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Petition for the Determination of Nonregulated Status for Dicamba-Tolerant Soybean MON 87708

The undersigned submits this petition under 7 CFR §340.6 to request that the Administrator make a determination that the article should not be regulated under 7 CFR Part 340

July 6, 2010

(Revised on October 10, 2011, March 1, 2012 and March 26, 2012)

OECD Unique Identifier: MON-877Ø8-9

Monsanto Petition Number: 10-SY-210U

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CERTIFICATION

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which to base a determination, and that it includes all relevant data and information known to the petitioner that are unfavorable to the petition.

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EXECUTIVE SUMMARY

The Animal and Plant Health Inspection Service (APHIS) of the United States (U.S.) Department of Agriculture (USDA) has responsibility, under the Plant Protection Act (Title IV Pub. L. 106-224, 114 Stat. 438, 7 U.S.C. § 7701-7772) to prevent the introduction and dissemination of plant pests into the U.S. APHIS regulation 7 CFR § 340.6 provides that an applicant may petition APHIS to evaluate submitted data to determine that a particular regulated article does not present a plant pest risk and should no longer be regulated. If APHIS determines that the regulated article does not present a plant pest risk, the petition is granted, thereby allowing unrestricted introduction of the article.

Monsanto Company is submitting this request to APHIS for a determination of nonregulated status in whole for the new biotechnology-derived soybean product, MON 87708, any progeny derived from crosses between MON 87708 and conventional soybean, and any progeny derived from crosses of MON 87708 with other biotechnology-derived soybean that has been granted nonregulated status under 7 CFR Part 340.

Product Description

Monsanto Company has developed biotechnology-derived soybean MON 87708 that is tolerant to dicamba (3,6-dichloro-2-methoxybenzoic acid) herbicide. MON 87708 offers growers an expanded use of dicamba in soybean production from the current preplant and preharvest labeled uses. The tolerance of MON 87708 to dicamba facilitates a wider window of application in soybean, allowing preemergence application up to the day of crop emergence and in-crop postemergence applications through the early reproductive (R1/R2) growth stage. Dicamba provides effective control of over 95 annual and biennial weed species, and suppression of over 100 perennial broadleaf and woody plant species. Dicamba is efficacious on broadleaf weeds that are hard-to-control with glyphosate, such as common lambsquarters, hemp sesbania, morning glory species, nightshade, Pennsylvania smartweed, prickly sida, velvetleaf, waterhemp and wild buckwheat. Hard-to-control weeds generally require a higher rate and/or application at a smaller growth stage in order to consistently achieve commercially acceptable control. Refer to the Roundup WeatherMax label (U.S. EPA Reg. No. 524-537) for a listing of these weeds.

Additionally, dicamba provides effective control of herbicide-resistant broadleaf weeds, including glyphosate-resistant weeds such as marestail, common ragweed, giant ragweed, palmer pigweed, and waterhemp. Herbicide resistant weeds are those listed on the International Survey of Resistant Weeds website (www.weedscience.org).

MON 87708 will be combined with MON 89788 (Roundup Ready 2 Yield® soybean) utilizing traditional breeding techniques. Dicamba is an effective broadleaf herbicide and the potential use of dicamba and glyphosate herbicides at the same time in mixtures for weed control will provide growers greater application flexibility prior to planting as well as in-crop for greater consistency of control in both conventional and conservation tillage situations. Use of dicamba, in addition to glyphosate and the other herbicide options currently labeled for use on soybean, provides more options to implement diversified weed management programs to control a broad

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spectrum of grass and broadleaf weed species. Successful adoption of the dicamba tolerance trait, into the Roundup Ready® soybean system, will provide: 1) growers with an opportunity for an efficient, effective weed management system; 2) an option to delay or prevent further resistance to glyphosate and other critically important soybean herbicides, in particular, herbicides in the ALS and PPO class of chemistry; 3) excellent crop safety, and 4) continue to provide soybean growers with effective weed control systems necessary for production yields to meet the growing needs of the food, feed, and industrial markets. The combination of dicamba and glyphosate tolerance in soybeans will also provide the basis for delaying or preventing the evolution of further weed resistance to glyphosate, dicamba, and herbicides in general, because of the ability to use these two modes of action in mixtures and sequences.

MON 87708 contains a gene from *Stenotrophomonas maltophilia* that expresses a mono-oxygenase enzyme that rapidly demethylates dicamba rendering it inactive, thereby conferring tolerance to dicamba. The demethylation of dicamba produces 3,6-dichlorosalicylic acid (DCSA), a known soybean, soil, and livestock metabolite whose safety has been evaluated by the Environmental Protection Agency (U.S. EPA). DCSA, in addition to dicamba, is included in the current 10 ppm pesticide residue tolerance for soybean seed that supports the existing uses of dicamba on commercial soybean (40 CFR § 180.227). Even with the expanded use of dicamba on MON 87708, compared to commercial soybean uses, the rapid metabolism of dicamba results in residues in dicamba-treated MON 87708 seed, including the DCSA metabolite, that are well below the established 10 ppm tolerance, and therefore no modification to the existing soybean seed tolerance is needed. Consequently, only approval for the expanded use pattern of dicamba on MON 87708 has been requested of EPA.

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Data and Information Presented Confirm the Lack of Plant Pest Potential of MON 87708 Compared to Conventional Soybean

The data and information presented in this petition demonstrate MON 87708 is agronomically, phenotypically, and compositionally comparable to conventional soybean with the exception of its tolerance to dicamba. Moreover, the data presented demonstrate MON 87708 is unlikely to pose an increased plant pest risk, including weediness or adverse environmental impact, compared to conventional soybean. The food, feed, and environmental safety of MON 87708 was confirmed based on multiple, well-established lines of evidence:

1. Soybean is a familiar crop that does not possess any of the attributes commonly associated with weeds and has a history of safe consumption.

2. A detailed molecular characterization of the inserted DNA demonstrated a single, intact copy of the T-DNA insert in a single locus within the soybean genome.

3. Data confirmed that the dicamba mono-oxygenase (DMO) in MON 87708 (MON 87708 DMO) is unlikely to be a toxin or allergen based on extensive information collected.

4. A compositional assessment of seed and forage confirmed that MON 87708 is compositionally equivalent to conventional soybean.

5. An extensive evaluation on phenotypic and agronomic characteristics and environmental interactions of MON 87708 demonstrated no increased plant pest potential compared to conventional soybean.

6. An assessment of potential impact on non-target organisms (NTOs) and endangered species indicated that, under normal agricultural conditions, MON 87708 is unlikely to have adverse effects on these organisms compared to conventional soybean.

7. Evaluation of MON 87708 using current cultivation and management practices for soybean concluded that deregulation of MON 87708 will not significantly impact soybean agronomic practices or land use, with the exception of the expanded window of dicamba application.

Soybean is a Familiar Crop Lacking Weedy Characteristics

There is a longstanding history of safe use and consumption of conventional soybean and processed products. Soybean is grown as a commercial crop in over 35 countries. Domestication occurred as early as 1000 B.C. and is now the most widely grown oilseed crop in the world, with approximately 211 million metric tons of harvested seed produced in 2008, which represented 56% of world oilseed seed production that year.

The commercial soybean species in the U.S. (*Glycine max* L. Merr.) does not exhibit weedy characteristics, does not invade established ecosystems, and does not outcross to weedy relatives. Soybean is not listed as a weed in major weed references, nor is it present on the lists of noxious weed species distributed by the federal government (7 CFR Part 360). During 2004 to 2008, U.S. growers planted between 64.7 and 75.7 million acres of soybean. Soybean does not possess any of the attributes commonly associated with weeds, such as long persistence of the seed in the soil, ability to disperse, invade, or become a dominant species in new or diverse landscapes, or the ability to compete well with native vegetation. However, due to a pronounced lack of dormancy it is known that soybean seed can germinate quickly under adequate temperature and moisture conditions, and can potentially grow as a volunteer plant. However, a volunteer soybean plant likely would be killed by frost during the autumn or winter of the year it germinated. Furthermore, if a volunteer plant were to survive, it would not compete well with the succeeding crop, and would be controlled readily via mechanical or other chemical means. Twenty commonly used agricultural herbicides, representing eight modes-of-action (*i.e.*, ALS-inhibitor, chloroacetamide, EPSPS, PPO inhibitor, PSI disruption, PSII inhibitor, synthetic auxin, and tubulin inhibitor classes) were tested as potential substrates for MON 87708 DMO. None of the herbicides tested were found to effect the tolerance of MON 87708 at commercial application rates, therefore, herbicides effective for control of volunteer soybean can still be used to control MON 87708 volunteers. Finally, since wild populations of *Glycine* species are not known to exist in the U.S., there is no potential for MON 87708 to outcross to wild or weedy relatives.

Conventional Soybean A3525 is an Appropriate Comparator to MON 87708

Soybean variety A3525 is the near isogenic line to MON 87708 and was used as the conventional soybean comparator to support the safety assessment of MON 87708. MON 87708 and the near isogenic conventional soybean control A3525 have similar genetic backgrounds

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with the exception of the *dmo* expression cassette, thus, the effect of the *dmo* expression cassette and the expressed MON 87708 DMO could be assessed in an unbiased manner.

Molecular Characterization Verifies the Integrity and Stability of the Inserted DNA in MON 87708

MON 87708 was developed through *Agrobacterium*-mediated transformation of conventional soybean A3525 meristem tissue with the 2T-DNA plasmid vector PV-GMHT4355. PV-GMHT4355 contains two separate T-DNAs that are each delineated by Left and Right Border sequences. The first T-DNA, designated as T-DNA I, contains the *dmo* expression cassette regulated by the peanut chlorotic streak virus (*PClSV*) promoter and the pea *E9* 3′ non-translated region. The second T-DNA, designated as T-DNA II, contains the *cp4 epsps* expression cassette under the regulation of the figwort mosaic virus (*FMV*) promoter and the pea *E9* 3′ non-translated region. During transformation, both T-DNAs were inserted into the soybean genome, where T-DNA II, containing the *cp4 epsps* expression cassette, functioned as a marker gene for the selection of transformed plantlets. Subsequently, conventional self-pollination breeding methods and segregation were used to isolate a plant containing the *dmo* expression cassette but not containing the *cp4 epsps* expression cassette, resulting in the production of marker-free, dicamba-tolerant soybean MON 87708.

Molecular characterization by Southern blot analyses determined that MON 87708 contains one copy of the T-DNA I at a single integration locus and all expression elements are present. These data also demonstrated that MON 87708 does not contain detectable backbone sequences from the plasmid vector or T-DNA II sequences. The complete DNA sequence of the insert and adjacent genomic DNA sequence in MON 87708 confirmed the integrity of the inserted *dmo* expression cassette within the inserted sequences and identified the 5′ and 3′ insert-to-genomic DNA junctions. Furthermore, Southern blot analysis demonstrated that the insert in MON 87708 has been maintained through at least five generations of breeding, thereby confirming the stability of the insert over multiple generations.

Data Confirm MON 87708 DMO Safety

MON 87708 contains a *dmo* expression cassette that results in two forms of the DMO protein; referred to as DMO and DMO+27 (Section V.A.). The active form of these proteins, necessary to confer dicamba tolerance, is a trimer comprised of three DMO monomers. In MON 87708, the trimer can be comprised of DMO, DMO+27, or a combination of both. Therefore, this document will refer to both forms of the protein and all forms of the trimer as MON 87708 DMO.

A multistep approach was used to characterize MON 87708 DMO. This detailed characterization and assessment confirmed that MON 87708 DMO is safe for human and animal consumption. The assessment involved: 1) characterization of the physicochemical and functional properties of MON 87708 DMO; 2) quantification of MON 87708 DMO levels in plant tissues; 3) comparison of the amino acid sequence of MON 87708 DMO to known allergens, gliadins, glutenins, toxins, and other biologically active proteins known to have adverse effects on mammals; 4) evaluation of the digestibility of MON 87708 DMO in simulated gastric and intestinal fluids; 5) endogenous and exogenous substrate specificity of DMO; 6)

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documentation of the history of safe consumption of mono-oxygenases (the class of enzymes to which MON 87708 DMO belongs); and 7) investigation of the potential mammalian toxicity through an oral gavage assay.

DMO was found to be specific to dicamba when tested using structurally similar endogenous substrates and exogenous herbicide substrates representing a wide range of modes-of-action. MON 87708 DMO has no relevant amino acid sequence similarities with known allergens, gliadins, glutenins, toxins, and other biologically active proteins that may have adverse effects on mammals. MON 87708 DMO was rapidly degraded in simulated gastric and intestinal fluids and a high dose of this protein in a mouse acute oral toxicity evaluation demonstrated that it is not acutely toxic, and does not cause any adverse effect. The safety assessment supports the conclusion that exposure to MON 87708 DMO poses no meaningful risk to the environment, or human and animal health.

MON 87708 is Compositionally Equivalent to Conventional Soybean

Detailed compositional analyses in accordance with OECD guidelines were conducted to assess whether levels of key nutrients and anti-nutrients in MON 87708 were comparable to levels present in the aforementioned near isogenic conventional soybean control A3525 and several commercial reference soybean varieties. Seed and forage were harvested from five individual sites in which MON 87708 (both treated with dicamba herbicide at the V2-V3 growth stage and not treated with dicamba herbicide), the conventional control, and a range of commercial reference varieties were grown concurrently in the same field trial. The commercial reference varieties used to establish a range of natural variability for the key nutrients and anti-nutrients in commercial soybean varieties have a history of safe consumption. Nutrients assessed in this analysis included proximates (ash, carbohydrates by calculation, moisture, protein, and fat), fiber, amino acids (18 components), fatty acids (FA, C8-C22), and vitamin E (α-tochopherol) in seed, and proximates (ash, carbohydrates by calculation, moisture, protein, and fat) and fiber in forage. The anti-nutrients assessed in seed included raffinose, stachyose, lectin, phytic acid, trypsin inhibitors, and isoflavones (daidzein, genistein, and glycitein).

The combined-site analysis was conducted to determine statistically significant differences (5% level of significance) between MON 87708 and the near isogenic conventional control A3525. The results from the combined-site data were reviewed using considerations relevant to food and feed safety and nutritional quality. These considerations included assessments of: 1) the relative magnitudes of the difference in the mean values of nutrient and anti-nutrient components of MON 87708 and the conventional control, 2) whether the MON 87708 component mean value was within the range of natural variability of that component as represented by the 99% tolerance interval of the commercial reference varieties grown concurrently in the same field trial, 3) analyses of the reproducibility of the statistically significant combined-site component differences at individual sites, and 4) assessing the differences within the context of natural variability of commercial soybean composition published in the scientific literature and in the International Life Sciences Institute (ILSI) Crop Composition Database.

Assessment of the analytical results confirmed that the differences observed in the combined-site analysis were not meaningful to food and feed safety or the nutritional quality of MON 87708 soybean. In addition, the levels of assessed components in MON 87708 were compositionally

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equivalent to the conventional control and within the range of variability of the commercial reference varieties that were grown concurrently in the same field trial.

MON 87708 Does Not Change Soybean Plant Pest Potential or Environmental Interactions

Assessing the plant pest potential of a biotechnology-derived crop includes the concept of familiarity that the USDA recognizes as an important consideration. Familiarity is based upon the fact that the new biotechnology-derived plant is developed from a conventional plant variety whose biological properties and plant pest potential are well known. Familiarity considers the biology of the plant, the introduced trait, the receiving environment, and the interactions among these factors that provides a basis for comparative risk assessment between a biotechnology-derived plant and the conventional control. Following this concept, the phenotypic, agronomic, and environmental interaction assessment of MON 87708 included the near isogenic conventional soybean control A3525 and the commercial reference varieties. Characteristics assessed included: seed dormancy and germination, pollen morphology, and symbiont interactions conducted in the laboratory and greenhouse; and plant phenotypic and agronomic evaluations and environmental interaction observations conducted in the field. The commercial soybean reference varieties grown concurrently were used to establish a range of natural variability for each assessed characteristic in soybean. The phenotypic, agronomic, and environmental interaction assessment demonstrated that MON 87708 is equivalent to the conventional control. Thus, MON 87708 is unlikely to have a changed plant pest potential compared to conventional soybean.

Seed dormancy and germination characterization demonstrated that MON 87708 seed had germination characteristics similar to seed of the conventional control. In particular, the lack of hard seed, a well-accepted characteristic of weediness affecting seed germination, supports a conclusion of no increased weediness of MON 87708 when compared to the conventional control. For pollen characteristics and symbiont interactions, there were no statistically significant differences (5% level of significance) observed between MON 87708 and the conventional control for any of the parameters measured, including pollen viability and diameter, nodule number and dry weight, shoot total nitrogen, and shoot and root dry weight. Collectively, these results support the conclusion that MON 87708 is not likely to exhibit increased plant pest potential compared to conventional soybean.

The field evaluation of phenotypic, agronomic, and environmental interaction characteristics of MON 87708 also support the conclusion that MON 87708 is not likely to have an increased plant pest potential compared to conventional soybean. The evaluations were conducted at 18 replicated field sites across North American soybean production regions. These assessments included plant growth and development characteristics, as well as observations for plant responses to abiotic stressors and plant-disease and plant-arthropod interactions. The observed phenotypic characteristics were similar between MON 87708 and the conventional control.

In a combined-site analysis, data show no statistically significant differences (5% level of significance) between MON 87708 and the conventional control for early stand count, seedling vigor, days to 50% flowering, lodging, pod shattering, final stand count, seed moisture, seed test weight, or yield. Two statistically significant differences were detected between MON 87708

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and the conventional control for plant height and 100 seed weight. MON 87708 was slightly taller and had a lower 100 seed weight than the conventional control. However, both differences were small in magnitude. Additionally, MON 87708 and the conventional control were within the same range of plant growth stages for 131 out of the 132 growth stage observations among the sites. Except for the differences in plant height, 100 seed weight, and a single growth stage observation at one site, all values for MON 87708 fell within the range of the commercial reference varieties grown concurrently. None of these differences were considered biologically meaningful in terms of increased plant pest potential of MON 87708 compared to conventional soybean.

In an individual-site assessment of abiotic stress response and disease damage, no differences were observed between MON 87708 and the conventional control for 193 out of 194 comparisons for the assessed abiotic stressors or for any of the 215 comparisons for the assessed diseases among all observations at the 18 sites. One difference was observed between MON 87708 and the conventional control for wind damage during a single observation at one site. The damage rating for MON 87708 (slight damage) was outside the range of the commercial reference varieties (no damage); however, the difference was not observed during any of the other 29 wind damage observations among the sites. Thus, the slight difference in wind damage rating was not indicative of a consistent plant response associated with MON 87708 and is not considered biologically meaningful in terms of increased plant pest potential or an altered environmental impact from MON 87708 compared to conventional soybean.

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In an assessment of arthropod-related damage, no statistically significant differences (5% level of significance) were detected between MON 87708 and the conventional control for 89 out of 95 comparisons for the assessed arthropods. Lack of variability in the data precluded statistical comparisons between MON 87708 and the conventional control for 121 additional comparisons; however, the means for MON 87708 and the conventional control were the same value for these comparisons, indicating no biological differences. For each of the six statistically significant differences between MON 87708 and the conventional control, the severity of arthropod-related damage to MON 87708 was within or slightly outside the range of the commercial reference varieties. The differences between MON 87708 and the conventional control were small in magnitude and were not consistent across observations or sites. Thus, the differences in arthropod-related damage are not indicative of a consistent plant response associated with MON 87708 and are not considered biologically meaningful in terms of increased plant pest potential or an altered environmental impact from MON 87708 compared to conventional soybean.

In an assessment of pest and beneficial arthropod abundance, no statistically significant differences (5% level of significance) were detected between MON 87708 and the conventional control for 142 out of 151 comparisons (including 74 arthropod pest and 77 beneficial arthropod comparisons) among the multiple collections conducted during the season at four sites. For the nine detected differences in arthropod abundance, seven were arthropod pests (green cloverworm, Japanese beetles, and stink bugs) and two were beneficial arthropods (spiders and *Nabis* spp). The differences detected in pest and beneficial arthropod abundance were small in magnitude and were not consistent with other collection times at the individual sites or across the sites. Consequently, it is concluded that the differences in pest and beneficial arthropod abundance are not indicative of a consistent plant response associated with MON 87708 and are not biologically meaningful in terms of increased plant pest potential or an altered environmental impact from MON 87708 compared to conventional soybean.

Field evaluations of phenotypic, agronomic, and environmental interaction characteristics of MON 87708 treated with dicamba herbicide were also conducted. Data were collected from field trials conducted at eight sites within the U.S. soybean producing regions. These assessments included plant growth and development characteristics, as well as observations for plant responses to abiotic stressors, plant-disease and plant-arthropod interactions. The phenotypic, agronomic, and environmental interaction assessment demonstrated that treated MON 87708 is equivalent to the conventional control. Thus, MON 87708 is unlikely to have an altered plant pest potential compared to conventional soybean.

The observed phenotypic characteristics were similar between the dicamba-treated MON 87708 and the conventional control. In a combined-site assessment, no statistically significant differences were detected between treated MON 87708 and the conventional control for early stand count, seedling vigor, days to 50% flowering, plant height, lodging, pod shattering, final stand count, seed moisture, or yield. One statistically significant difference was detected between treated MON 87708 and the control, for 100 seed weight. The difference in 100 seed weight was relatively small in magnitude and the mean 100 seed weight of treated MON 87708 was slightly below the reference range. It is unlikely that this small difference in 100 seed weight would contribute to increased weed potential of MON 87708 when treated with dicamba compared to conventional soybean. Additionally, treated MON 87708 and the control were within the same range of plant growth stages for all growth stage observations among the sites. None of these differences were considered biologically meaningful in terms of increased plant pest potential of treated MON 87708 compared to conventional soybean.

In an assessment of plant response to abiotic stressors and disease damage, no differences were observed between treated MON 87708 and the conventional control for 181 of 182 comparisons among all observations at the eight sites. One difference was observed between treated MON 87708 and the control for white mold during a single observation (slight vs. none). The damage rating for treated MON 87708 was outside of the reference range (no damage was observed in the references). This difference was not observed in any of the other two white mold evaluations across the sites and is not considered biologically meaningful in terms of increased plant pest potential or an altered environmental impact from treated MON 87708 compared to conventional soybean.

In an assessment of arthropod-related damage, there were no statistically significant differences detected between treated MON 87708 and the control for 56 out of 59 comparisons. Lack of variability in the data precluded statistical comparisons between treated MON 87708 and the conventional control for 34 additional comparisons. The mean damage ratings for bean leaf beetle and grasshopper damage was outside the reference range however the response was not consistent across observations or sites. Thus, the results are not considered biologically meaningful in terms of adverse environmental impacts of treated MON 87708 compared to the conventional soybean.

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In summary, the phenotypic, agronomic, and environmental interaction data were collected to provide a detailed characterization of MON 87708 and to assess whether the introduction of the dicamba tolerance trait in MON 87708 and the associated application of dicamba herbicide alters the plant pest potential compared to conventional soybean. The analysis considered the comparisons of MON 87708 to the conventional control, the reproducibility, magnitude, and direction of detected differences (trends), and comparison to the range of the commercial reference varieties. Results from the phenotypic, agronomic, and environmental interactions assessment indicated that MON 87708 does not possess weedy characteristics, increased susceptibility or tolerance to specific abiotic stress, diseases, or arthropods, or characteristics that would confer a plant pest risk or a significant environmental impact compared to conventional soybean.

MON 87708 Will Not Adversely Affect NTOs or Threatened and Endangered Species

Evaluation of the impacts of a biotechnology-derived crop on Non-Target Organisms (NTOs) and threatened and endangered species is a component of the plant pest risk assessment. Since MON 87708 does not possess pesticidal activity, all organisms that interact with MON 87708 are considered to be NTOs. The environmental assessment demonstrated that the presence of the dicamba tolerance trait in MON 87708 and the associated application of dicamba did not alter plant-arthropod interactions, including beneficial arthropods, or alter disease susceptibility compared to the conventional control.

The biochemical information and experimental data for evaluation of MON 87708 included molecular characterization, MON 87708 DMO safety assessments, the history of environmental exposure to mono-oxygenases (the class of enzymes to which MON 87708 DMO belongs), information from the environmental interaction assessment, demonstration of compositional equivalence to conventional soybean, and demonstration of agronomic and phenotypic equivalence to conventional soybean. Taken together, these data support the conclusion that MON 87708 has no reasonable mechanism for harm to NTOs, or to pose an additional risk to threatened and endangered species compared to the cultivation of conventional soybean.

The potential for outcrossing and gene introgression from MON 87708 to sexually-compatible species in the U.S. is unlikely since no known wild *Glycine* species related to cultivated soybean are known to be present in North America. Furthermore, should cross-pollination occur, MON 87708 and its progeny are not expected to exhibit a significant environmental impact because, as described above, evaluations have shown that the presence of the dicamba tolerance trait is not likely to enhance weediness or plant-pest potential. Therefore, the environmental consequence of pollen transfer from MON 87708 to other *Glycine* species is considered negligible.

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Deregulation of MON 87708 Will Not Significantly Impact Soybean Agronomic Practices or Land Use

Soybean fields are typically highly managed agricultural areas that are dedicated to crop production for many years. Cultivation of MON 87708 would not be expected to differ from typical soybean cultivation, with the sole exception of an expanded window of dicamba applications due to the presence of the dicamba tolerance trait in MON 87708. MON 87708 likely would be used in common rotations on land currently used for agricultural purposes. As demonstrated, MON 87708 is similar to conventional soybean in its agronomic, phenotypic, ecological, and compositional characteristics and has comparable levels of resistance to insects and diseases as compared to commercial soybean. Therefore, the introduction of MON 87708 into the Roundup Ready soybean system is not expected to have a significant impact on current cultivation and management practices for soybean. The adoption of MON 87708 into the Roundup Ready soybean system will provide growers with another herbicide mode-of-action and the means to control broadleaf weeds, including hard-to-control and herbicide-resistant broadleaf weeds, and will help preserve conservation tillage practices by providing growers with an additional weed management tool. Based on these considerations, there is no apparent potential for significant impacts on agronomic practices or land use, with the exception of the expanded application window of dicamba.

Conclusion

Based on the data and information presented in this petition, it is concluded that MON 87708 is not likely to be a plant pest. Therefore, Monsanto Company requests a determination from APHIS that MON 87708 and any progeny derived from crosses between MON 87708 and conventional soybean or previously deregulated biotechnology-derived soybean, be granted nonregulated status under 7 CFR Part 340.

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ABBREVIATION AND DEFINITIONS[*]

~	approximately
aadA	Bacterial promoter and coding sequence for an aminoglycoside-modifying enzyme, 3'(9)-O-nucleotidyltransferase from the transposon Tn7 that confers spectinomycin and streptomycin resistance
AAPSE	American Association of Pesticide Safety Educators
ADF	acid detergent fiber
ALS	acetolactate synthase
AOSA	Association of Official Seed Analysts
aPAD	acute population adjusted dose
APHIS	Animal and Plant Health Inspection Service
B. japonicum	*Bradyrhizobium japonicum*
BIO	Biotechnology Industry Organization
bp	base pair
BRS	Biotechnology Regulatory Services
BSA	bovine serum albumin
bu/A	bushels per acre
CEQ	Council on Environmental Quality
CES	Cooperative Extension Service
CFR	Code of Federal Regulations
CHT	ceramic hydroxyapatite column
cp4 epsps	codon modified coding sequence of the *aroA* gene from *Agrobacterium species* strain CP4 encoding CP4 EPSPS
CP4 EPSPS	5-Enolpyruvylshikimate-3-phosphate synthase protein
cPAD	chronic population adjusted dose
CTAB	Hexadecyltrimethylammonium bromide
CTP2	Sequences encoding the chloroplast transit peptide region of *Arabidopsis thaliana* EPSPS used to direct proteins into chloroplasts
CV	column volume
Da	Dalton
DAP	days after planting
dATP	Deoxyadenosine triphosphate
DCSA	3,6-dichlorosalicylic acid also known as 3,6-dichloro-2-hydroxybenzoic acid
DCGA	3,6-dichlorogentisic acid
dCTP	Deoxycytidine triphosphate
DDI	daily dietary intake
DEEM	dietary exposure evaluation model
DGA	Diglycolamine
DHB	dihydroxybenzoic acid
dicamba	3,6-dichloro-2-methoxybenzoic acid
dmo	Coding sequence of the dicamba mono-oxygenase gene from *Stenotrophomonas maltophilia* encoding DMO
DMO	full-length dicamba mono-oxygenase protein
DMO+27	full-length dicamba mono-oxygenase protein with an additional 24

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[*] Note: Standard abbreviations, *e.g.*, units of measure, are used according to the format described in 'Instructions to Authors' in the *Journal of Biological Chemistry*.

	amino acids from the Rubisco small subunit and 3 amino acids from an intervening sequence
DnaK	5′ non-translated leader sequence from the *Petunia hybrid Hsp70* gene that is involved in regulating gene expression
dNTP	deoxynucleoside triphosphate
DTT	dithiothreitol
DWCF	dry weight conversion factor
dwt	dry weight of tissue
E9	3′ non-translated region of the pea *RbcS2* gene that functions to direct polyadenylation of the mRNA
E. coli	*Escherichia coli*
EEC	estimated environmental exposure concentration
EFED	Environmental Fate and Effects Division
ELISA	enzyme-linked immunosorbent assay
EPA	U.S. Environmental Protection Agency
ERS	Economic Research Service
ETS	Excellence Through Stewardship
Exo	exonuclease I
FA	fatty acid
FASTA	algorithm used to find local high scoring alignments between a pair of protein or nucleotide sequences
FDA	U.S. Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FLt	*full-length transcript*
FMV	Promoter for the figwort mosaic virus 35S RNA
FQPA	Food Quality Protection Act
fwt	fresh weight of tissue
GLP	good laboratory practice
H.U.	hemagglutinating unit
HAL	health advisory level
HED	Health Effects Division
HPPD	4-hydroxyphenylpyruvate dioxygenase
HRP	horseradish peroxidase
IAA	indole acetic acid
ILSI	International Life Sciences Institute
IPM	integrated pest management
kb	kilobase
kDa	kiloDalton
LB	loading buffer
lb/bu	pounds per bushel
LC	lethal concentration
LD	lethal dose
Left Border	DNA region from *Agrobacterium tumefaciens* containing the left border sequence used for transfer of the T-DNA
LOAEL	lowest dosing level that produced an observable effect
LOC	level of concern
LOD	limit of detection
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
MALDI-TOF MS	matrix-assisted laser desorption/ionization time-of-flight mass

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	spectrometry
MMT	million metric tons
MOE	margin of exposure
MON 87708 DMO	The active form of DMO, a trimer comprised of three monmers. The DMO trimer can be comprised of DMO, DMO+27 or a combination of both forms.
MSTA	Monsanto Technology Stewardship Agreement
MW	molecular weight
MWCO	molecular weight cut off
N/A	not applicable
NADH	nicotinamide adenine dinucleotide
NASS	National Agricultural Statistics Service, a branch of the USDA
NAWQA	National Water-Quality Assessment
NDF	neutral detergent fiber
NEPA	National Environmental Policy Act
NFDM	non-fat dried milk
NOAEL	no observable adverse effect level
NOEC	no observable effect concentration
NTOs	non-target organisms
OECD	Organization of Economic Co-Operation and Development
OPP	Office of Pesticide Programs
ORETF	Outdoor Residential Exposure Task Force
ori-pBR322	Origin of replication from pBR322 necessary for maintenance of plasmid in *E. coli*
ori V	Origin of replication from the broad host range plasmid RK2 necessary for maintenance of plasmid in *Agrobacterium*
OSL	over-season leaf
PAD	population adjusted dose
PBS	phosphate buffered saline solution
PBST	phosphate buffered saline solution containing 0.05% (v/v) Tween-20
PC1SV	Promoter for the full length transcript of peanut chlorotic streak virus that directs transcription in plant cells
PCR	polymerase chain reaction
pea	*Pisum sativum*
PHED	Pesticide Handler Exposure Database
RED	Reregistration Eligibility Decision
RfD	reference dose
PMSF	phenylmethylsulfonyl fluoride
PPA	Plant Protection Act
PPO	protoporphyrinogen oxidase
PRZM/EXAMS	Pesticide Root Zone Model/Exposure Analysis Modeling System
PVDF	polyvinylidene difluoride
RbcS	Sequences encoding the transit peptide region of the ribulose-1,5-bisphosphate carboxylase oxygenase gene from *Pisum sativum*
Right Border	DNA region from *Agrobacterium tumefaciens* containing the right border sequence used for transfer of the T-DNA
rop	Coding sequence for repressor of primer protein used for maintenance of plasmid copy number in *E. coli*
RQ	risk quotient
RT	room temperature
SAP	shrimp alkaline phosphate

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SCI-GROW	Screening Concentration in Ground Water
SCN	soybean cyst nematode
SD	standard deviation
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
S.E.	standard error
SGF	simulated gastric fluid
SIF	simulated intestinal fluid
S. maltophilia	*Stenotrophomonas maltophilia*
soybean	*Glycine max* (L.) Merr.
T-DNA	transfer(ed) DNA
TBS	tris buffered saline
TES	threatened and endangered species
TEV	5′ non-translated region from the Tobacco Etch RNA virus genome that is involved in regulating gene expression
TFA	trifluoroacetic acid
TIU	trypsin inhibitor units
Tm	melting temperature
TMRC	theoretical maximum residue concentration
TMB	3,3',5,5' tetramethyl-benzidine
TRED	tolerance reregistration eligibility decision
TSSP	tissue-specific pool
TUG	Technology Use Guide
U.S.	United States of America
USDA	U.S. Department of Agriculture
v/v	volume per volume
VMD	volume median diameter
w/v	weight per volume
WAT	weeks after treatment
WPS	Worker Protection standard
WSSA	Weed Science Society of America

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I. RATIONALE FOR THE DEVELOPMENT OF MON 87708

I.A. Basis for the Request for a Determination of Nonregulated Status under 7 CFR § 340.6

The Animal and Plant Health Inspection Service (APHIS) of the United States (U.S.) Department of Agriculture (USDA) has responsibility, under the Plant Protection Act (Title IV Pub. L. 106-224, 114 Stat. 438, 7 U.S.C. § 7701-7772), to prevent the introduction and dissemination of plant pests into the U.S. APHIS regulation 7 CFR § 340.6 provides that an applicant may petition APHIS to evaluate submitted data to determine that a particular regulated article does not present a plant pest risk and no longer should be regulated. If APHIS determines that the regulated article does not present a plant pest risk, the petition is granted, thereby allowing unrestricted introduction of the article. A listing of all regulated MON 87708 field trials conducted under USDA notification can be found in Appendix A.

Monsanto Company is submitting this request to APHIS for a determination of nonregulated status for new biotechnology-derived soybean product, MON 87708, any progeny derived from crosses between MON 87708 and conventional soybean, and any progeny derived from crosses of MON 87708 with biotechnology-derived soybean that have previously been granted nonregulated status under 7 CFR Part 340.

I.B. Rationale for the Development of Dicamba-Tolerant Soybean MON 87708

The Roundup Ready® soybean system permits over-the-top application of Roundup® agricultural herbicides containing the active ingredient glyphosate for effective weed control. The value of the Roundup Ready soybean system has been demonstrated by the significant growth in the number of planted acres since its introduction in 1996. Today more than 90% of all soybean acres grown in the U.S. are Roundup Ready (USDA-NASS, 2009c). The Roundup Ready soybean system delivers effective broad spectrum weed control, provides flexibility of application timing, has facilitated increased adoption of reduced tillage practices, and has resulted in increased grower income (Carpenter and Gianessi, 2001; Bonny, 2008; Hurley et al., 2009). Additionally, the Roundup Ready soybean system provides incremental environmental benefits (Bonny, 2008; Brookes and Barfoot 2009), and glyphosate, as concluded by the U.S. EPA (1993), has a favorable safety profile. Continued use of the Roundup Ready soybean system will maintain effective and familiar weed control management practices that are fully compatible with all current tillage and land management systems including conservation tillage practices. Growth of conservation tillage in the U.S. was greatly accelerated with the introduction of glyphosate-tolerant crops in large part because of the broad spectrum postemergence control offered by glyphosate (Price et al. 2011).

As with all herbicides used in agriculture, there is potential for weeds to develop resistance to the herbicide over time.[1] If unmanaged, herbicide resistance can become a limiting factor in crop production. Glyphosate has had few cases of weed resistance,

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[1] http://www.weedscience.org/In.asp

particularly in relation to other herbicides. In the U.S., while there have been thirteen confirmed glyphosate-resistant weeds (Heap, 2011), glyphosate still controls more than 160 weed species (Roundup WeatherMax herbicide label, EPA Reg. No.524-537) and remains an extremely valuable tool for U.S, soybean crop production. Herbicide resistant weeds are those listed on the International Survey of Resistant Weeds website (www.weedscience.org). Additionally, studies have shown that resistance can be postponed, contained and managed through good management practices. One of the management practices most often recommended by University/Cooperative Extension Service and industry is the use of multiple herbicide modes-of-action. Simultaneously using two herbicides with different modes-of-action significantly reduces the probability of weeds developing resistance to either or both herbicides (Powles et al., 1996; Beckie and Reboud, 2009). Other recommended management practices to manage herbicide resistance includes the use of multiple herbicide modes-of-action in sequence, and/or the inclusion of mechanical or cultural practices in addition to the use of an herbicide.

Monsanto Company has developed biotechnology-derived soybean MON 87708 that is tolerant to dicamba (3,6-dichloro-2-methoxybenzoic acid) herbicide. Dicamba is a synthetic auxin herbicide that kills plants by mimicking naturally-occurring plant growth hormones called auxins, thereby destroying tissue through uncontrolled cell division and growth (Ahrens, 1994). Dicamba's mode-of-action is different from glyphosate, and it provides efficacious control of broadleaf weeds and is complementary to glyphosate on hard-to-control weeds such as common lambsquarters, hemp sesbania, morning glory species, nightshade, Pennsylvania smartweed, prickly sida, velvetleaf, waterhemp, and wild buckwheat (Johnson et al., 2010). Additionally, dicamba provides effective control of herbicide-resistant broadleaf weeds, including glyphosate-resistant weeds such as marestail, common ragweed, giant ragweed, palmer pigweed, and waterhemp (Johnson et al., 2010). Hard-to-control weeds generally require a higher rate and/or application at a smaller growth stage in order to consistently achieve commercially acceptable control. Refer to the Roundup WeatherMax label (U.S. EPA Reg. No. 524-537) for a listing of these weeds. Herbicide resistant weeds are those listed on the International Survey of Resistant Weeds website (www.weedscience.org). Since its introduction in 1967, only four species with known dicamba-resistant biotypes have been identified in North America (Heap, 2011).

MON 87708 will be combined with MON 89788 (Roundup Ready 2 Yield soybean) utilizing traditional breeding techniques. Dicamba is an effective broadleaf herbicide and the potential use of dicamba and glyphosate herbicides at the same time in mixtures for weed control will provide growers greater application flexibility prior to planting as well as in-crop for greater consistency of control in both conventional and conservation tillage situations (Johnson et al., 2010). Use of dicamba, in addition to glyphosate and the other herbicide options currently labeled for use on soybean, provides more options to implement diversified weed management programs to control a broad spectrum of grass and broadleaf weed species (Johnson et al, 2010). Successful adoption of the dicamba tolerance trait, into the Roundup Ready soybean system, will provide: 1) growers with an opportunity for an efficient, effective weed management system; 2) an effective tool for the management of glyphosate resistant weeds that will help to conserve reduced tillage practices; 3) an option to delay or prevent further resistance to glyphosate and other

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critically important soybean herbicides, in particular herbicides in the ALS and PPO class of chemistry; 4) excellent crop safety; and 5) soybean growers with effective weed control systems necessary for production yields to meet the growing needs of the food, feed, and industrial markets.

MON 87708 expresses a mono-oxygenase enzyme that rapidly demethylates dicamba rendering it inactive, thereby conferring tolerance to dicamba. The demethylation of dicamba produces 3,6-dichlorosalicylic acid (DCSA), a known soybean, soil, and livestock metabolite whose safety has been evaluated by the Environmental Protection Agency (U.S. EPA). DCSA, in addition to dicamba, is included in the current 10 ppm pesticide residue tolerance for soybean seed that supports the existing uses of dicamba on conventional soybean (40 CFR § 180.227). Even with the expanded use of dicamba on MON 87708, compared to conventional soybean uses, the rapid metabolism of dicamba results in residues in dicamba-treated MON 87708 seed, including the DCSA metabolite, that are well below the established 10 ppm tolerance, and therefore no modification to the existing soybean seed tolerance is needed. Consequently, only approval for the expanded use pattern of dicamba on MON 87708 has been requested of EPA. Furthermore, the U.S., Canada and the EU have recently completed reviews of dicamba where the safety of dicamba has been confirmed (U.S. EPA, 2009; PMRA, 2008; European Commission, 2008). The proposed use pattern of dicamba in MON 87708 falls within the use pattern criteria (rates and methods) evaluated and approved by EPA in association with existing dicamba agricultural uses.

I.C. Submissions to Other Regulatory Agencies

Under the Coordinated Framework for Regulation of Biotechnology, the responsibility for regulatory oversight of biotechnology-derived crops that do not include plant-incorporated protectants falls on two federal agencies: U.S. Food and Drug Administration (FDA) and United States Department of Agriculture (USDA). Deregulation of MON 87708 by USDA constitutes only one component of the overall regulatory oversight and review of this product. As a practical matter, MON 87708 cannot be released and marketed until FDA and USDA have completed their reviews and assessments under their respective jurisdictions. Additionally, EPA must complete its review and assessments prior to approving the use of dicamba on MON 87708.

I.C.1. Submission to FDA

MON 87708 falls within the scope of the 1992 FDA policy statement concerning regulation of products derived from new plant varieties, including those developed through biotechnology (U.S. FDA, 1992). In compliance with this policy, Monsanto has initiated a consultation with the FDA (BNF No. 125) on the food and feed safety and compositional assessment of MON 87708. A safety and nutritional assessment summary document for MON 87708 (BNF No. 125) was submitted to FDA on November 9, 2010. FDA completed the consultation process for MON 87708 on October 11, 2011.[2]

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[2] http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=bioListing&id=86

I.C.2. Submission to EPA

The EPA has authority over the use of pesticidal substances under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended (7 U.S.C. § 136 *et seq.*). Monsanto has submitted to the EPA an application to amend Registration Number 524-582 to register a new use pattern for dicamba on MON 87708. The new use pattern facilitates a wider window of application of dicamba on MON 87708, allowing dicamba to be applied preemergence through crop emergence (cracking) and in-crop postemergence through the early R1/R2 reproductive phase. EPA has reviewed the safety of dicamba and DCSA, the primary metabolite in MON 87708, during the reregistration of dicamba in 2006. EPA concluded in the 2006 dicamba Reregistration Eligibility Decision (RED) document that risks to human health and the environment associated with exposure to dicamba and its metabolites, including DCSA, were below the Agency's level of concern for all registered uses of dicamba including conventional soybean (U.S. EPA, 2009). Dicamba residues on soybean seed (less than 0.07 ppm average residue and less than 0.5 ppm maximum residue) resulting from its application on MON 87708 at the maximum labeled use rate are well below the established 10 ppm soybean seed pesticide residue tolerance. Therefore, a change to the current soybean seed tolerance is not needed to support the use of dicamba on MON 87708. However Monsanto has requested the establishment of new tolerances for soybean forage and hay, which will allow for the feeding of forage and hay to livestock. No other revisions to dicamba pesticide residue tolerances are needed including animal products such as meat or milk. Furthermore, the use of dicamba on MON 87708 does not present any new environmental exposure scenarios not previously evaluated and deemed acceptable by EPA. Additional details regarding dicamba and its use on MON 87708 are available in Appendix M.

I.C.3. Submissions to Foreign Government Agencies

To support commercial introduction of MON 87708 in the U.S., regulatory submissions will be made to countries that will eventually commercialize or import significant quantities of soybean or its processed fractions from the U.S. These will include submissions to a number of foreign government regulatory authorities, including: Ministry of Agriculture, People's Republic of China; Japan's Ministry of Agriculture, Forestry, and Fisheries, Ministry of Environment, and the Ministry of Health, Labor, and Welfare; the Canadian Food Inspection Agency and Health Canada; the Intersectoral Commission for Biosafety of Genetically Modified Organisms, Mexico; the European Food Safety Authority, as well as to regulatory authorities in other soybean importing countries with functioning regulatory systems. As appropriate, notifications of importation will be made to importing countries that do not have a formal approval process.

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II. THE BIOLOGY OF SOYBEAN

The Organization for Economic Co-Operation and Development (OECD) Consensus Document (OECD, 2000) on the biology of soybean provides key information on:

- a general description of soybean biology, including taxonomy and morphology as well as soybean use as a crop plant
- agronomic practices in soybean cultivation
- geographic centers of origin
- reproductive biology
- cultivated soybean as a volunteer weed
- inter-species/genus introgression into relatives and interactions with other organisms, and
- a summary of the ecology of soybean

The taxonomic information for soybean is available in the USDA's PLANTS Profile (USDA-NRCS, 2010).

To support the evaluation of the plant pest potential of MON 87708 relative to conventional soybean, additional information regarding several aspects of soybean biology can be found elsewhere in this petition. This includes: agronomic practices for soybean in Section VIII; volunteer management of soybean in Section VIII.J; and inter-species/genus introgression potential in Section VII.C.3.

II.A. Soybean as a Crop

Soybean is the most widely grown oilseed in the world, with approximately 211 million metric tons of harvested seed produced in 2008. This represents 56% of world oilseed seed production that year. Soybean is grown as a commercial crop in over 35 countries. The major producers are the U.S., Brazil, Argentina, China, India, and Paraguay, accounting for approximately 94% of the global soybean production in 2008. Approximately one-third of the 2008 world soybean production was in the U.S. (Soyatech, 2010). The U.S. was also the largest soybean seed exporting country in 2008 (ASA, 2009).

Soybean has a long history of planting and production in North America. Soybean was originally introduced into North America from China in 1765 and has since been reintroduced several times by scientists, seed dealers, merchants, military expeditions, and various individuals (Singh and Hymowitz, 1999). Conventional plant breeding is based on the interplay and combination of genes present in the particular crop genome, and soybean is limited with regard to genetic diversity (Chung and Singh, 2008).

II.B. Characteristics of the Recipient Plant

The conventional soybean variety A3525, used as the recipient for the *dmo* expression cassette insertion that produced MON 87708, was developed by Asgrow Seed Company. A3525 is a mid−maturity group III soybean variety with very high yield potential.

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A3525 has superior yields relative to varieties of similar maturity and has excellent agronomic characteristics (Steffen, 2004).

II.C. Soybean as a Test System in Product Safety Assessment

Soybean variety A3525 is the near isogenic line to MON 87708 and was used as the conventional soybean comparator (hereafter referred to as the conventional control) in the safety assessment of MON 87708. MON 87708 and the conventional control have similar genetic backgrounds with the exception of the *dmo* expression cassette, thus, the effect of the *dmo* expression cassette and the expressed MON 87708 DMO could therefore be assessed in an unbiased manner. In addition, commercial soybean varieties that were derived through conventional methods and Roundup Ready soybean varieties (hereafter referred to as commercial reference varieties) were used as reference materials to establish ranges of natural variability or responses representative of commercial soybean varieties. The commercial reference varieties used at each location were selected based on their availability and agronomic fit for the respective geographic region.

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III. DESCRIPTION OF THE GENETIC MODIFICATION

MON 87708 was developed through *Agrobacterium tumefaciens*-mediated transformation of conventional soybean A3525 meristem tissue utilizing transformation plasmid vector PV-GMHT4355. This section describes the plasmid vector, the donor genes, and the regulatory elements used in the development of MON 87708 and the deduced amino acid sequence of the MON 87708 DMO. In this section, transfer DNA (T-DNA) refers to DNA that is transferred to the plant during transformation. An expression cassette is comprised of sequences to be transcribed and the regulatory elements necessary for the expression of those sequences.

III.A. The Plasmid Vector PV-GMHT4355

PV-GMHT4355 was used for the transformation of conventional soybean to produce MON 87708 and is shown in Figure III-1; PV-GMHT4355 is approximately 11.4 kb and contains two T-DNAs, each delineated by Left and Right Border sequences to facilitate transformation. The first T-DNA, designated as T-DNA I, contains the *dmo* coding sequence under regulation of the peanut chlorotic streak virus (*PC1SV*) promoter and the pea *E9* 3′ non-translated region. The second T-DNA, designated as T-DNA II, contains the *cp4 epsps* coding sequence under the regulation of the figwort mosaic virus (*FMV*) promoter and the pea *E9* 3′ non-translated region. During transformation, both T-DNAs were inserted into the soybean genome (Section III.B) where T-DNA II, containing the *cp4 epsps* expression cassette, functioned as a marker gene for the selection of transformed plantlets. Subsequently, conventional self-pollinated breeding methods and segregation, along with a combination of analytical techniques, were used to isolate those plants that contain the *dmo* expression cassette (T-DNA I) and did not contain the *cp4 epsps* expression cassette (T-DNA II).

The backbone region of PV-GMHT4355 that is outside both of the T-DNAs contains two origins of replication for maintenance of the plasmid vector in bacteria (*ori V*, *ori-pBR322*), a bacterial selectable marker gene (*aadA*), and a coding sequence for repressor of primer (*rop*) protein which is necessary for the maintenance of the plasmid vector copy number in *E. coli*. A description of the genetic elements and their prefixes (*e.g.*, P-, L-, I-, TS-, OR-, B-, CS-, and T-) in PV-GMHT4355 is provided in Table III-1.

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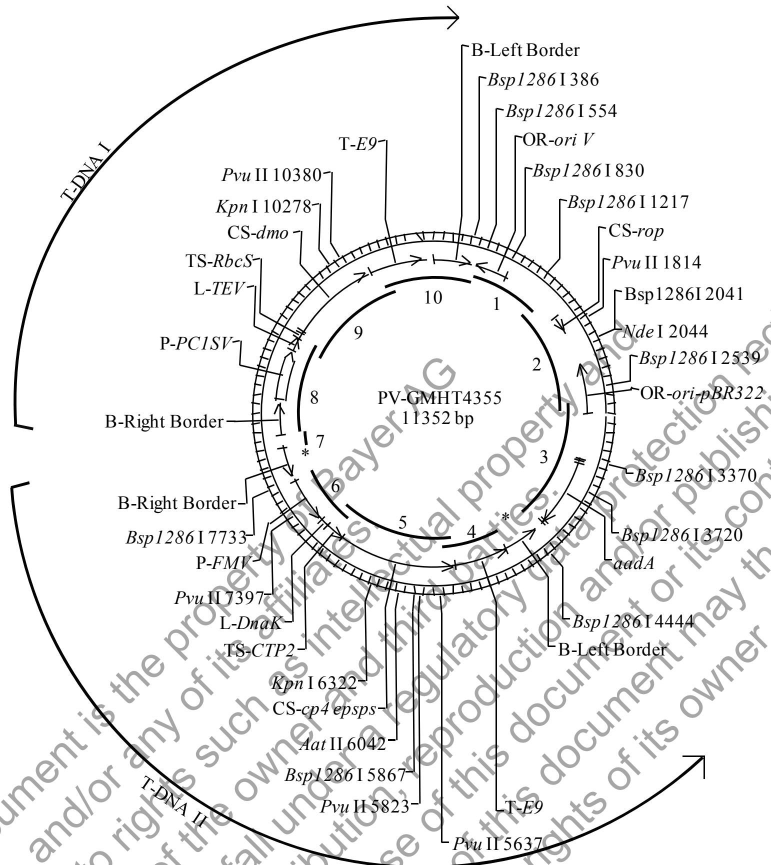

T-DNA I
T-DNA II
PV-GMHT4355
11352 bp
B-Left Border
Bsp1286 I 386
Bsp1286 I 554
OR-ori V
Bsp1286 I 830
Bsp1286 I 1217
CS-rop
Pvu II 1814
Bsp1286I 2041
Nde I 2044
Bsp1286 I 2539
OR-ori-pBR322
Bsp1286 I 3370
Bsp1286 I 3720
aadA
Bsp1286 I 4444
B-Left Border
T-E9
Pvu II 5637
Pvu II 5823
Bsp1286 I 5867
Aat II 6042
CS-cp4 epsps
Kpn I 6322
TS-CTP2
L-DnaK
Pvu II 7397
P-FMV
Bsp1286 I 7733
B-Right Border
B-Right Border
P-PC1SV
L-TEV
TS-RbcS
CS-dmo
Kpn I 10278
Pvu II 10380
T-E9
1
2
3
4
5
6
7
8
9
10
*
*

Probe Number	Probe Type	Probe Name	Start Position (bp)	End Position (bp)	Total Length (bp)
1	Backbone Probe	B1	443	1328	886
2	Backbone probe	B2	1250	2754	1505
3	Backbone Probe	B3	2625	4384	1760
4	T-DNA II Probe	TII-1	4796	5637	842
5	T-DNA II Probe	TII-2	5575	7021	1447
6	T-DNA II Probe	TII-3	6937	7761	825
7	Backbone Probe	B4	8119	8289	171
8	T-DNA I Probe	TI-1	8290	9523	1234
9	T-DNA I Probe	TI-2	9448	10668	1221
10	T-DNA I Probe	TI-3	10610	442	1185

Figure III-1. Circular Map of Plasmid Vector PV-GMHT4355 Showing Probes 1-10

The plasmid vector PV-GMHT4355 containing the T-DNAs used in *Agrobacterium*-mediated transformation to produce MON 87708. Genetic elements and restriction sites for enzymes used in the Southern blot analyses (with positions relative to the size of the plasmid vector) are shown on the exterior of the map. The probes used in the Southern blot analyses (labeled 1-10 on the interior of the map) are detailed in the accompanying table above.

*The Left and Right Border sequences of T-DNA II share 100% identity to those of T-DNA I, which were covered by probes 8 and 10 and thus not included in the T-DNA II probes.

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Table III-1. Summary of Genetic Elements in the Plasmid Vector PV-GMHT4355

Genetic Element	Location in Plasmid (bp)	Function (Reference)
T-DNA I (Present in MON 87708)		
B[1]-Right Border	8290-8646	DNA region from *Agrobacterium tumefaciens* containing the Right Border sequence used for transfer of the T-DNA (Depicker et al., 1982; Zambryski et al., 1982)
Intervening sequence	8647-8691	Sequence used in DNA cloning
P[2]-*PC1SV*	8692-9124	Promoter for the Full-Length Transcript (FLt) of peanut chlorotic streak caulimovirus (Maiti and Shepherd, 1998) that directs transcription in plant cells
Intervening sequence	9125-9144	Sequence used in DNA cloning
L[3]-*TEV*	9145-9276	5′ non-translated region from the Tobacco Etch virus genome (Niepel and Gallie, 1999) that is involved in regulating gene expression
Intervening sequence	9277	Sequence used in DNA cloning
TS[4]-*RbcS*	9278-9520	Sequences encoding the transit peptide and the first 24 amino acids of the mature protein of the *RbcS* gene from *Pisum sativum* (pea) (Fluhr et al., 1986) that directs transport to the DMO precursor protein of the chloroplast
Intervening Sequence	9521-9529	Sequence used in DNA cloning
CS[5]-*dmo*	9530-10552	Coding sequence for the dicamba mono-oxygenase from *Stenotrophomonas maltophilia* (Herman et al., 2005; Wang et al., 1997)
Intervening Sequence	10553-10620	Sequence used in DNA cloning
T[6]-*E9*	10621-11263	3′ non-translated region from the *RbcS2* gene of *Pisum sativum* (pea) encoding the Rubisco small subunit, which functions to direct polyadenylation of the mRNA (Coruzzi et al., 1984)
Intervening Sequence	11264-11352	Sequence used in DNA cloning
B-Left Border	1-442	DNA region from *Agrobacterium tumefaciens* containing the Left Border sequence used for transfer of the T-DNA (Barker et al., 1983)

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Table III-1 (continued). Summary of Genetic Elements in the Plasmid Vector PV-GMHT4355

Genetic Element	Location in Plasmid (bp)	Function (Reference)
Plasmid Vector Backbone (Not present in MON 87708)		
Intervening Sequence	443-528	Sequence used in DNA cloning
OR^7-*ori V*	529-925	Origin of replication from the broad host range plasmid RK2 for maintenance of plasmid in *Agrobacterium* (Stalker et al., 1981)
Intervening Sequence	926-1662	Sequence used in DNA cloning
CS-*rop*	1663-1854	Coding sequence for repressor of primer protein derived from the ColE1 plasmid for maintenance of plasmid copy number in *E. coli* (Giza and Huang, 1989)
Intervening Sequence	1855-2281	Sequence used in DNA cloning
OR-*ori-pBR322*	2282-2870	Origin of replication from pBR322 for maintenance of plasmid in *E. coli* (Sutcliffe, 1979)
Intervening Sequence	2871-3400	Sequence used in DNA cloning
aadA	3401-4289	Bacterial promoter, coding and 3′ UTR sequences for an aminoglycoside-modifying enzyme, 3″ (9)-O-nucleotidyltransferase from transposon Tn7 (Fling et al., 1985) that confers spectinomycin and streptomycin resistance
Intervening Sequence	4290-4384	Sequence used in DNA cloning
T-DNA II (Not present in MON 87708)		
B-Left Border	4385-4795	DNA region from *Agrobacterium tumefaciens* containing the Left Border sequence used for transfer of the T-DNA (Barker et al., 1983)
Intervening Sequence	4796-4809	Sequence used in DNA cloning
T-*E9*	4810-5452	3′ non-translated sequence from *RbcS2* gene of *Pisum sativum* (pea) encoding the Rubisco small subunit, which functions to direct polyadenylation of the mRNA (Coruzzi et al., 1984)
Intervening Sequence	5453-5458	Sequence used in DNA cloning
CS-*cp4 epsps*	5459-6826	Codon optimized coding sequence of the *aroA* gene from *Agrobacterium* spp. strain CP4 encoding CP4 EPSPS (Barry et al., 1997; Padgette et al., 1996a)

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Table III-1 (continued). Summary of Genetic Elements in the Plasmid Vector PV-GMHT4355

Genetic Element	Location in Plasmid (bp)	Function (Reference)
TS-*CTP2*	6827-7054	Sequences encoding the chloroplast transit peptide region from the *shkG* gene of *Arabidopsis thaliana* encoding EPSPS (Herrmann, 1995; Klee et al., 1987) that directs transport of the CP4 EPSPS precursor protein to the chloroplast
Intervening Sequence	7055-7063	Sequence used in DNA cloning
L-*DnaK*	7064-7159	5′ non-translated leader sequence from the *Petunia hybrida Hsp70* gene (Rensing and Maier, 1994) that is involved in regulating gene expression
Intervening Sequence	7160-7162	Sequence used in DNA cloning
P-*FMV*	7163-7714	Promoter for the 35S RNA from figwort mosaic virus (Rogers, 2000) that directs transcription in plant cells
Intervening Sequence	7715-7761	Sequence used in DNA cloning
B-Right Border	7762-8118	DNA region from *Agrobacterium tumefaciens* containing the Right Border sequence used for transfer of the T-DNA (Depicker et al., 1982; Zambryski et al., 1982)
Intervening sequence	8119-8289	Sequence used in DNA cloning

[1] B -border.
[2] P-promoter.
[3] L- leader.
[4] TS- targeting sequence.
[5] CS-coding sequence.
[6] T- 3' non-translated transcriptional termination sequence and polyadenylation signal sequences.
[7] OR-origin of replication.

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III.B. Description of the Transformation System

The *Agrobacterium*-mediated soybean transformation used to produce MON 87708 was based on the method described by Martinell et al. (2002), which allows for the generation of transformed plants without utilization of callus. Briefly, meristem tissues were excised from the embryos of germinated conventional seed. After co-culturing with the *Agrobacterium* carrying the vector, the meristems were placed on selection medium containing glyphosate, carbenicillin, cefotaxime, and ticarcillin/clavulanate acid mixture, to inhibit the growth of untransformed plant cells and excess *Agrobacterium*. The meristems were then placed in media conducive to shoot and root development. Rooted plants with normal phenotypic characteristics were selected and transferred to soil for growth and further assessment.

The R_0 plants generated through this transformation were self-pollinated to produce R_1 plants, and the unlinked insertions of T-DNA I and T-DNA II were segregated. A non-lethal dose of glyphosate was applied to R_1 plants and those plants with minor herbicide injury were selected for further analyses, whereas plants showing no injury, indicating that they contained the *cp4 epsps* coding sequence from T-DNA II, were eliminated from further development. Subsequently, plants that were homozygous for T-DNA I were identified by quantitative polymerase chain reaction (PCR) analysis. MON 87708 was selected as the lead event based on superior phenotypic characteristics, dicamba tolerance, and its molecular profile. The major development steps of MON 87708 are depicted in Figure III-2. The result of this process was the production of marker-free, dicamba-tolerant soybean MON 87708.

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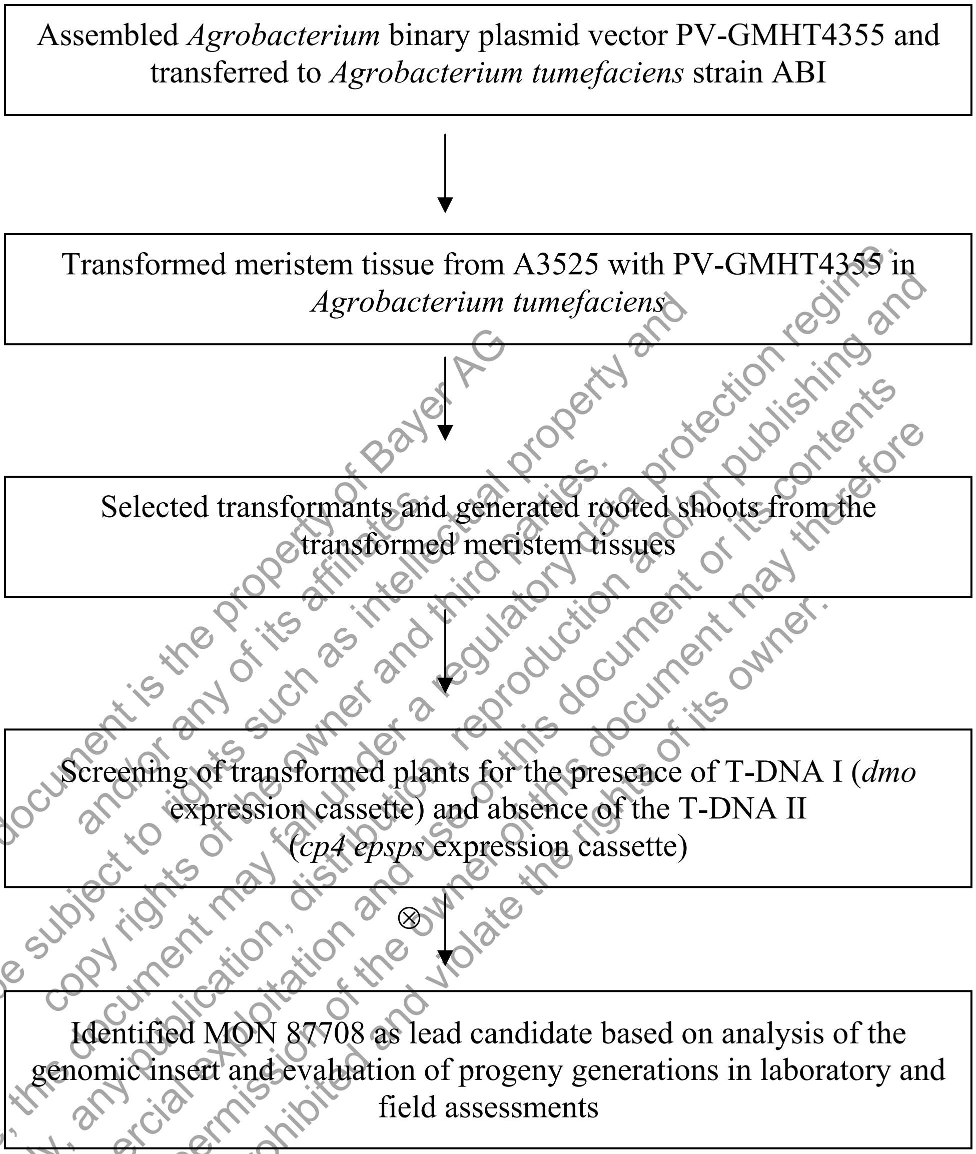
Assembled *Agrobacterium* binary plasmid vector PV-GMHT4355 and transferred to *Agrobacterium tumefaciens* strain ABI
Transformed meristem tissue from A3525 with PV-GMHT4355 in *Agrobacterium tumefaciens*
Selected transformants and generated rooted shoots from the transformed meristem tissues
Screening of transformed plants for the presence of T-DNA I (*dmo* expression cassette) and absence of the T-DNA II (*cp4 epsps* expression cassette)
⊗
Identified MON 87708 as lead candidate based on analysis of the genomic insert and evaluation of progeny generations in laboratory and field assessments

Figure III-2. Schematic of the Development of MON 87708

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III.C. The *dmo* Coding Sequence and MON 87708 DMO (T-DNA I)

The *dmo* expression cassette (T-DNA I) present in MON 87708 encodes MON 87708 DMO (Figure III-3). The *dmo* expression cassette contains the coding region for the DMO from *Stenotrophomonas maltophilia* (Herman et al., 2005; Wang et al., 1997). The presence of MON 87708 DMO confers tolerance to dicamba (refer to Section V.A for more details).

```
1   MASMISSSAV TTVSRASRGQ SAAMAPFGGL KSMTGFPVRK VNTDITSITS NGGRVKCMQV
61  WPPIGKKKFE TLSYLPPLTR DSRAMATFVR NAWYVAALPE ELSEKPLGRT ILDTPLALYR
121 QPDGVVAALL DICPHRFAPL SDGILVNGHL QCPYHGLEFD GGGQCVHNPH GNGARPASLN
181 VRSFPVVERD ALIWICPGDP ALADPGAIPD FGCRVDPAYR TVGGYGHVDC NYKLLVDNLM
241 DLGHAQYVHR ANAQTDAFDR LEREVIVGDG EIQALMKIPG GTPSVLMAKF LRGANTPVDA
301 WNDIRWNKVS AMLNFIAVAP EGTPKEQSIH SRGTHILTPE TEASCHYFFG SSRNFGIDDP
361 EMDGVLRSWQ AQALVKEDKV VVEAIERRRA YVEANGIRPA MLSCDEAAVR VSREIEKLEQ
421 LEAA
```

Figure III-3. Deduced Amino Acid Sequence of the *RbcS* Targeting Sequence and MON 87708 DMO

The transit peptide and the first 24 amino acids of the mature protein of the *RbcS* gene are underlined. Accumulation of MON 87708 DMO is targeted to the chloroplasts using the *RbcS* transit peptide. (see Section V.A for more detail).

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III.D. The *cp4 epsps* Coding Sequence and the CP4 EPSPS Protein (T-DNA II)

The *cp4 epsps* expression cassette (T-DNA II), that is not present in MON 87708, encoded a 47.6 kDa CP4 EPSPS protein, consisting of a single polypeptide of 455 amino acids (Padgette et al., 1996b). The *cp4 epsps* coding sequence is the codon optimized coding sequence of the *aroA* gene from *Agrobacterium* spp. strain CP4 encoding CP4 EPSPS (Barry et al., 1997; Padgette et al., 1996a). CP4 EPSPS confers tolerance to glyphosate and was used as a selectable marker during the transformation selection process. Through conventional self-pollinated breeding methods and segregation, along with a combination of analytical techniques, plants that did not contain the *cp4 epsps* expression cassette were isolated.

III.E. Regulatory Sequences

The *dmo* coding sequence in T-DNA I is under the regulation of the *PC1SV* promoter, *TEV* leader, the *RbcS* targeting sequence, and the *E9* 3′ non-translated region. The *PC1SV* promoter is the promoter for the Full-Length Transcript (FLt) of peanut chlorotic streak caulimovirus (Maiti and Shepherd, 1998) that directs transcription in plant cells. The *TEV* leader is the 5′ non-translated region from the Tobacco Etch virus (Niepel and Gallie, 1999) and is involved in regulating gene expression. The *RbcS* targeting sequence is the sequence encoding the chloroplast transit peptide and the first 24 amino acids of the mature protein of the ribulose-1,5-bisphosphate carboxylase oxygenase gene from pea (*Pisum sativum*) (Fluhr et al., 1986) that directs transport of the DMO precursor protein to the chloroplast. The *E9* 3′ non-translated region is the 3′ non-translated region from the *RbcS2* gene of pea encoding the Rubisco small subunit, which functions to direct polyadenylation of the mRNA (Coruzzi et al., 1984).

T-DNA II contains the *cp4 epsps* coding sequence under the regulation of the *FMV* promoter, *DnaK* leader, the *CTP2* targeting sequence, and the *E9* 3′ non-translated region. The *FMV* promoter is the promoter for the 35S RNA from figwort mosaic virus (Rogers, 2000) that directs transcription in plant cells. The *DnaK* leader is the 5′ non-translated leader sequence from the *Petunia hybrida Hsp70* gene (Rensing and Maier, 1994) that is involved in regulating gene expression. The *CTP2* targeting sequence is the sequence encoding the chloroplast transit peptide region from the *shkG* gene of *Arabidopsis thaliana* encoding EPSPS (Herrmann, 1995; Klee et al., 1987) that directs transport of the CP4 EPSPS precursor protein to the chloroplast. The *E9* 3′ non-translated region is the 3′ non-translated region from the *RbcS2* gene of pea encoding the Rubisco small subunit, which functions to direct polyadenylation of the mRNA (Coruzzi et al., 1984).

III.F. T-DNA Borders

PV-GMHT4355 contains Right and Left Border regions (Figure III-1 and Table III-1) that were derived from *Agrobacterium tumefaciens* (Barker et al., 1983; Depicker et al., 1982; Zambryski et al., 1982). The border regions each contain a 24-25 bp nick site that is the site of DNA exchange during transformation. The border regions separate the T-DNA from the backbone region and are involved in their efficient transfer into the soybean genome. Because PV-GMHT4355 is a 2T-DNA vector, it contains two Right Border regions and two Left Border regions, where one set flanks T-DNA I and the other set flanks T-DNA II.

III.G. Genetic Elements Outside of the T-DNA Borders

Genetic elements that exist outside of the T-DNA borders are those that are essential for the maintenance or selection of PV-GMHT4355 in bacteria and are referred to as the plasmid backbone. The *ori V*, derived from the broad host plasmid RK2, is required for the maintenance of the plasmid vector in *Agrobacterium* (Stalker et al., 1981), whereas the *ori-pBR322*, derived from the plasmid vector pBR322, is required for the maintenance of the plasmid vector in *E. coli* (Sutcliffe, 1979). The *rop* is necessary for the maintenance of plasmid vector copy number in *E. coli* (Giza and Huang, 1989). The *aadA* is a bacterial promoter and coding sequence for an enzyme from transposon Tn7 that confers spectinomycin and streptomycin resistance (Fling et al., 1985) in *E. coli* and *Agrobacterium* during molecular cloning. Because these elements are outside the border regions, they were not expected to be transferred into the soybean genome. The absence of the backbone sequence in MON 87708 was confirmed by Southern blot analyses (see Section IV.C).

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IV. CHARACTERIZATION OF THE GENETIC MODIFICATION

A multi-faceted approach was taken to characterize the genetic modification that produced MON 87708. The results confirmed that MON 87708 contains a single copy of the *dmo* expression cassette (T-DNA I) that is stably integrated at a single locus and is inherited according to Mendelian principles over multiple generations (Section IV.G). The results confirmed that no T-DNA II or plasmid vector backbone sequences are detected in MON 87708. These conclusions are based on several lines of evidence: 1) Southern blot analyses to assay the entire soybean genome for the presence of DNA derived from PV-GMHT4355, and to confirm that a single copy of T-DNA I was inserted at a single site and that the insert is stably inherited; 2) DNA sequencing analyses to determine the exact sequence of the inserted DNA and allowed a comparison to the T-DNA I sequence in PV-GMHT4355 to confirm that only the expected sequences were integrated; and 3) a comparison of the DNA flanking T-DNA I to the sequence of the insertion site in conventional soybean to identify any rearrangements that occurred at the insertion site during transformation. Taken together, the characterization of the genetic modification demonstrates that a single copy of the T-DNA I was inserted at a single locus of the genome.

Southern blot analyses were used to determine the number of copies and the insertion sites of T-DNA I as well as the presence or absence of T-DNA II and plasmid vector backbone sequences. The Southern blot strategy was designed to ensure that all potential inserted segments would be identified. The entire soybean genome was assayed with probes that spanned the complete plasmid vector PV-GMHT4355 to detect the presence of T-DNA I as well as confirm the lack of any detectable T-DNA II and plasmid vector backbone sequences. This was accomplished by using probes that were less than 2 kb in length, ensuring a high level of sensitivity. This high level of sensitivity was demonstrated for each blot by detection of a positive control added at 0.1 copies per genome equivalent. Two restriction enzyme sets were specifically chosen to fully characterize T-DNA I and look for any potential fragments of T-DNA I. This two enzyme set design also maximizes the possibility of detecting an insertion elsewhere in the genome that could be overlooked if that band comigrated with an expected band. Additionally, the restriction enzyme sets were chosen such that at least one enzyme from each set resides in the known 5′ or 3′ flanking sequence and that together the enzyme sets result in overlapping segments covering the entire insert. Therefore, at least one segment for each flank is of a predictable size and overlaps with another predictable size segment. This overlapping strategy confirms that the entire insert sequence is identified in a predictable hybridization pattern.

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To determine the number of copies and the insertion sites of T-DNA I, and the presence or absence of T-DNA II and the plasmid vector backbone sequences, duplicated samples that consisted of equal amounts of digested DNA were run on the agarose gel. One set of samples was run for a longer period of time (long run) than a second set (short run). The long run allows for greater resolution of large molecular weight DNA, whereas the short run allows the detection of small molecular weight DNA. The molecular weight markers on the left of the figures were used to estimate the sizes of the bands present in the long run lanes of the Southern blots, and the molecular weight markers on the right of the figures were used to estimate the sizes of bands present in the short run lanes of the Southern blots.

The DNA sequencing analyses complement the Southern blot analyses. Southern blot results demonstrated that MON 87708 contains a single copy of T-DNA I at a single insertion site. Sequencing of the insert and the flanking DNA confirmed the organization of the elements within the insert, determined the 5′ and 3′ insert-to-plant junctions, as well as the complete DNA sequence of the insert and adjacent DNA. In addition, DNA sequencing analyses confirmed that each genetic element in the insert is intact and the sequence of the insert matches the corresponding sequence in PV-GMHT4355. Furthermore, genomic organization at the insertion site was assessed by comparing the insert and flanking sequence to the insertion site in conventional soybean.

The stability of the T-DNA I present in MON 87708 across multiple generations (R_2-R_6) was demonstrated by Southern blot analysis. Genomic DNA from five generations of MON 87708 was digested with one of the enzyme sets used for the insert and copy number analysis and was hybridized with a probe that detects restriction segments that encompass the entire T-DNA I. This fingerprint strategy consists of two border segments that assess not only the stability of T-DNA I, but also the stability of genomic DNA directly adjacent to T-DNA I.

The results of these analyses for MON 87708 demonstrated that a single copy of the T-DNA I was inserted at a single locus of the genome. Generational stability analysis demonstrated that an expected Southern blot fingerprint of MON 87708 was maintained through five generations of the breeding history, thereby confirming the stability of T-DNA I in MON 87708. Results from segregation analyses showed heritability and stability of the insert occurred as expected across multiple generations, which corroborates the molecular insert stability analysis and establishes the genetic behavior of the T-DNA I at a single chromosomal locus.

The Southern blot analysis confirmed that T-DNA I reported in Figure IV-1 represents the only detectable insert in MON 87708. Figure IV-1 is a linear map depicting restriction sites within the insert as well as within the known soybean genomic DNA immediately flanking the insert in MON 87708. The circular map of PV-GMHT4355 annotated with the probes used in the Southern blot analysis is presented in Figure III-1. Based on the linear map of the insert and the plasmid map, a table summarizing the expected DNA segments for Southern analyses is presented in Table IV-1. The genetic elements integrated in MON 87708 are summarized in Table IV-2. The generations used are depicted in the breeding history shown in Figure IV-9. Materials and methods used for characterization of T-DNA I in MON 87708 are found in Appendix B.

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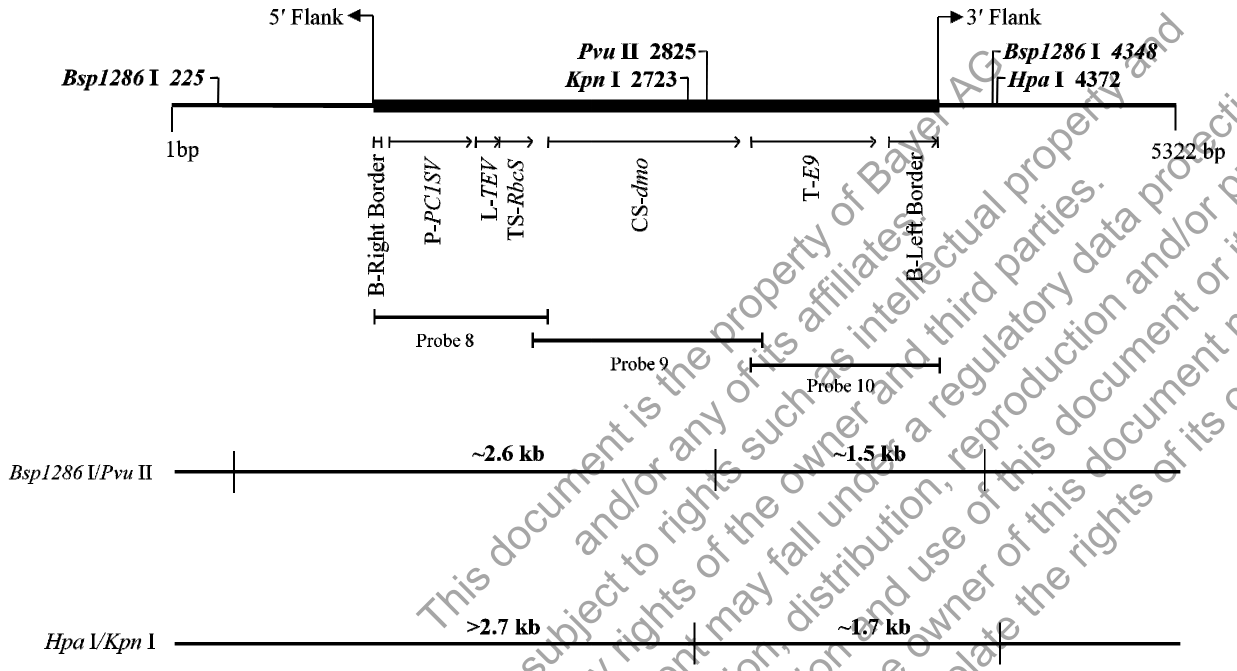

5′ Flank
3′ Flank
Pvu II 2825
Kpn I 2723
Bsp1286 I 225
Bsp1286 I 4348
Hpa I 4372
1bp
5322 bp
B-Right Border
P-*PC1SV*
L-*TEV*
TS-*RbcS*
CS-*dmo*
T-*E9*
B-Left Border
Probe 8
Probe 9
Probe 10
Bsp1286 I/*Pvu* II
~2.6 kb
~1.5 kb
Hpa I/*Kpn* I
>2.7 kb
~1.7 kb

Figure IV-1. Schematic Representation of the Insert and DNA Flanking Sequences in MON 87708

A linear map of the insert and genomic DNA flanking the insert in MON 87708 is shown. Identified on the map are genetic elements within the insert, as well as restriction sites with positions relative to the size of the linear map for enzymes used in the Southern analyses. The relative sizes and locations of the T-DNA I probes, which are described in Figure III-1, are shown on the middle portion. Shown on the lower portion of the map are the expected sizes of the DNA segments after digestion with respective restriction enzymes. Arrowheads (⟶) indicate the end of the insert and the beginning of the genomic DNA sequence flanking the 5′ and 3′ end of the insert. The arrows (→) indicate the sequence direction of the elements in MON 87708.

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Table IV-1. Summary Chart of the Expected DNA Segments Based on Hybridizing Probes and Restriction Enzymes Used in MON 87708 Analysis

Southern Blot Figure		IV-2	IV-3	IV-4	IV-5	IV-6	IV-7	IV-8	IV-10
Probe Used		8	9	10	4	5	6	1, 2, 3, and 7	9
Probing Target	Digestion Enzyme	Expected Band Sizes (kb) on Each Southern Blot							
Plasmid Vector PV-GMHT4355	*Aat* II/*Nde* I	~7.4	~7.4	~4.0 ~7.4	~4.0 ~7.4	~4.0 ~7.4	~7.4	~4.0 ~7.4	~7.4
Probe Templates[1]	N/A	~~[2]	~~[2]	~~[2]	~~[2]	~~[2]	~~[2]	~0.2 ~0.9 ~1.5 ~1.8	~~[2]
Conventional Control A3525	*Bsp1286* I/*Pvu* II	None	None	None	None	None	None	None	None
	Hpa I/*Kpn* I	None	None	None	None	None	None	None	None
MON 87708	*Bsp1286* I/*Pvu* II	~2.6	~2.6 ~1.5	~1.5	~1.5	None	None	None	~2.6 ~1.5
	Hpa I/*Kpn* I	>2.7*	>2.7* ~1.7	~1.7	~1.7	None	None	None	--[3]

[1] Probe templates were spiked when multiple probes are used in Southern blot analysis.

[2] '~~' indicates that only plasmid template was used since the Southern blot was hybridized with one probe.

[3] '--' indicates that the particular restriction enzyme or the combination of the enzymes was not used in the analysis.

* Southern analysis indicates this segment to be ~5.6 kb.

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Table IV-2. Summary of Genetic Elements in MON 87708

Genetic Element	Location (bp)	Function (Reference)
5′ Flanking Sequences	1-1048	DNA sequence adjacent to the 5′ end of the insertion site
B[1]-Right Border[*]	1049-1091	DNA region from *Agrobacterium tumefaciens* containing the Right Border sequence used for transfer of the T-DNA (Depicker et al., 1982; Zambryski et al., 1982)
Intervening sequence	1092-1136	Sequence used in DNA cloning
P[2]-*PC1SV*	1137-1569	Promoter for the Full-Length Transcript (FLt) of peanut chlorotic streak caulimovirus (Maiti and Shepherd, 1998) that directs transcription in plant cells
Intervening sequence	1570-1589	Sequence used in DNA cloning
L[3]-*TEV*	1590-1721	5' non-translated region from the Tobacco Etch virus genome (Niepel and Gallie, 1999) that is involved in regulating gene expression
Intervening sequence	1722-1722	Sequence used in DNA cloning
TS[4]-*RbcS*	1723-1965	Sequences encoding the transit peptide and the first 24 amino acids of the mature protein of the *RbcS* gene from *Pisum sativum* (pea) (Fluhr et al., 1986) that directs transport of the DMO precursor protein to the chloroplast
Intervening Sequence	1966-1974	Sequence used in DNA cloning
CS[5]-*dmo*	1975-2997	Coding sequence for the dicamba mono-oxygenase from *Stenotrophomonas maltophilia* (Herman et al., 2005; Wang et al., 1997)
Intervening Sequence	2998-3065	Sequence used in DNA cloning
T[6]-*E9*	3066-3708	3′ non-translated region from the *RbcS2* gene of *Pisum sativum* (pea) encoding the Rubisco small subunit, which functions to direct polyadenylation of the mRNA (Coruzzi et al., 1984)
Intervening Sequence	3709-3797	Sequence used in DNA cloning
B-Left Border[*]	3798-4051	DNA region from *Agrobacterium tumefaciens* containing the Left Border sequence used for transfer of the T-DNA (Barker et al., 1983)
3′ Flanking Sequences	4052-5322	DNA sequence adjacent to the 3′ end of the insertion site

[1] B-border.
[2] P-promoter.
[3] L-leader.
[4] TS- targeting sequence.
[5] S- coding sequence.
[6] T-3' non-translated transcriptional termination sequence and polyadenylation signal sequences.
*These borders are truncated.

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IV.A. Insert and Copy Number of T-DNA I in MON 87708

The copy number and insertion site of T-DNA I was assessed by digesting MON 87708 genomic DNA with the restriction enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I and hybridizing Southern blots with probes that span T-DNA I (Figure III-1). Each restriction digest is expected to produce a specific banding pattern on the Southern blots (Table IV-1). Since each detected segment contains flanking genomic DNA, any additional integrated sites would produce a different banding pattern with additional bands.

The restriction enzyme combination *Bsp1286* I/*Pvu* II cuts once within T-DNA I and once within each of the known genomic DNA sequences flanking the 5′ and 3′ ends of T-DNA I (Figure IV-1). Therefore, if T-DNA I sequences are present at a single integration site in MON 87708, the digestion with *Bsp1286* I/*Pvu* II was expected to generate two border segments with expected sizes of ~2.6 kb and ~1.5 kb (Figure IV-1, and Table IV-1). The ~2.6 kb restriction segment contained genomic DNA flanking the 5′ end of T-DNA I, the Right Border, the *PC1SV* promoter, the *TEV* leader, the *RbcS* targeting sequence, and a portion of the *dmo* coding sequence. The ~1.5 kb restriction segment contained a portion of the *dmo* coding sequence, the *E9* 3′ non-translated sequence, the Left Border, and genomic DNA flanking the 3′ end of T-DNA I.

The restriction enzyme combination *Hpa* I/*Kpn* I cuts once within T-DNA I and once within the known genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1). Therefore, if T-DNA I sequences are present at a single integration site in MON 87708, the digestion with *Hpa* I/*Kpn* I was expected to generate two border segments with expected sizes of ~1.7 kb and greater than 2.7 kb (Figure IV-1, and Table IV-1). Since the *Hpa* I/*Kpn* I restriction site in the genomic DNA flanking the 5′ end of the insert lies outside of the known sequence, it was not possible to predict a precise segment size. However, the segment size was determined by Southern blot analyses to be ~5.6 kb (Figures IV-2 and IV-3). The ~5.6 kb restriction segment contained genomic DNA flanking the 5′ end of T-DNA I, the Right Border, the *PC1SV* promoter, the *TEV* leader, the *RbcS* targeting sequence, and a portion of *dmo* coding sequence. The ~1.7 kb restriction segment contained a portion of the *dmo* coding sequence, the *E9* 3′ non-translated sequence, the Left Border, and genomic DNA flanking the 3′ end of T-DNA I.

In the Southern blot analyses performed, each Southern blot contained a negative and a positive control. Conventional control genomic DNA digested with either the restriction enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I was used as a negative control to determine if the probes hybridized to any endogenous soybean sequences. As a positive control on the Southern blots, PV-GMHT4355 digested with the restriction enzyme combination *Aat* II/*Nde* I was mixed with predigested conventional control DNA. The positive hybridization control was spiked at 0.1 and 1 genome equivalent to demonstrate sufficient sensitivity of the Southern blot. Individual Southern blots were hybridized with the following probes: probes 8, 9, and 10 (refer to Figure III-1 and Table IV-1). The results of this analysis are shown in Figures IV-2 through IV-4.

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IV.A.1. Probe 8

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-2, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-2, lanes 3 and 7) and hybridized with probe 8 (Figure III-1) produced no detectable hybridization bands as expected for the negative control. PV-GMHT4355, digested with the restriction enzyme combination *Aat* II/*Nde* I and mixed with conventional control DNA predigested with the restriction enzyme combination *Hpa* I/*Kpn* I (Figure IV-2, lanes 10 and 11), produced the expected size band at ~7.4 kb (refer to Figure III-1 and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II and hybridized with probe 8 (Figure III-1) produced one unique band at ~2.6 kb (Figure IV-2, lanes 2 and 6). The ~2.6 kb band is the expected size for the border segment containing the 5′ end of T-DNA I along with the adjacent genomic DNA flanking the 5′ end of T-DNA I (Figure IV-1).

MON 87708 DNA digested with the restriction enzyme combination *Hpa* I/*Kpn* I and hybridized with probe 8 (Figure III-1) produced one unique band at ~5.6 kb (Figure IV-2, lanes 4 and 8). The ~5.6 kb band is consistent with the expected band being greater than 2.7 kb for the border segment containing the 5′ end of T-DNA I along with the adjacent genomic DNA flanking the 5′ end of T-DNA I (Figure IV-1).

No additional bands were detected using probe 8. Based on the results presented in Figure IV-2, it was concluded that T-DNA I sequences covered by probe 8 reside at a single integration locus as one copy in MON 87708.

IV.A.2. Probe 9

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-3, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-3, lanes 3 and 7) and hybridized with probe 9 (Figure III-1) produced no detectable hybridization bands as expected for the negative control. PV-GMHT4355, digested with the restriction enzyme combination *Aat* II/*Nde* I and mixed with conventional control DNA predigested with the restriction enzyme combination *Hpa* I/*Kpn* I (Figure IV-3, lanes 10 and 11), produced the expected size band at ~7.4 kb (refer to Figure III-1 and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II and hybridized with probe 9 (Figure III-1) produced two unique bands at ~1.5 kb and ~2.6 kb (Figure IV-3, lanes 2 and 6). The ~1.5 kb band is the expected size for the border segment containing the 3′ end of T-DNA I along with the adjacent genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1). The ~2.6 kb band is the expected size for the border segment containing the 5′ end of T-DNA I along with the adjacent genomic DNA flanking the 5′ end of T-DNA I (Figure IV-1).

MON 87708 DNA digested with the restriction enzyme combination *Hpa* I/*Kpn* I and hybridized with probe 9 (Figure III-1) produced two unique bands at ~1.7 kb and ~5.6 kb

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(Figure IV-3, lanes 4 and 8). The ~1.7 kb band is the expected size for the border segment containing the 3′ end of T-DNA I along with the adjacent genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1). The ~5.6 kb band is consistent with the expected band being greater than 2.7 kb for the border segment containing the 5′ end of T-DNA I along with the adjacent genomic DNA flanking the 5′ end of T-DNA I (Figure IV-1).

No additional bands were detected using probe 9. Based on the results presented in Figure IV-3, it was concluded that T-DNA I sequences covered by probe 9 reside at a single integration locus as one copy in MON 87708.

IV.A.3. Probe 10

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-4, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-4, lanes 3 and 7) and hybridized with probe 10 (Figure III-1) produced no detectable hybridization bands as expected for the negative control. PV-GMHT4355, digested with the restriction enzyme combination *Aat* II/*Nde* I and mixed with conventional control DNA predigested with the restriction enzyme combination *Hpa* I/*Kpn* I (Figure IV-4, lanes 10 and 11), produced two bands at ~4.0 kb and ~7.4 kb. Both bands were expected because probe 10 contains E9 and left border sequences that hybridized to both the ~4.0 kb and the ~7.4 kb fragments from the digested plasmid (refer to Figure III-1 and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II and hybridized with probe 10 (Figure III-1) produced a unique band at ~1.5 kb (Figure IV-4, lanes 2 and 6). The ~1.5 kb band is the expected size for the border segment containing the 3′ end of T-DNA I along with the adjacent genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1).

MON 87708 DNA digested with the restriction enzyme combination *Hpa* I/*Kpn* I and hybridized with probe 10 (Figure III-1) produced a unique band at ~1.7 kb (Figure IV-4, lanes 4 and 8). The ~1.7 kb band is the expected size for the border segment containing the 3′ end of T-DNA I along with the adjacent genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1).

No additional bands were detected using probe 10. Based on the results presented in Figure IV-4, it was concluded that T-DNA sequences covered by probe 10 reside at a single integration locus as one copy in MON 87708.

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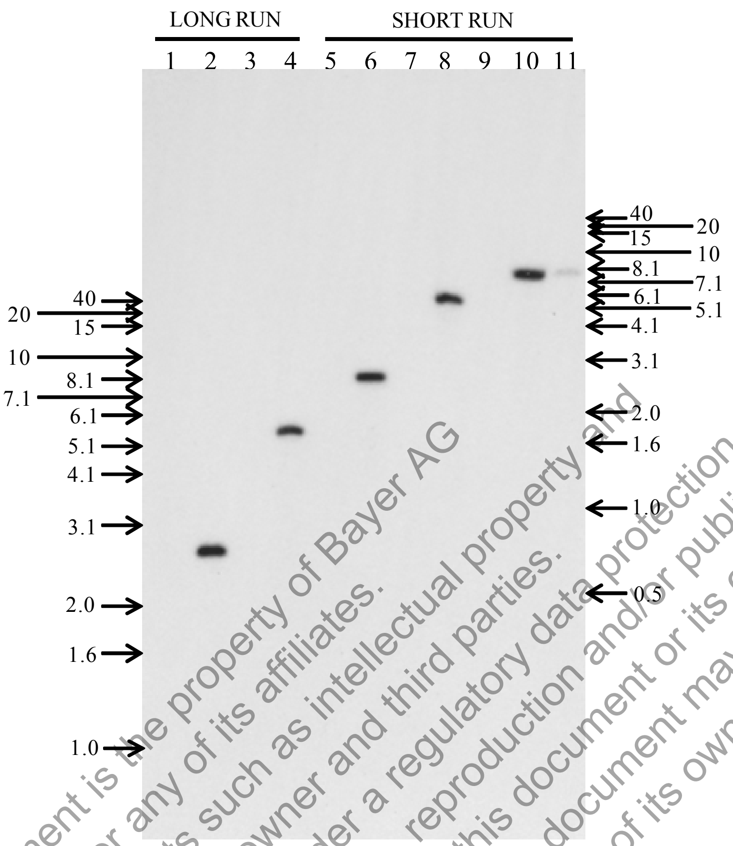

Figure IV-2. Southern Blot Analysis to Determine Insert and Copy Number of T-DNA I in MON 87708: Probe 8

The blot was hybridized with a ^{32}P labeled T-DNA I probe that spans a portion of the T-DNA I sequence (Probe 8, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	Description
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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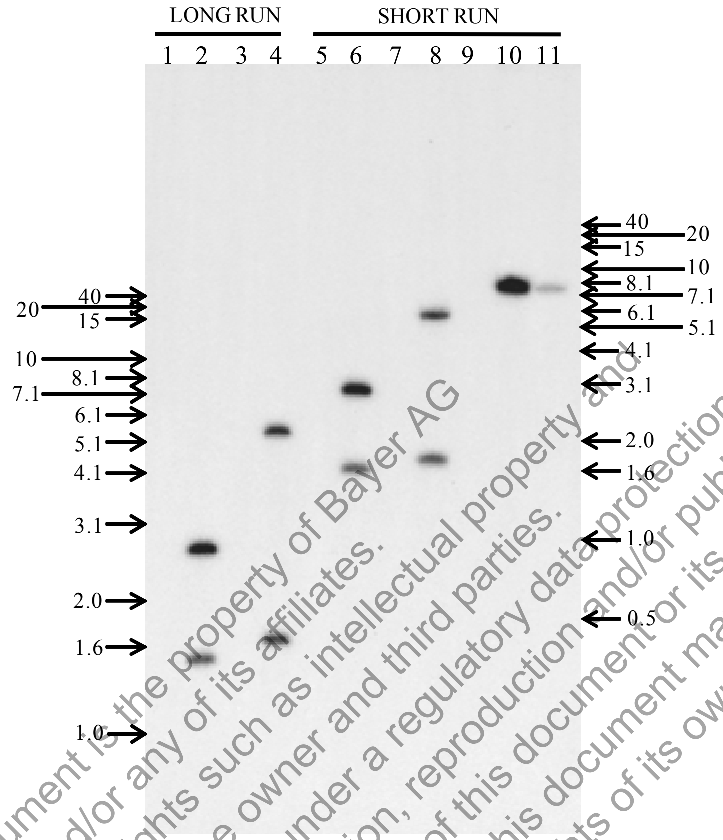

Figure IV-3. Southern Blot Analysis to Determine Insert and Copy Number of T-DNA I in MON 87708: Probe 9

The blot was hybridized with a ^{32}P labeled T-DNA I probe that spans a portion of the T-DNA I sequence (Probe 9, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	Description
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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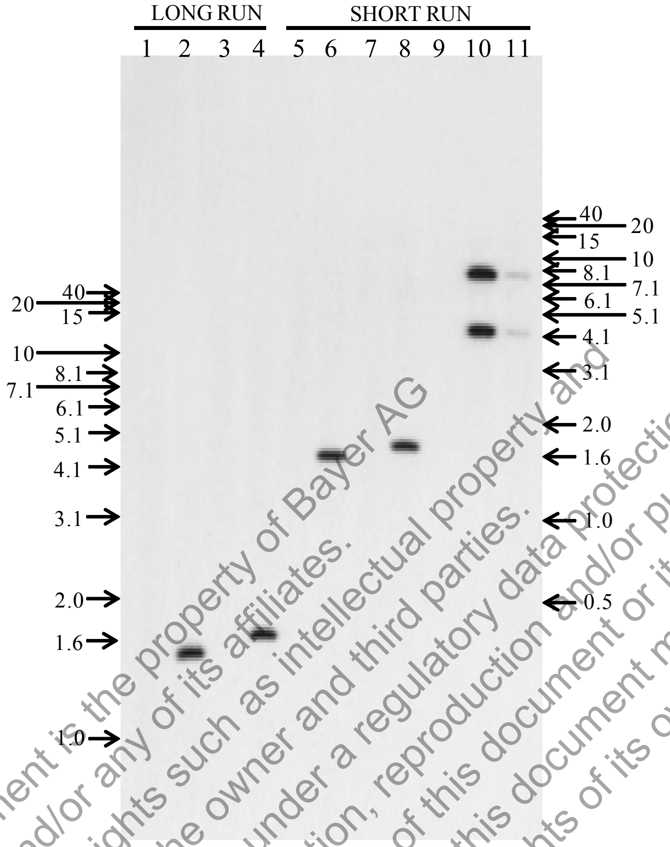

Figure IV-4. Southern Blot Analysis to Determine Insert and Copy Number of T-DNA I in MON 87708: Probe 10

The blot was hybridized with a ^{32}P labeled T-DNA I probe that spans a portion of the T-DNA I sequence (Probe 10, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	**Description**
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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IV.B. Southern Blot Analysis to Determine the Presence or Absence of T-DNA II Sequences in MON 87708

To determine the presence or absence of T-DNA II sequences, MON 87708 and conventional control genomic DNA were digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I and Southern blots were hybridized with probes that span the T-DNA II sequence (Figure III-1). As a positive control on the Southern blots, PV-GMHT4355 digested with the restriction enzyme combination *Aat* II/*Nde* I was mixed with predigested conventional control DNA. The positive hybridization control was spiked at 0.1 and 1 genome equivalent to demonstrate sufficient sensitivity of the Southern blot. Each blot was hybridized with one of three overlapping probes spanning the T-DNA II sequence other than the two border regions that share the same sequences as present in T-DNA I (Probes 4, 5 and 6, Figure III-1). If T-DNA II sequences were present in MON 87708, then probing with the T-DNA II sequences should result in unique hybridizing bands. The results of this analysis are shown in Figures IV-5 through IV-7.

IV.B.1. Probe 4

Conventional control DNA digested with *Bsp1286* I/*Pvu* II (Figure IV-5, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-5, lanes 3 and 7) and hybridized with probe 4 showed no detectable hybridization bands, as expected for the negative control. PV-GMHT4355, previously digested with *Aat* II/*Nde* I and mixed with conventional control DNA predigested with *Hpa* I/*Kpn* I (Figure IV-5, lanes 10 and 11), produced two bands at ~4.0 kb and ~7.4 kb. Both bands were expected because probe 4 contains E9 sequence that hybridized to both the ~4.0 kb and the ~7.4 kb fragments from the digested plasmid (refer to Figure III-1 and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II and hybridized with probe 4 (Figure III-1) produced one unique band at ~1.5 kb (Figure IV-5, lanes 2 and 6). MON 87708 DNA digested with *Hpa* I/*Kpn* I and hybridized with probe 4 (Figure III-1) produced one unique band at ~1.7 kb (Figure IV-5, lanes 4 and 8). Probe 4 contains the E9 3′ non-translated region sequence that is also contained in T-DNA I (Figure III-1). Therefore, probe 4 was expected to hybridize to the ~1.5 kb and ~1.7 kb fragments (Figure IV-1) derived from the T-DNA I insert. These bands were also detected by probe 10 (Figure IV-4, lanes 2 and 6, and lanes 4 and 8). Any T-DNA II sequences other than those associated with T-DNA I would be detected as novel bands. No unexpected bands were detected indicating that MON 87708 contains no detectable T-DNA II elements covered by probe 4.

IV.B.2. Probe 5

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-6, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-6, lanes 3 and 7) and hybridized with probe 5 (Figure III-1) showed no detectable hybridization bands, as expected for the negative control. PV-GMHT4355, previously digested with *Aat* II/*Nde* I

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and mixed with conventional control DNA predigested with *Hpa* I/*Kpn* I (Figure IV-6, lanes 10 and 11), produced two expected size bands at ~4.0 kb and ~7.4 kb (refer to Figure III-1 and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-6, lanes 2 and 6) or *Hpa* I/*Kpn* I (Figure IV-6, lanes 4 and 8) and hybridized with probe 5, produced no detectable hybridization bands. These results indicate that MON 87708 contains no detectable T-DNA II elements covered by probe 5.

IV.B.3. Probe 6

Conventional control DNA digested with *Bsp1286* I/*Pvu* II (Figure IV-7, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-7, lanes 3 and 7) and hybridized with probe 6 (Figure III-1) showed no detectable hybridization bands, as expected for the negative control. PV-GMHT4355 previously digested with *Aat* II/*Nde* I and mixed with conventional control DNA predigested with *Hpa* I/*Kpn* I (Figure IV-6, lanes 10 and 11) produced one expected size band at ~7.4 kb (refer to Figure III-1, and Table IV-1). These results indicate that the probe is hybridizing to its target sequence.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-7, lanes 2 and 6) or *Hpa* I/*Kpn* I (Figure IV-7, lanes 4 and 8) and hybridized with probe 6 produced no detectable hybridization bands. These results indicated that MON 87708 contains no detectable T-DNA II elements covered by probe 6.

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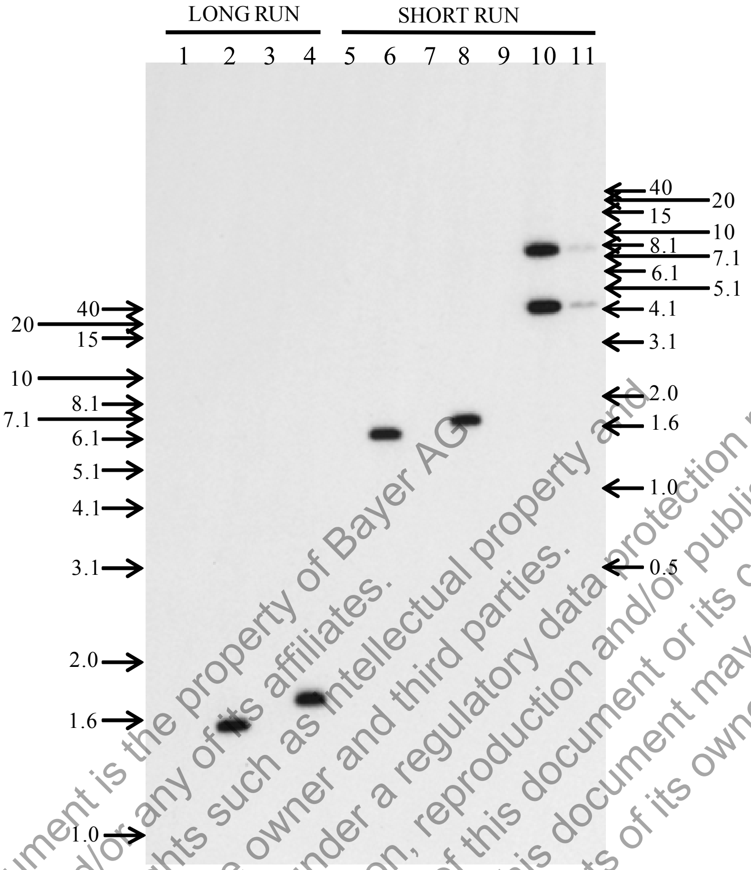

Figure IV-5. Southern Blot Analysis to Detect the Presence or Absence of T-DNA II Sequences in MON 87708: Probe 4

The blot was hybridized with a ^{32}P labeled T-DNA II probe that spans a portion of the T-DNA II sequence (Probe 4, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	**Description**
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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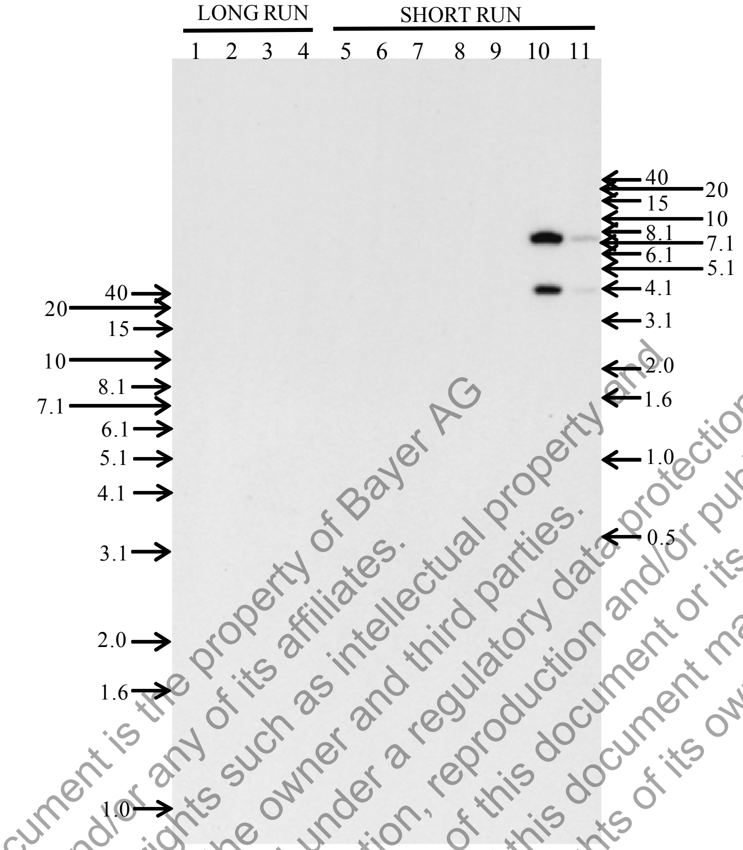

Figure IV-6. Southern Blot Analysis to Detect the Presence or Absence of T-DNA II Sequences in MON 87708: Probe 5

The blot was hybridized with a ^{32}P labeled T-DNA II probe that spans the coding region of the T-DNA II sequence (Probe 5, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	**Description**
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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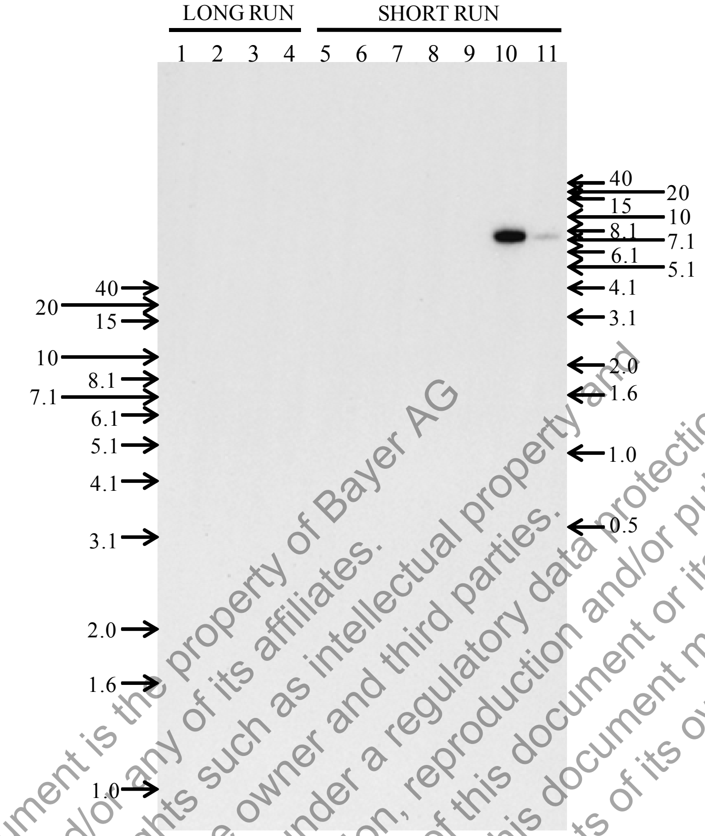

Figure IV-7. Southern Blot Analysis to Detect the Presence or Absence of T-DNA II Sequences in MON 87708: Probe 6

The blots were hybridized with a ^{32}P labeled T-DNA II probe that spans a portion of the T-DNA II sequence (Probe 6, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	**Description**
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/ *Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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IV.C. Southern Blot Analysis to Determine the Presence or Absence of PV-GMHT4355 Backbone Sequences in MON 87708

To determine the presence or absence of PV-GMHT4355 backbone sequences, MON 87708 and conventional control genomic DNA were digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I and Southern blots were hybridized with probes that span the plasmid vector backbone sequence (Figure III-1). As a positive control on the Southern blots, digested PV-GMHT4355 and probe templates generated from PV-GMHT4355 were used. Approximately 1 genome equivalent of PV-GMHT4355 digested with the restriction enzyme combination *Aat* II/*Nde* I was mixed with predigested conventional control DNA. As an additional positive control, approximately 0.1 and 1 genome equivalent of probe templates (Figure III-1, probes 1, 2, 3, and 7) generated from PV-GMHT4355 were mixed with predigested conventional control DNA. The blot was hybridized with probes 1, 2, 3, and 7 (Figure III-1). If backbone sequences are present in MON 87708, then probing with backbone probes should result in hybridizing bands. The results of this analysis are shown in Figure IV-8.

IV.C.1. Plasmid Vector Backbone Probes 1, 2, 3, and 7

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-8, lanes 1 and 5) or *Hpa* I/*Kpn* I (Figure IV-8, lanes 3 and 7) and hybridized simultaneously with the probes 1, 2, 3, and 7 (Figure III-1) spanning the entire backbone sequence of PV-GMHT4355 showed no detectable hybridization bands, as expected for the negative control. PV-GMHT4355, previously digested with *Aat* II/*Nde* I and mixed with conventional control DNA predigested with *Hpa* I/*Kpn* I (Figure IV-8, lane 10), produced two expected size bands at ~4.0 kb and ~7.4 kb (refer to Figure III-1 and Table IV-1). In addition, there are two faint hybridization bands at ~4.5 kb and ~11 kb (Figure IV-8, lane 10). The ~4.5 kb band was likely due to an artifact that occurred during the electrophoresis, and the ~11 kb band was likely due to undigested plasmid DNA or an artifact that occurred during the electrophoresis. Since these faint bands appeared only in the plasmid spike and the expected bands were observed, they have no negative impact on the conclusions made from this blot. Probe template spikes of probes 1, 2, 3, and 7 (Figure III-1) generated from PV-GMHT4355 mixed with conventional control DNA predigested with *Hpa* I/*Kpn* I (Figure IV-8, lanes 11 and 12) produced the expected size bands at ~0.2 kb, ~0.9 kb, ~1.5 kb, and ~1.8 kb, respectively. The 0.1 genome equivalent copy of the expected ~0.2 kb band was not observed on the exposure of the Southern blot that is reported in Figure IV-8, lane 12; however, the band was observed on the same blot with a longer exposure. These results indicate that the probes are hybridizing to their target sequences.

MON 87708 DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-8, lanes 2 and 6) or *Hpa* I/*Kpn* I (Figure IV-8, lanes 4 and 8) and hybridized simultaneously with probes 1, 2, 3, and 7 produced no detectable bands. The data indicate MON 87708 contains no detectable backbone sequences from PV-GMHT4355.

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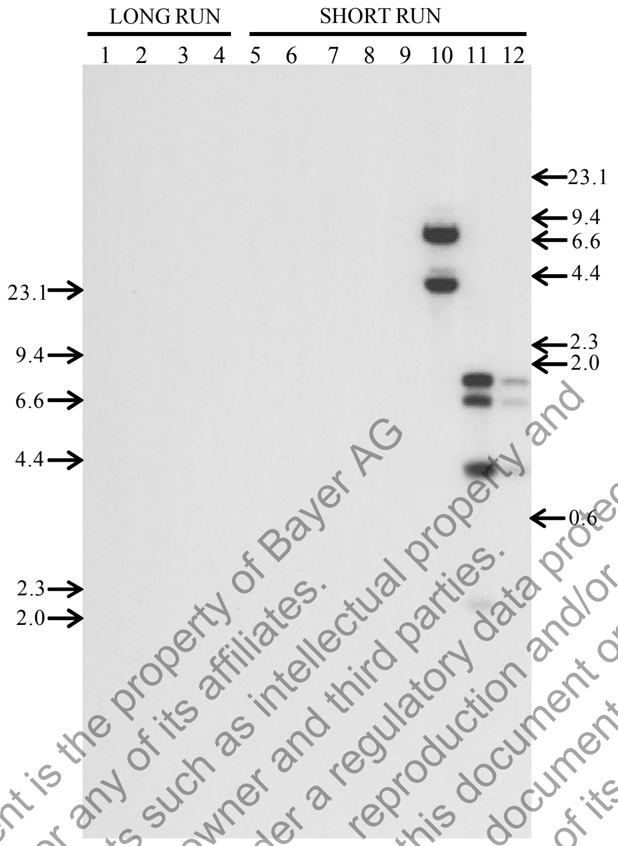

Figure IV-8. Southern Blot Analysis to Determine the Presence or Absence of PV-GMHT4355 Backbone Sequences in MON 87708: Probes 1, 2, 3, and 7

The blot was hybridized simultaneously with four ^{32}P labeled backbone probes (Probes 1, 2, 3, and 7, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	**Description**
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	MON 87708 (*Bsp1286* I/*Pvu* II)
3.	Conventional control (*Hpa* I/*Kpn* I)
4.	MON 87708 (*Hpa* I/*Kpn* I)
5.	Conventional control (*Bsp1286* I/*Pvu* II)
6.	MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Conventional control (*Hpa* I/*Kpn* I)
8.	MON 87708 (*Hpa* I/*Kpn* I)
9.	Blank
10.	Conventional control (*Hpa* I/*Kpn* I) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
11.	Conventional control (*Hpa* I/*Kpn* I) spiked with probe templates (~1 genome equivalent)
12.	Conventional control (*Hpa* I/*Kpn* I) spiked with probe templates (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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IV.D. Organization and Sequence of the Insert and Adjacent DNA in MON 87708

The organization of the elements within the T-DNA I was confirmed by DNA sequence analyses. PCR primers were designed with the intent to amplify two overlapping regions of the DNA that span the entire length of T-DNA I (Figure B-1, Appendix B). The amplified DNA segments were subjected to DNA sequencing analyses. The T-DNA I in MON 87708 is 3003 bp and matches the sequence of plasmid vector PV-GMHT4355, as described in Tables III-1 and IV-2.

IV.E. PCR and DNA Sequence Analyses to Examine the MON 87708 Insertion Site

PCR and sequence analyses were performed on genomic DNA extracted from MON 87708 and conventional control to examine the insertion sites. The PCR was performed with one primer specific to the genomic DNA sequence flanking the 5′ end of T-DNA I paired with a second primer specific to the genomic DNA sequence flanking the 3′ end of T-DNA I (Figure B-2, Appendix B). A sequence comparison between the PCR product generated from the conventional control and the sequence generated from the 5′ and 3′ flanking sequences of T-DNA I in MON 87708 indicates there was an 899 bp deletion and a 128 bp insertion just 5′ of T-DNA I, and a 35 bp insertion just 3′ of T-DNA I. These molecular rearrangements presumably resulted from double-stranded break repair mechanisms in the plant during the *Agrobacterium*-mediated transformation process (Salomon and Puchta, 1998).

IV.F. Southern Blot Analysis to Examine Insert Stability in Multiple Generations of MON 87708

In order to demonstrate the stability of the T-DNA I insert present in MON 87708 through multiple generations, Southern blot analysis was performed using DNA obtained from five breeding generations of MON 87708. For reference, the breeding history of MON 87708 is presented in Figure IV-9. The specific generations tested are indicated in the legend of Figure IV-10. The R_3 generation was used for the molecular characterization analyses shown in Figures IV-2 through IV-8. To analyze stability, four additional generations were evaluated by Southern blot analysis and compared to the fully characterized R_3 generation. Genomic DNA, isolated from each of the selected generations of MON 87708 and the conventional control, was digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-1) and hybridized with probe 9 (Figure III-1). Probe 9 will detect both border fragments generated by the *Bsp1286* I/*Pvu* II digestion. Any instability associated with the T-DNA I insert would be detected as novel bands within the fingerprint on the Southern blot. The Southern blot has the same positive hybridization controls as described in Section IV.A. The results are shown in Figure IV-10.

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IV.F.1. Probe 9

Conventional control DNA digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II produced no hybridization signals (Figure IV-10, lane 1) as expected for the negative control. PV-GMHT4355, digested with the restriction enzyme combination *Aat* II/*Nde* I and mixed with conventional control DNA predigested with the restriction enzyme combination *Bsp1286* I/*Pvu* II (Figure IV-10, lanes 8 and 9), produced the expected size band at ~7.4 kb (refer to Figure III-1 and Table IV-1). Additionally, there were two very faint hybridization bands in the ~1 genome equivalent plasmid vector PV-GMHT4355 spike at ~4.3 kb and ~6.5 kb observed in a longer exposure of the Southern blot (data not shown). These bands were likely due to an artifact that occurred during the electrophoresis. Since these faint bands appeared only in the plasmid vector spike and the expected ~7.4 kb band was observed, they do not have any negative impact on the conclusions from this Southern blot analysis. These results indicate that the probe is hybridizing to its target sequence.

Digestion of MON 87708 genomic DNA from multiple generations with the restriction enzyme combination *Bsp1286* I/*Pvu* II and hybridized with probe 9 (Figure III-1) produced two bands at ~1.5 kb and ~2.6 kb (Figure IV-10, lanes 2-6). The ~1.5 kb band is the expected size for the border segment containing the 3′ end of T-DNA I along with the adjacent genomic DNA flanking the 3′ end of T-DNA I (Figure IV-1). The ~2.6 kb band is the expected size for the border segment containing the 5′ end of T-DNA I along with the adjacent genomic DNA flanking the 5′ end of T-DNA I (Figure IV-1). The fingerprint of the Southern blot signals from multiple generations, R_2, R_4, R_5, and R_6 (Figure IV-10, lanes 2, 4, 5, and 6), of MON 87708 is consistent with the fully characterized generation R_3 (Figure IV-3, lanes 2 and 6; Figure IV-10, lane 3). No unexpected bands were detected, indicating that MON 87708 contains one copy of T-DNA I that is stably maintained across multiple generations.

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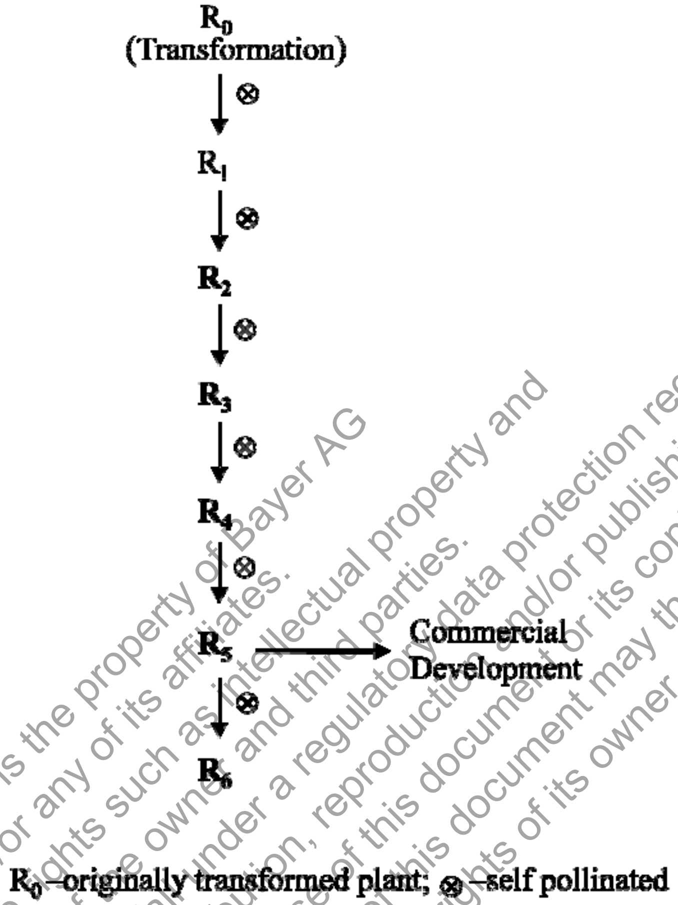
R0
(Transformation)
⊗
R1
⊗
R2
⊗
R3
⊗
R4
⊗
R5
Commercial Development
⊗
R6
R0 –originally transformed plant; ⊗ –self pollinated

Figure IV-9. Breeding History of MON 87708
The R_3 generation was used for the molecular analyses reported in Figures IV-2 through IV-8 and is referred to as MON 87708 in all Southern blot figures. The R_5 generation was used for development of all commercial products. MON 87708 from generations R_2, R_3, R_4, R_5, and R_6 (bolded in the breeding tree) were used for analyzing the stability of T-DNA I in MON 87708 across generations (Figure IV-10).

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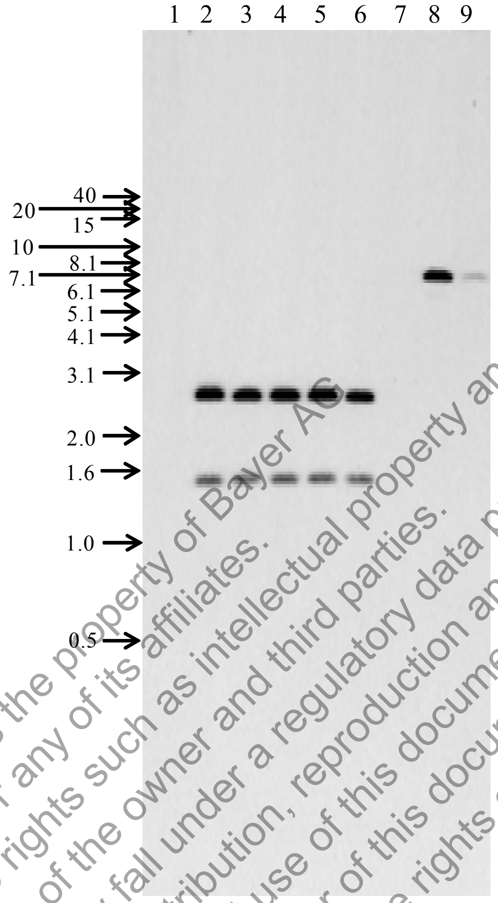

Figure IV-10. Southern Blot Analysis to Examine Insert Stability in Multiple Generations of MON 87708: Probe 9

The blot was hybridized with a ^{32}P labeled T-DNA I probe that spans the coding region of the T-DNA I (Probe 9, Figure III-1). Each lane contains approximately 10 µg of digested genomic DNA isolated from leaf tissue. Lane designations are as follows:

Lane	Description
1.	Conventional control (*Bsp1286* I/*Pvu* II)
2.	R_2 generation of MON 87708 (*Bsp1286* I/*Pvu* II)
3.	R_3 generation of MON 87708 (*Bsp1286* I/*Pvu* II)
4.	R_4 generation of MON 87708 (*Bsp1286* I/*Pvu* II)
5.	R_5 generation of MON 87708 (*Bsp1286* I/*Pvu* II)
6.	R_6 generation of MON 87708 (*Bsp1286* I/*Pvu* II)
7.	Blank
8.	Conventional control (*Bsp1286* I and *Pvu* II) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~1 genome equivalent)
9.	Conventional control (*Bsp1286* I and *Pvu* II) spiked with PV-GMHT4355 (*Aat* II/*Nde* I) (~0.1 genome equivalent)

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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IV.G. Inheritance of the Genetic Insert in MON 87708

During development of MON 87708, segregation data were generated to assess the heritability and stability of the T-DNA I present in MON 87708. Chi-square analysis was performed over several generations to confirm the segregation and stability of T-DNA I in MON 87708. The Chi-square analysis is based on testing the observed segregation ratio to the expected segregation ratio according to Mendelian principles.

The MON 87708 breeding path, from which segregation data were generated, is described in Figure IV-11. The transformed R_0 plant was self-pollinated to produce R_1 seed. An individual plant (#2, designated as MON 87708), that was homozygous for a single copy of the *dmo* expression cassette, was identified from the R_1 segregating population via Invader® and Southern blot analysis. Invader is a non-PCR based assay that can be used to accurately quantify transgene copy number in plant genomes (Gupta et al., 2008).

The selected R_1 MON 87708 plant was self-pollinated to give rise to a population of R_2 plants that were repeatedly self-pollinated through the R_4 generation. At each generation, the fixed homozygous plants were tested for the expected segregation pattern of 1:0 (positive:negative) for the *dmo* expression cassette using the Invader analysis, Southern blot analysis, and/or PCR.

At the R_4 generation, homozygous MON 87708 plants were bred via traditional breeding with a soybean variety that did not contain the *dmo* expression cassette to produce F_1 hemizygous seed. The resulting F_1 plants were then self-pollinated to produce F_2 seed. The F_2 plants were tested for the presence of the *dmo* expression cassette by Invader analysis, and hemizygous F_2 plants were selected and self-pollinated to produce F_3 seed. This process was repeated through the F_4 generation. The heritability and stability of the *dmo* expression cassette in MON 87708 was assessed in the F_2, F_3, and F_4 generations. A total of 2413 out of 3223 plants were positive for the presence of the *dmo* expression cassette in the F_2 generation; however, the zygosity of 200 of those 2413 plants could not be determined from the assay. Exclusion of these *dmo*-positive plants from the analysis likely would have skewed the distribution of homozygous positive: hemizygous positive:homozygous negative plants. Therefore, the segregation assessment in the F_2 generation was based on the presence or absence of the *dmo* expression cassette which was expected to segregate at a 3:1 (positive:negative) ratio according to Mendelian inheritance principles. Subsequently, assessment of segregation in the F_3 and F_4 generations was based on zygosity, and the *dmo* expression cassette was predicted to segregate at a 1:2:1 (homozygous positive:hemizygous positive :homozygous negative) ratio according to Mendelian inheritance principles.

A Chi-square (χ^2) analysis was used to compare the observed segregation ratios to the expected ratios according to Mendelian inheritance principles. The χ^2 was calculated as:

$$\chi^2 = \sum [(\,|\,o - e\,|\,)2 / e]$$

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where o = observed frequency of the phenotype and e = expected frequency of the phenotype. The level of statistical significance was predetermined to be 5%.

The results of the χ^2 analysis of the segregating progeny of MON 87708 are presented in Table IV-3. The χ^2 value for the F_2, F_3, and F_4 generations indicated no significant difference between the observed and expected segregation ratios. These results support the conclusion that the *dmo* expression cassette in MON 87708 resides at a single locus within the soybean genome and is inherited according to expected Mendelian inheritance principles. These results are also consistent with the molecular characterization data that indicate MON 87708 contains a single, intact copy of the *dmo* expression cassette that was inserted into the soybean genome at a single locus.

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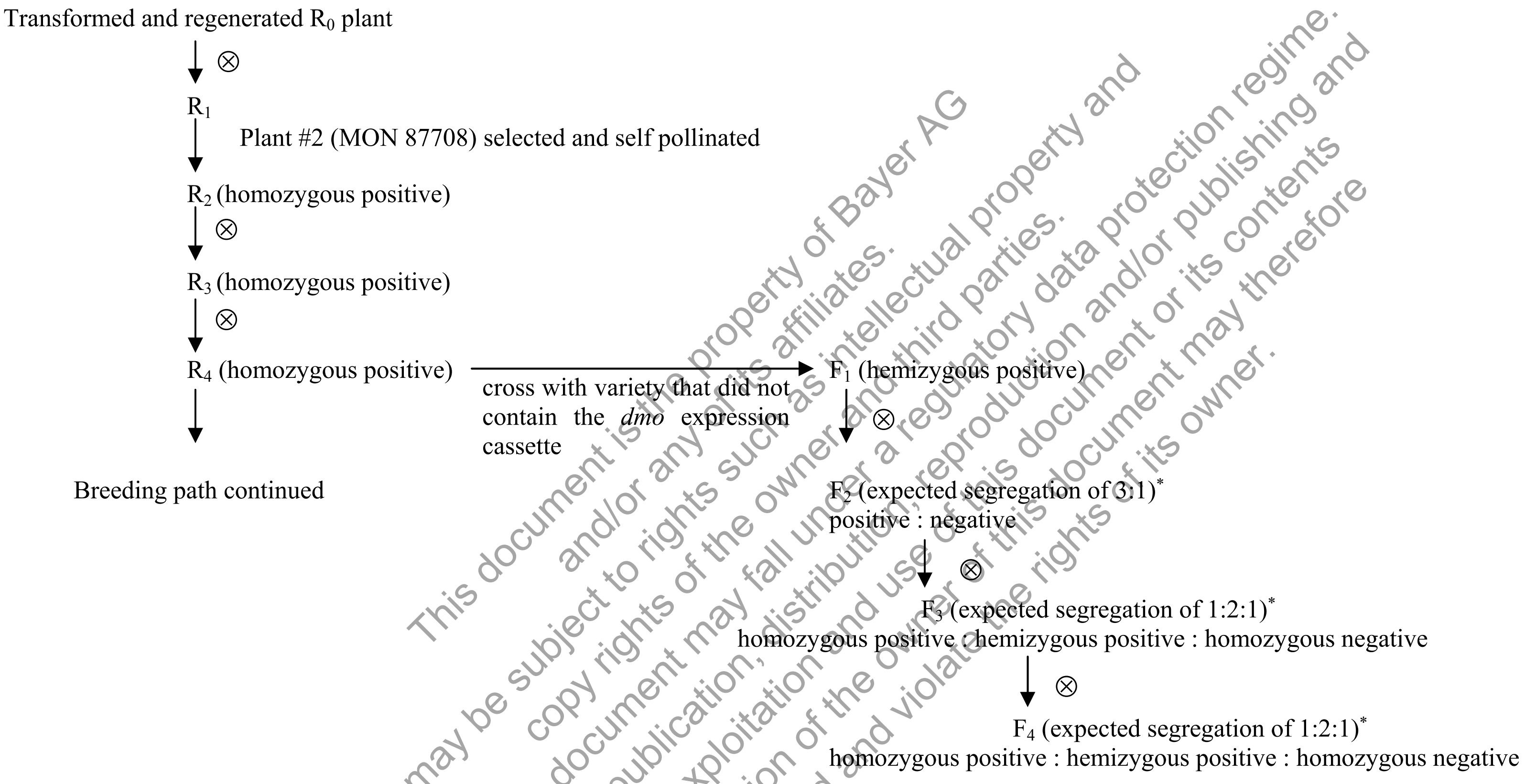
Transformed and regenerated R_0 plant
⊗
R_1
Plant #2 (MON 87708) selected and self pollinated
R_2 (homozygous positive)
⊗
R_3 (homozygous positive)
⊗
R_4 (homozygous positive)
Breeding path continued
cross with variety that did not contain the *dmo* expression cassette
F_1 (hemizygous positive)
⊗
F_2 (expected segregation of 3:1)*
positive : negative
⊗
F_3 (expected segregation of 1:2:1)*
homozygous positive : hemizygous positive : homozygous negative
⊗
F_4 (expected segregation of 1:2:1)*
homozygous positive : hemizygous positive : homozygous negative

⊗ = Self pollinated

Figure IV-11. Breeding Path for Generating Segregation Data for MON 87708

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[*] Chi-square analysis conducted on segregation data from the F_2, F_3, and F_4 generations.

Note: Hemizygous positive plants in the F_1, F_2, F_3, and F_4 generations were selected and self-pollinated to produce seed of the subsequent generation.

Table IV-3. Segregation of the *dmo* Expression Cassette During the Development of MON 87708

				3:1 Segregation[3]			
Generation[1]	Total Plants Tested[2]	Observed # Plants Positive	Observed # Plants Negative	Expected # Plants Positive	Expected # Plants Negative	χ^2	Probability
F_2	3223	2413	810	2417.25	805.75	0.03	0.863

					1:2:1 Segregation				
Generation[1]	Total Plants Tested[2]	Observed # Plants Homozygous Positive	Observed # Plants Hemizygous Positive	Observed # Plants Homozygous Negative	Expected # Plants Homozygous Positive	Expected # Plants Hemizygous Positive	Expected # Plants Homozygous Negative	χ^2	Probability
F_3	118	29	52	37	29.5	59	29.5	2.7	0.2534
F_4	343	83	171	89	85.75	171.5	85.75	0.2	0.8991

---

[1] F_2, F_3, and F_4 progeny were from self-pollinated F_1, F_2, and F_3 plants hemizygous positive for the *dmo* expression cassette, respectively.

[2] Plants were tested for the presence of the *dmo* expression cassette by Invader analysis.

[3] Assessment of segregation in the F_2 generation was based on the presence or absence of the *dmo* expression cassette due to an unacceptable number of *dmo*-positive plants for which zygosity could not be determined from the assay.

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IV.H. Genetic Modification Characterization Conclusion

Molecular characterization of MON 87708 by Southern blot analyses demonstrated that a single copy of the T-DNA I sequences from the plasmid vector PV-GMHT4355 was integrated into the soybean genome at a single locus. There were no additional genetic elements from the T-DNA II or backbone sequences of the plasmid vector PV-GMHT4355 detected, linked or unlinked to the intact T-DNA I present in MON 87708.

The PCR and DNA sequence analyses performed on MON 87708, which confirmed the organization of the elements within T-DNA I, demonstrated the 5′ and 3′ insert-to-plant junctions and determined the complete DNA sequence of T-DNA I and adjacent DNA sequence flanking the insert in MON 87708. Analysis of the T-DNA I insertion site indicates that there was an 899 bp deletion of genomic DNA at the insert-to-plant DNA junction. Additionally, a 128 bp insertion was identified in the 5′ adjacent flanking sequence of MON 87708 and a 35 bp insertion was identified in the 3′ adjacent flanking sequence of MON 87708.

Generational stability analysis by Southern blot demonstrated that MON 87708 has been maintained through five breeding generations, thereby confirming the stability of T-DNA I in MON 87708. Results from segregation analyses show heritability and stability of the insert occurred as expected across multiple generations, which corroborates the molecular insert stability analysis and establishes the genetic behavior of the T-DNA I in MON 87708 at a single chromosomal locus.

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V. CHARACTERIZATION AND SAFETY ASSESSMENT OF THE MON 87708 DMO

Characterization of the introduced protein in a biotechnology-derived crop product is important to establishing its food, feed, and environmental safety. As described in Section IV, MON 87708 contains a *dmo* expression cassette that upon translation results in two forms of the DMO protein; referred to as DMO and DMO+27 (Section V.A). The active form of these proteins, necessary to confer dicamba tolerance, is a trimer comprised of three DMO monomers (Chakraborty et al., 2005). In MON 87708, the trimer can be comprised of DMO, DMO+27, or a combination of both. Therefore, this document will refer to both forms of the protein and all forms of the trimer as MON 87708 DMO.

This section summarizes: 1) the functionality of DMO; 2) the characterization of MON 87708 DMO; 3) the levels of MON 87708 DMO in plant tissues; 4) assessment of the potential allergenicity of MON 87708 DMO and 5) the food, feed, and environmental safety assessment of MON 87708 DMO. The data support a conclusion that MON 87708 is safe for the environment and human or animal consumption based on several lines of evidence, all of which are summarized below.

V.A. Function of DMO and MON 87708 DMO

DMO was initially purified from *Stenotrophomonas maltophilia (S. maltophilia)* strain DI-6, isolated from soil at a dicamba manufacturing plant (Krueger et al., 1989). DMO is an enzyme that catalyzes the demethylation of dicamba to the non-herbicidal compound DCSA and formaldehyde (Chakraborty et al., 2005). DMO is a Rieske-type non-heme iron oxygenase, that is part of a three component system comprised of a reductase, a ferredoxin, and a terminal oxygenase, in this case the DMO. These three enzymes work together in a redox system similar to many other oxygenases to transport electrons from nicotinamide adenine dinucleotide (NADH) to oxygen and catalyze the demethylation (Behrens et al., 2007) as presented in Figure V-1.

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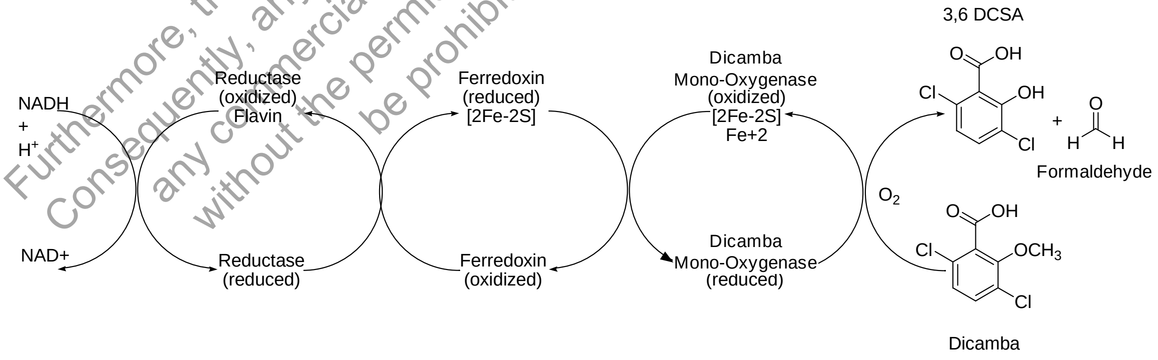

Figure V-1. Three Components of the DMO Oxygenase System

The crystal structure of a DMO has been solved (D'Ordine et al., 2009; Dumitru et al., 2009) and shows that the DMO monomers contain a Rieske [2Fe-2S] cluster domain and a non-heme iron center domain typical of all Rieske-type mono-oxygenases (Ferraro et al., 2005). To catalyze the demethylation of dicamba, electrons transferred from NADH are shuttled through an endogenous reductase and ferredoxin to the terminal DMO. The electrons are received by the Rieske [2Fe-2S] cluster on one DMO monomer and transferred to the non-heme iron center at the catalytic site of an adjacent monomer (D'Ordine et al., 2009; Dumitru et al., 2009), where it reductively activates oxygen to catalyze the final demethylation of dicamba. As a result of the reaction, 3.6 dichlorosalicylic acid (DCSA) and formaldehyde are formed. DCSA is a known soybean, soil, and livestock metabolite whose safety has been evaluated by the EPA. Formaldehyde is found naturally in many plants at levels up to several hundred ppm (Adrian-Romero et al, 1999). An assessment of the safety and potential effects of the DMO reaction products is provided in Section IX.B.3.6.

V.A.1. Formation of MON 87708 DMO

DMO is targeted to chloroplasts for co-localization with the endogenous reductase and ferredoxin enzymes that supply electrons for the DMO demethylation reaction as described by Behrens et al. (2007). The MON 87708 DMO precursor protein contains 84 additional amino acids corresponding to a 57 amino acid Chloroplast Transit Peptide (CTP) from pea and 24 amino acids from the N-terminal coding region of the pea Rubisco small (RbcS) subunit to target the protein to the chloroplast (Comai et al., 1988), and three amino acids from an intervening sequence used for cloning purposes (Table III-I). It was anticipated that during translocation of the DMO precursor into chloroplasts the introduced 84 amino acids would be fully cleaved resulting in the predicted N-terminus of the DMO protein. However, analysis of mature seed extracts by western blot demonstrated the presence of two immunoreactive bands (Figure C-2, Appendix C). Analysis of these two bands determined that the lower molecular weight band corresponded to the full-length DMO protein (referred to as DMO). DMO has an apparent molecular weight of 39.8 kDa and is a single polypeptide chain of 339 amino acids. The higher molecular weight band of approximately 42 kDa corresponded to the full-length DMO protein plus 27 amino acids originating from the pea Rubisco small subunit and intervening sequence on its N-terminus (referred to as DMO+27; 367 amino acid polypeptide). Both forms of the DMO protein were characterized (Appendix C).

As described previously the active form of DMO is a trimer (Chakraborty et al., 2005; Dumitru et al., 2009). For MON 87708 DMO to be functionally active and confer dicamba tolerance to MON 87708, a trimeric structure is required. This trimer contains either form of DMO or a mixture of both, and its activity was confirmed during characterization (Section V.B. and Appendix C).

V.A.2. Specificity of MON 87708 DMO

DMO has high specificity for its substrate dicamba (D'Ordine et al., 2009; Dumitru et al., 2009). The specificity of DMO for dicamba is likely due to the specific interactions that occur in the catalytic site between the dicamba substrate and DMO. Dicamba interacts with amino acids in the active site of DMO through both the carboxylate moiety and the

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chlorine atoms of dicamba, which are primarily involved in orienting the substrate in the catalytic pocket. These chlorine atoms are required for catalysis (D'Ordine et al., 2009; Dumitru et al., 2009).

The possibility that MON 87708 DMO can metabolize plant endogenous substrates was tested in *in vitro* experiments using an *Escherichia coli* (*E. coli*)-produced DMO. The *E. coli*-produced DMO is similar in sequence and function to MON 87708 DMO, therefore it is appropriate to extend specificity data generated with the *E. coli*-produced DMO to MON 87708 DMO (Appendix C.2.). A set of potential substrates was selected based on structural similarity to dicamba and abundance in soybean (Janas et al., 2000), including o-anisic acid (2-methoxybenzoic acid), vanillic acid (4-hydroxy-3-methoxybenzoic acid), syringic acid (3,5-dimethoxy-4-hydroxybenzoic acid), ferulic acid [3-(4-hydroxy-3-methoxy-phenyl)prop-2-enoic acid] and sinapic acid [3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enoic acid] (Figure V-2). The disappearance of potential substrates and the formation of potential oxidation products were monitored using LC-UV and LC-MS (Appendix C). None of the tested substrates was metabolized by the *E.coli*-produced DMO *in vitro.* Therefore, DMO, though structurally similar to other Rieske mono-oxygenases, is specific for dicamba (see Section V.E.3 for additional details).

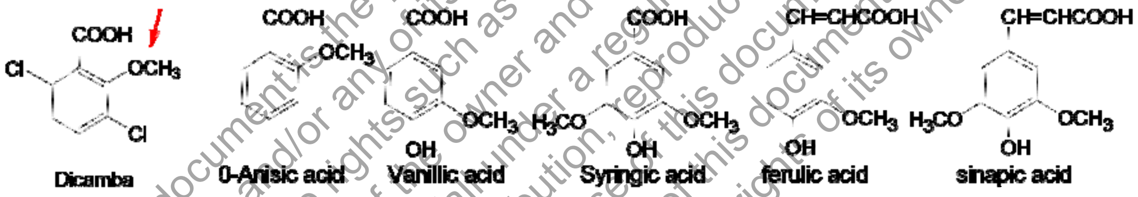

Figure V-2. Dicamba and Set of Potential Endogenous Substrates Tested in *in vitro* Experiments with DMO
The arrow indicates methyl group removed by DMO.

The possibility that MON 87708 DMO can metabolize exogenous substrates was tested in *in vivo* experiments. In addition to dicamba, a total of 19 herbicides representing eight families with distinct modes-of-action, some of which are approved for use in soybean, were tested with MON 87708 and the near isogenic conventional soybean control A3525 (Table V-1). Soybean naturally has varying levels of tolerance to different herbicides. For example, soybean is tolerant to in-crop postemergence applications of alachlor, but not atrazine. Each herbicide was applied at two spray rates, representative of potential commercial rates needed to control broadleaf weeds, at the V2-V3 soybean growth stage and then scored a visual rating based on the amount of injury observed on the plants. Across nearly all of the herbicides tested, MON 87708 and the conventional control were similar in their level of tolerance, indicating that these herbicides do not serve as a substrate for MON 87708 DMO. However, MON 87708 did show slightly more tolerance compared to the conventional control when treated with the three phenoxycarboxylic acid (phenoxy) synthetic auxin herbicides: 2,4-D (2,4-dichlorophenoxy acetic acid), MCPA (2-methyl-4-chlorophenoxy acetic acid) and

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2,4-DB (2,4-dichlorophenoxy butanoic acid). Chloramben and TBA are no longer available in the U.S and were excluded from this testing. See Appendix C, Section C.2.

As 2,4-D is the most structurally similar to dicamba of the three phenoxy auxin herbicides (2,4-D, 2,4-DB, and MCPA), it was selected as a representative for further *in vitro* experimentation. Subsequent experiments were performed to evaluate whether 2,4-D can be metabolized by *E. coli*-produced DMO. The presumptive product of the oxidative reaction between 2,4-D and DMO is 2,4-dichlorophenol (2,4-DCP), formed from the dealkylation of 2,4-D. The potential disappearance of 2,4-D and formation of 2,4-DCP were monitored using LC-UV and LC-MS (Appendix C, Section C.2). Neither the formation of 2,4-DCP nor any measurable decrease in 2,4-D were detected in the *in vitro* experiment. These results indicate that 2,4-D cannot be metabolized by *E. coli*-produced DMO, and demonstrate that DMO is specific to dicamba. The tolerance of MON 87708 to other herbicides at anticipated commercial application rates is no different than the conventional soybean, except for the phenoxy auxin herbicides where MON 87708 showed limited, but not commercially acceptable, tolerance when treated.

Table V-1. Herbicides Applied to MON 87708 and Conventional Control

Herbicide Active Ingredient	Herbicide Chemical Family (MOA)[1]
Dicamba	Benzoic acid (Synthetic Auxin)
2,4-D	Phenoxycarboxylic acid (Synthetic Auxin)
2,4-DB	Phenoxycarboxylic acid (Synthetic Auxin)
MCPA	Phenoxycarboxylic acid (Synthetic Auxin)
Triclopyr	Pyridinecarboxylic acid (Synthetic Auxin)
Clopyralid	Pyridinecarboxylic acid (Synthetic Auxin)
Picloram	Pyridinecarboxylic acid (Synthetic Auxin)
Alachlor	Chloroacetamide (Inhibition of VLCFAs)
Acetochlor	Chloroacetamide (Inhibition of VLCFAs)
Atrazine	Triazine (Inhibition of Photosynthesis at Photosytem II)
Linuron	Ureas (Inhibition of Photosynthesis at Photosytem II)
Oxyfluorofen	Diphenylether(Inhibition of PPO)
Lactofen	Diphenylether (Inhibition of PPO)
Chlorimuron	Sulfonylurea (Inhibition of ALS)
Chlorsulfuron	Sulfonylurea (Inhibition of ALS)
Halosulfuron	Sulfonylurea (Inhibition of ALS)
Imazapyr	Imidazolinone (Inhibition of ALS)
Trifluralin	Dinitroaniline (Microtubule Assembly Inhibition)
Paraquat	Bipyridilium (Photosystem I electron diversion)
Glyphosate	Glycine (Inhibition of EPSP synthase)

[1] HRAC (2009)

V.B. Characterization of MON 87708 DMO

The safety assessment of crops derived through biotechnology includes characterization of the functional and physicochemical properties, and confirmation of the safety of the introduced protein. As stated previously, both forms of the protein and all forms of the

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trimer are referred to as the MON 87708 DMO. MON 87708 DMO was purified in sufficient quantities directly from the seed of MON 87708 and used in subsequent safety assessment studies. Typically protein safety studies are conducted on proteins produced in heterologous expression systems, such as *E. coli*. Since the MON 87708 DMO used in the subsequent safety studies was purified directly from MON 87708 DMO, equivalence evaluations between plant-produced and bacterial-produced MON 87708 DMO was not necessary. The physicochemical characteristics and functional activity of the MON 87708 DMO were determined by a panel of analytical techniques, including: 1) western blot analysis to establish identity and immunoreactivity of MON 87708 DMO using an anti-DMO antibody, 2) N-terminal sequence analysis, 3) matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) to generate a tryptic peptide map of the MON 87708 DMO, 4) sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) to establish the apparent molecular weight of MON 87708 DMO, 5) glycosylation status of MON 87708 DMO, and 6) MON 87708 DMO activity analysis to demonstrate functional activity. The details of the materials, methods, and results are described in Appendix C, while the conclusions of the MON 87708 DMO characterization are summarized below.

The identities of both forms of the DMO protein produced in MON 87708 that constitute MON 87708 DMO were confirmed by western blot analysis by probing with an anti-DMO antibody, N-terminal sequencing, and MALDI-TOF MS analysis of peptides produced after trypsin digestion. The antibody specifically detected DMO and DMO+27 on a western blot. The N-terminal sequence of the first 15 amino acid residues of both DMO and DMO+27 was identical to the predicted amino acid sequence, with the exception of the N-terminal methionine residue. MALDI-TOF MS analyses of DMO and DMO+27 yielded peptide masses consistent with their expected sequence. The apparent molecular weights of DMO and DMO+27 were 39.8 and 42.0 kDa, respectively and neither were glycosylated. The MON 87708 DMO activity was determined by measuring the production of DCSA using dicamba as the substrate, resulting in a specific activity of 62.21 nmoles DCSA/min/mg of MON 87708 DMO. Taken together, these data provide a detailed characterization of the MON 87708 DMO isolated from the seed of MON 87708.

V.C. Expression Levels of MON 87708 DMO

The levels of MON 87708 DMO in various tissues of MON 87708 that are relevant to the risk assessment were determined by a validated ELISA. Tissues of MON 87708 and the near isogenic conventional soybean control A3525 were collected during the 2008 growing season from five field sites in the U.S.: Jefferson County, Iowa; Stark County, Illinois; Clinton County, Illinois; Parke County, Indiana; and Berks County, Pennsylvania. These field sites were representative of soybean producing regions suitable for commercial production. At each site, three replicated plots containing MON 87708, as well as the conventional control, were planted using a randomized complete block field design. Over-season leaf (OSL 1-4), root, forage, and seed tissues were collected from each replicated plot at all field sites (except for the conventional control from Berks County, Pennsylvania where only two replicates were collected). A description of tissues collected is provided in Table V-2.

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Table V-2. Tissues Collected and Analyzed for MON 87708 DMO

Tissue	Soybean Development Stage[1]	Days After Planting
OSL-1	V3-V4	21-30
OSL-2	V5-V8	31-42
OSL-3	R2-V12	43-58
OSL-4	R5-V16	55-78
Root	R6	70-91
Forage	R6	70-91
Seed	R8	109-147

[1] Soybean plant growth stages described in Soybean Growth and Development (ISU, 2004).

The levels of MON 87708 DMO were determined in all seven tissue types as described in Table V-3. The ELISA assay detected all forms of MON 87708 DMO and therefore the levels represent the total of MON 87708 DMO. The results obtained from the ELISA analysis are summarized in Table V-3 and the details of the materials and methods are described in Appendix D. In summary, expression analysis of the samples from the 2008 U.S. field trial showed that MON 87708 DMO was detected in all tissue types across all five sites ranging from 3.9 – 180 µg/g dry weight (dwt). The mean levels of the MON 87708 DMO across the five sites were highest in leaf (ranging from OSL-1 at 17 µg/g dwt, to OSL-4 at 69 µg/g dwt), followed by forage (53 µg/g dwt), seed (47 µg/g dwt), and root (6.1 µg/g dwt). As expected for the conventional control, the ELISA values for MON 87708 DMO were less than the limit of quantitation (LOQ) of the assay in all tissue types.

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Table V-3. Summary of the Levels of MON 87708 DMO in Leaf, Root, Forage, and Seed from MON 87708 Grown in 2008 U.S. Field Trials

Tissue Type	MON 87708 DMO[1] Mean (SD)[2] (µg/g fwt)[3]	Range[4] (µg/g fwt)	MON 87708 DMO Mean (SD) (µg/g dwt)[5]	Range (µg/g dwt)	LOQ/LOD (µg/g fwt)[6,7]
OSL-1	3.1 (1.9)	0.87 – 6.8	17 (7.7)	6.2 – 29	0.63/0.20
OSL-2	5.2 (2.6)	1.4 – 9.8	31 (13)	12 – 54	0.63/0.20
OSL-3	6.0 (2.2)	3.5 – 11	44 (14)	25 – 71	0.63/0.20
OSL-4	16 (12)	4.6 – 43	69 (46)	23 – 180	0.63/0.20
Root	1.9 (0.73)	1.2 – 3.6	6.1 (2.1)	3.9 – 11	0.031/0.015
Forage	12 (2.5)	7.0 – 17	53 (18)	25 – 84	0.63/0.10
Seed	43 (7.7)	31 – 55	47 (8.7)	34 – 59	1.3/0.21

[1] Represents total for MON 87708 DMO.

[2] The mean and standard deviation (SD) were calculated (n=15). The “n” values for the calculated mean and standard deviations represent the number of samples figured into the calculation.

[3] Protein levels are expressed as microgram (µg) of protein per gram (g) of tissue on a fresh weight (fwt) basis.

[4] Minimum and maximum values were determined for each tissue type.

[5] Protein levels are expressed as µg/g dwt. The dry weight values were calculated by dividing the µg/g fwt by the dry weight conversion factors obtained from moisture analysis data.

[6] The limit of quantitation (LOQ) was calculated based on the lowest DMO standard concentration. The “ng/ml” value was converted to “µg/g fwt” using the respective dilution factor and tissue-to-buffer ratio.

[7] The limit of detection (LOD) was calculated as the mean value plus three SD using the data generated with conventional control sample extracts for each tissue type. The LOD value in “ng/ml” was converted to “µg/g fwt” using the respective dilution factor and tissue-to-buffer ratio.

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V.D. Assessment of Potential Allergenicity of MON 87708 DMO

The allergenic potential of an introduced protein is assessed by comparing the biochemical characteristics of the introduced protein to biochemical characteristics of known allergens (Codex Alimentarius, 2003). A protein is not likely to be associated with allergenicity if: 1) the protein is from a non-allergenic source, 2) the protein represents a very small portion of the total plant protein, 3) the protein does not share structural similarities to known allergens based on the amino acid sequence, and 4) the protein is rapidly digested in mammalian gastrointestinal systems. MON 87708 DMO, as defined above, refers to all forms of the protein and the resulting trimer, has been assessed for its potential allergenicity according to these safety assessment guidelines.

> 1) MON 87708 DMO originates from *S. maltophilia*, an organism that has not been reported to be a source of known allergens.
>
> 2) MON 87708 DMO represents no more than 0.01% of the total protein in the seed of MON 87708.
>
> 3) Bioinformatics analyses demonstrated that the DMO+27 form of MON 87708 DMO, that also contains the DMO sequence, does not share amino acid sequence similarities with known allergens and, therefore, is highly unlikely for DMO or DMO+27 to contain immunologically cross-reactive allergenic epitopes.
>
> 4) *In vitro* digestive fate experiments conducted with the MON 87708 DMO demonstrate that the proteins are rapidly digested in simulated gastric fluid (SGF) and in simulated intestinal fluid (SIF).

Taken together, these data support the conclusion that MON 87708 DMO does not pose a significant allergenic risk to humans or animals.

V.E. Safety Assessment Summary of MON 87708 DMO

Numerous factors have been considered in the safety assessment of MON 87708 DMO. A comprehensive food, feed, and environmental safety assessment of the MON 87708 DMO was conducted. The results are summarized below along with the conclusions reached from the assessment.

V.E.1. The Donor Organism is Safe

The *dmo* gene is derived from the bacterium *Stenotrophomonas maltophilia* (Palleroni and Bradbury, 1993). *S. maltophilia* is an aerobic, ubiquitous environmental gram negative bacterium commonly present in aquatic environments, soil, and plants. *S. maltophilia* is ubiquitously associated with plants and has been isolated from the rhizosphere of wheat, maize, grasses, beet, cucumber, chicory, potato, strawberry, sugarcane, and rapeseed (Berg et al., 1996; Berg et al., 1999; Berg et al., 2002; Denton et al., 1998; Echemendia, 2007; Juhnke and des Jardin, 1989; Juhnke et al., 1987; Lambert et al., 1987). *S. maltophilia* was isolated from cotton seed, bean pods, and coffee (Nunes and de Melo, 2006; Swings et al., 1983), thus, *S. maltophilia* can be found in a variety of

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foods and feeds. It is also widespread in the home environment and can be found around dishwashers, sponges, toothbrushes, flowers, plants, fruits, vegetables, frozen fish, milk, and poultry (Ryan et al., 2009). Strains of *S. maltophilia* have been found in the transient flora of hospitalized patients as a commensal organism (Echemendia, 2007). Infections caused by *S. maltophilia* are extremely uncommon ([redacted], 2006) and *S. maltophilia* can be found in healthy individuals without causing any harm to human health (Denton et al., 1998). Similar to the indigenous bacteria of the gastrointestinal tract, *S. maltophilia* can be an opportunistic pathogen (Berg, 1996). As such, *S. maltophilia* is of low virulence in immuno-compromised patients where a series of factors must occur for colonization by *S. maltophilia* on humans (Ryan et al., 2009). The ubiquitous presence of *S. maltophilia* in the environment, the presence in healthy individuals, and the incidental presence on foods without any adverse safety reports establishes the safety of the donor organism.

V.E.2. MON 87708 DMO Belongs to a Common Class of Mono-Oxygenases

MON 87708 DMO is classified as an oxygenase. Oxygenases are enzymes that incorporate one or two oxygen atoms into substrates and are widely distributed in many universal metabolic pathways (Harayama et al., 1992). Within this large enzymatic class are mono-oxygenases that incorporate a single oxygen atom as a hydroxyl group with the concomitant production of water and oxidation of NAD(P)H (Harayama et al., 1992). Non-heme iron oxygenases, where iron is involved in the catalytic site, are an important class of oxygenases. Within this class are Rieske oxygenases, which contain a Rieske iron-sulfur [2Fe-2S] cluster. All Rieske non-heme iron oxygenases contain two catalytic domains, a non-heme iron domain (nh-Fe) that is a site of oxygen activation, and a Rieske [2Fe-2S] domain (Ferraro et al., 2005). MON 87708 DMO belongs to this class of oxygenases which are found in diverse phyla ranging from bacteria to plants (Ferraro et al., 2005; Schmidt and Shaw, 2001).

As discussed previously, the crystal structure of a DMO has been solved (D'Ordine et al., 2009; Dumitru et al., 2009). The crystallography results demonstrated that, similar to all Rieske non-heme iron oxygenases, DMO contains two catalytically important and highly conserved domains; a mononuclear non-heme iron domain (nh-Fe) that is a site of oxygen activation, and a Rieske [2Fe-2S] domain (D'Ordine et al., 2009; Dumitru et al., 2009; Ferraro, et al., 2005). The amino acids binding the non-heme iron and those that constitute the Rieske [2Fe-2S] domain in the DMO protein are also highly conserved in these plant proteins, as is their spatial orientation (D'Ordine et al., 2009; Ferraro et al., 2005). Rieske domains are ubiquitous in numerous bacterial and plant proteins like the iron-sulfur protein of the cytochrome bc1 complex, chloroplast cytochrome b6/f complex, and choline mono-oxygenases (Breyton, 2000; Darrouzet et al., 2004; Gray et al., 2004; Hibino et al., 2002; Rathinasabapathi et al., 1997; Russell et al., 1998). The presence of two conserved domains, a Rieske [2Fe-2S] domain and a mononuclear iron domain, suggests that all Rieske type non-heme iron oxygenases share the same reaction mechanism, by which the Rieske domain transfers electrons from the ferredoxin to the mononuclear iron to allow catalysis (Chakraborty et al., 2005; Dumitru et al., 2009; Ferraro et al., 2005). The structure and mechanistic homologies are further evidence of the evolutionary relatedness of all Rieske non-heme iron oxygenases to each other (Nam et al., 2001; Rosche et al., 1997; Werlen et al., 1996). Additionally, a FASTA alignment

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search of publicly available databases using the DMO+27 sequence as a query yielded homologous sequences from many different species, predominantly bacteria, with amino acid sequence identity ranging up to approximately 42%. Homologous oxygenases are also present in plants, including such crops as rice (*Orysa sativa*), canola (*Brassica napus*), and corn (*Zea mays*), with sequence identity up to 24%. The highest homology was observed to pheophorbide A oxygenases from corn, canola and pea (*Pisum sativum*). Pheophorbide A oxygenase is also a Rieske-type oxygenase that plays a key role in the overall regulation of chlorophyll degradation in plants (Rodoni et al., 1997). The protein is constitutively present in all green tissues and, at slightly lower levels, in etiolated and non-photosynthetic tissues including seeds (Yang et al., 2004).

Therefore, MON 87708 DMO shares sequence identity and many catalytic and domain structural similarities with a wide variety of oxygenases present in bacteria and plants currently widely prevalent in the environment and consumed, establishing that animals and humans are extensively exposed to these types of enzymes.

V.E.3. DMO is a Dicamba-Specific Mono-Oxygenase

DMO converts dicamba to DCSA. This demethylation is very specific to dicamba, where both the carboxylate moiety and the chlorine atoms help position the substrate at the active site of the enzyme (D'Ordine et al., 2009; Dumitru et al., 2009). Crystallography studies of the substrate in the active site demonstrated that these chlorines function as steric “handles” that position the substrate in the proper orientation in the binding pocket (Dumitru et al., 2009). Potential substrates abundant in soybean (o-anisic acid, vanillic acid, syringic acid, ferulic acid and sinapic acid) that are structurally similar to dicamba, were not metabolized by an *E. coli*-produced DMO in laboratory tests indicating that the DMO enzyme is specific for dicamba (Section V.A.2). The *E. coli*-produced DMO is similar in sequence and function to MON 87708 DMO, therefore it is appropriate to extend specificity data generated with the *E. coli*-produced DMO to MON 87708 DMO. Given the limited amount of chlorinated metabolites with structures similar to dicamba in plants and other eukaryotes (Wishart, 2010; Wishart et al., 2009) it is unlikely that MON 87708 DMO will catalyze the conversion of other endogenous substrates. Therefore, the activity of the enzyme is specific for dicamba while it maintains many structural properties common to oxygenases that are ubiquitous to all organisms.

V.E.4. MON 87708 DMO is Not a Known Allergen or Toxin

Bioinformatics analyses were performed to assess the allergenic potential, toxicity, or biological activity of MON 87708 DMO. The bioinformatics assessment was performed on DMO+27, which includes the amino acid sequence of DMO. The analysis demonstrated that MON 87708 DMO does not share amino acid sequence similarities with known allergens, gliadins, glutenins, or protein toxins which could have adverse effects to human or animal health (Section V.D).

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V.E.5. MON 87708 DMO is Labile in *in vitro* Digestion Assays

MON 87708 DMO was readily digestible in SGF and SIF. Rapid degradation of the MON 87708 DMO in SGF and SIF makes it highly unlikely that the MON 87708 DMO would be absorbed in the small intestine and have any adverse effects on human or animal health.

V.E.6. MON 87708 DMO is Not a Toxin

An acute oral toxicology study was conducted with MON 87708 DMO. Results indicate that MON 87708 DMO did not cause any adverse effects in mice, with a No Observable Adverse Effect Level (NOAEL) of 140 mg/kg body weight (BW), the highest dose level tested.

Potential human health risks from consumption of foods derived from MON 87708 were evaluated using a Margin of Exposure (MOE) approach. A MOE was calculated between the acute mouse NOAEL (140 mg/kg BW) for the MON 87708 DMO and 95th percentile "eater-only" estimates of acute dietary exposure determined using the Dietary Exposure Evaluation Model (DEEM-FCID version 2.03, Exponent Inc.). DEEM food consumption data are obtained from the 1994-1996 and 1998 USDA Continuing Survey of Food Intakes by Individuals (CSFII). The MOEs for acute dietary intake of MON 87708 DMO were estimated to be 24,800 and 600 for the general population and non-nursing infants, the sub-population with the highest estimated exposure, respectively. These very large MOEs, in addition to the above mentioned protein safety data for MON 87708 DMO, support the conclusion that there is no meaningful risk to human health from dietary exposure to MON 87708 DMO.

Potential health risks to animals from the presence of MON 87708 DMO in feed were evaluated by calculating an estimate of daily dietary intake (DDI). In the worst case scenario, the percentage of MON 87708 DMO consumed from MON 87708 as a percentage of the daily protein intake for a dairy cow is 0.0396% and for both the broiler and pig is less than 0.0121%. These very small levels of exposure of animals to MON 87708 DMO in their feed, in addition to the above mentioned safety data for MON 87708 DMO, support the conclusion that there is no meaningful risk to animal health when MON 87708 is present in their diets.

Using the guidance provided by the FDA in its 1992 Policy Statement regarding the evaluation of New Plant Varieties, a conclusion of "no concern" is reached for the donor organism and MON 87708 DMO. The food and feed products containing MON 87708 or derived from MON 87708 are as safe as soybean currently on the market for human and animal consumption.

V.F. MON 87708 DMO Characterization and Safety Conclusion

MON 87708 DMO is an oxygenase that catalyzes the O-demethylation of the herbicide dicamba. MON 87708 DMO was derived from *S. maltophilia*, which is an environmentally ubiquitous bacterium that does not pose a health risk to healthy individuals. MON 87708 DMO is a Rieske-type mono-oxygenase that has homologs in

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bacteria and plants that share many of the typical structural and functional characteristics of these types of oxygenases, while maintaining specificity for its substrate. MON 87708 DMO was fully characterized confirming both the N-terminal and internal amino acid sequence and the lack of glycosylation. MON 87708 DMO was isolated from MON 87708 and was used for the described safety studies; therefore an equivalence evaluation to the protein produced in a heterologous expression system was not required. Expression studies using ELISA demonstrated that MON 87708 DMO was expressed in all tissues assayed at levels ranging from 3.9 – 180 µg/g dwt, representing a low percentage of the total protein in soybean. Bioinformatics analysis determined that MON 87708 DMO does not share amino acid sequence similarities with known allergens, gliadins, glutenins, or protein toxins. MON 87708 DMO was rapidly digested in *in vitro* assays using simulated gastric and intestinal fluids and did not show any adverse effects when administered to mice via oral gavage at levels that resulted in large MOEs. Together with the safety data, these data support a conclusion that there is no meaningful risk to human health from dietary exposure to MON 87708 DMO. Therefore, the food and feed products containing MON 87708 or derived from MON 87708 are as safe as soybean currently on the market for human and animal consumption.

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VI. COMPOSITIONAL ASSESSMENT OF MON 87708

Safety assessments of biotech crops typically include comparisons of the composition of forage and whole grain of the GM crop to that of conventional counterparts (Codex Alimentarius, 2003). Compositional assessments are performed using the principles and analytes outlined in the OECD consensus documents for soybean composition (OECD, 2001).

A recent review of compositional assessments conducted according to OECD guidelines that encompassed a total of seven GM crop varieties, nine countries and eleven growing seasons concluded that incorporation of biotechnology-derived agronomic traits has had little impact on natural variation in crop composition; most compositional variation is attributable to growing region, agronomic practices and genetic background (Harrigan et al., 2010). Numerous scientific publications have further documented the extensive variability in the concentrations of crop nutrients and anti-nutrients that reflect the influence of environmental and genetic factors as well as extensive conventional breeding efforts to improve nutrition, agronomics and yield. (Reynolds et al., 2005). Compositional equivalence between biotechnology-derived and conventional crops provides an “equal or increased assurance of the safety of foods derived from genetically modified plants” (OECD, 2001). The OECD consensus documents emphasize quantitative measurements of essential nutrients and known anti-nutrients. This is based on the premise that such comprehensive and detailed analyses will most effectively discern any compositional changes that imply potential safety and nutritional concerns. Levels of the components in seed and forage of the biotechnology-derived crop are compared to: 1) corresponding levels in a conventional comparator, the non-biotechnology near isogenic line, grown concurrently, under identical field conditions, and 2) natural ranges generated from an evaluation of commercial reference varieties grown concurrently and from data published in the scientific literature.

The latter comparison places any potential differences between the assessed crop and its comparator in the context of the well-documented variation in the concentrations of crop nutrients and anti-nutrients.

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VI.A. Compositional Equivalence of MON 87708 Seed and Forage to Conventional Soybean

Seed and forage samples were collected from MON 87708 and the near isogenic conventional soybean control A3525 grown in a 2008 U.S. field production. Four different commercial reference varieties were included at each site of the field production to provide data on natural variability of each compositional component analyzed. The field production was conducted at five sites: Jefferson County, Iowa; Stark County, Illinois; Clinton County, Illinois; Parke County, Indiana; and Berks County, Pennsylvania. All soybean plants including MON 87708, the conventional control, and the commercial reference varieties were treated with maintenance pesticides as necessary throughout the growing season. In addition, MON 87708 plots were either treated at the V2-V3 growth stage with dicamba herbicide at the maximum in-crop label rate (0.5 lb acid equivalence (a.e.)/acre) or not treated with dicamba herbicide.

Compositional analyses were conducted to assess whether levels of key nutrients and anti-nutrients in MON 87708 were equivalent to levels in the conventional control and to the composition of the commercial reference varieties. A description of nutrients and anti-nutrients present in soybean is provided in the OECD consensus document on compositional considerations for soybean (OECD, 2001). Nutrients assessed included proximates (ash, carbohydrates by calculation, moisture, protein, and fat), fiber, amino acids (18 components), fatty acids (FA, C8-C22), and vitamin E (α-tochopherol) in seed, and proximates (ash, carbohydrates by calculation, moisture, protein, and fat) and fiber in forage. Anti-nutrients assessed in seed included raffinose, stachyose, lectin, phytic acid, trypsin inhibitors, and isoflavones (daidzein, genistein, and glycitein).

In all, 64 different components were measured (seven in forage and 57 in seed). Components that had more than 50% of the observations below the assay limit of quantitation (LOQ) were excluded from statistical analysis. Therefore, 50 components for both dicamba-treated and untreated MON 87708 were statistically assessed using a mixed-model analysis of variance method. Values for all assessed components were reported on a dry weight basis with the exception of moisture, which was reported as % fresh weight (fwt) and fatty acids, which were reported as % of total FA.

For MON 87708, six statistical comparisons to the conventional control were conducted. One comparison was based on compositional data combined across all five field sites (combined-site analysis) and five separate comparisons were conducted on data from each of the individual field sites. Statistically significant differences were identified at a 5% level of significance. Data from the commercial reference varieties were combined across all sites and used to calculate a 99% tolerance interval for each compositional component to define the natural variability of each component in soybean varieties that have a history of safe consumption and that were grown concurrently with MON 87708 and the conventional control in the same trial.

For the combined-site analysis, statistically significant differences in nutrient and anti-nutrient components were further evaluated using considerations relevant to the safety and nutritional quality of MON 87708 when compared to the conventional control A3525, the conventional counterpart with a history of safe consumption: 1) the relative magnitude of the difference in the mean values of nutrient and anti-nutrient components of MON 87708 and the conventional control, 2) whether the MON 87708 component mean value is within the range of natural variability of that component as represented by the 99% tolerance interval of the commercial varieties grown concurrently in the same trial, 3) analyses of the reproducibility of the statistically significant combined-site component differences at individual sites, and 4) assessing the differences within the context of natural variability of commercial soybean composition published in the scientific literature and in the International Life Sciences Institute (ILSI) Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

This analysis provides a comprehensive comparative assessment of the levels of key nutrients and anti-nutrients in seed, and of key nutrients in forage of MON 87708 and the conventional control, discussed in the context of natural variability in commercial soybean. Results of the comparison indicate that the composition of the seed and forage of MON 87708 is equivalent to that of the near isogenic conventional control A3525 and within the range of natural variability of the commercial reference varieties.

VI.A.1. Composition of Soybean Seed and Forage (Treated)

VI.A.1.1. Nutrient Levels in Soybean Seed (Treated)

In the combined-site analysis of nutrient levels in seed, the following components showed no statistically significant differences in mean values between MON 87708 and the conventional control: moisture, total fat, six amino acids (alanine, lysine, methionine, serine, threonine, and tryptophan), and three fatty acids (18:0 stearic acid, 20:0 arachidic acid, and 20:1 eicosenoic acid) (Table VI-2).

The components that showed statistically significant differences in mean values between MON 87708 and the conventional control in the combined-site analysis were: three proximates (ash, carbohydrates by calculation, and protein), 12 amino acids (arginine, aspartic acid, cystine, glutamic acid, glycine, histidine, isoleucine, leucine, phenylalanine, proline, tyrosine, and valine), three types of fiber (acid detergent fiber -ADF, neutral detergent fiber -NDF, and crude fiber), five fatty acids (16:0 palmitic acid, 18:1 oleic acid, 18:2 linoleic acid, 18:3 linolenic acid, and 22:0 behenic acid), and vitamin E (Tables VI-1 and VI-2).

These statistically significant differences in nutrients were evaluated using considerations relevant to the safety and nutritional quality of MON 87708 when compared to the conventional control:

1) All nutrient component differences observed in the combined-site analysis, whether reflecting increased or decreased MON 87708 mean values with respect to the conventional control were small. Relative magnitude of differences ranged from 2.65 to 7.91% for amino acids, 1.51 to 8.19% for fatty acids, 15.13% for vitamin E, and 2.41 to 12.37% for proximates and fibers.

2) Mean values for all of these statistically different nutrient components from the combined-site analysis of MON 87708 were within the 99% tolerance interval established from the commercial reference varieties grown concurrently and were, therefore, within the range of natural variability of that component in commercial soybean varieties with a history of safe consumption (Tables VI-1 and VI-2).

3) Assessment of the reproducibility of the combined-site differences at the five individual sites showed: statistically significant differences for carbohydrates by calculation, crude fiber, cystine, and glycine at one site; aspartic acid, phenylalanine, proline, tyrosine, valine, 16:0 palmitic acid, and 18:2 linoleic acid at two sites; protein, arginine, glutamic acid, histidine, isoleucine, leucine, and 22:0 behenic acid at three sites; vitamin E at four sites; and 18:1 oleic acid and 18:3 linolenic acid differed across all five sites. Although they were different in the combined-site analysis, no differences were observed for ash, ADF or NDF at

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any of the individual sites. Individual site mean values of MON 87708 for all nutrient components with statistically significant differences fell within the 99% tolerance interval established from the commercial reference varieties grown concurrently and were, therefore, within the range of natural variability of that component in commercial soybean varieties with a history of safe consumption.

4) All mean values of MON 87708 for all nutrient components were within the context of the natural variability of commercial soybean composition as published in the scientific literature and available in the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

Thirteen of the 24 differences between MON 87708 and the conventional control observed in the combined-site data analysis were attributable to small differences in protein and 12 individual amino acids (all expressed as % dwt). The relative magnitude of the difference between the mean protein values for MON 87708 and the conventional control was small (a decrease of 3.65% in the combined-site analysis for MON 87708) and reached statistical significance at only three of the five individual sites. Correspondingly, differences in all amino acids were small and not observed consistently as statistically significant differences at all individual sites. Eleven of the 12 amino acids observed to be different in the combined-site analysis were decreased (2.65-7.91%) relative to the conventional control and, as with protein, statistically significant differences were not consistently observed at all individual sites. Cystine showed a relative increase of 3.01% but was statistically significantly different at only one site. Four of the six amino acids (alanine, lysine, serine, and threonine) not observed to be statistically different in the combined-site analysis also showed modest decreases ranging from ~ 1.5-2.3% (Table VI-2) consistent with the directionality of the changes observed in protein content. Overall, observed differences in protein and amino acid levels are not considered to be meaningful from a food and feed safety and nutritional perspective because they were small, and the mean MON 87708 values were within the 99% tolerance interval established by the commercial reference varieties grown concurrently in the same trial.

Five of the combined-site differences between MON 87708 and the conventional control were attributable to fatty acid levels (all expressed as % total FA) in seed, whereas total fat content was not statistically significantly different. For 18:1 oleic acid and 18:3 linolenic acid, the relative magnitude of differences between the mean values for MON 87708 and conventional control were small in the combined-site analysis (a decrease of 8.19% and an increase of 6.65% compared to the conventional control, respectively) and at the five individual sites (levels were <11% decreased for 18:1 oleic acid and <10% increased for 18:3 linolenic acid at all sites compared to conventional control) (Tables VI-2, E-4, E-7, E-10, E-13, and E-16).

By comparison, the observed differences between MON 87708 and conventional control for 18:1 oleic and 18:3 linolenic acids are markedly less than differences in soybean varieties developed through conventional breeding (Fehr, 2007; Clemente and Cahoon, 2009). The average relative levels of 18:3 linolenic acid in commercial soybean are approximately 10% total FA, while the average relative level of 18:1 oleic acid in

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commercial soybean is approximately 18-25% total FA. In the compositional analysis presented here, the values of FA components in the conventional control, when assessed as individual replicates across all five individual sites, ranged from 19.6 to 22.4% total FA for 18:1 oleic acid and from 8.4 to 10.1% total FA for 18:3 linolenic acid (Table VI-2). The values from the commercial reference varieties ranged from 17.9 to 25.3% total FA for 18:1 oleic acid and 7.4 to 11.4% total FA for 18:3 linolenic acid (Table VI-2). Additionally, literature data from Lundry et al. (2008) and Berman et al. (2009) and the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004) highlight the extensive natural variability in fatty acid levels in soybean, as presented in Table VI-9. The small relative magnitudes of the differences in 18:3 linolenic acid and 18:1 oleic acid compared to the conventional control as well the broad range of these fatty acids present in commercial soybean varieties, suggest that the differences are not meaningful to food and feed safety and nutritional quality in MON 87708.

The relative magnitudes of differences between the mean values for MON 87708 and the conventional control for the other three ftty acids observed in the combined-site analysis were small (2.29% increase for 16:0 palmitic acid, 1.51% increase for 18:2 linoleic acid and a 4.70% decrease for 22:0 behenic acid). The small magnitude of differences as well as the lack of statistical differences across all individual sites (Tables VI-2, E-4, E-7, E-10, E-13, and E-16) further confirmed that the differences observed in fatty acid composition are not meaningful to food and feed safety and nutritional quality.

One of the combined-site differences observed between MON 87708 and the conventional control was attributable to vitamin E (expressed as mg/100g dwt). The relative magnitude of difference between the mean values of MON 87708 and conventional control for vitamin E in the combined-site analysis was an increase of 15.1% with respect to the conventional control (Tables VI-1).

Levels of vitamin E are known to be affected by environmental growing conditions (E) and germplasm (G) as demonstrated in results from recent assessments on soybean varieties grown at three locations in the U.S. over a period of four years (Britz et al., 2008) and across six environments in Eastern Canada in a single year (Seguin et al., 2009). Britz et al. (2008) showed more than a two-fold variation in levels across their study (units expressed as the ratio of α-tocopherol (vitamin E) to total tocopherol content). Vitamin E values in Seguin et al. (2009) ranged from 0.87 to 3.32 mg/100g dwt. Both assessments showed that G and E effects as well as G × E interaction effects influenced vitamin E content. In the compositional analysis presented here, values of vitamin E in the conventional control, when assessed as individual replicates across all sites, ranged by as much as 0.89 to 2.11 mg/100g dwt (Table VI-2). Ranges of vitamin E values from the concurrently grown commercial reference varieties were even greater and ranged from 0.69 to 2.91 mg/100g dwt (Table VI-2). Literature data from other compositional assessments (Berman et al., 2009; Lundry et al., 2008; ILSI, 2006; Ridley et al., 2004) that further highlight the extensive natural variability in vitamin E levels in soybean are presented in Table VI-9. Therefore, given this established variability of vitamin E levels in conventional soybean and the fact that soybean is not an important nutritional source of vitamin E in human or animal diets, this increase in vitamin E levels in MON 87708

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compared to the conventional control supports the conclusion that this observed difference is not meaningful to food and feed safety and nutritional quality.

The remaining combined-site differences between MON 87708 and the conventional control were attributable to two proximates (ash and carbohydrates by calculation) and three fibers (ADF, NDF, and crude fiber). The relative magnitude of these increases were small (2.41% to 12.37%) and there was no consistency of these combined-site differences at the individual sites (carbohydrates by calculation and crude fiber were different at only one site, whereas ash, ADF and NDF were not different at any of the individual sites). The combined-site mean values for these nutrient components also were within the 99% tolerance interval established from the commercial reference varieties grown concurrently establishing that these differences are not meaningful to food and feed safety and nutrition.

In summary, statistical analyses found no consistent differences across sites in the levels of nutrient components in seed from MON 87708 and the conventional control, except for differences in 18:1 oleic acid, 18:3 linoleic acid, and vitamin E levels that were of small magnitude and were within the natural variability of the concurrently grown commercial soybean varieties. These data support the conclusion that MON 87708 is compositionally equivalent to conventional soybean.

VI.A.1.2. Anti-Nutrient Levels in Soybean Seed (Treated)

In the combined-site analysis, no statistically significant differences were observed in four of the eight anti-nutrient component comparisons (lectin, trypsin inhibitors, genistein, and glycitein) between MON 87708 and the conventional control. Statistically significant differences were observed between MON 87708 and the conventional control in the other four anti-nutrient components that were measured (Tables VI-1 and VI-3). The differences included decreased mean values for phytic acid, raffinose, stachyose, and an increased mean level of daidzein, compared to the conventional control.

The statistically significant differences in anti-nutrients were evaluated using considerations relevant to the safety and nutritional quality of MON 87708 when compared to the conventional control:

1) All anti-nutrient component differences observed in the combined-site analysis, whether reflecting increased or decreased MON 87708 mean values with respect to the conventional control were small. Relative magnitude of differences in the combined-site analysis for the anti-nutrients that were decreased in MON 87708 ranged from 6.1% (phytic acid) to 7.73% (raffinose). The relative magnitude of difference (increase) in daidzein was 11.5%.

2) MON 87708 mean values for these anti-nutrient components from the combined-site analysis were within the 99% tolerance interval established from the commercial reference varieties concurrently grown in the same trial and, therefore were within the range of natural variability of these components in commercial soybean varieties with a history of safe consumption (Tables V1-1 and V1-3).

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3) Assessment of the reproducibility of the combined-site differences at the five individual sites showed no consistent pattern across sites. A statistically significant decrease was observed for stachyose at one site and phytic acid at two sites, whereas a significant increase was seen for daidzein at two sites. No differences for raffinose were observed at any of the individual sites. Mean values for all of the above anti-nutrient components in MON 87708 at the individual sites were within the 99% tolerance interval established from the concurrently grown commercial reference varieties.

4) All mean values of MON 87708 for all anti-nutrients were within the context of the natural variability of commercial soybean composition as published in the scientific literature and available in the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

In summary, statistical analyses found no consistent differences across sites in the levels of anti-nutrient components in seed from MON 87708 and the conventional control. Thus, a comprehensive evaluation of anti-nutrient components in seed support the conclusion that MON 87708 is compositionally equivalent to conventional soybean.

VI.A.1.3. Nutrient Levels in Soybean Forage (Treated)

In the combined-site analysis of forage, six of the seven nutrient component comparisons did not have a statistically significant difference between MON 87708 and the conventional control (Tables VI-1 and VI-4). The only statistical difference was for the ADF mean value and it was evaluated using considerations relevant to the safety and nutritional quality of MON 87708 when compared to the conventional control.

1) The relative magnitude of difference in ADF, with respect to the conventional control, was small with an increase of 10.45%.

2) The mean value for ADF from the combined-site analysis of MON 87708 was within the 99% tolerance interval established from the commercial reference varieties grown concurrently in the same trial and, therefore within the range of natural variability of that component in commercial soybean varieties with a history of safe consumption (Tables V1-1 and V1-4).

3) Assessment of the reproducibility of the combined-site difference of ADF across the individual sites showed no statistically significant differences at any of the five individual sites.

4) The level of ADF was within the natural variability observed for commercial soybean varieties as published in the scientific literature and available in the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

In summary, statistical analyses found no consistent differences across sites in the levels of nutrient components in forage from MON 87708 and the conventional control. Thus, a comprehensive evaluation of nutrient components in forage supports the conclusion that MON 87708 is compositionally equivalent to conventional soybean.

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VI.A.2. Composition of Soybean Seed and Forage (Untreated)

VI.A.2.1. Nutrient Levels in Soybean Seed (Untreated)

In the combined-site analysis of nutrient levels in seed, the following components showed no statistically significant differences in mean values between MON 87708 (untreated) and the conventional control: ash, carbohydrates by calculation, moisture, total fat, crude fiber, ten amino acids (alanine, aspartic acid, glycine, histidine, lysine, methionine, serine, threonine, tryptophan, tyrosine), and three fatty acids (18:0 stearic acid, 20:0 arachidic acid, and 20:1 eicosenoic acid) (Table VI-6).

The components that showed statistically significant differences in mean values between MON 87708 (untreated) and the conventional control in the combined-site analysis were: protein, eight amino acids (arginine,cystine, glutamic acid, isoleucine, leucine, phenylalanine, proline, and valine), two types of fiber (acid detergent fiber (ADF), and neutral detergent fiber (NDF)), five fatty acids (16:0 palmitic acid, 18:1 oleic acid, 18:2 linoleic acid, 18:3 linolenic acid, and 22:0 behenic acid), and vitamin E (Tables VI-5 and VI-6).

These statistically significant differences in nutrients were evaluated using considerations relevant to the safety and nutritional quality of MON 87708 (untreated) when compared to the conventional control:

1) All nutrient component differences observed in the combined-site analysis, whether reflecting increased or decreased MON 87708 (untreated) mean values with respect to the conventional control were small. Relative magnitude of differences ranged from 2.27 to 5.88% or protein and amino acids, 1.45 to 7.60% for fatty acids, 18.16% for vitamin E, and 3.99 to 6.33% for fibers.

2) Mean values for all of these statistically different nutrient components from the combined-site analysis of MON 87708 (untreated) were within the 99% tolerance interval established from the commercial reference varieties grown concurrently and were, therefore, within the range of natural variability of that component in commercial soybean varieties with a history of safe consumption (Tables VI-5 and VI-6).

3) Assessment of the reproducibility of the combined-site differences at the five individual sites showed: statistically significant differences for cystine, isoleucine, valine, and 16:0 palmitic acid at one site; protein, arginine, glutamic acid, and leucine at two sites; phenylalanine, proline, 18:2 linoleic acid, and 22:0 behenic acid at three sites; 18:1 oleic acid, 18:3 linolenic acid, and vitamin E at four sites. No components were statistically significantly different at all five sites. Although they were different in the combined site analysis, no differences were observed for ADF or NDF at any of the individual sites. Individual site mean values of MON 87708 (untreated) for all nutrient components with statistically significant differences fell within the 99% tolerance interval established from the commercial reference varieties grown concurrently and were, therefore, within the range of natural variability of that component in commercial soybean varieties with a history of safe consumption.

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4) All mean values of MON 87708 (untreated) for all nutrient components were within the context of the natural variability of commercial soybean composition as published in the scientific literature and available in the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

Nine of the 17 differences between MON 87708 (untreated) and the conventional control observed in the combined-site data analysis were attributable to small differences in protein and eight individual amino acids (all expressed as % dwt). The relative magnitude of the difference between the mean protein values for MON 87708 (untreated) and the conventional control was small (a decrease of 2.94% in the combined-site analysis for MON 87708 (untreated) and reached statistical significance at only two of the five individual sites. Correspondingly, differences in all amino acids were small and not observed consistently as statistically significant differences at all individual sites. Seven of the 8 amino acids observed to be different in the combined-site analysis were decreased (2.27 to 5.88%) relative to the conventional control. Cystine showed a relative increase of 3.27% but was statistically significantly different at only one site. Overall, observed differences in protein and amino acid levels are not considered to be meaningful from a food and feed safety and nutritional perspective because they were small, and the mean MON 87708 (untreated) values were within the 99% tolerance interval established by the commercial reference varieties grown concurrently in the same trial.

Five of the combined-site differences between MON 87708 (untreated) and the conventional control were attributable to fatty acid levels (all expressed as % total FA) in seed, whereas total fat content was not statistically significantly different. For 18:1 oleic acid and 18:3 linolenic acid, the relative magnitude of differences between the mean values for MON 87708 (untreated) and conventional control were small in the combined-site analysis (a decrease of 7.60% and an increase of 5.78% compared to the conventional control, respectively) and at the individual sites (levels were <12% decreased for 18:1 oleic acid and <8% increased for 18:3 linolenic acid at all sites compared to conventional control) (Tables VI-6, E-19, E-22, E-25, E-28, and E-31).

By comparison, the observed differences between MON 87708 (untreated) and conventional control for 18:1 oleic and 18:3 linolenic acids are markedly less than differences in soybean varieties developed through conventional breeding (Clemente and Cahoon, 2009; Fehr, 2007). The average relative levels of 18:3 linolenic acid in commercial soybean are approximately 10% total FA, while the average relative level of 18:1 oleic acid in commercial soybean is approximately 18-25% total FA. In the compositional analysis presented here, the values of FA components in the conventional control, when assessed as individual replicates across all five individual sites, ranged from 19.6 to 22.4% total FA for 18:1 oleic acid and from 8.4 to 10.1% total FA for 18:3 linolenic acid (Table VI-6). The values from the commercial reference varieties ranged from 17.9 to 25.3% total FA for 18:1 oleic acid and 7.4 to 11.4% total FA for 18:3 linolenic acid (Table VI-6). Additionally, literature data from Lundry et al. (2008) and Berman et al. (2009) and the ILSI Crop Composition Database highlight the extensive natural variability in fatty acid levels in soybean, as presented in Table VI-9. The small relative magnitudes of the differences in 18:3 linolenic acid and 18:1 oleic acid compared to the conventional control as well the broad range of these fatty acids present in

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commercial soybean varieties, suggest that the differences are not meaningful to food and feed safety and nutritional quality in MON 87708 (untreated).

The relative magnitudes of differences between the mean values for MON 87708 (untreated) and the conventional control for the other three fatty acids observed in the combined-site analysis were small (2.37% increase for 16:0 palmitic acid, 1.45% increase for 18:2 linoleic acid and a 3.71% decrease for 22:0 behenic acid). The small magnitude of differences as well as the lack of statistical differences across all individual sites (Tables VI-6, E-19, E-22, E28 and E-28) further confirmed that the differences observed in fatty acid composition are not meaningful to food and feed safety and nutritional quality.

One of the combined-site differences observed between MON 87708 (untreated) and the conventional control was attributable to vitamin E (expressed as mg/100g dwt). The relative magnitude of difference between the mean values of MON 87708 (untreated) and conventional control for vitamin E in the combined-site analysis was an increase of 18.16% with respect to the conventional control (Table VI-6).

Levels of vitamin E are known to be affected by environmental growing conditions and germplasm as demonstrated in results from recent assessments on soybean varieties grown at three locations in the U.S. over a period of four years (Britz et al., 2008) and across six environments in Eastern Canada in a single year (Seguin et al., 2009). Britz et al. (2008) showed more than a two-fold variation in levels across their study (units expressed as the ratio of α tocopherol (vitamin E) to total tocopherol content). Vitamin E values in Seguin et al. (2009) ranged from 0.87 to 3.32 mg/100g dwt. In the compositional analysis presented here, values of vitamin E in the conventional control, when assessed as individual replicates across all sites, ranged by as much as 0.89 to 2.11 mg/100g dwt (Table VI-6). Ranges of vitamin E values from the concurrently grown commercial reference varieties were even greater and ranged from 0.69 to 2.91 mg/100g dwt (Table VI-6). Literature data from other compositional assessments (Berman et al., 2009; ILSI, 2006; Lundry et al., 2008; Ridley et al., 2004) that further highlight the extensive natural variability in vitamin E levels in soybean are presented in Table VI-9. Therefore, given this established variability of vitamin E levels in conventional soybean and the fact that soybean is not an important nutritional source of vitamin E in human or animal diets, this increase in vitamin E levels in MON 87708 (untreated) compared to the conventional control supports the conclusion that this observed difference is not meaningful to food and feed safety and nutritional quality.

The remaining combined-site differences between MON 87708 (untreated) and the conventional control were attributable to two fibers (ADF and NDF). The relative magnitude of these increases were small (3.99% to 6.33%) and ADF and NDF were not different at any of the individual sites. The combined-site mean values for these nutrient components also were within the 99% tolerance interval established from the commercial reference varieties grown concurrently establishing that these differences are not meaningful to food and feed safety and nutrition.

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In summary, statistical analyses found no consistent differences across sites in the levels of nutrient components in seed from MON 87708 (untreated) and the conventional control, except for differences in 18:1 oleic acid, 18:3 linoleic acid, and vitamin E levels that were of small magnitude and were within the natural variability of the concurrently grown commercial soybean varieties. These data support the conclusion that MON 87708 (untreated) is compositionally equivalent to conventional soybean.

VI.A.2.2. Anti-Nutrient Levels in Soybean Seed (Untreated)

In the combined-site analysis, no statistically significant differences were observed in five of the eight anti-nutrient component comparisons (lectin, phytic acid, raffinose, stachyose, and glycitein) between MON 87708 (untreated) and the conventional control. Statistically significant differences were observed between MON 87708 (untreated) and the conventional control in the other three anti-nutrient components that were measured (Tables VI-5 and VI-7). The differences included increased mean values trypsin inhibitors, daidzein, and genistein compared to the conventional control.

The statistically significant differences in anti-nutrients were evaluated using considerations relevant to the safety and nutritional quality of MON 87708 (untreated) when compared to the conventional control:

1) All anti-nutrient component differences observed in the combined-site analysis reflected increased MON 87708 (untreated) mean values with respect to the conventional control, but were all less than 20%. Relative magnitude of differences in the combined-site analysis for the anti-nutrients were 15.37% (trypsin inhibitor), 17.24% (daidzein) and 11.59% (genistein).

2) MON 87708 (untreated) mean values for these anti-nutrient components from the combined-site analysis were within the 99% tolerance interval established from the commercial reference varieties concurrently grown in the same trial and, therefore were within the range of natural variability of these components in commercial soybean varieties with a history of safe consumption (Tables VI-5 and VI-7).

3) Assessment of the reproducibility of the combined-site differences at the five individual sites showed no consistent pattern across sites. None of the anti-nutrient components found to be different in the combined site analysis were observed to be statistically different at more than one of the five individual sites. Mean values for all of the above anti-nutrient components in MON 87708 (untreated) at the individual sites were within the 99% tolerance interval established from the concurrently grown commercial reference varieties.

4) All mean values of MON 87708 (untreated) for all anti-nutrients were within the context of the natural variability of commercial soybean composition as published in the scientific literature and available in the ILSI Crop Composition Database (ILSI, 2006; Ridley et al., 2004).

In summary, statistical analyses found no consistent differences across sites in the levels of anti-nutrient components in seed from MON 87708 (untreated) and the conventional

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control. Thus, a comprehensive evaluation of anti-nutrient components in seed support the conclusion that MON 87708 is compositionally equivalent to conventional soybean.

VI.A.2.3. Nutrient Levels in Soybean Forage (Untreated)

In the combined-site analysis of forage, none of the seven nutrient component comparisons had a statistically significant difference between MON 87708 (untreated) and the conventional control (Tables VI-5 and VI-8). In summary, statistical analyses found no consistent differences across sites in the levels of nutrient components in forage from MON 87708 (untreated) and the conventional control. Thus, a comprehensive evaluation of nutrient components in forage supports the conclusion that MON 87708 (untreated) compositionally equivalent to conventional soybean.

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Table VI-1. Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Combined-Site Analysis						
Seed Proximate (% dwt)						
Ash	5.24	5.12	2.41	0.031	4.94 - 5.69	4.74, 6.01
Carbohydrates	37.93	36.64	3.50	0.012	35.65 - 39.21	32.07, 40.08
Protein	40.86	42.41	-3.65	0.016	39.00 - 42.53	35.50, 45.19
Seed Fiber (% dwt)						
Acid Detergent Fiber	13.55	12.86	5.30	0.009	12.45 - 15.57	10.06, 18.04
Crude Fiber	8.29	7.37	12.37	<0.001	6.23 - 9.65	5.76, 10.76
Neutral Detergent Fiber	15.29	14.34	6.63	0.028	13.11 - 17.83	11.36, 19.38
Seed Amino Acid (% dwt)						
Arginine	3.30	3.58	-7.91	0.006	3.09 - 3.50	2.55, 3.83

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708 minus Control) Mean Difference (% of Control)	Mean Difference (MON 87708 minus Control) Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Combined-Site Analysis						
Seed Amino Acid (% dwt)						
Aspartic Acid	4.63	4.78	-3.18	0.016	4.44 - 4.80	4.04, 5.13
Cystine	0.61	0.59	3.01	<0.001	0.58 - 0.63	0.50, 0.68
Glutamic Acid	7.38	7.69	-4.03	0.010	7.05 - 7.73	6.28, 8.30
Glycine	1.76	1.81	-2.65	0.020	1.67 - 1.83	1.53, 1.92
Histidine	1.06	1.09	-3.07	0.017	1.02 - 1.10	0.93, 1.16
Isoleucine	1.88	1.95	-3.58	0.006	1.75 - 1.97	1.65, 2.06
Leucine	3.06	3.17	-3.37	0.008	2.93 - 3.19	2.72, 3.39
Phenylalanine	2.06	2.13	-3.33	0.034	1.92 - 2.18	1.80, 2.30

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Combined-Site Analysis						
Seed Amino Acid (% dwt)						
Proline	1.99	2.05	-3.24	0.017	1.90 - 2.09	1.65, 2.26
Tyrosine	1.37	1.42	-3.47	0.048	1.28 - 1.46	1.24, 1.50
Valine	1.98	2.06	-3.89	0.006	1.82 - 2.09	1.72, 2.20
Seed Fatty Acid (% Total FA)						
16:0 Palmitic	11.59	11.33	2.29	0.002	11.25 - 12.16	8.44, 12.56
18:1 Oleic	19.20	20.91	-8.19	<0.001	17.85 - 19.94	15.73, 27.19
18:2 Linoleic	54.40	53.59	1.51	0.010	53.42 - 55.67	48.61, 59.37
18:3 Linolenic	10.12	9.49	6.65	<0.001	8.99 - 10.88	6.01, 12.58
22:0 Behenic	0.27	0.28	-4.70	0.001	0.25 - 0.29	0.24, 0.40

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Combined-Site Analysis						
Seed Vitamin (mg/100g dwt)						
Vitamin E	1.41	1.23	15.13	0.001	1.08 - 2.17	0, 3.49
Seed Anti-nutrient (% dwt)						
Phytic Acid	1.30	1.39	-6.14	0.043	1.08 - 1.51	0.77, 1.91
Raffinose	0.43	0.47	-7.73	0.045	0.32 - 0.59	0.13, 0.70
Stachyose	3.36	3.62	-7.24	0.011	3.07 - 4.02	2.30, 4.07
Seed Isoflavone (µg/g dwt)						
Daidzein	1494.97	1340.71	11.51	0.046	899.83 - 2305.26	0, 2271.38
Forage Fiber (% dwt)						
Acid Detergent Fiber	30.58	27.69	10.45	0.021	23.30 - 45.11	16.54, 41.80

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708 minus Control) Mean Difference (% of Control)	Mean Difference (MON 87708 minus Control) Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Five Individual Sites						
Seed Fatty Acid (% Total FA)						
18:1 Oleic Site IARL	19.38	21.67	-10.58	0.001	19.07 - 19.73	15.73, 27.19
18:1 Oleic Site ILCY	19.74	21.57	-8.46	0.011	19.44 - 19.94	15.73, 27.19
18:1 Oleic Site ILWY	19.52	21.14	-7.66	0.010	19.34 - 19.64	15.73, 27.19
18:1 Oleic Site INRC	18.78	20.19	-6.96	<0.001	18.58 - 18.95	15.73, 27.19
18:1 Oleic Site PAHM	18.58	20.01	-7.13	0.015	17.85 - 19.42	15.73, 27.19
18:3 Linolenic Site IARL	10.64	10.04	5.94	0.033	10.58 - 10.74	6.01, 12.58
18:3 Linolenic Site ILCY	9.07	8.58	5.78	0.007	8.99 - 9.16	6.01, 12.58
18:3 Linolenic Site ILWY	10.54	10.05	4.92	0.026	10.51 - 10.59	6.01, 12.58

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Five Individual Sites						
Seed Fatty Acid (% Total FA)						
18:3 Linolenic Site INRC	10.03	9.31	7.65	<0.001	9.89 - 10.10	6.01, 12.58
18:3 Linolenic Site PAHM	10.33	9.47	9.02	0.006	9.91 - 10.88	6.01, 12.58
Statistically Significant Differences Observed in Four Individual Sites						
Seed Vitamin (mg/100g dwt)						
Vitamin E Site IARL	1.15	0.94	22.25	0.033	1.10 - 1.22	0, 3.49
Vitamin E Site ILCY	2.13	1.86	14.43	0.038	2.10 - 2.17	0, 3.49
Vitamin E Site ILWY	1.18	0.94	24.64	0.011	1.08 - 1.26	0, 3.49
Vitamin E Site PAHM	1.32	1.23	7.90	0.010	1.21 - 1.54	0, 3.49
Statistically Significant Differences Observed in Three Individual Sites						
Seed Proximate (% dwt)						
Protein Site ILCY	40.17	41.72	-3.72	0.047	39.44 - 40.96	35.50, 45.19

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Three Individual Sites						
Seed Proximate (% dwt)						
Protein Site ILWY	40.88	41.99	-2.64	0.042	40.56 - 41.37	35.50, 45.19
Protein Site PAHM	40.25	43.69	-7.86	0.002	39.00 - 41.05	35.50, 45.19
Seed Amino Acid (% dwt)						
Arginine Site ILWY	3.30	3.57	-7.58	0.002	3.24 - 3.33	2.55, 3.83
Arginine Site INRC	3.44	3.72	-7.37	0.011	3.39 - 3.50	2.55, 3.83
Arginine Site PAHM	3.25	3.88	-16.13	0.001	3.09 - 3.36	2.55, 3.83
Glutamic Acid Site ILCY	7.43	7.61	-2.38	0.032	7.27 - 7.54	6.28, 8.30
Glutamic Acid Site ILWY	7.29	7.51	-2.86	0.002	7.20 - 7.35	6.28, 8.30
Glutamic Acid Site PAHM	7.28	8.00	-9.08	0.003	7.06 - 7.40	6.28, 8.30

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Three Individual Sites						
Seed Amino Acid (% dwt)						
Histidine Site ILCY	1.06	1.08	-1.84	0.022	1.04 - 1.07	0.93, 1.16
Histidine Site ILWY	1.05	1.07	-1.62	0.019	1.05 - 1.05	0.93, 1.16
Histidine Site PAHM	1.05	1.13	-7.52	0.002	1.02 - 1.06	0.93, 1.16
Isoleucine Site ILCY	1.89	1.97	-3.98	0.010	1.87 - 1.93	1.65, 2.06
Isoleucine Site ILWY	1.87	1.90	-1.22	0.004	1.85 - 1.89	1.65, 2.06
Isoleucine Site PAHM	1.85	2.00	-7.59	0.014	1.79 - 1.90	1.65, 2.06
Leucine Site ILCY	3.09	3.17	-2.42	0.002	3.04 - 3.14	2.72, 3.39
Leucine Site ILWY	3.02	3.10	-2.49	<0.001	3.00 - 3.04	2.72, 3.39

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Three Individual Sites						
Seed Amino Acid (% dwt)						
Leucine Site PAHM	3.03	3.28	-7.42	0.002	2.96 - 3.09	2.72, 3.39
Seed Fatty Acid (% Total FA)						
22:0 Behenic Site IARL	0.26	0.28	-5.49	0.022	0.25 - 0.27	0.24, 0.40
22:0 Behenic Site ILWY	0.26	0.28	-6.67	0.008	0.26 - 0.27	0.24, 0.40
22:0 Behenic Site INRC	0.28	0.29	-4.85	0.038	0.27 - 0.29	0.24, 0.40
Statistically Significant Differences Observed in Two Individual Sites						
Seed Proximate						
Moisture (% fwt) Site ILWY	6.96	6.16	12.99	0.022	6.80 - 7.17	4.27, 9.58
Moisture (% fwt) Site PAHM	7.84	10.50	-25.30	<0.001	7.38 - 8.47	4.27, 9.58
Seed Amino Acid (% dwt)						
Aspartic Acid Site ILWY	4.59	4.67	-1.90	0.011	4.55 - 4.61	4.04, 5.13

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Two Individual Sites						
Seed Amino Acid (% dwt)						
Aspartic Acid Site PAHM	4.56	4.94	-7.65	0.002	4.45 - 4.63	4.04, 5.13
Phenylalanine Site ILWY	2.01	2.07	-2.95	0.046	1.96 - 2.06	1.80, 2.30
Phenylalanine Site PAHM	2.04	2.21	-7.96	0.010	2.00 - 2.07	1.80, 2.30
Proline Site ILWY	1.94	2.05	-5.09	0.020	1.93 - 1.96	1.65, 2.26
Proline Site PAHM	1.98	2.10	-5.98	0.016	1.94 - 2.00	1.65, 2.26
Threonine Site ILWY	1.52	1.55	-1.69	0.005	1.51 - 1.53	1.40, 1.69
Threonine Site PAHM	1.55	1.62	-4.23	0.029	1.52 - 1.57	1.40, 1.69
Tyrosine Site INRC	1.38	1.44	-4.49	0.044	1.35 - 1.43	1.24, 1.50

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708 minus Control): Mean Difference (% of Control)	Mean Difference (MON 87708 minus Control): Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Two Individual Sites						
Seed Amino Acid (% dwt)						
Tyrosine Site PAHM	1.35	1.49	-9.43	0.011	1.28 - 1.43	1.24, 1.50
Valine Site ILCY	1.96	2.05	-4.37	0.013	1.94 - 2.01	1.72, 2.20
Valine Site PAHM	1.95	2.13	-8.17	0.012	1.89 - 2.00	1.72, 2.20
Seed Fatty Acid (% Total FA)						
16:0 Palmitic Site IARL	11.49	11.00	4.47	0.001	11.44 - 11.54	8.44, 12.56
16:0 Palmitic Site ILWY	11.26	11.04	2.02	0.017	11.25 - 11.27	8.44, 12.56
18:2 Linoleic Site ILCY	54.54	53.26	2.40	0.021	54.45 - 54.70	48.61, 59.37
18:2 Linoleic Site INRC	54.98	54.43	1.00	0.019	54.80 - 55.14	48.61, 59.37

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Two Individual Sites						
Seed Anti-nutrient (% dwt)						
Phytic Acid Site IARL	1.36	1.53	-11.28	0.018	1.33 - 1.38	0.77, 1.91
Phytic Acid Site ILWY	1.40	1.55	-9.34	0.030	1.33 - 1.46	0.77, 1.91
Seed Isoflavone (µg/g dwt)						
Daidzein Site ILWY	1458.08	1271.60	14.67	0.004	1416.31 - 1535.98	0, 2271.38
Daidzein Site INRC	1683.50	1419.40	18.61	0.049	1593.24 - 1777.49	0, 2271.38
Glycitein Site ILWY	111.77	79.70	40.23	<0.001	109.88 - 113.86	31.24, 233.60
Glycitein Site INRC	111.51	98.42	13.31	0.016	110.91 - 112.28	31.24, 233.60
Forage Proximate (% dwt)						
Protein Site IARL	25.21	23.00	9.63	0.043	24.71 - 25.52	15.69, 26.63

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in Two Individual Sites						
Forage Proximate (% dwt)						
Protein Site INRC	21.78	23.33	-6.63	0.019	20.99 - 22.51	15.69, 26.63
Statistically Significant Differences Observed in One Individual Site						
Seed Proximate (% dwt)						
Carbohydrates Site PAHM	38.30	35.23	8.71	0.008	37.69 - 38.65	32.07, 40.08
Seed Fiber (% dwt)						
Crude Fiber Site INRC	8.06	6.89	17.03	0.009	7.76 - 8.47	5.76, 10.76
Seed Amino Acid (% dwt)						
Alanine Site PAHM	1.75	1.86	-5.81	0.010	1.74 - 1.77	1.56, 1.91
Cystine Site PAHM	0.62	0.59	4.79	0.024	0.60 - 0.63	0.50, 0.68
Glycine Site PAHM	1.73	1.86	-6.78	0.004	1.69 - 1.75	1.53, 1.92

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Table VI-1 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Treated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Commercial Tolerance Interval[5]
Statistically Significant Differences Observed in One Individual Site						
Seed Amino Acid (% dwt)						
Lysine Site PAHM	2.60	2.75	-5.39	0.009	2.53 - 2.65	2.33, 2.84
Serine Site ILWY	1.98	2.06	-3.83	0.003	1.97 - 2.00	1.78, 2.27
Tryptophan Site ILCY	0.51	0.48	6.21	0.024	0.49 - 0.53	0.38, 0.52
Seed Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt) Site ILWY	1.10	2.33	-52.88	0.045	0.59 - 1.51	0, 7.73
Stachyose Site INRC	3.14	3.46	-9.18	0.043	3.12 - 3.17	2.30, 4.07
Forage Proximate (% dwt)						
Carbohydrates Site PAHM	70.95	65.81	7.81	0.015	69.23 - 73.31	60.69, 73.46
Moisture (% fwt) Site PAHM	74.27	74.91	-0.86	0.021	73.40 - 75.40	62.08, 89.80

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid; H.U. = Hemagglutinating Units.
[2] MON 87708 was treated with dicamba.
[3] Mean = least-square mean.
[4] Control refers to the near isogenic conventional soybean control A3525.
[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference varieties. Negative limits set to zero.

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Table VI-2. Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	5.24 (0.067) (4.94 - 5.69)	5.12 (0.067) (4.73 - 5.47)	0.12 (0.055) (-0.28 - 0.45)	0.011, 0.24	0.031	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	37.93 (0.50) (35.65 - 39.21)	36.64 (0.50) (34.11 - 38.45)	1.28 (0.40) (-0.38 - 4.07)	0.36, 2.20	0.012	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	6.88 (0.65) (5.17 - 8.47)	7.14 (0.65) (5.79 - 10.60)	-0.26 (0.52) (-3.12 - 1.43)	-1.46, 0.94	0.629	4.27, 9.58 (5.50 - 9.23)
Protein	40.86 (0.39) (39.00 - 42.53)	42.41 (0.39) (40.69 - 43.85)	-1.55 (0.51) (-4.84 - 0.088)	-2.73, -0.37	0.016	35.50, 45.19 (37.06 - 43.42)
Total Fat	15.97 (0.59) (14.00 - 18.56)	15.84 (0.59) (14.40 - 18.39)	0.13 (0.31) (-1.90 - 2.37)	-0.58, 0.84	0.691	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	13.55 (0.40) (12.45 - 15.57)	12.86 (0.40) (11.62 - 14.57)	0.68 (0.25) (-0.71 - 2.13)	0.18, 1.19	0.009	10.06, 18.04 (12.07 - 17.46)

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Table VI-2 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Crude Fiber	8.29 (0.26) (6.23 - 9.65)	7.37 (0.26) (6.05 - 8.64)	0.91 (0.26) (-0.34 - 2.67)	0.40, 1.43	<0.001	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	15.29 (0.59) (13.11 - 17.83)	14.34 (0.59) (11.81 - 17.99)	0.95 (0.41) (-1.31 - 4.57)	0.11, 1.79	0.028	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.76 (0.018) (1.66 - 1.83)	1.80 (0.018) (1.69 - 1.90)	-0.037 (0.017) (-0.16 - 0.042)	-0.075, 0.0018	0.059	1.56, 1.91 (1.59 - 1.86)
Arginine	3.30 (0.069) (3.09 - 3.50)	3.58 (0.069) (3.19 - 3.93)	-0.28 (0.078) (-0.83 - 0.0059)	-0.46, -0.10	0.006	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.63 (0.044) (4.44 - 4.80)	4.78 (0.044) (4.46 - 5.01)	-0.15 (0.050) (-0.56 - 0.12)	-0.27, -0.037	0.016	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0049) (0.58 - 0.63)	0.59 (0.0049) (0.56 - 0.62)	0.018 (0.0046) (-0.0071 - 0.053)	0.0085, 0.027	<0.001	0.50, 0.68 (0.53 - 0.66)

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Table VI-2 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.38 (0.085) (7.05 - 7.73)	7.69 (0.085) (7.12 - 8.14)	-0.31 (0.093) (-1.09 - 0.17)	-0.53, -0.095	0.010	6.28, 8.30 (6.69 - 7.92)
Glycine	1.76 (0.016) (1.67 - 1.83)	1.81 (0.016) (1.70 - 1.89)	-0.048 (0.017) (-0.20 - 0.042)	-0.086, -0.0096	0.020	1.53, 1.92 (1.58 - 1.84)
Histidine	1.06 (0.0095) (1.02 - 1.10)	1.09 (0.0095) (1.02 - 1.14)	-0.033 (0.011) (-0.12 - 0.031)	-0.059, -0.0076	0.017	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.88 (0.019) (1.75 - 1.97)	1.95 (0.019) (1.79 - 2.04)	-0.070 (0.019) (-0.24 - 0.11)	-0.11, -0.026	0.006	1.65, 2.06 (1.68 - 2.02)
Leucine	3.06 (0.029) (2.93 - 3.19)	3.17 (0.029) (2.96 - 3.32)	-0.11 (0.031) (-0.36 - 0.072)	-0.18, -0.035	0.008	2.72, 3.39 (2.80 - 3.27)
Lysine	2.64 (0.019) (2.53 - 2.71)	2.68 (0.019) (2.54 - 2.77)	-0.041 (0.023) (-0.23 - 0.090)	-0.094, 0.012	0.110	2.33, 2.84 (2.38 - 2.74)

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Table VI-2 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.58 (0.0053) (0.53 - 0.60)	0.58 (0.0053) (0.53 - 0.60)	0.00012 (0.0062) (-0.039 - 0.071)	-0.013, 0.013	0.985	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.06 (0.028) (1.92 - 2.18)	2.13 (0.028) (1.95 - 2.27)	-0.071 (0.028) (-0.27 - 0.048)	-0.13, -0.0067	0.034	1.80, 2.30 (1.85 - 2.21)
Proline	1.99 (0.021) (1.90 - 2.09)	2.05 (0.021) (1.89 - 2.13)	-0.067 (0.022) (-0.17 - 0.065)	-0.12, -0.015	0.017	1.65, 2.26 (1.74 - 2.16)
Serine	2.04 (0.023) (1.92 - 2.12)	2.09 (0.023) (1.95 - 2.21)	-0.048 (0.026) (-0.19 - 0.054)	-0.11, 0.013	0.105	1.78, 2.27 (1.90 - 2.18)
Threonine	1.56 (0.015) (1.48 - 1.62)	1.58 (0.015) (1.51 - 1.64)	-0.023 (0.015) (-0.10 - 0.052)	-0.058, 0.012	0.169	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.47 (0.0085) (0.44 - 0.53)	0.46 (0.0085) (0.43 - 0.50)	0.0070 (0.0097) (-0.035 - 0.064)	-0.015, 0.029	0.494	0.38, 0.52 (0.39 - 0.50)

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Table VI-2 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Tyrosine	1.37 (0.018) (1.28 - 1.46)	1.42 (0.018) (1.34 - 1.52)	-0.049 (0.021) (-0.20 - 0.078)	-0.098, -0.00046	0.048	1.24, 1.50 (1.26 - 1.49)
Valine	1.98 (0.020) (1.82 - 2.09)	2.06 (0.020) (1.90 - 2.17)	-0.080 (0.022) (-0.27 - 0.13)	-0.13, -0.030	0.006	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.59 (0.16) (11.25 - 12.16)	11.33 (0.16) (10.92 - 12.08)	0.26 (0.060) (-0.15 - 0.62)	0.12, 0.40	0.002	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.06 (0.10) (3.60 - 4.40)	4.04 (0.10) (3.67 - 4.31)	0.028 (0.049) (-0.19 - 0.42)	-0.085, 0.14	0.584	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.20 (0.30) (17.85 - 19.94)	20.91 (0.30) (19.60 - 22.44)	-1.71 (0.19) (-2.71 - -0.90)	-2.15, -1.27	<0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.40 (0.37) (53.42 - 55.67)	53.59 (0.37) (52.33 - 54.99)	0.81 (0.24) (-0.59 - 1.68)	0.25, 1.37	0.010	48.61, 59.37 (50.95 - 56.68)

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Table VI-2 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.12 (0.27) (8.99 - 10.88)	9.49 (0.27) (8.42 - 10.14)	0.63 (0.072) (0.36 - 1.20)	0.46, 0.80	<0.001	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0052) (0.23 - 0.27)	0.26 (0.0052) (0.24 - 0.27)	-0.0012 (0.0031) (-0.013 - 0.020)	-0.0082, 0.0059	0.707	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.093 (0.017) (0.069 - 0.16)	0.090 (0.017) (0.068 - 0.17)	0.0029 (0.0042) (-0.010 - 0.050)	-0.0056, 0.011	0.495	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.27 (0.0038) (0.25 - 0.29)	0.28 (0.0038) (0.27 - 0.30)	-0.013 (0.0029) (-0.023 - 0.0024)	-0.020, -0.0066	0.001	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	1.41 (0.18) (1.08 - 2.17)	1.23 (0.18) (0.89 - 2.11)	0.19 (0.038) (0.018 - 0.42)	0.098, 0.27	0.001	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference varieties. Negative limits set to zero.

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Table VI-3. Statistical Summary of Combined-Site Soybean Seed Anti-Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dwt)	3.17 (0.76) (0.59 - 10.27)	3.16 (0.76) (0.46 - 10.38)	0.013 (0.67) (-4.27 - 8.13)	-1.54, 1.57	0.984	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dwt)	1.30 (0.071) (1.08 - 1.51)	1.39 (0.071) (1.09 - 1.62)	-0.085 (0.035) (-0.29 - 0.15)	-0.17, -0.0034	0.043	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dwt)	0.43 (0.038) (0.32 - 0.59)	0.47 (0.038) (0.36 - 0.60)	-0.036 (0.018) (-0.24 - 0.069)	-0.072, -0.00077	0.045	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dwt)	3.36 (0.078) (3.07 - 4.02)	3.62 (0.078) (3.07 - 4.15)	-0.26 (0.099) (-1.00 - 0.40)	-0.46, -0.062	0.011	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	32.27 (1.40) (26.09 - 39.27)	30.37 (1.40) (25.22 - 34.22)	1.90 (1.79) (-4.76 - 8.72)	-2.23, 6.04	0.319	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dwt)						
Daidzein	1494.97 (155.94) (899.83 - 2305.26)	1340.71 (155.94) (762.49 - 1729.91)	154.26 (65.62) (-258.27 - 795.19)	2.95, 305.57	0.046	0, 2271.38 (451.33 - 2033.05)

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Table VI-3 (continued). Statistical Summary of Combined-Site Soybean Seed Anti-Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	967.01 (90.36) (594.13 - 1496.78)	886.57 (90.36) (588.17 - 1162.01)	80.44 (41.86) (-185.98 - 513.56)	-4.30, 165.19	0.062	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	108.01 (5.24) (77.67 - 119.09)	95.85 (5.24) (68.68 - 122.09)	12.16 (6.91) (-43.86 - 50.41)	-3.77, 28.09	0.116	31.24, 233.60 (73.61 - 231.75)

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[1] dwt = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference varieties. Negative limits set to zero.

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Table VI-4. Statistical Summary of Combined-Site Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	7.29 (0.54) (5.94 - 9.65)	7.39 (0.54) (6.10 - 10.46)	-0.10 (0.27) (-0.89 - 1.56)	-0.71, 0.51	0.712	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	66.48 (1.03) (62.21 - 73.31)	65.66 (1.04) (62.91 - 67.94)	0.83 (0.96) (-3.95 - 6.90)	-1.40, 3.05	0.414	60.69, 73.46 (62.73 - 71.72)
Moisture (% fwt)	75.63 (1.82) (72.40 - 82.80)	75.55 (1.82) (71.60 - 82.70)	0.081 (0.27) (-1.40 - 1.30)	-0.55, 0.71	0.775	62.08, 89.80 (70.40 - 84.10)
Protein	21.52 (0.95) (15.23 - 25.52)	22.32 (0.95) (20.88 - 24.11)	-0.80 (0.80) (-6.26 - 2.75)	-2.67, 1.07	0.350	15.69, 26.63 (18.50 - 25.86)
Total Fat	4.67 (0.66) (2.00 - 7.34)	4.64 (0.66) (2.01 - 6.72)	0.032 (0.26) (-0.68 - 1.96)	-0.57, 0.63	0.904	0, 10.04 (1.57 - 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	30.58 (1.79) (23.30 - 45.11)	27.69 (1.80) (21.79 - 38.15)	2.89 (1.19) (-4.78 - 16.24)	0.45, 5.34	0.021	16.54, 41.80 (20.98 - 39.23)

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Table VI-4 (continued). Statistical Summary of Combined-Site Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	29.63 (1.68) (24.21 - 38.51)	30.49 (1.70) (23.66 - 39.42)	-0.86 (1.22) (-8.13 - 11.03)	-3.65, 1.94	0.503	20.28, 44.03 (24.81 - 42.80)

[1] dwt = dry weight; fwt = fresh weight.
[2] MON 87708 was treated with dicamba.
[3] Mean (S.E.) = least-square mean (standard error).
[4] Control refers to the near isogenic conventional soybean control A3525.
[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference varieties. Negative limits set to zero.

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Table VI-5. Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in Combined-Site Analysis						
Seed Proximate (% dw)						
Protein	41.17	42.41	-2.94	0.040	39.96 - 43.06	35.50, 45.19
Seed Fiber (% dw)						
Acid Detergent Fiber	13.38	12.86	3.99	0.046	11.01 - 15.72	10.06, 18.04
Neutral Detergent Fiber	15.24	14.34	6.33	0.035	12.91 - 18.38	11.36, 19.38
Seed Amino Acid (% dw)						
Arginine	3.37	3.58	-5.88	0.026	3.12 - 3.60	2.55, 3.83
Cystine	0.61	0.59	3.27	<0.001	0.59 - 0.64	0.50, 0.68
Glutamic Acid	7.46	7.69	-3.03	0.037	7.25 - 7.88	6.28, 8.30
Isoleucine	1.90	1.95	-2.42	0.039	1.80 - 2.02	1.65, 2.06

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in Combined-Site Analysis						
Seed Amino Acid (% dw)						
Leucine	3.10	3.17	-2.27	0.049	3.01 - 3.24	2.72, 3.39
Phenylalanine	2.06	2.13	-3.04	0.048	1.98 - 2.14	1.80, 2.30
Proline	1.98	2.05	-3.39	0.014	1.89 - 2.05	1.65, 2.26
Valine	2.00	2.06	-2.76	0.030	1.90 - 2.13	1.72, 2.20
Seed Fatty Acid (% Total FA)						
16:0 Palmitic	11.60	11.33	2.37	0.002	11.02 - 12.15	8.44, 12.56
18:1 Oleic	19.32	20.91	-7.60	<0.001	18.26 - 20.73	15.73, 27.19
18:2 Linoleic	54.37	53.59	1.45	0.012	52.18 - 55.62	48.61, 59.37
18:3 Linolenic	10.04	9.49	5.78	<0.001	8.94 - 10.90	6.01, 12.58

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control (continued)

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708 minus Control) Mean Difference (% of Control)	Mean Difference (MON 87708 minus Control) Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in Combined-Site Analysis						
Seed Fatty Acid (% Total FA)						
22:0 Behenic	0.27	0.28	-3.71	0.006	0.25 - 0.29	0.24, 0.40
Seed Vitamin (mg/100g dw)						
Vitamin E	1.45	1.23	18.16	<0.001	1.11 - 2.27	0, 3.49
Seed Anti-nutrient						
Trypsin Inhibitor (TIU/mg dw)	35.03	30.37	15.37	0.031	23.32 - 51.50	22.05, 41.12
Seed Isoflavone (µg/g dw)						
Daidzein	1571.79	1340.71	17.24	0.007	910.73 - 2297.58	0, 2271.38
Genistein	989.28	886.57	11.59	0.018	654.16 - 1469.13	78.36, 1869.48
Statistical Differences Observed in More than One Individual Site						
Seed Fatty Acid (% Total FA)						
18:1 Oleic Site IARL	19.28	21.67	-11.02	0.001	18.77 - 19.68	15.73, 27.19

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708minus Control) Mean Difference (% of Control)	Mean Difference (MON 87708minus Control) Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in More than One Individual Site						
Seed Fatty Acid (% Total FA)						
18:1 Oleic Site ILCY	19.85	21.57	-7.98	0.013	19.62 - 20.22	15.73, 27.19
18:1 Oleic Site INRC	18.80	20.19	-6.90	<0.001	18.63 - 18.96	15.73, 27.19
18:1 Oleic Site PAHM	18.45	20.01	-7.78	0.011	18.26 - 18.80	15.73, 27.19
18:3 Linolenic Site ILCY	9.09	8.58	5.96	0.006	8.94 - 9.23	6.01, 12.58
18:3 Linolenic Site ILWY	10.65	10.05	5.95	0.014	10.37 - 10.90	6.01, 12.58
18:3 Linolenic Site INRC	10.05	9.31	7.94	<0.001	10.00 - 10.10	6.01, 12.58
18:3 Linolenic Site PAHM	10.03	9.47	5.87	0.026	9.74 - 10.18	6.01, 12.58
Seed Vitamin (mg/100g dw)						
Vitamin E Site IARL	1.26	0.94	33.64	0.008	1.11 - 1.42	0, 3.49

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)^1	MON 87708^2 Mean^3	Control^4 Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval^5
Statistical Differences Observed in More than One Individual Site						
Seed Vitamin (mg/100g dw)						
Vitamin E Site ILCY	2.21	1.86	18.85	0.016	2.11 - 2.27	0, 3.49
Vitamin E Site ILWY	1.15	0.94	21.98	0.017	1.11 - 1.20	0, 3.49
Vitamin E Site PAHM	1.37	1.23	12.00	0.002	1.26 - 1.59	0, 3.49
Seed Amino Acid (% dw)						
Phenylalanine Site ILCY	2.07	2.13	-3.03	0.024	2.05 - 2.08	1.80, 2.30
Phenylalanine Site INRC	2.08	2.20	-5.54	0.037	2.03 - 2.14	1.80, 2.30
Phenylalanine Site PAHM	2.08	2.21	-6.07	0.025	2.03 - 2.11	1.80, 2.30
Proline Site ILCY	1.95	2.06	-5.34	0.004	1.90 - 1.98	1.65, 2.26
Proline Site INRC	2.01	2.06	-2.63	0.020	1.99 - 2.04	1.65, 2.26

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in More than One Individual Site						
Seed Amino Acid (% dw)						
Proline Site PAHM	2.00	2.10	-5.09	0.028	1.93 - 2.04	1.65, 2.26
Seed Fatty Acid (% Total FA)						
18:2 Linoleic Site IARL	54.30	52.70	3.04	0.025	53.70 - 55.34	48.61, 59.37
18:2 Linoleic Site ILCY	54.31	53.26	1.97	0.040	53.67 - 54.63	48.61, 59.37
18:2 Linoleic Site INRC	54.94	54.43	0.93	0.024	54.79 - 55.13	48.61, 59.37
22:0 Behenic Site IARL	0.26	0.28	-4.96	0.030	0.26 - 0.27	0.24, 0.40
22:0 Behenic Site INRC	0.28	0.29	-5.54	0.025	0.27 - 0.28	0.24, 0.40
22:0 Behenic Site PAHM	0.26	0.27	-4.78	0.018	0.25 - 0.27	0.24, 0.40

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)^{1}	MON 87708^{2} Mean^{3}	Control^{4} Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval^{5}
Statistical Differences Observed in More than One Individual Site						
Seed Proximate (% dw)						
Moisture (% fw) Site IARL	7.84	6.07	29.21	0.010	7.39 - 8.73	4.27, 9.58
Moisture (% fw) Site PAHM	9.53	10.50	-9.24	0.011	9.21 - 9.91	4.27, 9.58
Protein Site INRC	41.47	43.58	-4.85	0.049	40.22 - 43.06	35.50, 45.19
Protein Site PAHM	40.38	43.69	-7.57	0.002	39.96 - 40.97	35.50, 45.19
Seed Amino Acid (% dw)						
Arginine Site INRC	3.40	3.72	-8.50	0.007	3.35 - 3.50	2.55, 3.83
Arginine Site PAHM	3.39	3.88	-12.75	0.002	3.35 - 3.44	2.55, 3.83
Glutamic Acid Site ILCY	7.44	7.61	-2.24	0.039	7.33 - 7.51	6.28, 8.30
Glutamic Acid Site PAHM	7.42	8.00	-7.24	0.007	7.32 - 7.50	6.28, 8.30

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)¹	MON 87708² Mean³	Control⁴ Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval⁵
Statistical Differences Observed in More than One Individual Site						
Seed Amino Acid (% dw)						
Leucine Site ILCY	3.11	3.17	-1.82	0.008	3.08 - 3.13	2.72, 3.39
Leucine Site PAHM	3.10	3.28	-5.46	0.009	3.08 - 3.11	2.72, 3.39
Lysine Site ILWY	2.68	2.63	1.76	0.006	2.66 - 2.69	2.33, 2.84
Lysine Site PAHM	2.64	2.75	-4.02	0.025	2.62 - 2.65	2.33, 2.84
Seed Isoflavone (µg/g dw)						
Glycitein Site ILWY	96.96	79.70	21.65	0.001	92.19 - 103.25	31.24, 233.60
Glycitein Site INRC	119.27	98.42	21.19	0.003	113.04 - 124.24	31.24, 233.60
Statistical Differences Observed in One Individual Site						
Seed Amino Acid (% dw)						
Alanine Site PAHM	1.79	1.86	-3.65	0.046	1.76 - 1.81	1.56, 1.91

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

			Mean Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (% of Control)	Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in One Individual Site						
Seed Amino Acid (% dw)						
Aspartic Acid Site PAHM	4.66	4.94	-5.62	0.008	4.64 - 4.69	4.04, 5.13
Cystine Site INRC	0.62	0.59	5.30	0.029	0.60 - 0.63	0.50, 0.68
Glycine Site PAHM	1.77	1.86	-4.84	0.014	1.76 - 1.78	1.53, 1.92
Histidine Site PAHM	1.07	1.13	-5.37	0.008	1.07 - 1.08	0.93, 1.16
Isoleucine Site PAHM	1.89	2.00	-5.67	0.035	1.88 - 1.91	1.65, 2.06
Serine Site ILWY	2.10	2.06	2.11	0.026	2.09 - 2.11	1.78, 2.27
Threonine Site ILWY	1.59	1.55	2.85	<0.001	1.58 - 1.60	1.40, 1.69
Valine Site PAHM	2.00	2.13	-5.93	0.035	2.00 - 2.00	1.72, 2.20

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Table VI-5 (continued). Summary of Differences (α=0.05) for the Comparison of Soybean Component Levels for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean[3]	Control[4] Mean	Mean Difference (MON 87708 minus Control): Mean Difference (% of Control)	Mean Difference (MON 87708 minus Control): Significance (p-Value)	MON 87708 Range	Conventional Tolerance Interval[5]
Statistical Differences Observed in One Individual Site						
Seed Fatty Acid (% Total FA)						
16:0 Palmitic Site IARL	11.51	11.00	4.67	0.001	11.39 - 11.63	8.44, 12.56
20:1 Eicosenoic Site ILCY	0.15	0.16	-4.82	0.028	0.15 - 0.16	0.022, 0.24
Seed Anti-nutrient						
Trypsin Inhibitor (TIU/mg dw) Site ILWY	38.93	29.73	30.95	0.033	37.89 - 39.49	22.05, 41.12
Forage Proximate (% dw)						
Ash Site INRC	6.20	6.95	-10.70	0.047	5.87 - 6.72	3.36, 10.84
Moisture (% fw) Site IARL	83.47	81.97	1.83	0.027	82.70 - 84.10	62.08, 89.80
Protein Site IARL	25.76	23.00	12.02	0.022	24.63 - 27.04	15.69, 26.63

[1] dw = dry weight; fw = fresh weight; FA = fatty acid; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean = least-square mean.

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table VI-6. Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708 ² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Proximate (% dw)						
Ash	5.22 (0.067) (4.89 - 5.51)	5.12 (0.067) (4.73 - 5.47)	0.10 (0.055) (-0.28 - 0.55)	-0.010, 0.21	0.073	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	37.30 (0.50) (35.27 - 39.79)	36.64 (0.50) (34.11 - 38.45)	0.66 (0.40) (-1.89 - 4.52)	-0.26, 1.58	0.138	32.07, 40.08 (33.82 - 39.26)
Moisture (% fw)	7.30 (0.65) (5.68 - 9.91)	7.14 (0.65) (5.79 - 10.60)	0.16 (0.52) (-1.19 - 2.89)	-1.04, 1.36	0.771	4.27, 9.58 (5.50 - 9.23)
Protein	41.17 (0.39) (39.96 - 43.06)	42.41 (0.39) (40.69 - 43.85)	-1.25 (0.51) (-3.89 - 0.47)	-2.42, -0.069	0.040	35.50, 45.19 (37.06 - 43.42)
Total Fat	16.32 (0.59) (13.95 - 18.66)	15.84 (0.59) (14.40 - 18.39)	0.48 (0.31) (-1.73 - 1.70)	-0.23, 1.19	0.155	12.33, 24.10 (15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	13.38 (0.40) (11.01 - 15.72)	12.86 (0.40) (11.62 - 14.57)	0.51 (0.25) (-0.72 - 2.45)	0.0084, 1.02	0.046	10.06, 18.04 (12.07 - 17.46)

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Table VI-6 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Crude Fiber	7.50 (0.26) (6.14 - 8.89)	7.37 (0.26) (6.05 - 8.64)	0.13 (0.26) (-1.33 - 1.19)	-0.39, 0.64	0.620	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	15.24 (0.59) (12.91 - 18.38)	14.34 (0.59) (11.81 - 17.99)	0.91 (0.41) (-2.27 - 4.17)	0.064, 1.75	0.035	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.78 (0.018) (1.72 - 1.84)	1.80 (0.018) (1.69 - 1.90)	-0.025 (0.017) (-0.10 - 0.043)	-0.063, 0.014	0.174	1.56, 1.91 (1.59 - 1.86)
Arginine	3.37 (0.069) (3.12 - 3.60)	3.58 (0.069) (3.19 - 3.93)	-0.21 (0.078) (-0.55 - 0.051)	-0.39, -0.031	0.026	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.68 (0.044) (4.57 - 4.90)	4.78 (0.044) (4.46 - 5.01)	-0.10 (0.050) (-0.35 - 0.10)	-0.22, 0.014	0.078	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0049) (0.59 - 0.64)	0.59 (0.0049) (0.56 - 0.62)	0.019 (0.0046) (-0.0068 - 0.047)	0.010, 0.029	<0.001	0.50, 0.68 (0.53 - 0.66)

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Table VI-6 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Glutamic Acid	7.46 (0.085) (7.25 - 7.88)	7.69 (0.085) (7.12 - 8.14)	-0.23 (0.093) (-0.70 - 0.12)	-0.45, -0.018	0.037	6.28, 8.30 (6.69 - 7.92)
Glycine	1.77 (0.016) (1.74 - 1.85)	1.81 (0.016) (1.70 - 1.89)	-0.034 (0.017) (-0.13 - 0.041)	-0.073, 0.0042	0.074	1.53, 1.92 (1.58 - 1.84)
Histidine	1.07 (0.0095) (1.05 - 1.11)	1.09 (0.0095) (1.02 - 1.14)	-0.021 (0.011) (-0.073 - 0.029)	-0.047, 0.0044	0.092	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.90 (0.019) (1.80 - 2.02)	1.95 (0.019) (1.79 - 2.04)	-0.047 (0.019) (-0.22 - 0.085)	-0.091, -0.0028	0.039	1.65, 2.06 (1.68 - 2.02)
Leucine	3.10 (0.029) (3.01 - 3.24)	3.17 (0.029) (2.96 - 3.32)	-0.072 (0.031) (-0.23 - 0.055)	-0.14, -0.00024	0.049	2.72, 3.39 (2.80 - 3.27)
Lysine	2.65 (0.019) (2.60 - 2.76)	2.68 (0.019) (2.54 - 2.77)	-0.026 (0.023) (-0.13 - 0.083)	-0.079, 0.027	0.295	2.33, 2.84 (2.38 - 2.74)

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Table VI-6 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Methionine	0.58 (0.0053) (0.55 - 0.61)	0.58 (0.0053) (0.53 - 0.60)	0.0013 (0.0062) (-0.036 - 0.056)	-0.011, 0.014	0.834	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.06 (0.028) (1.98 - 2.14)	2.13 (0.028) (1.95 - 2.27)	-0.065 (0.028) (-0.18 - 0.023)	-0.13, -0.00067	0.048	1.80, 2.30 (1.85 - 2.21)
Proline	1.98 (0.021) (1.89 - 2.05)	2.05 (0.021) (1.89 - 2.13)	-0.070 (0.022) (-0.17 - 0.043)	-0.12, -0.018	0.014	1.65, 2.26 (1.74 - 2.16)
Serine	2.07 (0.023) (1.91 - 2.11)	2.09 (0.023) (1.95 - 2.21)	-0.021 (0.026) (-0.19 - 0.073)	-0.081, 0.039	0.449	1.78, 2.27 (1.90 - 2.18)
Threonine	1.57 (0.015) (1.49 - 1.61)	1.58 (0.015) (1.51 - 1.64)	-0.0093 (0.015) (-0.088 - 0.052)	-0.044, 0.026	0.556	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.47 (0.0085) (0.41 - 0.50)	0.46 (0.0085) (0.43 - 0.50)	0.0095 (0.0097) (-0.053 - 0.049)	-0.013, 0.032	0.359	0.38, 0.52 (0.39 - 0.50)

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Table VI-6 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.41 (0.018) (1.35 - 1.48)	1.42 (0.018) (1.34 - 1.52)	-0.015 (0.021) (-0.086 - 0.098)	-0.064, 0.034	0.506	1.24, 1.50 (1.26 - 1.49)
Valine	2.00 (0.020) (1.90 - 2.13)	2.06 (0.020) (1.90 - 2.17)	-0.057 (0.022) (-0.25 - 0.097)	-0.11, -0.0069	0.030	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.60 (0.16) (11.02 - 12.15)	11.33 (0.16) (10.92 - 12.08)	0.27 (0.060) (-0.094 - 0.59)	0.13, 0.41	0.002	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.04 (0.10) (3.55 - 4.57)	4.04 (0.10) (3.67 - 4.31)	0.0057 (0.049) (-0.23 - 0.38)	-0.11, 0.12	0.909	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.32 (0.30) (18.26 - 20.73)	20.91 (0.30) (19.60 - 22.44)	-1.59 (0.19) (-2.82 - -0.045)	-2.03, -1.15	<0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.37 (0.37) (52.18 - 55.62)	53.59 (0.37) (52.33 - 54.99)	0.78 (0.24) (-0.98 - 2.61)	0.22, 1.34	0.012	48.61, 59.37 (50.95 - 56.68)

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Table VI-6 (continued). Statistical Summary of Combined-Site Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Compoent (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.04 (0.27) (8.94 - 10.90)	9.49 (0.27) (8.42 - 10.14)	0.55 (0.072) (-0.18 - 1.01)	0.38, 0.72	<0.001	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0052) (0.23 - 0.29)	0.26 (0.0052) (0.24 - 0.27)	-0.0013 (0.0031) (-0.014 - 0.022)	-0.0083, 0.0058	0.684	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.092 (0.017) (0.065 - 0.16)	0.090 (0.017) (0.068 - 0.17)	0.0011 (0.0042) (-0.013 - 0.058)	-0.0074, 0.0096	0.795	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.27 (0.0038) (0.25 - 0.29)	0.28 (0.0038) (0.27 - 0.30)	-0.010 (0.0029) (-0.023 - 0.0054)	-0.017, -0.0038	0.006	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	1.45 (0.18) (1.11 - 2.27)	1.23 (0.18) (0.89 - 2.11)	0.22 (0.038) (0.0086 - 0.49)	0.14, 0.31	<0.001	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table VI-7. Statistical Summary of Combined-Site Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	3.05 (0.76) (1.18 - 6.35)	3.16 (0.76) (0.46 - 10.38)	-0.12 (0.67) (-7.83 - 3.07)	-1.67, 1.44	0.867	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.33 (0.071) (1.05 - 1.48)	1.39 (0.071) (1.09 - 1.62)	-0.060 (0.035) (-0.21 - 0.26)	-0.14, 0.022	0.129	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.46 (0.038) (0.34 - 0.58)	0.47 (0.038) (0.36 - 0.60)	-0.0069 (0.018) (-0.065 - 0.056)	-0.042, 0.029	0.697	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.48 (0.078) (2.94 - 3.85)	3.62 (0.078) (3.07 - 4.15)	-0.15 (0.099) (-0.82 - 0.53)	-0.35, 0.054	0.147	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	35.03 (1.40) (23.32 - 51.50)	30.37 (1.40) (25.22 - 34.22)	4.67 (1.79) (-2.94 - 18.17)	0.53, 8.80	0.031	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	1571.79 (155.94) (910.73 - 2297.58)	1340.71 (155.94) (762.49 - 1729.91)	231.08 (65.62) (-187.35 - 691.83)	79.76, 382.39	0.007	0, 2271.38 (451.33 - 2033.05)

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Table VI-7 (continued). Statistical Summary of Combined-Site Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708 [2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	989.28 (90.36) (654.16 - 1469.13)	886.57 (90.36) (588.17 - 1162.01)	102.71 (41.86) (-116.63 - 400.27)	17.96, 187.46	0.018	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	110.40 (5.24) (83.25 - 133.73)	95.85 (5.24) (68.68 - 122.09)	14.55 (6.91) (-2.04 - 37.48)	-1.38, 30.48	0.068	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table VI-8. Statistical Summary of Combined-Site Soybean Forage Nutrients for MON 87708 (Untreated) Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	7.01 (0.54) (4.92 - 9.45)	7.39 (0.54) (6.10 - 10.46)	-0.39 (0.27) (-1.57 - 0.97)	-0.99, 0.22	0.183	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	65.55 (1.03) (61.64 - 71.05)	65.66 (1.04) (62.91 - 67.94)	-0.11 (0.96) (-6.11 - 4.64)	-2.33, 2.12	0.913	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	75.81 (1.82) (72.30 - 84.10)	75.55 (1.82) (71.60 - 82.70)	0.25 (0.27) (-1.00 - 2.70)	-0.37, 0.88	0.379	62.08, 89.80 (70.40 - 84.10)
Protein	22.70 (0.95) (16.28 - 27.04)	22.32 (0.95) (20.88 - 24.11)	0.38 (0.80) (-5.21 - 4.89)	-1.49, 2.25	0.648	15.69, 26.63 (18.50 - 25.86)
Total Fat	4.70 (0.66) (2.61 - 6.52)	4.64 (0.66) (2.01 - 6.72)	0.055 (0.26) (-1.38 - 1.63)	-0.55, 0.66	0.838	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	27.72 (1.79) (23.32 - 34.63)	27.69 (1.80) (21.79 - 38.15)	0.036 (1.19) (-7.68 - 4.38)	-2.41, 2.48	0.976	16.54, 41.80 (20.98 - 39.23)

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Table VI-8 (continued). Statistical Summary of Combined-Site Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	30.98 (1.68) (25.38 - 37.80)	30.49 (1.70) (23.66 - 39.42)	0.49 (1.22) (-5.93 - 10.81)	-2.31, 3.29	0.698	20.28, 44.03 (24.81 - 42.80)

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[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table VI-9. Literature and ILSI Database Ranges for Components in Soybean Seed and Forage

Seed Tissue Components[1]	Literature Range[2]	ILSI Range[3]
Seed Nutrients		
Proximates (% dwt)		
Ash	4.61 – 6.32[a]; 4.32 – 5.88[b]	3.89 – 6.99
Carbohydrates by calculation	32.75 – 40.98[a]; 29.88 – 43.48[b]	29.6 – 50.2
Moisture (% fwt)	6.24 – 12.10[a]; 5.44 – 11.70[b]	4.7 – 34.4
Protein	34.78 – 43.35[a]; 32.29 – 42.66[b]	33.19 – 45.48
Total Fat	14.40 – 20.91[a]; 15.10 – 23.56[b]; 15.5[c] – 24.7[c]	8.10 – 23.56
Fiber (% dwt)		
Acid Detergent Fiber	9.22 – 26.26[a]; 11.81 – 19.45[b]	7.81 – 18.61
Neutral Detergent Fiber	10.79 – 23.90[a]; 13.32 – 23.57[b]	8.53 – 21.25
Amino Acids (% dwt)		
Alanine	1.62 – 1.89[a]; 1.43 – 1.93[b]	1.51 – 2.10
Arginine	2.57 – 3.34[a]; 2.15 – 3.05[b]	2.29 – 3.40
Aspartic acid	4.16 – 5.02[a]; 4.01 – 5.72[b]	3.81 – 5.12
Cystine/Cysteine	0.52 – 0.69[a]; 0.41 – 0.71[b]	0.37 – 0.81
Glutamic acid	6.52 – 8.19[a]; 5.49 – 8.72[b]	5.84 – 8.20
Glycine	1.59 – 1.90[a]; 1.41 – 1.99[b]	1.46 – 2.00
Histidine	0.96 – 1.13[a]; 0.86 – 1.24[b]	0.88 – 1.18
Isoleucine	1.59 – 2.00[a]; 1.41 – 2.02[b]	1.54 – 2.08
Leucine	2.79 – 3.42[a]; 2.39 – 3.32[b]	2.59 – 3.62
Lysine	2.36 – 2.77[a]; 2.19 – 3.15[b]	2.29 – 2.84
Methionine	0.45 – 0.63[a]; 0.39 – 0.65[b]	0.43 – 0.68
Phenylalanine	1.82 – 2.29[a]; 1.62 – 2.44[b]	1.63 – 2.35
Proline	1.83 – 2.23[a]; 1.63 – 2.25[b]	1.69 – 2.28
Serine	1.95 – 2.42[a]; 1.51 – 2.30[b]	1.11 – 2.48
Threonine	1.44 – 1.71[a]; 1.23 – 1.74[b]	1.14 – 1.86
Tryptophan	0.30 – 0.48[a]; 0.41 – 0.56[b]	0.36 – 0.50
Tyrosine	1.27 – 1.53[a]; 0.74 – 1.31[b]	1.02 – 1.61
Valine	1.68 – 2.11[a]; 1.50 – 2.13[b]	1.60 – 2.20
Fatty Acids (% total FA)		
8:0 Caprylic	not available	0.148 – 0.148
10:0 Capric	0.15 – 0.27[b]	not available
12:0 Lauric	not available	0.082 – 0.132
14:0 Myristic	0.063 – 0.11[b]	0.071 – 0.238
14:1 Myristoleic	not available	0.121 – 0.125
15:0 Pentadecanoic	not available	not available
15:1 Pentadecenoic	not available	not available
16:0 Palmitic	9.80 – 12.63[b]	9.55 – 15.77
16:1 Palmitoleic	0.055 – 0.14[b]	0.086 – 0.194
17:0 Heptadecanoic	0.076 – 0.13[b]	0.085 – 0.146
17:1 Heptadecenoic	0.019 – 0.064[b]	0.073 – 0.087
18:0 Stearic	3.21 – 5.63[b]	2.70 – 5.88
18:1 Oleic	16.69 – 35.16[b]	14.3 – 32.2
18:2 Linoleic	44.17 – 57.72[b]	42.3 – 58.8
18:3 Gamma Linolenic	not available	not available
18:3 Linolenic	4.27 – 9.90[b]	3.00 – 12.52

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Table VI-9 (continued). Literature and ILSI Database Ranges for Components in Soybean Seed and Forage

Seed Tissue Components[1]	Literature Range[2]	ILSI Range[3]
Seed Nutrients		
Fatty Acids (% total FA)		
20:0 Arachidic	0.35 – 0.57[b]	0.163 – 0.482
20:1 Eicosenoic	0.13 – 0.30[b]	0.140 – 0.350
20:2 Eicosadienoic	0.016 – 0.071[b]	0.077 – 0.245
20:3 Eicosatrienoic	not available	not available
20:4 Arachidonic	not available	not available
22:0 Behenic	0.35 – 0.59[b]	0.277 – 0.595
22:1 Erucic	not available	not available
Vitamins (mg/100g dwt)		
Vitamin E	1.29 – 4.80[a]; 1.12 – 8.08[b]	0.19 – 6.17
Seed Anti-Nutrients		
Lectin (H.U./mg fwt)	0.45 – 10.87[a]; 0.090 – 11.18[b]	0.09 – 8.46
Trypsin Inhibitor (TIU/mg dwt)	20.79 – 59.03[a]; 18.14 – 42.51[b]	19.59 – 118.68
Phytic Acid (% dwt)	0.41 – 1.92[a]; 0.81 – 2.66[b]	0.63 – 1.96
Raffinose (% dwt)	0.26 – 0.84[a]; 0.43 – 1.85[b]	0.21 – 0.66
Stachyose (% dwt)	1.53 – 3.04[a]; 1.97 – 6.65[b]	1.21 – 3.50
Isoflavones	**(µg/g dwt)**	**(mg/kg dwt)**
Daidzein	224.03 – 1571.91[a]; 198.95 – 1458.24[b]	60.0 – 2453.5
Genistein	338.24 – 1488.89[a]; 148.06 – 1095.57[b]	144.3 – 2837.2
Glycitein	52.72 – 298.57[a]; 32.42 – 255.94[b]	15.3 – 310.4

Forage Tissue Components[1]	Literature Range[2]	ILSI Range[3]
Forage Nutrients		
Proximate (% dwt)		
Ash	5.28 – 9.24[a]; 4.77 – 8.54[b]	6.72 – 10.78
Carbohydrates by calculation	62.25 – 72.30[a]; 60.61 – 77.26[b]	59.8 – 74.7
Moisture (% fwt)	68.50 – 78.40[a]; 62.76 – 80.20[b]	73.5 – 81.6
Protein	16.48 – 24.29[a]; 12.68 – 23.29[b]	14.38 – 24.71
Total Fat	2.65[4] – 9.87[a]; 2.96 – 7.88[b]	1.302 – 5.132
Fiber (% dwt)		
Acid Detergent Fiber	23.86 – 50.89[a]; 25.49 – 47.33[b]	not available
Neutral Detergent Fiber	19.61 – 43.70[a]; 30.96 – 54.55[b]	not available

[1] fwt = fresh weight; dwt = dry weight; H.U. = hemagglutinating unit; TIU = trypsin inhibitor unit.

[2] Literature range references: [a](Lundry et al., 2008); [b](Berman et al., 2009); [c](OECD, 2001).

[4] ILSI Crop Composition Database (2006).

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VI.B. Compositional Assessment Conclusion

Analyses of nutrient and anti-nutrient levels in both dicamba-treated and untreated MON 87708 and the near isogenic conventional control A3525 were conducted to assess compositional equivalence. The tissues analyzed included seed and forage harvested from plants grown at five field sites in the U.S. during the 2008 field season. The composition analysis, conducted in accordance with OECD guidelines, also included measurement of nutrients and anti-nutrients in the commercial reference varieties concurrently grown with MON 87708 to provide data on natural variability of each compositional component. All soybean plants including MON 87708, the conventional control, and the commercial reference varieties were treated with maintenance pesticides as necessary throughout the growing season. In addition, MON 87708 plots were either treated at the V2-V3 growth stage with dicamba herbicide at the maximum in-crop label rate (0.5 lb a.e./acre) or not treated with dicamba herbicide.

For MON 87708 treated, the combined-site analysis of both seed and forage showed no statistically significant differences between MON 87708 and conventional control for 21 (42.0%) of the 50 mean value comparisons. Of the statistically significant differences observed, one was from the forage analysis, and 28 were from the seed analysis. Nutrient component differences in seed included mean values for ash, carbohydrates by calculation, protein and 12 amino acids, five fatty acids, ADF, NDF, crude fiber, and vitamin E. In the combined-site analysis, all nutrient component differences in seed between MON 87708 and the conventional control were of small relative magnitude with respect to the conventional control and, whether increased or decreased, ranged from 1.51% to 12.37% for the three proximates, amino acids, fatty acids, and fibers, and 15.13% for vitamin E. Two of the nutrient components in the combined-site analysis (decreased levels of 18:1 oleic acid and increased levels of 18:3 linolenic acid) were also observed to be statistically different at all five individual sites, and one nutrient component (vitamin E) was observed to be increased at four of the five individual sites as in the combined-site analysis. The other combined-site differences occurred at fewer or none of the individual sites. Anti-nutrient component differences in seed were observed in mean values for phytic acid, raffinose, stachyose, and daidzein. In the combined-site analysis, all anti-nutrient component differences in seed between MON 87708 and the conventional control were of small relative magnitude, with respect to the conventional control, and ranged from a 6.14% decrease (phytic acid) to an 11.51% increase (daidzein). None of the anti-nutrient components were observed to be statistically different at more than two of the five individual sites. The only nutrient component difference in forage for the combined-site analysis was observed in ADF and its relative magnitude of difference, with respect to the conventional control, was 10.45%. No differences between MON 87708 and the conventional control ADF mean values were observed at any of the five individual sites. Mean values of MON 87708 components with statistically significant differences to the conventional control were all within the 99% tolerance interval established from the commercial reference varieties grown concurrently and at the same field sites, as well as ranges in the scientific literature and the ILSI Crop Composition Database.

For MON 87708 (untreated) the combined-site analysis of both seed and forage showed no statistically significant differences between MON 87708 (untreated) and conventional control for 30 (60.0%) of the 50 mean value comparisons. Of the statistically significant differences observed, none were from the forage analysis, and 20 were from the seed analysis. Nutrient component differences in seed included mean values for protein and eight amino acids, five fatty acids, ADF, NDF, and vitamin E. In the combined-site analysis, all nutrient component differences in seed between MON 87708 (untreated) and the conventional control were of small relative magnitude with respect to the conventional control and, whether increased or decreased, ranged from 1.45% to 7.60% for protein and amino acids, fatty acids, and fibers, and 18.16% for vitamin E. None of the nutrient components in the combined-site analysis were observed to be statistically different at all five individual sites. Anti-nutrient component differences in seed were observed in mean values for trypsin inhibitor, daidzein, and genistein. In the combined-site analysis, all anti-nutrient component differences in seed between MON 87708 (untreated) and the conventional control were of small relative magnitude, with respect to the conventional control, and ranged from an 11.59% increase (genistein), 15.37% increase (trypsin inhibitor), and a 17.24% increase (daidzein). None of the anti-nutrient components from the combined-site analysis were observed to be statistically different at more than one of the five individual sites. No nutrient component differences in forage for the combined-site analysis were observed. Mean values of MON 87708 components with statistically significant differences to the conventional control were all within the 99% tolerance interval established from the commercial reference varieties grown concurrently and at the same field sites, as well as ranges in the scientific literature and the ILSI Crop Composition Database.

In summary, a comprehensive evaluation of key nutrients and anti-nutrients in seed and key nutrients in forage for both dicamba-treated and untreated MON 87708 supports the conclusion that soybean seed and forage produced from MON 87708 are compositionally equivalent to that of conventional soybean and that neither the dicamba tolerance trait in MON 87708, nor the dicamba herbicide treatment, applied according to maximum in-crop label rates (including the associated dicamba residue levels) have a meaningful impact on the composition and therefore on the food and feed safety or the nutritional quality of MON 87708 compared to conventional soybean.

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VII. PHENOTYPIC, AGRONOMIC, AND ENVIRONMENTAL INTERACTIONS ASSESSMENT

This section provides an assessment of the phenotypic, agronomic, and environmental interaction characteristics, including plant-symbiont associations of both dicamba treated and untreated MON 87708 compared to the near isogenic conventional soybean control A3525. Analysis of the untreated MON 87708 allows an assessment of the effect of the inserted gene only. However, for this product, since DCSA and formaldehyde are reaction products formed in the presence of dicamba herbicide, and since salicylic acid and formaldehyde are known to be involved in plant defense responses, dicamba treated MON 87708 data are supplied as well. The data support a determination that MON 87708 is similar to conventional soybean with the exception of the dicamba tolerance trait and, therefore, is no more likely to pose a plant pest risk than conventional soybean. These conclusions are based on the results of multiple evaluations.

Phenotypic, agronomic, and environmental interaction characteristics of both dicamba-treated and untreated MON 87708 were evaluated in a comparative manner to assess plant pest potential. These assessments included evaluation of seed germination characteristics, plant growth and development characteristics, observations for plant responses to abiotic stress, plant-disease and plant-arthropod interactions, pollen characteristics, and plant-symbiont interaction characteristics. Results from the phenotypic, agronomic, and environmental interactions assessment demonstrate that MON 87708 does not possess weedy characteristics, increased susceptibility or tolerance to specific abiotic stress, diseases, or arthropods, or characteristics that would confer a plant pest risk compared to the conventional control.

VII.A. Characteristics Measured for Assessment

A detailed phenotypic description of the regulated article is requested as part of the petition for determination of nonregulated status in 7 CFR § 340.6 including differences from the unmodified recipient organism that would "substantiate that the regulated article is unlikely to pose a greater plant pest risk than the unmodified organism from which it was derived". As part of the characterization of MON 87708, data were collected to provide a detailed phenotypic, agronomic, and environmental interaction description of both dicamba-treated and untreated MON 87708 and included an evaluation of specific characteristics related to altered weediness or plant pest potential.

The plant characterization and assessment of MON 87708 encompassed six general data categories: 1) seed germination, dormancy, and emergence; 2) vegetative growth; 3) reproductive development (including pollen characteristics); 4) seed retention on the plant and lodging; 5) plant response to abiotic stress and interactions with diseases and arthropods; and 6) plant-symbiont interactions. An overview of the characteristics assessed is presented in Table VII-1.

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The data were evaluated from a basis of familiarity (OECD, 1993) and were comprised of a combination of field, greenhouse, and laboratory assessments conducted by scientists who are familiar with the production and evaluation of soybean. In each of these assessments, the dicamba-treated and/or untreated MON 87708 was compared to the near isogenic conventional soybean control A3525 that has a genetic background similar to MON 87708 but does not possess the dicamba tolerance trait. In addition, multiple commercial reference varieties (see Appendices F-I and Tables F-1, G-1, and I-1) were included to provide a range of comparative values that are representative of existing commercial soybean varieties for each measured phenotypic, agronomic, and environmental interaction characteristic. Commercial reference soybean varieties are developed through a process of selecting and breeding for various desirable soybean characteristics and can provide a range of natural variability for characteristics and context for interpreting experimental results.

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Table VII-1. Phenotypic, Agronomic, and Environmental Interaction Characteristics Evaluated in U.S. Field Trials, Laboratory, or Greenhouse Tests

Data category	Characteristics measured (associated section where discussed)	Evaluation timing (setting of evaluation)[1]	Evaluation description (measurement endpoints)
Seed germination, dormancy, and emergence	Normal germinated (VII.C.1)	Day 5 and 8 (20/30°C) (laboratory)	Percentage of seed producing seedlings exhibiting normal developmental characteristics
	Abnormal germinated (VII.C.1)	Day 8 (20/30°C) (laboratory)	Percentage of seed producing seedlings that could not be classified as normal germinated
	Germinated (VII.C.1)	Day 5, 8, and 13 (10, 20, 30, 10/20 and 10/30°C) (laboratory)	Percentage of seed that had germinated normally and abnormally
	Dead (VII.C.1)	Day 5 and 8 (10, 20, 30, 10/20, 10/30, and 20/30°C); Day 13 (10, 20, 30, 10/20 and 10/30°C) (laboratory)	Percentage of seed that had visibly deteriorated and become soft to the touch (also included non-viable hard and non-viable firm-swollen seed)
	Viable hard (VII.C.1)	Day 8 (20/30°C); Day 13 (10, 20, 30, 10/20 and 10/30°C) (laboratory)	Percentage of seed that did not imbibe water and remained hard to the touch (viability determined by a tetrazolium test[2])
	Viable firm-swollen (VII.C.1)	Day 8 (20/30°C); Day 13 (10, 20, 30, 10/20 and 10/30°C) (laboratory)	Percentage of seed that imbibed water and were firm to the touch but did not germinate (viability determined by a tetrazolium test[2])
	Early stand count (VII.C.2.3)	V2 - V4 (Field)	Number of emerged plants in two rows, standardized to 20 ft rows
	Final stand count (VII.C.2.3)	Maturity, R8 (Field)	Number of plants in two rows, standardized to 20 ft rows
Vegetative growth	Seedling vigor (VII.C.2.3)	V2 - V4 (Field)	Rated on a 1-9 scale, where 1 = excellent, 5 = average, and 9 = poor vigor
	Growth stage assessment (VII.C.2.3)	Every 2-3 weeks, V2-R8 (Field)	Average soybean plant growth stage per plot
	Flower color (VII.C.2.3)	Flowering, R2 (Field)	Color of flowers: purple, white, or mixed
	Plant pubescence[3] (VII.C.2.3)	Maturity, R8 (Field)	Pubescence on plants in each plot categorized as hairy or hairless
	Plant height (VII.C.2.3)	Maturity, R8 (Field)	Distance (in) from the soil surface to the uppermost node on the main stem of five representative plants per plot
Reproductive development	Days to 50% flowering (VII.C.2.3)	Flowering, R1-R2 (Field)	Calendar day number (days from January 1) when approximately 50% of the plants in each plot were flowering
	Pollen viability (VII.C.3)	Flowering, R1-R2 (laboratory)	Percentage of viable pollen based on pollen grain staining characteristics
	Pollen morphology (VII.C.3)	Flowering, R1-R2 (laboratory)	Diameter (µm) of viable pollen grains
	Seed moisture (VII.C.2.3	Harvest (Field)	Percent moisture content of harvested seed
	100 seed weight (VII.C.2.3)	Harvest (Field)	Mass (g) of 100 harvested seed
	Test weight[3] (VII.C.2.3)	Harvest (Field)	Mass (lb) of a bushel of harvested seed
	Yield (VII.C.2.3)	Harvest (Field)	Bushels of harvested seed per acre, adjusted to 13% moisture

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Table VII-1 (continued). Phenotypic, Agronomic and Environmental Interaction Characteristics Evaluated in U.S. Field Trials, Laboratory or Greenhouse Tests

Data category	Characteristics measured (associated section where discussed)	Evaluation timing (setting of evaluation)[1]	Evaluation description (measurement endpoints)
Seed retention and lodging	Lodging (VII.C.2.3)	Maturity, R8 (Field)	Rated on 0-9 scale, where 0 = completely erect and 9 = completely flat or lodged
	Pod shattering (VII.C.2.3)	Maturity, R8 (Field)	Rated on 0-9 scale, where 0 = no shattering and 9 = completely shattered
Plant-environment interactions	Plant response to abiotic stress (VII.C.2.4)	Four times per growing season (Field)	Qualitative assessment of each plot, with rating on a 0-9 scale, where 0 = no symptoms and 9 = severe symptoms
	Disease damage (VII.C.2.4)	Four times per growing season (Field)	Qualitative assessment of each plot, with rating on a 0-9 scale, where 0 = no symptoms and 9 = severe symptoms
	Arthropod-related damage (VII.C.2.4)	Four times during growing season (Field)	Damage assessed on upper four nodes of 10 representative plants per plot using arthropod-specific 0-5 rating scales of increasing severity
	Arthropod abundance (VII.C.2.4) [3]	Four times during growing season (Field)	Quantitative assessment of pest and beneficial arthropods
Plant-symbiont interactions[3]	Biomass (VII.C.4)	6 weeks after emergence (Greenhouse)	Nodule, root, and shoot dry weight (g/plant)
	Nodule number (VII.C.4)	6 weeks after emergence (Greenhouse)	Nodule number
	Total nitrogen (VII.C.4)	6 weeks after emergence (Greenhouse)	Shoot total nitrogen (% and g/plant)

[1] Soybean plant growth stages were determined using descriptions and guidelines outlined in Soybean Growth and Development (ISU, 2004).

[2] Viability of hard and firm-swollen seed were determined by a tetrazolium test (AOSA, 2000).

[3] Plant pubescence, test weight, arthropod abundance, and plant symbiont interactions were recorded only in the 2008 (untreated) field trials.

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VII.B. Interpretation of Phenotypic and Environmental Interaction Data

Plant pest risk assessments for biotechnology-derived crops are comparative assessments. Familiarity provides a basis from which the potential environmental impact of a biotechnology-derived plant can be evaluated. The concept of familiarity is based on the fact that the biotechnology-derived plant is developed from a well-characterized conventional plant variety. Familiarity considers the biology of the crop, the introduced trait, the receiving environment and the interaction of these factors, and provides a basis for comparative environmental risk assessment between a biotechnology-derived plant and its conventional counterpart.

Expert knowledge and experience with conventionally bred soybean was the basis for selecting appropriate endpoints and estimating the range of responses that would be considered typical for soybean. As such, both dicamba-treated and untreated MON 87708 was compared to the conventional control in the assessment of phenotypic, agronomic, and environmental interaction characteristics. An overview of the characteristics assessed is presented in Table VII-1. A subset of the data relating to well-understood weedy characteristics (*e.g.*, seed dormancy, pre-harvest seed loss characteristics, and lodging) was used to assess whether there is an increase in weediness of MON 87708, an element of APHIS's plant pest determination. Evaluation of environmental interaction characteristics (*e.g.*, plant-abiotic stress, plant-disease, and plant-arthropod interactions) was also considered in the plant pest assessment. Based on all of the data collected, an assessment was made to determine if MON 87708 is likely to pose an increased plant pest risk compared to conventional soybean. Prior to analysis, the overall dataset was evaluated for evidence of biologically relevant changes, and for possible evidence of an unexpected plant response. No unexpected observations or issues were identified.

VII.B.1. Interpretation of Detected Differences Criteria

Comparative plant characterization data from a biotechnology-derived crop and the conventional control are interpreted in the context of contributions to increased plant pest potential as assessed by APHIS. Under the framework of familiarity, characteristics for which no differences are detected support a conclusion of no increased plant pest potential of the biotechnology-derived crop compared to the conventional crop. Characteristics for which differences are detected are considered in a step-wise method (Figure VII-1). All detected differences for a characteristic are considered in the context of whether or not the difference would increase the plant pest potential of the biotechnology-derived crop. Ultimately, a weight of evidence approach considering all characteristics and data is used for the overall risk assessment of differences and their significance. Figure VII-1 illustrates the stepwise assessment process employed in detail:

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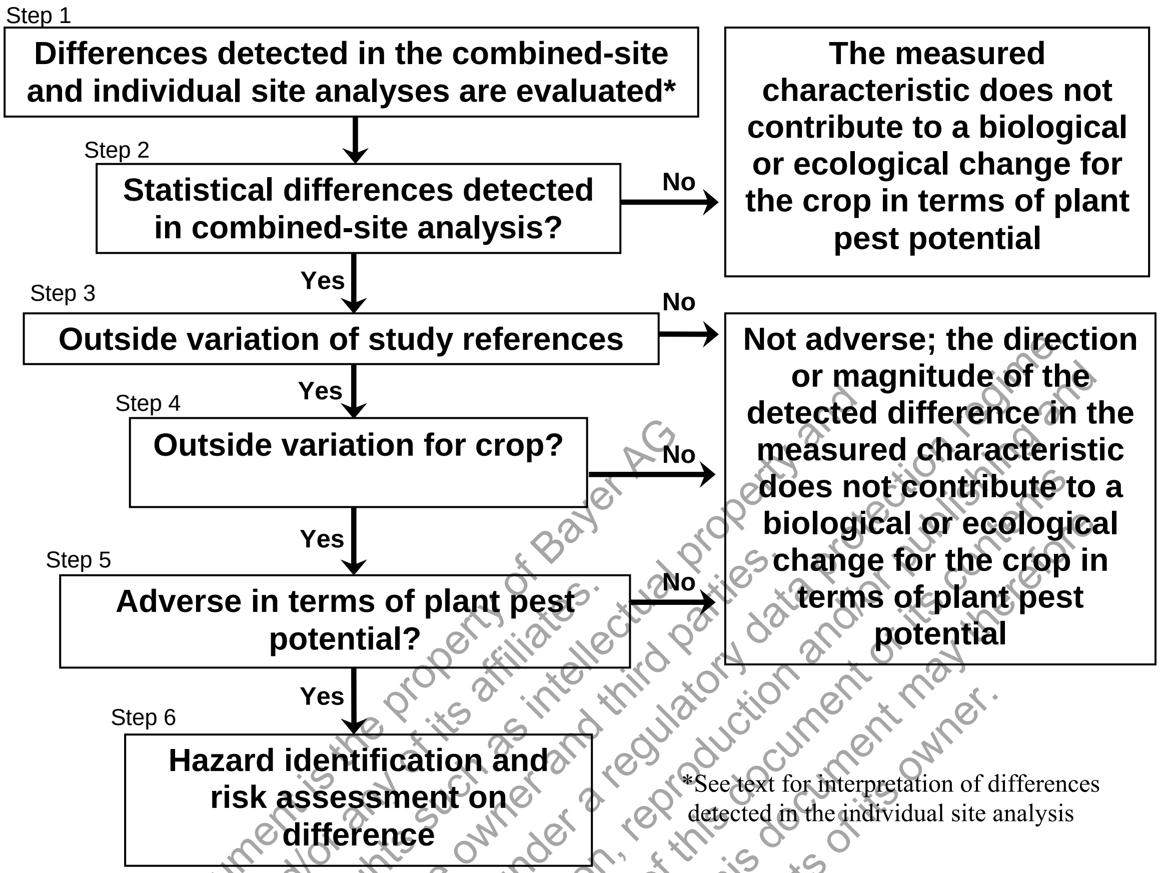
Step 1
Differences detected in the combined-site and individual site analyses are evaluated*
Step 2
Statistical differences detected in combined-site analysis?
No
The measured characteristic does not contribute to a biological or ecological change for the crop in terms of plant pest potential
Yes
Step 3
Outside variation of study references
No
Not adverse; the direction or magnitude of the detected difference in the measured characteristic does not contribute to a biological or ecological change for the crop in terms of plant pest potential
Yes
Step 4
Outside variation for crop?
No
Yes
Step 5
Adverse in terms of plant pest potential?
No
Yes
Step 6
Hazard identification and risk assessment on difference
*See text for interpretation of differences detected in the individual site analysis

Note: A "no" answer at any step indicates that the characteristic does not contribute to a biological or ecological change for the crop in terms of plant pest potential and subsequent steps are not considered. If the answer is "yes" or "uncertain", the subsequent step is considered.

Figure VII-1. Schematic Diagram of Agronomic and Phenotypic Data Interpretation Methods

Steps 1 and 2 - Evaluate Detected Statistically Significant Differences

Data on each measured characteristic are statistically analyzed, where appropriate, within each individual site and in a combined-site analysis, in which the data are pooled among sites. All statistically significant differences are evaluated and considered in the context of a change in plant pest potential. Differences detected in individual-site analyses that are not consistently observed across multiple environments in the combined-site analysis are considered not biologically meaningful in terms of plant pest potential and, therefore, are not further considered in subsequent steps. Any difference detected in the combined-site analysis is further assessed.

Step 3 - Evaluate Differences Relative to Commercial Reference Varieties Range

If a difference for a characteristic is detected in the combined-site analysis across multiple environments, then the mean value of the biotechnology-derived crop for the characteristic is assessed relative to the commercial reference varieties.

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Step 4 - Evaluate Differences in the Context of the Crop

If the mean value of the biotechnology-derived crop is outside the variation of the commercial reference varieties (*e.g.*, reference range), the mean value of the biotechnology-derived crop for the characteristic is assessed relative to known values common for the crop (*e.g.*, published values).

Step 5 - Plant Pest Potential

If the mean value of the biotechnology-derived crop is outside the range of values common for the crop, the detected difference for the characteristic is then assessed for whether or not it is adverse in terms of plant pest potential.

Step 6 - Conduct Risk Assessment on Identified Hazard

If an adverse effect (hazard) is identified, risk assessment on the difference is conducted. The risk assessment considers contributions to enhanced plant pest potential of the crop itself, the impact of differences detected in other measured characteristics, and potential for and effects of trait transfer to feral populations of the crop or to a sexually-compatible species.

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VII.C. Comparative Assessments of the Phenotypic, Agronomic, and Environmental Interaction Characteristics of MON 87708

This section provides the results of comparative assessments conducted in replicated laboratory, greenhouse, and/or multi-site field experiments to provide a detailed phenotypic, agronomic, and environmental interaction description of MON 87708. The MON 87708 characteristics evaluated in these assessments included: seed dormancy and germination characteristics (Section VII.C.1), plant phenotypic and environmental interaction observations under field conditions (Section VII.C.2), pollen characteristics (Section VII.C.3), and symbiont interactions (Section VII.C.4). Additional details for each assessment are provided in Appendices F through I.

VII.C.1. Seed Dormancy and Germination Characteristics

USDA-APHIS considers the potential for weediness to constitute a plant pest factor (7 CFR § 340.6). Seed germination and dormancy mechanisms vary among species and their genetic basis tends to be complex. Seed dormancy (*e.g.*, hard seed) is an important characteristic that is often associated with plants that are considered weeds (Anderson, 1996; Lingenfelter and Hartwig, 2003); however, it is not uncommon to observe low levels of hard seed in conventional soybean (Mullin and Xu, 2001). Standardized germination assays are available and routinely used to measure the germination characteristics of soybean seed. The Association of Official Seed Analysts (AOSA), an internationally recognized seed testing organization, recommends a temperature range of 20/30°C as optimal for testing the germination characteristics of soybean seed (AOSA, 2007).

Comparative assessments of seed dormancy and germination characteristics were conducted on MON 87708 and the conventional control. In addition, eight commercial reference varieties were included to provide a range of comparative values that are representative of existing commercial soybean varieties. The seed lots for MON 87708, conventional control, and the commercial reference varieties were produced in replicated field trials during 2008 in Iowa, Illinois, and Missouri, geographic areas which represent environmentally relevant conditions for soybean production for this product. In addition to the AOSA recommended temperature range of 20/30°C, seed was tested at five additional temperature regimes of 10, 20, 30, 10/20, and 10/30°C to assess seed germination properties. The details of the materials, experimental methods, and germination data from all individual production sites are presented in Appendix F.

In a combined-site analysis, in which the data were pooled among the three seed production sites, no statistically significant differences (5% level of significance) were detected between MON 87708 and the conventional control for percent viable hard seed or percent viable firm-swollen seed in any temperature regime (Table VII-2). Within some temperature regimes, it was not possible to conduct an analysis of variance for percent viable firm-swollen seed due to no variance in the data. For these data, the values for MON 87708 and the conventional control were all zero, indicating no biological differences. No statistically significant differences were detected between MON 87708

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and the conventional control for percent germinated or percent dead seed in the 20, 30, 10/20, and 20/30°C temperature regimes.

Four statistically significant differences were detected between MON 87708 and the conventional control in the combined-site analysis (Table VII-2). MON 87708 had lower percent germinated seed than the conventional control at 10°C (98.9% vs. 99.7%) and 10/30°C (98.6% vs. 99.7%). Concurrently, MON 87708 had higher percent dead seed than the conventional control at 10°C (0.8% vs. 0.2%) and 10/30°C (1.4% vs. 0.3%). The differences in percent germinated and dead seed of MON 87708 were small in magnitude, and the mean values of MON 87708 were all within the range of the commercial reference varieties produced in the field trials along with MON 87708 and the conventional control. Furthermore, lower percent germinated seed and higher percent dead seed would not contribute to increased weediness.

The biological characteristics evaluated were used to characterize MON 87708 in the context of plant pest risk assessment. Based on the seed dormancy and germination characteristics assessed, the results, particularly MON 87708's lack of hard seed, demonstrate there were no changes indicative of increased weediness or plant pest potential of MON 87708 compared to conventional soybean.

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Table VII-2. Combined-Site Comparison of MON 87708 to Conventional Control for Seed Dormancy and Germination Characteristics

Temperature Regime	Germination Characteristic[1]	Mean % (S.E.)[2]		Reference Range[3]	
		MON 87708	Control	Min.	Max.
10 °C	Germinated	98.9 (0.4)*	99.7 (0.2)	94.4	99.8
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0	0.3
	Dead	0.8 (0.4)*	0.2 (0.1)	0.2	5.3
	Viable Firm-swollen	0.3 (0.1)	0.2 (0.1)	0.0	0.4
20 °C	Germinated	99.3 (0.4)	99.3 (0.3)	95.3	100.0
	Viable Hard	0.0 (0.0)	0.1 (0.1)	0.0	0.4
	Dead	0.8 (0.4)	0.6 (0.3)	0.0	4.8
	Viable Firm-swollen	0.0 (0.0)	0.0 (0.0)	0.0	0.3
30 °C	Germinated	98.7 (0.6)	99.3 (0.3)	93.3	100.0
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0	0.1
	Dead	1.3 (0.6)	0.7 (0.3)	0.0	6.8
	Viable Firm-swollen	0.0 (0.0)†	0.0 (0.0)	0.0	0.0
10/20 °C	Germinated	99.3 (0.3)	99.3 (0.3)	95.9	100.0
	Viable Hard	0.1 (0.1)	0.1 (0.1)	0.0	0.4
	Dead	0.6 (0.3)	0.6 (0.3)	0.0	3.9
	Viable Firm-swollen	0.0 (0.0)	0.1 (0.1)	0.0	0.3
10/30 °C	Germinated	98.6 (0.5)*	99.7 (0.2)	95.9	99.8
	Viable Hard	0.0 (0.0)	0.1 (0.1)	0.0	0.0
	Dead	1.4 (0.5)*	0.3 (0.2)	0.3	4.1
	Viable Firm-swollen	0.0 (0.0)	0.0 (0.0)	0.0	0.1
20/30 °C	Normal Germinated	95.9 (1.2)	96.6 (1.0)	86.0	99.0
	Abnormal Germinated	2.9 (0.7)	2.8 (0.8)	0.8	9.8
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0	0.3
	Dead	1.2 (0.5)	0.7 (0.3)	0.3	4.1
	Viable Firm-swollen	0.0 (0.0)†	0.0 (0.0)	0.0	0.0

Note: The data in this table are the combined-site results for the seeds from three 2008 field sites. The experimental design was a split-plot where the whole-plot treatment was seed production site and the sub-plot treatment was seed material (*i.e.*, MON 87708, conventional control, or commercial reference varieties).

*Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

† No statistical comparisons were made due to lack of variability in the data.

[1] Germinated seed in the AOSA temperature regime (20/30°C) were categorized as either normal germinated or abnormal germinated seed.

[2] Means based on twelve replicates (n = 12) of 100 seeds. The total percentage of all germination characteristics of MON 87708 or conventional control in some temperature regimes is greater than 100.0% due to numerical rounding of the means. S.E. = Standard Error.

[3] Minimum and maximum mean values from among eight commercial reference varieties.

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VII.C.2. Phenotypic, Agronomic, and Environmental Interaction Characteristics Evaluated under Field Conditions

Plant growth, development, and yield characteristics were evaluated under field conditions as part of the plant characterization assessment of MON 87708. These data were developed to provide USDA-APHIS with a detailed description of MON 87708 relative to the conventional --control and commercial reference varieties. According to 7 CFR § 340.6, as part of the petition to seek deregulation, a petitioner must submit "a detailed description of the phenotype of the regulated article." This information is being provided to assess whether there are phenotypic differences between MON 87708 and the conventional control that may impact its pest potential. Certain growth, reproduction, and pre-harvest seed loss characteristics (*e.g.*, lodging, pod shattering) were used to assess whether there is an increase in weediness of MON 87708, an element of APHIS's plant pest determination. Environmental interactions were also assessed as an indirect indicator of phenotypic changes to MON 87708 compared to the same comparators described above and are also considered in the plant pest assessment.

VII.C.2.1. Phenotypic, Agronomic, and Environmental Interaction Characteristics for Untreated MON 87708 Evaluated under 2008 Field Conditions

Data were collected from field trials located at 16 field sites in the U.S. and two field sites in Canada during 2008 to evaluate phenotypic, agronomic, and environmental interaction characteristics. These 18 field sites provided a diverse range of environmental and agronomic conditions representative of commercial soybean production areas in North America (Table VII-3). The experiments were arranged as randomized complete block designs with three replications at each field site. All plots of MON 87708, the conventional control, and the commercial reference varieties at each site were uniformly managed in order to assess whether the introduction of the dicamba tolerance trait altered the phenotypic and agronomic characteristics or the environmental interactions of MON 87708 compared to the conventional control. Therefore, dicamba herbicide was not applied to MON 87708 during the study. A description of the evaluated phenotypic and environmental interaction characteristics and the designated developmental stages when evaluations occurred are listed in Table VII-1. The methods and detailed results of the individual-site data comparisons are presented and discussed in Appendix G, while the combined-site analyses are summarized below. The results of this assessment demonstrated that the introduction of the dicamba tolerance trait did not alter MON 87708 compared to the conventional control in terms of weediness. The lack of differences in plant response to abiotic stress, disease damage, arthropod-related damage, and pest and beneficial arthropod abundance further support the conclusion that the introduction of the dicamba tolerance trait is not likely to result in increased plant pest potential or an altered environmental impact from untreated MON 87708 compared to conventional soybean.

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Table VII-3. 2008 Field Phenotypic Evaluation Sites for Untreated MON 87708

Location	Location Code	USDA-APHIS Notification Number
Jackson County, Arkansas	AR	08-072-110n
Norfolk County, Ontario, Canada	Can1	N/A
Kent County, Ontario, Canada	Can2	N/A
Jefferson County, Iowa	IA1	08-058-101n
Benton County, Iowa	IA2	08-058-101n
Howard County, Iowa	IA3	08-072-110n
Clinton County, Illinois	IL1	08-058-101n
Stark County, Illinois	IL2	08-058-101n
Boone County, Indiana	IN1	08-072-110n
Clinton County, Indiana	IN2	08-072-110n
Parke County, Indiana	IN3	08-058-101n
Pawnee County, Kansas	KS	08-072-110n
Ottawa County, Michigan	MI	08-072-110n
Shelby County, Missouri	MO1	08-072-110n
Macon County, Missouri	MO2	08-072-110n
York County, Nebraska	NE	08-072-110n
Berks County, Pennsylvania	PA	08-058-101n
Walworth County, Wisconsin	WI	08-058-101n

N/A = Not applicable, trial was conducted under a Canadian confined research field testing permit.

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VII.C.2.2. Phenotypic, Agronomic, and Environmental Interaction Characteristics for Dicamba-Treated Evaluated under 2009 Field Conditions

In addition to the data from 2008 field trials, data were collected from field trials conducted in 2009 at eight sites within U.S. soybean production regions (Table VII-4). MON 87708, the conventional control variety A3525, and three commercially-released reference soybean varieties were evaluated at each site. A total of 14 reference varieties were evaluated among the sites. The experimental design at each site was a randomized complete block with four replications. All plots of MON 87708, the conventional control, and the commercial reference varieties at each site were uniformly managed in order to assess whether the introduction of the dicamba tolerance trait in the presence of dicamba altered the phenotypic and agronomic characteristics or the environmental interactions of MON 87708 compared to the conventional control. Therefore, MON 87708, in each replication at all sites, received an application of a commercial formulation of dicamba (Clarity) at 0.5 pound a.e dicamba per acre. Treated MON 87708 was compared to the control within each site (i.e., individual-site analysis) and in a combined-site analysis, in which the data were pooled across the eight sites, for 12 plant characteristics. The minimum and maximum mean values (reference range) were determined from the references to provide phenotypic characteristic and environmental interaction values representative of commercial soybean varieties.

Table VII-4. 2009 Field Phenotypic Evaluation Sites for Dicamba Treated MON 87708

County, State	Location Code	USDA-APHIS Notification Number
Jackson County, Arkansas	ARNE	09-061-108n
Jefferson County, Iowa	IARL	09-061-108n
Clinton County, Illinois	ILCY	09-061-108n
Stark County, Illinois	ILWY	09-061-108n
Parke County, Indiana	INRC	09-061-108n
Boone County, Indiana	INSH	09-061-108n
Pawnee County, Kansas	KSLA	09-061-108n
York County, Nebraska	NEYO	09-061-108n

VII.C.2.3. Field Phenotypic and Agronomic Characteristics

VII.C.2.3.1. 2008 Field Phenotypic and Agronomic Characteristics for Untreated MON 87708

A total of 14 phenotypic and agronomic characteristics were evaluated (Table VII-5 and Table G-5 of Appendix G). In a combined-site analysis in which the data were pooled among the sites, no statistically significant differences were detected (5% level of significance) between untreated MON 87708 and the conventional control for early stand count, seedling vigor, days to 50% flowering, lodging, pod shattering, final stand count, seed moisture, test weight, or yield (Table VII-5). A statistically significant difference was detected between untreated MON 87708 and the conventional control for plant height and 100 seed weight in the combined-site analysis. Untreated MON 87708 was 6% taller (33.5 vs. 31.6 inches) and had 3.3% lower 100 seed weight than the conventional control (15.0 vs. 15.5 grams). However, the differences in plant height and 100 seed weight were small in magnitude, and the mean values of untreated MON 87708 for both plant height and 100 seed weight were within the range of the commercial reference varieties grown in the trials along with untreated MON 87708 and the conventional control. The difference in 100 seed weight did not result in a statistically significant difference in final yield, and it is unlikely that a difference in seed weight or plant height would contribute to increased weediness of MON 87708 compared to the conventional control.

Flower color, plant pubescence, and plant growth stage data were categorical and were not statistically analyzed; however, at each site, all plants of untreated MON 87708 and the conventional control had purple flowers and hairy pubescence as expected. Additionally, untreated MON 87708 and the conventional control were within the same range of plant growth stages for 131 out of the 132 growth stage gobservations among all sites (Appendix G; Table G-4). During the second observation at the WI site, untreated MON 87708 plants were at the V5 growth stage while the conventional control was at V4.

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The growth stage of untreated MON 87708, however, was within the range of growth stages observed for the commercial reference varieties grown concurrently (V4 − V5). Thus, there were no biologically meaningful differences in plant development observed between untreated MON 87708 and the conventional control.

Table VII-5. Combined-Site Comparison of Untreated MON 87708 to Conventional Control during 2008 for Phenotypic and Agronomic Characteristics

Phenotypic Characteristic (units)	Mean (S.E.)		Reference Range[1]	
	MON 87708	Control[2]	Minimum	Maximum
Early stand count (#/plot)	271.1 (9.0)	265.2 (9.8)	195.7	452.5
Seedling vigor (1-9 scale)	3.5 (0.2)	3.4 (0.2)	1.8	4.5
Days to 50% flowering[3]	206.4 (1.2)	206.2 (1.3)	199.6	216.7
Flower color[4]	Purple	Purple	Purple	Purple
Plant pubescence[4]	Hairy	Hairy	Hairy	Hairy
Plant height (in.)	33.5 (0.9)*	31.6 (0.8)	25.4	42.4
Lodging (0-9 scale)	1.2 (0.2)	0.9 (0.1)	0.1	2.9
Pod shattering (0-9 scale)	0.1 (0.0)	0.1 (0.0)	0.0	0.3
Final stand count (#/plot)	251.1 (8.4)	243.4 (8.7)	178.3	338.0
Seed moisture (%)	11.8 (0.3)	11.7 (0.3)	10.4	13.9
100 seed weight (g)[5]	15.0 (0.2)*	15.5 (0.2)	14.2	18.7
Test weight (lb/bu)	56.2 (0.3)	55.9 (0.3)	53.6	57.6
Yield (bu/A)	55.4 (2.0)	55.1 (2.3)	37.7	72.7

Note: The experimental design was a randomized complete block. S.E. = Standard Error. Means based on n = 54 for MON 87708 and n = 53 for the conventional control with exception of 100 seed weight for the control where n = 52.

* Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

[1] Reference ranges were determined from the minimum and maximum mean values from among 18 commercial reference varieties.

[2] Excessive water damage from heavy precipitation early in the season at the WI site resulted in a poor stand in one replicate of the conventional control. Therefore, the data for all characteristics from the single replicate at the WI site were excluded from the statistical analysis.

[3] Calendar day number (from 1 Jan 2008) when approximately 50% of the plants in each plot were flowering.

[4] Flower color and plant pubescence data were categorical and not statistically analyzed (see Appendix G, Table G-3).

[5] Data on 100 seed weight were inadvertently not collected from one replicate of the conventional control at the MO1 site.

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VII.C.2.3.2. 2009 Field Phenotypic and Agronomic Characteristics for Dicamba-Treated MON 87708

A total of 12 phenotypic and agronomic characteristics were evaluated (Table VII-6 and Table G-6 of Appendix G). In the combined-site analysis, no statistically significant differences were detected between treated MON 87708 and the conventional control for early stand count, seedling vigor, days to 50% flowering, plant height, lodging, pod shattering, final stand count, seed moisture, or yield (Table VII-6). One statistically significant difference was detected between treated MON 87708 and the control, where MON 87708 had a lower 100 seed weight than the control (14.6 vs. 15.6 g). The difference in 100 seed weight is relatively small in magnitude and the mean 100 seed weight of treated MON 87708 was slightly below the reference range. It is unlikely that a difference in 100 seed weight would contribute to increased weed potential of MON 87708 when treated with dicamba compared to conventional soybean. Flower color and plant growth stage data were categorical and were not statistically analyzed; however, at each site, all plants of treated MON 87708 and the control had purple flowers as expected. Additionally, treated MON 87708 and the control were within the same range of plant growth stages for all growth stage observations among the sites. Thus, there were no biologically-meaningful differences in plant development observed between treated MON 87708 and conventional soybean.

The results of this assessment demonstrated that the introduction of the dicamba tolerance trait and the associated dicamba application does not alter MON 87708 compared to the conventional control in terms of weediness. The lack of differences in plant response to abiotic stress, disease damage, and arthropod-related damage further support the conclusion that the introduction of the dicamba tolerance trait is not likely to result in increased plant pest potential or an altered environmental impact for dicamba-treated MON 87708 compared to conventional soybean.

Table VII-6. Combined-Site Comparison of Dicamba Treated MON 87708 to Conventional Control during 2009 for Phenotypic and Agronomic Characteristics

Phenotypic Characteristic (units)	MON 87708 (S.E.)		Reference Range[1]	
	MON 87708	Control	Minimum	Maximum
Early stand count (#/plot)	298.9 (5.20)	301.1 (3.58)	263.4	340.8
Seedling vigor (1-9 scale)	3.0 (0.33)	3.0 (0.31)	1.0	4.5
Days to 50% flowering[2]	214.7 (1.12)	214.6 (1.19)	205.0	226.0
Plant height (in)	31.6 (0.78)	31.2 (0.92)	25.3	38.3
Lodging (1-9 scale)	2.2 (0.27)	2.4 (0.31)	1.0	4.5
Pod shattering (1-9 scale)	1.1 (0.05)	1.1 (0.07)	1.0	1.5
Final stand count (#/plot)	264.8 (6.81)	266.8 (5.20)	219.5	305.5
Seed moisture (%)	13.1 (0.38)	13.4 (0.37)	11.1	17.0
100 seed weight (g)	14.6* (0.23)	15.6 (0.23)	15.0	17.7
Yield (bu/ac)	46.7 (2.37)	46.8 (2.23)	29.4	59.9

Note: The experimental design was a randomized complete block with four replications. Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

* Statistically significant differences ($\alpha=0.05$) between MON 87708(T) and the conventional soybean control.

[1] Reference range = Minimum and maximum mean values among the 14 commercially-released reference soybean varieties.

[2] Calendar day number (days after 1 Jan 2009) when approximately 50% of the plants in each plot were flowering.

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VII.C.2.3.3. Field Phenotypic and Agronomic Characteristics for Both Dicamba-Treated and Untreated MON 87708 - Conclusion

The phenotypic and agronomic characteristics were used to provide a detailed description of both dicamba-treated and untreated MON 87708 compared to the conventional control. A subset of these characteristics was useful to assess the weediness potential of MON 87708. Based on the assessed phenotypic and agronomic characteristics, the results support a determination that both dicamba-treated and untreated MON 87708 are similar to conventional soybean and are no more weedy or likely to pose a plant pest risk than conventional soybean.

VII.C.2.4. Environmental Interaction Characteristics

USDA-APHIS considers the environmental interaction of the biotechnology-derived crop compared to its conventional counterpart to determine the potential for increased plant pest characteristics. Evaluations of environmental interactions were conducted as part of the plant characterization for untreated MON 87708. In the 2008 North American field trials conducted for evaluation of phenotypic and agronomic characteristics of MON 87708, data were also collected on plant response to abiotic stress (drought, wind, nutrient deficiency, etc.), disease damage, arthropod-related damage, and arthropod abundance (Appendix G; Tables G-9, G-10, G-11, G-12, and G-13). Similarly these data, except for arthropod abundance, were also collected for the 2009 U.S. field trials (Appendix G; Tables G-14, G-15, and G-16). These data were used as part of the environmental consequences (Section IX) to assess plant pest potential and provide an indication of potential effects of untreated MON 87708 on non-target organisms (NTOs) and threatened and endangered species compared to the conventional control. In addition, multiple commercial reference varieties were included in the analysis to establish a range of natural variability for each assessed characteristic. The results of the field evaluations showed that the dicamba tolerance trait did not unexpectedly alter the assessed environmental interactions of untreated MON 87708 compared to the conventional control. Additionally, results of field evaluations showed that the dicamba tolerance trait in the presence of dicamba herbicide did not unexpectedly alter the assessed environmental interactions of treated MON 87708 compared to the conventional control. The lack of significant biologically meaningful differences in plant response to abiotic stress, disease damage, arthropod-related damage, and pest and beneficial arthropod abundance support the conclusion that the introduction of the dicamba tolerance trait is unlikely to result in increased plant pest potential or an altered environmental impact from MON 87708 compared to conventional soybean.

In the 2008 field trials, the observations of plant response to abiotic stress, disease damage, and arthropod-related damage were performed four times during the growing season at all 18 sites, and arthropod abundance was assessed quantitatively from collections performed four times during the growing season at four of the 18 sites (*i.e.*, IL2, IN1, MI, and MO1 sites). In the 2009 field trials, the observations of plant response

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to abiotic stress, disease damage, and arthropod-related damage were performed four times during the growing season at all eight sites.

The assessed stressors (abiotic, diseases, and arthropods) were at natural levels as no artificial infestation or imposed abiotic stress was used and, therefore, typically varied between observations at a site and among sites. Abiotic stress and disease damage data were collected from each plot using a non-specific 0 – 9 scale of increasing severity of observed damage. The 0 – 9 scale was not designed to rate specific damage symptoms. However, the non-specific scale was utilized to allow for the evaluation of the wide variety of potential abiotic stressor and disease damage symptoms potentially occurring across the season and across sites. Due to the non-specific nature of the scale used, the data were not statistically analyzed but rather assessed qualitatively and placed into one of the following categories: none, slight, moderate, or severe. The response of MON 87708 and the conventional control to an abiotic stress or disease were considered different on a particular observation date at a site if the range of injury severity to MON 87708 did not overlap with the range of injury severity to the control across all three replications (*e.g.*, "none" vs. "slight-moderate" rating). For each observation at a site, the range of injury severity across the commercial reference varieties provided assessment data that are representative of commercial soybean varieties. Arthropod-related damage was assessed from each plot on the upper four nodes of 10 representative plants using a 0 – 5 pest-specific rating scale of increasing severity of observed damage. These numerical data along with the quantitative arthropod abundance data were subjected to statistical analysis.

VII.C.2.4.1. 2008 Environmental Interaction Characteristics for Untreated MON 87708

In an assessment of abiotic stress response and disease damage, no differences were observed between untreated MON 87708 and the conventional control for 193 out of 194 comparisons for the assessed abiotic stressors or for any of the 215 comparisons for the assessed diseases among all observations at the sites (Appendix G; Tables G-9 and G-10). One difference was observed in abiotic stress response during the fourth observation at the WI site where minor wind damage was observed in MON 87708 ("slight" rating) and no wind damage was observed in the conventional control or commercial reference varieties ("none" rating). The difference, however, was not observed during any of the other 29 wind damage observations among the sites. Thus, the small difference in wind damage rating during the single observation was not indicative of a consistent response associated with the trait and was considered not biologically meaningful in terms of increased weediness or plant pest potential or an altered environmental impact from untreated MON 87708 compared to conventional soybean.

In an assessment of arthropod-related damage, no statistically significant differences were detected (5% level of significance) between untreated MON 87708 and the conventional control for 89 out of 95 comparisons for the assessed arthropods (Appendix G; Table G-11). Statistical comparisons could not be made between MON 87708 and the conventional control for 121 additional arthropod-related damage comparisons due to no variance in the data; however, the means for MON 87708 and the

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conventional control were the same value for these comparisons, indicating no biological differences. A total of six statistically significant differences involving four taxa were detected between MON 87708 and the conventional control. MON 87708 had less damage than the conventional control from aphids in the third observation at the IA2 site (0.3 vs. 0.5 rating) and second observation at the IA3 site (0.8 vs. 0.9 rating). MON 87708 had less damage than the conventional control from blister beetles in the second observation at the MO1 site (0.1 vs. 0.4 rating) and more damage than the conventional control from potato leafhopper in the first observation at the PA site (1.1 vs. 0.6 rating). MON 87708 had less damage than the conventional control from Japanese beetle in the second observation at the IN1 site (0.6 vs. 0.9 rating) and more damage in the fourth observation at the PA site (0.6 vs. 0.4 rating). The mean damage ratings for MON 87708 were within the range of the commercial reference varieties grown concurrently with MON 87708 and the conventional control for all differences detected in arthropod-related damage with the exception of the differences in Japanese beetle damage at the IN1 and PA sites. The mean Japanese beetle damage rating for MON 87708 at the IN1 site was slightly lower than the range of commercial reference varieties for the difference detected (MON 87708 mean = 0.6 rating; range of commercial reference varieties = 0.7 – 0.9 ratings) and slightly higher than the range of commercial reference varieties for the difference detected at the PA site (MON 87708 mean = 0.6 rating; range of commercial reference varieties = 0.3 – 0.5 ratings). Furthermore, the differences detected in arthropod-related damage were all small in magnitude and were not consistent across observations or sites. These results support a conclusion that the detected differences in arthropod-related damage were not indicative of a consistent response associated with the trait and were not considered biologically meaningful in terms of increased weediness or plant pest potential or an altered environmental impact from untreated MON 87708 compared to conventional soybean.

In an assessment of pest and beneficial arthropod abundance, no statistically significant differences were detected (5% level of significance) between untreated MON 87708 and the conventional control for 142 out of 151 comparisons, including 74 arthropod pest abundance comparisons and 77 beneficial arthropod abundance comparisons, among the collection intervals at the four sites (Appendix G; Tables G-12 and G-13). Statistical comparisons could not be made between MON 87708 and the conventional control for eight additional comparisons, including three arthropod pest abundance comparisons and five beneficial arthropod abundance comparisons, due to no variance in the data; however, the means for MON 87708 and the conventional control were the same value for these comparisons, indicating no biological differences. A total of nine statistically significant differences were detected between MON 87708 and the conventional control for arthropod abundance, including seven for pest arthropods and two for beneficial arthropods.

The seven differences detected for pest arthropod abundance included observations for green cloverworm, Japanese beetles, and stink bugs (Table G-12). MON 87708 had lower green cloverworm abundance than the conventional control in the first collection from the IL2 site (0.0 vs. 2.0 per plot), third collection from the IN1 site (7.0 vs. 11.3 per plot), and fourth collection from the MI site (0.0 vs. 0.7 per plot); and higher green cloverworm abundance than the conventional control in the first collection from the MI

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site (1.7 vs. 0.0 per plot). MON 87708 had lower Japanese beetle abundance than the conventional control in the first collection from the MI site (2.3 vs. 8.0 per plot). In addition, MON 87708 had lower stink bug abundance than the conventional control in the third collection from the IL2 site (0.0 vs. 1.3 per plot) and higher stink bug abundance in the third collection from the IN1 site (2.0 vs. 0.0 per plot). The mean arthropod abundance values for MON 87708 were within the range of the commercial reference varieties grown concurrently with MON 87708 and the conventional control for all differences detected with the exception of the difference detected for green cloverworm abundance at the IL2 site (MON 87708 mean = 0.0 per plot; range of commercial reference varieties = 0.3 – 2.7 per plot) and the IN1 site (MON 87708 = 7.0 per plot; range of commercial reference varieties = 8.0 – 13.0 per plot) and stink bug abundance at the IN1 site (MON 87708 = 2.0 per plot; range of commercial reference varieties = 0.0 – 0.7 per plot). Furthermore, the differences detected in green cloverworm, Japanese beetle, and stink bug abundance were all small in magnitude and were not detected in other collections or sites where these pests were present. These results support a conclusion that the detected differences in pest arthropod abundance were not indicative of a consistent response associated with the trait and were not considered biologically meaningful in terms of increased weediness or plant pest potential or an altered environmental impact from MON 87708 compared to conventional soybean.

The two differences detected for beneficial arthropod abundance included observations for *Araneae* (spiders) and *Nabis* spp. (Table G-13). MON 87708 had lower Araneae abundance (0.0 vs. 3.0 per plot) and higher *Nabis* spp. abundance (4.7 vs. 1.7 per plot) than the conventional control in the fourth collection from the MI site. The mean *Araneae* abundance value for MON 87708 was slightly lower than the range of commercial reference varieties (0.7 – 1.0 per plot), while the mean *Nabis* spp. abundance value for MON 87708 was within the range of commercial reference varieties (2.0 – 6.3 per plot). Furthermore, the differences detected for both *Araneae* and *Nabis* spp. abundance were small in magnitude and were not consistent across collections or sites. The results support a conclusion that the detected differences in beneficial arthropod abundance were not indicative of a consistent response associated with the dicamba tolerance trait and were not considered biologically meaningful in terms of increased weediness or plant pest potential or an altered environmental impact from untreated MON 87708 compared to conventional soybean.

VII.C.2.4.2. 2009 Environmental Interaction Characteristics for Treated MON 87708

In an assessment of plant response to abiotic stressors and disease damage for the 2009 field trials (Appendix G; Table G-14 and G-15), no differences were observed between treated MON 87708 and the conventional control for 181 of 182 comparisons (including 89 abiotic stress response and 92 disease damage comparisons) among all observations at the sites. One difference was observed between treated MON 87708 and the control for white mold during a single observation (slight vs. none). The damage rating for treated MON 87708 was outside of the reference range (no damage was observed in the references), and this difference was not observed in any of the other two white mold evaluations across the sites.

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In an assessment of arthropod-related damage (Appendix G; Table G-16) there were a total of 93 comparisons. No statistically significant differences were detected between treated MON 87708 and the control for 56 out of 59 comparisons. In addition, no numerical differences were observed for the 34 comparisons for which *p*-values could not be generated due to lack of variability in the data. Treated MON 87708 had lower bean leaf beetle damage than the control for Observation 3 at the KSLA site (0.00 vs. 0.08), and greater grasshopper damage for Observation 3 at the INRC site (0.45 vs. 0.10) and at the KSLA site (0.20 vs. 0.03). The mean damage ratings for bean leaf beetle damage and grasshopper damage at the KSLA site were within the respective reference ranges. For the remaining difference, the mean damage rating for grasshopper damage at the INRC site from treated MON 87708 was outside the reference range; however, this difference was not consistent across observations or sites. Thus, there was not a consistent response associated with the dicamba tolerance trait or the herbicide treatment, and the results are not considered biologically meaningful in terms of adverse environmental impacts of treated MON 87708 compared to the conventional soybean.

VII.C.2.4.3. Environmental Interaction Characteristics for Both Dicamba Treated and Untreated MON 87708 - Conclusion

The results of the 2008 field evaluations showed that the dicamba tolerance trait did not unexpectedly alter the assessed environmental interactions of untreated MON 87708 compared to the conventional control. Additionally, the results of the 2009 field evaluations showed that the dicamba tolerance trait in the presence of dicamba herbicide did not unexpectedly alter the assessed environmental interactions of MON 87708 compared to the conventional control. The lack of significant biological differences in plant responses to abiotic stress, disease damage, arthropod-related damage for both dicamba treated and untreated MON 87708, and pest and beneficial arthropod abundance for untreated MON 87708 support the conclusion that the introduction of the dicamba tolerance trait is unlikely to result in increased plant pest potential compared to conventional soybean.

VII.C.3. Pollen Characteristics

USDA-APHIS considers the potential for gene flow and introgression of the biotechnology-derived trait into other soybean varieties and wild relatives to determine the potential for increased weedy or invasive characteristics of the receiving species. Pollen morphology and viability information are pertinent to this assessment and, therefore, were assessed for MON 87708. In addition, characterization of pollen produced by MON 87708 and the conventional control is relevant to the plant pest risk assessment because it adds to the detailed description of the phenotype of MON 87708 compared to the conventional control.

The purpose of this evaluation was to assess the morphology and viability of pollen collected from MON 87708 compared to that of the conventional control. Pollen was collected from MON 87708, the conventional control, and four commercial reference varieties grown under similar agronomic conditions in a field trial in Illinois. The trial was arranged in a randomized complete block design with three replications. Twenty

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flowers were collected from each plot. Pollen was extracted, combined among flowers collected from the same plot, and stained with Alexander's stain (Alexander, 1980). Pollen viability was evaluated for each sample, and pollen grain diameter was measured for ten representative viable pollen grains per replication. General morphology of the pollen was observed for each of the three replications of MON 87708, the conventional control, and the commercial reference varieties (see Appendix H).

No statistically significant differences were detected (5% level of significance) between MON 87708 and the conventional control for percent viable pollen or pollen grain diameter (Table VII-7). Furthermore, no visual differences in general pollen morphology were observed between MON 87708 and the conventional control. These results demonstrate that the introduction of the dicamba tolerance trait did not alter the overall morphology or viability of MON 87708 pollen compared to the conventional control. The pollen characterization data contribute to the detailed phenotypic description of MON 87708 compared to the conventional control. The result supports an overall conclusion that MON 87708 is similar to conventional soybean and is no more likely to pose a plant pest risk than conventional soybean.

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Table VII-7. Pollen Characteristics of MON 87708 Compared to Conventional Control

Pollen Characteristic	Mean (S.E.)[1]		Reference Range[2]	
	MON 87708	Control	Minimum	Maximum
Viability (%)	99.3 (0.3)	98.4 (0.9)	98.1	98.4
Diameter (µm)	24.4 (0.5)	24.3 (0.7)	23.4	24.3

Note: No statistically significant differences were detected between MON 87708 and the conventional control (α=0.05).

[1] Means based on n = 3. S.E. = Standard Error

[2] Reference ranges were determined from the minimum and maximum mean value from among the four commercial reference varieties.

VII.C.4. Symbiont Interactions

As part of the plant pest risk assessment, USDA-APHIS considers the impact of the biotechnology-derived crop on plant pest potential and the environment as well as on agricultural or cultivation practices compared to its conventional counterpart. Changes in the symbiotic relationship with rhizosphere-inhabiting bacteria *Rhizobiaceae* and *Bradyrhizobiaceae* could directly impact pest potential, the environment, or cultivation practices (*i.e.*, the need to add additional nitrogen to sustain soybean production). Thus, the purpose of this evaluation was to assess whether the introduction of the dicamba tolerance trait altered the symbiotic interaction of MON 87708 with *Bradyrhizobium japonicum* (*B. japonicum*) compared to that of the conventional control.

Members of the bacterial family *Rhizobiaceae* and *Bradyrhizobiaceae* form a highly complex and specific symbiotic relationship with leguminous plants, including soybean (Gage, 2004). The nitrogen-fixing plant-microbe symbiosis results in the formation of root nodules, providing an environment in which differentiated bacteria called bacteroids are capable of reducing or fixing atmospheric nitrogen. The product of nitrogen fixation, ammonia, then can be utilized by the plant. In soybean, atmospheric nitrogen is fixed into ammonia through a symbiotic association with the bacterium *B. japonicum*. As a result of this relationship, nitrogen inputs are typically not necessary for agricultural production of soybean.

The relative effectiveness of the symbiotic association between a leguminous plant and its rhizobial symbiont can be assessed by various methods. Assessment of nodule number and mass along with plant growth and nitrogen status are commonly used to assess differences in the symbiotic association between a legume and its associated rhizobia (Israel et al., 1986). It should be noted, however, that nodule number relative to nodule dry weight may be variable in soybean experiments because nodules may be larger in diameter and less numerous, while others are not as developed (smaller) but more abundant (Appunu and Dhar, 2006; Israel et al., 1986).

MON 87708, the conventional control, and six commercial reference varieties were produced from seeds planted in pots containing nitrogen-deficient potting medium grown in a greenhouse. Seeds were inoculated with a solution of *B. japonicum*. The pots were arranged in a randomized complete block design with eight replicates. At six weeks after emergence, plants were excised at the surface of the potting medium, and shoot and root plus nodule material were removed from the pots. Nodules were separated from roots prior to enumeration and determination of dry weight. MON 87708 was compared to the conventional control for key characteristics related to their association with the soybean-*B. japonicum* symbiosis. Detailed information on materials and methods used for the symbiont evaluation is presented in Appendix I.

No statistically significant differences were detected (5% level of significance) between MON 87708 and the conventional control for any of the measured characteristics, including nodule number, nodule dry weights, root dry weights, shoot dry weights, and shoot total nitrogen (percent and mass) (Table VII-8).

Based on the assessed characteristics, the results support the conclusion that the introduction of the dicamba tolerance trait does not alter the symbiotic relationship between *B. japonicum* and MON 87708 compared to the conventional control. Thus, these data further support a conclusion of no change in plant pest potential and no expected impact to cultivation practices relative to nitrogen inputs for MON 87708 compared to conventional soybean.

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Table VII-8. Symbiont Interaction Assessment of MON 87708 and Conventional Control

	Mean (S.E.)[1]		Reference Range[2]	
Characteristic	MON 87708	Control	Minimum	Maximum
Nodule Number (per plant)	264 (25)	238 (13)	148	346
Nodule Dry Weight (g/plant)	0.58 (0.03)	0.56 (0.02)	0.43	0.66
Root Dry Weight (g/plant)	1.33 (0.07)	1.15 (0.04)	1.09	1.89
Shoot Dry Weight (g/plant)	6.95 (0.46)	6.03 (0.23)	5.93	8.68
Shoot Total Nitrogen (% dwt)	4.46 (0.05)	4.48 (0.06)	3.51	4.26
Shoot Total Nitrogen (g)	0.31 (0.02)	0.27 (0.01)	0.25	0.32

Note: Pots were arranged in a greenhouse in a randomized complete block design. No statistically significant differences were detected between MON 87708 and the conventional control (α=0.05).

[1] Means based on n = 8. S.E. = Standard Error.

[2] Reference ranges were determined from the minimum and maximum mean value from among the six commercial reference varieties.

VII.D. Phenotypic, Agronomic, and Environmental Interactions Assessment Conclusion

An extensive and robust set of information and data were used to assess whether the introduction of the dicamba tolerance trait or the introduction of the dicamba tolerance trait in the presence of dicamba herbicide altered the plant pest potential of MON 87708 compared to the conventional control. Phenotypic, agronomic, and environmental interaction characteristics of both dicamba-treated and untreated MON 87708 were evaluated and compared to those of the conventional control and considered within the variation among commercial reference varieties. These assessments included plant growth and development characteristics; seed dormancy and germination characteristics; pollen characteristics; observations of abiotic stress response, disease damage, arthropod-related damage and arthropod abundance; and plant-symbiont interaction characteristics. Results from the phenotypic, agronomic, and environmental interactions assessment demonstrate that MON 87708 does not possess weedy characteristics, increased susceptibility or tolerance to specific abiotic stress, diseases, or arthropods, or characteristics that would confer a plant pest risk or significant environmental impact compared to conventional soybean.

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VIII. U.S. AGRONOMIC PRACTICES

VIII.A. Introduction

As part of the plant pest assessment required by 7 CFR § 340.6(c)(4), impacts to agricultural and cultivation practices must be considered. This section provides a summary of current agronomic practices in the U.S. for producing soybean and is included in this petition as a baseline to assess possible impacts to agricultural practices due to the cultivation of MON 87708. Discussions include soybean production, seed production, plant growth and development, general management practices during the season, management of weeds, insects and diseases, soybean rotational crops, and volunteer soybean management. Information presented in Section VII.C.2 demonstrated that MON 87708 is no more susceptible to diseases or pests than conventional soybean. Additionally data presented in Section VII.C show that, with the exception of tolerance to the herbicide dicamba, MON 87708 is phenotypically equivalent to conventional soybean. Thus, there are no changes to the inputs needed for MON 87708, and no specific impacts to most of the agronomic practices employed for production of soybean. In the areas where there is potential for impact on agronomic practices from the deregulation of MON 87708, the scope and magnitude of those impacts will be discussed.

Soybean is planted in over 30 states, demonstrating its wide adaptation to varied soils and climate. The soil, moisture, and temperature requirements for producing soybean are generally similar to those for corn, and thus the two crops share a similar cultivation area. Proper seedbed preparation, appropriate variety selection, appropriate planting dates and plant population, and good integrated pest management practices are important for optimizing the yield potential and economic return for soybean.

Annual and perennial weeds are perceived to be the greatest pest problem in soybean production (Aref and Pike, 1998). Weeds compete with soybean for water, nutrients, and light resulting in substantial yield losses when left uncontrolled. Weed species in soybean vary from region to region and state to state. Economic thresholds for controlling weeds in soybean require some form of weed management practice on all soybean acreage. Weed management practices include mechanical tillage, crop rotations, cultural practices, and herbicide application. Numerous selective herbicides are available for preplant, preemergence, and postemergence control of annual and perennial weeds in soybean. Approximately 98% of the soybean acreage in the U.S. receives an herbicide application (USDA-NASS, 2006). Soybean insects and diseases generally are considered less problematic, although infestations can reach economic thresholds requiring treatment.

Volunteer soybean, *i.e.*, soybean plants that have germinated and emerged unintentionally in a subsequent crop, are not considered a significant concern in rotational crops primarily because of climatic conditions and adequate control of volunteer soybean from tillage practices. Additionally, mechanical and chemical control methods are available to manage the occasional volunteer soybean plant. Due to its lack of weediness potential, introduction of MON 87708 in the soybean production system would have a negligible impact on managing soybean volunteer plants in rotational crops such as corn, cotton,

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and wheat. The numerous control measures that are effective on conventional and Roundup Ready soybean volunteer plants will continue to be effective on volunteer MON 87708 plants when they arise.

As shown in Sections VI and VII, with the exception of the dicamba tolerance trait, no phenotypic, compositional, or environmental differences between MON 87708 and conventional soybean have been observed. Moreover herbicide-tolerant soybean is currently grown on 91% of U.S. soybean acres (USDA-NASS, 2009c). MON 87708 will facilitate a wider window of application of dicamba (at planting and in-crop) and will replace or supplement the use of other soybean herbicides. Therefore, it is not anticipated that commercialization of MON 87708 in the U.S. would have a notable impact on current soybean cultivation practices, including the management of weeds, diseases, and insects other than the in-crop use of dicamba in soybean production.

VIII.B. Overview of U.S. Soybean Production

VIII.B.1. Soybean Production

Soybean first entered North America in the 18th century (Hoeft et al., 2000). During the 1930s, soybean started to be processed industrially in the U.S. for edible oil and protein meal. In 2008, soybean represented 56 percent of world oilseed production, and about a third of those soybeans were produced in the U.S. (ASA, 2009). In 2008, the U.S. exported 1.16 billion bushels (31.6 million metric tons) of soybean, which accounted for 40 percent of the world's soybean exports (ASA, 2009). In total, the U.S. exported $[redacted] worth of soybean and soybean products globally in 2008 (ASA, 2009). China was the largest export market for U.S. soybean with purchases totalling $[redacted]. Mexico was the second largest export market with purchases of $[redacted]. Other significant markets include the European Union ($[redacted]) and Japan ($[redacted]).

Approximately 94% of the world's soybean seed supply was crushed to produce soybean meal and oil in 2008 (Soyatech, 2010), and the majority was used to supply the feed industry for livestock use or the food industry for edible vegetable oil and soybean protein isolates.

The productivity of soybean is highly dependent upon soil and climatic conditions. In the U.S., the soil and climatic requirements for growing soybean are very similar to corn. The soils and climate in the Midwestern, Eastern, and portions of the Great Plains regions of the U.S. provide sufficient water under normal climatic conditions to produce a soybean crop. The general water requirement for a high-yielding soybean crop is approximately 20 inches of water during the growing season (Hoeft et al., 2000). Soil texture and structure are key components determining water availability in soils, where medium-textured soils hold more water, allowing soybean roots to penetrate deeper in medium-textured soils than in clay soils. Irrigation is used on approximately 9% of the soybean acreage to supplement the water supply during dry periods in the Western and Southern soybean growing regions (USDA-ERS, 2008).

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Most of the soybean acreage is grown as a full-season crop. Approximately 8% of the soybean acres are planted in a double-crop system following winter wheat south of 35º North latitude (Boerma and Specht, 2004). However, this percentage can vary significantly from year to year. The decision to plant double-crop soybean is influenced by both agronomic and economic factors. Agronomic factors include harvest date of the wheat crop, which determines the double-crop soybean planting date, and available soil moisture. Economic factors include expected soybean price and anticipated economic return (Boerma and Specht, 2004).

The U.S. soybean acreage in the past 10 years has varied from approximately 64.7 to 75.7 million acres, with the lowest acreage recorded in 2007 and the highest in 2008 (Table VIII-1). Average soybean yields have varied from 33.9 to 43.3 bushels per acre over this same time period. Annual soybean production ranged from 2.45 to 3.19 billion bushels over the past ten years. According to data from USDA-NASS (2009a), soybean was planted on approximately 75.7 million acres in the U.S. in 2008, producing 2.96 billion bushels of soybean (Table VIII-1). Soybean acreage and production in 2008 was up from 2007, mainly due to a decrease in corn acreage. The value of soybean reached $[redacted] in the U.S. in 2008 (USDA-NASS, 2009b). In comparison, corn and wheat values in 2008 were $[redacted] and $[redacted], respectively (USDA-NASS, 2009a, b).

For purposes of this agronomic practices discussion, soybean production is divided into three major soybean growing regions accounting for 99.1% of the 2008 U.S. soybean acreage: Midwest/Great Plains region (IL, IN, IA, KS, KY, MI, MN, MO, NE, ND, OH, SD, and WI), Southeast region (AL, AR, GA, LA, MS, NC, SC, and TN) and the Eastern Coastal region (DE, MD, NJ, NY, PA, and VA) (Table VIII-2). The vast majority of soybean was grown in the Midwest region, representing 82.1% of the total U.S. acreage. The Southeast and Eastern Coastal regions represented 14.3% and 2.7% of the acreage, respectively. Among the three regions, the Midwest region produced the highest average yield at 38.6 bushels per acre in 2008, and average state yields in this region ranged from 28.0 to 47.0 bushels per acre. The average yield in the Southeast region was 34.4 bushels per acre, with states within this region averaging from 30.0 to 40.0 bushels per acre. The average yield in the Eastern Coastal region was 34.1 bushels per acre, with individual state averages ranging from 27.5 to 46.0 bushels per acre.

Managing input costs is a major component to the economics of producing a soybean crop (Helsel and Minor, 1993). Key decisions on input costs include choosing what soybean varieties to plant, amounts of fertilizer to apply, and what herbicide program to use. The average operating cost for producing soybean in the U.S. in 2008 was [redacted] per acre, according to statistics compiled by the USDA-Economic Research Service (USDA-ERS, 2008). The value of the production less operating cost was reported to be $[redacted] per acre. A summary of potential production costs and returns are presented in Table VIII-3.

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Table VIII-1. Soybean Production in the U.S., 1999 – 2008[1]

Year	Acres Planted (×1000)	Acres Harvested (×1000)	Average Yield (bushels/acre)	Total Production (×1000 bushels)	Value ([redacted] $)
2008	75,718	74,641	39.6	2,959,174	[redacted]
2007	64,741	64,146	41.7	2,677,117	[redacted]
2006	75,522	74,602	42.7	3,188,247	[redacted]
2005	72,142	71,361	43.3	3,086,432	[redacted]
2004	75,208	73,958	42.2	3,123,686	[redacted]
2003	73,404	72,476	33.9	2,453,665	[redacted]
2002	73,963	72,497	38.0	2,756,147	[redacted]
2001	74,075	72,975	39.6	2,890,682	[redacted]
2000	74,266	72,408	38.1	2,757,810	[redacted]
1999	73,730	72,446	36.6	2,653,758	[redacted]
Ave.	73,277	72,151	39.6	2,854,672	[redacted]

[1] Source is USDA-NASS (2009a,b).

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Table VIII-2. U.S. Soybean Production by Region and State in 2008[1]

Region/State	Acres Planted (thousands)	Acres Harvested (thousands)	Average Yield (bushels/acre)	Total Production (×1000 bushels)	Value ([redacted] $)
Midwest Region					
Illinois	9,200	9,100	47.0	427,700	[redacted]
Indiana	5,450	5,430	45.0	244,350	[redacted]
Iowa	9,750	9,670	46.0	444,820	[redacted]
Kansas	3,300	3,250	37.0	120,250	[redacted]
Kentucky	1,390	1,380	34.0	46,920	[redacted]
Michigan	1,900	1,890	37.0	69,930	[redacted]
Minnesota	7,050	6,950	38.0	264,100	[redacted]
Missouri	5,200	5,030	38.0	191,140	[redacted]
Nebraska	4,900	4,860	46.5	225,990	[redacted]
North Dakota	3,800	3,760	28.0	105,280	[redacted]
Ohio	4,500	4,480	36.0	161,280	[redacted]
South Dakota	4,100	4,060	34.0	138,040	[redacted]
Wisconsin	1,610	1,590	35.0	55,650	[redacted]
Region Totals	**62,150**	**61,450**	**38.6**	**2,495,450**	[redacted]
Southeast Region					
Alabama	360	350	35.0	12,250	[redacted]
Arkansas	3,300	3,250	38.0	123,500	[redacted]
Georgia	430	415	30.0	12,450	[redacted]
Louisiana	1,050	950	33.0	31,350	[redacted]
Mississippi	2,000	1,960	40.0	78,400	[redacted]
North Carolina	1,690	1,670	33.0	55,110	[redacted]
South Carolina	540	530	32.0	16,960	[redacted]
Tennessee	1,490	1,460	34.0	49,640	[redacted]
Region Totals	**10,860**	**10,585**	**34.4**	**379,660**	[redacted]
Eastern Coastal Region					
Delaware	195	193	27.5	5,308	[redacted]
Maryland	495	485	30.0	14,550	[redacted]
New Jersey	92	90	29.0	2,610	[redacted]
New York	230	226	46.0	10,396	[redacted]
Pennsylvania	435	430	40.0	17,200	[redacted]
Virginia	580	570	32.0	18,240	[redacted]
Region Totals	**2027**	**1994**	**34.1**	**68,304**	[redacted]

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Table VIII-3. U.S. Soybean Production Costs and Returns in 2008[1]

Production Cost or Return Category	Itemized Costs	Return per Planted Acre ($ USD)
Total Gross Value of Production		[redacted]
Operating Costs:	Seed	[redacted]
	Fertilizer	[redacted]
	Chemicals	[redacted]
	Custom operations	[redacted]
	Fuel, lube and electricity	[redacted]
	Repairs	[redacted]
	Purchased irrigation water	[redacted]
	Interest on operating capital	[redacted]
Total, operating costs		[redacted]
Allocated overhead:	Hired labor	[redacted]
	Opportunity cost of unpaid grower's labor	[redacted]
	Capital recovery of machinery and equipment	[redacted]
	Opportunity cost of land (rental rate)	[redacted]
	Taxes and insurance	[redacted]
	General farm overhead	[redacted]
Total, allocated overhead		[redacted]
Total cost listed		[redacted]
Value of production less total cost listed		[redacted]
Value of production less operating costs		[redacted]

Supporting Information: Yield = 43 bushels/acre, Price = $[redacted]/bushel, Enterprise size = 303 planted acres, Irrigated = 9%, Dry land = 91%.

[1] Source is USDA-ERS (2008).

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VIII.B.2. Soybean Seed Production

Standardized seed production practices are responsible for maintaining high-quality seed stocks, an essential basis for U.S. agriculture. By the early 20th century, agronomists learned how to develop specific plant varieties with desirable traits. In the U.S., state agricultural experiment stations developed many seed varieties that were distributed to growers for use. Seed was saved by growers and later sold to neighbors; however, the desirable traits of the varieties often were lost through random genetic changes and contamination with other crop and weed seed (Sundstrom et al., 2002). The value of seed quality (including genetic purity, vigor, and presence of weed seed, seed-borne diseases, and inert materials, such as dirt) was quickly identified as a major factor impacting crop yields. States developed seed laws and certification agencies to ensure that purchasers who received certified seed could be assured that the seed met established seed quality standards (Bradford, 2006). The federal government passed the U.S. Federal Seed Act of 1939 to recognize seed certification and the establishment of official certifying agencies. Regulations first adopted in 1969 under the Federal Seed Act recognize land history, field isolation, and varietal purity standards for foundation, registered, and certified seed. Under international agreements such as the Organization for Economic Co-Operation and Development (OECD) scheme, the U.S. and other countries mutually recognize minimum seed quality standards (Bradford, 2006). The Association of Official Seed Certifying Agencies (AOSCA) represents state and private seed certification organizations in the U.S., and includes international member countries in North and South America, Australia, and New Zealand.

Soybean seed is separated into four seed classes: 1) breeder, 2) foundation, 3) registered, and 4) certified (AOSCA, 2009). Breeder seed is seed directly controlled by the originating or sponsoring plant breeding organization or firm. Foundation seed is first-generation seed increased from breeder seed and is handled in a manner to maintain specific levels of varietal purity and identity. Registered seed is the progeny of foundation seed that is handled to maintain satisfactory varietal purity and identity. Certified seed is the progeny of breeder, foundation or registered seed, and is typically two generations removed from foundation seed. While not all soybean seed sold to growers is officially certified, commercial soybean seed sold and planted for typical soybean production is produced predominately to meet or exceed certified seed standards. This section of the petition will provide a broad overview of the practices used in producing certified seed.

Soybean seed breeders and producers have put in place practical measures to assure the quality and genetic purity of soybean varietal seed for commercial planting. The need for such systems arose from the recognition that the quality of improved soybean varieties quickly deteriorated in the absence of monitoring for quality and genetic purity (CAST, 2007). Seed certification programs were initiated in the early 1900s in the U.S. to preserve the genetic identity and variety purity of seed. There are special land requirements, seed stock eligibility requirements, field inspections and seed labeling standards for seed certification. Seed certification services are available through various state agencies affiliated with AOSCA. Large seed producers implement their own seed quality assurance programs. However, large seed producers often will utilize the services

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of state certifying agencies as a third party source to perform certain field inspections and audits.

U.S soybean production for all purposes has varied from approximately 64.7 to 75.7 million acres in the past ten years (USDA-NASS, 2009a; Table VIII-1). To plant this area of soybean acreage requires 105 to 125 million units (50 lbs/unit) of soybean seed. This seed volume includes allowances for seed losses due to weather, poor yields, and quality issues. Additional allowances are included for distribution excess, seed returns, replants, and potential increases in soybean acreage. Assuming an average soybean yield of 45 bushels, or 54 units (50 lbs/unit) per acre, 1.9 to 2.3 million acres would be required to produce this volume of commercial certified soybean seed each year.

Certified soybean seed is produced throughout most of the U.S. soybean-growing regions. Soybean varieties are developed and adapted to certain geographical zones and are separated into ten maturity groups – Group 00 to Group VIII (see Section VIII.C). Seed production for these maturity groups is grown in the respective geographical zone for each maturity group. However, the production areas generally are on the northern edge of the respective zone to minimize incidences of disease.

Soybean seed is produced by a number of companies that produce and sell seed, such as Monsanto Company, Pioneer Hi-Bred International, Syngenta Seeds, Kruger Seed Co., and Becks Hybrids. In addition, certified seed is produced by toll seed producers, or tollers, which are companies that produce but do not directly sell certified seed, such as Remington Seeds LLC and Precision Soya. Seed companies and tollers in turn contract acreage with growers to produce the needed amount of soybean seed. Seed production or processing plants at these seed companies identify local soybean growers to produce the seed and also monitor and inspect seed fields throughout the growing season. The seed production plants also clean, condition, and bag the harvested soybean seed as well as monitor and inspect all the processes at the plant. Production plants typically produce between 100,000 units to 2,000,000 units of soybean seed. Production plants will produce the various soybean varieties in different climates or environments to spread production risks.

The entire seed production process at the majority of the seed companies and tollers operate using International Organization for Standardization (ISO) certification standards and, therefore, include internal and external audits (ISO, 2009). ISO standards ensure desirable characteristics of seeds and services, such as quality, safety, reliability, and efficiency. The ISO standards represent an international consensus on good management practices with the aim of ensuring that the organization can consistently deliver excellent product or services. The standards not only must meet the customer's requirements and applicable seed regulatory requirements, but must aim to enhance customer satisfaction and achieve continual improvement of its performance in pursuit of these objectives (ISO, 2009).

The field operations and management practices for producing soybean seed are similar to normal soybean production. However, special attention is needed in certain areas to produce seed with high quality, high germination rates, and high genetic purity (Helsel

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and Minor, 1993). General guidelines specific for seed production are discussed below. Importantly, the seed production field should not have been planted with soybean in the previous crop season in order to avoid potential volunteer soybean plants (even though the risk of soybean volunteer plants is negligible) and to ensure genetic purity.

Very early planting is typically avoided because the seed produced from early planting often results in poorer quality seed (Helsel and Minor, 1993). Every effort must be made to eliminate weeds in a seed field through the use of herbicides and cultivation practices to prevent weed seed in the harvested soybean seed. Fields are scouted frequently for insect pests and insecticides are applied when insect pest infestations reach economical threshold levels. Foliar-applied fungicides should be considered when disease infestations are predicted in the area. Harvest should occur as soon as the mature soybean seed reaches 13% moisture content. Harvesting soybean seed with less than 13% moisture can cause damage to the seed coat and result in split soybean seed that can affect germination and viability. Harvesting equipment must be adjusted to minimize or avoid seed damage. Harvesting equipment must be cleaned before entering the seed fields to assure genetic purity. Certain seed handling equipment, such as auger elevators, should be avoided because they can increase seed damage.

Field inspections are vital to ensure the soybean seed meets seed certification requirements, ISO certification standards, regulatory standards, and trait licensing agreement standards. Field inspections are conducted on seed production fields throughout the soybean growing season to visually evaluate variety purity, ensure soybean plants are developing properly, and fields are maintained free of weeds, insects, and diseases. The fields are also mapped to ensure the seed field has the minimum federal isolation requirement of five feet as a physical barrier (AOSCA, 2009). Some states and seed producers have a stricter isolation requirement of 10 feet.

Production plant personnel make every effort to avoid mechanical damage to the harvested seed during the screening, cleaning, and bagging process. Specific methods are used to assure the genetic purity and the identity of the seed is maintained throughout the handling and storage operation. Bin inspections and sample collections are conducted at storage locations at the seed production plant to examine the physical characteristics of the soybean seed and to ensure proper bin cleanout. Seed is inspected for appearance, disease, discoloration, seed coat, mechanical damage, inert matter, and weed seed. Warm and cold germination tests are conducted on all seed lots to verify acceptable germination rates. Many seed companies will also conduct tetrazolium staining tests to assess seed viability.

Commercially certified soybean seed must meet state and federal seed standards and labeling requirements. AOSCA standards for certified soybean seed are as follows: 98% pure seed (minimum), 2% inert matter (maximum), 0.05% weed seed (maximum, not to exceed 10 per lb.), 0.60% total of other crop seeds (maximum), 0.5% other varieties (maximum, includes off-colored beans and off-type seeds), 0.10% other crop seeds (maximum, not to exceed three per lb.), and 80% germination and hard seed (minimum) (AOSCA, 2009). State seed certification standards vary slightly from state to state and can be more restrictive than the seed standards of AOSCA.

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When deregulated, MON 87708 seed will be produced in the same manner as commercially certified soybean seed, such that it will meet all state and federal seed standards and labeling requirements.

VIII.C. Production Management Considerations

VIII.C.1. Pre-Season

Well in advance of planting a soybean crop, decisions are made regarding the planned crop rotation, the tillage system and row spacing that will be implemented, the planting equipment that will be used, the seed or variety that will be planted, and soil fertility management requirements. Many of the decisions in this area are made prior to or immediately after harvest of the previous crop. There are many benefits to crop rotation, with the majority of the soybean acreage planted in a two-year corn-soybean rotation (see Section VIII.I). Crop rotation is generally a long-term decision, but the rotation sequence can be modified to take advantage of a particular economic or market opportunity. The decision to plant soybean in a conservation tillage or no-till system may require special equipment and will be made long before planting. In addition, this decision on tillage system usually will be a long-term commitment, provided the system is successful. A decision to change row spacing is a similar long-term commitment that generally requires new equipment.

The benefits of conservation tillage or no-till systems are well documented and include reduced soil erosion, reduced fuel and labor costs, and conservation of soil moisture (CTIC, 2011). In 2004, approximately 27.5 million acres (39.6%) of soybean were planted in a no-till system (CTIC, 2007). Slow soybean emergence and growth leading to lower yields have been some of the concerns associated with adoption of conservation tillage systems in soybean, especially no-till. Research in Wisconsin and Minnesota shows that soil temperatures can be four to five degrees colder in no-till than conventional tillage systems, which can slow seedling emergence, but have little effect on soybean yield (Pedersen, 2008a). Improved planters for establishment of good soybean populations and planting Roundup Ready soybean allowing the use of glyphosate to effectively control weeds in no-till fields have made no-till a viable production system for soybean (Pedersen, 2008a). Extension specialists still recommend some spring tillage on fine-textured and poorly drained soils for proper seedbed preparation (Pedersen, 2008a).

Most field crops, including soybean, respond well to fertilizer when planted in soils with low fertility levels. Soybean requires 16 essential elements for growth and development. Deficiencies in any of these elements can reduce yields (Hoeft et al., 2000). The primary or major essential nutrients are nitrogen, phosphorus and potassium. The soybean plant is a member of the legume family, like alfalfa and clover, and fixes a significant portion of its own nitrogen through the symbiotic relationship with the nitrogen-fixing Bradyrhizobia bacteria (*Bradyrhizobium japonicum*) that live in the nodules on its roots. Bradyrhizobia are unicellar, microscopic bacteria that invade the soybean plant through its root hairs (Hoeft et al., 2000). The plant responds to this invasion by forming nodules which contain colonies of bacteria. Once established on the soybean root, bacteria in the nodule take gaseous nitrogen from the atmosphere and fix it in forms easily used by the

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soybean plant. Since these bacteria are not native to U.S. soils and would not normally be found in these soils, inoculation of the soybean seed with these bacteria is recommended when soybean has not been grown in a field for three to five years. Nitrogen fertilizer applications at planting generally do not improve yield and decrease nodulation while increasing the plant's dependency on the soil for nitrogen (Pedersen, 2008a). Therefore, nitrogen fertilizer is seldom applied prior to planting a soybean crop.

Soil tests are the only reliable way to determine the pH, phosphorus, and potassium levels in the soil. Liming and fertilizer requirements subsequently are determined based on soil test results. Ideal soil test results for corn are also ideal for soybean (Scott and Aldrich, 1970). In corn-soybean rotations in the Midwest, phosphorus and potassium fertilizers are applied prior to a corn crop in accordance with soil test recommendations, but are seldom applied prior to a soybean crop. However, in some of the southern growing areas, differences in crop rotations and soil types may require a fertilizer application prior to planting soybean.

Although not common, deficiencies in soil can occur in secondary nutrients (calcium, magnesium, and sulfur) or micronutrients (boron, chloride, copper, iron, manganese, molybdenum, and zinc). The availability of soil nutrients is dependent on soil acidity or pH level. Because soybean is adversely affected when the pH is below approximately 5.8 (Hoeft et al., 2000), soil pH should be maintained at about 6.0 to 6.5 through the addition of limestone.

Soybean varieties are developed and adapted to certain geographical zones and are separated into ten maturity groups – Group 00 to Group VIII (Pimentel, 1991; Zhang et al., 2004). Groups 00 and 0 are the earliest maturity groups and are adapted best to the area north of latitude 46º North. Succeeding groups are adapted further south with Groups I and II within latitudes 41º and 46º North, and Group III within latitudes 38º and 41º North. Group 00 through Group IV soybean varieties are planted in the Midwest and Eastern Coastal regions. Groups II, III and IV account for approximately 76% (24%, 36%, and 16%, respectively) of the soybean planted in the U.S. ([redacted] personal communication, August 2008). Groups IV through VIII are planted in the southern states with Groups V, VI and VII representing 7%, 2%, and 2% of the planted soybean, respectively ([redacted] personal communication, August 2008).

Soybean variety selection is crucial for high yield and quality, and is the foundation of an effective management plan (Pedersen, 2008a). Characteristics to consider in selecting a variety include maturity, yield potential, disease and pest resistance, iron deficiency tolerance (chlorosis), lodging score, height, and specific soybean quality traits, such as protein and oil content. If a field has a history of a particular disease or pest, planting soybean varieties that have resistance or tolerance to these pests and diseases can be an effective and economical method of control.

VIII.C.2. Planting and Early Season

An understanding of the growth stages of soybean is also important for the proper timing of certain management practices, such as herbicide and insecticide applications. In

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addition, the impact of certain weather conditions, insect pests, and diseases on soybean yield is dependent on growth stage. The system of soybean growth stages divides plant development into vegetative (V) and reproductive (R) stages (Pedersen, 2008a). The vegetative stages begin with VE, which designates emergence. V stages continue and are numbered according to how many fully developed trifoliate leaves are present (*i.e.*, V1, V2, etc.). The reproductive (R) stages begin at flowering (R1) and include pod development and plant maturation. Full maturity is designated as R8.

Adequate soil moisture and warm temperatures facilitate rapid seed germination and emergence. The ideal soil temperature for soybean germination and emergence is 77ºF (Pedersen, 2008a). However, waiting for soils to reach this soil temperature will delay planting beyond the optimum planting date that will maximize yield. Soybean can germinate at a soil temperature of 50ºF when planted at a depth of two inches. However, emergence is slow and can take up to three weeks in northern climates. Because of fluctuations in soil temperature in early spring, soil temperature should not be the only criteria for optimum planting time. Planting into a good seedbed is the most important consideration. Planting into soil that is too wet will reduce emergence and plant population, and can lead to reduced yield.

Planting date has the greatest impact on yield, according to research conducted in the Northern states (Hoeft et al., 2000). Highest yields are generally obtained when planting in early to mid May. Yields begin to decline quite rapidly when planting is delayed until late May. For example, the optimum planting dates for soybean in Iowa are the last week of April in the southern two-thirds of the state and the first week of May in the northern one-third of the state (Pedersen, 2008a). In the Southern U.S., planting adapted varieties before late April results in shorter plants and, in many cases, lower yields than when the same varieties are planted in May or early June. Planting after early June generally decreases plant height and yield due to water shortages in July and August.

Variations in plant spacing through row spacing and plant population have a significant effect on canopy development and soybean yield. Row spacing is important to maximize soybean yield. Research in the Midwest over the past 20 years consistently shows that row spacing of less than 20 inches is preferred for soybean regardless of tillage system, rotation sequence or planting date (Pedersen, 2008a). In the Southern states, the advantage from narrow rows is less consistent and less beneficial. In 2000, approximately 40% of soybean was planted in row spacing of 10 inches or less, 27% in 10.1 to 28.5 inches, and 33% in rows wider than 28.5 inches (Hoeft et al., 2000).

Soybean has the ability to produce good yield over a wide range of plant populations. Most soybean varieties have the ability to branch and adjust the number of pods on branches to compensate for large differences in seeding rate. Maximum yields generally require planting rates that result in about 2.5 to 5 plants per square foot (Hoeft et al., 2000). Therefore, a full stand of soybean is approximately eight to ten plants per foot of row at harvest for 40-inch rows, six to eight plants per foot of row in 30-inch rows, four to six plants in 20-inch rows, and two to three plants in 10-inch rows. This translates to 109,000 to 218,000 plants per acre at harvest. Higher populations are recommended in narrow rows for maximum yields because plants are more uniformly spaced in narrow

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rows. Seeding rates are generally 10 to 25% higher than the desired harvest population, especially in no-till fields, to account for the losses in germination, emergence, and seedling diseases. The accuracy of the planting equipment also can impact the decision on seeding rate. Soybean seed traditionally has been sold by weight. Therefore, the grower must know the number of seeds per pound for the particular soybean varieties being planted for accurate seeding rates.

Treating soybean seed with a fungicide (*e.g.*, metalaxyl or mefenoxam) to prevent damping-off diseases may be beneficial when planting in cold, wet soils, using reduced till and no-till planting systems, and when planting seed with a low germination rate (<80%) or low seed vigor (Pedersen, 2008a).

Annual and perennial weeds are considered to be the greatest pest problem in soybean production (Aref and Pike, 1998). In order to maximize yields, weeds must be controlled during the early growth stages of soybean because weeds compete with soybean for water, nutrients, and light. There have been many studies examining the loss in soybean yield due to weed competition. The amount of loss is dependent upon the species, time when the weed is growing with the crop, and crop cultural practices, particularly row spacing. A sampling of these studies show that soybean yield reductions are generally in the range from 10% to 50% (Norsworthy et al., 2002; Shurtleff and Coble, 1985; Vail et al., 1993, Hock et al., 2006). In one study, yield loss due to several annual grasses ranged from 13% to 16% while yield losses due to various annual broadleaf weeds ranged from 23% to 52% (Hock et al. 2006). A combination of tillage and herbicides are used to control weeds throughout the growing season (Section VIII.F).

VIII.C.3. Mid to Late Season

Ideal daytime temperatures for soybean growth are between 75ºF and 85ºF (Hoeft et al., 2000). Warmer temperatures result in larger plants and earlier flowering. Sustained temperatures below 75ºF will delay the beginning of flowering significantly. Seed set also is affected by temperature. Seed set is generally good when pollination follows night temperatures around 70ºF. Soybean varieties differ in their response and tolerance to temperatures.

Soybean is photoperiod sensitive, which means that it transitions from vegetative to flowering stage in direct response to length of daylight (Scott and Aldrich, 1970). Most soybean varieties begin flowering soon after the day length begins to shorten. Flowering of southern varieties is initiated by a shorter day than that of varieties adapted to the north. The extent of vegetative growth occurring after the initiation of flowering depends not only on environmental factors but also the growth habit. Soybean varieties are described as either indeterminate or determinate in their growth habit (Scott and Aldrich, 1970). Indeterminate varieties increase their height by two to four times after flowering begins. Indeterminate varieties are typically grown in the northern and central U.S. Determinate varieties increase their height very little after flowering and generally are grown in the southern U.S. Indeterminate and determinate varieties also differ in flowering characteristics. Indeterminate plants generally bloom first at the fourth or fifth

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node and progress upward. Flowering on determinate plants begins at the eight or tenth node and progresses both downward and upward.

The first appearance of flowers signals the beginning of the reproductive stage, namely the R1 stage (Hoeft et al., 2000). The reproductive period consists of flowering, pod set, and seed formation. Climatic conditions such as temperature and moisture supply during the flowering period will affect the number of flowers. The soybean plant does not form a pod from each flower. It is common for the soybean plant to have 75% of the flowers fail to develop a pod (Scott and Aldrich, 1970). This characteristic makes soybean less susceptible than corn to short periods of adverse weather during flowering. Under normal conditions, pod set occurs over about a three week period. Good soil moisture is most critical during the pod-filling stages to prevent pod abortion and to ensure high yields (Hoeft et al., 2000). Another critical requirement during the seed-filling stages is a high rate of photosynthesis to maximize yield. High humidity and temperatures during seed development and maturity can result in poor seed quality because these conditions promote the development of reproductive-stage diseases.

VIII.C.4. Harvest Season

When dry matter accumulation ends, the plant is considered to be physiologically mature. The seed moisture content is approximately 55 to 60% at this stage (Hoeft et al., 2000). At this stage, namely R7, at least one normal pod on the plant reaches the mature pod color. Under warm and dry weather conditions, seed moisture content will drop to 13 to 14% in 10 to 14 days from physiological maturity (Hoeft et al., 2000). Soybean can be harvested when the moisture content drops below 15%. However, soybean should be at 13% moisture to be stored without artificial drying (Scott and Aldrich, 1970). Moisture content below 12% may increase seed cracking and seed coat damage.

Pre-harvest losses are influenced by soybean variety, weather, and timeliness of harvest (Scott and Aldrich, 1970). Timely harvest when the moisture content is 13 to 14% also will minimize losses. Proper operation and adjustment of the combine is essential to minimizing harvest losses in the field.

VIII.D. Management of Insects

Although insects are rated as less problematic than weeds in U.S. soybean production, management of insect pests during the growth and development of soybean is important for protecting the yield of soybean (Aref and Pike, 1998). Understanding the impact of insects on soybean growth is essential for proper management (Higley and Boethel, 1994). It is important to understand the way that insects injure soybean as well as how the soybean plant responds to insect injury. Insect injury can impact yield, plant maturity, and seed quality. Insect injury in soybean seldom reaches levels to cause an economic loss, as indicated by the low percentage (16%) of soybean acreage that receives an insecticide treatment (USDA-NASS, 2007b).

Characterizing soybean responses to insect injury is essential in establishing economic injury levels (Higley and Boethel, 1994). Most often, soybean insects are categorized or

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defined by the plant parts they injure, namely root-feeding, stem-feeding, leaf-feeding, or pod-feeding insects. The root- and stem-feeding insect groups are often the hardest to scout and typically are not detected until after they have caused their damage. The leaf-feeding insects comprise the biggest group of soybean insect pests, but not necessarily the most economically damaging insects. Research on defoliation has determined that a major effect of leaf injury is to reduce light interception by the soybean canopy which in turn can have a significant effect on yield (Higley and Boethel, 1994). Soybean has an extraordinary capacity to withstand considerable defoliation early in the season without significant yield loss. By contrast, defoliation during the flowering and pod filling stages poses a greater threat to yield because the soybean plant has less time to compensate for injury compared to other growth stages. Research indicates that the soybean plant can sustain a 35% leaf loss prior to the pre-bloom period without lowering yield (NDSU, 2002). However, from pod-set to maturity, the plant can tolerate only a 20% defoliation level before yield is impacted.

VIII.E. Management of Diseases and Other Pests

More than 100 pathogens are known to affect soybean, of which 35 are considered to be of economic importance (Heatherly and Hodges, 1999). The estimated yield losses to soybean diseases in the U.S. were 12.5, 13.2, and 13.0 million metric tons in 2008, 2009, and 2010, respectively (Wrather and Koenning, 2011), which equated to 15.5%, 14.4%, and 14.4% of total soybean production, respectively (ASA, 2011). Pathogens can affect all parts of the soybean plant, resulting in reduced quality and yield. The extent of losses depends upon the pathogen, the state of plant development and health when infection occurs, the severity of the disease on individual plants, and the number of plants affected (Heatherly and Hodges, 1999).

One or more diseases can generally be found in fields wherever soybean is grown (Heatherly and Hodges, 1999). However, a pathogen may be very destructive one season and difficult or impossible to find the next season. The extent and severity of soybean diseases depend on the degree of compatibility between the host and the pathogen and the influence of the environment.

According to field surveys conducted in soybean-producing states during 1996 to 2010, soybean cyst nematode (SCN), *Heterodera glycines*, caused the greatest soybean yield losses (Wrather and Koenning, 2011). *Phytophthora* root and stem rot (*Phytophthora sojae*), brown spot (*Septoria glycines*), charcoal rot (*Macrophomina phaseolina*), *Sclerotinia* stem rot (*Sclerotinia sclerotiorum*), seedling diseases, and sudden death syndrome (*Fusarium solani f.sp. glycines*) followed in economical importance. As expected, yield losses vary by region. *Sclerotinia* stem rot caused yield losses in several Northern states, but not in other states. *Rhizoctonia* foliar blight losses were greatest in Arkansas, Louisiana, and Texas where humidity and temperature conditions are suitable for disease development (Wrather et al., 2001).

Selecting resistant varieties is the primary tool growers have for disease control (Heatherly and Hodges, 1999). Resistant varieties may have morphological or physiological characteristics that provide immunity, resistance, tolerance or avoidance to

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certain pathogens. Cultural practices can also play an important role in disease management by reducing initial inoculums or reducing the rate of disease development (Heatherly and Hodges, 1999). Preplant tillage can bury crop residue, which encourages the decomposition of fungal-resting structures. Crop rotation is routinely recommended as a disease-management strategy. Rotating crops interrupts the disease cycle and allows time for the decomposition of inoculums. One exception is *Rhizontonia* spp., a soil-inhabitant pathogen that grows on a wide variety of crops and can survive sufficiently in the soil to make crop rotation as a means of controlling this pest impractical. Row spacing, plant population, and planting date also can be changed to manage soybean diseases.

Soybean cyst nematode is one of the most damaging pathogens of soybean throughout the soybean growing regions of the U.S. (Pedersen, 2008b). Losses have been estimated to be at about $[redacted] in the U.S. (Pedersen, 2008a). SCN can cause yield losses up to 50%, where this pest in 2004 alone caused an estimated loss of 50 million bushels of soybean in Iowa (Pedersen, 2008c). Soybean cyst nematodes feed on the roots, causing severely stunted and yellow plants. The simplest, least expensive method to reduce populations of this pest is to rotate soybean with a non-host crop such as corn, small grains, or sorghum. Planting resistant varieties is regarded as the best and most effective management practice to prevent losses from this pest. Several public and private soybean varieties offer sources of resistance to certain races of nematode. Alternating varieties with different sources of resistance also is beneficial.

High-quality seed is essential for controlling seedling diseases. The most important seedling diseases in soybean are *Phytophthora* spp., *Pythium* spp., *Rhizoctonia* spp., and *Fusarium* spp. (Pedersen, 2008a). Many soybean varieties demonstrate resistance to specific taxonomic races of *Phytophthora*. Treating soybean seed with a fungicide (*e.g.*, metalaxyl or mefenoxam) is effective against damping-off disease (seedling blight) caused by common soil fungi, such as *Phytophthora* spp. and *Pythium* spp. Fungicide seed treatments are recommended where there is a history of these seedling diseases.

Asian soybean rust is a foliar fungal disease that typically infests soybean during reproductive stages of development and can cause defoliation and reduce yields significantly in geographies such as Brazil (Dorrance et al., 2007). Soybean rust is caused by the fungus *Phakopsora pachyrhizi*. This disease in the U.S. was first detected in Louisiana in 2004 (LSU, 2009). At this time, foliar application of fungicides is the standard disease-management practice to limit yield losses due to soybean rust.

Foliar fungicide applications can effectively reduce the incidence of many fungal diseases (Heatherly and Hodges, 1999). However, the economic return from a fungicide application may be limited to select soybean production systems; for example, high-yield environments or when producing soybean seed. According to USDA-NASS (2007b) statistics, fungicides were applied on approximately 4% of the soybean acreage in 2006.

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VIII.F. Weed Management

Annual weeds are perceived to be the greatest pest problem in soybean production, followed by perennial weeds (Aref and Pike, 1998). Soybean insects and diseases are rated less problematic but may reach economic thresholds requiring treatment. Weed control in soybean is essential to optimizing yields. Weeds compete with soybean for light, nutrients, and soil moisture. Weeds can harbor insects and diseases, and also can interfere with harvest, causing extra wear on harvest equipment (Pedersen, 2008a). The primary factors affecting soybean yield loss from weed competition are the weed species, weed density, and the duration of the competition. When weeds are left to compete with soybean for the entire growing season, yield losses can exceed 75% (Dalley et al., 2001). Generally, the competition between crops and weeds increases with higher levels of weed density. The time period that weeds compete with the soybean crop influences the level of yield loss. In general, early season weed competition will have the greatest negative impact on yield (Dalley et al., 2001). Soybean plants withstand early-season weed competition longer than corn without affecting yield, and the canopy closes earlier in soybean than corn. In addition, canopy closure is much sooner when soybean is drilled or planted in narrow rows. The most common weeds in soybean for each of the three major U.S. growing regions are presented in Tables VIII-4, VIII-5 and VIII-6.

Crop rotations and environment have a significant impact on the adaptation and occurrence of weeds in soybean. Foxtail spp. (*Setaria* spp.), pigweed (*Amaranthus* spp.), velvetleaf (*Abutilon theophrasti*), lambsquarters (*Chenopodium album*), and cocklebur (*Xanthium strumarium*) are common weeds in Midwest corn and soybean fields. However, growers consider giant ragweed (*Ambrosia artemisiifolia*), lambsquarters, Canada thistle (*Cirsium arvense)*, cocklebur, and velvetleaf to be the top five most problematic weeds in corn and soybean because of difficulty controlling these weeds (Nice and Johnson, 2005). In a recent survey of growers utilizing glyphosate-tolerant crops, pigweed, morningglory (*Ipomoea* spp.), Johnsongrass (*Sorghum halepense*), ragweed spp. (*Ambrosia* spp.), foxtail, and velvetleaf were mentioned as the most problematic weeds, depending on the state and cropping system (Kruger et al., 2009). With the exception of morningglory and pigweed, these problematic weed species were present before the introduction of glyphosate-tolerant crops, and some improvement in weed control was realized after the implementation of glyphosate-tolerant cropping systems (Kruger et al., 2009). Common waterhemp (*Amaranthus rudis*) and ragweed were the most frequently mentioned problematic weeds in glyphosate-tolerant crops in Illinois, Indiana and Iowa.

The most frequently reported common weeds in the Southeast region were morningglory (*Ipomoea* spp.), prickly sida (*Sida spinosa*), johnsongrass (*Sorghum halepense*), sicklepod (*Cassia obtusifolia*), and broadleaf signalgrass (*Brachiaria platyphylla*) (Webster et al., 2005, 2009). Morningglory, sicklepod, and pigweed are the most frequently mentioned problematic weeds in glyphosate-tolerant crops in Mississippi and North Carolina (Kruger et al., 2009).

Cultural and mechanical weed control practices can be important components of an effective weed management program (Loux et al., 2009). Crop rotation, narrow row

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spacing and planting date are a few of the crop management practices that are implemented to provide the crop with a competitive edge over weeds. Although the primary purpose of tillage is for seedbed preparation, tillage is still used to supplement weed control with selective herbicides in soybean production. Approximately 98% of the soybean acreage received an herbicide application in 2006, indicating the importance of excellent weed control in maximizing soybean yield (USDA-NASS, 2007b).

Herbicide-tolerant soybean was introduced to provide growers with additional options to improve crop safety and/or improve weed control. The Roundup Ready soybean system (planting Roundup Ready soybean and applying glyphosate in crop to provide primary weed control) was introduced in 1996 and has become the standard weed control program in U.S. soybean production and is utilized on 91% of U.S. soybean acreage (USDA-NASS, 2009c).

Herbicides provide effective and economical control of weeds in soybean. The risk of weeds developing resistance to herbicides and the potential impact of resistance on the usefulness of an herbicide vary greatly across different mechanisms of action and are dependent on a combination of factors, such as selection pressure, herbicide soil residual activity, herbicide chemistry, prolific seed production and high genetic variation in plants (see Appendix K for a more detailed discussion of herbicide resistance in weeds). Weed-resistance management programs that integrate the use of herbicides with different mechanisms of action and short residual activity times in soil reduce selection pressure exerted on weed species (Prather et al., 2000). Crop rotation can also be beneficial in managing resistance because it may allow the grower to manipulate planting times to avoid early-season weed germination and to use mechanical as well as chemical weed control methods (Jordan et al., 1995). As described in Appendix K, when utilized in an integrated manner, these management practices can be used to impede the development of herbicide resistance in weeds.

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Table VIII-4. Common Weeds in Soybean Production: Midwest Region

Foxtail spp. (12)[1]
Pigweed spp. (11)
Velvetleaf (11)
Lambsquarters (10)
Cocklebur (9)
Ragweed, common (7)
Smartweed spp. (6)
Morningglory spp. (5)
Sunflower, spp. (5)
Waterhemp spp. (5)
Horseweed (marestail) (3)
Panicum, fall (3)
Ragweed, giant (3)
Shattercane (3)
Quackgrass (3)
Buckwheat, wild (2)
Crabgrass spp. (2)
Kochia (2)
Mustard, wild (2)
Nightshade, Eastern black (2)
Palmer pigweed (2)
Canada thistle (1)
Chickweed (1)
Cupgrass, woolly (1)
Dandelion (1)
Johnson grass (1)
Milkweed, honeyvine (1)
Nightshade, hairy (1)
Oats, wild (1)
Pokeweed, common (1)
Prickly sida (1)
Proso millet, wild (1)
Sandbur, field (1)
Venice mallow (1)
Volunteer cereal (1)
Volunteer corn (1)

[1] Number provided in parenthesis is the number of states out of the thirteen total states in the Midwest region reporting each weed as a common weed.

Sources:

IL: University of Illinois (2002) and [redacted] Extension Weed Specialist, University of Illinois - Personal Communication (2006).

IN: 2003-2005 Statewide Purdue Horseweed Weed Survey, Special database query and personal communication (2006), [redacted] Extension Weed Specialist, Purdue University.

IA, MN, OH, WI: WSSA, 1992.

KS: [redacted] Extension Weed Specialist, Kansas State - Personal communication (2006).

KY, MO: Webster et al., 2005.

MI: Davis et al., 2005.

NE: [redacted] Extension Weed Specialist, University of Nebraska – Personal communication (2006).

ND: Zollinger, 2000.

SD: [redacted] Extension Weed Specialist, South Dakota State University – Personal communication (2006).

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Table VIII-5. Common Weeds in Soybean Production: Southeast Region

Morningglory spp. (8)[1]
Crabgrass spp. (6)
Prickly sida (6)
Nutsedge spp. (6)
Sicklepod (5)
Signalgrass, broadleaf (5)
Palmer pigweed (4)
Pigweed spp. (4)
Barnyard grass (3)
Florida pusely (3)
Goosegrass (3)
Johnsongrass (3)
Ragweed, common (3)
Cocklebur (2)
Florida beggarweed (2)
Hemp sesbania (2)
Horseweed (marestail) (2)
Texas millet (2)
Browntop millet (1)
Copperleaf, hophorn (1)
Cutleaf evening-primrose (1)
Groundcherry (1)
Henbit (1)
Lambsquarters (1)
Ragweed, giant (1)
Smartweed (1)
Spurge, nodding/hyssop (1)
Spurge, Prostrate (1)
Tropic croton (1)

[1] Number provided in parenthesis is the number of states out of the eight total states in the Southeast region reporting each weed as a common weed.

Sources:
AL, AR, GA, LA, NC, SC: Webster et al., 2009.
MS, TN: Webster et al., 2005.

Table VIII-6. Common Weeds in Soybean Production: Eastern Coastal Region

Foxtail spp. (6)[1]
Ragweed, common (6)
Velvetleaf (6)
Lambsquarters (5)
Pigweed spp. (5)
Cocklebur (4)
Jimson weed (4)
Morningglory spp. (4)
Panicum, fall (4)
Crabgrass spp. (3)
Nutsedge spp. (3)
Quackgrass (2)
Canada thistle (1)
Burcucumber (1)
Dandelion (1)
Goosegrass (1)
Johnson grass (1)
Nightshade, Eastern black (1)
Prickly sida (1)
Shattercane (1)
Smartweed spp. (1)

[1] Number provided in parenthesis is the number of states out of the six total states in the Eastern Coastal region reporting each weed as a common weed. Data were not available for DE in soybean.

Sources:
DE, MD, NJ, PA: WSSA, 1992.
NY: [redacted] Extension Weed Specialist, Cornell University – Personal Communication (2006).
VA: Webster et al., 2009.

VIII.F.1. Methods of Weed Control in Soybean

Mechanical methods of weed control including tillage have been used for centuries to control weeds in crop production. Spring or fall preplant tillage and in-crop shallow cultivation can effectively reduce the competitive ability of weeds by burying the plants, disturbing or weakening their root systems, or causing sufficient physical injury to kill the weeds. Research in the early 1900s centered on determining the economic benefits of removing weeds with the use of cultivation (Klingman et al., 1975). A consequence of in-crop cultivation for weed control can be injury to crop roots and moisture loss. Selective herbicides have proved more efficacious and reduced the need for in-crop tillage or cultivation to control weeds in soybean production. The development of selective herbicides has progressed rapidly since the introduction of the first synthetic

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herbicide (2,4-D) for weed control in corn in the early 1940s. Although the primary purpose of tillage is for seedbed preparation, tillage still is used to supplement weed control with selective herbicides in soybean production.

Alanap (1949), amiben (1958), trifluralin (1959), linuron (1960), and alachlor (1966) led the way for numerous selective herbicides in soybean (Agranova, 2010). Bentazone (1968) was one of the early selective postemergence herbicides used in soybean production. By the early 1990s, there were over 70 registered herbicides or premix herbicides for weed control in soybean (Gianessi et al., 2002). Table VIII-7 provides a summary of herbicide use in soybean production in the U.S. from 1995 through 2001. Weed control programs in soybean production during this time period consisted of preemergence herbicides used alone or in a tank mixture with other preemergence herbicides. Applications were made as preplant incorporated or preemergence surface applications prior to or at planting. Tank mixtures of two preemergence herbicides were used to broaden the spectrum of control to both grasses and broadleaf weed species. Preemergence herbicides are followed by postemergence applications to control weed escapes that emerge later in the crop. Total postemergence programs were seldom used in soybean production prior to 1995. For soybean planted in a no-till system, an additional preplant burndown herbicide application for broad-spectrum control of existing weeds at time of planting was also applied. Therefore, multiple herbicides and/or multiple applications were generally made in soybean production. The average number of herbicide applications per acre in soybean rose from 1.5 in 1990 to 1.7 applications in 1995 reflecting the use of at-plant and postemergence applications or two postemergence applications (Gianessi et al., 2002).

It is important to understand herbicide use in 1995, as this was prior to the introduction of Roundup Ready soybean system. The most widely used herbicides in 1995 were the sulfonylurea (chlorimuron, thifensulfuron) and imidazolinone (imazethapyr, imazaquin) herbicide classes that are applied preemergence and postemergence in a soybean crop. These two classes of herbicides, both acetolactate synthase (ALS) inhibitors, were applied on approximately 87% of the soybean treated acres in 1995 (Table VIII-7). The dinitroanaline herbicides (trifluralin and pendimethalin) were the second most widely used preemergence herbicides. Selective postemergence herbicides were used on 52% of the treated acres and were generally either effective on grass species or broadleaf species. Sethoxydim, clethodim, quizalofop, and fluazifop were among the postemergence grass herbicides. Acifluorfen and bentazon were the main postemergence broadleaf herbicides. Glyphosate was used on 20% of the treated acres, mainly as a preplant burndown treatment, but it also was used in spot treatments or ropewick applications to control weed escapes or volunteer corn in soybean.

Herbicide programs used in conventional soybean have not changed significantly since 1995, with many of the traditional herbicides still in use. Although, new active ingredients have been introduced, including carfentrazone, sulfentrazone, flufenacet, flumetsulam, flumiclorac, flumioxazin, cloransulam, and imazamox. These new active ingredients improve the level or spectrum of weed control. Numerous products have been introduced that are a pre-mixture product of two active ingredients for broad spectrum weed control. Some of the new active ingredients and pre-mixtures are more

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effective in controlling waterhemp, ALS-resistant weeds, and other hard-to-control weeds. Hard-to-control weeds generally require a higher rate and/or application at a smaller growth stage in order to consistently achieve commercially acceptable control. Refer to the Roundup WeatherMax label (U.S. EPA Reg. No. 524-537) for a listing of these weeds. Herbicide resistant weeds are those listed on the International Survey of Resistant Weeds website (www.weedscience.org).

Table VIII-8 provides a summary of the herbicide use in soybean in the U.S. in 2006. In 2006, herbicide-tolerant soybean (glyphosate-tolerant) was planted on 89% of the 75.5 million acres of soybean (USDA-NASS, 2007a). With the high percentage of glyphosate-tolerant soybean and the additional use of glyphosate for preplant burndown applications on both glyphosate-tolerant and conventional soybean, it is not surprising that glyphosate was used on 97% of the total soybean acres in 2006. The percentage of herbicide-tolerant soybean has subsequently increased to 91% in 2009 (USDA-NASS, 2009c). The remaining preemergence and postemergence herbicides are utilized in conventional soybean as well as glyphosate-tolerant soybean. A grower survey conducted in 2006 showed that 15 to 21% of growers applied non-glyphosate herbicides as another mode-of-action in addition to glyphosate for weed control in glyphosate-tolerant soybean (Givens et al., 2009). These non-glyphosate herbicides were applied prior to planting, at planting and postemergence in soybean. The non-glyphosate herbicides mainly included applications of chlorimuron, flumiclorac, pendimethalin, imazethapyr, and 2,4-D, which were commonly used herbicides in weed management programs prior to the introduction of glyphosate-tolerant soybean. Although these non-glyphosate herbicides were applied to supplement the weed control provided by glyphosate, researchers report that approximately 40 to 55% of the growers utilizing glyphosate-tolerant crops indicate that rotating herbicides or tank mixing glyphosate with other herbicides is an effective management practice to minimize glyphosate resistance development (Johnson et al., 2009). It should be noted that in 2006 approximately 16,000 lbs of dicamba was used in soybean production which would be a sufficient amount of dicamba to treat 64,000 acres assuming the average application rate of 0.25 lb dicamba acid equivalent (a.e.) per acre (see TableVIII-7). Dicamba is currently labeled only for preplant and preharvest applications in soybean, where restrictions on days after preplant treatment are required due to insufficient ability of soybean to tolerate applications of the herbicide, referred to as "crop tolerance." Similarly, dicamba currently cannot be used in-crop postemergence applications on soybean due to a lack of crop tolerance.

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Tables VIII-9 and VIII-10 provide a summary of the crop tolerance to herbicides applied in soybean production and the efficacy of these herbicides on 25 of the common weed species identified in Section VIII.F. These tables list only the most commonly used herbicides in soybean production. Glyphosate applied postemergence (as part of the Roundup Ready soybean system) and four other herbicides applied either preemergence or postemergence have the highest crop tolerance rating of excellent. The other herbicides are rated only good to poor. Seldom would one field or farm have all 25 weed species, but they generally have a mixture of grass and broadleaf weed species. These ratings can be used by growers to facilitate the selection of an herbicide program for a soybean crop, which offers the best overall control of the weed species. Based on Tables

VIII-9 and VIII-10, glyphosate is considered to have better control (>80%) on more grass and broadleaf weed species than any other herbicide. Glyphosate/imazethapyr has the next highest overall rating, but it is rated only good on crop tolerance. S-Metolachlor and pendimethalin are rated high on many grass species, but are rated low on most of the broadleaf weed species. Chlorimuron/tribenuron, fomesafen, and flumioxazin/cloransulam are rated high on the broadleaf species, but are rated low on grass species.

Table VIII-7. Herbicide Use in Soybean in the U.S. from 1995 through 2001[1]

	Percent-Treated Acres						
Active Ingredient	1995	1996	1997	1998	1999	2000	2001
2,4-D	10	13	8	7	5	5	4
2,4-DB	1	<1	1	<1	<1	NA	NA
Acifluorfen	12	11	12	7	3	3	3
Alachlor	4	5	3	2	2	1	<1
Bentazon	12	11	11	7	4	2	1
Chlorimuron	16	14	13	12	12	10	5
Clethodim	5	7	4	4	5	4	4
Clomazone	4	3	5	4	1	<1	<1
Cloransulam	NA	NA	NA	1	5	4	5
Dimethenamid	1	1	1	1	<1	<1	NA
Ethalfluralin	1	1	<1	NA	<1	<1	NA
Fenoxaprop	6	4	6	4	4	4	3
Fluazifop	10	7	7	5	4	5	3
Flumetsulam	2	2	4	2	2	2	<1
Flumiclorac	NA	2	1	<1	<1	<1	<1
Fomesafen	4	5	6	6	4	7	7
Glyphosate	20	25	29	47	62	66	76
Imazamox	NA	NA	NA	7	3	6	5
Imazaquin	15	15	13	8	5	4	2
Imazethapyr	44	43	38	17	16	12	9
Lactofen	5	8	4	2	2	2	1
Linuron	2	1	1	<1	<1	<1	NA
Metolachlor	7	5	7	4	4	2	NA
Metribuzin	11	9	10	6	5	4	2
Paraquat	2	1	2	1	1	<1	NA
Pendimethalin	26	27	25	18	14	11	10
Quizalofop	6	7	4	3	1	<1	<1
S-Metolachlor	NA	NA	NA	NA	NA	NA	<1
Sethoxydim	7	9	7	5	3	2	1
Sulfentrazone	NA	NA	NA	3	4	4	5
Thifensulfuron	12	10	9	5	5	6	2
Trifluralin	20	22	21	16	14	14	7

[1] Source is Gianessi et al. (2002).

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Table VIII-8. Agricultural Chemical Applications Registered for Soybean Use in AR, IA, IL, IN, KS, KY, LA, MI, MN, MS, MO, NE, NC, ND, OH, SD, TN, VA, and WI in 2006[1]

Herbicide	Chemical Family	Mode-of-Action (MOA)	Percent-Treated Acres	Total Area Applied (Percent/MOA)	Quantity Applied (1000 lbs)	Total Quantity Applied (1000 lbs/MOA)
Glyphosate	glycine	EPSPS inhibitor	4	97	2,841	92,856
Glyphosate, amm. Salt	glycine		*		142	
Glyphosate, iso. salt	glycine		92		88,903	
Sulfosate	glycine		1		970	
Pendimethalin	dinitroanaline	Tubulin inhibitor	3	5	1,894	3,348
Trifluralin	dinitroanaline		2		1,454	
Bentazon	benzothiadiazinone	PSII inhibitor	*	3	70	577
Metribuzin	triazinone		2		437	
Sulfentrazone	triazolinone		1		70	
Chlorimuron-ethyl	sulfonylurea	ALS inhibitor	4	11	52	265
Cloransulam-methyl	triazolopyrimidine		1		17	
Flumetsulam	triazolopyrimidine		*		8	
Imazamox	imidazolinone		*		9	
Imazaquin	imidazolinone		1		66	
Imazethapyr	imidazolinone		3		100	
Imazethapyr, ammon.	Imidazolinone		*		5	
Thifensulfuron	sulfonylurea		1		3	
Tribenuron-methyl	sulfonylurea		1		5	
Alachlor	chloroacetamide	Cell division inhibitor	*	1	485	1,402
S-Metolachlor	chloroacetamide		1		837	
Flufenacet	oxyacetamide		*		80	
Paraquat	bipyridilium	PSI disruption	1	1	335	335

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Table VIII-8 (continued). Agricultural Chemical Applications Registered for Soybean Use in AR, IA, IL, IN, KS, KY, LA, MI, MN, MS, MO, NE, NC, ND, OH, SD, TN, VA, and WI in 2006[1]

Herbicide	Chemical Family	Mode-of-Action (MOA)	Percent-Treated Acres	Total Area Applied (Percent/MOA)	Quantity Applied (1000 lbs)	Total Quantity Applied (1000 lbs/MOA)
Clethodim	cyclohexenone	ACCase inhibitor	3	4	190	266
Fenoxaprop	aryloxyphenoxy propionate		*		9	
Fluazifop-P-butyl	aryloxyphenoxy propionate		1		43	
Quizalofop-P-ethyl	aryloxyphenoxy propionate		*		14	
Sethoxydim	cyclohexenone		*		10	
Acifluorfen	diphenyl ether	PPO inhibitor	*	6	47	565
Carfentrazone-ethyl	triazolinones		*		10	
Flumiclorac-pentyl	N-phenylphthalimide		1		17	
Flumioxazin	N-phenylphthalimide		3		138	
Fomesafen	diphenyl ether		2		330	
Lactofen	diphenyl ether		*		23	
2,4-D, 2-EHE	phenoxy	Synthetic auxin	7	10	2,505	3,542
2,4-D, dimeth. salt	phenoxy		3		953	
2,4-D (butoxy ester)	phenoxy		*		68	
Dicamba, digly salt	benzoic acid		*		16	
					Total	**103,156**

* Area receiving application is less than 0.5 percent.

[1] Data derived from USDA-NASS (2007b). Planted acreage for the nineteen primary soybean production states was 72.9 million acres, which represented 96.5% of total planted acres.

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Table VIII-9. Crop Tolerance and Common Grass Weed Responses to Herbicides Applied in Soybean Production

Herbicide/Application	CT[3]	Common Grass Weeds[1,2]										
		BY	BS	CG	FP	FT	GG	SC	JGs	JGr	RR	NSy
Preplant Incorporated												
Trifluralin	1	9	9	9	9	9	9	7	7	3	9	-
Preplant or Preemergence												
Chlorimuron/tribenuron	2	-	8	-	-	-	7	-	-	2	8	-
Cloransulam	0	-	NA	-	-	-	NA	-	-	NA	NA	-
Flumioxazin	2	-	5	-	-	-	5	-	-	0	8	-
Flumioxazin/cloransulam	2	-	5	-	-	-	5	-	-	0	8	-
Imazaquin	1	-	7	-	-	-	5	-	-	2	5	6
Imazethapyr	1	6	NA	7	7	7	NA	6	6	NA	NA	-
Metribuzin	2	2	6	6	5	6	7	6	-	0	4	-
Pendimethalin	2	8	9	9	9	8	9	7	7	3	4	-
s-Metolachlor	1	8	8	9	8+	8+	9	-	-	0	3	8+
Postemergence												
Bentazon	1	-	0	-	-	-	0	-	-	0	NA	8+
Chlorimuron	2	-	0	-	-	-	0	-	-	0	0	8
Clethodim	0	9	9	8+	9	9	9	9	9	9	8	-
Cloransulam	1	-	0	-	-	-	0	-	-	0	0	6
Clorimuron/thifensulfuron	0**	-	NA	-	-	-	NA	-	-	NA	NA	8
Fluazifop/fenoxaprop	0	9	8	8+	9	9	9	9	9	9	7	-
Flumiclorac	2	-	NA	-	-	-	NA	-	-	NA	NA	-
Fomesafen	2	-	3	-	-	-	3	-	-	3	0	-
Glyphosate	0*	8+	9	8+	8+	9	8	8	9	9	8	7
Glyphosate/imazethapyr	1*	9	NA	8+	9	9	NA	9	9	NA	NA	7
Imazamox	2	6	NA	7	7	7-8+	NA	-	-	NA	NA	-
Imazethapyr	1	6	7	7	7	7-8	5	8	8	6	4	-
Lactofen	3	-	4	-	-	-	4	-	-	2	0	-
Thifensulfuron	2	-	NA	-	-	-	NA	-	-	NA	NA	-

[1] All weed control ratings except for BS, GG, JGr and RR are from the 2009 Weed Control Guide for Ohio and Indiana, Ohio State University and Purdue University (Loux et al., 2009). Ratings for BS, GG, JGr and RR are from the 2009 Weed Control Guidelines for Mississippi, Mississippi State University (MSU, 2010). Weed control rating for weeds, except BS, GG, and RR, are: 9 = 90% to 100%, 8 = 80% to 90%, 7 = 70% to 80%, 6 = 60% to 70%, - = less than 60% control, not recommended. Weed control ratings for BS, GG, and RR are: 9-10 = excellent, 7-8 = good, 4-6 = fair, 0-3 = none to slight. Ratings assume the herbicides are applied in the manner suggested in the guidelines and according to the label under optimum growing conditions.

[2] Weed species: BY = barnyardgrass, BS = broadleaf signalgrass, CG = crabgrass, FP = fall panicum, FT = giant and yellow foxtail, GG = goosegrass, SC = shattercane, JGs = seedling Johnsongrass, JGr = rhizome Johnsongrass, RR = red rice, and NSy = yellow nutsedge.

[3] All crop tolerance ratings are from the 2009 Weed Control Guide for Ohio and Indiana, Ohio State University and Purdue University (Loux et al., 2009). Crop tolerance (CT) rating: 0 = excellent, 1 = good, 2 = fair, 3 = poor.

NA denotes not available. *Rating based on application to Roundup Ready soybean. **Ratings based on application to STS soybean.

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Table VIII-10. Common Broadleaf Weed Responses to Herbicides Applied in Soybean Production

Herbicide/Application	Common Broadleaf Weeds[1,2]													
	BN	CB	CR	GR	HS	LQ	MG	PA	PW	PS	SP	SW	VL	WH
Preplant Incorporated Only														
Trifluralin	-	-	-	-	0	8+	2	7	9	0	4	-	-	8
Preplant or Preemergence														
Chlorimuron/tribenuron	-	8	9	7	9	9	8	8	9	7	NA	9	8+	-
Cloransulam	-	8	9	7	NA	9	NA	NA	9	NA	NA	8	8+	-
Flumioxazin	9	-	7	-	9	9	6-8	9	9	8	7	7	7	8
Flumioxazin/cloransulam	9	8	9	7	9	9	7-8	9	9	8	7	9	8+	8
Imazaquin	9	8	8	7	0	9	6-8	9	9	9	5	9	7	-
Imazethapyr	9	7	6	-	NA	9	NA	NA	9	NA	NA	9	8	-
Metribuzin	-	-	-	7	9	7	2-8	9	8	9	8	9	9	7
Pendimethalin	-	-	-	-	0	8+	2	7	9	4	2	-	-	7
s-Metolachlor	8	-	-	-	0	6	0	8	8	4	2	-	-	7
Postemergence														
Bentazon	-	9	7	6	4	7	2-9	4	-	8	0	9	8+	-
Chlorimuron	-	9	8	7+	8	-	8-9	6	9	2	7	8	8	-
Cloransulam	-	9	9	9	3	-	8-9	2	-	2	7	8	9	-
Clorimuron/thifensulfuron	-	9	8	7+	NA	8	NA	NA	9	NA	NA	9	9	-
Flumiclorac	-	7	7	-	NA	7	NA	NA	7	NA	NA	-	9	7
Fomesafen	8	7	8+	8	9	-	8-9	8	9	2	3	7	6	9
Glyphosate	8	9	8+	8	7	8	7-9	9	9	7	8	8	8	8
Glyphosate/imazethapyr	9	9	8+	8+	NA	8+	NA	NA	9	NA	NA	9	9	8
Imazamox	9	8	7	8	NA	8	NA	NA	9	NA	NA	8	9	-
Imazethapyr	9	9	6	7	0	6	7-9	6	9	6	0	9	9	-
Lactofen	8+	8	9	8	9	-	8-9	8	9	8	5	6	7	9
Thifensulfuron	-	6	-	-	NA	8	NA	NA	9	NA	NA	8	9	-

[1] All weed control ratings except for HS, MG, PA, PS, and SP are from the 2009 Weed Control Guide for Ohio and Indiana, Ohio State University and Purdue University (Loux et al., 2009). Ratings for HS, MG, PA, PS, and SP are from the 2009 Weed Control Guidelines for Mississippi, Mississippi State University (MSU, 2010). Weed control ratings for weeds, except HS, MG, PA, PS, and SP, are: 9 = 90% to 100%, 8 = 80% to 90%, 7 = 70% to 80%, 6 = 60% to 70%, - = less than 60% control, not recommended. Weed control ratings for HS, MG, PA, PS, and SP are: 9-10 = excellent, 7-8 = good, 4-6 = fair, 0-3 = none to slight. Ratings assume the herbicides are applied in the manner suggested in the guidelines and according to the label under optimum growing conditions.

[2] Weed species: BN = black nightshade, CB = cocklebur, CR = common ragweed, GR = giant ragweed, LQ = lambsquarters, MG = morningglory spp., HS = hemp sesbania, PA = palmer and spiny pigweed, PW = pigweed, PS= prickly sida, SP = sicklepod, SW = smartweed, VL = velvetleaf, and WH = waterhemp. NA denotes not available.

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VIII.G. Dicamba Herbicide Use in the U.S.

Dicamba was approved by the U.S. EPA for agricultural uses in 1967 (U.S. EPA, 2009). Dicamba is formulated as a stand-alone herbicide product and marketed by several companies under various trade names such as Banvel®, Clarity®, Diablo®, Rifle®, and Sterling® that are various salt formulations of dicamba. These dicamba products can be tank mixed with one or more active ingredients depending on the treated crop. For example, Clarity can be tank mixed with over 75 herbicide products in labeled crops. Additionally, dicamba is formulated as a registered premix product with one or more other herbicide active ingredients such as glyphosate, 2,4-D, diflufenzopyr, atrazine, nicosulfuron, metsulfuron, primsulfuron, triazulfuron, rimsulfuron and halosulfuron. Dicamba herbicide (*e.g.*, Clarity – diglycolamine (DGA) salt of dicamba) is currently labeled for weed control in soybean, corn, cotton, sorghum, wheat, barley, oats, millet, pasture, rangeland, asparagus, sugarcane, turf, grass grown for seed, conservation reserve programs, and fallow croplands. Table VIII-11 provides a summary of dicamba-treated acres (crop acreage that has dicamba applied to it) and the amount of dicamba active ingredient applied for all labeled crops each year from 1990 through 2008. Dicamba-treated acreage has ranged from 17.4 to 36.3 million acres during this period. Usage of dicamba peaked during the period of 1994 through 1997, where 1994 was the peak year when 36.3 million acres were treated with 9.4 million pounds of dicamba. Since 1994, the use of dicamba has steadily declined to 20.2 million treated-acres with 2.7 million pounds in 2008 due to the competitive market introductions of sulfonylurea herbicides (chlorsulfuron, metsulfuron-methyl, and thifensulfuron-methyl) in wheat, new broadleaf herbicide active ingredients in corn, and Roundup Ready corn. Usage in cotton is one exception, where dicamba-treated acres (preplant applications) have increased from 140,000 to 590,000 acres from 2004 to 2008 (AgroTrak, 2009).

Table VIII-12 provides a summary of the dicamba-treated acres by crop in 2008. Approximately 20.2 million acres were treated with dicamba in 2008. Over 8 million acres of corn were treated, which is 40.1% of the total dicamba-treated acres for all crops. The next highest levels of treated acres are in wheat (25.2%) and fallow land (14.9%). The crops with the highest percentage of dicamba-treated acres are sugarcane (21.9%), fallow land (19.2%), sorghum (15.8%), and wheat (8.4%). Although corn represents the crop with the highest dicamba-treated acres, only 9.4% of the total corn acreage was treated with dicamba in 2008. For comparison, the treated percentage in corn was at approximately 29% as recently as 2000 (USDA-NASS, 2001).

Approximately 2.67 million pounds of dicamba active ingredient were applied for all agricultural uses in 2008 (Table VIII-12). The distribution of dicamba active ingredient across the various labeled uses is similar to the distribution of treated acres. Based on USDA-NASS (2004, 2006, 2007b, 2008) statistics, dicamba application rates ranged from 0.03 to 0.25 pounds per acre with the number of applications ranging from 1 to 1.2 applications per cropping season (Table VIII-13). Dicamba rates are the lowest in barley, wheat, and oats, where typically more than one application is made in these crops per cropping season. The average application rate in corn is 0.19 pounds of dicamba per acre with slightly over one application per season.

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Dicamba is currently labeled for use in conventional or Roundup Ready soybean, although dicamba use is extremely limited because applications are restricted to very early preplant and/or preharvest applications due to soybean tolerance concerns. The dicamba-treated acreage in 2008 soybean production was approximately 530,000 acres that represented 0.7% of the total soybean acreage.

Table VIII-11. Dicamba Use in All Labeled Crops from 1990 to 2008[1]

Year	Treated Acres (000,000 acres)	Dicamba (a.e.) (000,000 lbs)
1990	26.8	6.7
1991	24.5	6.3
1992	30.3	7.4
1993	27.7	7.0
1994	36.3	9.4
1995	34.3	8.7
1996	33.3	8.2
1997	33.1	8.6
1998	32.2	8.0
1999	29.8	6.3
2000	29.4	5.4
2001	30.6	5.4
2002	29.4	5.0
2003	27.1	4.3
2004	22.3	3.9
2005	21.3	3.4
2006	17.4	2.7
2007	18.6	2.7
2008	20.2	2.7

[1] Source is AgroTrak (2009).

Shaded bar indicates the year with maximum dicamba-treated acres.

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Table VIII-12. Dicamba-Treated Acres and Amounts Applied to Labeled Crops and Uses in 2008[1]

Crop	Total Crop Acres (000)	Dicamba-Treated Acres (000)	Dicamba-Treated Acres (% of Total)[2]	Dicamba Treated Crop (%)	Dicamba Pounds (000 a.e.)
Asparagus	34	1	<0.1	1.8	0.1
Barley	3,868	211	1.0	5.5	23
Corn	87,245	8,115	40.1	9.4	961
Cotton	9,309	590	2.9	6.3	139
Fallow	15,751	3,018	14.9	19.2	420
Pastureland	96,151	1,218	6.0	1.3	254
Sorghum	7,035	1,114	5.5	15.8	137
Soybean	74,405	530	2.6	0.7	118
Sugarcane	810	177	0.9	21.9	40
Wheat, all	60,835	5,094	25.2	8.4	549
All other uses	NA	139	NA	NA	30
Total		20,207			2,670

NA denotes not applicable.

[1] Source is AgroTrak (2009).

[2] The percentage of the total dicamba-treated acres for all labeled crops and uses.

Table VIII-13. Dicamba Applications – Average Number and Rates to Labeled Crops[1]

Crop	# of Dicamba Applications	Rate of Dicamba per Application	Rate of Dicamba per Crop Year
Corn	1.02	0.188	0.192
Cotton	1.00	0.191	0.192
Sorghum	1.05	0.205	0.215
Soybean	1.00	0.250	0.250
Barley	1.20	0.060	0.080
Wheat, spring	1.13	0.032	0.085
Wheat, winter	1.20	0.122	0.149
Oats	1.00	0.088	0.088

[1] USDA-NASS, 2004 (sorghum), 2006 (corn and oats), 2007b (soybean, barley and wheat), and 2008 (cotton)

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VIII.G.1. Dicamba Application Timing for Labeled Crops

Label recommendations on the application timing of dicamba are highly dependent on the crop being treated to ensure adequate crop safety. Many of the field crops currently labeled for dicamba, such as soybean and cotton, include preplant applications but certain timing intervals are required between application and planting to avoid crop injury. However, dicamba can be applied in other field crops such as corn, sorghum, barley, and wheat either as preplant or postemergence applications with restrictions regarding the crop stage of growth. Broadcast applications in corn can be made up to the 5-leaf stage or 8 inches tall, whichever occurs first. Sorghum can be treated with broadcast applications from after the spike stage up to the 5-leaf stage or 8 inches tall[3]. These applications are considered early-postemergence since they occur relatively early in the growing season, typically ending sometime in June. Post-directed applications can be made in corn (up to 36 inches tall) and sorghum (15 inches tall), which would be much later in the season than an early-postemergence application. However, growers seldom make these applications in corn and sorghum since post-directed applications require special spraying equipment and equipment setup. Applications in wheat and barley must be made prior to the jointing stage except in spring seeded wheat where application can be made up to the 6-leaf stage of wheat. These applications are relatively early in the spring or late in the fall.

Preharvest applications of dicamba are permitted in several crops including soybean, sorghum, barley, and wheat. Preharvest applications are only allowed after the crops reach a certain maturity stage and then harvesting must be delayed for a given time period depending on the crop[4]. This type of application is infrequently used since it is considered a rescue or harvest-aid treatment intended to remove weeds which interfere with the harvesting equipment or operation.

Table VIII-14 provides a summary of the application timings of dicamba in labeled crops. Approximately 24% of the dicamba treated acres are treated either in the fall or spring as preplant applications to the crop. Over 50% of the treated acres are treated postemergence. Postemergence applications represent the primary timing in corn, sorghum, and wheat.

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[3] Clarity product label can be found at: http://www.cdms.net/LDat/ld797002.pdf.

[4] Clarity label specifies that preharvest application requires that soybean pods must have reached mature brown color and at least 75% leaf drop has occurred. Harvest of soybean is allowed 14 or more days after preharvest application.

Table VIII-14. Dicamba-Treated Acres (000) by Application Timing and Crop in 2008[1]

	Application Timing[2]						
Crop	Fall Preplant	Spring Preplant	At Planting	Pre-Crop Emergence	In-Crop Postemergence	Other Timings[3]	Totals
Asparagus	-	-	-	-	-	1	**1**
Barley	8	41	-	-	162	-	**211**
Corn	136	851	71	285	6,771	-	**8,114**
Cotton	41	549	-	-	-	-	**590**
Fallow	647	-	-	-	-	2,371	**3,018**
Sorghum	439	380	12	81	202	-	**1,114**
Soybean	43	486	-	-	-	-	**529**
Sugarcane	13	-	-	15	149	-	**177**
Wheat, spring	341	193	-	26	791	-	**1,351**
Wheat, winter	608	-	13	71	3,050	-	**3,742**
Pastures	84	-	-	-	-	1,134	**1,218**
Totals	**2,360**	**2,500**	**96**	**478**	**11,125**	**3,506**	**20,065**
% of Applications	**11.8**	**12.5**	**0.5**	**2.4**	**55.4**	**17.5**	

- denotes no application at the timing for the listed crop.

[1] Source is AgroTrak (2009).

[2] Dicamba-treated acres are expressed as dicamba a.e.

[3] Application timing could be throughout the season since applications are made between harvests or are not dependent on a specific stage of growth.

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VIII.G.2. Distribution of Dicamba Use in the U.S.

Table VIII-15 provides a summary of the dicamba-treated acres by crop for each of the states in the U.S. soybean growing regions. As expected, based on the dicamba use data previously presented, over one-half of the dicamba-treated acres (58%) are in the Midwest region representing approximately 11.8 million acres. The primary dicamba-treated crops/uses in this region are corn, wheat, barley, and fallow. Although the Plains and Western States regions are not considered a soybean producing region, it represents a large portion (32%) of the dicamba-treated acres (6.4 million). Only 1.4 and 0.6 million acres are treated with dicamba in the Southeast and Eastern Coastal regions, respectively. Soybean producing states with over one million dicamba-treated acres include Illinois, Kansas, and North Dakota. The state of Kansas, which grows many of the primary dicamba-labeled crops, has the largest amount of dicamba-treated acres at approximately 4.6 million acres (22.6% of total dicamba-treated acres), which is 2.5 times more than the next largest use states of North Dakota, Colorado, Montana, and Texas. Dicamba is used on less than 1% of U.S. soybean acres, but in Arkansas dicamba is used on 12.6% of the soybean acres, and accounts for the majority of dicamba-treated soybean acres in the U.S. (~78%). The primary reason for the relatively higher use of dicamba in Arkansas, compared to other soybean producing states, is that dicamba is being recommended by academics and extension agents in the Delta to control glyphosate resistant marestail.

The maps presented in Figures VIII-1 and VIII-2 provide a visual illustration of the historical distribution and intensity of dicamba-treated acres for all labeled crops and the current U.S. soybean production acres at the county level, respectively. By overlaying the geographical representations from Figures VIII-1 and VIII-2, it can be concluded that the historical use and intensity of total dicamba-treated acres align with soybean acreage.

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Table VIII-15. Dicamba-Treated Acres by State and Labeled Crop in 2008[1]

Region/State	Soybean Acres (000)	Total Dicamba Acres (000)	Percent U.S. Dicamba Acres[2]	Crop Acres Treated With Dicamba (000)							
				Corn	Small Grains[3]	Fallow	Pasture	Cotton	Sorghum	Soybean	Other Crops[4]
Midwest Region											
Illinois	9,200	1,213	6.0	1,204	-	-	-	-	3	6	-
Indiana	5,450	494	2.4	489	-	-	-	-	-	5	-
Iowa	9,750	580	2.9	576	-	-	4	-	-	-	-
Kansas	3,300	4,558	22.6	658	2,198	901	30	2	675	61	33
Kentucky	1,390	36	0.2	36	-	-	-	-	-	-	-
Michigan	1,900	294	1.5	285	8	-	-	-	-	-	1
Minnesota	7,050	628	3.1	606	21	-	<1	-	-	-	-
Missouri	5,200	341	1.7	205	<1	-	36	99	-	-	-
Nebraska	4,900	946	4.7	558	222	134	6	-	<1	21	4
North Dakota	3,800	1,670	8.3	740	846	64	-	-	-	9	11
Ohio	4,500	270	1.3	247	23	-	-	-	-	-	-
South Dakota	4,100	502	2.5	183	88	198	-	-	16	13	4
Wisconsin	1,610	261	1.3	250	-	-	11	-	-	-	-
Region Totals	**62,150**	**11,793**	**58.4**	**6,037**	**3,407**	**1,297**	**88**	**101**	**695**	**115**	**53**

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Table VIII-15 (continued). Dicamba-Treated Acres by State and Labeled Crop in 2008[1]

Region/State	Soybean Acres (000)	Total Dicamba Acres (000)	Percent U.S. Dicamba Acres[2]	Crop Acres Treated With Dicamba (000)							
				Corn	Small Grains[3]	Fallow	Pasture	Cotton	Sorghum	Soybean	Other Crops[4]
Southeast Region											
Alabama	360	119	0.6	54	-	-	14	51	-	-	-
Arkansas	3,300	791	3.9	-	-	-	92	262	-	415	22
Georgia	430	32	0.2	17	-	-	15	-	-	-	-
Louisiana	1,050	215	1.1	17	-	23	-	-	-	-	175
Mississippi	2,000	102	0.5	-	-	-	50	52	-	-	-
North Carolina	1,690	53	0.3	39	-	-	14	-	-	-	-
South Carolina	540	6	0.0	-	-	-	-	-	-	-	6
Tennessee	1,490	102	0.5	5	-	-	<1	96	-	-	-
Region Totals	**10,860**	**1,420**	**7.0**	**132**	**-**	**23**	**186**	**461**	**-**	**415**	**203**
Eastern Coastal Region											
Delaware	195	0	0	-	-	-	-	-	-	-	-
Maryland	495	268	1.3	268	-	-	-	-	-	-	-
New Jersey	92	0	0	-	-	-	-	-	-	-	-
New York	230	62	0.3	62	-	-	-	-	-	-	-
Pennsylvania	435	170	0.8	168	-	-	2	-	-	-	-
Virginia	580	118	0.6	104	5	-	9	-	-	-	-
Region Totals	**2,027**	**618**	**3.1**	**602**	**5**	**-**	**11**	**-**	**-**	**-**	**-**

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Table VIII-15 (continued). Dicamba-Treated Acres by State and Labeled Crop in 2008[1]

				Crop Acres Treated With Dicamba (000) expressed as a.e.							
Region/State	Soybean Acres (000)	Total Dicamba Acres (000)	Percent U.S. Dicamba Acres[2]	Corn	Small Grains[3]	Fallow	Pasture	Cotton	Sorghum	Soybean	Other Crops[4]
Plains and Western States Region											
California	0	95	0.5	32	63	-	-	-	-	-	-
Colorado	0	1,606	8.0	248	253	958	3	-	122	-	22
Florida	327	142	0.7	-	-	-	140	-	-	-	2
Idaho	0	170	0.8	114	51	<1	<1	-	-	-	4
Montana	0	1,657	8.2	-	955	686	-	-	-	-	16
New Mexico	0	46	0.2	37	-	-	-	-	9	-	-
Oklahoma	400	622	3.1	8	84	5	409	-	113	-	3
Oregon	0	222	1.1	-	218	-	4	-	-	-	-
Texas	230	1,641	8.1	850	212	14	360	27	175	-	3
Utah	0	22	0.1	3	<1	12	-	-	-	-	6
Washington	0	96	0.5	-	55	31	5	-	-	-	5
Wyoming	0	57	0.3	54	-	3	-	-	-	-	-
Region Totals	**957**	**6,376**	**31.6**	**1,346**	**1,892**	**1,710**	**934**	**27**	**419**		**61**
U.S. Totals	**75,994**	**20,207**	**100**	**8,117**	**5,304**	**3,030**	**1,207**	**589**	**1,114**	**530**	**317**

- denotes no dicamba-treated acres for listed crop/use.

[1] Source is AgroTrak (2009).

[2] Percent of total U.S. Dicamba Acres = Total Dicamba-Treated Acres (per state)/U.S. Total Dicamba-Treated Acres (20,207,000) × 100

[3] Small grains include barley, winter wheat and spring wheat.

[4] Other labeled crops include asparagus and sugarcane.

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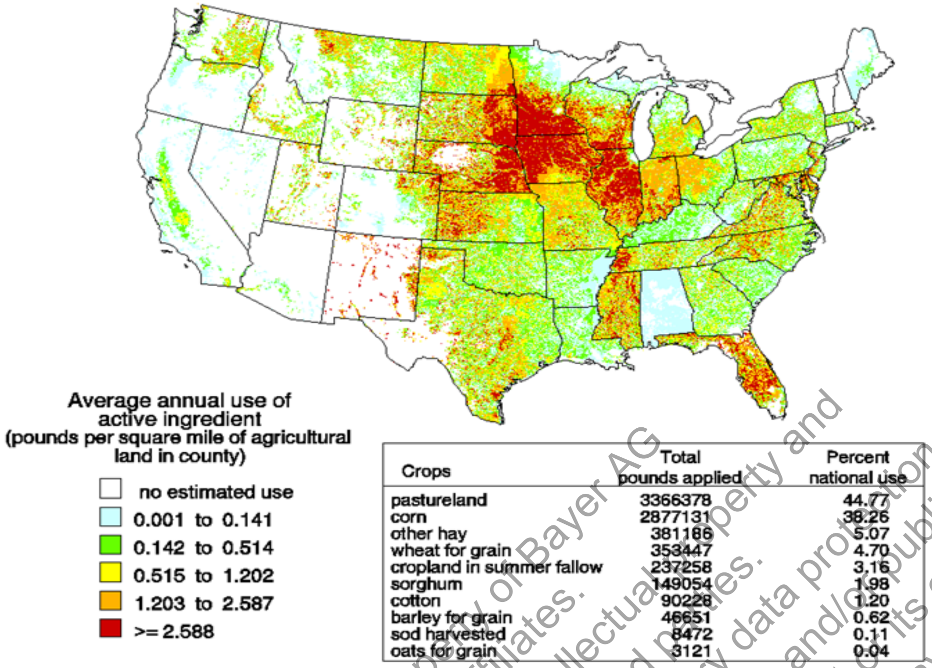
Average annual use of active ingredient (pounds per square mile of agricultural land in county)
☐ no estimated use
0.001 to 0.141
0.142 to 0.514
0.515 to 1.202
1.203 to 2.587
>= 2.588

Crops	Total pounds applied	Percent national use
pastureland	3366378	44.77
corn	2877131	38.26
other hay	381186	5.07
wheat for grain	353447	4.70
cropland in summer fallow	237258	3.16
sorghum	149054	1.98
cotton	90228	1.20
barley for grain	46651	0.62
sod harvested	8472	0.11
oats for grain	3121	0.04

Figure VIII-1. Mean Annual Dicamba Use for Agricultural Uses in the U.S. During 1999-2004[1]

[1]Based on 2002 Census of Agriculture county crop acreage (USGS, 2004).

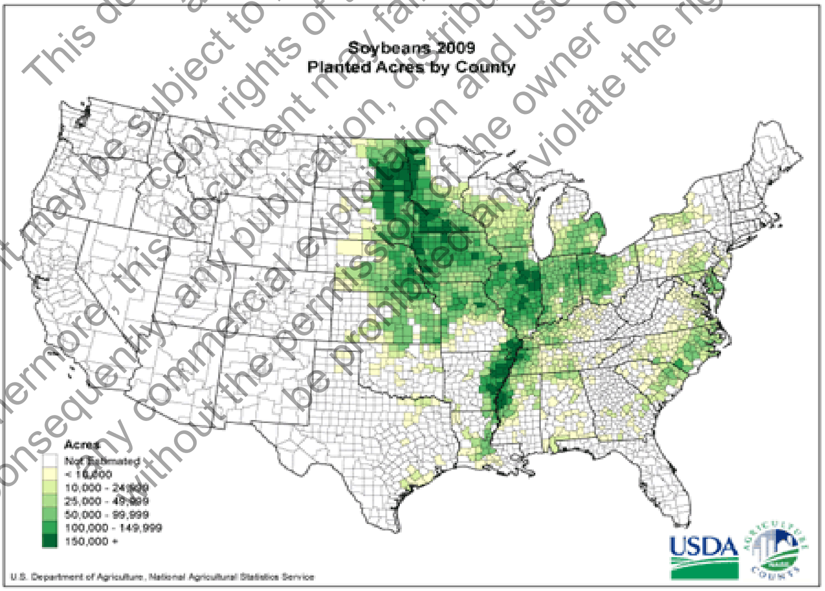
Soybeans 2009
Planted Acres by County
Acres
Not Estimated
< 10,000
10,000 - 24,999
25,000 - 49,999
50,000 - 99,999
100,000 - 149,999
150,000 +
U.S. Department of Agriculture, National Agricultural Statistics Service
USDA
AGRICULTURE COUNTS

Figure VIII-2. Planted Soybean Acreage by County in the U.S. in 2009[1]

[1]Source is USDA-NASS (2010).

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VIII.G.3. Potential Impacts to Adjacent Crops

U.S. EPA considers possible effects from offsite movement as part of the pesticide registration process. In order to approve the use of a pesticide (herbicide) under FIFRA, U.S. EPA must conclude that no unreasonable adverse effects on non-target vegetation will result from offsite movement when the herbicide is used according to the product label. Thus, when herbicides are applied in accordance with the pertinent label restrictions, offsite impacts can be avoided. EPA reassessed the potential risks to non-target plants in its analysis in the dicamba RED, and it concluded that no specific additional drift mitigations were needed to support the continued registration of all dicamba uses (U.S. EPA, 2009). Since the proposed use pattern for dicamba on MON 87708 is consistent with use patterns evaluated and deemed eligible for reregistration in the dicamba RED, it is reasonable to conclude that dicamba use on MON 87708 meets the FIFRA standards related to offsite movement and does not pose any greater risk to non-target vegetation over existing dicamba agricultural uses approved by EPA when used according to the product label.

Growers and commercial herbicide applicators have been applying dicamba to agricultural row crops for over 40 years. This practice has provided valuable experience and knowledge on the proper application of dicamba for effective weed control and also for minimizing offsite movement to sensitive crops. Dicamba herbicide spray drift can be reduced during application by using industry standard procedures for minimizing spray drift. These procedures include making applications with coarse droplet size through appropriate nozzle selection, using lower spray pressure, applying at the lowest nozzle height that provides uniform coverage, and making applications when wind speeds are low and consistent in direction (SDTF, 1997). In addition, growers and commercial applicators are legally required to follow label requirements and are educated by university specialists and industry representatives on the proper application equipment, equipment setup, and climatic conditions to maximize herbicide performance and minimize offsite movement of herbicides. For example, with the introduction of Roundup Ready crops and the subsequent increase in glyphosate use, university specialists conducted extensive education programs on proper application procedures and precautions ([redacted] – Purdue University, 2010 personal communication). Equipment manufacturers have developed spray nozzles that provide uniform coverage for effective weed control while applying larger spray droplets to reduce the potential for particle drift. Similarly, offsite movement of dicamba has been managed with the knowledge of the proper spray equipment and equipment setup, climatic conditions for accurate, on-target applications, and based on the requirements for applying dicamba at an appropriate distance from adjacent crops and plants (Jordan et al., 2009).

Monsanto plans to further address the use of dicamba on MON 87708 with US EPA to evaluate whether any additional measures may be appropriate to further address potential drift and offsite movement.

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VIII.H. Dicamba-Tolerant Soybean MON 87708

Monsanto has developed a new herbicide-tolerant soybean, MON 87708, to offer growers an expanded use of the herbicide dicamba in soybean production. MON 87708 will facilitate a wider window of dicamba application in soybean, allowing preemergence application up to the day of crop emergence (cracking) and in-crop postemergence applications through the R1/R2 growth stage. MON 87708 will be combined with MON 89788 (Roundup Ready 2 Yield soybean) utilizing traditional breeding techniques. The combination of herbicide-tolerance traits will allow the pre- and postemergence use of both dicamba and glyphosate herbicides in an integrated weed management program to control a broad spectrum of grass and broadleaf weed species (Johnson et al., 2010). Increasing postemergence herbicide options is important, especially in conservation tillage situations, where the performance consistency of postemergence herbicides has generally been greater than that of soil active residual products. Dicamba will improve the control of glyphosate's hard-to-control broadleaf weeds (*e.g.*, common lambsquarters, hemp sesbania, morningglory species, nightshade, Pennsylvania smartweed, prickly sida, and wild buckwheat) and also offer an effective control option for glyphosate-resistant broadleaf weed species, namely marestail, common ragweed, giant ragweed, palmer pigweed, and waterhemp (Johnson et al., 2010). Dicamba will also offer an effective control option for broadleaf species resistant to ALS and PPO chemistries. In the case of PPO resistance, a primary dicamba benefit will be to provide options for delaying the further spread of PPO resistant amaranthus species (University of Tennessee, 2010).

Upon integration of MON 87708 into the Roundup Ready soybean system, growers will have the ability to continue to use established soybean production practices including crop rotation, tillage systems, labeled herbicides, and row spacing, thereby using the same planting and harvesting machinery currently being utilized. Growers will also continue to have the flexibility and simplicity in weed control provided by glyphosate that will allow growers to continue to reap the environmental benefits associated with the use of conservation-tillage that is facilitated by the use of glyphosate for postemergence weed control in the Roundup Ready soybean system (CTIC, 2011; CTIC, 2004).

Current labeled uses of dicamba in soybean are limited to early preplant and late postemergence (preharvest) applications. Significant planting restrictions exist in soybean for preplant applications of dicamba, including a maximum application rate of 0.5 lbs a.e. per acre, a 28-day interval between application and planting soybean, and a minimum of one inch of rainfall must occur before planting soybean to avoid soybean injury. Monsanto has submitted an application to U.S. EPA to amend Registration Number 524-582, a DGA salt formulation, to remove all preemergence planting restrictions (intervals and rainfall) and to allow in-crop postemergence dicamba applications to MON 87708 through the R1/R2 growth stage of soybean. Once approved, growers would be authorized to apply dicamba alone or in mixtures with glyphosate or other herbicides for preplant or in-crop postemergence applications on MON 87708. Dicamba would be authorized to be applied preemergence up to crop emergence as a single application or split applications up to a total of 1.0 lb a.e. per acre, and up to two postemergence applications up to 0.5 lb a.e. per acre each through the R1/R2 growth stage of soybean. The maximum annual application rate of dicamba on MON 87708 is 2.0 lb dicamba a.e. per acre. Furthermore, Monsanto's proposed

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dicamba label does not allow aerial applications of dicamba on MON 87708, a stewardship measure intended to address potential offsite impacts. As indicated, Monsanto also plans to further address the use of dicamba on MON 87708 with US EPA to evaluate whether any additional measures may be appropriate to further address potential drift and offsite movement.

The potential increase in dicamba use in U.S. soybean production upon deregulation of MON 87708 was assessed by estimating the total dicamba use across soybean acres. Assuming 100% adoption of MON 87708 across all U.S. soybean acreage[6] and an application of dicamba at the maximum labeled use rate on all soybean acres, dicamba use on MON 87708 could potentially total 150 million pounds. In practice, however, a single early season in-crop application per year of dicamba at 0.38 lb a.e. per acre is expected on the majority of MON 87708 planted acres. However, in no-till or conservation tillage soybean systems, an additional preplant application at 0.50 lb a.e. per acre could also be common practice, and in areas where glyphosate resistant weeds, especially *Ambrosia* and *Amaranthus* species, are present two in-crop applications at 0.5 lb a.e. each may be needed in some situations. These anticipated use patterns represent a high-end estimate for prediciting dicamba use associated with MON 87708 integrated with the Roundup Ready soybean system.

Furthermore, consistent with recommendations by academics and weed scientists, Monsanto will recommend the use of a third herbicide mode-of-action with soil residual activity as part of a comprehensive weed resistance management program to assure that at least two effective modes-of-action are always used in the cultivated soybean field. A summary of the anticipated weed control recommendations for the combined MON 87708 and Roundup Ready soybean system is provided in Table VIII-16.

In 2010, Monsanto conducted an informal survey of weed scientists across the country to estimate the number of crop acres with glyphosate resistant weed populations. Based upon this survey it was estimated that approximately 14-16 million acres of planted row-crops (i.e. corn, soybeans, cotton) had populations of glyphosate resistant weeds. Of these acres, the majority of acres (~ 10 million) are infested with glyphosate resistant marestail populations where a preplant application of dicamba and glyphosate described above will be effective for control. The remainder of resistant acres (~5 million) have resistant *Ambrosia* (common and giant ragweed) and *Amaranthus* (palmer pigweed and water hemp,) species present. A conservative estimate of 5 million resistant acres is assumed for this assessment, which overestimates current resistant acres in soybean producing areas and also accounts for potential increases in resistant acres because not all resistant crop acres would be planted to soybean in any given year.

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[6] Based on approximately 75 million acres planted to soybean in 2008, see Table VIII-1.

Table VIII-16. Anticipated Weed Management Recommendations for MON 87708 Combined with the Roundup Ready 2 Yield Soybean System[1]

	Conventional Tillage[2]			Conservation Tillage [2] (No-till or reduced till)		
	No GR Weeds	GR Weeds or Suspected GR Weeds		No GR Weeds	GR Weeds or Suspected GR Weeds	
Application Timing		**Option 1[3]**	**Option 2[4]**		**Option 1[3]**	**Option 2[4]**
Preemergence (burndown, at planting) [5]	Residual	Residual	Residual	Residual + Glyphosate + Dicamba	Residual + Glyphosate + Dicamba	Residual + Glyphosate + Dicamba
Postemergence 1 (V1-V3)	Glyphosate + Dicamba	Glyphosate + Dicamba	Glyphosate + Dicamba	Glyphosate + Dicamba	Glyphosate + Dicamba	Glyphosate + Dicamba
Postemergence 2 (V4-R2)	---	Glyphosate + Dicamba	---	---	Glyphosate + Dicamba	---

[1] The anticipated use patterns represent a high-end estimate for prediciting dicamba use associated with MON 87708 integrated with the Roundup Ready soybean system. Actual weed control practices by growers will vary depending on the specific weed spectrum and agronomic situation of the individual soybean field, specifically dicamba use could be lower especially for the preemergence and second postemergence applications.

[2] Average rate for dicamba is 0.38 pound a.e. per acre except for fields with glyphosate resistant (GR) species where a 0.5 pound a.e. per acre postemergence application rate will be recommended. In some situations, the second postemergence application may not be needed.

[3] Option 1 would be used for more aggressive glyphosate resistant weed species, such as *Ambrosia* or *Amaranthus* species.

[4] Option 2 would be used for less aggressive glyphosate resistant weed species, such as marestail.

[5] Monsanto and academics recommend the use of soil residuals as part of a comprehensive weed resistance management program to ensure that two effective herbicide modes-of-action are used in soybean and to provide protections against additional resistance development to existing soybean herbicides.

Assuming the anticipated use rate of 0.5 lb a.e. per acre dicamba for preemergence applications and 0.38 lb a.e. per acre dicamba for postemergence applications, and using a conservative assumption that MON 87708 has 100% adoption across all U.S. geographies and conservation tillage systems are used on approximately 40% of the U.S. soybean acres (CTIC, 2007), dicamba use on MON 87708 would total approximately 44 million pounds. When considering a more realistic adoption rate for MON 87708 of 40% (refer to Section VIII.H.2), dicamba use on MON 87708 would total approximately 17 million pounds. In areas where resistant *Ambrosia* and *Amaranthus* species are present requiring two in-crop applications, the use of an additional 5 million pounds of dicamba per year is estimated.

It is anticipated that dicamba applications will continue for currently labeled crops at the dicamba-treated acreage levels and amounts presented in Table VIII-12, such that the dicamba treatment to MON 87708 will thereby result in a total U.S. dicamba use of approximately 25 million pounds annually. This level of dicamba use would be

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approximately double the historical peak level (Table VIII-11) experienced since dicamba's introduction in 1967.

Upon integration of MON 87708 into the Roundup Ready soybean system, dicamba will provide excellent control of numerous annual and perennial broadleaf weed species, including populations of broadleaf weeds that are resistant to ALS, atrazine, or glyphosate herbicides. Table VIII-17 shows weed control ratings for dicamba, glyphosate and several glyphosate tank mixtures when applied as a preplant burndown application to common broadleaf weed species found in soybean fields of the Midwest and Southeast regions. An application of dicamba alone provides effective control of a broad spectrum of winter and summer annual and perennial broadleaf weed species. In comparison, glyphosate alone provides excellent control of many grass species in addition to many of the annual and perennial broadleaf species listed. However, dicamba provides a higher level of control of certain broadleaf weeds including common lambsquarters, Pennsylvania smartweed, red clover, alfalfa, marestail, hairy vetch, and prickly lettuce. Dicamba will be very complementary in mixtures with glyphosate for weed control in a preplant application (Johnson et al, 2010) and will offer growers equal or superior weed control to other glyphosate mixtures because it offers reduced potential herbicide antagonism, improved efficacy and broader weed spectrum.

The dicamba tolerance trait in MON 87708 will permit in-crop applications of dicamba to soybean with excellent crop safety (crop tolerance). Dicamba will also complement the weed control of in-crop applications of glyphosate when applied as a mixture or in sequence. Table VIII-18 shows common broadleaf weed responses to dicamba compared to glyphosate and several glyphosate labeled tank mixtures in soybean. Since dicamba is not currently labeled for in-crop applications in soybean, weed control ratings for dicamba were taken from labeled in-crop applications of dicamba in corn for comparison purposes. Glyphosate will continue to provide broad spectrum control of annual grasses and broadleaf weeds, while dicamba will provide improved control of common ragweed, giant ragweed, hemp sesbania, morningglory species, and prickly sida. As presented in Table VIII-17, dicamba is more effective in controlling marestail then glyphosate. Likewise, in comparison to glyphosate, dicamba is expected to also improve the control of lambsquarters, eastern black nightshade, kochia, palmer pigweed, and wild buckwheat. In addition to complementing the weed control of glyphosate, dicamba will provide another mode of action in the Roundup Ready soybean system to lower the potential risk of weeds developing resistance to glyphosate (see Section L.5.3.3 of Appendix L). Furthermore, dicamba will provide an alternative mode of action for control of broadleaf weeds with populations known to be resistant to ALS and PPO classes of herbicides (see Table VIII-8 for herbicide listings).

Application of both dicamba and glyphosate to MON 87708 integrated with the Roundup Ready soybean system will provide effective control of both dicamba- and glyphosate-resistant broadleaf weeds (Johnson et al, 2010). In the U.S., kochia (*Kochia scoparia*) and prickly lettuce (*Lactula serriola*) are the only species with biotypes confirmed to be resistant to dicamba after 40+ years of use (Heap, 2009). Additionally, a population of lambsquarters (*Chenopodium album*) has been confirmed as resistant in New Zealand, and in Canada common hempnettle (*Galeopsis tetrahit*) and wild mustard (*Sinapis arvensis*) have been

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confirmed as resistant, for a total of five species worldwide with confirmed resistance to dicamba. Glyphosate has been shown to provide good to excellent control of all five of these broadleaf weeds. In addition, there are 3 species (spreading dayflower (*Commelina diffusa*), field bindweed (*Convolvulus arvensis*) and wild carrot (*Daucus carota*)) in the U.S. with confirmed resistance to 2,4-D. Of the dicamba and 2,4-D species with known resistance in the U.S. and Canada, cross resistance between dicamba and 2,4-D has only been documented in wild mustard. However, cross resistance within the other species can not be totally ruled out nor assumed to be present. Currently in the U.S., six grass species and seven broadleaf species have been confirmed to have resistance to glyphosate. Dicamba provides good to excellent control of all seven of these broadleaf species. None of these broadleaf weed biotypes have been shown to have populations that are resistant to both glyphosate and dicamba. However, there are known resistant populations of kochia that are either resistant to glyphosate or to dicamba, but no population with known resistance to both glyphosate and dicamba. Since there is no cross resistance between dicamba and glyphosate either product can be effective on kochia populations resistant to the other. A more detailed discussion regarding the potential development of dicamba resistance in weeds can be found in Appendix K.

The introduction of MON 87708 into the Roundup Ready soybean system will allow dicamba to effectively compete with and provide an additional mode-of-action to the alternative herbicides that are currently used in combination with glyphosate in preplant and in-crop postemergence applications in soybean (for a comparison of dicamba to alternative non-glyphosate herbicides, see Appendix L). This will provide an additional mode-of action into the soybean weed management system that was previously not available. A comparison of dicamba to alternative herbicides, in terms of human health effects (acute toxicity, cancer risk, chronic risk, and risk to infants and children), ecological effects (aquatic animal risk and aquatic plant risk), weed management efficacy, herbicide-resistant weed frequency, rotational crop restrictions, and the potential for injury to the soybean crop, is presented in Table VIII-19. In this analysis, dicamba offers an improved risk profile over each alternative herbicide in at least one and up to five of the comparative categories; however all alternative herbicides are safe when used according to label directions. Additionally, dicamba is expected to offer greater benefits than some alternative herbicides as a supplement to glyphosate for in-crop applications on MON 87708 since planting interval restrictions following preplant applications of dicamba in soybean will be removed and allowing dicamba to be applied through planting and up to crop emergence (cracking). Dicamba will have greater flexibility for preplant applications than current preplant applications of 2,4-D and potentially will replace some 2,4-D applications in soybean. The superior broadleaf weed control provided by dicamba and excellent crop tolerance when applied to MON 87708 will provide an additional mode-of-action and an alternative to the herbicides used for broadleaf weed control in soybean, particularly acifluorfen, lactofen, chlorimuron, and flumiclorac. The human health and environmental safety of dicamba relative to other non-glyphosate alternative herbicides is discussed in greater detail in Appendix L. Considering the characteristics of dicamba from a weed control, compatibility with glyphosate, and human and environmental safety perspective, it is concluded that MON 87708 will complement the established safety and efficacy of glyphosate use in the Roundup Ready soybean system.

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Table VIII-17. Common Broadleaf Weed Responses to Preplant Burndown Herbicides

	Common Broadleaf Weeds[1,2]														
Herbicide/Application	LQ	CR	GR	SW	CC	M, SP	CT	RC	AL	HV	MT	PL	DN, HB	DL	CG
Spring Preplant Application															
2,4-D (0.5 lb/1.0 lb)	-	-	-	-	-	9	-/6	6/8	-/7	6/8	8/9	8/9	-/8	6/7	9/9
Dicamba	9	9	9	9	6	7	-	9	8	8	7	9	-	7	-
Dicamba + 2,4-D	9	9	9	9	6	9	6	9	8	9	9	9	-	8	9
Glyphosate	8	9	8	7	7	8	6	7	6	6	6	8	-	7	7
Glyphosate + 2,4-D	9	9	9	8	7	9	6	8	8	8	8+	9	6	8	9
Glyphosate + Canopy	8	9	9	9	7	8	6	7	6	6	8	8+	9	8+	9
Glyphosate + Canopy + 2,4-D	9	9	9	9	7	9	6	8	8	8	9	9	9	8+	9
Glyphosate + Gangster + 2,4-D	9	9	9	9	7	9	6	8	8	8	9	9	8	8	9
Glyphosate + Python + 2,4-D	9	9	9	8	7	9	6	8	8	8	9	9	6	8	9
Glyphosate + Scepter + 2,4-D	9	9	9	8	7	9	6	8	8	8	8+	9	6	8	9
Gly + Sonic/Authority First + 2,4-D	9	9	9	9	7	9	6	8	8	8	9	9	8	8	9
Glyphosate + Valor + 2,4-D	9	9	9	8	7	9	6	8	8	8	8+	9	8	7	9

[1] All weed control ratings are from the 2009 Weed Control Guide for Ohio and Indiana – Weed Responses to Burndown Herbicides, Ohio State University and Purdue University (Loux et al., 2009). Weed control ratings for weeds are: 9 = 90% to 100%, 8 = 80% to 90%, 7 = 70% to 80%, 6 = 60% to 70%, and - = less than 60% control, not recommended. Ratings assume the herbicides are applied in the manner suggested in the guidelines and according to the label under optimum growing conditions.

[2] Weed species: LQ = lambsquarters, CR = common ragweed, GR = giant ragweed, SW = annual smartweed, CC = common chickweed, M & SP = mustard and shephard's purse, CT = Canada thistle, RC = red clover, AL = alfalfa, HV = hairy vetch, MT = marestail, PL = prickly sida, DN & HB = deadnettle & henbit, DL = dandelion, and CG = crested groundsel

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Table VIII-18. Common Broadleaf Weed Responses to Dicamba Compared to Labeled Postemergence Herbicides in Soybean Production

	Common Broadleaf Weeds[1,2]													
Herbicide/Application	BN	CB	CR	GR	HS	LQ	MG	PA	PW	PS	SP	SW	VL	WH
Postemergence														
Bentazon	-	9	7	6	4	7	2-9	4	-	8	0	9	8+	-
Chlorimuron	-	9	8	7+	8	-	8-9	6	9	2	7	8	8	-
Cloransulam	-	9	9	9	3	-	8-9	2	-	2	7	8	9	-
Chlorimuron/thifensulfuron	-	9	8	7+	NA	8	NA	NA	9	NA	NA	9	9	-
Dicamba[3]	8	9	9	9	9	8	9	9	8	8	8	8	7+	8
Flumiclorac	-	7	7	-	NA	7	NA	NA	7	NA	NA	-	9	7
Fomesafen	8	7	8+	8	9	-	8-9	8	9	2	3	7	6	9
Glyphosate	8	9	8+	8	7	8	7-9	9	9	7	8	8	8	8
Glyphosate/imazethapyr	9	9	8+	8+	NA	8+	NA	NA	9	NA	NA	9	9	8
Imazamox	9	8	7	8	NA	8	NA	NA	9	NA	NA	8	9	-
Imazethapyr	9	9	6	7	0	6	7-9	6	9	6	0	9	9	-
Lactofen	8+	8	9	8	9	-	8-9	8	9	8	5	6	7	9
Thifensulfuron	-	6	-	-	NA	8	NA	NA	9	NA	NA	8	9	-

[1] All weed control ratings except for HS, MG, PA, PS, and SP are from the 2009 Weed Control Guide for Ohio and Indiana – Ohio State University and Purdue University (Loux et al., 2009). Ratings for HS, MG, PA, PS, and SP are from the 2009 Weed Control Guidelines for Mississippi, Mississippi State University (MSU, 2010), except for dicamba ratings for PA are from the 2010 Weed Control Manual for Tennessee (University of Tennessee, 2010). Weed control ratings for weeds, except HS, MG, PA, PS, and SP, are: 9 = 90% to 100%, 8 = 80% to 90%, 7 = 70% to 80%, 6 = 60% to 70%, and - = less than 60% control, not recommended. Weed control ratings for HS, MG, PA, PS, and SP are: 9-10 = excellent, 7-8 = good, 4-6 = fair, 0-3 = none to slight. Ratings assume the herbicides are applied in the manner suggested in the guidelines and according to the label under optimum growing conditions. NA denotes not available.

[2] Weed species: BN = black nightshade, CB = cocklebur, CR = common ragweed, GR = giant ragweed, LQ = lambsquarters, MG = morningglory spp., HS = hemp sesbania, PA = palmer and spiny pigweed, PW = pigweed, PS= prickly sida, SP = sicklepod, SW = smartweed, VL = velvetleaf, and WH = waterhemp

[3] Weed control ratings for dicamba are from postemergence applications in corn.

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Table VIII-19. Summary of Comparative Analysis of Dicamba and Alternative Herbicides

Herbicide Active Ingredient	Mode-of-Action[1]	Human Health Risk Measures				Aquatic Non-Target Species Risk Measures		Known Resistant Weed Species[2]	Herbicidal Efficacy (< 50% of dicamba)	Long Rotational Crop Restriction	Serious Crop Injury Potential	Number of "Yes" Entries[3]	Number of "No" Entries[4]
		Acute Toxicity Risk	Cancer Risk	Chronic Risk	Infants & Children Risk	Aquatic Animal Risk	Aquatic Plant Risk						
2,4-D acid / esters	Aux (4)	**Yes**	**Yes**	**Yes**	Neutral	**Yes**	**Yes**	28	Neutral	Neutral	Neutral	**6**	**0**
2,4-DB	Aux (4)	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral		**Yes**	Neutral	Neutral	**2**	**0**
imazethapyr	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	Neutral	**Yes** (107)	**Yes**	**Yes**	Neutral	**3**	**1**
cloransulam-methyl	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	Neutral		**Yes**	**Yes**	Neutral	**4**	**1**
chlorimuron-ethyl	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	NA		**Yes**	**Yes**	Neutral	**3**	**1**
thifensulfuron	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	**Yes**		**Yes**	**Yes**	Neutral	**4**	**1**
imazaquin	ALS (2)	No	No	Neutral	Neutral	Neutral	NA		**Yes**	**Yes**	Neutral	**3**	**2**
imazamox-ammonium	ALS (2)	No	Neutral	No	Neutral	Neutral	Neutral		**Yes**	**Yes**	Neutral	**4**	**2**
flumioxazin	PPO (14)	Neutral	Neutral	**Yes**	Neutral	**Yes**	**Yes**	5	**Yes**	**Yes**	Neutral	**5**	**0**
fomesafen	PPO (14)	**Yes**	Neutral	**Yes**	Neutral	Neutral	Neutral		Neutral	**Yes**	**Yes**	**4**	**0**
flumiclorac-pentyl	PPO (14)	No	No	Neutral	Neutral	Neutral	NA		**Yes**	Neutral	Neutral	**1**	**2**
sulfentrazone	PPO (14)	**Yes**	Neutral	Neutral	Neutral	Neutral	**Yes**		**Yes**	Neutral	Neutral	**4**	**0**
lactofen	PPO (14)	No	**Yes**	Neutral	**Yes**	**Yes**	**Yes**	5	Neutral	Neutral	**Yes**	**5**	**1**
fluthiacet-methyl	PPO (14)	No	**Yes**	Neutral	Neutral	Neutral	Neutral	5	**Yes**	Neutral	**Yes**	**3**	**1**
acifluorfen sodium	PPO (14)	**Yes**	**Yes**	Neutral	**Yes**	Neutral	Neutral	5	**Yes**	Neutral	**Yes**	**5**	**0**
glufosinate-ammonium	Glu (10)	**Yes**	No	**Yes**	Neutral	Neutral	Neutral	No reports	Neutral	Neutral	Neutral	**3**	**0**
paraquat dichloride	BiPyr (22)	**Yes**	No	**Yes**	Neutral	Neutral	**Yes**	24	**Yes**	Neutral	Neutral	**4**	**0**
mesotrione	HPPD (28)	No	Neutral	Neutral	**Yes**	Neutral	**Yes**	No reports	**Yes**	**Yes**	Neutral	**4**	**1**

Refer to Appendix L for additional details on the comparison of alternative herbicides to dicamba.

"Yes", indicates that dicamba has an improved risk profile based on presented categories. Entries not indicated with a "Yes" mean that dicamba is either comparable or less favorable than the alternative herbicide. "Neutral" entries indicate similar risks exist for dicamba and the alternative herbicide. "No" means the alternative herbicide offers a risk benefit compared to dicamba

[1] Mode-of-Action based upon WSSA (2010) classifications.

[2] A listing of the worldwide numbers of known resistant weeds for each herbicide based on its mode-of-action group. Dicamba has five known resistant weed biotypes worldwide (www.weedscience.org/summary/MOASummary.asp *Accessed May 28, 2010*). A "Yes" indicates that the

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number of resistant weeds in this herbicide class is many more than the known five dicamba resistant species biotypes. A comparison of each individual herbicide in the class is not provided. See Section L.5.3.3 in Appendix L.

[3] Number of "Yes" entries in each row is a summation for all the categories assessed, indicating a total score for improved risk profile for dicamba.

[4] Number of "No" entries in each row is a summation for all the categories assessed, indicating a total score for worse risk profile for dicamba.

NA – not available

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VIII.H.1. Potential Impact of Dicamba Application Timing to MON 87708

The proposed label directions for dicamba applications in MON 87708 will permit preplant applications up to the crop emergence and in-crop postemergence applications up to the R1/R2 soybean growth stage. Most in-crop applications are expected to be made up to the V4 growth stage, when germinated weeds are more easily and economically controlled and broadcast applications can be uniformly applied to the weeds (reduced crop canopy compared to later vegetative growth stages); with limited applications up to R1/R2, where this application is primarily anticipated to control missed weeds, treat a flush of broadleaf weeds germinating after the V4 application, or for control of more aggressive glyphosate-resistant weed species such as *Amaranthus* or *Ambrosia* species. Currently, in-crop postemergence applications of dicamba, except for preharvest applications, are not permitted or practical on commercially available soybean due to the lack of crop tolerance. An application of dicamba at or following the V4 soybean growth stage is expected to be later in the growing season than the current latest in-crop application timings to corn, sorghum, and wheat.

To assess the potential impact related to an anticipated difference in application timing of dicamba to MON 87708 compared to current labeled uses of dicamba, the latest timing of in-crop postemergence dicamba applications in corn was assessed. The comparison to corn application timing is pertinent since corn is grown in the same general areas where soybean is grown and a high percentage of the total dicamba-treated acres occur in corn (see Table VIII-15). Table VIII-20 provides the typical date and days from planting for corn and soybean to reach various growth stages. According to USDA-NASS (2009e) planting progress reports, the dates at which 50% of the corn and soybean are planted in Illinois are April 25 and May 17, respectively. The current dicamba label[7] specifies an allowable use pattern relative to corn growth stages as defined by the number of leaves and plant height. Dicamba can be broadcast applied to corn up to a height of 8 inches, which is roughly equivalent to the 5-leaf stage. To relate these application timings to soybean, it is necessary to convert the timing of the 5-leaf stage of corn to a comparable soybean vegetative growth stage (V stage). The 5-leaf stage of corn is equivalent to a V4 growth stage (Personal communication, [redacted] – Purdue University, 2010). Corn will generally reach this growth stage in 37 days from planting based on central Illinois temperatures. Presuming corn planting occurs on April 25, corn would reach the comparable V4 stage on June 1. Soybean will typically reach the V4 growth stage in 35 days. Presuming soybean planting on average occurs on May 17, soybean will reach the V4 stage on approximately June 21. Therefore, based on planting and environmental data from central Illinois, the most likely application timing for dicamba to MON 87708 is approximately 20 days later than the current latest application timing for corn. The timing difference is expected to be applicable to much of the Midwest region where the majority of the soybean is grown.

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[7] Clarity product label can be found at:http://www.cdms.net/Images/acroiconwblue.gif. Label specifies when applying to corn not to apply Clarity when soybean are growing nearby if any of the following conditions exist: 1) corn is more than 24" tall, 2) soybean is more than 10" tall, and 3) soybean has begun to bloom.

Table VIII-20. Dates and Days to Reach Various Growth Stages in Corn and Soybean in Central Illinois

Growth Stage	Corn[1] Date & Calendar Day	Corn[1] Days From Planting	Soybean[2] Date & Calendar Day	Soybean[2] Days From Planting
Planting	April 25 (115)[3]		May 17 (137)[3]	
VE	May 10 (130)	15	May 27 (147)	10
VC			June 1 (152)	15
V1	May 27 (137)	22	June 6 (157)	20
V2	May 22 (142)	27	June 11(162)	25
V3	May 27 (147)	32	June 16 (167)	30
V4	June 1 (152)	37	June 21 (172)	35
V5	June 5 (156)	41	June 26 (177)	40
V6	June 9 (160)	45	June 29 (180)	43
V7	June 13 (164)	49	July 2 (183)	46
V8	June 17 (168)	53	July 5 (186)	49

[1] Corn growth based on Nielsen (2008) and average growing degree days at Champaign, IL (1971-2000).

[2] Soybean growth is based on Naeve (2005).

[3] Average date when 50% of the crop acreage was planted in Illinois during the 5-year period 2004-2008 (USDA-NASS, 2009d).

Corn and soybean planting dates and climates are considerably different in the Southeast region states than the Midwest region states. Thus, a second analysis was conducted to assess the potential difference in timing between current dicamba applications in corn and the likely dicamba application to MON 87708 in a southern location. Table VIII-21 provides the typical date and days for plantings of corn and soybean to reach various growth stages in western Tennessee. The dates at which 50% of the corn and soybean are planted in Tennessee are April 15 and May 25, respectively. Corn will generally reach the 5-leaf growth stage (comparable to the V4 soybean growth stage) in approximately 30 days from planting based on western Tennessee's climate. Typical corn plantings occur on April 15, such that corn will reach the V4 stage on May 15. Soybean will reach the V4 growth stage in 27 days. Typical soybean planting occurs on May 25, such that soybean will typically reach the V4 stage on June 21. Therefore, based on planting and environmental data from western Tennessee, the expected postemergence dicamba application timing (V4 growth stage) to MON 87708 is approximately 37 days later than the current latest application timing for corn. Although the difference between application timings is greater in this southern location compared to a northern location, the estimated dates for the V4 stage in soybean for the two locations are the same.

As presented in Appendix M, Monsanto has submitted an application to EPA to amend Registration Number 524-582 to add the new use on MON 87708 to the product label. Registration Number 524-582 is a DGA salt formulation of dicamba, which is a formulation with low volatility. Monsanto also plans to further address the use of dicamba on MON 87708 with EPA to evaluate whether any additional measures may be appropriate. In addition, Monsanto in cooperation with public sector scientists and organizations will

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implement robust stewardship programs to assist in the education of applicators on the best application practices to minimize the potential for offsite movement, including the use of low volatility formulations.

Table VIII-21. Dates and Days to Reach Various Growth Stages in Corn and Soybean in Western Tennessee

	Corn[1]		Soybean[2]	
Growth Stage	Date & Calendar Day	Days From Planting	Date & Calendar Day	Days From Planting
Planting	April 15 (108)[3]		May 25(148)[3]	
VE	April 25 (118)	10	June 1 (155)	7
VC			June 5 (159)	11
V1	May 1 (124)	16	June 9 (163)	15
V2	May 6 (129)	21	June 13 (167)	19
V3	May 10 (133)	25	June 17 (171)	23
V4	May 15 (138)	30	June 21 (175)	27
V5	May 19 (142)	34	July 25 (179)	31
V6	May 23 (146)	38	July 28 (182)	34
V7	May 26 (149)	41	July 1 (185)	37
V8	May 30 (153)	45	July 4 (188)	40

[1] Corn growth based on Nielsen (2008) and 30-year average growing degree days at West Memphis, TN.

[2] Soybean growth is based on Naeve (2005).

[3] Average date when 50% of the crop acreage was planted in Tennessee during the 5-year period 2004-2008 (USDA-NASS, 2009d).

Table VIII-22. Average Daily Temperatures in Major Soybean Producing States[1]

	Average Daily Temperature (°F)			
	April	**May**	**June**	**July**
IN	51	62	71	74
IA	49	60	70	74
IL	52	62	72	75
MN	42	56	65	69
MO	55	64	73	78
OH	50	60	69	73
AR	60	69	76	81
NE	48	59	69	74
ND	42	55	64	69
SD	45	57	66	72

[1] Earth System Research Laboratory of National Oceanic and Atmospheric Administration (NOAA-ESRL 2011).

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Table VIII-23. Average Relative Humidity (1971-2000) in Major Soybean Producing States[1]

	Morning				Afternoon			
	April	May	June	July	April	May	June	July
IN	78	80	81	84	56	57	57	59
IA	77	78	81	85	61	62	64	66
IL	73	75	76	79	60	60	61	63
MN	75	76	81	84	59	58	62	64
MO	76	82	84	84	61	66	66	65
OH	76	78	80	83	54	54	55	55
AR	80	86	86	85	61	61	64	63
NE	77	79	81	81	56	58	58	58
ND	77	76	81	81	59	56	60	58
SD	78	79	81	82	58	58	60	57

[1] National Climatic Data Center of National Oceanic and Atmospheric Administration (NOAA-NCDC 2011).

VIII.H.2. Impact on Dicamba Use in U.S. Soybean Production Following Integration of MON 87708 into the Roundup Ready Soybean System

Upon integration of MON 87708 into the Roundup Ready soybean system, dicamba herbicide use will be expanded to in-crop postemergence applications for those hard-to-control and herbicide-resistant broadleaf weeds found in U.S. soybean production. The impact that MON 87708 will have on overall dicamba use will be dependent upon the level of MON 87708 adoption by growers. Thus, the extent of dicamba-treated soybean acreage following the deregulation of MON 87708 is difficult to forecast. Monsanto estimates dicamba-treated acres to ultimately be in the range of 30 to 50% of the total U.S. soybean acres. This estimate is based on a number of factors: 1) the percentage of non-glyphosate herbicides currently used in Roundup Ready soybean, 2) current and historical use of dicamba in corn, 3) the development of glyphosate-resistant weeds in soybean cultivation areas, 4) the effectiveness of other non-glyphosate herbicides used in the Roundup Ready soybean system, 5) compliance with EPA mandatory label instructions may have the practical affect of limiting the use in some soybean growing areas; and 6) the foreseeable future introduction of new competitive biotechnology-derived traits in soybean.

Approximately 15 to 21% of growers used a non-glyphosate herbicide in addition to glyphosate in the Roundup Ready soybean system in 2005 (Givens et al., 2009). The reasons growers stated for their use of a non-glyphosate herbicide in the Roundup Ready soybean system were generally for early weed control, residual weed control, improvement in the control of specific hard-to-control weeds, and/or glyphosate-resistant weed management. Frisvold et al. (2009) reported that in 2007 approximately 30% of the growers often or always use herbicides with different modes-of-action in the Roundup Ready soybean system. The future use of non-glyphosate herbicides would be expected to increase

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in order to support the management of glyphosate-resistant weeds. Additionally, grower educational programs on weed resistance management conducted by industry and universities encourage the use of non-glyphosate herbicides with alternative modes-of-action in Roundup Ready cropping systems as a proactive measure to minimize the potential for development of glyphosate-resistant weeds (Beckie, 2006; Powles, 2008). These programs, along with Monsanto's support for the use of another herbicide mode-of-action to control glyphosate-resistant weeds, will likely drive a further increase in non-glyphosate herbicides applied in soybean production.

A second factor that can be used as an indicator of potential future dicamba-treated soybean acreage is the current and historical use of dicamba in corn. Dicamba has been applied for many years in conventional and Roundup Ready corn for supplemental broadleaf weed control very similar to the proposed uses of dicamba on MON 87708. Therefore, information on dicamba use in corn will provide an indication of the potential demand for dicamba applied to MON 87708 when planted as a combined trait with Roundup Ready 2 Yield soybean. The use of non-glyphosate herbicides in Roundup Ready corn was reported to be 43 to 44% in 2005, which is significantly higher than presently used in Roundup Ready soybean (Givens et al., 2009). More recent market research data indicate a higher adoption rate of non-glyphosate herbicides in the corn, where market estimates were around 70% in 2010 (Agro Trak, 2010). Although, the reasons for using a non-glyphosate herbicide in the Roundup Ready corn system are the same as in Roundup Ready soybean, the benefits of using residual herbicides are greater in Roundup Ready corn because of the need for early season weed control and greater application flexibility with postemergence application of glyphosate (Dalley et al., 2001). Arguably for these reasons, the use of non-glyphosate herbicides applied to MON 87708 as a combined trait with Roundup Ready 2 Yield soybean will not likely exceed the current levels in Roundup Ready corn.

Prior to the introduction of Roundup Ready corn, the use of dicamba in corn production was greater since it was used mainly to complement the control of residual grass herbicides by providing postemergence control of annual broadleaf weed escapes. Dicamba-treated acres in conventional corn peaked at 29% of the corn acres in 1994. Dicamba use in corn dropped to 9.4% of the corn acres in 2008 following the commercial introduction of Roundup Ready corn (Table VIII-12). Therefore, considering the current use of dicamba in Roundup Ready corn (conservatively assumed to be 43 to 70%), the historical use of dicamba in conventional corn (peaking at 29% of the corn acres in 1994), and the current use of non-glyphosate herbicides in soybean (15 to 21% of growers applied a non-glyphosate herbicide in 2005), it can reasonably be concluded that dicamba-treated acres of MON 87708 will not likely exceed 50% of the total soybean acres following introduction of MON 87708.

A third factor impacting dicamba-treated soybean acreage is the current and future need for control of glyphosate-resistant weeds. Glyphosate-resistant weeds have been identified in multiple states (Heap, 2009). When a glyphosate-resistant weed biotype has been confirmed to be present in a geographical area, growers in that area are recommended by Monsanto, glyphosate distributors, and university specialists to proactively implement glyphosate-resistant weed management programs to ensure effective control of the resistant weed biotype regardless of whether the weed species has been confirmed to be resistant on a grower's farm. Therefore, the acreage in an area where responsive weed resistance

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management practices are implemented is potentially greater than the actual acres known to be impacted by glyphosate-resistant weeds. University weed scientists are recommending growers proactively implement best management practices, including a non-glyphosate herbicide with a second mode-of-action, in their cropping systems to minimize the development and potential spread of glyphosate-resistant weeds in the future (Owen et al., 2009; Frisvold et al., 2009). Monsanto supports this recommendation where glyphosate-resistant biotypes are present, such that MON 87708 integrated into the Roundup Ready soybean system should be treated with glyphosate and dicamba plus another herbicide mode-of-action to ensure at least two effective modes-of-action cover the spectrum of weeds present in a grower's soybean field. In this case, the other herbicide mode-of-action that will be recommended in the MON 87708 plus Roundup Ready soybean system is likely to be a soil active residual preemergence herbicide.

It is anticipated that even in locations where glyphosate-resistant weeds are present, glyphosate will continue to be the base herbicide applied to MON 87708 as a combined trait product with MON 89788 (Roundup Ready 2 Yield soybean), thereby providing broad spectrum control of grass and broadleaf weeds. MON 87708 allows the use of dicamba in the Roundup Ready soybean system for control of glyphosate-resistant weeds and to improve the control of dicotyledonous weeds that are hard to control with glyphosate alone. As described in Section VIII.F.1 and Table VIII-8, numerous residual and postemergence herbicides are utilized currently to complement the control of glyphosate for hard-to-control weeds and to mitigate or control glyphosate-resistant weeds. These alternative herbicides will compete with dicamba and undoubtedly will reduce the potential dicamba use on MON 87708 integrated into the Roundup Ready soybean system and in future combined trait products containing dicamba tolerance.

An additional factor influencing the number of dicamba-treated soybean acres in the future will be the introduction of competing herbicide-tolerant traits in soybean. Currently, there are numerous herbicide-tolerant soybean products under regulatory review or recently authorized (see Appendix J, Table J-4). This includes several products that have tolerance to multiple herbicides with different modes-of-action. These new biotechnology-derived herbicide-tolerant soybean products are anticipated to be introduced in future years and will compete with Monsanto's MON 87708 × MON 89788 combined-trait soybean product, further reducing the ultimate potential of dicamba applications in soybean. A grower may chose to not cultivate MON 87708 or to use an alternative soybean herbicide for their weed control. Furthermore, compliance with EPA mandatory label instructions may have the practical affect of limiting the use in some soybean growing areas.

Taking into consideration the above assessment, the potential dicamba-treated MON 87708 acreage is estimated to be 40% of the U.S. soybean acres, and would represent approximately 30 million dicamba-treated soybean acres. Considering the acreage currently treated with dicamba (20.2 million acres of which 0.53 million acres area soybean), this would potentially result in a total of 50.2 million acres treated with dicamba. As presented previously, dicamba was used on approximately 36 million acres at its peak use in 1994. Furthermore, considering the anticipated weed control recommendations for dicamba use in MON 87708, as outlined in Section VIII.H, combined with current dicamba usage in other crops (2.7 million pounds), a total of 25 million pounds a.e. of dicamba is estimated (high-

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end) to be applied annually, compared to 9.4 million pounds a.e. of dicamba applied at its peak use in 1994.

VIII.H.3. Conclusions on Dicamba-Tolerant Soybean MON 87708

Upon integration of MON 87708 into the Roundup Ready soybean system, growers will have the ability to continue use of established soybean production practices including tillage systems; the same planting and harvesting machinery; traditional management of insects, diseases, and other pests; and many of the current herbicides used for weed control, including glyphosate with its established environmental benefits. Similarly, certified seed production will continue to use well-established industry practices to deliver high quality seed to growers. Due to the excellent crop safety of MON 87708 to dicamba, growers will have a new herbicide mode-of-action for in-crop control of hard-to-control and herbicide resistant broadleaf weeds that are present in U.S. soybean production. As expected with a new use of herbicide in U.S. soybean production, the number of dicamba-treated soybean acres and the total dicamba use will increase. The total dicamba use is expected to be about double the historical peak levels experienced since dicamba's introduction in 1967. Additionally, due to the expanded timing of in-crop applications to soybean, dicamba treatments may be later in the growing season than currently occurs for most labeled dicamba uses, including applications to corn. Monsanto has requested EPA approval for the use of a low volatility dicamba (DGA salt) formulation, together with allowing only ground application on MON 87708, subject to certain limitations specified on the label. With these additional limitations, the potential for offsite movement (spray drift and volatility) onto adjacent crops due to applications on MON 87708 later in the season is not expected to significantly impact adjacent crops. In addition, Monsanto will consult with U.S. EPA to identify what additional measures, if any, are appropriate to address any potential impact of dicamba offsite movement. In addition, to reinforce anticipated EPA label requirements, Monsanto will implement a robust stewardship program that will include a strong emphasis on grower and applicator training.

VIII.I. Crop Rotation Practices in Soybean

The well-established farming practice of crop rotation is still a key management tool for growers. The purpose of growing soybean in rotation is to improve yield and profitability of one or both crops over time, decrease the need for nitrogen fertilizer on the crop following soybean, increase residue cover, mitigate or break disease, insect, and weed cycles, reduce soil erosion, increase soil organic matter, improve soil tilth and soil physical properties, and reduce runoff of nutrients, herbicides, and insecticides (Boerma and Specht, 2004; Al-Kaisi et al., 2003). According to USDA Economic Research Service, 95% of the soybean-planted acreage has been in some form of a crop rotation system since 1991 (USDA-ERS, 2001). Corn- and wheat-planted acreage has been rotated at a slightly lower level of 75% and 70%, respectively. Although the benefits of crop rotations can be substantial, the grower must make cropping decisions by evaluating both the agronomic and economic returns of various cropping systems. Crop rotations also afford growers the opportunity to diversify farm production in order to minimize market risks.

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Continuous soybean production is not a common practice in the Midwest and is discouraged by most extension soybean specialists to reduce the risk of damage from diseases and nematodes (Hoeft et al., 2000; Al-Kaisi et al., 2003). Corn and soybean occupy more than 80% of the farmland in many of the Midwestern states, and the two-year cropping sequence of soybean-corn is used most extensively in this region. However, a soybean crop sometimes is grown after soybean and then rotated to corn in a 3-year rotation sequence (soybean-soybean-corn) in the Midwest. Compared to corn, soybean shows a greater yield response to being grown after a number of years without soybean. The yield of both corn and soybean is approximately 10% higher when grown in rotation than when either crop is grown continuously (Hoeft et al., 2000).

A combination of conservation tillage practices and crop rotation has been shown to be very effective in improving soil physical properties. Long-term studies in the Midwest indicate that the corn-soybean rotation improves yield potential of no-till systems compared to continuous corn production (Al-Kaisi, 2001). The reduction in yield of continuous corn production in no-till systems is attributed to low soil temperature during seed germination, which is evident on poorly drained soils under no-till practices.

Unique to the southern portion of the Midwest and the Southeast regions, soybean is grown in a double-cropping system. Double-cropping refers to the practice of growing two crops in one year. This practice can improve income and reduce soil and water losses by having the soil covered with a plant canopy most of the year (Hoeft et al., 2000). In the Midwest, winter wheat is harvested in late June or July, and then soybean is planted into the wheat residue in a no-till system to conserve moisture. Due to the uncertainty of double-cropping yields, growers sometimes do not plant if soils are too dry at the time of wheat harvest. Soybean typically is grown in a corn-wheat-soybean rotation sequence when soybean is grown in a double-cropping system.

Rotation practices for soybean vary from state to state. However, there are similarities among states within certain growing regions. This section provides a detailed description and quantitative assessment of the rotational cropping practices immediately following soybean production, by region and state. This assessment accounts for about 99% of total U.S. soybean acreage. This assessment is based on current agronomic practices following soybean production and current dicamba herbicide usage in labeled crops. USDA-NASS (2004, 2006, 2007b, 2008) and AgroTrak (2009) data on dicamba herbicide usage for corn, sorghum, cotton, wheat, barley, and oats were utilized for this assessment. For the purpose of this assessment, a 50% adoption rate in U.S. soybean production was assumed for MON 87708. These data on rotational patterns are presented in Tables VIII-24 through VIII-27.

The majority of the U.S. soybean acreage (68.6%) is rotated to corn (Table VIII-24). The second largest rotational crop following soybean is soybean. Approximately 14.5% of the soybean acreage is rotated back to soybean the following year. Wheat follows soybean on approximately 11.2% of the U.S. soybean acreage, with cotton, rice, and sorghum the next largest rotational crops. However, these three crops were planted on only 4.6% of the soybean acreage. Other minor rotational crops that follow soybean production are listed in Table VIII-24.

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Column J of each table provides the percentage of soybean acreage as a function of the total rotational crop acreage to indicate the level that soybean is the primary crop preceding the rotational crops. For the entire country (Table VIII-24), this percentage is 35.3% indicating that soybean is a major crop preceding these rotational crops. The percentage of soybean as a preceding crop varies widely in different states, which ranges from 16.8% (KS, Table VIII-25) to 95.2% (NJ, Table VIII-27). In the Midwest region where 82% of the soybean is grown, 34.6% of the rotational crop area was planted with soybean during the previous growing season.

Dicamba-tolerant soybean can be followed by dicamba-tolerant soybean or another rotational crop with a labeled application of dicamba. To determine the likelihood that the rotational crops planted after MON 87708 will be a rotational crop where dicamba application is possible, an assessment also has been provided in Column K of Tables VIII-24 through VIII-27. This assessment showed that the percentage of the total rotational crop acreage that may be rotated from MON 87708 to another crop with a potential for dicamba application (Table VIII-24 - Column K) is estimated to be 4.9% in the U.S., with ranges from32.3% in Mississippi to Georgia and New Jersey having essentially no rotational crop acres with dicamba usage since these states have essentially no continuous soybean acres and USDA-NASS and AgroTrak statistics show no use of dicamba currently in labeled crops in these states. The percentage is 4.1% in the Midwest region, which is the largest soybean production region.

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Table VIII-24. Rotational Practices in the U.S. Following Soybean Production

A	B	C	D	E	F	G	H	I	J	K
State	Total Soybean Acres[1]	Major Crops Following Soybean in Rotation	Total Acreage of Rotational Crop in the U.S.[1]	Rotational Crop Acres Following Soybean[2]	% Rotational Crop Following Soybean[3]	% Rotational Crop of Total Soybean[4]	Acreage of Dicamba in Rotational Crop Option[5]	% Dicamba Usage in Rotational Crop Option[6]	% Soybean Acres Preceding Major Rotations[7]	Estimated % Dicamba Usage in Major Rotations[8]
United States	**75037**	Corn	80130	51500	64.3	68.6	4431	8.6%		
		Soybean	75037	10866	14.5	14.5	5438	40.0%		
		Sorghum	4020	841	20.9	1.1				
		Cotton	3767	1570	41.7	2.1	153	9.7%		
		Wheat	37414	8396	22.4	11.2	448	5.3%		
		Barley	2159	41	1.9	0.05				
		Oats	1995	98	4.9	0.1				
		Rice	2301	1042	45.3	1.4				
		Alfalfa	1864	162	8.7	0.2				
		Sugar Beets	830	144	17.3	0.19				
		Potatoes	334	32	9.6	0.04				
		Dry Beans	1183	35	3.0	0.05				
		Dry Peas	520	38	7.3	0.05				
		Millet	250	41	16.4	0.05				
		Flax	345	76	22.0	0.10				
		Other[9]	452	155	34.3	0.2				
			Total: 212601	**Total: 75037**			**Total: 10470**		**35.3**	**4.9**

This U.S. summary was developed by compiling the data from all three regional summaries. All acreage is expressed as 1000s of acres.

[1] Acreage planted of the specific crops is based on 2008 planting data (USDA-NASS, 2009a); "other" crop and newly seeded alfalfa acreages are based on 2008 planting data from the Individual States data which was obtained from Quick Stat searches on http://www.nass.usda.gov/Data_and_Statistics/Quick_Stats/index.asp.

[2] Column E is obtained by compiling the data from all three regional summaries.

[3] Column F is obtained by dividing Column E by Column D.

[4] Column G is obtained by dividing Column E by Column B.

[5] Column H is obtained by compiling the data from all three regional summaries.

[6] Column I is obtained by dividing Column H by Column E.[7] Column J is obtained by dividing Column B by Column D Total.

[8] Column K is obtained by dividing Column H Total by Column D Total.

[9] Various vegetables.

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Table VIII-25. Rotational Practices Following Soybean Production in the Midwest Region

A	B	C	D	E	F	G	H	I	J	K
State	**Total Soybean Acres[1]**	**Major Crops Following Soybean in Rotation**	**Total Acreage of Rotational Crop in States[1]**	**Rotational Crop Acres Following Soybean[2]**	**% Rotational Crop Following Soybean[3]**	**% Rotational Crop of Total Soybean[4]**	**Acreage of Dicamba in Rotational Crop Option[5]**	**% Dicamba Usage in Rotational Crop Option[6]**	**% Soybean Acres Preceding Major Rotations[7]**	**Estimated % Dicamba Usage in Major Rotations[8]**
Region	**62150**	Corn	72260	47480	65.7	76.4	4591	9.7		
		Soybean	62150	4885	7.9	7.9	1954	40		
		Sorghum	3553	670	18.8	1.1	313	46.8		
		Cotton	341	78	22.9	0.1	14	18		
		Wheat	32039	8102	25.3	13.0	448	5.5		
		Barley	1929	41	2.1	0.07	6	15		
		Oats	1590	98	6.2	0.2		*		
		Rice	200	182	91.0	0.3		NA		
		Alfalfa[9]	1617	162	10.0	0.3		NA		
		Sugar Beets	830	144	17.3	0.2		NA		
		Potatoes	278	32	11.6	0.05		NA		
		Dry Beans	1166	35	3.0	0.06		NA		
		Dry Peas	520	38	7.3	0.06		NA		
		Millet	250	41	16.4	0.07		*		
		Flax	345	76	22.0	0.1		NA		
		Other[10]	342	87	25.3	0.1		NA		
			Total: 179410	**Total: 62150**			**Total: 7326**		**34.6**	**4.1**
IL	**9200**	Corn	12100	8556	71	93.0	1711	20		
		Soybean	9200	230	3	2.5	92	40		
		Sorghum	80	74	92	0.8	265	4[6]		
		Wheat	1200	340	28	3.7		*		
			Total: 22580	**Total: 9200**			**Total: 2068**		**40.7**	**9.2**
IN	**5450**	Corn	5700	4905	86	90	343	7		
		Soybean	5450	273	5	5	109	40		
		Wheat	580	273	47	5		*		
			Total: 11730	**Total: 5450**			**Total: 453**		**46.5**	**3.9**

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Table VIII-25 (continued). Rotational Practices Following Soybean Production in the Midwest Region

A	B	C	D	E	F	G	H	I	J	K
State	**Total Soybean Acres[1]**	**Major Crops Following Soybean in Rotation**	**Total Acreage of Rotational Crop in States[1]**	**Rotational Crop Acres Following Soybean[2]**	**% Rotational Crop Following Soybean[3]**	**% Rotational Crop of Total Soybean[4]**	**Acreage of Dicamba in Rotational Crop Option[5]**	**% Dicamba Usage in Rotational Crop Option[6]**	**% Soybean Acres Preceding Major Rotations[7]**	**Estimated % Dicamba Usage in Major Rotations[8]**
IA	**9750**	Corn	13300	9458	71	97	378	4		
		Soybean	9750	195	2	2	78	40		
		Alfalfa[9]	125	98	78	1		NA		
			Total: 23175	**Total: 9750**			**Total: 456**		**42.1**	**2.0**
KS	**3300**	Corn	3850	1650	43	50	297	18		
		Soybean	3300	330	10	10	132	40		
		Sorghum	2900	165	6	5	13	8		
		Wheat	9600	1155	12	35	58	5		
			Total: 19650	**Total: 3300**			**Total: 500**		**16.8**	**2.5**
KY	**1390**	Corn	1210	1182	98	85	106	9		
		Soybean	1390	139	10	10	56	40		
		Wheat	580	70	12	5		*		
			Total: 3180	**Total: 1390**			**Total: 162**		**43.7**	**5.1**
MI	**1900**	Corn	2400	1330	55	70	160	12		
		Soybean	1900	95	5	5	38	40		
		Wheat	730	475	65	25	5	1[6]		
			Total: 5030	**Total: 1900**			**Total: 202**		**37.8**	**4.0**
MN	**7050**	Corn	7700	5358	70	76	697	13		
		Soybean	7050	212	3	3	85	40		
		Wheat	1925	1269	66	18	14	1[6]		
		Sugar beets	440	106	24	1.5		NA		
		Dry Beans	150	35	24	0.5		NA		
		Other[11]	203	71	35	1		NA		
			Total: 17468	**Total: 7050**			**Total: 796**		**40.4**	**4.6**

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Table VIII-25 (continued). Rotational Practices Following Soybean Production in the Midwest Region

A	B	C	D	E	F	G	H	I	J	K
State	Total Soybean Acres[1]	Major Crops Following Soybean in Rotation	Total Acreage of Rotational Crop in States[1]	Rotational Crop Acres Following Soybean[2]	% Rotational Crop Following Soybean[3]	% Rotational Crop of Total Soybean[4]	Acreage of Dicamba in Rotational Crop Option[5]	% Dicamba Usage in Rotational Crop Option[6]	% Soybean Acres Preceding Major Rotations[7]	Estimated % Dicamba Usage in Major Rotations[8]
MO	**5200**	Corn	2800	2756	98	53	201	7[6]		
		Soybean	5200	1560	30	30	624	40		
		Sorghum	90	104	116	2		*		
		Cotton	306	78	25	1.5	14	18		
		Wheat	1250	520	42	10		*		
		Rice	200	182	91	3.5		NA		
			Total: 9846	**Total: 5200**			**Total: 839**		**52.8**	**8.5**
NE	**4900**	Corn	8800	3675	42	75	147	4		
		Soybean	4900	490	10	10	196	40		
		Sorghum	300	245	82	5	22	9		
		Wheat	1750	490	28	10	15	3		
			Total: 15750	**Total: 4900**			**Total: 380**		**31.1**	**2.4**
ND	**3800**	Corn	2550	1140	45	30	331	29		
		Soybean	3800	798	21	21	319	50		
		Wheat	9230	1710	19	45	274	16		
		Sugar Beets	208	38	18	1		NA		
		Dry Peas	520	38	7	1		NA		
		Flax	335	76	23	2		NA		
			Total: 16643	**Total: 3800**			**Total: 923**		**22.8**	**5.6**
OH	**4500**	Corn	3300	3150	95	70	32	1		
		Soybean	4500	450	10	10	180	40		
		Wheat	1120	900	80	20	18	2[5]		
			Total: 8920	**Total: 4500**			**Total: 230**		**50.4**	**2.6**

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Table VIII-25 (continued). Rotational Practices Following Soybean Production in the Midwest Region

A	B	C	D	E	F	G	H	I	J	K
State	Total Soybean Acres[1]	Major Crops Following Soybean in Rotation	Total Acreage of Rotational Crop in States[1]	Rotational Crop Acres Following Soybean[2]	% Rotational Crop Following Soybean[3]	% Rotational Crop of Total Soybean[4]	Acreage of Dicamba in Rotational Crop Option[5]	% Dicamba Usage in Rotational Crop Option[6]	% Soybean Acres Preceding Major Rotations[7]	Estimated % Dicamba Usage in Major Rotations[8]
SD	**4100**	Corn	4750	2952	62	72	148	5		
		Soybean	4100	82	2	2	33	40		
		Sorghum	170	82	48	2	13	16		
		Wheat	3661	820	22	20	66	8		
		Barley	63	41	65	1	6	15		
		Oats	220	82	37	2		*		
		Millet	110	41	37	1		*		
			Total: 13074	**Total: 4100**			**Total: 266**		**31.4**	**2.0**
WI	**1610**	Corn	3800	1369	36	85	41	3		
		Soybean	1610	32	2	2	13	40		
		Wheat	373	81	22	5		*		
		Oats	270	16	6	1		*		
		Alfalfa[9]	420	64	15	4		NA		
		Potatoes	63.5	32	51	2		NA		
		Other[12]	139.2	16	12	1		NA		
			Total: 6676	**Total: 1610**			**Total: 54**		**24.1**	**0.8**

This Midwest region summary table was developed by compiling the data from all the states within the region except where noted in footnotes. NA denotes Not Applicable. An asterisk (*) indicates no usage reported. All acreage are expressed as 1000s of acres.

[1] Acreage planted of the specific crops is based on 2008 planting data (USDA-NASS, 2009a); "other" crop and newly seeded alfalfa acreages are based on 2008 planting data from the Individual States data which were obtained from Quick Stat searches on http://www.nass.usda.gov/Data_and_Statistics/Quick_Stats/index.asp. [2] Column E for the regional summary is obtained by compiling data from all the states within the region. Column E for the individual states is obtained by multiplying Column B by Column G.

[3] Column F is obtained by dividing Column E by Column D.

[4] Column G for the regional summary is obtained by dividing Column E by Column B. The rotational crop percentages in Column G for the individual states are based on estimates from personal communications (2006) with individual state Extension Crop Production Specialist; Extension Agronomists – Soybean, Corn and Cotton; Extension Weed Control Specialist on Soybean and Corn; and/or Monsanto Technology Development Representatives.

[5] Column H for the regional summary is obtained by compiling the data from all the states within the region. Column H for the individual states is obtained by multiplying Column E by Column I.

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[6] Column I for the regional summary is obtained by dividing Column H by Column E. Dicamba usage except for individual states for soybean is based on most recent statistics from USDA-NASS (2004 -sorghum, 2006 - corn and oats, 2007b - wheat and barley, 2008 -cotton). Percentages with the superscript 6 are usage statistics from AgroTrak (2009), due to USDA-NASS data not being reported for the particular crop and state. Dicamba usage in soybean (40%) is a future market adoption estimate.[7] Column J is obtained by dividing Column B by Column D Total.

[8] Column K is obtained by dividing Column H Total by Column D Total.

[9] Newly seeded alfalfa.

[10] Various vegetables.

[11] Sweet corn and green peas.

[12] Sweet corn, green peas and onions.

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Table VIII-26. Rotational Practices Following Soybean Production in the Southeast Region

A	B	C	D	F	E	G	H	I	J	K
State	**Total Soybean Acres[1]**	**Major Crops Following Soybean in Rotation**	**Total Acreage of Rotational Crop in States[1]**	**Rotational Crop Acres Following Soybean[2]**	**% Rotational Crop of Total Soybean[3]**	**% Rotational Crop Following Soybean[4]**	**Acreage of Dicamba in Rotational Crop Option[5]**	**% Dicamba Usage in Rotational Crop Option[6]**	**% Soybean Acres Preceding Major Rotations[7]**	**Estimated % Dicamba Usage in Major Rotations[8]**
Region	**10860**	Corn	3535	2284	21.0	64.6	72	3.2		
		Soybean	10430	5748	52.9	55.1	2299	40		
		Sorghum	245	171	1.6	69.8		*		
		Cotton	2380	1469	13.5	61.7	139	9.4		
		Wheat	1530	294	2.7	19.2		*		
		Rice	1631	860	7.9	52.7		NA		
		Other*	65	34	0.3	52.0				
			Total: 19816	**Total:10860**			**Total: 2510**		**54.8**	**12.7**
AL	**360**	Corn	260	126	35	48	26	21[6]		
		Soybean	360	18	5	5	7	40		
		Cotton	290	180	50	62	13	7		
		Wheat	240	36	10	15		*		
			Total: 1150	**Total: 360**			**Total: 46**		**31.3**	**4.0**
AR	**3300**	Corn	440	231	7	53		*		
		Soybean	3300	2112	64	64	845	40		
		Sorghum	125	66	2	53		*		
		Wheat	1070	231	7	22		*		
		Rice	1401	660	20	47		NA		
			Total: 6336	**Total: 3300**			**Total: 845**		**52.1**	**13.3**
GA	**430**	Corn	370	43	10	12	2	5[6]		
		Cotton	940	387	90	41		*		
			Total: 1310	**Total: 430**			**Total: 2**		**32.8**	**0.2**
LA	**1050**	Corn	520	105	10	20	3	3[6]		
		Soybean	1050	683	65	65	273	40		
		Sorghum	120	105	10	88		*		
		Cotton	300	158	15	53		*		
			Total: 1990	**Total: 1050**			**Total: 276**		**52.8**	**13.9**

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Table VIII-26 (continued). Rotational Practices Following Soybean Production in the Southeast Region

A	B	C	D	E	F	G	H	I	J	K
State	Total Soybean Acres[1]	Major Crops Following Soybean in Rotation	Total Acreage of Rotational Crop in States[1]	Rotational Crop Acres Following Soybean[2]	% Rotational Crop of Total Soybean[3]	% Rotational Crop Following Soybean[4]	Acreage of Dicamba in Rotational Crop Option[5]	% Dicamba Usage in Rotational Crop Option[6]	% Soybean Acres Preceding Major Rotations[7]	Estimated % Dicamba Usage in Major Rotations[8]
MS	**2000**	Soybean	2000	1800	90	90	720	40		
		Rice	230	200	10	87		NA		
			Total: 2230	**Total: 2000**			**Total: 720**		**89.7**	**32.3**
NC	**1690**	Corn	900	811	48	90	36	4[6]		
		Soybean	1690	423	25	25	169	40		
		Cotton	430	423	25	98		*		
		Other[9]	65	34	2	52		NA		
			Total: 3085	**Total: 1690**			**Total: 205**		**54.8**	**6.7**
TN	**1490**	Corn	690	671	45	97	5	1[6]		
		Soybean	1490	551	37	37	220	40		
		Cotton	285	268	18	94	126	47		
			Total: 2465	**Total: 1490**			**Total: 351**		**60.4**	**14.2**
SC	**540**	Corn	355	297	55	84		*		
		Soybean	540	162	30	30	65	40		
		Cotton	135	54	10	40		*		
		Wheat	220	27	5	12		*		
			Total: 1250	**Total: 540**			**Total: 65**		**43.2**	**5.2**

This Mid-South region summary table was developed by compiling the data from all the states within the region except where noted otherwise in footnotes. NA denotes not applicable. An asterisk (*) indicates no usage reported. All acreage are expressed as 1000s of acres.

[1] Acreage planted of the specific crops is based on 2008 planting data (USDA-NASS, 2009a); "other" crop and newly seeded alfalfa acreages are based on 2008 planting data from the Individual States data which were obtained from Quick Stat searches on http://www.nass.usda.gov/Data_and_Statistics/Quick_Stats/index.asp. [2] Column E for the regional summary is obtained by compiling data from all the states within the region. Column E for individual states is obtained by multiplying Column B by Column G.

[3] Column F is obtained by dividing Column E by Column D.

[4] Column G for the regional summary is obtained by dividing Column E by Column B. The rotational crop percentages in Column G for the individual states are based on estimates from personal communications (2006) with individual state Extension Crop Production Specialist; Extension Agronomists – Soybean, Corn and Cotton; Extension Weed Control Specialist on Soybean and Corn ;and/or Monsanto Technology Development Representatives.

[5] Column H for the regional summary is obtained by compiling the data from all the states within the region. Column H for individual states is obtained by multiplying Column E by Column I.

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[6] Column I for the regional summary is obtained by dividing Column H by Column E. Dicamba usage except for individual sites for soybean is based on most recent statistics from USDA-NASS (2004 - sorghum, 2006 - corn and oats, 2007b - wheat and barley, 2008 - cotton). Percentages with the superscript 5 are usage statistics from AgroTrak (2009) because USDA-NASS data was not reported for the particular crop and state. Dicamba usage in soybean (40%) is a future market adoption estimate. [7] Column J is obtained by dividing Column B by Column D Total.

[8] Column K is obtained by dividing Column H Total by Column D Total.

[9] Cucumbers and sweet potatoes.

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Table VIII-27. Rotational Practices Following Soybean Production in the East Coastal Region

A	B	C	D	E	F	G	H	I	J	K
State	Total Soybean Acres[1]	Major Crops Following Soybean In Rotation	Total Acreage of Rotational Crop in States[1]	Rotational Crop Acres Following Soybean[2]	% Rotational Crop Following Soybean[3]	% Rotational Crop of Total Soybean[4]	Acreage of Dicamba in Rotational Crop Option[5]	% Dicamba Usage in Rotational Crop Option[6]	% Soybean Acres Preceding Major Rotations[7]	Estimated % Dicamba Usage in Major Rotations[8]
Region	**4687**	Corn	3615	1741	48.2	85.9	390	22.4		
		Soybean	1705	242	14.2	11.9	97	40		
		Cotton	61	23	38.0	1.1		*		
		Other[9]	45	21	45.9	1.0		NA		
			Total: 5426	**Total: 2027**			**Total: 487**		**37.4**	**9.0**
DE	**195**	Corn	160	156	98	80		*		
		Soybean	195	39	20	20	16	40		
			Total: 355	**Total: 195**			**Total: 16**		**54.9**	**4.5**
MD	**495**	Corn	460	446	97	90	258	58[6]		
		Soybean	495	50	10	10	20	40		
			Total: 955	**Total: 495**			**Total: 278**		**51.8**	**29.1**
NJ	**92**	Corn	85	83	97	90		*		
		Other[9]	11.6	9	79	10		NA		
			Total: 97	**Total: 92**			**Total: 0**		**95.2**	**0**
NY	**230**	Corn	1090	219	20	95	11	5		
		Other[10]	33.5	12	34	5		*		
			Total: 1124	**Total: 230**			**Total: 11**		**20.5**	**1.0**
PA	**435**	Corn	1350	426	32	98	30	7		
		Soybean	435	9	2	2	4	40		
			Total: 1785	**Total: 435**			**Total: 34**		**24.4**	**1.9**
VA	**580**	Corn	470	412	88	71	91	22[6]		
		Soybean	580	145	25	25	58	40		
		Cotton	61	23	38	4		*		
			Total: 1111	**Total: 580**			**Total: 149**		**52.2**	**13.4**

This Eastern Coastal region summary table was developed by compiling the data from all the states within the region except where noted in footnotes. NA denotes not applicable. An asterisk (*) indicates no usage reported. All acreage are expressed as 1000s of acres.

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[1] Acreage planted of the specific crops is based on 2008 planting data (USDA-NASS, 2009a); "other" crop and newly seeded alfalfa acreages are based on 2008 planting data from the Individual States data which were obtained from Quick Stat searches on http://www.nass.usda.gov/Data_and_Statistics/Quick_Stats/index.asp.

[2] Column E for the regional summary obtained by compiling data from all of the states within the region. Column E for individual states is obtained by multiplying Column B by Column G.

[3] Column F is obtained by dividing Column E by Column D.

[4] Column G for the regional summary is obtained by dividing Column E by Column B. The rotational crop percentages in Column G for the individual states are based on estimates from personal communications (2006) with individual state Extension Crop Production Specialist; Extension Agronomists – Soybean, Corn and Cotton; Extension Weed Control Specialist on Soybean and Corn; and/or Monsanto Technology Development Representatives.[5] Column H for the regional summary is obtained by compiling the data from all the states within the region. Column H for the individual states is obtained by multiplying Column E by Column I.

[6] Column I for the regional summary is obtained by dividing Column H by Column E. Dicamba usage except for individual states for soybean is based on most recent statistics from USDA-NASS (2004 -sorghum, 2006 -corn and oats, 2007b -wheat and barley, 2008 -cotton). Percentages with the superscript 6 are usage statistics from AgroTrak (2009) because USDA-NASS data was not reported for the particular crop and state. Dicamba usage in soybean (40%) is a future market adoption estimate.

[7] Column J is obtained by dividing Column B by Column D Total.

[8] Column K is obtained by dividing Column H Total by Column D Total.

[9] Sweet corn and other vegetables.

[10] Sweet corn and onions.

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VIII.J. Soybean Volunteer Management

Volunteer soybean is defined as a plant that has germinated and emerged unintentionally in a subsequent crop. Soybean seeds can remain in a field after soybean harvest as a result of pods splitting before or during harvest. Soybean seeds also can remain in a field when pod placement on the plants is too close to the ground for the combine head to collect all the pods or when the combine is improperly adjusted for efficient harvesting. Volunteer soybean in rotational crops is not a concern in the Midwest region because the soybean seed is typically not viable after the winter period (Carpenter et al., 2002; OECD, 2000). In southern soybean growing areas of the U.S. where the winter temperatures are milder, it is possible for soybean seed to remain viable over the winter and germinate the following spring.

Volunteer soybean normally is not a concern in rotational crops, such as corn, cotton, rice, and small grains (*e.g.*, wheat, barley, sorghum, and oats), that are the significant rotational crops following soybean due to control measures that are available for volunteer soybean when they arise (Carpenter et al., 2002; OECD, 2000). Because of these control measures and field testing which confirmed that MON 87708 has equivalent volunteer potential as other soybean, the introduction of MON 87708 plus Roundup Ready soybean will not elevate concerns about managing volunteer soybeans nor will it result in more dependence on preplant or in-crop tillage and cultivation because there are adequate alternative herbicide options. Preplant tillage and/or herbicides are the first management tool for control of emerging volunteer soybean in the spring, where this may be an issue, such as in the south. If volunteer soybean should emerge after planting, shallow cultivation and/or use of another herbicide will control volunteers and effectively reduce competition with the crop. Several postemergence herbicides also are available to control volunteer soybean (conventional or glyphosate-tolerant soybean, and by extension dicamba-tolerant soybean) in each of the major soybean rotational crops. Table VIII-28 provides control ratings on volunteer soybean for several herbicides used in the major rotational crops. Additionally, 19 commonly used herbicides in agriculture, representing eight modes-of-action (*i.e.*, ALS inhibitor, chloroacetamide, EPSPS, PPO inhibitor, PSI disruption, PSII inhibitor, synthetic auxin, and tubulin inhibitor classes) were tested as potential substrates for the MON 87708 DMO present in MON 87708 (Section V.A). Across nearly all of the herbicides tested, MON 87708 and the conventional control were similar in their level of tolerance, except for the three phenoxy synthetic auxin herbicides (2,4-D, 2,4-DB, and MCPA). These results indicate that herbicides which are effective for the control of volunteer soybean can still be used to control MON 87708.

To provide control of volunteer soybean in corn, postemergence applications of AAtrex® (atrazine), Hornet® (flumetsulam + clopyralid) and Widematch® (clopyralid + fluroxypyr) provide excellent control (Zollinger, 2009). AAtrex and Permit® (halosufuron) provide excellent volunteer control in sorghum. In small grains (wheat, barley, oats), Bronate® Advanced (bromoxynil/MCPA), and Widematch® applied postemergence provide excellent control of volunteer soybean (Zollinger, 2009).

Volunteer soybean in cotton is normally not a concern. However, hurricanes or other extreme weather conditions can damage a soybean crop preceding cotton production in the

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Mid-South region states, where the unharvested soybean seed can produce volunteer plants. Preplant applications of paraquat or herbicide mixtures containing paraquat will effectively control volunteer glyphosate-tolerant soybean (Montgomery et al., 2002; Murdock et al., 2002). Recent research in North Carolina indicates Envoke (trifloxysulfuron) will provide excellent postemergence control of (volunteer) soybean containing traits for glyphosate and sulfonylurea herbicide tolerance in Roundup Ready cotton (York et al., 2005).

Volunteer soybean in rice is rarely a concern due to the combination of preplant tillage, flooding practices, and herbicides used in producing rice. If volunteer plants should emerge in rice, postemergence applications of Grandstand (triclopyr), Regiment (bispyribac), Grasp (penoxsulam), and Permit (halosulfuron) typically used for weed control in rice will effectively alleviate competition from volunteer soybean (Dillon et al., 2006; Bond and Walker, 2009).

Given the low potential for soybean to volunteer in subsequent crops, the availability of multiple herbicidal and cultivation methods for controlling volunteers, as well as the demonstrated lack of difference in germination of MON 87708 compared to conventional soybean (see Section VII.C.1), the introduction of MON 87708 into the Roundup Ready soybean system is not expected to impact the management of soybean volunteer plants.

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Table VIII-28. Ratings for Postemergence Control of Volunteer Soybean in Labeled Rotational Crops[1]

Product	Rate (Product/Acre)	Soybean V2 – V3	Soybean V4- V6
Corn[2]			
AAtrex 4L (atrazine)	0.38 qts	E	P
	0.50 qts	E	F
Hornet WDG (flumetsulam/clopyralid)	1 – 2 oz	E	F-G
Widematch (clopyralid/fluroxypyr)	0.25 pt	E	G
Sorghum[2,4]			
AAtrex 4L (atrazine)	0.38 qts	E	P
	0.50 qts	E	F
Permit (halosulfuron)	2/3 oz	E	E
Buctril® (bromoxynil)	1 pt		
Wheat, Barley & Oats[2]			
Buctril (bromoxynil)	1 pt	E	E
Widematch (clopyralid/fluroxypyr)	0.25 pt	E	G
Cotton[3]			
Envoke® (trifloxysulfuron)	0.1 oz	E	E
Rice[4]			
Grandstand® CA (triclopyr)	0.5 pint	E	E
Regiment® (bispyribac)	0.4 oz	E	E
Grasp® SC (penoxsulam)	2 oz	E	E
Permit (halosulfuron)	2/3 oz	E	E

NA denotes "not applicable."

[1] Weed control ratings: E = Excellent (90 to 99% control), G = Good (80 to 90% control), F = Fair (65 to 80 control), and P = Poor (40 to 65% control).

[2] Source is Zollinger (2009).

[3] Source is York et al. (2005).

[4] Sources are Dillon et al. (2006); Bond and Walker (2009).

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VIII.K. Weed Resistance to Dicamba Herbicide

The risk of weeds developing resistance and the potential impact of resistance on the usefulness of an herbicide vary greatly across different herbicide modes-of-action and is dependent on a combination of different factors. Monsanto considers product stewardship to be a fundamental component of customer service and business practices, and invests considerably in research to understand the proper uses and stewardship of our herbicide-tolerant soybean systems. This research includes an evaluation of the factors that can contribute to the development of weed resistance. Detailed information regarding dicamba stewardship is presented in Appendix K.

VIII.L. Stewardship of MON 87708

Monsanto Company develops effective products and technologies and is committed to assuring that its products and technologies are safe and environmentally responsible. Monsanto demonstrates this commitment by implementing product stewardship processes throughout the lifecycle of a product and by participation in the Excellence Through Stewardship$^{\text{SM}}$ (ETS) Program[8]. These policies and practices include rigorous field compliance and quality management systems and verification through auditing. Monsanto's Stewardship Principles are also articulated in Technology Use Guides[9] that are distributed annually to growers who utilize Monsanto branded traits. Growers who purchase seeds containing Monsanto's proprietary biotechnology traits are contractually required to comply with stewardship measures outlined in the Technology Use Guide.

As an integral action of fulfilling our stewardship commitment, Monsanto will seek biotechnology regulatory approvals for MON 87708 in all key soybean import countries with a functioning regulatory system to assure global compliance and support the flow of international trade. These actions will be consistent with the Biotechnology Industry Organization (BIO) Policy on Product Launch.[10] Monsanto continues to monitor other countries that are key importers of soybean from the U.S. for the development of formal biotechnology approval processes. If new functioning regulatory processes are developed, Monsanto will make appropriate and timely regulatory submissions.

Monsanto also commits to best industry practices on seed quality assurance and control to ensure the purity and integrity of MON 87708 seed. As with all of Monsanto's products, before commercializing MON 87708 in any country, a MON 87708 detection method will be made available to soybean producers, processors, and buyers.

Dicamba is a selective herbicide registered with the U.S. EPA for the preemergent and postemergent control of certain broadleaf weeds in agriculture. Dicamba has a long

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[8] Excellence Through Stewardship Program can be found at: http://www.excellencethroughstewardship.org/.

[9] Monsanto Technology Use Guides can be found at:http://www.monsanto.com/SiteCollectionDocuments/Technology-Use-Guide.pdf.

[10] BIO's Product Launch guidelines can be found at: http://www.excellencethroughstewardship.org/LinkClick.aspx?fileticket=ppgyTABguQs%3d&tabid=84.

history of effective use in U.S. crop production, including corn, soybean, cotton, sorghum, wheat, barley, oats, millet, pasture, rangeland, asparagus, sugarcane, turf, grass grown for seed, conservation reserve programs, and fallow croplands (as described in Section VIII.G). Although herbicide resistance may eventually occur in a weed species when an herbicide is widely used, research, education and best management practices can be utilized to potentially delay, contain and manage resistance. The addition of dicamba tolerance to the Roundup Ready soybean system will provide an efficient method for incorporation of an additional herbicide mode-of-action in the system, and reduce the potential for further resistance development to glyphosate and dicamba as well as other critical soybean herbicides. Current research conducted by Monsanto to define the optimum weed management systems indicate the following: 1) in the absence of glyphosate resistant populations, the recommendation will be to apply a soil active preemergence residual herbicide followed by an in-crop postemergence application of glyphosate plus dicamba to control weed escapes, and 2) in the presence of glyphosate resistant populations, the same system will be recommended with a potential second application of glyphosate plus dicamba if needed. In this latter case, the preemergence herbicide to be recommended will be one with activity against the targeted glyphosate resistant species. This will ensure more than one mode of action against the targeted species. These management systems will reduce the potential for further resistance development to glyphosate, dicamba and other critical soybean herbicides. In conservation tillage systems, a preplant application of glyphosate plus dicamba may be recommended in some situations in addition to the in-crop applications described above. This is not expected to increase selection pressure on either product since the preplant weed spectrum is generally different from the in-crop spectrum.

Stewardship of dicamba to preserve its usefulness for growers is an important aspect of Monsanto's stewardship commitment, as is discussed in Appendix K. Specifically, Monsanto will develop weed resistance management practices, and utilize multiple methods to distribute technical and stewardship information to growers, academics and grower advisors through a variety of communication tools. Monsanto's Technology Use Guide (TUG) will set forth the requirements and best practices for the cultivation of MON 87708 including recommendations on weed resistance management practices. Growers purchasing products containing dicamba tolerance will be obligated to follow all practices outlined in the TUG as required in the Monsanto Technology Stewardship Agreement (MTSA). Furthermore, Monsanto is committed to actively evaluate herbicide performance and weed efficacy on a continuing basis, and develop additional mitigation plans as necessary to manage resistance development for glyphosate and dicamba. Dicamba tolerance integrated into the Roundup Ready soybean system will enable expanded use of dicamba herbicide in soybean production when and in the manner appropriate. Monsanto is seeking regulatory approvals with the U.S. EPA for the expanded application of dicamba herbicide, as a weed control tool, as well as establishing appropriate dicamba Maximum Residue Levels (MRLs) for key soybean import countries, including the EU, Canada, and Japan, and CODEX, to support importing countries that do not have an established regulatory system to set MRLs including China.

As with all U.S. EPA registered herbicides for agricultural use, it is possible that offsite movement during and/or following application can occur such that non-target plants may

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be exposed to direct spray or to spray drift. Research has demonstrated that herbicide formulation, application equipment and application procedures can be optimized to significantly reduce spray drift potential in most circumstances (Jordan et al, 2009; STDF, 1997).

Monsanto is addressing such issues in its application to U.S. EPA to amend Registration Number 524-582. Specifically, Monsanto seeks approval of a low volatility dicamba (DGA salt) formulation that will only be applied to MON 87708 using ground application equipment. In addition, Monsanto will consult with U.S. EPA to identify what additional measures, if any, are necessary to address any potential impact of dicamba offsite movement. To reinforce EPA's label requirements, Monsanto will implement a robust stewardship program that will include a strong emphasis on grower and applicator training. Such training will, for example, teach growers and applicators that dicamba herbicide spray drift can be further reduced during ground application by using industry standard procedures for minimizing spray drift, e.g. making applications with coarse droplet size through appropriate nozzle selection, using lower spray pressure, applying at the lowest nozzle height that provides uniform coverage, and making applications when wind speeds are low and consistent in direction (SDTF, 1997).

VIII.M. Impact of the Introduction of MON 87708 on Agricultural Practices

Introduction of MON 87708 is expected to have no impact on current cultivation and management practices for soybean, with the exception of expanded dicamba application timings. Monsanto recommends the use of preemergent soil residual herbicides as part of our current weed control programs for soybean. Dicamba has been used in corn, soybean and small grain cropping systems since 1967. MON 87708 with its excellent crop tolerance to dicamba allows preemergence applications through crop emergence (cracking) and in-crop postemergence applications through the R1/R2 growth stage. MON 87708 will be combined with MON 89788 (Roundup Ready 2 Yield) utilizing traditional breeding techniques. Soybean containing both MON 87708 and MON 89788 will allow the use of glyphosate and dicamba herbicides in an integrated weed management program to control a broad spectrum of grasses and broadleaf weed species, and sustain and compliment the benefits and value of the glyphosate use in the Roundup Ready soybean system. The addition of another herbicide with a different mode-of-action for preemergence and in-crop postemergence control of broadleaf weeds in soybean that is compatible with glyphosate will help to preserve the growth in conservation tillage acres associated with Roundup Ready cropping systems. For an overview of the cumulative impacts on agricultural practices (weed control, tillage and crop rotation) from deregulation of MON 87708, see Appendix J.

MON 87708 has been shown to be no different from conventional soybean in its agronomic, phenotypic, and compositional characteristics (refer to Sections VI, VII, and VIII), and has the same levels of susceptibility to insects and diseases as commercial soybean. Like other herbicide-tolerant soybean, such as Roundup Ready and Roundup Ready 2 Yield that have been cultivated and consumed in the U.S. since 1996, dicamba-tolerant soybean MON 87708 will improve the current agricultural practices for U.S. soybean growers by providing another preemergence and in-crop postemergence

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herbicide mode-of-action for the control of hard-to-control and herbicide resistant broadleaf weeds, thereby improving the efficiency in the U.S. soybean production system to maximize or maintain soybean yield potential.

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IX. ENVIRONMENTAL CONSEQUENCES

IX.A. Introduction

This section provides a brief review and assessment of the plant pest potential of MON 87708 and its impact on current agronomic practices. USDA-APHIS has responsibility, under the Plant Protection Act (7 U.S.C. § 7701-7772), to prevent the introduction and dissemination of plant pests into the U.S. APHIS regulation 7 CFR § 340.6 provides that an applicant may petition APHIS to evaluate submitted data to determine that a particular regulated article does not present a plant pest risk and no longer should be regulated. If APHIS determines that the regulated article does not present a plant pest risk, the petition must be granted, thereby allowing unrestricted introduction of the article.

The definition of "plant pest" in the Plant Protection Act (PPA) includes living organisms that could directly or indirectly injure, damage, or cause disease in any plant or plant product (7 U.S.C. § 7702[14]).

The regulatory endpoint under the PPA for biotechnology-derived crop products is that deregulation of the regulated article is not likely to pose a plant pest risk. The approach used to assess the plant pest potential of MON 87708 is a weight of the evidence approach based primarily on eight lines of evidence: 1) insertion of a single functional copy of the *dmo* expression cassette, 2) characterization of MON 87708 DMO expressed in MON 87708, 3) safety of MON 87708 DMO, 4) compositional equivalence of harvested MON 87708 seed and forage to conventional soybean, 5) phenotypic, agronomic, and environmental interaction characteristics demonstrating no increased plant pest potential compared to conventional soybean, 6) negligible risk to NTOs and threatened or endangered species, 7) familiarity with soybean as a cultivated crop and the inherently low plant pest potential of soybean, and (8) no greater likelihood to impact agronomic practices, including land use, cultivation practices, or the management of weeds (other than the intended benefit of dicamba weed control), diseases, and insects than conventional soybean.

Using the assessment above, the data and analysis presented in this petition lead to a conclusion that MON 87708 is unlikely to be a plant pest and, therefore, should no longer be subject to regulation under 7 CFR § 340.

Under current regulations, APHIS's noxious weed authorities are not at issue unless a petition is filed under7 C.F.R. Part 360. Although no such issues are posed by a Part 340 petition for non-regulated status, the data presented in this petition nevertheless demonstrate that MON 87708 is neither noxious nor a weed and could not be designated as such even in the appropriate procedural context.

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IX.B. Plant Pest Assessment of the MON 87708 Insert and Expressed Protein

IX.B.1. Characteristics of the Genetic Insert and the Expressed Protein

This section summarizes the details of the genetic insert, characteristics of the genetic modification, and safety and expression of the MON 87708 DMO used to evaluate the food, feed, and environmental safety of MON 87708.

IX.B.1.1. Genetic Insert

As described in more detail in Section III, MON 87708 was produced by *Agrobacterium tumefaciens*-mediated transformation of soybean with PV-GMHT4355, which is a binary vector containing two T-DNAs (Figure III-1). T-DNA I contains the *dmo* expression cassette and T-DNA II contains the *cp4 epsps* expression cassette. During plant transformation, both T-DNAs were inserted into the soybean genome, with the *cp4 epsps* expression cassette functioning as a selectable marker. Subsequently, conventional self-pollinated breeding methods and segregation were used to isolate those plants that contain the *dmo* expression cassette (T-DNA I) and do not contain the *cp4 epsps* expression cassette (T-DNA II), resulting in the production of marker-free MON 87708. T-DNA I contains the *dmo* coding sequence under the regulation of the *PC1SV* promoter, *TEV* leader, the *RbcS* targeting sequence, and the *E9* 3′ non-translated region. In addition, T-DNA I contains Left and Right Border sequences. The promoter, leader, targeting, and border sequences of T-DNA I are not known to cause plant disease. Furthermore, these sequences are well characterized, are noncoding regions, and will not cause MON 87708 to promote plant disease.

Molecular analyses demonstrated that MON 87708 contains one copy of the inserted T-DNA I at a single integration locus. No T-DNA II or backbone sequences from PV-GMHT4355 were detected in the genome of MON 87708. Additionally, the data confirmed the organization and sequence of the insert and demonstrated the stability of the insert over several generations. These data demonstrated that there are no unintended changes in the MON 87708 genome as a result of the insertion of the *dmo* expression cassette, and support the overall conclusion that MON 87708 is unlikely to be a plant pest.

IX.B.1.2. Protein Safety

MON 87708 exhibits tolerance to the herbicide dicamba through the insertion of a demethylase gene from *Stenotrophomonas maltophilia* that encodes for DMO. *S. maltophilia* is an environmentally ubiquitous bacterium. Infections caused by *S. maltophilia* are extremely uncommon and it can be found in healthy individuals without any harmful effects. DMO is a Rieske type non-heme iron oxygenase that catalyzes the demethylation of dicamba to the non-herbicidal compound DCSA (Section V.A). DMO is specific for dicamba (Dumitru et al., 2009).

DMO is a trimer comprised of three DMO monomers (Chakraborty et al., 2005). MON 87708 DMO is comprised of two forms of the DMO protein; denoted as DMO and DMO+27. Since DMO can be formed by DMO, DMO+27, or a combination of both, all forms of the trimer are referred to as MON 87708 DMO (Section V). MON 87708 DMO

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was fully characterized confirming the N-terminal and internal sequence of both protein forms, neither of which were glycosylated. MON 87708 DMO is structurally and functionally similar to oxygenase homologs present in bacteria and plants, where a history of safe use is established (Section V.E.2).

The MON 87708 DMO levels in MON 87708 tissue samples ranged from 6.1 to 69 µg/g dwt in root, forage, harvested seed, and overseason leaf, and represent a low percentage of the total protein in soybean (Section V.C). MON 87708 DMO was rapidly digested in simulated gastric fluids, lacked homology with known toxins and allergens, and lacked acute toxicity in a mouse oral gavage study, which taken together, support the conclusion that there is no meaningful risk to human or animal health from dietary exposure to MON 87708 DMO.

The low level of MON 87708 DMO expressed in MON 87708 tissues taken together with the safety of MON 87708 DMO support the conclusion that food and feed products containing or derived from MON 87708 are as safe for human and animal consumption as soybean currently on the market. Therefore, unintended environmental effects are not anticipated from dietary exposure to MON 87708 DMO, and support the overall conclusion that MON 87708 is unlikely to be a plant pest.

IX.B.2. Compositional Characteristics

Detailed compositional analyses in accordance with OECD guidelines were conducted to assess whether levels of key nutrients and anti-nutrients in MON 87708, both dicamba-treated and untreated, were comparable to levels present in the near isogenic conventional soybean control A3525 and several commercial reference varieties. Seed and forage were harvested from five individual sites in which MON 87708, the conventional control, and a range of commercial reference varieties were grown concurrently in the same field trial. The commercial reference varieties were used to establish a range of natural variability for the key nutrients and anti-nutrients in commercial soybean varieties that have a history of safe consumption.

The combined-site analysis was conducted to determine statistically significant differences (5% level of significance) between MON 87708, both dicamba-treated and untreated, and the conventional control A3525. The results from the combined-site data were reviewed using considerations relevant to food and feed safety and nutritional quality. These considerations included the relative magnitudes of the difference in the mean values of nutrient and anti-nutrient components of MON 87708 and the conventional control, whether the MON 87708 component mean value was within the range of natural variability of that component as represented by the 99% tolerance interval of the commercial reference varieties grown concurrently in the same field trial, and analyses of the reproducibility of the statistically significant combined-site component differences at individual sites.

Assessment of the analytical results confirmed that the differences observed in the combined-site analysis were not meaningful to food and feed safety or the nutritional quality of MON 87708 soybeans. In addition, the levels of assessed components in

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MON 87708 were compositionally equivalent to the conventional control and within the range of variability of commercial soybeans that were grown concurrently in the same field trial. These results support the overall conclusion that MON 87708 is unlikely to be a plant pest.

IX.B 3. Phenotypic and Agronomic and Environmental Interaction Characteristics

An extensive set of comparative plant characterization data were used to assess whether the introduction of the dicamba tolerance trait and the associated treatment of dicamba herbicide altered the plant pest potential of MON 87708 compared to the conventional control (Section VII). Phenotypic, agronomic, and environmental interaction characteristics of MON 87708 were evaluated and compared to those of the conventional control (Section VII.B). As described below, these assessments included: seed dormancy and germination characteristics; plant growth and development characteristics; observations for abiotic stress response, disease damage, arthropod-related damage; pollen characteristics; and arthropod abundance; and plant-symbiont interaction characteristics. Results from the phenotypic, agronomic, and environmental interaction assessments demonstrated that MON 87708 does not possess weedy characteristics, or increased susceptibility or tolerance to specific diseases, insects, or abiotic stressors, or altered symbiont interactions compared to conventional soybean, and the dicamba treatment does not alter the plant pest potential of MON 87708. Taken together, the results of the analysis support a determination that MON 87708 is no more likely to pose a plant pest risk or have a biologically meaningful change in environmental impact than conventional soybean.

IX.B.3.1. Seed Dormancy and Germination

Seed dormancy and germination characterization demonstrated that MON 87708 seed had germination characteristics similar to those of the conventional control (Section VII.C.1). In particular, the lack of hard seed, a well-accepted characteristic often associated with plants that are weeds, supports a conclusion of no increased weediness or plant pest potential of MON 87708 compared to conventional soybean.

IX.B.3.2. Plant Growth and Development

Evaluations of plant growth and development characteristics in the field are useful for assessing potential weediness characteristics such as lodging and pod shattering (Section VII.C.2.3). Of the growth and development characteristics assessed between MON 87708 and the conventional control, no statistically significant differences were detected (5% level of significance) with the exception of plant height and 100 seed weight in a combined-site analysis of the data. The differences in these parameters were relatively small in magnitude, and the mean values of MON 87708 were within the range of the commercial reference varieties for these characteristics. Thus, the differences in these parameters are not considered to be biologically meaningful in terms of increased weediness or plant pest potential of MON 87708 compared to conventional soybean.

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IX.B.3.3. Response to Abiotic Stressors

No biologically meaningful differences were observed during comparative field observations between MON 87708 and the conventional control and their response to abiotic stressors, such as drought, heat stress, high winds, nutrient deficiency, etc. (Section VII.C.2.4). The lack of significant biologically meaningful differences in the MON 87708 response to abiotic stress support the conclusion that the introduction of the dicamba tolerance trait is unlikely to result in increased weediness or plant pest potential compared to conventional soybean.

IX.B.3.4. Pollen Morphology and Viability

Evaluations of pollen morphology and viability from field-grown plants provide information useful in a plant pest assessment as it relates to the potential for gene flow to, and introgression of, the biotechnology-derived trait into other soybean varieties and wild relatives (Section VII.C.3). Pollen morphology and viability evaluations demonstrated no statistically significant differences between MON 87708 and the conventional control. Taken together, these comparative assessments indicate that MON 87708 is not likely to have increased weediness or plant pest potential compared to conventional soybean.

IX.B.3.5. Interactions with Non-Target Organisms Including Threatened and Endangered Species

Evaluation of MON 87708 for potential adverse impacts on NTOs is a component of the plant pest risk assessment. Since MON 87708 is a product with no pesticidal activity, all organisms that interact with MON 87708 are considered to be NTOs. In a 2008 U.S. phenotypic and agronomic assessment, observational data on environmental interactions were collected for MON 87708 and the conventional control. In addition, multiple commercial reference varieties were included in the analysis to establish a range of natural variability for each characteristic. The environmental interactions assessment (Section VII.C.2.4) included data collected on plant-arthropod and plant-disease interactions. The results of this assessment indicated that the presence of the dicamba tolerance trait did not alter plant-arthropod interactions, including beneficial arthropods and arthropod pests, nor did it alter disease susceptibility of MON 87708 compared to conventional soybean. The lack of differences in disease damage, arthropod-related damage, and pest and beneficial arthropod abundance demonstrate that the introduction of the dicamba tolerance trait is unlikely to be biologically meaningful in terms of increased plant pest potential.

In the field, soybean forms a complex symbiotic relationship with members of the bacterial family *Rhizobiaceae* and *Bradyrhizobiaceae*. This symbiosis results in the formation of root nodules in which the bacteria reduce or fix atmospheric nitrogen-producing ammonia that can be used by the plant. MON 87708 was assessed for changes in the symbiotic relationship with *B. japonicum* relative to the conventional control by evaluating shoot total nitrogen, nodule number, and nodule, root, and shoot dry weights (Section VII.C.4). No statistically significant differences were detected between MON 87708 and the conventional control for the parameters measured, indicating no

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impact on either the symbiotic relationship or the symbiotic nitrogen-fixing bacteria. These data support a conclusion of no change in plant pest potential and no expected impact to cultivation practices relative to nitrogen inputs for MON 87708 compared to conventional soybean.

The potential for MON 87708 to harm NTOs was evaluated using a combination of biochemical information and experimental data. The biochemical information and experimental data included molecular characterization, the MON 87708 DMO safety assessments, the history of environmental exposure to mono-oxygenases (the class of enzymes to which DMO belongs), results from the environmental assessment described above, and the demonstration of compositional, agronomic and phenotypic equivalence to conventional soybean. Taken together, these data support the conclusion that MON 87708 is unlikely to adversely affect NTOs, or pose an additional risk to threatened and endangered species above those posed by the cultivation of conventional soybean.

Furthermore, according to APHIS, the only listed threatened or endangered animal that occupies a habitat where it is likely to include soybean fields, and that might feed on soybean, is the federally endangered Delmarva Peninsula Fox Squirrel, (*Sciurus niger cinereus*), found in areas of the mid-Atlantic Eastern seaboard (USDA-APHIS, 2007). It is known to utilize certain agricultural lands readily, but its diet includes acorns; nuts/seeds of hickory, beech, walnut, and loblolly pine; buds and flowers of trees; fungi; insects; fruit; and an occasional bird egg (NatureServe, 2007). The safety of the MON 87708 DMO, the compositional, agronomic and phenotypic equivalence of MON 87708 to conventional soybean, and the diversity of the Fox Squirrel diet, support a conclusion that no biologically significant changes to the habitat or diet of the Delmarva Peninsula Fox Squirrel are expected. Consequently, the planting of MON 87708 is not expected to affect the Delmarva Peninsula Fox Squirrel.

IX.B.3.6. Effects of dicamba reaction products

MON 87708 DMO rapidly demethylates dicamba rendering it inactive, thereby conferring tolerance to dicamba in MON 87708. In dicamba-treated MON 87708 the demethylation of dicamba produces 3,6-dichlorosalicylic acid (DCSA), a known soybean, soil, and livestock metabolite whose safety has been evaluated by the Environmental Protection Agency (U.S. EPA), and formaldehyde. In the absence of a dicamba treatment on MON 87708, DCSA and formaldehyde would not be produced. DCSA is structurally similar to salicylic acid (SA). Numerous studies have reported on the stress defense activities of SA, although most studies have looked at the protective effects of exogenously applied SA (Janda et al, 2007). Formaldehyde has a potential linkage to apoptosis in plants (Szende and Tyihak, 2010), and formaldehyde concentrations in plants have been found to increase under certain stress conditions (Szabo et al, 2003). The National Toxicology Program (NTP) 12th Report on Carcinogens has reclassified formaldehyde as a known human carcinogen (USHHS-NTP, 2011). The relevant route of exposure for this health risk is from repeated inhalation at levels associated with indoor or occupational environments, which are generally higher than outdoor environments (USHHS-NTP, 2011). Formaldehyde is present in food and in the human body naturally,

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and there is no evidence to suggest that dietary intake of formaldehyde is important (USHHS-NTP, 2011).

A full discussion on DCSA, and the safety of this metabolite, is provided in Appendix M. DCSA as well as other dicamba metabolite products were measured in the residue study provided to the EPA to demonstrate that dicamba and dicamba metabolite residues are well below the current MRL set for dicamba in soybeans in the U.S.

Formaldehyde is ubiquitous in the environment and present in plants and animals. Formaldehyde was not considered a relevant metabolite in the demethylation of dicamba by the EPA. According to the guidelines published by Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency (US EPA OPPTS 860.1300), the methoxy sidechain that is cleaved from dicamba to form formaldehyde would specifically not be chosen to be labeled in a metabolism study (U.S. EPA, 1996). This is because it is not metabolically stable and would not be considered a significant moiety as it would be readily metabolized and incorporated into the 1-carbon pool of the plant through known pathways. Therefore, formaldehyde was not measured in the residue study when dicamba was applied to MON 87708.

Data from both dicamba-treated and non-treated MON 87708 compared to a conventional control are available from multiple sites across the U.S. where agronomic, phenotypic and observational environmental interaction data were collected. The results of this assessment demonstrate no biologically meaningful difference between MON 87708 treated with dicamba, or MON 87708 not treated with dicamba compared to the conventional control, and support a conclusion that the formation of DCSA and formaldehyde does not alter the weedy characteristics, or increased susceptibility and tolerance to diseases, insects or abiotic stresses. Therefore, MON 87708, as cultivated, is no more likely to be a plant pest risk or have a biologically meaningful change in environmental impact than conventional soybean.

Further, the metabolism of formaldehyde in plants is well understood, and there are a number of natural occurring sources of formaldehyde in plants. For example, it is produced during the process of photorespiration (Oliver, 1994) and during oxidative demethylation of DNA (Zhu, 2009), which supports why it is not considered a byproduct of interest as dicamba is demethylated. It is well known and understood that formaldehyde is rapidly metabolized in plants through two basic routes: 1) it can be incorporated into the one-carbon folate pool via spontaneous or enzyme-mediated formation of methylene tetrahydrofolate (Hanson and Roje, 2001); or 2) it can be oxidized to formate by a detoxification pathway that begins with spontaneous formation of the glutathione adduct *S*-hydroxymethylglutathione (Hanson and Roje, 2001). In each case, formaldehyde is further metabolized to carbon dioxide or entered into the 1C folate pool (Hanson and Roje, 2001; Giese et al., 1994). The maximum theoretical production of formaldehyde produced from dicamba-treated MON 87708 is estimated to be 16.7 and 37.5 mg/kg[11]. This is well within the range of formaldehyde concentrations measured for

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[11] Calculation based on an assumption that the entire 0.56 kg/ha (0.5 lb/acre a.e.) application of dicamba to MON 87708 soybean at the V3 growth stage is intercepted by the soybean plants, is instantaneously and

a variety of agricultural commodities – up to 60 mg/kg in fruits and vegetables (WHO-IPCS, 1989). Plants have a large capacity to metabolize formaldehyde naturally produced from internal processes (A. Hanson (2011), [redacted] Eminent Scholar, Horticulture Department, University of Florida, Personal Communication), and any additional amount of formaldehyde that could be theoretically produced in the plant by dicamba treatment in MON 87708 would be metabolized very quickly. Additionally, as dicamba would not be instantaneously absorbed and metabolized, the incremental increase in formaldehyde over and above the levels already presumed to be present in the soybean plant would be small and transient. Further, since current literature supports that formaldehyde is only emitted from foliage under certain conditions (Nemecek-Marshall et al., 1995; Cojocariu et al., 2004; Cojocariu et al., 2005) and that emission rates are low (Nemecek-Marshall et al., 1995), little opportunity exists for formaldehyde to be released from MON 87708 after dicamba treatment.

In addition to formaldehyde production in plants, plants and animals are constantly exposed to low levels of formaldehyde. Formaldehyde is already present in the environment and the atmosphere from a variety of biogenic (e.g. plant and animal) and anthropogenic (e.g. automotive or industrial emissions) sources. Additionally, formaldehyde degrades rapidly in environmental compartments (air, soil, and water). In water, formaldehyde dissipates through biodegradation to low levels in a few days (USHHS-ATSDR, 1999). Aerobic biodegradation half-lives are estimated to be 1-7 days for surface water and 2-14 days for ground water (US EPA, 2008). The half-life of formaldehyde in air is dependent on a number of factors (light intensity, temperature and location). Through reaction with hydroxyl radical, the half-life of formaldehyde in air varies from 7 to 70 hours (US EPA, 2008). The photolytic half-life of formaldehyde in air (e.g., in the presence of sunlight) is estimated to be 1.6-6 hours (US EPA, 2008; USHHS-ATSDR, 1999). The rapid degradation of formaldehyde in the environment combined with the understanding that formaldehyde is widely used by living organisms as a 1C source, support a conclusion that any environmental effects of formaldehyde, including effects on other plants and NTO's, resulting from dicamba-treated MON 87708 would be negligible.

Humans are also constantly exposed to low levels of formaldehyde. Human exposure to formaldehyde is primarily due to indoor air exposures (USHHS-ATSDR, 1999). Formaldehyde is also found in a variety of consumer products such as cosmetics and paints, often as an antimicrobial agent, and is used extensively in urea-formaldehyde "slow-release" fertilizer formulations and adhesives (USHHS-ATSDR, 1999). Indoor formaldehyde air concentrations are generally significantly higher than outdoor air concentrations (USHHS-ATSDR, 1999) as a result of combustion (cooking, heating, tobacco use) and the emission of formaldehyde from a variety of construction materials (e.g., particle board, plywood or foam insulation) as well as permanent press fabrics (clothing or draperies) (US CPSC, 1997). Formaldehyde present in outdoor air results

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completely absorbed, and then instantaneously metabolized by the DMO enzyme (Complete demethylation of 560 g (2.5 mol)/ ha dicamba would yield 2.5 mol/ha formaldehyde). Above ground biomass of V3 plants is estimated at 2 metric tons/ha, and results in 37.5 mg/kg formaldehyde in planta. For dicamba applications at R1 growth stage, the crop biomass is estimated to be 4.5 metric tons/ha, and level of formaldehyde produced in planta is 16.7 mg/kg.

from a number of sources, and levels of formaldehyde are generally higher in urban areas than in rural areas (WHO-IPCS, 1989). Direct contributions of formaldehyde to the atmosphere (i.e., those in the form of formaldehyde itself) from man-made sources are present, but are generally considered to be small relative to natural sources or indirect production of formaldehyde in the atmosphere (WHO, 2002). Formaldehyde is rapidly consumed in the atmosphere through direct photolysis or by oxidation with hydroxyl or nitrate radicals (USHHS-ATSDR, 1999).

The National Toxicology Program (NTP) 12th Report on Carcinogens has reclassified formaldehyde as a known human carcinogen (USHHS-NTP, 2011). However, the relevant route of exposure for this health risk is from repeated inhalation of concentrated levels associated with indoor or occupational environments. As previously discussed, formaldehyde may only be released by plants in very small quantities and under certain conditions. Any incremental exposure to formaldehyde associated with the application of dicamba to MON 87708 would occur outdoors, would be minimal, and also transient in nature. Therefore human safety concerns of formaldehyde released from dicamba treated MON 87708 are considered to be negligible. USHHS-NTP (2011) has already stated that there is no evidence to suggest that dietary intake of formaldehyde is important. In addition, commodity soybean seed is not directly consumed by humans, and would be processed into food products, limiting potential exposure to humans to any formaldehyde in dicamba-treated MON 87708 seed.

IX.C. Weediness Potential of MON 87708

The commercial *Glycine* species in the U.S. (*Glycine max L.*) does not exhibit weedy characteristics and is not effective in invading established ecosystems. Soybean is not listed as a weed in the major weed references (Crockett, 1977; Holm et al., 1979; Holm et al., 1997), nor is it present on the lists of noxious weed species distributed by the federal government (7 CFR Part 360). Soybean does not possess any of the attributes commonly associated with weeds (Baker, 1965), such as long persistence of seed in the soil, the ability to disperse, invade, and become a dominant species in new or diverse landscapes or the ability to compete well with native vegetation. Due to the lack of dormancy, which is a trait that has been removed from soybean through commercial breeding, soybean seed can germinate quickly under adequate temperature and moisture conditions, and potentially grow as volunteer plants. However, volunteer plants likely would be killed by frost during autumn or winter of the year they were produced. If they did become established, volunteer plants would not compete well with the succeeding crop, and could be controlled readily by either mechanical or chemical means (Carpenter et al., 2002; Dillon et al., 2006; OECD, 2000; York et al., 2005; Zollinger, 2009). In addition, since wild populations of *Glycine* species are not known to exist in the U.S., the potential does not exist for MON 87708 to outcross to wild or weedy relatives and to alter their weediness potential.

In comparative studies between MON 87708 and the conventional control, phenotypic, agronomic, and environmental interaction data were evaluated (Section VII) for changes that would impact the plant pest potential and, in particular, plant weediness potential.

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Results of these evaluations show that there is no biologically meaningful difference between MON 87708 and the conventional control for characteristics potentially associated with weediness. Furthermore, comparative field observations between MON 87708 and its conventional control in their response to abiotic stressors, such as drought, heat stress, and high winds, indicated no biologically meaningful differences and, therefore, no increased weediness potential. Data on environmental interactions also indicate that MON 87708 does not confer any biologically meaningful increased susceptibility or tolerance to specific diseases or insect pests. Collectively, these findings support the conclusion that MON 87708 has no increased weediness potential compared to conventional soybean.

Because MON 87708 has the same limited weediness potential as conventional soybean, it is similarly unlikely to survive as a volunteer plant. Under 7 C.F. R. Part 340, no "noxious weed" issues are reviewed by APHIS. Nevertheless, even if APHIS's Part 360 noxious weed authorities were at issue here, MON 87708 could pose no "noxious weed" risks under the Plant Protection Act because it would not be "noxious" as APHIS ordinarily interprets that term. APHIS has made clear that "noxious" weeds refer to weeds that are "likely to be aggressively invasive, have significant negative impacts," and are "extremely difficult to manage or control once established." 73 Fed. Reg. 60,008, 60,013 (Oct. 9, 2008). Volunteer MON 87708—like volunteer conventional soybean—would compete poorly with any succeeding crops and soon be killed, making it extremely unlikely to have any prolonged negative effects. Volunteer MON 87708 would also not be "extremely difficult to manage" because it can be controlled easily with numerous alternative herbicides and other mechanical means. (Carpenter et al., 2002; Dillon et al., 2006; OECD, 2000; York et al., 2005; Zollinger, 2009). The conclusion that MON 87708 does not pose noxious weed risks is consistent with APHIS's historical interpretations of the Plant Protection Act, as APHIS has never before considered a genetically engineered crop to be a noxious weed.

IX.D. Potential for Pollen Mediated Gene Flow

Gene introgression is a process whereby one or more genes successfully integrate into the genome of a recipient plant population. Introgression is affected by many factors, including the frequency of the initial pollination event, environmental factors, sexual compatibility of pollen donor and recipient plants, pollination biology, flowering phenology, hybrid stability and fertility, selection, and the ability to backcross repeatedly. Because gene introgression is a natural biological process, it does not constitute an environmental risk in and of itself (Sutherland and Poppy, 2005). Gene introgression must be considered in the context of the transgene(s) inserted into the biotechnology-derived plant, and the likelihood that the presence of the transgene(s) and their subsequent transfer to recipient plants will result in increased plant pest potential. The potential for gene introgression from MON 87708 is discussed below.

The assessment for gene introgression from MON 87708 with other cultivated or wild relatives of soybean, discussed in detail below, indicates that MON 87708 is no more likely to become a weed than conventional soybean, and MON 87708 is expected to be similar to conventional soybean regarding its potential for and impacts from gene flow.

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Soybean lacks sexually-compatible relatives in the U.S.; therefore, the only pollen-mediated gene flow would be within cultivated soybean.

IX.D.1. Hybridization with Cultivated Soybean

Although soybean is largely a self-pollinated species, low levels of natural cross-pollination can occur (Caviness, 1966; OECD, 2000; Ray et al., 2003; Yoshimura et al., 2006). In studies with cultivated soybean, where conditions have been optimized to ensure close proximity and flowering synchrony, natural cross-pollination generally has been found to be very low. Most outcrossing occurred with surrounding plants, and cross-pollination frequencies varied depending on growing season and genotype. Insect activity does increase the outcrossing rate, but soybean generally is not a preferred plant for pollinators (Abrams et al, 1978; Erickson 1975; Jaycox 1970a, b).

Numerous studies on soybean cross-pollination have been conducted, and the published results, with and without supplemental pollinators, are summarized in Table IX-1. Under natural conditions, cross-pollination among adjacent plants in a row or among plants in adjacent rows ranged from 0 to 6.3%. In experiments where supplemental pollinators (usually bees) were added to the experimental area, cross-pollination ranged from 0.5 to 7.74% in adjacent plants or adjacent rows. However, cross-pollination does not occur at these levels over long distances. Cross-pollination rates decrease to less than 1.5% beyond one meter from the pollen source, and rapidly decrease with greater distances from the source. The following cross-pollination rates at extended distances have been reported: 0.05% at 5.4 meters (Ray et al., 2003), 0% at 6.5 meters (Abud et al., 2003), 0% at 10.5 m (Yoshimura et al., 2006), and 0.004% at 13.7 meters of separation (Caviness, 1966).

The potential for cross-pollination in soybean is limited. This is recognized in certified seed regulations for foundation seed in the U.S., which permit any distance between different soybean cultivars in the field as long as the distance is adequate to prevent mechanical mixing (USDA-APHIS, 2006).

The consequence of introgression of the dicamba tolerance trait from MON 87708 into other soybean is negligible since soybean gene flow is naturally low; therefore the dicamba tolerance trait confers no increased plant pest potential to cultivated soybean.

IX.D.2. Hybridization with Wild Annual Species within Subgenus *Soja*

The subgenus *Soja* includes the cultivated soybean *Glycine max* and the wild annual species *Glycine soja*. *Glycine soja* is found in China, Taiwan, Japan, Korea, and Russia and can hybridize naturally with the cultivated soybean, *G. max* (Hymowitz, 2004; Lu, 2004). Hybridization between female *G. soja* and male *G. max* was less successful than hybridization in the opposite direction (Dorokhov et al., 2004), where frequency of spontaneous cross pollination in reciprocal combinations of *G. max* and *G. soja* varied from 0.73 (♀ *G. soja* × ♂ *G. max*) to 12.8% (♀ *G. max* × ♂ *G. soja*). Species relationships in the subgenus *soja* indicated that F_1 hybrids of *G. max* and *G. soja* carry similar genomes and are fertile (Singh and Hymowitz, 1989). Abe et al. (1999) note that

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"natural hybrids between *G. max* and *G. soja* are rare and hybrid swarms involving both species have never been reported." This is also supported by work from Kuroda et al. (2008) in which molecular markers were used and no gene flow from *G. max* to *G. soja* was detected. Many barriers to natural hybridization exist between soybean and wild relatives, including the highly selfing nature of both plants, required proximity of wild soybean to cultivated soybean, synchrony of flowering, and presence of pollinators. As such, it is highly unlikely that naturally occurring, pollen-mediated gene flow and transgene introgression into wild soybean relatives from incidentally released biotechnology-derived soybean will occur at any meaningful frequency.

The subgenus *Soja* also contains an unofficial species, *G. gracilis* (Hymowitz, 2004). *Glycine gracilis* is known only from Northeast China, and is considered to be a weedy or semi-wild form of *G. max*, with some phenotypic characteristics intermediate to those of *G. max* and *G. soja*. *Glycine gracilis* may be a hybrid between *G. soja* and *G. max* (Hymowitz, 1970; Lu, 2004). Interspecific fertile hybrids formed by intentional crosses between *G. max* and *G. soja* and between *G. max* and *G. gracilis* have been easily obtained (Dorokhov et al., 2004; Singh and Hymowitz, 1989). Although hybridization between *G. max* and members of the subgenus *Soja* can take place, *G. soja* is not found in North or South America, and it is highly unlikely that gene transfer will occur.

IX.D.3. Hybridization with the Wild Perennial Species of *Glycine* Subgenus

Wild perennial species of the *Glycine* subgenus occur in Australia; West, Central and South Pacific Islands; China; Papua New Guinea; Philippines; and Taiwan (Hymowitz et al., 1992). Therefore, the only opportunities for inter-subgeneric hybridization would occur in areas where those species are endemic. Nonetheless, the likelihood of interspecific hybridization between *G. max* and the wild perennial *Glycine* species is extremely low because they are genomically dissimilar (Hymowitz, 2004; Lu, 2004) and pod abortion is common. From time to time, immature seeds of the crosses have been germinated aseptically *in vitro*, but the resulting F1 hybrids are slow-growing, morphologically weak, and completely sterile. Their sterility is due to poor chromosome pairing. Furthermore, species distantly related usually produce nonviable F1 seeds that either have premature death of the germinating seedlings or suffer from seedling and vegetative lethality (Kollipara et al., 1993). In North and South America, it is not possible for gene transfer to occur between cultivated soybean and wild perennial species of *Glycine* subgenera because these wild species do not exist in these regions.

IX.D.4. Transfer of Genetic Information to Species with Which Soybean Cannot Interbreed (Horizontal Gene Flow)

Monsanto is unaware of any reports regarding the unaided transfer of genetic material from soybean species to other sexually-incompatible plant species. The likelihood for horizontal gene flow to occur is exceedingly small. Therefore, potential ecological risk associated with horizontal gene flow from MON 87708 due to the presence of the dicamba tolerance trait is not expected. The consequence of horizontal gene flow of the dicamba tolerance trait into other plants that are sexually-incompatible is negligible since, as data presented in this petition confirm, the gene and trait confer no increased plant pest

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potential to soybean. Thus in the highly unlikely event that horizontal gene transfer were to occur, the presence of the dicamba tolerance trait would not be expected to increase pest potential in the recipient species.

IX.E. Potential Impact on Soybean Agronomic Practices

An assessment of current soybean agronomic practices was conducted to determine whether the cultivation of MON 87708 has the potential to impact current soybean and weed management practices (Section VIII). Soybean fields are typically highly managed agricultural areas that are dedicated to crop production. MON 87708 is likely to be used in common rotations on land previously used for agricultural purposes. Certified seed production will continue to use well-established industry practices to deliver high quality seed containing MON 87708 to growers. Cultivation of MON 87708 is not expected to differ from typical soybean cultivation, with the exception of an expanded window of dicamba applications. Due to the excellent crop safety of MON 87708 to dicamba, growers will have a new herbicide mode-of-action for in-crop control of glyphosate's hard-to-control and resistant broadleaf weeds that are present in U.S. soybean production. As a result of cultivation of MON 87708 integrated into the Roundup Ready soybean system, the number of dicamba-treated soybean acres is expected to double from historic peak levels. Additionally, due to the expanded timing of in-crop applications to soybean, dicamba treatments will be later in the growing season than most current labeled dicamba uses. These later applications of dicamba to MON 87708 are not expected to impact dicamba-sensitive crops from drift (spray or volatility) because, in its application to U.S. EPA, Monsanto is registering the use on MON 87708 on a low volatility dicamba (DGA salt) formulation, not allowing aerial application on MON 87708, and will consult with U.S. EPA to develop any necessary additional measures to protect against offsite impacts.

MON 87708 is similar to conventional soybean in its agronomic, phenotypic, ecological, and compositional characteristics and has levels of resistance to insects and diseases comparable to conventional soybean. Therefore, no significant impacts on current cultivation and management practices for soybean are expected following the introduction of MON 87708. Based on this assessment, the introduction of MON 87708 will not impact current U.S. soybean cultivation practices or weed management practices, other than intended weed control benefits.

IX.F. Summary of Plant Pest Assessments

Plant pests are defined in the Plant Protection Act as certain living organisms that can directly or indirectly injure, cause damage to, or cause disease to any plant or plant product (7 U.S.C. § 7702[14]). Characterization data presented in Sections III through VII of this petition confirm that although MON 87708 contains the dicamba-tolerant trait, it is not different from conventional soybean in terms of pest potential in its phenotypic, agronomic, and environmental interaction characteristics. Monsanto is not aware of any study results or observations associated with MON 87708 that would suggest an increased plant pest risk would result from its introduction.

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The plant pest assessment was based on multiple lines of evidence developed from a detailed characterization of MON 87708 compared to conventional soybean, followed by a risk assessment on detected differences. The risk assessment considered various factors including: 1) insertion of a single functional copy of the *dmo* expression cassette, 2) characterization of the MON 87708 DMO, 3) safety of the MON 87708 DMO, 4) compositional equivalence of harvested MON 87708 soybean seed and forage as compared to conventional soybean, 5) phenotypic, agronomic, and environmental interaction characteristics demonstrating no increased plant pest potential compared to conventional soybean, 6) negligible risk to NTOs and threatened or endangered species, 7) familiarity with soybean as a cultivated crop and the inherently low plant pest potential of soybean, and 8) no greater likelihood to impact agronomic practices, including land use, cultivation practices, or the management of weeds, diseases, and insects than conventional soybean, with the exception of the expanded window of dicamba application.

Based on the data and information presented in this petition, it is concluded that, like conventional soybean and currently deregulated biotechnology-derived soybean, MON 87708 is highly unlikely to be a plant pest. Therefore, Monsanto Company requests a determination from APHIS that MON 87708 and any progeny derived from crosses between MON 87708 and other commercial soybean be granted nonregulated status under 7 CFR Part 340.

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Table IX-1. Summary of Published Literature on Soybean Cross Pollination

Distance from Pollen Source (meters)	Cross-Pollination (%)	Comments	Reference
0.3	0.04 (estimated per pod)	Interspaced plants within a row. Experiment conducted in a single year. Single male and female parental varieties. Percent outcrossing calculated per pod rather than per seed.	(Woodworth, 1922)
0.8	0.07 to 0.18	Adjacent rows. Experiment conducted over two years. Several male and female parental varieties.	(Garber and Odland, 1926)
0.1	0.38 to 2.43	Adjacent plants within a row. Experiment conducted in a single year. Several male and female parental varieties.	(Cutler, 1934)
0.1	0.2 to 1.2	Adjacent plants within a row. Experiment conducted in single year at two locations. Several male and female parental varieties.	(Weber and Hanson, 1961)
0.9 2.7–4.6 6.4–8.2 10–15.5	0.03 to 0.44 0.007 to 0.06 0 to 0.02 0 to 0.01	Frequency by distance was investigated. Experiment conducted over three years. Single male and female parental varieties.	(Caviness, 1966)
0.8 m	0.3 to 3.62	Various arrangements within and among adjacent rows. Experiment conducted over three years. Several male and female parental varieties.	(Beard and Knowles, 1971)
One row (undefined)	1.15 to 7.74	Bee pollination of single-row, small-plots of pollen receptor surrounded by large fields (several acres) of pollen donor soybean. Soybean is not a preferred flower for alfalfa leafcutting bees.	(Abrams et al., 1978)
0.1–0.6	0.5 to 1.03 (depending on planting design)	Bee pollination of soybean grown in various spatial arrangements. Experiment conducted over four years. Several soybean cultivars.	(Chiang and Kiang, 1987)
1.0	0.09 to 1.63	Adjacent rows. Experiment conducted over two years. Several male and female parental varieties.	(Ahrent and Caviness, 1994)
0.5 1.0 6.5	0.44 to 0.45 0.04 to 0.14 none detected	Frequency by distance was investigated. Experiment conducted in a single year. Single male and female parental varieties.	(Abud et al., 2003)
0.9 5.4	0.29 to 0.41 0.03 to 0.05	Frequency by distance was investigated. Experiment conducted in a single year. Single male and female parental varieties.	(Ray et al., 2003)
0.15	0.65 to 6.32 (avg. 1.8)	Interspaced plants within a row. Experiment conducted in a single year. Single male and female parental varieties.	(Ray et al., 2003)
0.7 1.4 2.1 2.8 3.5 7.0 10.5	0 to 0.19 0 to 0.04 0 to 0.05 0 to 0.08 0 to 0.04 0 to 0.04 0	Interspaced plants within a row arranged in small plots. Experiment conducted in a four year period. Single male and two female parental varieties.	(Yoshimura et al., 2006)

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X. ADVERSE CONSEQUENCES OF INTRODUCTION

Monsanto knows of no results or observations associated with MON 87708 or the MON 87708 DMO indicating that there would be an adverse environmental consequence from the introduction of MON 87708. MON 87708 contains DMO that renders the soybean plant tolerant to the herbicide dicamba. As demonstrated by field results and laboratory tests, the only phenotypic difference between MON 87708 and conventional soybean is tolerance to dicamba.

The data and information presented in this petition demonstrate that MON 87708 is unlikely to pose an increased plant pest risk or to have an adverse environmental consequence compared to conventional soybean. This conclusion is based on multiple lines of evidence developed from a detailed characterization of the product compared to conventional soybean, followed by risk assessment on detected differences: 1) characterization evaluations included molecular analyses, which confirmed the insertion of a single functional copy of the *dmo* expression cassette at a single locus within the soybean genome; 2) measurement of the MON 87708 DMO levels in various soybean tissues; 3) characterization of the MON 87708 DMO confirming it is not novel and is structurally and functionally similar to oxygenase homologs widely present in bacteria and plants, where a history of safe use is established; and 4) extensive characterization of the plant phenotype, including compositional analysis of key nutrients and antinutrients, and environmental interactions. Therefore, based on the lack of increased pest potential or adverse environmental consequences compared to conventional soybean, the risks for humans, animals, and other NTOs from MON 87708 are negligible under the conditions of use. Additionally the introduction of MON 87708 will not adversely impact cultivation practices or the management of weeds, diseases, and insects in soybean production systems, other than the use of dicamba postemergence in soybean.

Successful integration of MON 87708 into the Roundup Ready soybean system will provide growers with an opportunity for an efficient, effective weed management system for the management of glyphosate's hard-to-control and resistant broadleaf weeds; provide an easy system for inclusion of a second herbicide mode-of-action in soybean production practices as recommended by weed science experts to manage weed resistance development; and continue to provide soybean growers with effective weed control systems necessary for production yields to meet the growing needs of the food, feed and industrial markets.

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APPENDICES

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Appendix A: USDA Notifications

Field trials of MON 87708 have been conducted in the U.S. since 2005. The protocols for these trials included field performance, breeding and observation, agronomics, and generation of field materials and data necessary for this petition. In addition to MON 87708 phenotypic assessment data, observational data on pest and disease stressors were collected from these product development trials. The majority of the final reports have been submitted to the USDA. However, some final reports, mainly from the 2008-2009 seasons, are still in preparation. A list of trials conducted under USDA notifications and the status of the final reports for these trials are provided in Table A-1.

Table A-1. USDA Notifications Approved for MON 87708 and Status of Trials Conducted under These Notifications and Permits

USDA Number	Effective Date	Release Site (State)	Trial Status
2005			
05-269-02n	11/16/2005	PR	Submitted to USDA
2006			
06-045-15n	5/18/2006	HI(5)	Submitted to USDA
06-045-17n	5/18/2006	PR(3)	Submitted to USDA
06-052-01n	3/20/2006	IL(7), KS(5)	Submitted to USDA
06-052-02n	4/24/2006	IA(7), IL(5), IN(2)	Submitted to USDA
06-052-09n	4/24/2006	IA(2), IL(6), IN(2)	Submitted to USDA
06-067-05n	4/24/2006	IL(2)	Submitted to USDA
06-090-03n	5/5/2006	IL(2)	Submitted to USDA
06-275-102n	11/14/2006	PR	Submitted to USDA
06-345-101n	1/10/2007	PR(3)	Submitted to USDA
2007			
07-018-103n	2/17/2007	IL(10), IN(3), MO, PR	Submitted to USDA
07-018-106n	2/17/2007	IA(7), KS(6)	Submitted to USDA
07-018-109n	2/17/2007	IA, IL(10), IN(3), MO	Submitted to USDA
07-024-101n	3/18/2007	IA(7), KS(6)	Submitted to USDA
07-039-101n	3/18/2007	IA(4), IL(5), IN(3), KS(3)	Submitted to USDA
07-043-102n	4/10/2007	IA, IL(2), KS, MD, WI	Submitted to USDA
07-050-107n	4/9/2007	IA, IL(2), IN, KS, KY, MN, NE, SD	Submitted to USDA
07-057-109n	4/6/2007	AL, IA(3), IL, IN, LA, MN, MO(2), MS, NE, SD, TN	Submitted to USDA
07-094-104n	5/4/2007	IA(2)	Submitted to USDA
07-094-116n	5/4/2007	MN	Submitted to USDA
07-113-103n	6/4/2007	PR(2)	Submitted to USDA
07-241-103n	9/28/2007	PR	Submitted to USDA
07-250-102n	10/7/2007	PR(2)	Submitted to USDA
07-261-101n	10/18/2007	PR	Submitted to USDA
07-271-101n	10/28/2007	PR(2)	Submitted to USDA
07-312-101n	12/5/2007	PR	Submitted to USDA

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Table A-1 (continued). USDA Notifications Approved for MON 87708 and Status of Trials Conducted under These Notifications and Permits

USDA Number	Effective Date	Release Site (State)	Trial Status
2008			
07-352-101rm	3/26/2008	IA(8), IL(16), IN(4), KS(7), MO	Submitted to USDA
08-030-103n	2/29/2008	PR(2)	Submitted to USDA
08-031-105n	3/13/2008	IA(5), IL(4), KS(5)	Submitted to USDA
08-031-106n	3/1/2008	IA(2), IL(5), IN(3)	Submitted to USDA
08-039-107n	3/9/2008	IA(5), IL, IN(3), KS(5), MO	Submitted to USDA
08-043-107n	3/13/2008	IA(3), IL(10), IN, OH	Submitted to USDA
08-049-101n	3/19/2008	IL, MD, WI	Submitted to USDA
08-058-101n	3/28/2008	IA(3), IL(2), IN, MO, PA, WI(2)	Submitted to USDA
08-059-109n	3/29/2008	IA	Submitted to USDA
08-059-110n	3/29/2008	IL	Submitted to USDA
08-059-112n	3/29/2008	IN	Submitted to USDA
08-060-103n	4/2/2008	MN	Submitted to USDA
08-063-112n	4/2/2008	IA(4), IL(2), IN, MI, MO, NE(2)	Submitted to USDA
08-063-113n	4/4/2008	MN(2), ND, SD(5), WI(5)	Submitted to USDA
08-065-101n	4/4/2008	IL(2), IN	Submitted to USDA
08-064-102n	4/3/2008	PA	Submitted to USDA
08-064-103n	4/3/2008	IL	Submitted to USDA
08-064-104n	4/3/2008	AR, GA, KS(5), LA, MO, SC	Submitted to USDA
08-064-105n	4/3/2008	AR, IL(2), IN, KS(3), MD, MN(3), NC, SD, WI, ND	Submitted to USDA
08-072-110n	4/25/2008	AR, IA, IN(3), KS, MI, MO(2), NE	Submitted to USDA
08-079-101n	4/17/2008	IA(3)	Submitted to USDA
08-084-102n	4/24/2008	IA, NE	Submitted to USDA
08-182-101n	8/1/2008	PR(2)	Submitted to USDA
08-219-101n	9/5/2008	PR	Submitted to USDA
08-263-101n	10/19/2008	AR, IA, IL, MO	Submitted to USDA
08-266-105n	10/22/2008	PR	Submitted to USDA
08-323-101n	12/18/2008	PR	Submitted to USDA
08-352-108n	1/26/2009	PR	Submitted to USDA
08-357-101rm	3/17/2009	IA(8), IL(7), IN(3), KS(5), NE	Submitted to USDA

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Table A-1 (continued). USDA Notifications Approved for MON 87708 and Status of Trials Conducted under These Notifications and Permits

USDA Number	Effective Date	Release Site (State)	Trial Status
2009			
09-007-106n	2/25/2009	PR	Submitted to USDA
09-036-103n	3/7/2009	IA(2), IL(2), IN, NE	Submitted to USDA
09-042-103n	3/19/2009	MS	Submitted to USDA
09-049-110n	3/20/2009	IA	Submitted to USDA
09-050-136n	4/3/2009	IA(2), IL(2), IN(2), MD, MN, OH, PR, SD	Submitted to USDA
09-061-108n	4/1/2009	AR, IA, IL(3), KS	Submitted to USDA
09-061-117n	4/1/2009	IL, MO(2)	Submitted to USDA
09-068-111n	4/8/2009	IL(2), IN(2), MS, NE(2), OH	Submitted to USDA
09-071-102n	4/11/2009	NE, SD, TN(2)	Submitted to USDA
09-082-103n	4/22/2009	IN(2)	Submitted to USDA
09-091-103n	5/1/2009	AR	Submitted to USDA
09-093-120n	5/3/2009	AR	Submitted to USDA
09-124-102n	6/3/2009	PR	Submitted to USDA
09-124-105n	5/13/2009	IA	Submitted to USDA
09-135-104n	6/14/2009	IL	Submitted to USDA
09-162-105n	7/11/2009	PR	Submitted to USDA
09-162-106n	7/11/2009	PR	Submitted to USDA
09-222-101n	9/9/2009	PR(2)	Submitted to USDA
09-237-104n	9/24/2009	PR	Submitted to USDA
09-247-101rm	11/17/2009	PR	Submitted to USDA

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Appendix B: Materials, Methods, and Results for Molecular Analyses of MON 87708

B.1. Materials

The genomic DNA used in molecular analyses was isolated from leaf tissue harvested from MON 87708 and the near isogenic conventional soybean control A3525 (seed lot: GLP-0707-18882-S, and GLP-0707-18884-S, respectively). Additional DNA extracted from leaf tissue of various MON 87708 generations was used in generational stability analyses. The control was conventional soybean variety A3525 that has a similar genetic background as MON 87708. Plasmid vector PV-GMHT4355 (Figure III-1) was used as a positive hybridization control in Southern blot analyses. Probe templates generated from PV-GMHT4355 were used as additional positive hybridization controls. As additional reference standards, the 1 kb DNA extension ladder and λ DNA/*Hind* III segments from Invitrogen (Carlsbad, CA) were used for size estimations on Southern blots and agarose gels. The GeneRuler™ 1 kb Plus DNA ladder from Fermentas (Hanover, MD) was used for size estimations on agarose gels for polymerase chain reaction (PCR) analyses.

B.2. Characterization of the Materials

The identity of the leaf material from MON 87708 and the conventional control was verified by event-specific PCR analysis to confirm the presence or absence of the *dmo* expression cassette. The stability of the genomic DNA was confirmed in each Southern blot analysis by observation of the digested DNA sample on an ethidium bromide-stained agarose gel, and/or interpretable signals on Southern blots, and/or produced specific PCR products.

B.3. DNA Isolation for Southern Blot and PCR Analyses

Genomic DNA from MON 87708 and the conventional control was isolated from leaf tissue. The leaf tissue was ground to a fine powder in liquid nitrogen using a mortar and pestle. DNA was extracted using a hexadecyltrimethylammonium bromide (CTAB)-based method. Briefly, 20 ml of CTAB buffer (1.5% w/v CTAB, 75 mM Tris HCl, 100 mM EDTA, 1.05 M NaCl, and 0.75% w/v PVP) and 10 mg RNase A were added to approximately 4 ml of ground leaf tissue and incubated at 60-70°C for 40-50 minutes with intermittent mixing. Twenty ml of chloroform was added to the samples and mixed by hand for 2-3 minutes, then centrifuged at 10,300 × g for 8-10 minutes. The upper aqueous phase was put into a clean tube and the chloroform step was repeated twice. After the last chloroform step, the aqueous phase was put into a clean tube and the DNA was precipitated with 20 ml of 100% ethanol. The sample was centrifuged for one minute to condense the pellet, and then the precipitated DNA was hooked out and put into a tube with 4-6 ml of 70% ethanol to wash the DNA pellet. The samples were centrifuged at 5,100 × gravity for 5 minutes to pellet the DNA. DNA pellets were air dried, then resuspended in 300 µl of TE buffer (10 mM Tris HCl, 1 mM EDTA, pH8.0). All extracted DNA was stored in a 4°C refrigerator or a -20°C freezer.

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B.4. Quantification of Genomic DNA

Extracted genomic DNA was quantified using a Hoefer DyNA Quant 200 Fluorometer. Molecular size marker IX (Roche, Indianapolis, IN) was used as the calibration standard.

B.5. Restriction Enzyme Digestion of Genomic DNA

Approximately 10 µg of genomic DNA extracted from MON 87708 and the conventional control was digested with appropriate combinations of restriction enzymes *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I (New England Biolabs, Ipswich, MA). All digests were conducted in 1 × NEBuffer 4 (New England Biolabs) plus 1 × BSA (New England Biolabs) at 37 °C in a total volume of ~500 µl with ~50 units of each restriction enzyme. For the purpose of running positive hybridization controls, ~10 µg of genomic DNA extracted from the conventional control was digested with the restriction enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I and the appropriate positive hybridization control(s) were added to these digests.

B.6. Agarose Gel Electrophoresis

Digested genomic DNA was resolved on ~0.8% (w/v) agarose gels. Individual digests of MON 87708 and the conventional control genomic DNA were loaded on the same gel in a long-run/short-run format. The long-run allows for greater resolution of large molecular weight DNA, whereas the short-run allows for the detection of small molecular weight DNA. For the insert stability analysis, individual digests of genomic DNA extracted from leaf tissue across multiple generations were loaded on the agarose gel in a single short-run format. The positive hybridization controls were only run in the short-run format.

B.7. DNA Probe Preparation for Southern Blot Analyses

Probe templates were prepared by PCR amplification from plasmid vector PV-GMHT4355. Approximately 25 ng of each probe template were radiolabeled with ^{32}P-deoxycytidine triphosphate (dCTP) (6000 Ci/mmol) or ^{32}P-deoxyadenosine triphosphate (dATP) (6000 Ci/mmol) using the RadPrime DNA Labeling System (Invitrogen). Probe locations relative to the genetic elements in plasmid vector PV-GMHT4355 are depicted in Figure III-1.

B.8. Southern Blot Analyses of Genomic DNA

Digested genomic DNA isolated from MON 87708 and the conventional control was evaluated using Southern blot analyses. The plasmid vector PV-GMHT4355 DNA digested with the enzyme combination *Aat* II/*Nde* I was added to the conventional control genomic DNA previously digested with the enzyme combination *Bsp1286* I/*Pvu* II or *Hpa* I/*Kpn* I to serve as a positive hybridization control. When multiple probes were hybridized simultaneously to one Southern blot, the appropriate probe templates generated from PV-GMHT4355 were mixed with previously digested conventional control genomic DNA to serve as additional positive hybridization controls. The digested DNA was then separated by agarose gel electrophoresis and transferred onto a

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nylon membrane. Southern blots were hybridized and washed at 55, 60, or 65°C, depending on the melting temperature (Tm) of the probes. Table B-1 lists the radiolabeling conditions and hybridization temperatures of the probes used in this study. Multiple exposures of each blot were then generated using Kodak Biomax MS film in conjunction with one or two Kodak Biomax MS intensifying screen(s) in a -80°C freezer.

Table B-1. Hybridization Conditions of Utilized Probes

Probe	DNA Probe	Element Sequence Spanned by DNA Probe	Probe labeled with dNTP (^{32}P)	Hybridization Temperature (°C)
1	Backbone Probe	Backbone sequence	dCTP	60
2	Backbone Probe	Backbone sequence	dCTP	60
3	Backbone Probe	Backbone sequence	dCTP	60
4	T-DNA II Probe	T-*E9,* and CS-*cp4 epsps* (portion)	dATP	55
5	T-DNA II Probe	CS-*cp4 epsps* (portion), and TS-*CTP2* (portion)	dCTP	60
6	T-DNA II Probe	TS-*CTP2* (portion), L-*DnaK*, P-*FMV*	dATP	55
7	Backbone Probe	Backbone sequence	dCTP	60
8	T-DNA I Probe	B-Right Border, P-*PC1SV*, L-*TEV,* TS-*RbcS*	dATP	60
9	T-DNA I Probe	TS-*RbcS* (portion), CS-*dmo*, T-*E9* (portion)	dCTP	65
10	T-DNA I Probe	T-*E9*, and B-Left Border	dATP	55

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B.9. DNA Sequence Analyses of the Insert

Overlapping PCR products that span the insert and adjacent 5′ and 3′ flanking DNA sequences in MON 87708 (Figure B-1) were generated. These products were sequenced to determine the nucleotide sequence of the insert in MON 87708 as well as the nucleotide sequence of the DNA flanking the 5′ and 3′ ends of the insert.

The PCR analyses were conducted using 50 ng of genomic DNA template in a 25 µl reaction volume containing a final concentration of 1 M betaine, 1 mM $MgSO_4$, 0.8 µM of each primer, 0.2 mM of each dNTP, and 0.5 units of KOD Hot Start DNA polymerase (Novagen, Madison, WI). The amplification of Product A (Figure B-1) was performed under the following cycling conditions: one cycle at 94°C for 2 minutes; 35 cycles at 94°C for 45 seconds, 60.2°C for 45 seconds, 72°C for 5 minutes; one cycle at 72°C for 10 minutes. The amplification of Product B (Figure B-1) was performed under the following cycling conditions: one cycle at 94°C for 2 minutes; 35 cycles at 94°C for 45 seconds, 60.8°C for 45 seconds, 72°C for 5 minutes; one cycle at 72°C for 10 minutes.

Following PCR amplification, exonuclease I (Exo; US Biochemicals, Cleveland, OH)/ shrimp alkaline phosphatase (SAP; US Biochemicals) purification of the PCR products used for sequencing was performed in a 21 µl reaction volume containing 15 µl of the PCR product and a final concentration of 0.1 units/µl of Exo and 0.1 units/µl of SAP. The reaction was incubated at 37ºC for 15 minutes, followed by 80ºC for an additional 15 minutes.

Prior to sequencing, aliquots of untreated and Exo/SAP treated PCR product were separated on 0.8% (w/v) agarose E-gels (Invitrogen) and visualized by ethidium bromide staining to verify that the products were of the expected size. The PCR products were sequenced using multiple primers including primers used for PCR amplification and primers designed internal to the amplified sequences. All sequencing was performed by the Monsanto Genomics Sequencing Center using BigDye terminator chemistry (ABI, Foster City, CA).

B.10. PCR and DNA Sequence Analysis to Examine the MON 87708 Insertion Site

To examine the insertion site of conventional soybean and MON 87708, PCR analysis was performed on genomic DNA from both MON 87708 and the conventional control (Figure B-2). The primers used in this analysis were designed from the genomic DNA sequences flanking the insert in MON 87708. One primer designed from the genomic DNA sequence flanking the 5′ end of the insert was paired with a second primer located in the genomic DNA sequence flanking the 3′ end of the insert.

The PCR analysis was conducted using approximately 50 ng of genomic DNA template in a 25 µl reaction volume containing a final concentration of 1 M betaine, 1 mM $MgSO_4$, 0.8 µM of each primer, 0.2 mM of each dNTP, and 0.5 units of KOD Hot Start DNA polymerase (Novagen). The amplification of the product was performed under the following cycling conditions: one cycle at 94°C for 2 minutes; 35 cycles at 94°C for 45 seconds, 60.2°C for 45 seconds, 72°C for 5 minutes; one cycle at 72°C for 10 minutes.

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Following PCR amplification, Exo/SAP purification of the PCR products used for sequencing was performed in a 21 µl reaction volume containing 15 µl of the PCR product and a final concentration of 0.1 units/µl of Exo and 0.1 units/µl of SAP (U.S. Biochemicals). The reaction was incubated at 37ºC for 15 minutes, followed by 80ºC for an additional 15 minutes.

Prior to sequencing, aliquots of untreated and Exo/SAP treated PCR product were separated on 0.8 % (w/v) agarose E-gels (Invitrogen) and visualized by ethidium bromide staining to verify that the products were of the expected size prior to sequencing. The PCR products were sequenced using multiple primers, including primers used for PCR amplification and primers designed internal to the amplified sequences. All sequencing was performed by the Monsanto Genomics Sequencing Center using BigDye terminator chemistry.

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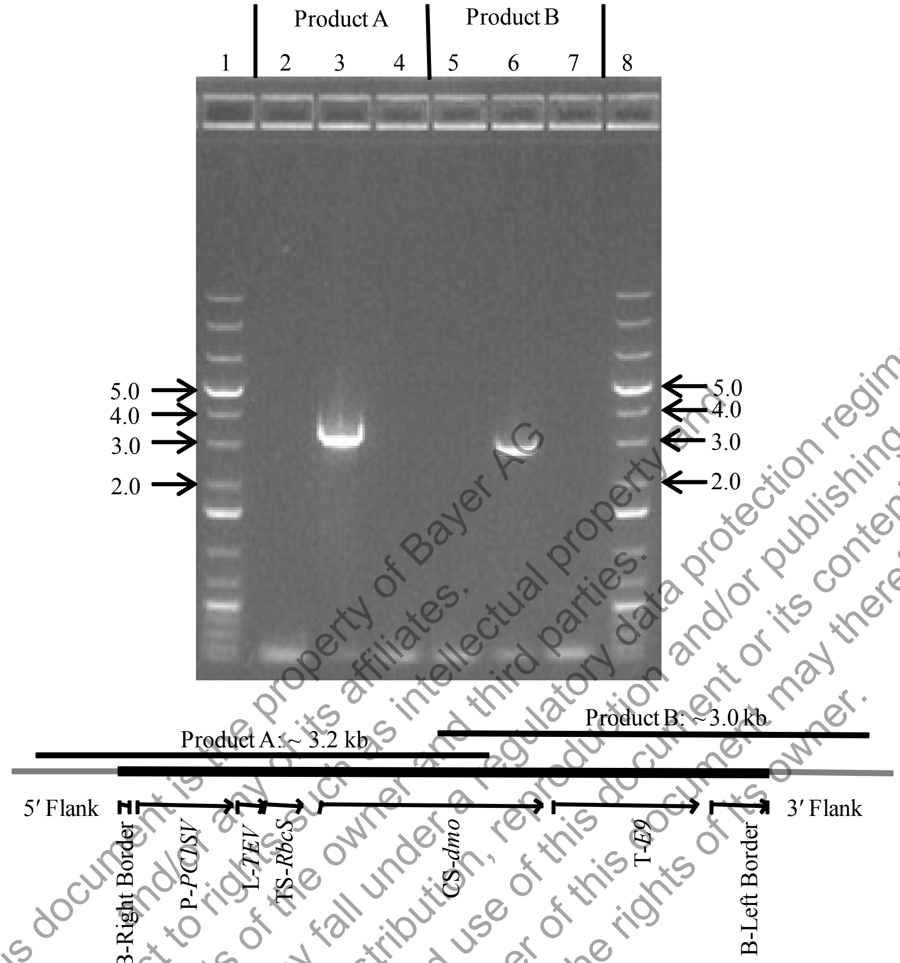

Figure B-1. Overlapping PCR Analysis Across the Insert in MON 87708

PCR analyses were performed on MON 87708 genomic DNA extracted from leaf (Lanes 3 and 6). Lanes 2 and 5 contain reactions with conventional control DNA while lanes 4 and 7 are reactions containing no template DNA. Lanes 1 and 8 contain Fermentas GeneRuler™ 1 kb Plus DNA Ladder. Lanes are marked to show which product has been loaded and is visualized on the agarose gel. The expected product size for each amplicon is provided in the illustration of the insert in MON 87708 that appears at the bottom of the figure. Five microliters of each of the PCR products was loaded on the gel. This figure is representative of the data generated; however, the specific bands from this gel were not excised and sequenced.

Lane:

1. GeneRuler™ 1 kb Plus DNA Ladder
2. Conventional control DNA
3. MON 87708 genomic DNA
4. No template DNA control
5. Conventional control DNA
6. MON 87708 genomic DNA
7. No template DNA control
8. GeneRuler™ 1 kb Plus DNA Ladder

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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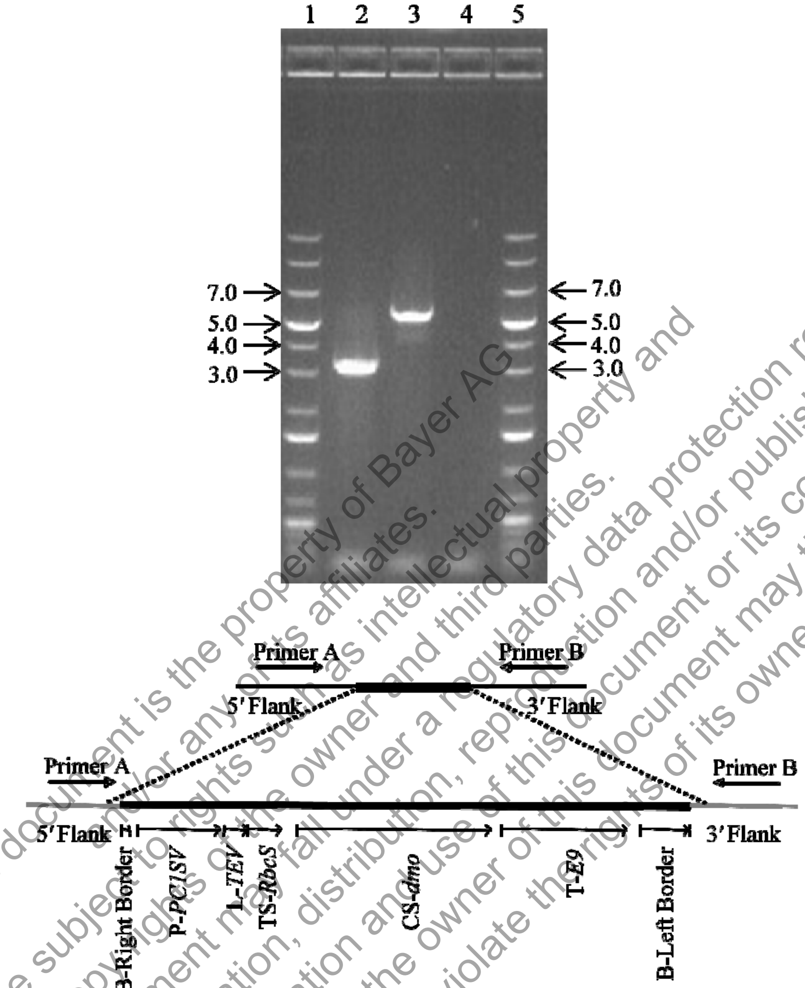
1
2
3
4
5
7.0
5.0
4.0
3.0
7.0
5.0
4.0
3.0
Primer A
Primer B
5′ Flank
3′ Flank
Primer A
Primer B
5′ Flank
3′ Flank
B-Right Border
P-*PC1SV*
L-*TEV*
TS-*RbcS*
CS-*dmo*
T-*E9*
B-Left Border

Figure B-2. PCR Amplification of the MON 87708 Insertion Site

Depiction of the MON 87708 insertion locus in conventional control and MON 87708. PCR amplification was performed using Primer A in the 5′ flanking sequence and Primer B in the 3′ flanking sequence of the insert in MON 87708 to verify to examine the insertion site in conventional soybean and MON 87708.

Lane	**Description**
1	GeneRuler™ 1 kb Plus DNA Ladder
2	Conventional control DNA
3	MON 87708 genomic DNA
4	No template DNA control
5	GeneRuler™ 1 kb Plus DNA Ladder

Arrows denote sizes of DNA, in kilobase pairs, obtained from molecular weight markers on ethidium bromide stained gel.

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Appendix C: Materials, Methods, and Results for the Characterization of MON 87708 DMO and Substrate Specificity of DMO

C.1. Characterization of MON 87708 DMO

C.1.1. Materials

MON 87708 DMO (lot 11261646) was purified from defatted soybean flour as described in C.3. As described in Section V, MON 87708 produces two forms of DMO. In MON 87708, the DMO trimer can be comprised of DMO, DMO+27, or a combination of both. Therefore, this document will refer to both forms of the protein and all forms of the trimer as the MON 87708 DMO. The identity of the MON 87708 harvested seed processed to make the defatted soybean flour was confirmed by event-specific polymerase chain reaction (PCR) and a copy of the verification of identity is archived in the Monsanto Regulatory archives with the records documenting protein isolation. The purified MON 87708 DMO was stored in a -80 ºC freezer in a buffer solution containing 50 mM potassium phosphate, pH 8.0, 100 mM NaCl, 1 mM dithiothreitol (DTT) and 5% glycerol. The records describing the purification of the MON 87708 DMO are archived in the Monsanto Regulatory archives under Orion lot 11261646.

C.1.2. Description of Assay Control

Protein molecular weight standards (SeeBlue® Plus2 Pre-stained, Invitrogen,) were used to calibrate SDS-PAGE gels and verify protein transfer to polyvinylidene difluoride (PVDF) membranes. The broad range SDS-PAGE molecular weight standards (Bio-Rad, Hercules, CA) were used to determine the apparent molecular weight of both forms of the MON 87708 DMO protein. A peptide mixture (Sequazyme™ Peptide Mass Standards kit, Applied Biosystems, Foster City, CA) was used to calibrate the MALDI-TOF mass spectrometer for tryptic mass and intact mass analysis. Transferrin provided with the kit (GE Healthcare, Piscataway, NJ) was used as a positive control for glycosylation analysis.

C.1.3. MON 87708 DMO Purification

MON 87708 DMO was purified from defatted flour processed from harvested seed of MON 87708. MON 87708 DMO was purified using a combination of extraction, filtration and diafiltration, and various chromatographic separations. A brief description of the purification process is below.

Defatting of seed from MON 87708 was completed at Pilot Plant Corporation in Saskatoon, Canada. The seed was cracked, dehulled, and ground to meal in the presence of dry ice. The meal was then solvent extracted, dried, and shipped to Monsanto and stored in a -20°C cold room.

Aliquots of the defatted flour were used as starting material in the purification process. Approximately 7.5 kg of defatted MON 87708 flour were extracted with 75 liters (L) of extraction buffer (25 mM potassium phosphate, pH 7.2, 10 mM MgCl2, 1 mM DTT,

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1 mM benzamidine-HCl, 1 mM phenylmethylsulfonyl fluoride (PMSF), 1 µM E-64, and 0.1 µM bestatin). The extraction was conducted at room temperature (RT) for 2 hours using a Lightnin® mixer with slow stirring (Graham Transmissions Inc, Menomonee Falls, WI). The resulting slurry was filtered using an Ertel Alsop filter press (Kingston, NY) with Die 42 micro media filter pads and a Cuno filter (Hagedorn and Gannon Co., Inc) after the addition of 7.5 kg of diatomaceous earth (5.6 kg fine hy-flo (Celite Corporation, Lompoc, CA) and 1.9 kg Celite 560 coarse (Sigma-Aldrich, St Louis, MO)). The pads on the press were pre-coated with 1.8 kg of fine hy-flo prior to the filtration of the extract. After washing the press with an additional volume of extraction buffer, the filtrate was collected (final volume: 150 L).

The filtrate was then concentrated at RT to 75 L using a hollow fiber cartridge with a 30,000 kDa molecular weight cutoff (MWCO) (GE Healthcare) at RT to remove small molecules. Solid KCl was added to a final concentration of 0.15 M. The concentrated filtrate was dialfiltered with four exchanges of 25 L each of a phenyl sepharose equilibration buffer (25 mM potassium phosphate, pH 8.0, 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 µM E-64, 0.1 µM bestatin, and 0.15 M KCl).

The first chromatographic step was performed at RT. A 30 L phenyl sepharose (GE Healthcare) column equilibrated with phenyl sepharose equilibration buffer was charged with the dialfiltered extract and then washed with three column volumes (CV) of the phenyl sepharose equilibration buffer. A single CV of elution buffer (50 mM triethanolamine, pH 8.0, 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 µM E-64, 0.1 µM bestatin, and 100 µM dicamba) was loaded onto the column, the flow stopped and the column incubated for 1 hour. The released proteins were eluted with an additional CV of elution buffer and stored at 4°C.

Solid potassium phosphate was added to the phenyl column elution to a final concentration of 25 mM and the pH adjusted to 8.0, followed by the addition of 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 µM E-64, and 0.1 µM bestatin. A 3 L ceramic hydroxyapatite column (CHT) (Bio-Rad) was packed at 4 °C and equilibrated in a buffer containing 25 mM potassium phosphate, pH 8.0, 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 µM E-64, 0.1 µM bestatin, and 100 µM dicamba. Half of the adjusted phenyl elution was charged on the CHT column. The column was washed with two CV of the CHT equilibration buffer. The bound proteins were then eluted with 400 mM potassium phosphate, pH 8.0. The flow-through containing the MON 87708 DMO, detected by immunoblot analysis, was collected. The eluted fractions without the MON 87708 DMO were discarded and the column was re-equilibrated. The second half of the phenyl elution was processed with the CHT column in the same manner as the first half. The flow-through collected from each CHT column run was combined into a single pool.

Before charging onto the next column, fresh, solid DTT and protease inhibitors were added to the CHT column flow-through pool. The flow-through pool from the CHT step was then charged on a 5 L DEAE macroprep (Bio-Rad) column at 4°C and equilibrated in a buffer containing 25 mM Tris-HCl, pH 8.0, 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 µM E-64, 0.1 µM bestatin, and 100 µM dicamba. The DEAE column

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was then washed with five CV of the DEAE equilibration buffer followed by five CV of the equilibration buffer plus 100 mM NaCl. The MON 87708 DMO was eluted with a 20 CV linear NaCl gradient from 100 mM to 350 mM in the equilibration buffer. The fractions collected throughout the gradient were analyzed by immunoblot and those fractions containing the MON 87708 DMO were pooled.

To concentrate the DEAE macroprep pool, it was first diluted with the DEAE equilibration buffer (to reduce the conductivity) and then charged onto a 1 L DEAE macroprep column. After charging, the column was washed with three CV of equilibration buffer and then eluted with minimal volume of the equilibration buffer plus 1 M NaCl. This concentrated the DEAE macroprep pool from 16 to 1.6 L.

The concentrated DEAE macroprep pool was mixed with 1 L of concanavalin A (Con A) sepharose 4B (Sigma-Aldrich) that was previously equilibrated with the DEAE equilibration buffer with fresh, solid DTT and protease inhibitors added. The purification step was run in batch mode at RT and was intended to remove contaminants that bind to Con A, while not binding MON 87708 DMO. The concentrated DEAE macroprep pool was stirred Con A resin for 1 hour, the resin was filtered out using a Büchner funnel and Whatman® filter paper (GE Healthcare). The resin was washed with 3 L of equilibration buffer. All filtrates containing MON 87708 DMO were combined.

The Con A filtrate pool was concentrated on ice for approximately 4 hours using a tangential flow membrane (Sartorius-Stedim, Goettingen, Germany) with a 100 kDa MWCO. After a 10× concentration step, the retentate containing MON 87708 DMO was dialfiltered with 10 volume exchanges of DEAE macroprep equilibration buffer containing 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 μM E-64, and 0.1 μM bestatin.

The concentrated and dialfiltered Con A pool was further purified on CHT at RT, this time in a binding mode where MON 87708 DMO was bound to the resin. This is achieved in the complete absence of phosphate where MON 87708 DMO binds to the CHT column and is then eluted. A 1 L CHT column was packed and equilibrated with the DEAE macroprep equilibration buffer with fresh DTT and protease inhibitors. The column was washed with three CV of equilibration buffer. The protein was eluted with a linear phosphate gradient using an elution buffer (400 mM potassium phosphate, pH 8.0, 1 mM DTT, 1 mM benzamidine-HCl, 1 mM PMSF, 1 μM E-64, 0.1 μM bestatin, and 100 μM dicamba) increasing from 0% to 50% over 10 CV. The fractions were collected and analyzed by SDS-PAGE. Those containing at least 80% pure MON 87708 DMO as estimated by gel densitometry were pooled.

This entire purification procedure was repeated with two additional batches of 7.5 kg of defatted flour from MON 87708. After analysis, all final CHT pools were combined into a single final pool that was concentrated on ice for approximately 2 hours to 370 ml with a tangential flow membrane with a 30 kDa MWCO. The concentrated pool was dialyzed against enzyme storage buffer (50 mM potassium phosphate, pH 8.0, 100 mM NaCl, 5% glycerol, and 1 mM DTT). Four liters of storage buffer were used and exchanged

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twice over two days and the dialysis was conducted at 4°C. The dialysate was aliquoted, assigned APS lot 11261646 and stored at -80°C.

C.1.4. Molecular Weight and Purity Estimation using SDS-PAGE Method

SDS-PAGE analysis was performed to determine the molecular weight and purity of MON 87708 DMO.

An aliquot of MON 87708 DMO was mixed with 5 × loading buffer (LB) to a final total protein concentration of 0.09 µg/µl and heated at 99°C for three minutes. A molecular weight marker (Broad Range MW Marker, Bio-Rad) was diluted to a final total protein concentration of 0.9 µg/µl. MON 87708 DMO was loaded in duplicate at 0.5, 1.0 and 1.5 µg of total protein per lane onto a pre-cast Tris glycine 4-20% polyacrylamide gradient 10-well gel (Invitrogen). The molecular weight markers were loaded in parallel at 4.5 µg protein per lane. Electrophoresis was performed at a constant 125 V for 90 minutes. Proteins were fixed by placing the gel in a solution of 40% (v/v) methanol and 7% (v/v) acetic acid for 30 minutes, stained for 16 hours with Brilliant Blue G Colloidal stain (Sigma-Aldrich), destained 30 seconds with a solution containing 10% (v/v) acetic acid and 25% (v/v) methanol, and finally destained with 25% (v/v) methanol for 6 hours. Analysis of the gel was performed using a Bio-Rad GS-800 densitometer with the supplied Quantity One® software (version 4.4.0). Molecular weight markers were used to estimate the apparent molecular weight of each observed band. All visible bands within each lane were quantified using Quantity One software. Apparent molecular weight was obtained for both forms of the MON 87708 DMO protein while the purity was calculated based on the addition of the average purity of both proteins. The results were reported as an average of all six samples loaded onto the gel containing MON 87708 DMO.

C.1.5. Immunoblot Analysis Method

Immunoblot analysis was performed to confirm the identity of MON 87708 DMO.

An aliquot of MON 87708 DMO was diluted with water and mixed with 5 × LB (312 mM Tris-HCl, 20% (v/v) 2-mercaptoethanol, 10% (w/v) SDS, 0.025% (w/v) bromophenol blue, and 50% (v/v) glycerol, pH 6.8), heated at 99°C for 3 minutes, and applied on a pre-cast Tris glycine 4- 20% polyacrylamide gradient 10-well gel (Invitrogen). Three amounts (20, 30, and 40 ng) of MON 87708 DMO were loaded in duplicate on the gel. Electrophoresis was performed at a constant 125 V for 90 minutes. Pre-stained molecular weight markers (SeeBlue® Plus2 Pre-stained, Invitrogen) were loaded in parallel to verify electrotransfer of the proteins to the membrane and estimate the size of the immunoreactive bands observed. Electrotransfer to a 0.45 µm PVDF membrane (Invitrogen) was performed for 90 minutes at a constant 25 V.

For immunodetection, the membrane was blocked for 1 hour with 10% (w/v) Non-Fat Dried Milk (NFDM) in 1× Phosphate Buffered Saline containing 0.05% (v/v) Tween-20 (PBST). The membrane was then probed with a 1:3,000 dilution of goat anti-DMO antibody, which is specific for both forms of the MON 87708 DMO protein, in 5% (w/v)

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NFDM in PBST for one hour. Excess antibody was removed using three 10 minutes washes with PBST. Finally, the membrane was probed with horseradish peroxidase (HRP)-conjugated rabbit anti-goat IgG (Thermo, Rockford, IL) at a dilution of 1:10,000 in 5% (w/v) NFDM in PBST for 1 hour. Excess HRP-conjugate was removed using three 10 minutes washes with PBST. All incubations were performed at RT. Immunoreactive bands were visualized using the ECL (Enhanced Chemiluminescence) detection system (GE Healthcare) and exposed to Amersham Hyperfilm (GE, Healthcare). The film was developed using a Konica SRX-101A automated film processor (Tokyo, Japan). Three exposures (20, 30, and 60 seconds) were taken and the 20 second exposure was scanned using a Bio-Rad GS-800 densitometer with the supplied Quantity One software (version 4.4.0).

C.1.6. MALDI-TOF Tryptic Mass Map Analysis Method

MALDI-TOF mass spectrometry was used to confirm the identity of both forms of the MON 87708 DMO proteins. The proteins were first separated by SDS-PAGE prior to trypsinization.

An aliquot (89.5 µl) of MON 87708 DMO was mixed with 22.5 µl of 5 × LB, heated at 99°C for 3 minutes and loaded in four lanes (three lanes each loaded with 4.2 µg and one lane with 3.1 µg of total protein) onto a pre-cast Tris glycine 4-20% polyacrylamide gradient 10-well gel (Invitrogen). Pre-stained MW markers (SeeBlue Plus2 Pre-stained, Invitrogen) were loaded in parallel to estimate the size of the stained bands observed. Electrophoresis was carried out at a constant 150 V for 80 minutes. Following electrophoresis, the gel was stained with Brilliant Blue G Colloidal (Sigma-Aldrich). The bands corresponding to DMO or DMO+27 were excised from four lanes of the gel, destained, reduced, and alkylated. Each gel band was destained for 30 minutes by incubation in 100 µl of destain solution (40% methanol, 50% water, and 10% glacial acetic acid) in a microfuge tube. This step was repeated twice for 60 minutes each, removing all visible Brilliant Blue G Colloidal stain. Following destaining, the gel bands were incubated in 100 µl per band of 100 mM ammonium bicarbonate buffer for 16 hours at RT. The protein was reduced in 100 µl of 10 mM DTT solution for two hours at 37 °C. After removing the reducing solution, the protein in the gel was alkylated by incubating in 100 µl of 20 mM iodoacetic acid. The alkylation reaction was allowed to proceed at RT for 20 minutes in the dark. The gel containing the protein band was incubated in 200 µl of 25 mM ammonium bicarbonate buffer for 15 minutes at RT. This step was repeated two additional times for 15 minutes each; then the gel band was dried using a Savant Speed Vac concentrator (Holbrook, NY). Each gel band was rehydrated with 20 µl of 0.02 µg/µl trypsin in 25 mM ammonium bicarbonate and 10% acetonitrile, and the incubated for approximately one hour at RT. Following incubation, the excess solution was removed and the gel/trypsin reaction mixture was incubated overnight at 37°C in 40 µl of 25 mM ammonium bicarbonate and 10% acetonitrile. The following day, the sample was sonicated for 5 minutes, and the supernatant transferred to a new tube and dried using a Speed Vac concentrator (Extract 1). The gel band(s) was resuspended in 30 µl of a solution consisting of 60% acetonitrile, 0.1% trifluoroacetic acid (TFA), and 0.1% octyl-β-D-glucopyranoside, and then sonicated for 5 minutes. After transfer of the supernatant to a new microcentrifuge tube, this step was repeated

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once and the combined supernatants were dried using the Speed Vac concentrator (Extract 2). Extracts 1 and 2 were separately dissolved in 20 µl 0.1% TFA and then dried using a Speed Vac concentrator. Finally, Extract 1 was dissolved in 5 µl of 50% acetonitrile/0.1% TFA, while Extract 2 was dissolved in 10 µl of the same solution. To maximize the solubilization, each sample was sonicated for 5 minutes.

Mass calibration of the mass spectrometer was performed using an external peptide mixture (Sequazyme™ Peptide Mass Standards Kit, Calibration Mixture 2, Applied Biosystems). The samples Extract 1 and Extract 2 (0.3 µl) were co-crystallized with 0.75 µl each of the following matrix solutions: dihydroxybenzoic acid (DHB), α-cyano-4-hydroxy cinnamic acid (α-cyano), and 3,5 dimethoxy-4 hydroxycinnamic acid (sinapinic acid) at separate locations on the analysis plate. The samples in DHB matrix were analyzed in the 300 to 5,000 Dalton (Da) range. The samples in α-cyano matrix were analyzed in the 500 to 5,000 Da range. The samples in sinapinic acid matrix were analyzed in the 500 to 7,000 Da range. Protonated (MH+) peptide masses were observed monoisotopically in reflector mode (Aebersold, 1993), except above 3,000 Da, where mass-averaged values were used. GPMAW32® software (Lighthouse data, Denmark) was used to generate a theoretical trypsin digestion of the deduced DMO and DMO+27 amino acid sequences. Masses were calculated for each theoretical peptide and compared to the raw experimental mass data. Below 1000 Da, experimental masses (MH+) were assigned to peaks when two or more isotopically resolved peaks were observed. Above 1000 Da, experimental masses (MH+) were assigned to peaks when three or more isotopically resolved peaks were observed. Peaks were not assessed if the peak heights were less than approximately twice the baseline noise, or when a mass could not be assigned due to overlap with a stronger mass signal. Known autocatalytic segments from trypsin digestion were identified in the raw data. The list of experimental masses was compared to the theoretical list from the GPMAW software. Those experimental masses within 1 Da of a theoretical mass were matched. All matching masses were tallied and a coverage map was generated. The tryptic mass map coverage was considered acceptable if ≥ 40% of the protein sequence was identified by matching experimental masses observed for the tryptic peptide segments to the expected masses for the segments.

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C.1.7. N-Terminal Sequencing Method

N-terminal sequencing using automated Edman degradation chemistry (Hunkapiller et al., 1983) was used to confirm the identity of both forms of the MON 87708 DMO proteins.

Ninety microliters of MON 87708 DMO were mixed with 22.5 µl of 5× LB, heated at 99°C for 3 minutes and loaded in four lanes (10 µl/lane) onto a pre-cast Tris glycine 4-20% polyacrylamide gradient 10-well gel (Invitrogen). Electrophoresis was carried out at a constant voltage of 150 V for 80 minutes. Proteins in the gel were electrotransferred to a PVDF (Invitrogen) membrane for 90 minutes in a buffer containing 10 mM CAPS, pH 11 and 10% methanol at a constant voltage of 25 V. Pre-stained molecular weight markers (SeeBlue Plus2 Pre-stained, Invitrogen) were loaded in parallel to verify the electrotransfer of protein to the membrane and estimate the size of the stained bands observed. The blot was stained with Ponceau S (Sigma-Aldrich).

Following electrotransfer and staining, the bands corresponding to DMO and DMO+27 were excised based on apparent molecular weight from the blot and N-terminal sequence analyses were performed for 15 cycles using automated Edman degradation chemistry (Hunkapiller et al., 1983). An Applied Biosystems 494 Procise™ Protein Sequencing System with 140C Microgradient HPLC pump, ABI 785A Programmable Absorbance Detector and Procise™ Control Software (version 2.1) were used. Chromatographic data were collected using Atlas™ 2003 software (Thermo Fisher Scientific Inc, Waltham, MA). A PTH (Phenylthiohydantoin) -amino acid standard mixture (Applied Biosystems) was used as the calibration standard in the chromatographic analysis. This mixture served to verify system suitability criteria such as percent peak resolution and relative amino acid chromatographic retention times. A control protein, 10 pmol β lactoglobulin (Applied Biosystems), was analyzed before and after the analysis to verify that the sequencer met performance criteria for repetitive yield and sequence identity.

C.1.8. Glycosylation Analysis Method

Glycosylation analysis was used to determine whether either form of the MON 87708 DMO proteins were post-translationally modified with covalently bound carbohydrate moieties.

An aliquot of MON 87708 DMO and the positive control, transferrin (GE Healthcare) were each diluted with water and mixed with 5 × LB. These samples were heated at 101.0 °C for three minutes, cooled, and loaded on a Tris glycine 4-20% polyacrylamide gradient 10-well mini-gel (Invitrogen). Three amounts of transferrin (50, 100, and 200 ng) and two amounts (100 and 200 ng) of the purity-corrected DMO enzyme was loaded in the gel. SeeBlue® Plus2 Pre-stained protein molecular weight markers (Invitrogen) were loaded to verify electrotransfer of the proteins to the membrane. Electrophoresis was performed at a constant 150 V for 87 minutes. Electrotransfer to a 0.45 μm PVDF membrane (Invitrogen) was performed for 60 minutes at a constant 25 V, followed by 30 minutes at 30 V.

Carbohydrate detection was performed directly on the PVDF membrane using the GE Healthcare Glycosylation Detection Module (Cat. No. RPN 2190). The manufacturer's protocol was followed and all the reagents except phosphate buffered saline (PBS) were provided with the kit. All steps were performed at RT. Following electrotransfer to PVDF membrane, the blot was incubated in 30 ml of PBS for 10 minutes, followed by incubation with 20 ml of 10 mM NaIO4 for 20 minutes in the dark. The membrane was rinsed twice with PBS and washed three times with 20 ml PBS for 10 minutes each. The membrane was incubated with 20 ml solution consisting of 0.125 mM biotin-hydrazide, 100 mM acetate, pH 5.5 for 60 minutes followed by two PBS rinses and three 10 minute washes with PBS. The membrane was blocked for 60 minutes using 5% blocking reagent in PBS followed by two PBS rinses and three 10 minute washes with PBS. The membrane was incubated with strepavidin-HRP at 1:6000 dilution for 30 minutes. After two PBS rinses and three 10 minute washes with PBS, the membrane was developed with

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ECL detection reagents by mixing 1 ml of Reagent 1 and 1 ml of Reagent 2. After one minute incubation, the excess detection solution was removed by blotting with paper towels and the blot was exposed to Hyperfilm ECL (GE Healthcare). The film was developed using a Konica SRX-101A automated film processor (Tokyo, Japan). Three exposures (30 seconds, 1 and 2 minutes) were performed. The image was captured using a Bio-Rad GS-800 densitometer with the supplied Quantity One® software (version 4.4.0).

C.1.9. Functional Activity Analysis Method

The specific activity of MON 87708 DMO was determined by quantifying the conversion of 3,6-dichloro-2-methoxybenzoic acid (dicamba) to 3,6 dichlorosalicylic acid (DCSA) via HPLC (Agilent Technologies 1100 series, Santa Clara, CA) separation and fluorescence detection (Agilent Technologies 1200 series, G1321A). The standard assays were conducted in 200 µl solutions consisting of 25 mM potassium phosphate, pH 7.2, 3.4 µg Ferredoxin, 3.4 µg Reductase, 0.5 mM FeSO4, 10 mM MgCl2, 0.7 mM NADH, 0.3 mM dicamba, 2 µl (42.48 U/ml) of formaldehyde dehydrogenase and either 2 µg MON 87708 DMO or 1 µg HIS-DMO as an assay positive control. The reactions were performed in PCR tubes (Sorenson, Salt Lake City, UT) and incubated at 30°C for 15 minutes. Reactions were initiated by the addition of dicamba and quenched with the addition of 50 µl of 5% H_2SO_4. Reactions were then filtered using Whatman Anotop 10 filters (0.2 µm, GE healthcare), and 40 µl was transferred to a HPLC sample vial (200 µl, Agilent) for analysis. Twenty-five microliters of the filtered reaction was injected onto a Phenomenex® Synergi 4 µm C18/ODS Hydro-RP column (150 x 4.6 mm ID, Torrance, CA). The mobile phase consisted of solvent A (21.5 mM phosphoric acid) and solvent B (100% acetonitrile) running at 1.5 ml/min. DCSA was eluted from the column using a linear gradient from 90% to 40% solvent A for the first 14 minutes, followed by a step to 10% solvent A for 1 minute and then re-equilibration at 90% solvent A for 10 minutes before the next injection. DCSA was monitored by the detection of fluorescent emission at 424 nm (excitation 306 nm) and quantified relative to a standard curve of DCSA generated using 0.1, 0.3, 0.6, 0.9, 1.2, 2.4, and 4.8 nmol/250 µl. Chromatographic data were collected using Atlas™ 2003 software (Thermo Fisher Scientific Inc). The specific activity was calculated based on the amount of purity corrected MON 87708 DMO added to the reaction mixture and expressed as nmol of DCSA produced per minute per mg of MON 87708 DMO (nmol/min/mg).

C.1.10. Results of MON 87708 DMO Proteins Molecular Weight and Purity

The apparent molecular weights of the MON 87708 DMO proteins were determined by using SDS-PAGE and the gel stained using Brilliant Blue G Colloidal stain (Sigma-Aldrich). Purity and apparent molecular weight of DMO and DMO+27 were determined using densitometric analysis of the gel (Figure C-1). As summarized in Table C-1, apparent molecular weight values were averaged from duplicated loads of 0.5, 1.0, and 1.5 µg of total protein (Figure C-1, lanes 2-7). The predominant bands identified as DMO and DMO+27 were estimated to have apparent molecular weights of 39.8 kDa and 42.0 kDa, respectively. The average purity of the combined DMO proteins was 81%.

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Table C-1. Molecular Weight and Purity of the MON 87708-Produced DMO Proteins

Total Protein Loaded	Apparent Molecular Weight (kDa)		Purity (%)		
	DMO	DMO+27	DMO	DMO+27	DMO Proteins
0.5 µg in lane 3	39.2	41.6	34	44	
0.5 µg in lane 4	39.2	41.5	33	43	
1.0 µg in lane 5	39.5	41.7	36	46	
1.0 µg in lane 6	39.8	42.0	34	46	
1.5 µg in lane 7	40.3	42.4	37	47	
1.5 µg in lane 8	40.7	42.8	35	47	
Average	39.8	42.0	35	46	81

The apparent molecular weight and the purity of DMO and DMO+27 were determined by densitometric analysis of SDS PAGE shown in Figure C-1. Final molecular weight was rounded to one decimal place and purity was reported as a whole number percentage. Purity of the MON 87708 DMO proteins equals the average purity of DMO plus the average purity of DMO+27.

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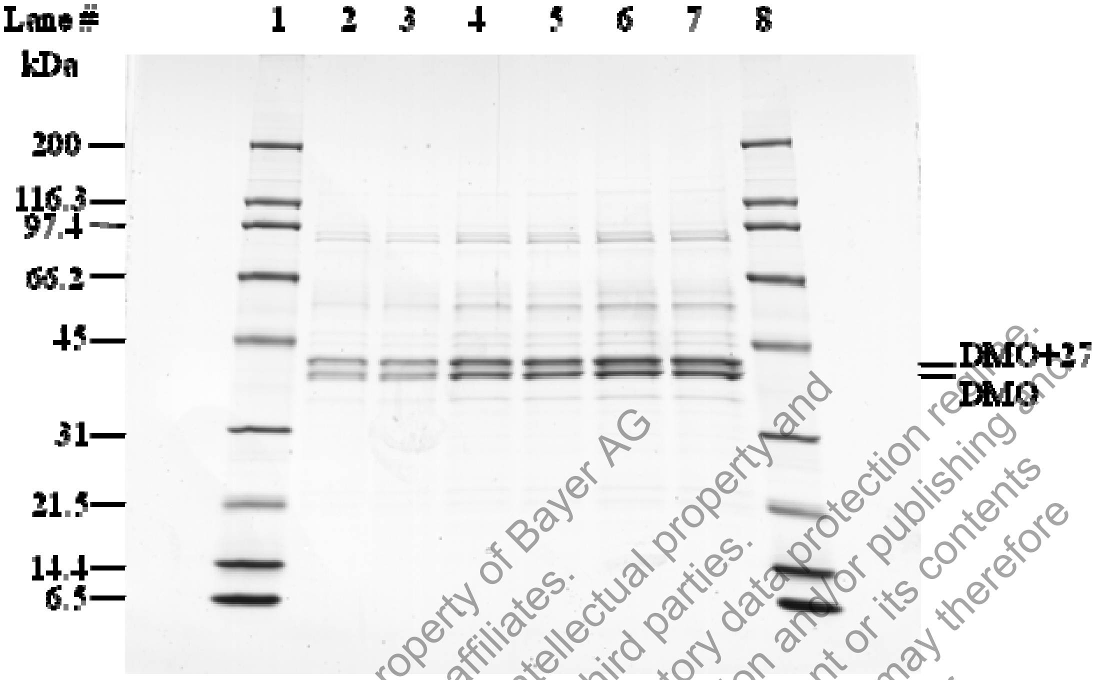

Figure C-1. Molecular Weight and Purity Analysis of MON 87708 DMO Proteins
An aliquot of MON 87708 DMO was separated on a 4 - 20% Tris glycine polyacrylamide gradient gel and then stained with Brilliant Blue G Colloidal stain. Approximate apparent molecular weights (kDa) are shown on the left and correspond to the markers loaded in Lanes 1 and 8. Empty lanes were cropped.

Lane	Sample	Amount (µg)
1	Broad Range MW markers	4.5
2	MON 87708 DMO proteins	0.5
3	MON 87708 DMO proteins	0.5
4	MON 87708 DMO proteins	1.0
5	MON 87708 DMO proteins	1.0
6	MON 87708 DMO proteins	1.5
7	MON 87708 DMO proteins	1.5
8	Broad Range MW markers	4.5

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C.11. Results of Immunoblot Analysis

On the immunoblot, the goat anti-DMO antibody recognized two bands migrating at the expected apparent molecular weights of approximately 39.8 kDa (DMO) and 42.0 kDa (DMO+27), respectively (Figure C-2). As expected, the intensity of the immunoreactive bands increased with increasing amount of total protein loaded. No additional bands were observed. This immunoblot analysis confirmed the identity of both forms of the MON 87708 DMO protein.

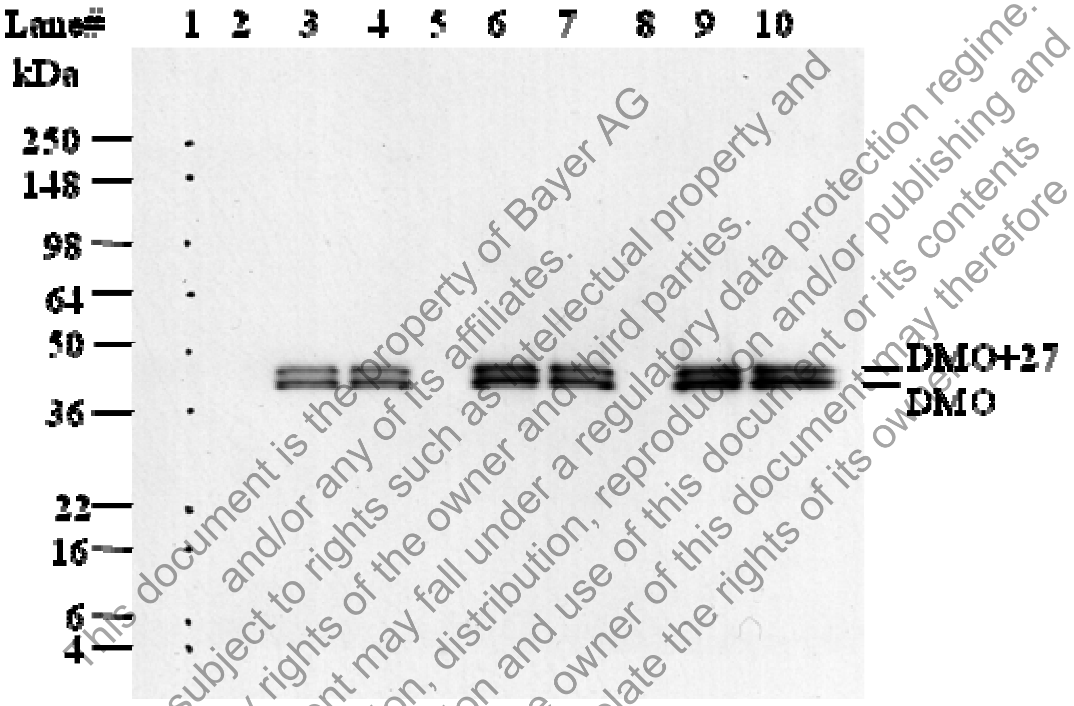

Figure C-2. Immunoblot Analysis of MON 87708 DMO Proteins
An aliquot of MON 87708 DMO and molecular weight markers were separated by SDS-PAGE and electrotransferred to a PVDF membrane. The membrane was incubated with goat anti-DMO antibody and immunoreactive bands were visualized using an ECL system. Approximate MWs (kDa) are shown on the left and correspond to the markers loaded in Lane 1. The 20 second exposure is shown.

Lane	Sample	Amount (ng)
1	See Blue Plus2 Pre-Stained MW markers	—
2	empty	
3	MON 87708 DMO proteins	20
4	MON 87708 DMO proteins	20
5	empty	
6	MON 87708 DMO proteins	30
7	MON 87708 DMO proteins	30
8	empty	
9	MON 87708 DMO proteins	40
10	MON 87708 DMO proteins	40

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C.12. Results of MALDI-TOF Tryptic Mass Map Analysis

The identity of both forms of the MON 87708 DMO proteins was confirmed by tryptic mapping using MALDI-TOF MS analysis of the fragments. Prior to analysis, DMO and DMO+27 were separated by SDS-PAGE, reduced, alkylated and digested with trypsin. The ability to identify a protein using this method is dependent upon matching a sufficient number of observed tryptic peptide fragment masses with predicted tryptic peptide fragment masses. In general, protein identification made by peptide mapping is considered to be reliable if the measured coverage of the sequence is 15% or higher with a minimum of five matched peptides (Jensen et al., 1997).

There were 26 unique peptides identified from DMO that corresponded to the expected masses of the DMO trypsin-digested peptides while 29 fragments from DMO+27 were found to match the expected peptides (Tables C-2 and C-3, respectively). The identified peptides were used to assemble a coverage map indicating the matched peptide sequences for the entire DMO and DMO+27 protein sequences, resulting in 77.4% (263/340) and 82.0% (301/367) coverage of the amino acid sequence, respectively (Figures C-3 and C-4). N-terminal peptides of both DMO and DMO+27 were identified and consistent with the N-terminal sequencing data that determined the N-terminal methionine was missing in DMO and methylated in DMO+27 (Tables C-2 and C-3; Figures C-3 and C-4). These results confirm the identity of both forms of the MON 87708 DMO proteins.

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Table C-2. Summary of the Tryptic Masses Identified for the MON 87708 DMO Protein Using MALDI-TOF MS

Matrix						Expected Mass[1]	Difference[2]	AA position[3]	Fragment
α-Cyano		DHB		Sinapinic acid					
Ext.1	Ext.2	Ext.1	Ext.2	Ext.1	Ext.2				
			331.20			331.22	0.02	304-305	RR
		391.34				391.18	0.16	293-295	EDK
		435.38	435.38			435.27	0.11	206-208	FLR
593.61	593.61	593.51	593.53			593.34	0.27	2-6	ATFVR
720.67	720.68	720.60	720.60			720.37	0.30	131-136	VDPAYR
833.78	833.80	833.74	833.77			833.45	0.33	99-105	SFPVVER
856.77	856.78	856.72	856.75			856.43	0.34	242-248	EQSIHSR
914.89	914.91	914.84	914.88			914.53	0.36	296-303	VVVEAIER
1030.96	1030.97	1030.92	1030.92			1030.57	0.39	284-292	SWQAQALVK
1108.93	1108.95	1108.89	1108.94			1108.50	0.43	167-176	ANAQTDAFDR
		1171.08				1170.63	0.45	194-205	IPGGTPSVLMAK
1276.17	1276.20	1276.19	1276.21	1276.19		1275.73	0.44	26-36	TILDTPLALYR
1287.14		1287.19				1286.70	0.44	293-303	EDKVVVEAIER
1429.18	1429.20	1429.23	1429.26	1429.20		1428.69	0.49	209-221	GANTPVDAWNDIR
		1502.35	1502.37	1502.34		1501.79	0.56	180-193	EVIVGDGEIQALMK
1507.27	1507.27	1507.32				1506.73	0.54	167-179	ANAQTDAFDRLER
1578.24	1578.27	1578.32	1578.33	1578.30		1577.73	0.51	270-283	NFGIDDPEMDGVLR
1745.42	1745.51	1745.59		1745.56		1744.93	0.49	225-241	VSAMLNFIAVAPEGTPK
1762.48	1762.48	1762.62		1762.54		1761.90	0.58	37-52	QPDGVVAALLDICPHR
1994.65	1994.67	1994.76		1994.78		1994.03	0.62	150-166	LLVDNLMDLGHAQYVHR
2143.78	2143.84	2143.94		2143.96	2143.95	2143.12	0.66	7-25	NAWYVAALPEELSEKPLGR
2294.97				2294.93		2294.09	0.88	306-326	AYVEANGIRPAMLSCDEAAVR
2398.86	2398.77			2399.15		2398.08	0.78	249-269	GTHILTPETEASCHYFFGSSR
2581.87				2582.22		2582.34	0.47	225-248	VSAMLNFIAVAPEGTPKEQSIHSR
2700.08				2700.31		2699.25	0.83	106-130	DALIWICPGDPALADPGAIPDFGCR
				4218.47[4]		4217.77[4]	0.70	99-136	SFPVVERDALIWICPGDPALADPGAIPDFGCRVDPAYR

---

[1] Only experimental masses that matched expected masses are listed in the table.

[2] The number represents the difference between the expected mass and the first column, which has the corresponding numbers.

[3] AA position refers to amino acid position within the predicted DMO sequence as depicted in Figure C-3.

[4] Mass average.

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Table C-3. Summary of the Tryptic Masses Identified for the MON 87708 DMO+27 Protein Using MALDI-TOF MS

Matrix						Expected Mass[1]	Difference[2]	AA position[3]	Fragment
α-Cyano		DHB		Sinapinic acid					
Ext.1	Ext.2	Ext.1	Ext.2	Ext.1	Ext.2				
			331.19			331.22	0.03	331-332	RR
		435.30				435.27	0.03	233-235	FLR
720.55	720.64	720.47	720.55			720.37	0.18	158-163	VDPAYR
795.61	795.71	795.54	795.66			795.42	0.19	27-33	AMATFVR
833.65	833.73	833.59	833.69			833.45	0.20	126-132	SFPVVER
856.64	856.72	856.58	856.64			856.43	0.21	269-275	EQSIHSR
914.74		914.69				914.53	0.21	323-330	VVVEAIER
1030.80	1030.89	1030.75				1030.57	0.23	311-319	SWQAQALVK
1069.78	1069.92					1069.57	0.21	1-9	M*QVWPPIGK
1108.75	1108.90	1108.71				1108.50	0.25	194-203	ANAQTDAFDR
			1170.98			1170.66	0.32	221-232	IPGGTPSVLMAK
1275.97	1276.12	1275.98	1276.14	1275.97		1275.73	0.24	53-63	TILDTPLALYR
1286.95		1286.97				1286.70	0.25	320-330	EDKVVVEAIER
1428.95	1429.10	1429.00	1429.26	1428.93		1428.69	0.26	236-248	GANTPVDAWNDIR
		1470.93		1469.94		1470.63	0.30	164-176	TVGGYGHVDCNYK
				1502.10		1501.79	0.31	207-220	EVIVGDGEIQALMK
1507.01	1507.18	1507.03				1506.73	0.28	194-206	ANAQTDAFDRLER
1565.13	1565.30	1565.22	1565.34			1564.87	0.26	11-23	KFETLSYLPPLTR
1578.02	1578.14	1578.06	1578.29	1578.04		1577.73	0.29	297-310	NFGIDDPEMDGVLR
1693.26	1693.38	1693.29				1692.97	0.29	10-23	KKFETLSYLPPLTR
1745.17	1745.36	1745.28	1745.51	1745.22		1744.93	0.24	252-268	VSAMLNFIAVAPEGTPK
1762.17	1762.37	1762.29				1761.90	0.27	64-79	QPDGVVAALLDICPHR
1994.34	1994.55	1994.48		1994.42		1994.03	0.31	177-193	LLVDNLMDLGHAQYVHR
2143.46	2143.63	2143.57	2143.98	2143.57		2143.12	0.34	34-52	NAWYVAALPEELSEKPLGR
				2294.62		2294.09	0.53	333-353	AYVEANGIRPAMLSCDEAAVR
	2398.72	2398.49		2398.52		2398.08	0.64	276-296	GTHILTPETEASCHYFFGSSR
				2581.78		2582.34	0.56	252-275	VSAMLNFIAVAPEGTPKEQSIHSR
		2699.73		2699.84		2699.25	0.48	133-157	DALIWICPGDPALADPGAIPDFGCR
				4215.70		4215.03	0.67	126-163	SFPVVERDALIWICPGDPALADPGAIPDFGCRVDPAYR

[1] Only experimental masses that matched expected masses are listed in the table.

[2] The number represents the difference between the expected mass and the first column, which has the corresponding numbers.

[3] AA position refers to amino acid position within the predicted DMO+27 sequence as depicted in Figure C-4.

*Methylated methionine.

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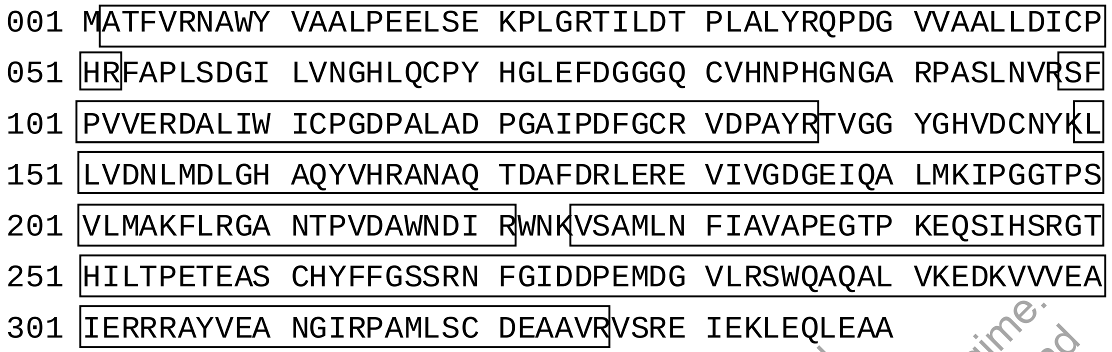
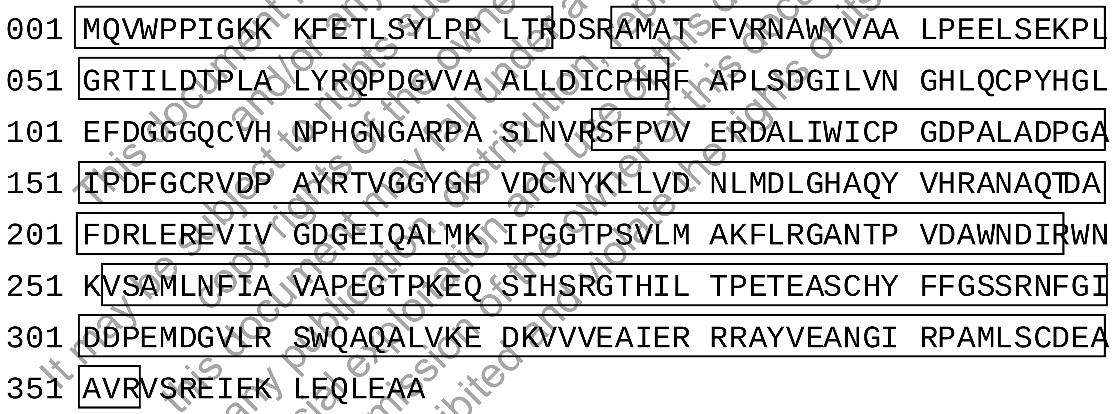


```
001 MATFVRNAWY VAALPEELSE KPLGRTILDT PLALYRQPDG VVAALLDICP
051 HRFAPLSDGI LVNGHLQCPY HGLEFDGGGQ CVHNPHGNGA RPASLNVRSF
101 PVVERDALIW ICPGDPALAD PGAIPDFGCR VDPAYRTVGG YGHVDCNYKL
151 LVDNLMDLGH AQYVHRANAQ TDAFDRLERE VIVGDGEIQA LMKIPGGTPS
201 VLMAKFLRGA NTPVDAWNDI RWNKVSAMLN FIAVAPEGTP KEQSIHSRGT
251 HILTPETEAS CHYFFGSSRN FGIDDPEMDG VLRSWQAQAL VKEDKVVVEA
301 IERRRAYVEA NGIRPAMLSC DEAAVRVSRE IEKLEQLEAA
```

Figure C-3. MALDI-TOF MS Coverage Map of the MON 87708 DMO Protein
The amino acid sequence of DMO was deduced from the *dmo* coding region present in MON 87708. Boxed regions correspond to tryptic peptides that were identified from DMO using MALDI-TOF MS. In total, 77.4% (263 of 340 total amino acids) of the expected protein sequence was identified.



```
001 MQVWPPIGKK KFETLSYLPP LTRDSRAMAT FVRNAWYVAA LPEELSEKPL
051 GRTILDTPLA LYRQPDGVVA ALLDICPHRF APLSDGILVN GHLQCPYHGL
101 EFDGGGQCVH NPHGNGARPA SLNVRSFPVV ERDALIWICP GDPALADPGA
151 IPDFGCRVDP AYRTVGGYGH VDCNYKLLVD NLMDLGHAQY VHRANAQTDA
201 FDRLEREVIV GDGEIQALMK IPGGTPSVLM AKFLRGANTP VDAWNDIRWN
251 KVSAMLNFIA VAPEGTPKEQ SIHSRGTHIL TPETEASCHY FFGSSRNFGI
301 DDPEMDGVLR SWQAQALVKE DKVVVEAIER RRAYVEANGI RPAMLSCDEA
351 AVRVSREIEK LEQLEAA
```

Figure C-4. MALDI-TOF MS Coverage Map of the MON 87708 DMO+27 Protein
The amino acid sequence of DMO+27 was deduced from the *dmo* coding region and *RbcS* present in MON 87708. Boxed regions correspond to tryptic peptides that were identified from DMO+27 using MALDI-TOF MS. In total, 82.0% (301 of 367 total amino acids) of the expected protein sequence was identified.

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C.13. Results of N-terminal Sequencing

N-terminal sequence analysis of the two major protein bands on the PVDF membrane (Figure C-2) returned a sequence of 15 amino acids per band that matched the expected N-terminal sequences of DMO and DMO+27 (Figures C-5 and C-6, respectively), which were deduced from the *dmo* coding region present in the seed of MON 87708 (Section IV). The N-terminal methionine residue in DMO was not observed, indicating that it was removed during posttranslational processing of the protein. Removal of the N-terminal methionine occurs through methionine aminopeptidase (Arfin and Bradshaw, 1988; Bradshaw et al., 1998; Polevoda and Sherman, 2000) and is common in many organisms.

In the case of DMO+27, the first cycle of N-terminal sequence analysis resulted in a PTH-amino acid derivative that corresponds to a methylated modification of the N-terminal methionine. It is well-known that the amino-terminal methionine of the Rubisco small subunit is post-translationally modified to N-methyl-methionine *in vivo* in pea and other plant species (Grimm et al., 1997; Whitney and Andrews, 2001).

The N-terminal sequencing results clearly confirm the identity of the DMO and DMO+27 isolated from the seed of MON 87708.

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Amino acid residue # from the N-terminus →	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Expected Sequence	M	A	T	F	V	R	N	A	W	Y	V	A	A	L	P	E
	|	|	|	|	|	|	|	|	|	|	|	|	|	|	|	|
Experimental Sequence	-	A	T	F	V	R	N	A	W	Y	V	A	A	L	P	E

Figure C-5. N-Terminal Sequence of the MON 87708 DMO Protein
The expected amino acid sequence of the N-terminus of DMO was deduced from the *dmo* coding region present in MON 87708. The experimental sequence obtained from DMO was compared to the expected sequence. (-) indicates the residue was not observed.

Amino acid residue # from the N-terminus →	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Expected Sequence	M	Q	V	W	P	P	I	G	K	K	K	F	E	T	L
	|	|	|	|	|	|	|	|	|	|	|	|	|	|	|
Experimental Sequence	M*	Q	V	W	P	P	I	G	K	K	K	F	E	T	L

Figure C-6. N-Terminal Sequence of the MON 87708 DMO+27 Protein
The expected amino acid sequence of the N-terminus of DMO+27 was deduced from the *dmo* coding region present in MON 87708. The experimental sequence obtained from DMO+27 was compared to the expected sequence. M*, methylated methionine.

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C.1.14. Results of Glycosylation Analysis

To test whether DMO or DMO+27 was glycosylated when expressed in the seed of MON 87708, the MON 87708 DMO proteins were analyzed for glycosylation using a GE Glycoprotein Detection Module (GE healthcare). Transferrin, a naturally glycosylated protein, was used as a positive control in the assay. The results of this analysis are presented in Figure C-7. The positive control was clearly detected at the expected molecular weight and the bands increased with increasing protein concentration (Figure C-7, lanes 2-4). No bands were observed for DMO or DMO+27 at their expected molecular weight positions (39.8 and 42.0 kDa) (Figure C-7, lanes 5 and 6) indicating that both forms of the DMO protein are not glycosylated.

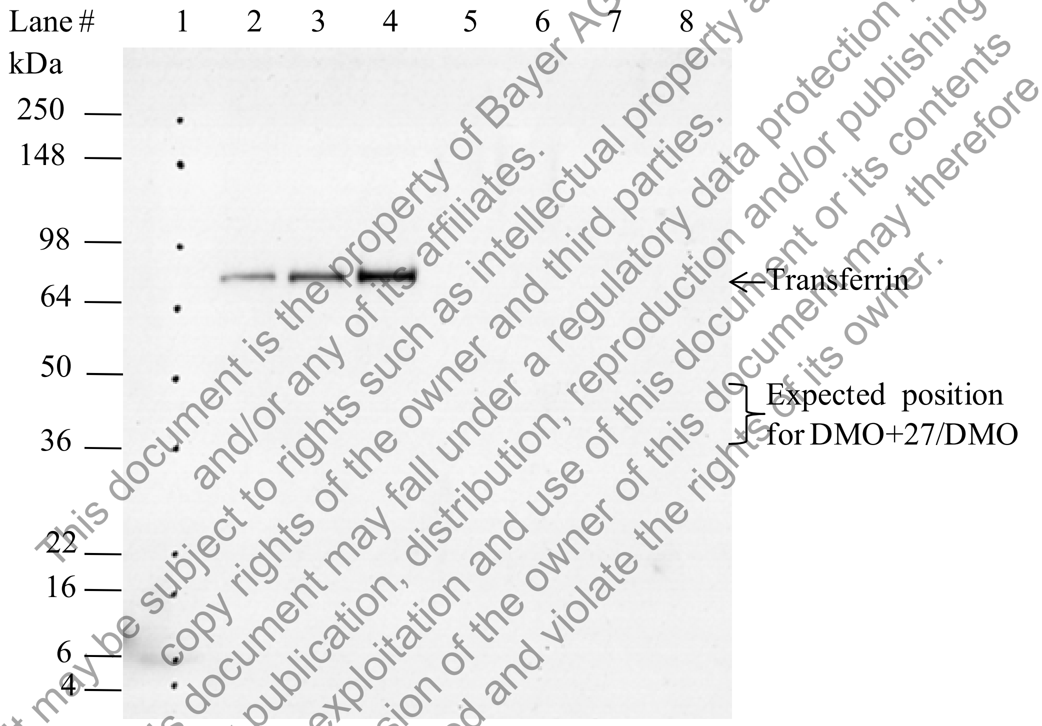

Figure C-7. Glycosylation Analysis of the MON 87708 DMO Proteins
Molecular weight markers, transferrin (positive control) and an aliquot of the MON 87708 DMO were separated by SDS-PAGE (4 - 20%) and electrotransferred to a PVDF membrane. The image was captured using a Bio-Rad GS800 with Quantity One software (version 4.4.0). The 30 second exposure is shown.

Lane	Sample	Amount (ng)
1	See Blue Plus2 Pre-Stained MW markers	—
2	Transferrin	50
3	Transferrin	100
4	Transferrin	200
5	MON 87708 DMO proteins	100
6	MON 87708 DMO proteins	200
7	Empty lane	
8	Empty lane	

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C.15. Results of Functional Activity

MON 87708 DMO activity was determined by measuring the production of DCSA. The specific activity was 62.21 nmol/min/mg of MON 87708 DMO (Table C-4). The value represents an average of three independent assays. This result demonstrates that MON 87708 DMO isolated from the seed of MON 87708 is functionally active.

Table C-4. MON 87708 DMO Functional Activity Assay

Assay#	Specific activity (DCSA nmol/min/mg)	Average (nmol/min/mg) ±Standard Deviation
1	61.92	62.21 ± 11.03
2	51.33	
3	73.39	

C.2. Substrate Specificity of DMO

C.2.1. Materials

MON 87708 (lot 11225299-114) and the near isogenic conventional soybean control A3525 (lot 11225301-104) were used for the exogenous specificity greenhouse tests conducted in 2009 and 2010. At the V2-V3 growth stage, MON 87708 and the conventional control plants were sprayed with different herbicides. The herbicides tested are listed in Table C-5.

The DMO protein used in the endogenous and exogenous specificity *in vitro* experiments was generated in *Escherichia coli* with a histidine-tag at the N-terminus and has an identical amino acid sequence to MON 87708 DMO with the exception of a single amino acid change at position 112 (W112C) and the lack of alanine at the second position. The compounds tested and standards used in the *in vitro* experiments are listed in Table C-6.

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Table C-5. Herbicides Tested in Exogenous Specificity Herbicide Tolerance Greenhouse Trials

Manufacturer/ Retailer	Chemistry/ Compound	Formulation	Lot Number
Agriliance	MCPA	MCPA L.V.Ester 4	RUD-0102-11027-F
Albaugh	2,4-DB	Butyrac® 200	HPR-0404-14987-F
BASF	dicamba	Clarity®	KIH-0702-18134-F
BASF	imazapyr	Arsenal®	KIH-0408-15423-F
Dow	picloram	Tordon® 22K	ABR-9912-99121-F
Dow	clopyralid	Stinger®	AGD-0104-11295
Dow	triclopyr	Garlon® 3A	AGD-0205-12641
Dow	atrazine	Atrazine®	AGT-0804-19336-F
Dow	trifluralin	Treflan®	MB231656T7
Dow	oxyfluorfen	Goal® 2XL	EWP-0107-11628-F
DuPont	chlorimuron	Classic®	MPO-9304-19319
DuPont	chlorsulfuron	Glean®	MPO-9910-9869
DuPont	linuron	Lorox®	NIF-0103-1173-F
Helena	2,4-D	2,4-D Amine 4	RUD-0502-15805-F
Monsanto	alachlor	Lasso®	MUS-0905-19849-F
Monsanto	acetochlor	Harness®	MUS-0704-18520-F
Monsanto	glyphosate	Roundup WeatherMax®	MUS-0905-19887-F
Monsanto	halosulfuron	Permit®	MUS-0405-15154-F
Syngenta	paraquat	Gramoxone®	GTA-0606-17421
Valent	lactofen	Cobra®	LVT-0905-19884-F

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® Roundup WeatherMax is a trademark of Monsanto Technology LLC. All other trademarks are the property of their respective owners.

Table C-6. Compounds Used in Specificity *In Vitro* Experiments

Manufacturer/ Retailer	Compound	Common Name	Lot/Product Number
Compounds Tested:			
Aldrich	2-methoxybenzoic acid	o-anisic acid	A0230443
Chem Service	3,6-dichloro-2-methoxybenzoic acid	dicamba	341-9143
Sigma	2,4-dichlorophenoxyacetic acid	2,4-D	D7299-100G
Sigma	3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enoic acid	sinapic acid	D7927-1G
Fluka	3,5-dimethoxy-4-hydroxybenzoic acid	syringic acid	86230
Fluka	4-hydroxy-3-methoxybenzoic acid	vanillic acid	94770
Fluka	3-(4-hydroxy-3-methoxy-phenyl)prop-2-enoic acid	ferulic acid	46278
Compounds Used as Standards:			
Monsanto	3,6-dichlorosalicylic acid	DCSA	GLP-0603-16959-T
Riedel-de Haen	2,4-dichlorophenol	2,4-DCP	35811

C.2.2. Exogenous Specificity Herbicide Tolerance Greenhouse Method

MON 87708 and the conventional control were planted in pots containing Redi-earth® and Osmocote® 14-14-14 slow release fertilizer or Peters® 20-20-20 fertilizer. There were ten replicate pots each (MON 87708 and the conventional control) with one plant per replicate. The pots were placed in a greenhouse and grown under normal agronomic conditions for soybean (relative humidity 10-70%, temperature 21-29°C, 14 hour photoperiod, and watering as needed). When the plants were at the V2-V3 growth stage, the replicates were sprayed with an herbicide (10 replicates of MON 87708 and the conventional control per each treatment of each tested herbicide; Table C-5). Two different application rates of each herbicide were applied to different replicate sets. Twenty to 21 days after treatment, all plants were rated for percent of injury. Ratings were based on visual assessment of chlorosis, necrosis, malformation, stunting, and biomass reduction with 100% equaling completely dead and 0% equaling no visual adverse effects. All ten replicate ratings were averaged.

C.2.3. *In Vitro* Specificity Experiments Enzymatic Reaction Mixture Method

The reaction of *E. coli*-produced DMO with different compounds evaluated as potential substrates was carried out using similar reaction conditions described in the characterization portion of this appendix (Appendix C.1.9.). The compounds (Table C-6) were combined with *E. coli*-produced DMO at 0.2 and/or 0.012 mM. The concentrations tested ensured adequate reaction conditions in terms of the substrate for the detection of product formation or disappearance of substrate.

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C.2.4. *In Vitro* Experiments Liquid Chromatography Separation Method

The reaction mixture was separated by Ultra Performance Liquid Chromatography (UPLC) using an ACQUITY UPLC BEH C18 Column containing 1.7 µm Bridged Ethyl Hybrid (BEH) particles and an ACQUITY BEH C18 VanGuard Pre-column. The column was heated to 40°C. The tested substrates and potential oxidative by-products were monitored by ACQUITY UPLC photodiode array (PDA) with wavelength range from 200nm to 320nm with 1.2nm resolution. The chromatography was performed at 0.25ml/min and directed to the mass spectrometer following the separation. Both mobile phase A (water) and solvent B (acetonitrile) contained 0.1% v/v formic acid. Gradients used were substrate specific:

- The gradient for dicamba was run from 40 to 50% solvent B in 3min, 50 to 100% solvent B in 0.1 min and then kept at 100% solvent B for 1min before returning to 40% solvent B in 0.1 min.

- The gradient for 2,4-D was run from 40 to 45% solvent B in 6min, held at 45% solvent B for 1min, 45 to 100% solvent B in 0.1 min, and then held at 100% solvent B for 0.5 min before returning to 40% solvent B in 0.1 min.

- The gradient for ferulic acid, o-anisic acid, sinapic acid, syringic acid, and vanillic acid were run from 0 to 100% solvent B in 4 min and then held at 100% solvent B for 1 min before returning to 0% solvent B in 0.1 min.

Five microliters injection of each sample was used for UPLC analysis where the disappearance of the potential substrate was monitored, and a 50 µl injection was used for UPLC analysis where formation of potential oxidative by-products was monitored.

C.2.5. *In Vitro* Experiments Mass Spectrometry Detection Method

Elution from the UPLC column (C.2.4) flowed directly to a Waters Micro Q-TOF mass spectrometer. The parameters used for the mass determination were: negative mode, capillary voltage of 2800 V, sample cone voltage of 26 V for all analytes with the exception of 2,4-D and 2,4-DCP, which was 10 V. The extraction cone was 1.5 V. The source temperature was 150 °C and the desolvation temperature was 390 °C. The desolvation gas flow was 500 L/hour. Scan time was 0.76 seconds and inter scan delay was 0.1 seconds. The m/z range used was specific to each substrate and product. The m/z range for dicamba and DCSA was from 160 to 225 from 0 to 4 minutes. The m/z at 175, which is the fragment ion of dicamba, was used as a detection method for dicamba. This fragment ion of dicamba gave better sensitivity, than the parent ion. The m/z at 205 or 207was used to detect DCSA. The m/z range for 2,4-D and 2,4-DCP was from 160-164 or 160-225 dependent on the specific experiment from 0 to 6 minutes. The m/z range for all other acids is from 120 to 230 within 4 minutes.

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C.2.6. Results of Herbicide Tolerance Greenhouse Trials

MON 87708 plants demonstrated similar levels of tolerance as the conventional control for 16 of the 19 herbicides tested (Table C-7). When 2,4-D, 2,4-DB, and MCPA were applied, the MON 87708 plants showed higher tolerance (expressed as injury rating in Table C-8) than the conventional control. Based on these results 2,4-D was further examined as a potential substrate for DMO in *in vitro* experiments. 2,4-D was selected as representative of the three auxin herbicides (2,4-D, 2,4-DB, and MCPA) as it is the most structurally similar to dicamba.

C.2.7. Results of *In Vitro* Experiments with 2,4-D

The reaction of dicamba with *E. coli*-produced DMO has been well characterized utilizing an *in vitro* enzymatic assay that monitors the formation of DCSA by LC-MS, which allows for the detection of the product with high sensitivity. Both the substrate and reaction products can be detected by LC-UV and LC-MS after separation by UPLC (Figure C-8).

The same enzymatic assay using LC-MS as the detection method was used to look for the potential conversion of 2,4-D to 2,4-DCP by *E. coli*-produced DMO. 2,4-DCP is predicted to be the product formed from the possible oxidative reaction of 2,4-D and DMO, based on the mechanism of action for dicamba conversion to DCSA by DMO. Both the amount of substrate and product were monitored in reactions using dicamba and 2,4-D as the substrate (Figure C-9). Using dicamba as a substrate, the formation of DCSA is clearly observed in the presence of *E. coli*-produced DMO (Figure C-9A). When 2,4-D is utilized as a possible substrate, there is no significant formation of product, as minimal amounts of 2,4-DCP are observed with and without *E. coli*-produced DMO as well as in a substrate only control (Figure C-9B).

C.2.8. Results of *In Vitro* Experiments with Endogenous Soybean Compounds

Compounds structurally similar to dicamba and found in soybean were used as potential substrates to determine if these compounds could be metabolized by DMO (Table C-6). The compounds tested were: syringic acid, o-anisic acid, vanillic acid, ferulic acid, and sinapic acid. Mass spectrometry scans were taken from 120 m/z to 250 m/z to cover the range of all potential oxidation products formed by DMO. Standard reaction conditions of dicamba with *E. coli*-produced DMO were used as a positive control. LC-MS data demonstrated that there are no additional peaks formed when reactions of each compound incubated with *E. coli*-produced DMO and without *E. coli*-produced DMO are compared (Figure C-10) (dicamba m/z 205, 2, 4-D m/z 163, ferulic acid m/z 175, o-anisic acid m/z 137, sinapic acid m/z 209, syringic acid m/z 183, and vanillic acid m/z 153). There were no peaks observed at the respective masses for the predicted reaction products of each compound incubated with *E. coli*-produced DMO, indicating these compounds are not catabolized by DMO.

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Table C-7. Herbicide Tolerance Trials Injury Ratings

Formulation	Manufacturer	Active Ingredient	Labeled Rate Range (g/ha)[1]	Rates Applied (g/ha)[1]	Injury Observations (days after application)	Injury ratings (%)[2] Control[3] Average (Range)	MON 87708[4] Average (Range)
Clarity	BASF	dicamba	0.13-2.00 (a.e.)	0.50 (a.e.)	20	100[a]	0[a]
				1.00 (a.e.)		100[a]	1.8 (0-5)
2,4-D Amine 4	Helena	2,4-D	0.13-2.00 (a.e.)	0.25 (a.e.)	20	96 (90-100)	59 (50-70)
				0.50 (a.e.)		98 (90-100)	70 (60-80)
Butyrac 200	Albaugh	2,4-DB	0.12-1.50 (a.e.)	0.25 (a.e.)	20	92 (85-100)	52 (40-65)
				0.50 (a.e.)		93 (85-100)	61 (50-70)
MCPA L.V.Ester 4	Agriliance	MCPA	0.12-1.50 (a.e.)	0.25 (a.e.)	20	95 (90-100)	61 (30-80)
				0.50 (a.e.)		97 (95-100)	82 (65-95)
Stinger	Dow	clopyralid	0.09-0.49 (a.e.)	0.25 (a.e.)	20	98 (95-100)	95 (90-100)
				0.50 (a.e.)		100[a]	100[a]
Garlon 3A	Dow	triclopyr	0.25-9.01 (a.e.)	0.25 (a.e.)	20	97 (90-100)	98 (95-100)
				0.50 (a.e.)		99 (95-100)	99 (95-100)
Tordon 22K	Dow	picloram	0.06-1.00 (a.e.)	0.25 (a.e.)	20	98 (95-100)	98 (90-100)
				0.50 (a.e.)		100 (95-100)	100 (99-100
Classic	DuPont	chlorimuron	0.02-0.08 (a.i.)	0.07 (a.i.)	20	88 (85-98)	88 (85-90)
				0.18 (a.i.)		90 (85-98)	89 (85-90)
Glean	DuPont	chlorsulfuron	0.008-0.046 (a.i.)	0.07 (a.i.)	20	89 (85-95)	89 (85-95)
				0.18 (a.i.)		94 (90-98)	93 (85-98)
Gramoxone	Syngenta	paraquat	0.25-1.00 (a.e.)	0.50 (a.e.)	20	98 (95-99)	97 (95-98)
				0.75 (a.e.)		99 (98-99)	98 (95-99)
Lasso	Monsanto	alachlor	0.15-4.00 (a.i.)	4.00 (a.i.)	21	21 (10-35)	19 (15-30)
				6.01 (a.i.)		45 (30-60)	34 (20-50)
Harness	Monsanto	acetochlor	0.83-4.00 (a.i.)	4.00 (a.i.)	21	71 (50-85)	88 (60-98)
				6.01 (a.i.)		92 (80-98)	97 (90-100)

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Table C-7 (continued). Herbicide Tolerance Trials Injury Ratings

						Injury ratings (%)[2]	
Formulation	Manufacturer	Active Ingredient	Labeled Rate Range (lb/acre)[1]	Rates Applied (lb/acre)[1]	Injury Observations (days after application)	Control[3] Average (Range)	MON 87708[4] Average (Range)
Atrazine®	Dow	atrazine	0.98-3.39 (a.i.)	1.50 (a.i.)	21	80 (50-100)	83 (40-100)
				3.00 (a.i.)		97 (85-100)	98 (90-100)
Lorox®	DuPont	linuron	0.25-2.50 (a.i.)	4.00 (a.i.)	21	58 (30-100)	55 (35-100)
				6.01 (a.i.)		70 (45-100)	79 (40-100)
Treflan®	Dow	trifluralin	0.50-2.00 (a.i.)	4.00 (a.i.)	21	9 (5-15)	8 (5-15)
				6.01 (a.i.)		11 (5-15)	10 (5-15)
Roundup WeatherMax®	Monsanto	glyphosate	0.25-3.72 (a.e.)	0.07 (a.e.)	21	47 (40-55)	48 (35-55)
				0.21 (a.e.)		64 (60-70)	62 (55-70)
Goal® 2XL	Dow	oxyfluorfen	0.25-2.00 (a.i.)	0.50 (a.i.)	21	54 (40-70)	56 (40-70)
				0.75 (a.i.)		67 (50-80)	69 (65-80)
Cobra®	Valent	lactofen	0.06-0.39 (a.i.)	0.50 (a.i.)	21	33 (25-50)	34 (25-50)
				0.75 (a.i.)		41 (25-50)	45 (35-60)
Arsenal®	BASF	imazapyr	0.21-1.50 (a.i.)	0.07 (a.i.)	21	58 (50-65)	60 (55-70)
				0.18 (a.i.)		67 (60-75)	66 (55-75)
Permit®	Monsanto	halosulfuron	0.032-0.13 (a.i.)	0.07 (a.i.)	21	43 (30-50)	50 (45-60)
				0.18 (a.i.)		52 (40-60)	55 (45-60)

[1] a.e. = acid equivalent; a.i. = active ingredient. Each herbicide contains the active ingredient directly or the salt form of the active ingredient. When determining the rate of application, the salt form is calculated back to the acid that is the active ingredient and therefore called acid equivalent. Each labeled rate is for cereal or/and broad acre row crops since these herbicides are not labeled to be sprayed on soybeans or are labeled for soybeans only as a pre-plant treatment. Based on the labeled rates, the rates for the experiments were chosen and then adjusted for use in-crop on soybeans and for the optimal growing conditions in the greenhouse.

[2] Injury ratings were determined by visual inspection of each plant. Ratings were based on visual assessment of chlorosis, necrosis, malformation, stunting, and biomass reduction. 100 percent = completely dead and 0 percent = no visual adverse effects.

[3] Control plants were near isogenic conventional soybean control A3525. Reported average and range of 10 replicate plants.

[4] Reported average and range of 10 replicate plants.

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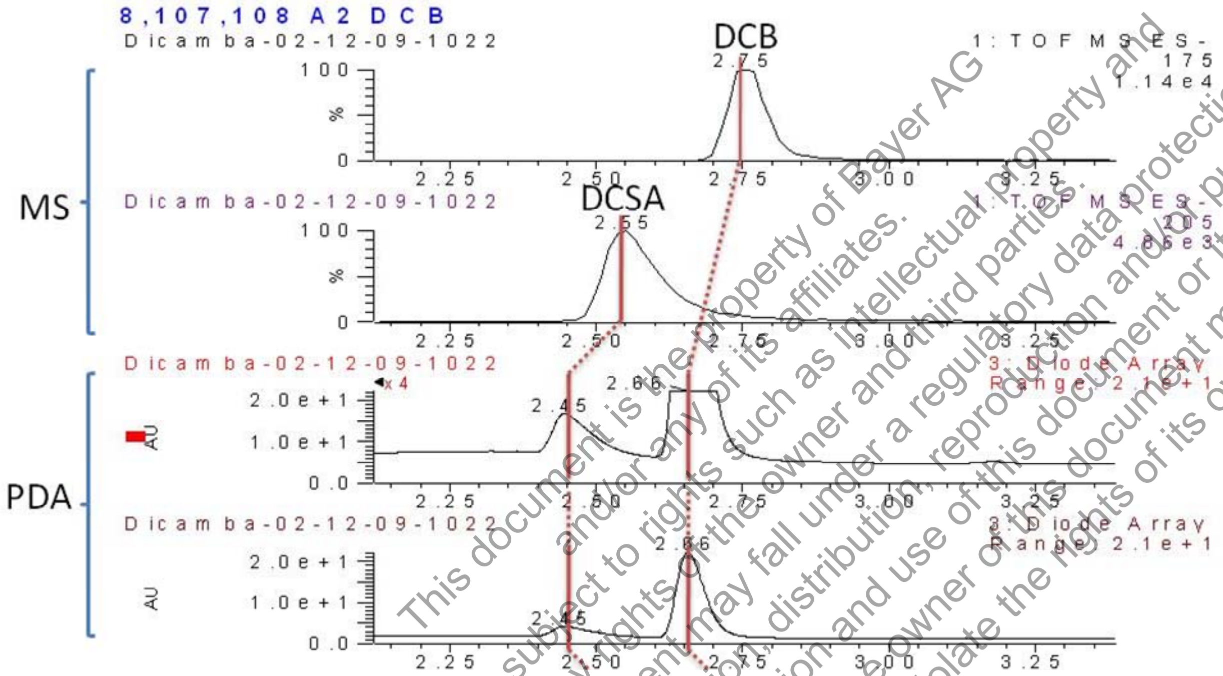

Figure C-8. UPLC separation of dicamba (DCB) and DCSA

Dicamba and DCSA were separated by UPLC and detected by UV absorbance using a Photo Diode Array (PDA) and mass spectrometry (MS).

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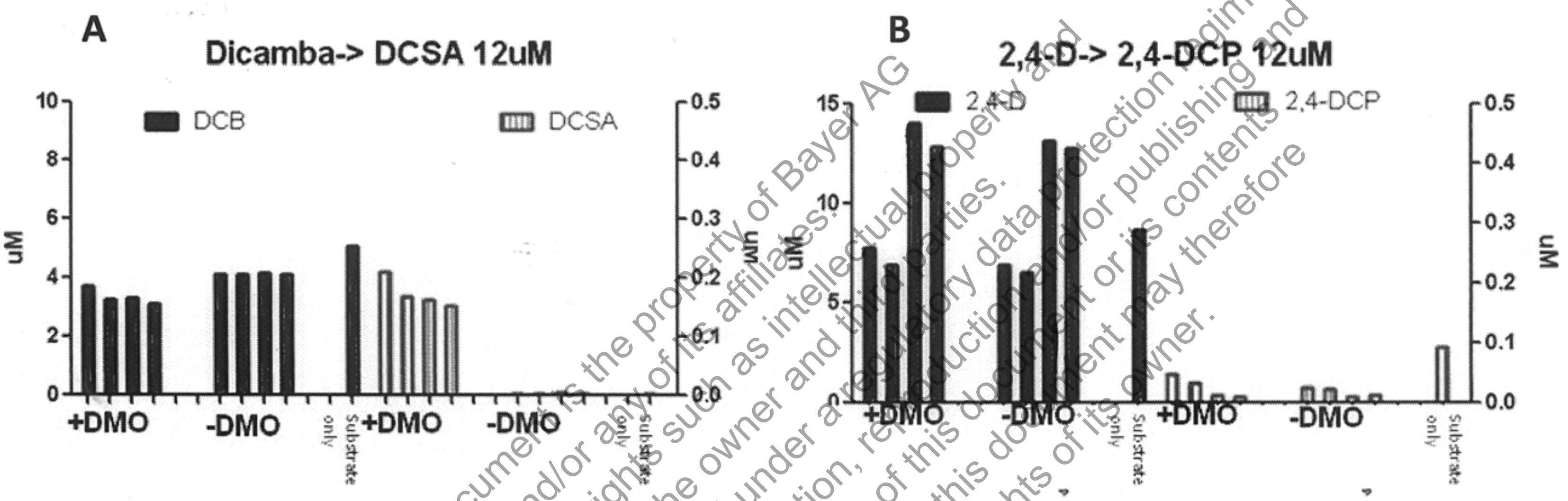

Figure C-9. *E. coli*-produced DMO Conversion of Dicamba (DCB) to DCSA and 2,4-D to 2,4-Dichlorophenol (2,4-DCP)
The formation of DCSA from dicamba (Panel A) and 2,4-DCP from 2,4-D (Panel B) due to *E. coli*-produced DMO were determined. The scale on the lefthand side of each graph represents the concentration of the potential substrate, and the scale on the righthand side of each graph represents the concentration of the predicted oxidative product. Each bar represents a replicate assay. Substrate only refers to either DCB or 2,4-D in the 25 mM KPi, 10 mM MgCl2 buffer. The concentration of the dicamba or 2,4-D used in each experiment was 12μM.

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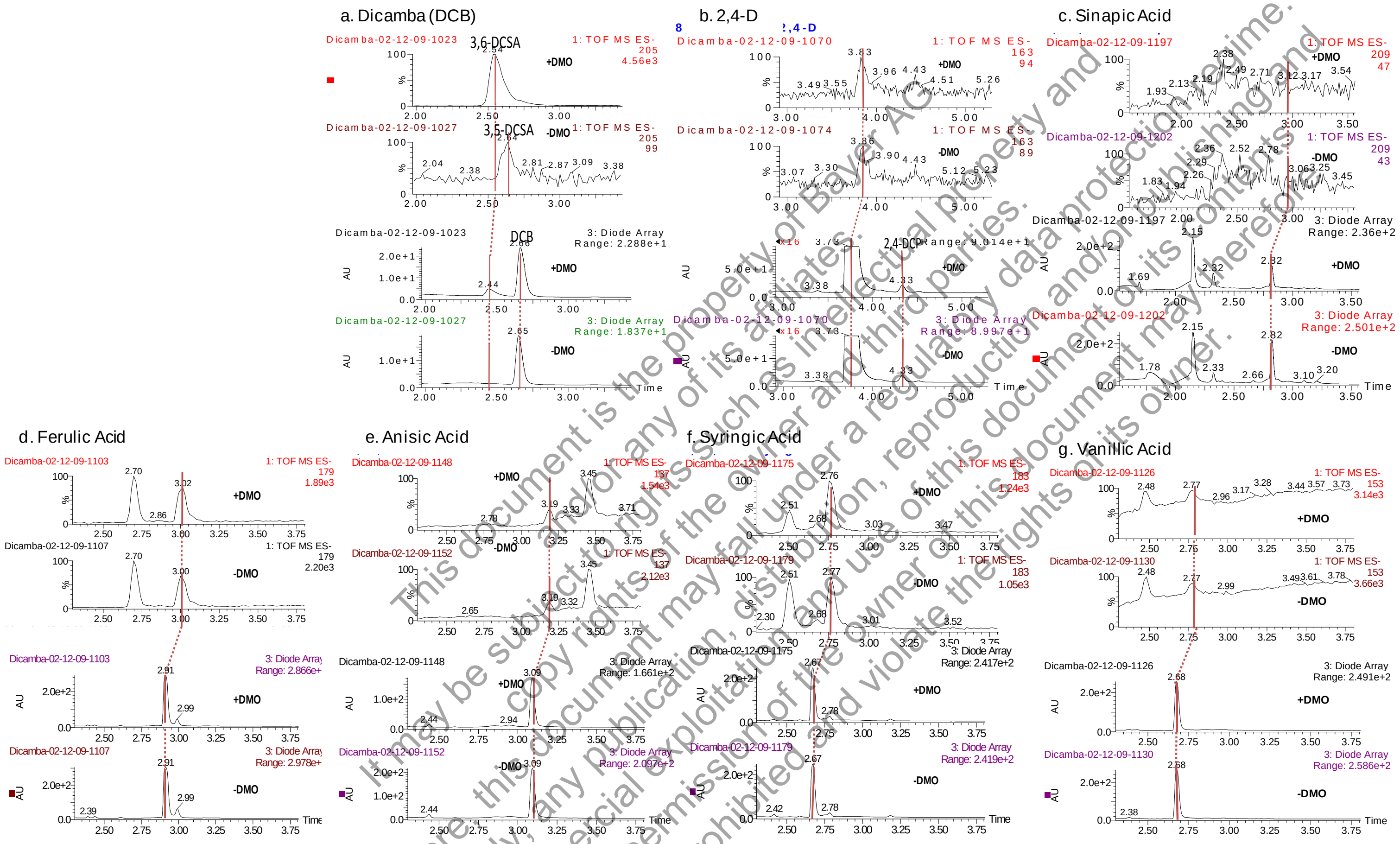

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Figure C-10. *E. coli*-produced DMO Conversion of Endogenous Substrates

Endogenous substrates, as well as dicamba and 2,4-D, were incubated with *E. coli*-produced DMO and the formation of products and disappearance of substrate was monitored by LC-MS (top two chromatograms) and LC-UV (bottom to chromatograms) for a positive control (dicamba (a)), (2,4-D (b)) and each endogenous compound:, sinapic acid(c), ferulic acid (d), anisic acid (e), syringic acid (f), and vanillic acid (g). For each experiment the reaction mixture was made with (+*E. coli*-produced DMO, upper) and without (-*E. coli*-produced DMO, lower). The red line indicates the migration of the substrates (and DCSA in the case of dicamba) in each chromatogram.

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Appendix D: Materials and Methods Used for the Analysis of the Levels of MON 87708 DMO

D.1. Materials

Over-season leaf, root, forage, and seed tissue samples from MON 87708 and the near isogenic conventional soybean control A3525 were harvested from five field sites in the U.S. during 2008 from plants grown from starting seed lot 10001256 and 10001257, respectively. An *E. coli*-produced DMO protein (lot 11247247) was used as the analytical reference standard.

The identities of MON 87708 and the conventional control samples were confirmed by verifying the chain of custody documentation prior to analysis. To further confirm the identities of MON 87708 and the conventional control samples, event specific polymerase chain reaction (PCR) analyses were conducted on the seed tissue samples from each site to confirm the presence or absence of the *dmo* expression cassette. The PCR analyses and the resulting verification of identities were archived under the starting seed lot numbers.

D.2. Field Design and Tissue Collection

Field trials were initiated during the 2008 planting season to generate MON 87708 and the conventional control samples at the following locations in the U.S.: Jefferson County, Iowa; Stark County, Illinois; Clinton County, Illinois; Parke County, Indiana; and Berks County, Pennsylvania. The field sites were representative of soybean producing regions suitable for commercial soybean production. At each site, three replicated plots containing MON 87708, as well as the conventional control, were planted using a randomized complete block field design. Over-season leaf (OSL), root, forage, and seed samples were collected from each replicated plot at each field site (except for the conventional control from Berks County, Pennsylvania where only two replicates were tested).

The OSL tissue samples were collected from the youngest set of fully expanded trifoliate leaves at the following growth stages: OSL-1 at V3-V4; OSL-2 at V5-V8; OSL-3 at R2-V12; and OSL-4 at R5-V16. The root and forage tissue samples were collected at approximately the R6 growth stage. Seed tissue samples were collected at the R8 growth stage.

D.3. Tissue Processing and Protein Extraction

All tissue samples harvested were shipped to Monsanto's processing facility and were prepared by the Monsanto Sample Management Team. The prepared tissue samples were stored in a -80°C freezer until transferred on dry ice to the analytical facility.

MON 87708 DMO was extracted from the seed tissue samples at a tissue to buffer ratio of 1:100 with a Tris-borate buffer (0.1 M Tris, 0.1 M Na2B4O7 • 10H2O, 0.01 M MgCl2, 0.05% (v/v) Tween-20 at pH 7.8). MON 87708 DMO was extracted from OSL, forage,

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and root tissues samples at a tissue to buffer ratio of 1:100, 1:50, and 1:50, respectively, using phosphate buffered saline (PBS) with Tween 20 and 0.5% (w/v) bovine serum albumin (BSA) (1 × PBST with 0.5% (w/v) BSA). Extractions were done using 8 1/4″ chrome-steel beads, and shaking in a Harbil mixer (Fluid Management, Wheeling, Illinois). Insoluble material was removed from all tissue extracts using a serum filter (Fisher Scientific, Pittsburgh, PA). The extracts were aliquotted and stored frozen in a -80°C freezer until enzyme-linked immunosorbent assay (ELISA) analysis.

D.4. DMO Antibodies

Goat polyclonal anti-DMO antibodies were purified using Protein-G Agarose affinity chromatography. The concentration of the purified IgG was determined to be 8.1 mg/ml by spectrophotometric methods. The purified antibody was stored in 1× PBS, pH 7.4. The purified anti-DMO antibodies were coupled with biotin (Pierce, Rockford, IL) according to the manufacturer's instructions. The detection reagent was NeutrAvidin (Pierce, Rockford, IL) conjugated to horseradish peroxidase (HRP). The goat polyclonal anti-DMO antibodies react with the DMO and DMO+27 present in the MON 87708 DMO and were used as capture antibodies for the DMO ELISA method.

D.5. DMO ELISA Method

Goat polyclonal anti-DMO antibodies were diluted in coating buffer (15 mM Na2CO3, 35 mM NaHCO3, and 150 mM NaCl, pH 9.6) to a final concentration of 5.0 µg/ml and then immobilized onto 96-well microtiter plates followed by incubation in a 4 °C refrigerator for ≥8 hours. Plates were washed with 1 × PBS containing 0.05% (v/v) Tween-20 (1 × PBST). The plates were blocked using 10% Casein in tris buffered saline (TBS) blocking buffer (Pierce, Rockford, IL) at 200 µl per well for 1 hour at room temperature. The blocking buffer was aspirated and DMO standard or tissue sample extract was added at 100 µl per well and incubated for 1 hour at 37°C. Prior to the addition of biotinylated antibody, NuetrAvidin-HRP and 3,3',5,5' tetramethyl-benzidine (TMB; Kirkegaard & Perry, Gaithersburg, MD) reagents, plates were washed with 1 × PBST. The captured MON 87708 DMO was detected by the addition of 100 µl per well of biotinylated goat anti-DMO antibodies and NeutrAvidin-HRP. Plates were developed by adding 100 µl per well of TMB. The enzymatic reaction was terminated by the addition of 100 µl per well of 3 M H3PO4. Quantification of MON 87708 DMO was accomplished by interpolation on a DMO standard curve that ranged from 0.313-20 ng/ml.

D.6. Moisture Analysis

Tissue moisture content was determined using an IR-200 Moisture Analyzer (Denver Instrument Company, Arvada, CO). A homogeneous site and tissue-specific pool (TSSP) was prepared using MON 87708 and the conventional control samples from each tissue type grown at each site. The average percent moisture for each TSSP was calculated from triplicate analyses. A TSSP Dry Weight Conversion Factor (DWCF) was calculated as follows:

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$$\text{DWCF} = 1 - \frac{(\text{Mean \% TSSP Moisture})}{(100)}$$

The DWCF was used to convert protein levels from a µg/g fresh weight (fwt) basis into a µg/g dry weight (dwt) basis using the following calculation:

$$\text{Protein Level in Dry Weight} = \frac{(\text{Protein Level Fresh Weight})}{(\text{DWCF})}$$

The protein levels that were reported on a fwt basis to be less than or equal to the limit of detection or less than the limit of quantification (LOQ) were not reported on a dwt basis.

D.7. Data Analyses

All MON 87708 DMO ELISA plates were analyzed on a SPECTRAmax Plus 384 (Molecular Devices, Sunnyvale, CA) microplate spectrophotometer, using a dual wavelength detection method. All protein concentrations were determined by optical absorbance at a wavelength of 450 nm with a simultaneous reference reading of 620-650 nm. Data reduction analyses were performed using Molecular Devices SOFTmax PRO GxP version 5.0.1 software. Absorbance readings and protein standard concentrations were fitted with a four parameter logistic curve fit. Following the interpolation from the standard curve, the amount of protein (ng/ml) in the tissue was reported on a µg/g fwt basis for data that were greater than or equal to the LOQ. For MON 87708 DMO, this conversion utilized a sample dilution factor and a tissue-to-buffer ratio. The enzyme values in µg/g fwt were converted to µg/g dwt by applying the DWCF. Microsoft Excel 2007 (Version 12.0.6514.5000 SP2 Microsoft, Redmond, WA) was used to calculate MON 87708 DMO levels in tissue samples. The sample mean, standard deviations, and ranges were also calculated using Microsoft Excel 2007.

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Appendix E: Materials, Methods, and Individual-Site Results for Compositional Analysis of MON 87708 Soybean Seed and Forage

Compositional comparisons between MON 87708 and the near isogenic conventional soybean control A3525 were performed using the principles and analytes outlined in the OECD consensus documents for soybean composition (OECD, 2001). These principles are accepted globally and have been employed previously in assessments of soybean products derived through biotechnology. The compositional assessment was conducted on seed and forage samples harvested from a single growing season conducted in the U.S. during 2008 under typical agronomic practices.

The materials and methods for compositional analysis, as well as the individual-site results (Tables E-4 to E-18), are provided below.

E.1. Materials

Forage and harvested seed from MON 87708, a near isogenic conventional soybean control A3525 that has similar genetic background to that of MON 87708, and commercial reference varieties were compositionally assessed. The commercial reference varieties are listed in Table E-1.

Table E-1. Commercial Reference Varieties

Material Name	Seed Lot#	Field Site Code
CST3461	10000890	IARL
Wilken 3316	10001505	IARL
Midland 363	10001570	IARL
Stine 3300-0	10001312	IARL
Croplan HT3596STS	10001450	ILWY
FS 3591	10001448	ILWY
Garst 3585N	10000883	ILWY
Pioneer 93M52	10001311	ILWY
Stine 3608-0	10001392	ILCY
Quality Plus 365C	10001608	ILCY
Crows C37003N	10001508	ILCY
NK S38-T8	10001509	ILCY
Lewis 372	10001475	INRC
Pioneer 93M50	10000888	INRC
Dekalb DKB34-51	10000889	INRC
Stewart SB3454	10000887	INRC
Dekalb DKB31-51	10001285	PAHM
NK 32Z3	10001607	PAHM
Hoegemeyer 333	10001590	PAHM
Pioneer 93B15	10001304	PAHM

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E.2. Characterization of the Materials

The identities of the forage and seed samples from MON 87708, the conventional control, and the commercial reference varieties were verified by the Study Director prior to the study by confirming the chain-of-custody documentation supplied with the forage and seed harvested from the field sites. The seed of MON 87708, the conventional control, and the commercial reference varieties were characterized by event-specific polymerase chain reaction (PCR) analysis to confirm the presence or absence of the *dmo* expression cassette.

E.3. Field Production of the Samples

Harvested seed and forage of MON 87708, the conventional control, and the commercial reference varieties were collected from five replicated sites in the U.S. during the 2008 growing season. These sites are Jefferson County, Iowa (IARL); Stark County, Illinois (ILWY); Clinton County, Illinois (ILCY); Parke County, Indiana (INRC); and Berks County, Pennsylvania (PAHM). Starting seeds were planted in a randomized complete block design with three plots for each of MON 87708, the conventional control, and the commercial reference varieties. The production was conducted under normal agronomic field conditions. All soybean plants including MON 87708, the conventional control, and commercial reference varieties were treated with maintenance pesticides as necessary throughout the growing season. In addition, MON 87708 plots were treated at the V2-V3 growth stage with dicamba herbicide at the target label rate (0.5 lb/Acre a.e.). Seed and forage samples were harvested from all plots and shipped on dry ice (forage) or at ambient temperature (harvested seed) to Monsanto Company, St. Louis, MO. A subsample for compositional analysis was obtained for each tissue sample collected. These subsamples were ground and stored in a freezer set to maintain -20°C until their shipment on dry ice to Covance Laboratories Inc. (Madison, WI) for analysis.

E.4. Summary of Analytical Methods

Nutrients assessed in this study included proximates (ash, carbohydrates by calculation, moisture, protein, and fat), fiber, amino acids (18 components), fatty acids (FA, C8-C22), and vitamin E (α-tochopherol) in seed, and proximates (ash, carbohydrates by calculation, moisture, protein, and fat) and fiber in forage. Anti-nutrients assessed in seed included raffinose, stachyose, lectin, phytic acid, trypsin inhibitors, and isoflavones (daidzein, genistein, and glycitein).

All compositional analyses were performed at Covance Laboratories, Inc. (Madison, WI). Methods for analysis were based on internationally-recognized procedures and literature publications. Brief descriptions of the methods utilized for the analyses are described below.

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E.5. Analytical Method Summaries and Reference Standards

E.5.1. Acid Detergent Fiber

The sample was placed in a fritted vessel and washed with an acidic boiling detergent solution that dissolved the protein, carbohydrate, and ash. An acetone wash removed the fats and pigments. The lignocellulose fraction was collected on the frit and determined gravimetrically (Goering and Van Soest, 1970). The limit of quantitation (LOQ) for this analysis was 0.100%.

E.5.2. Amino Acid Composition

The sample was assayed by three methods to obtain the full profile. Tryptophan required a base hydrolysis with sodium hydroxide. The sulfur-containing amino acids required an oxidation with performic acid prior to hydrolysis with hydrochloric acid. Analysis of the samples for the remaining amino acids was accomplished through direct acid hydrolysis with hydrochloric acid. Once hydrolyzed, the individual amino acids were then quantitated using an automated amino acid analyzer (AOAC-International, 2005a). The LOQ for this analysis was 0.100 mg/g.

Reference Standards:

- ThermoScientific K18, 2.5 µmol/mL per constituent except cystine (1.25 µmol/mL), Lot Number JK126327
- Sigma, L-Tryptophan, 100%, Lot Number 076K0075
- Sigma/BioChemika, L-Cysteic Acid Monohydrate, 99.5% (used as 100%), Lot Number 1305674
- Sigma, L-Methionine Sulfone, 100%, Lot Number 047K1321

E.5.3. Ash

The sample was placed in an electric furnace at 550 °C and ignited to drive off all volatile organic matter. The nonvolatile matter remaining was quantitated gravimetrically and calculated to determine percent ash (AOAC-International, 2005b). The LOQ for this analysis was 0.100%.

E.5.4. Carbohydrates

The total carbohydrate level was calculated by difference using the fwt-derived data and the following equation (USDA, 1973):

% carbohydrates = 100 % - (% protein + % fat + % moisture + % ash)

The LOQ for this analysis was 0.100%.

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E.5.5. Crude Fiber

Crude fiber was quantitated as the loss on ignition of dried residue remaining after digestion of the sample with 1.25% sulfuric acid and 1.25% sodium hydroxide solutions under specific conditions (AOAC-International, 2005c). The limit of quantitation for this study was 0.100%.

E.5.6. Fat by Acid Hydrolysis

The sample was hydrolyzed with hydrochloric acid at an elevated temperature. The fat was extracted with ether and hexane. The extract was evaporated on a steambath, re-dissolved in hexane and filtered through a sodium sulfate column. The hexane extract was then evaporated again on a steambath under nitrogen, dried, and weighed (AOAC-International, 2005d). The LOQ for this analysis was 0.100%.

E.5.7. Fat by Soxhlet Extraction

The sample was weighed into a cellulose thimble containing sodium sulfate and dried to remove excess moisture. Pentane was dripped through the sample to remove the fat. The extract was then evaporated, dried, and weighed (AOAC-International, 2005e). The LOQ for this analysis was 0.100%.

E.5.8. Fatty Acids

The lipid was extracted and saponified with 0.5 N sodium hydroxide in methanol. The saponification mixture was methylated with 14% boron trifluoride in methanol. The resulting methyl esters were extracted with heptane containing an internal standard. The methyl esters of the fatty acids were analyzed by gas chromatography using external standards for quantitation (AOAC-International, 2005f; AOCS, 1997a, c). The limit of quantitation was 0.0200%.

Reference Standards:

- Nu Chek Prep GLC Reference Standard Hazleton No. 1, *, Lot Number AU18-S
- Nu Chek Prep GLC Reference Standard Hazleton No. 2, *, Lot Number M13-O
- Nu Chek Prep GLC Reference Standard Hazleton No. 3, *, Lot Number MA18-S
- Nu Chek Prep GLC Reference Standard Hazleton No. 4, *, Lot Number JA16-T
- Nu Chek Prep Methyl Gamma Linolenate, used as 100%, Lot Number U-63M-JY12-R
- Nu Chek Prep Methyl Tridecanoate, used as 100%, Lot Number N-13M-JA16-T

* Overall purity of the sum of the mixture of components is used as 100%.

E.5.9. Isoflavones

The sample was extracted using a solution of hydrochloric acid and reagent alcohol heated on steam baths or hot plates. The extract was brought to volume, diluted, and centrifuged. An aliquot of the supernatant was placed onto a C18 solid-phase extraction column. Unwanted components of the matrix were rinsed off with 20% methanol and then the isoflavones were eluted with 80% methanol. The sample was analyzed on a

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high-performance liquid chromatography system with ultraviolet detection and was compared to an external standard curve of known standards for quantitation (Pettersson and Kiessling, 1984; Seo and Morr, 1984). The LOQ for each component was 10.0 ppm (µg/g).

Reference Standards:

- Chromadex, Daidzein, 96.5%, Lot Number 04007-120
- Chromadex, Glycitein, 96.3%, Lot Number 07344-571
- Indofine, Genistein, ≥99% (100% used in calculations), Lot Number 0309074

E.5.10. Lectin

The sample was suspended in phosphate buffered saline (PBS), shaken, and filtered. An aliquot of the resulting extract was serially diluted in 10 cuvettes containing PBS. A 10% hematocrit of lyophilized rabbit blood in PBS was added to each dilution. After 2.5 hours, the absorbance of each dilution of the sample and lectin control was measured on a spectrophotometer at 620 nm, using PBS to zero the instrument. One hemagglutinating unit (H.U.) was defined as the level that caused 50% of the standard cell suspension to sediment in 2.5 hours (Klurfeld and Kritchevsky, 1987; Liener, 1955). The LOQ for this analysis was 0.10 H.U./mg.

Reference Standard:

- Sigma-Aldrich, Red Blood Cells, Rabbit, Product #R1629, Lot Number 105K6042

E.5.11. Moisture

The sample was dried in a vacuum oven at approximately 100°C to a constant weight. The moisture weight loss was determined and converted to percent moisture (AOAC-International, 2005g). The LOQ for this analysis was 0.100%.

E.5.12. Neutral Detergent Fiber, Enzyme Method

The sample was placed in a fritted vessel and washed with a neutral boiling detergent solution that dissolved the protein, carbohydrate, enzyme, and ash. An acetone wash removed the fats and pigments. Hemicellulose, cellulose, and lignin fractions were collected on the frit and determined gravimetrically (AACC, 1998; Goering and Van Soest, 1970). The LOQ for this analysis was 0.100%.

E.5.13. Phytic Acid

The sample was extracted using 0.5 M HCl with ultrasonication. Purification and concentration were accomplished on a silica-based anion-exchange column. The sample was analyzed on a polymer high-performance liquid chromatography column PRP-1, 5 µm (150 × 4.1 mm) with a refractive index detector (Lehrfeld, 1989; Lehrfeld, 1994). The LOQ for this analysis was 0.100%.

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Reference Standard:

- Aldrich, Phytic Acid, Dodecasodium Salt Hydrate, 98%, Lot Number 068K0755

E.5.14. Protein

Nitrogenous compounds in the sample were reduced in the presence of boiling sulfuric acid and a mercury catalyst mixture to form ammonia. The acid digest was made alkaline. The ammonia was distilled and then titrated with a previously standardized acid. The percent nitrogen was calculated and converted to equivalent protein using the factor 6.25 (AOAC-International, 2005h; Bradstreet, 1965; Kolthoff and Sandell, 1948). The LOQ for this analysis was 0.100%.

E.5.15. Raffinose and Stachyose

The sample was extracted with deionized water and the extract treated with a hydroxylamine hydrochloride solution in pyridine, containing phenyl-β-D-glucoside as an internal standard. The resulting oximes were converted to silyl derivatives by treatment with hexamethyldisilazane and trifluoracetic acid and analyzed by gas chromatography using a flame ionization detector (Brobst, 1972; Mason and Slover, 1971). The LOQ for this analysis was 0.0500%.

Reference Standards:

- Sigma, D-(+)-Raffinose Pentahydrate, 95.5% after correction for degree of hydration, Lot Number 037K1059
- Sigma, Stachyose, 97.1% after correction for degree of hydration, Lot Number 078K3802

E.5.16. Trypsin Inhibitor

The sample was ground and defatted with petroleum ether. A sample of matrix was extracted with 0.01 N sodium hydroxide. Varying aliquots of the sample suspension were exposed to a known amount of trypsin and benzoy1-DL-arginine~p~nitroanilide hydrochloride. The sample was allowed to react for 10 minutes at 37°C. After 10 minutes, the reaction was halted by the addition of acetic acid. The solution was centrifuged and then the absorbance was determined at 410 nm. Trypsin inhibitor activity was determined by photometrically measuring the inhibition of trypsin's reaction with benzoyl-DL-arginine~p~nitroanilide hydrochloride (AOCS, 1997b). The LOQ for this analysis was 1.00 Trypsin Inhibitor Units (TIU)/mg.

E.5.17. Vitamin E

The sample was saponified to break down any fat and release vitamin E. The saponified mixture was extracted with ethyl ether and then quantitated by high-performance liquid chromatography using a silica column (Cort et al., 1983; McMurray et al., 1980; Speek et al., 1985). The LOQ for this analysis was 0.500 mg/100g.

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Reference Standard:

- USP, Alpha Tocopherol, 100%, Lot Number M

E.6. Data Processing and Statistical Analysis

After compositional analyses were performed, data spreadsheets were forwarded to Monsanto Company. The data were reviewed, formatted, and sent to Certus International, Inc. for statistical analysis.

The following formulas were used for re-expression of soybean composition data for statistical analysis (Table E-2):

Table E-2. Re-Expression Formulas for Statistical Analysis of Composition Data

Component	From (X)	To	Formula[1]
Proximates (excluding Moisture), Fiber, Phytic Acid, Raffinose, Stachyose	% fwt	% dwt	X/d
Isoflavones	µg/g fwt	µg/g dwt	X/d
Lectin	H.U./fwt	H.U./dwt	X/d
Trypsin Inhibitor	TIU/mg fwt	TIU/mg dwt	X/d
Vitamin E	mg/100g fwt	mg/100g dwt	X/d
Amino Acids (AA)	mg/g fwt	% dwt	X/(10d)
Fatty Acids (FA)	% fwt	% Total FA	$(100)X_j/\Sigma X$, for each FA_j where ΣX is over all the FA

[1] 'X' is the individual sample value; 'd' is the fraction of the sample that is dry matter.

In order to complete a statistical analysis for a compositional analyte, at least 50% of the values for an analyte had to be greater than the assay LOQ. The following 14 analytes with more than 50% of observations below the assay LOQ were excluded from statistical analysis: 8:0 caprylic acid, 10:0 capric acid, 12:0 lauric acid, 14:0 myristic acid, 14:1 myristoleic acid, 15:0 pentadecanoic acid, 15:1 pentadecenoic acid, 16:1 palmitoleic acid, 17:0 heptadecanoic acid, 17:1 heptadecenoic acid, 18:3 gamma-linolenic acid, 20:3 eicosatrienoic acid, 20:2 eicosadienoic acid, and 20:4 arachidonic acid.

If less than 50% of the observations for a component were below the LOQ, individual analyses that were below the LOQ were assigned a value equal to one-half the LOQ. The following analyte was assigned a value (Table E-3):

Table E-3. Component with Observations Below the Assay Limit of Quantitation Not Excluded from Statistical Analysis

		Obs. Below LOQ		Total		Value
Component	Units	N	(%)	N	LOQ	Assigned
Seed Fatty Acid						
20:1 Eicosenoic	% fwt	45	42.9	105	0.020	0.010

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The data were assessed for potential outliers using a studentized PRESS residuals calculation. A PRESS residual is the difference between any value and its predicted value from a statistical model that excludes the data point. The studentized version scales these residuals so that the values tend to have a standard normal distribution when outliers are absent. Thus, most values are expected to be between ± 3. Extreme data points that are also outside of the ± 6 studentized PRESS residual range are considered for exclusion, as outliers, from the final analyses. No results had PRESS residual values outside of the ± 6 range.

All soybean compositional components were statistically analyzed using a mixed model analysis of variance. The five replicated sites were analyzed both separately and combined. Individual replicated site analyses used model *(1)*.

(1) $Y_{ij} = U + T_i + B_j + e_{ij}$,

where Y_{ij} = unique individual observation, U = overall mean, T_i = substance effect, B_j = random block effect, and e_{ij} = residual error.

Combined-site analyses used model *(2)*.

(2) $Y_{ijk} = U + T_i + L_j + B(L)_{jk} + LT_{ij} + e_{ijk}$,

where Y_{ijk} = unique individual observation, U = overall mean, T_i = substance effect, L_j = random site effect, $B(L)_{jk}$ = random block within site effect, LT_{ij} = random site by substance interaction effect, and e_{ijk} = residual error.

A range of observed values from the reference varieties was determined for each analytical component. Additionally, data from the reference varieties were used to develop tolerance intervals. A tolerance interval is an interval that one can claim, with a specified degree of confidence, contains at least a specified proportion, p, of an entire sampled population for the parameter measured.

For each compositional component, 99% tolerance intervals were calculated that are expected to contain, with 95% confidence, 99% of the quantities expressed in the population of commercial reference varieties. Because negative quantities are not possible, negative calculated lower tolerance bounds were set to zero.

SAS® (Version 9.2) software was used to generate all summary statistics and perform all analyses.

Report tables present p-values from SAS as either <0.001 or the actual value truncated to three decimal places.

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Table E-4. Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	5.30 (0.070) (5.20 - 5.37)	5.29 (0.070) (5.19 - 5.47)	0.0063 (0.098) (-0.27 - 0.17)	-0.27, 0.28	0.952	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	38.55 (0.56) (38.03 - 39.11)	37.97 (0.56) (37.17 - 38.45)	0.57 (0.55) (-0.27 - 1.33)	-0.96, 2.11	0.358	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	7.13 (0.28) (6.92 - 7.27)	6.07 (0.28) (5.84 - 6.36)	1.06 (0.39) (0.56 - 1.43)	-0.033, 2.15	0.054	4.27, 9.58 (5.50 - 9.23)
Protein	40.92 (0.27) (40.40 - 41.41)	41.09 (0.27) (40.69 - 41.74)	-0.18 (0.16) (-0.33 - 0.088)	-0.63, 0.28	0.342	35.50, 45.19 (37.06 - 43.42)
Total Fat	15.22 (0.47) (14.77 - 15.62)	15.61 (0.47) (15.38 - 15.82)	-0.40 (0.66) (-1.05 - -0.017)	-2.23, 1.43	0.579	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	13.03 (0.38) (12.68 - 13.58)	12.60 (0.38) (11.92 - 13.17)	0.43 (0.54) (-0.34 - 1.66)	-1.08, 1.94	0.472	10.06, 18.04 (12.07 - 17.46)

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Table E-4 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Crude Fiber	7.71 (0.33) (7.26 - 8.48)	7.41 (0.33) (7.17 - 7.60)	0.30 (0.46) (-0.34 - 1.03)	-0.98, 1.58	0.545	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	14.25 (0.89) (13.11 - 16.38)	13.27 (0.89) (11.81 - 14.42)	0.98 (1.25) (-1.31 - 4.57)	-2.51, 4.46	0.479	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.72 (0.026) (1.66 - 1.76)	1.74 (0.026) (1.69 - 1.77)	-0.027 (0.036) (-0.11 - 0.042)	-0.13, 0.074	0.502	1.56, 1.91 (1.59 - 1.86)
Arginine	3.28 (0.055) (3.26 - 3.30)	3.45 (0.055) (3.27 - 3.56)	-0.17 (0.061) (-0.26 - -0.013)	-0.33, 0.0040	0.053	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.55 (0.060) (4.44 - 4.63)	4.63 (0.060) (4.46 - 4.74)	-0.076 (0.084) (-0.29 - 0.12)	-0.31, 0.16	0.416	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0094) (0.60 - 0.62)	0.59 (0.0094) (0.56 - 0.62)	0.018 (0.013) (-0.0056 - 0.053)	-0.019, 0.054	0.257	0.50, 0.68 (0.53 - 0.66)

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Table E-4 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.24 (0.10) (7.05 - 7.38)	7.41 (0.10) (7.12 - 7.58)	-0.16 (0.15) (-0.53 - 0.17)	-0.57, 0.25	0.332	6.28, 8.30 (6.69 - 7.92)
Glycine	1.72 (0.024) (1.67 - 1.76)	1.76 (0.024) (1.70 - 1.79)	-0.037 (0.034) (-0.12 - 0.042)	-0.13, 0.057	0.331	1.53, 1.92 (1.58 - 1.84)
Histidine	1.04 (0.014) (1.02 - 1.06)	1.06 (0.014) (1.02 - 1.08)	-0.018 (0.019) (-0.066 - 0.031)	-0.071, 0.036	0.408	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.84 (0.038) (1.75 - 1.90)	1.88 (0.038) (1.79 - 1.94)	-0.036 (0.054) (-0.16 - 0.11)	-0.19, 0.11	0.540	1.65, 2.06 (1.68 - 2.02)
Leucine	3.01 (0.041) (2.93 - 3.07)	3.07 (0.041) (2.96 - 3.14)	-0.055 (0.058) (-0.21 - 0.072)	-0.22, 0.11	0.401	2.72, 3.39 (2.80 - 3.27)
Lysine	2.60 (0.030) (2.53 - 2.64)	2.62 (0.030) (2.54 - 2.66)	-0.017 (0.042) (-0.12 - 0.090)	-0.13, 0.10	0.710	2.33, 2.84 (2.38 - 2.74)

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Table E-4 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.58 (0.013) (0.56 - 0.60)	0.56 (0.013) (0.53 - 0.60)	0.016 (0.019) (-0.022 - 0.071)	-0.037, 0.068	0.452	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	1.98 (0.036) (1.92 - 2.04)	2.03 (0.036) (1.95 - 2.09)	-0.052 (0.050) (-0.17 - 0.023)	-0.19, 0.087	0.357	1.80, 2.30 (1.85 - 2.21)
Proline	1.92 (0.035) (1.90 - 1.96)	1.98 (0.035) (1.89 - 2.07)	-0.063 (0.050) (-0.17 - 0.065)	-0.20, 0.076	0.274	1.65, 2.26 (1.74 - 2.16)
Serine	1.98 (0.044) (1.92 - 2.03)	2.00 (0.044) (1.95 - 2.08)	-0.024 (0.036) (-0.087 - 0.047)	-0.12, 0.076	0.545	1.78, 2.27 (1.90 - 2.18)
Threonine	1.53 (0.023) (1.48 - 1.56)	1.54 (0.023) (1.51 - 1.58)	-0.011 (0.023) (-0.051 - 0.052)	-0.075, 0.053	0.653	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.45 (0.0092) (0.45 - 0.46)	0.45 (0.0092) (0.44 - 0.47)	0.00085 (0.013) (-0.0079 - 0.0069)	-0.035, 0.037	0.950	0.38, 0.52 (0.39 - 0.50)

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Table E-4 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Tyrosine	1.34 (0.013) (1.32 - 1.37)	1.38 (0.013) (1.37 - 1.42)	-0.042 (0.016) (-0.079 - -0.00044)	-0.087, 0.0035	0.062	1.24, 1.50 (1.26 - 1.49)
Valine	1.95 (0.046) (1.82 - 2.03)	1.99 (0.046) (1.90 - 2.05)	-0.042 (0.065) (-0.20 - 0.13)	-0.22, 0.14	0.552	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.49 (0.051) (11.44 - 11.54)	11.00 (0.051) (10.92 - 11.08)	0.49 (0.062) (0.39 - 0.62)	0.32, 0.66	0.001	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.06 (0.067) (3.99 - 4.19)	4.00 (0.067) (3.99 - 4.01)	0.059 (0.095) (-0.016 - 0.20)	-0.21, 0.32	0.568	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.38 (0.20) (19.07 - 19.73)	21.67 (0.20) (21.48 - 21.78)	-2.29 (0.28) (-2.71 - -1.75)	-3.07, -1.52	0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	53.85 (0.33) (53.42 - 54.07)	52.70 (0.33) (52.66 - 52.73)	1.16 (0.46) (0.68 - 1.41)	-0.13, 2.44	0.066	48.61, 59.37 (50.95 - 56.68)

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Table E-4 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.64 (0.13) (10.58 - 10.74)	10.04 (0.13) (10.00 - 10.12)	0.60 (0.19) (0.46 - 0.74)	0.074, 1.12	0.033	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.25 (0.0038) (0.25 - 0.26)	0.25 (0.0038) (0.25 - 0.26)	0.0016 (0.0054) (-0.0021 - 0.0080)	-0.013, 0.017	0.777	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.073 (0.0020) (0.071 - 0.075)	0.070 (0.0020) (0.069 - 0.071)	0.0030 (0.0028) (0.0011 - 0.0062)	-0.0048, 0.011	0.348	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.26 (0.0035) (0.25 - 0.27)	0.28 (0.0035) (0.27 - 0.28)	-0.015 (0.0042) (-0.023 - -0.0038)	-0.027, -0.0036	0.022	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	1.15 (0.058) (1.10 - 1.22)	0.94 (0.058) (0.89 - 0.97)	0.21 (0.066) (0.18 - 0.24)	0.027, 0.39	0.033	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-5. Statistical Summary of Site IARL Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt)	2.04 (0.64) (0.80 - 3.44)	1.53 (0.64) (0.46 - 2.70)	0.52 (0.90) (-0.81 - 2.98)	-1.98, 3.02	0.595	0, 7.73 (0.68 - 8.34)
Phytic Acid	1.36 (0.032) (1.33 - 1.38)	1.53 (0.032) (1.47 - 1.62)	-0.17 (0.045) (-0.29 - -0.10)	-0.30, -0.048	0.018	0.77, 1.91 (1.00 - 1.64)
Raffinose	0.38 (0.022) (0.34 - 0.42)	0.43 (0.022) (0.40 - 0.45)	-0.051 (0.020) (-0.10 - -0.018)	-0.11, 0.0034	0.059	0.13, 0.70 (0.26 - 0.59)
Stachyose	3.61 (0.20) (3.15 - 4.02)	3.89 (0.20) (3.76 - 4.15)	-0.29 (0.28) (-1.00 - 0.26)	-1.06, 0.49	0.365	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	33.59 (2.63) (29.66 - 37.60)	29.67 (2.63) (25.64 - 32.71)	3.92 (3.19) (-3.05 - 7.87)	-4.94, 12.79	0.286	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dwt)						
Daidzein	1489.23 (145.92) (1175.46 - 1654.49)	1447.97 (145.92) (1404.40 - 1505.77)	41.27 (206.36) (-258.27 - 233.35)	-531.67, 614.20	0.851	0, 2271.38 (451.33 - 2033.05)

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Table E-5 (continued). Statistical Summary of Site IARL Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	1050.87 (83.29) (1019.09 - 1070.05)	954.99 (83.29) (900.10 - 984.62)	95.88 (117.79) (38.84 - 163.37)	-231.16, 422.92	0.461	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	108.39 (5.35) (97.06 - 117.44)	106.40 (5.35) (97.49 - 111.71)	1.98 (2.24) (-0.44 - 5.73)	-4.23, 8.20	0.425	31.24, 233.60 (73.61 - 231.75)

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[1] dwt= dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-6. Statistical Summary of Site IARL Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	9.44 (0.62) (9.14 - 9.65)	8.87 (0.62) (7.58 - 10.46)	0.57 (0.52) (-0.81 - 1.56)	-0.88, 2.03	0.334	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	63.02 (0.80) (62.21 - 63.79)	65.57 (0.80) (63.58 - 67.74)	-2.55 (1.13) (-3.95 - -1.37)	-5.69, 0.60	0.087	60.69, 73.46 (62.73 - 71.72)
Moisture (% fwt)	82.60 (0.33) (82.40 - 82.80)	81.97 (0.33) (81.40 - 82.70)	0.63 (0.44) (0.10 - 1.20)	-0.59, 1.86	0.223	62.08, 89.80 (70.40 - 84.10)
Protein	25.21 (0.54) (24.71 - 25.52)	23.00 (0.54) (22.15 - 24.07)	2.21 (0.76) (1.33 - 2.75)	0.098, 4.33	0.043	15.69, 26.63 (18.50 - 25.86)
Total Fat	2.30 (0.32) (2.00 - 2.59)	2.52 (0.32) (2.01 - 3.27)	-0.22 (0.46) (-0.68 - 0.042)	-1.49, 1.06	0.662	0, 10.04 (1.57 - 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	40.04 (2.83) (32.90 - 45.11)	32.62 (2.83) (28.87 - 38.15)	7.42 (3.30) (2.07 - 16.24)	-1.75, 16.59	0.088	16.54, 41.80 (20.98 - 39.23)

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Table E-6 (continued). Statistical Summary of Site IARL Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	35.16 (2.66) (30.00 - 38.51)	35.01 (2.66) (27.47 - 39.42)	0.15 (3.76) (-8.13 - 11.03)	-10.30, 10.60	0.969	20.28, 44.03 (24.81 - 42.80)

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[1] dwt = dry weight; fwt = fresh weight.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-7. Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)^1	MON 87708^2 Mean (S.E.)^3 (Range)	Control^4 Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval^5 (Range)
Proximate (% dwt)						
Ash	5.10 (0.080) (5.07 - 5.13)	5.05 (0.080) (4.88 - 5.22)	0.050 (0.089) (-0.14 - 0.23)	-0.20, 0.30	0.602	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	36.35 (0.68) (35.65 - 36.91)	35.77 (0.68) (34.11 - 37.16)	0.58 (0.97) (-0.38 - 2.37)	-2.11, 3.26	0.583	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	5.73 (0.20) (5.17 - 6.25)	6.44 (0.20) (6.20 - 6.63)	-0.71 (0.28) (-1.46 - -0.24)	-1.49, 0.062	0.062	4.27, 9.58 (5.50 - 9.23)
Protein	40.17 (0.40) (39.44 - 40.96)	41.72 (0.40) (40.81 - 42.67)	-1.55 (0.55) (-2.56 - -0.73)	-3.08, -0.024	0.047	35.50, 45.19 (37.06 - 43.42)
Total Fat	18.39 (0.45) (18.25 - 18.56)	17.49 (0.45) (16.81 - 18.39)	0.89 (0.63) (-0.047 - 1.74)	-0.87, 2.65	0.231	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	15.13 (0.45) (14.86 - 15.57)	14.04 (0.45) (13.47 - 14.57)	1.10 (0.61) (0.41 - 2.10)	-0.59, 2.78	0.144	10.06, 18.04 (12.07 - 17.46)

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Table E-7 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control)			Commercial Tolerance Interval[5] (Range)
			Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	
Fiber (% dwt)						
Crude Fiber	9.13 (0.29) (8.84 - 9.39)	8.38 (0.29) (8.20 - 8.64)	0.76 (0.41) (0.55 - 0.97)	-0.38, 1.90	0.139	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	16.62 (0.63) (16.34 - 16.77)	16.85 (0.63) (15.19 - 17.99)	-0.23 (0.73) (-1.23 - 1.56)	-2.27, 1.81	0.766	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.80 (0.014) (1.77 - 1.82)	1.81 (0.014) (1.78 - 1.84)	-0.0030 (0.020) (-0.028 - 0.034)	-0.060, 0.054	0.891	1.56, 1.91 (1.59 - 1.86)
Arginine	3.22 (0.053) (3.14 - 3.28)	3.30 (0.053) (3.19 - 3.43)	-0.081 (0.049) (-0.20 - 0.0059)	-0.22, 0.056	0.174	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.67 (0.037) (4.59 - 4.75)	4.76 (0.037) (4.73 - 4.82)	-0.089 (0.034) (-0.15 - -0.043)	-0.18, 0.0051	0.058	4.04, 5.13 (4.22 - 4.94)
Cystine	0.60 (0.0078) (0.58 - 0.62)	0.59 (0.0078) (0.58 - 0.60)	0.010 (0.011) (-0.0071 - 0.034)	-0.021, 0.041	0.416	0.50, 0.68 (0.53 - 0.66)

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Table E-7 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.43 (0.073) (7.27 - 7.54)	7.61 (0.073) (7.52 - 7.76)	-0.18 (0.056) (-0.25 - -0.067)	-0.34, -0.024	0.032	6.28, 8.30 (6.69 - 7.92)
Glycine	1.79 (0.013) (1.75 - 1.81)	1.81 (0.013) (1.79 - 1.83)	-0.021 (0.014) (-0.049 - 0.0022)	-0.059, 0.018	0.213	1.53, 1.92 (1.58 - 1.84)
Histidine	1.06 (0.0071) (1.04 - 1.07)	1.08 (0.0071) (1.07 - 1.09)	-0.020 (0.0055) (-0.030 - -0.0050)	-0.035, -0.0046	0.022	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.89 (0.013) (1.87 - 1.93)	1.97 (0.013) (1.97 - 1.97)	-0.078 (0.017) (-0.10 - -0.037)	-0.13, -0.031	0.010	1.65, 2.06 (1.68 - 2.02)
Leucine	3.09 (0.022) (3.04 - 3.14)	3.17 (0.022) (3.14 - 3.19)	-0.077 (0.012) (-0.10 - -0.051)	-0.11, -0.044	0.002	2.72, 3.39 (2.80 - 3.27)
Lysine	2.66 (0.017) (2.62 - 2.69)	2.67 (0.017) (2.65 - 2.69)	-0.013 (0.013) (-0.041 - 0.0088)	-0.048, 0.022	0.366	2.33, 2.84 (2.38 - 2.74)

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Table E-7 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.55 (0.012) (0.53 - 0.59)	0.57 (0.012) (0.56 - 0.58)	-0.017 (0.017) (-0.039 - 0.024)	-0.064, 0.030	0.370	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.11 (0.022) (2.08 - 2.14)	2.13 (0.022) (2.09 - 2.19)	-0.016 (0.018) (-0.048 - 0.011)	-0.067, 0.035	0.429	1.80, 2.30 (1.85 - 2.21)
Proline	2.02 (0.019) (1.98 - 2.04)	2.06 (0.019) (2.04 - 2.09)	-0.044 (0.019) (-0.063 - -0.016)	-0.096, 0.0082	0.079	1.65, 2.26 (1.74 - 2.16)
Serine	2.10 (0.027) (2.06 - 2.12)	2.08 (0.027) (2.01 - 2.15)	0.023 (0.025) (-0.027 - 0.054)	-0.046, 0.093	0.404	1.78, 2.27 (1.90 - 2.18)
Threonine	1.59 (0.015) (1.55 - 1.62)	1.59 (0.015) (1.58 - 1.59)	0.0058 (0.019) (-0.035 - 0.046)	-0.046, 0.058	0.772	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.51 (0.0090) (0.49 - 0.53)	0.48 (0.0090) (0.47 - 0.50)	0.030 (0.0084) (0.015 - 0.045)	0.0064, 0.053	0.024	0.38, 0.52 (0.39 - 0.50)

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Table E-7 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Tyrosine	1.44 (0.033) (1.43 - 1.46)	1.43 (0.033) (1.39 - 1.51)	0.014 (0.045) (-0.079 - 0.078)	-0.11, 0.14	0.773	1.24, 1.50 (1.26 - 1.49)
Valine	1.96 (0.015) (1.94 - 2.01)	2.05 (0.015) (2.05 - 2.06)	-0.090 (0.021) (-0.12 - -0.048)	-0.15, -0.031	0.013	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	12.05 (0.073) (11.95 - 12.16)	11.95 (0.073) (11.73 - 12.08)	0.096 (0.089) (-0.082 - 0.29)	-0.15, 0.34	0.340	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	3.91 (0.044) (3.88 - 3.93)	3.93 (0.044) (3.86 - 4.02)	-0.025 (0.062) (-0.086 - 0.018)	-0.20, 0.15	0.705	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.74 (0.29) (19.44 - 19.94)	21.57 (0.29) (21.07 - 22.44)	-1.83 (0.41) (-2.51 - -1.21)	-2.96, -0.69	0.011	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.54 (0.25) (54.45 - 54.70)	53.26 (0.25) (52.77 - 53.74)	1.28 (0.35) (0.73 - 1.68)	0.31, 2.26	0.021	48.61, 59.37 (50.95 - 56.68)

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Table E-7 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range))
Fatty Acid (% Total FA)						
18:3 Linolenic	9.07 (0.074) (8.99 - 9.16)	8.58 (0.074) (8.42 - 8.71)	0.50 (0.099) (0.36 - 0.56)	0.22, 0.77	0.007	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0035) (0.26 - 0.26)	0.26 (0.0035) (0.26 - 0.27)	-0.0048 (0.0050) (-0.012 - 0.00087)	-0.019, 0.0091	0.393	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.16 (0.0016) (0.16 - 0.16)	0.16 (0.0016) (0.16 - 0.17)	-0.0064 (0.0023) (-0.010 - -0.0034)	-0.013, 0.00005	0.051	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.28 (0.0030) (0.27 - 0.28)	0.29 (0.0030) (0.28 - 0.30)	-0.011 (0.0042) (-0.019 - -0.0066)	-0.023, 0.00033	0.054	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	2.13 (0.077) (2.10 - 2.17)	1.86 (0.077) (1.71 - 2.11)	0.27 (0.089) (0.059 - 0.42)	0.022, 0.52	0.038	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-8. Statistical Summary of Site ILCY Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt)	6.89 (1.81) (4.28 - 10.27)	5.54 (1.81) (2.14 - 10.38)	1.34 (2.55) (-4.27 - 8.13)	-5.75, 8.43	0.626	0, 7.73 (0.68 - 8.34)
Phytic Acid	1.12 (0.032) (1.08 - 1.20)	1.16 (0.032) (1.10 - 1.22)	-0.037 (0.045) (-0.14 - 0.10)	-0.16, 0.088	0.456	0.77, 1.91 (1.00 - 1.64)
Raffinose	0.58 (0.013) (0.57 - 0.59)	0.57 (0.013) (0.54 - 0.60)	0.011 (0.018) (-0.027 - 0.046)	-0.039, 0.061	0.575	0.13, 0.70 (0.26 - 0.59)
Stachyose	3.33 (0.10) (3.25 - 3.46)	3.64 (0.10) (3.43 - 3.83)	-0.31 (0.14) (-0.58 - 0.023)	-0.70, 0.085	0.095	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	31.75 (1.10) (30.61 - 33.32)	32.78 (1.10) (31.06 - 34.22)	-1.02 (1.56) (-2.43 - 0.26)	-5.35, 3.30	0.546	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dwt)						
Daidzein	925.54 (72.66) (899.83 - 974.38)	922.21 (72.66) (762.49 - 1098.08)	3.32 (102.76) (-198.25 - 139.91)	-281.99, 288.63	0.975	0, 2271.38 (451.33 - 2033.05)

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Table E-8 (continued). Statistical Summary of Site ILCY Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	655.78 (45.60) (594.13 - 712.01)	653.27 (45.60) (588.17 - 770.79)	2.51 (64.49) (-58.78 - 60.35)	-176.54, 181.56	0.970	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	98.02 (8.11) (77.67 - 112.00)	113.29 (8.11) (96.25 - 122.09)	-15.27 (11.47) (-43.86 - 15.75)	-47.13, 16.59	0.254	31.24, 233.60 (73.61 - 231.75)

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[1] dwt = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-9. Statistical Summary of Site ILCY Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	6.45 (0.22)	6.27 (0.22)	0.18 (0.32)	-0.70, 1.05	0.601	3.36, 10.84
	(6.12 - 6.70)	(6.10 - 6.49)	(-0.37 - 0.48)			(5.20 - 9.81)
Carbohydrates	65.26 (0.61)	66.38 (0.61)	-1.12 (0.87)	-3.53, 1.29	0.265	60.69, 73.46
	(64.42 - 65.78)	(65.53 - 67.94)	(-3.52 - 0.11)			(62.73 - 71.72)
Moisture (% fwt)	73.13 (0.25)	73.53 (0.25)	-0.40 (0.35)	-1.37, 0.57	0.316	62.08, 89.80
	(72.40 - 73.70)	(73.20 - 73.80)	(-1.20 - 0.50)			(70.40 - 84.10)
Protein	22.20 (0.51)	21.64 (0.51)	0.56 (0.68)	-1.33, 2.46	0.454	15.69, 26.63
	(21.25 - 23.11)	(20.88 - 23.03)	(-0.78 - 2.23)			(18.50 - 25.86)
Total Fat	6.11 (0.38)	5.77 (0.38)	0.34 (0.52)	-1.09, 1.77	0.549	0, 10.04
	(5.62 - 6.88)	(5.15 - 6.72)	(0.17 - 0.47)			(1.57 - 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	30.24 (1.09)	28.46 (1.09)	1.78 (1.54)	-2.49, 6.05	0.310	16.54, 41.80
	(28.75 - 32.14)	(27.05 - 30.90)	(-2.15 - 5.09)			(20.98 - 39.23)

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Table E-9 (continued). Statistical Summary of Site ILCY Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	27.72 (1.65) (27.34 - 27.98)	28.06 (1.65) (23.66 - 32.73)	-0.35 (2.33) (-4.90 - 3.68)	-6.82, 6.13	0.889	20.28, 44.03 (24.81 - 42.80)

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[1] dwt = dry weight; fwt = fresh weight.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-10. Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	5.43 (0.084) (5.24 - 5.69)	5.23 (0.084) (5.13 - 5.29)	0.20 (0.084) (0.097 - 0.40)	-0.031, 0.44	0.073	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	38.84 (0.44) (38.13 - 39.21)	38.29 (0.44) (38.19 - 38.42)	0.54 (0.45) (-0.064 - 0.96)	-0.71, 1.79	0.292	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	6.96 (0.16) (6.80 - 7.17)	6.16 (0.16) (5.79 - 6.41)	0.80 (0.22) (0.63 - 1.01)	0.18, 1.42	0.022	4.27, 9.58 (5.50 - 9.23)
Protein	40.88 (0.28) (40.56 - 41.37)	41.99 (0.28) (41.72 - 42.25)	-1.11 (0.38) (-1.54 - -0.63)	-2.15, -0.062	0.042	35.50, 45.19 (37.06 - 43.42)
Total Fat	14.83 (0.38) (14.00 - 15.90)	14.49 (0.38) (14.40 - 14.54)	0.34 (0.44) (-0.53 - 1.49)	-0.89, 1.57	0.487	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	13.43 (0.43) (12.71 - 14.61)	12.96 (0.43) (12.48 - 13.69)	0.47 (0.61) (-0.71 - 2.13)	-1.21, 2.15	0.480	10.06, 18.04 (12.07 - 17.46)

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Table E-10 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Crude Fiber	8.22 (0.52) (7.39 - 9.07)	7.58 (0.52) (7.39 - 7.82)	0.64 (0.74) (-0.14 - 1.68)	-1.40, 2.69	0.430	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	15.62 (0.72) (13.84 - 17.83)	13.78 (0.72) (13.44 - 14.00)	1.84 (0.94) (-0.064 - 4.39)	-0.77, 4.45	0.122	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.74 (0.0076) (1.73 - 1.76)	1.75 (0.0076) (1.75 - 1.76)	-0.014 (0.0093) (-0.024 - -0.0071)	-0.039, 0.012	0.219	1.56, 1.91 (1.59 - 1.86)
Arginine	3.30 (0.037) (3.24 - 3.33)	3.57 (0.037) (3.55 - 3.60)	-0.27 (0.040) (-0.32 - -0.23)	-0.38, -0.16	0.002	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.59 (0.017) (4.55 - 4.61)	4.67 (0.017) (4.67 - 4.68)	-0.089 (0.020) (-0.13 - -0.065)	-0.14, -0.034	0.011	4.04, 5.13 (4.22 - 4.94)
Cystine	0.62 (0.0090) (0.62 - 0.63)	0.61 (0.0090) (0.58 - 0.62)	0.014 (0.0092) (-0.0029 - 0.036)	-0.012, 0.039	0.205	0.50, 0.68 (0.53 - 0.66)

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Table E-10 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.29 (0.030) (7.20 - 7.35)	7.51 (0.030) (7.49 - 7.53)	-0.21 (0.031) (-0.29 - -0.16)	-0.30, -0.13	0.002	6.28, 8.30 (6.69 - 7.92)
Glycine	1.75 (0.0053) (1.74 - 1.76)	1.77 (0.0053) (1.76 - 1.77)	-0.021 (0.0075) (-0.034 - -0.0096)	-0.042, 0.00033	0.052	1.53, 1.92 (1.58 - 1.84)
Histidine	1.05 (0.0032) (1.05 - 1.05)	1.07 (0.0032) (1.06 - 1.07)	-0.017 (0.0046) (-0.027 - -0.0057)	-0.030, -0.0046	0.019	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.87 (0.012) (1.85 - 1.89)	1.90 (0.012) (1.88 - 1.91)	-0.023 (0.0040) (-0.033 - -0.017)	-0.034, -0.012	0.004	1.65, 2.06 (1.68 - 2.02)
Leucine	3.02 (0.011) (3.00 - 3.04)	3.10 (0.011) (3.09 - 3.13)	-0.077 (0.0062) (-0.086 - -0.061)	-0.094, -0.060	<0.001	2.72, 3.39 (2.80 - 3.27)
Lysine	2.63 (0.0062) (2.63 - 2.64)	2.63 (0.0062) (2.62 - 2.64)	0.0011 (0.0088) (-0.011 - 0.0071)	-0.023, 0.026	0.904	2.33, 2.84 (2.38 - 2.74)

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Table E-10 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.59 (0.0074) (0.57 - 0.60)	0.58 (0.0074) (0.56 - 0.59)	0.0079 (0.010) (-0.016 - 0.029)	-0.021, 0.037	0.492	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.01 (0.019) (1.96 - 2.06)	2.07 (0.019) (2.05 - 2.10)	-0.061 (0.021) (-0.085 - -0.047)	-0.12, -0.0015	0.046	1.80, 2.30 (1.85 - 2.21)
Proline	1.94 (0.020) (1.93 - 1.96)	2.05 (0.020) (2.01 - 2.09)	-0.10 (0.028) (-0.16 - -0.048)	-0.18, -0.027	0.020	1.65, 2.26 (1.74 - 2.16)
Serine	1.98 (0.013) (1.97 - 2.00)	2.06 (0.013) (2.02 - 2.09)	-0.079 (0.013) (-0.095 - -0.048)	-0.11, -0.044	0.003	1.78, 2.27 (1.90 - 2.18)
Threonine	1.52 (0.0042) (1.51 - 1.53)	1.55 (0.0042) (1.54 - 1.55)	-0.026 (0.0049) (-0.030 - -0.022)	-0.040, -0.013	0.005	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.44 (0.0083) (0.44 - 0.45)	0.47 (0.0083) (0.45 - 0.48)	-0.025 (0.011) (-0.035 - -0.015)	-0.055, 0.0061	0.089	0.38, 0.52 (0.39 - 0.50)

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Table E-10 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Tyrosine	1.35 (0.024) (1.32 - 1.41)	1.36 (0.024) (1.34 - 1.40)	-0.013 (0.027) (-0.032 - 0.0095)	-0.090, 0.063	0.651	1.24, 1.50 (1.26 - 1.49)
Valine	1.99 (0.013) (1.95 - 2.01)	2.01 (0.013) (2.01 - 2.02)	-0.022 (0.012) (-0.053 - 0.0028)	-0.057, 0.012	0.149	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.26 (0.041) (11.25 - 11.27)	11.04 (0.041) (10.97 - 11.12)	0.22 (0.057) (0.15 - 0.28)	0.063, 0.38	0.017	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.32 (0.063) (4.23 - 4.40)	4.25 (0.063) (4.16 - 4.31)	0.076 (0.089) (0.067 - 0.085)	-0.17, 0.32	0.439	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.52 (0.25) (19.34 - 19.64)	21.14 (0.25) (20.78 - 21.55)	-1.62 (0.36) (-1.97 - -1.43)	-2.62, -0.62	0.010	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	53.74 (0.32) (53.55 - 54.06)	52.90 (0.32) (52.33 - 53.20)	0.85 (0.46) (0.47 - 1.22)	-0.43, 2.12	0.139	48.61, 59.37 (50.95 - 56.68)

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Table E-10 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.54 (0.10) (10.51 - 10.59)	10.05 (0.10) (9.89 - 10.14)	0.49 (0.14) (0.39 - 0.65)	0.095, 0.89	0.026	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.27 (0.0041) (0.26 - 0.27)	0.27 (0.0041) (0.26 - 0.27)	-0.00093 (0.0058) (-0.0057 - 0.0027)	-0.017, 0.015	0.879	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.075 (0.0020) (0.070 - 0.079)	0.076 (0.0020) (0.075 - 0.077)	-0.0014 (0.0023) (-0.0071 - 0.0019)	-0.0076, 0.0049	0.583	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.26 (0.0032) (0.26 - 0.27)	0.28 (0.0032) (0.28 - 0.29)	-0.019 (0.0040) (-0.021 - -0.017)	-0.030, -0.0079	0.008	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	1.18 (0.037) (1.08 - 1.26)	0.94 (0.037) (0.89 - 0.99)	0.23 (0.053) (0.19 - 0.31)	0.086, 0.38	0.011	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.
[2] MON 87708 was treated with dicamba.
[3] Mean (S.E.) = least-square mean (standard error).
[4] Control refers to the near isogenic conventional soybean control A3525.
[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-11. Statistical Summary of Site ILWY Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt)	1.10 (0.44) (0.59 - 1.51)	2.33 (0.44) (1.34 - 3.68)	-1.23 (0.43) (-2.17 - -0.75)	-2.43, -0.035	0.045	0, 7.73 (0.68 - 8.34)
Phytic Acid	1.40 (0.033) (1.33 - 1.46)	1.55 (0.033) (1.47 - 1.61)	-0.14 (0.044) (-0.22 - -0.054)	-0.27, -0.023	0.030	0.77, 1.91 (1.00 - 1.64)
Raffinose	0.37 (0.026) (0.32 - 0.45)	0.41 (0.026) (0.41 - 0.41)	-0.037 (0.036) (-0.086 - 0.040)	-0.14, 0.065	0.371	0.13, 0.70 (0.26 - 0.59)
Stachyose	3.44 (0.19) (3.07 - 4.02)	3.76 (0.19) (3.68 - 3.85)	-0.33 (0.27) (-0.78 - 0.34)	-1.08, 0.43	0.294	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	34.32 (2.07) (29.54 - 39.27)	29.73 (2.07) (25.43 - 32.22)	4.59 (2.89) (-2.68 - 8.72)	-3.43, 12.62	0.187	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dwt)						
Daidzein	1458.08 (35.08) (1416.31 - 1535.98)	1271.60 (35.08) (1196.71 - 1354.96)	186.48 (31.48) (153.17 - 225.25)	99.09, 273.88	0.004	0, 2271.38 (451.33 - 2033.05)

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Table E-11 (continued). Statistical Summary of Site ILWY Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	898.89 (28.15) (873.39 - 913.50)	860.58 (28.15) (784.27 - 913.26)	38.31 (39.82) (-10.80 - 129.23)	-72.23, 148.86	0.390	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	111.77 (2.15) (109.88 - 113.86)	79.70 (2.15) (77.14 - 81.62)	32.07 (2.23) (31.24 - 32.73)	25.87, 38.27	<0.001	31.24, 233.60 (73.61 - 231.75)

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[1] dwt = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.
[2] MON 87708 was treated with dicamba.
[3] Mean (S.E.) = least-square mean (standard error).
[4] Control refers to the near isogenic conventional soybean control A3525.
[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-12. Statistical Summary of Site ILWY Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	6.61 (0.23) (6.02 - 7.21)	6.88 (0.23) (6.82 - 6.99)	-0.27 (0.30) (-0.79 - 0.37)	-1.10, 0.56	0.416	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	67.99 (0.77) (66.09 - 69.50)	66.26 (0.77) (65.71 - 66.67)	1.73 (1.08) (-0.30 - 3.78)	-1.28, 4.74	0.185	60.69, 73.46 (62.73 - 71.72)
Moisture (% fwt)	75.17 (0.55) (74.10 - 76.70)	75.40 (0.55) (75.10 - 75.60)	-0.23 (0.65) (-1.40 - 1.10)	-2.04, 1.57	0.737	62.08, 89.80 (70.40 - 84.10)
Protein	20.93 (0.58) (19.27 - 22.70)	21.97 (0.58) (21.81 - 22.13)	-1.03 (0.82) (-2.69 - 0.57)	-3.32, 1.25	0.278	15.69, 26.63 (18.50 - 25.86)
Total Fat	4.44 (0.52) (3.92 - 5.10)	4.91 (0.52) (4.50 - 5.63)	-0.47 (0.35) (-0.67 - -0.19)	-1.44, 0.50	0.252	0, 10.04 (1.57 - 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	29.18 (1.73) (26.72 - 31.00)	27.77 (1.73) (25.12 - 31.00)	1.41 (2.44) (-4.28 - 4.71)	-5.36, 8.19	0.593	16.54, 41.80 (20.98 - 39.23)

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Table E-12 (continued). Statistical Summary of Site ILWY Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	28.64 (1.83) (27.22 - 31.26)	33.25 (1.83) (31.89 - 34.06)	-4.61 (2.59) (-6.63 - -0.62)	-11.80, 2.58	0.149	20.28, 44.03 (24.81 - 42.80)

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[1] dwt = dry weight; fwt = fresh weight.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-13. Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	5.03 (0.11) (4.94 - 5.18)	4.95 (0.11) (4.73 - 5.23)	0.075 (0.15) (-0.28 - 0.45)	-0.35, 0.50	0.644	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	37.60 (0.78) (37.15 - 38.07)	35.95 (0.78) (35.27 - 37.04)	1.65 (1.10) (1.03 - 2.05)	-1.41, 4.71	0.208	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	6.74 (0.20) (6.48 - 7.13)	6.53 (0.20) (6.32 - 6.84)	0.21 (0.29) (-0.23 - 0.69)	-0.59, 1.01	0.513	4.27, 9.58 (5.50 - 9.23)
Protein	42.11 (0.53) (41.33 - 42.53)	43.58 (0.53) (43.50 - 43.69)	-1.48 (0.76) (-2.36 - -0.97)	-3.57, 0.62	0.122	35.50, 45.19 (37.06 - 43.42)
Total Fat	15.30 (0.45) (14.54 - 15.95)	15.55 (0.45) (14.52 - 16.10)	-0.25 (0.56) (-0.63 - 0.025)	-1.82, 1.32	0.678	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	13.22 (0.35) (12.64 - 13.79)	12.77 (0.35) (12.28 - 13.25)	0.46 (0.46) (-0.14 - 1.52)	-0.81, 1.73	0.374	10.06, 18.04 (12.07 - 17.46)

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Table E-13 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Crude Fiber	8.06 (0.18) (7.76 - 8.47)	6.89 (0.18) (6.59 - 7.12)	1.17 (0.25) (0.64 - 1.51)	0.47, 1.88	0.009	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	15.98 (0.67) (14.97 - 16.49)	14.66 (0.67) (13.24 - 15.56)	1.32 (0.95) (0.93 - 1.73)	-1.32, 3.96	0.237	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.81 (0.021) (1.80 - 1.83)	1.84 (0.021) (1.80 - 1.87)	-0.032 (0.022) (-0.072 - 0.013)	-0.093, 0.029	0.223	1.56, 1.91 (1.59 - 1.86)
Arginine	3.44 (0.044) (3.39 - 3.50)	3.72 (0.044) (3.64 - 3.81)	-0.27 (0.062) (-0.38 - -0.15)	-0.45, -0.10	0.011	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.76 (0.062) (4.70 - 4.80)	4.89 (0.062) (4.80 - 4.95)	-0.13 (0.078) (-0.23 - 0.0034)	-0.34, 0.087	0.173	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0067) (0.61 - 0.61)	0.59 (0.0067) (0.59 - 0.60)	0.020 (0.0094) (0.0087 - 0.029)	-0.0067, 0.046	0.107	0.50, 0.68 (0.53 - 0.66)

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Table E-13 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval⁵ (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.66 (0.11) (7.57 - 7.73)	7.93 (0.11) (7.75 - 8.02)	-0.26 (0.14) (-0.45 - -0.018)	-0.66, 0.13	0.138	6.28, 8.30 (6.69 - 7.92)
Glycine	1.82 (0.020) (1.80 - 1.83)	1.85 (0.020) (1.82 - 1.87)	-0.035 (0.027) (-0.072 - 0.013)	-0.11, 0.039	0.257	1.53, 1.92 (1.58 - 1.84)
Histidine	1.09 (0.012) (1.07 - 1.10)	1.11 (0.012) (1.10 - 1.12)	-0.028 (0.016) (-0.056 - -0.0026)	-0.073, 0.018	0.166	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.94 (0.042) (1.90 - 1.97)	2.00 (0.042) (1.95 - 2.03)	-0.060 (0.057) (-0.11 - 0.025)	-0.22, 0.099	0.354	1.65, 2.06 (1.68 - 2.02)
Leucine	3.16 (0.041) (3.11 - 3.19)	3.24 (0.041) (3.20 - 3.26)	-0.082 (0.052) (-0.14 - -0.0086)	-0.23, 0.061	0.186	2.72, 3.39 (2.80 - 3.27)
Lysine	2.70 (0.030) (2.66 - 2.71)	2.72 (0.030) (2.68 - 2.76)	-0.030 (0.035) (-0.070 - 0.031)	-0.13, 0.068	0.446	2.33, 2.84 (2.38 - 2.74)

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Table E-13 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.58 (0.0086) (0.58 - 0.59)	0.59 (0.0086) (0.58 - 0.60)	-0.0055 (0.012) (-0.017 - 0.00070)	-0.039, 0.028	0.674	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.15 (0.030) (2.12 - 2.18)	2.20 (0.030) (2.13 - 2.23)	-0.049 (0.040) (-0.11 - 0.048)	-0.16, 0.062	0.289	1.80, 2.30 (1.85 - 2.21)
Proline	2.07 (0.010) (2.06 - 2.09)	2.06 (0.010) (2.05 - 2.07)	0.0045 (0.015) (-0.0071 - 0.016)	-0.036, 0.045	0.771	1.65, 2.26 (1.74 - 2.16)
Serine	2.09 (0.028) (2.06 - 2.12)	2.13 (0.028) (2.13 - 2.14)	-0.038 (0.029) (-0.070 - -0.016)	-0.12, 0.043	0.260	1.78, 2.27 (1.90 - 2.18)
Threonine	1.60 (0.019) (1.57 - 1.62)	1.61 (0.019) (1.60 - 1.62)	-0.014 (0.027) (-0.040 - 0.012)	-0.089, 0.060	0.622	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.47 (0.013) (0.44 - 0.50)	0.45 (0.013) (0.43 - 0.46)	0.019 (0.018) (-0.015 - 0.064)	-0.032, 0.069	0.365	0.38, 0.52 (0.39 - 0.50)

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Table E-13 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Tyrosine	1.38 (0.024) (1.35 - 1.43)	1.44 (0.024) (1.38 - 1.47)	-0.065 (0.022) (-0.12 - -0.036)	-0.13, -0.0024	0.044	1.24, 1.50 (1.26 - 1.49)
Valine	2.05 (0.045) (2.01 - 2.09)	2.12 (0.045) (2.06 - 2.16)	-0.074 (0.063) (-0.14 - 0.026)	-0.25, 0.10	0.305	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.42 (0.068) (11.39 - 11.46)	11.19 (0.068) (11.14 - 11.21)	0.23 (0.097) (0.19 - 0.26)	-0.036, 0.50	0.074	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.18 (0.047) (4.11 - 4.27)	4.25 (0.047) (4.16 - 4.31)	-0.064 (0.066) (-0.19 - 0.11)	-0.25, 0.12	0.387	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	18.78 (0.085) (18.58 - 18.95)	20.19 (0.085) (20.12 - 20.23)	-1.41 (0.093) (-1.64 - -1.27)	-1.66, -1.15	<0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.98 (0.10) (54.80 - 55.14)	54.43 (0.10) (54.32 - 54.64)	0.54 (0.14) (0.16 - 0.82)	0.15, 0.94	0.019	48.61, 59.37 (50.95 - 56.68)

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Table E-13 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.03 (0.050) (9.89 - 10.10)	9.31 (0.050) (9.26 - 9.40)	0.71 (0.070) (0.60 - 0.84)	0.52, 0.91	<0.001	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0029) (0.26 - 0.27)	0.27 (0.0029) (0.26 - 0.27)	-0.0053 (0.0041) (-0.013 - 0.0051)	-0.017, 0.0062	0.270	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.072 (0.0020) (0.069 - 0.076)	0.071 (0.0020) (0.069 - 0.076)	0.0010 (0.0025) (-0.00013 - 0.0025)	-0.0059, 0.0079	0.701	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.28 (0.0033) (0.27 - 0.29)	0.29 (0.0033) (0.29 - 0.30)	-0.014 (0.0047) (-0.023 - 0.00015)	-0.027, -0.0012	0.038	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	1.28 (0.054) (1.25 - 1.30)	1.16 (0.054) (1.10 - 1.23)	0.12 (0.067) (0.018 - 0.18)	-0.065, 0.31	0.146	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference varieties. Negative limits set to zero.

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Table E-14. Statistical Summary of Site INRC Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt)	3.03 (0.32) (2.75 - 3.45)	2.56 (0.32) (2.33 - 3.02)	0.47 (0.45) (-0.26 - 1.13)	-0.79, 1.74	0.357	0, 7.73 (0.68 - 8.34)
Phytic Acid	1.27 (0.071) (1.22 - 1.34)	1.19 (0.071) (1.09 - 1.36)	0.078 (0.087) (-0.022 - 0.15)	-0.16, 0.32	0.421	0.77, 1.91 (1.00 - 1.64)
Raffinose	0.37 (0.023) (0.33 - 0.43)	0.40 (0.023) (0.36 - 0.43)	-0.032 (0.033) (-0.098 - 0.069)	-0.12, 0.060	0.384	0.13, 0.70 (0.26 - 0.59)
Stachyose	3.14 (0.077) (3.12 - 3.17)	3.46 (0.077) (3.33 - 3.67)	-0.32 (0.11) (-0.51 - -0.21)	-0.62, -0.015	0.043	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	29.17 (1.79) (26.09 - 33.09)	29.28 (1.79) (25.22 - 31.77)	-0.12 (1.83) (-4.76 - 3.09)	-5.21, 4.97	0.952	22.05, 41.12 (22.81 - 44.56)
Isoflavone (μg/g dwt)						
Daidzein	1683.50 (67.03) (1593.24 - 1777.49)	1419.40 (67.03) (1416.92 - 1421.55)	264.10 (94.79) (173.52 - 360.58)	0.92, 527.28	0.049	0, 2271.38 (451.33 - 2033.05)

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Table E-14 (continued). Statistical Summary of Site INRC Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	1033.37 (50.59) (963.43 - 1092.19)	862.03 (50.59) (840.10 - 890.94)	171.34 (71.54) (108.39 - 204.37)	-27.29, 369.97	0.074	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	111.51 (3.23) (110.91 - 112.28)	98.42 (3.23) (89.42 - 103.14)	13.10 (3.31) (7.77 - 21.94)	3.91, 22.29	0.016	31.24, 233.60 (73.61 - 231.75)

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[1] dwt = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.
[2] MON 87708 was treated with dicamba.
[3] Mean (S.E.) = least-square mean (standard error).
[4] Control refers to the near isogenic conventional soybean control A3525.
[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-15. Statistical Summary of Site INRC Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	6.45 (0.24) (5.94 - 7.05)	6.95 (0.24) (6.84 - 7.07)	-0.50 (0.26) (-0.89 - 0.11)	-1.23, 0.23	0.128	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	65.19 (0.69) (63.10 - 66.54)	63.82 (0.69) (62.91 - 64.44)	1.38 (0.98) (-1.34 - 3.03)	-1.34, 4.10	0.232	60.69, 73.46 (62.73 - 71.72)
Moisture (% fwt)	73.00 (0.32) (72.40 - 73.70)	72.27 (0.32) (71.60 - 72.70)	0.73 (0.39) (-0.10 - 1.30)	-0.34, 1.80	0.129	62.08, 89.80 (70.40 - 84.10)
Protein	21.78 (0.41) (20.99 - 22.51)	23.33 (0.41) (22.64 - 24.11)	-1.55 (0.41) (-2.26 - -0.73)	-2.69, -0.41	0.019	15.69, 26.63 (18.50 - 25.86)
Total Fat	6.54 (0.27) (6.12 - 7.34)	5.88 (0.27) (5.39 - 6.19)	0.66 (0.39) (-0.069 - 1.96)	-0.42, 1.73	0.164	0, 10.04 (1.57 - 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	26.46 (1.50) (23.30 - 31.06)	23.83 (1.50) (22.93 - 25.53)	2.63 (2.13) (-0.51 - 8.13)	-3.27, 8.54	0.283	16.54, 41.80 (20.98 - 39.23)

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Table E-15 (continued). Statistical Summary of Site INRC Soybean Forage Nutrients for MON 87708 Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	27.20 (1.62) (24.21 - 31.27)	26.11 (1.62) (23.91 - 29.42)	1.08 (2.04) (0.30 - 1.85)	-4.59, 6.76	0.623	20.28, 44.03 (24.81 - 42.80)

[1] dwt = dry weight; fwt = fresh weight.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-16. Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	5.33 (0.11) (5.27 - 5.39)	5.05 (0.11) (4.96 - 5.17)	0.28 (0.16) (0.15 - 0.44)	-0.16, 0.72	0.148	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	38.30 (0.51) (37.69 - 38.65)	35.23 (0.51) (34.49 - 35.75)	3.07 (0.64) (2.23 - 4.07)	1.29, 4.84	0.008	32.07, 40.08 (33.82 - 39.26)
Moisture (% fwt)	7.84 (0.22) (7.38 - 8.47)	10.50 (0.22) (10.40 - 10.60)	-2.66 (0.22) (-3.12 - -2.13)	-3.27, -2.04	<0.001	4.27, 9.58 (5.50 - 9.23)
Protein	40.25 (0.41) (39.00 - 41.05)	43.69 (0.41) (43.46 - 43.85)	-3.43 (0.51) (-4.84 - -2.70)	-4.86, -2.01	0.002	35.50, 45.19 (37.06 - 43.42)
Total Fat	16.10 (0.63) (14.95 - 18.03)	16.05 (0.63) (15.64 - 16.85)	0.050 (0.89) (-1.90 - 2.37)	-2.41, 2.51	0.957	12.33, 24.10 (15.47 - 21.34)
Fiber (% dwt)						
Acid Detergent Fiber	12.91 (0.35) (12.45 - 13.21)	11.96 (0.35) (11.62 - 12.17)	0.96 (0.43) (0.37 - 1.44)	-0.24, 2.15	0.089	10.06, 18.04 (12.07 - 17.46)

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Table E-16 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Crude Fiber	8.30 (0.63) (6.23 - 9.65)	6.61 (0.63) (6.05 - 6.98)	1.68 (0.71) (0.18 - 2.67)	-0.30, 3.66	0.077	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	13.97 (0.36) (13.43 - 14.97)	13.11 (0.36) (12.63 - 13.62)	0.86 (0.50) (-0.18 - 1.88)	-0.54, 2.25	0.164	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dwt)						
Alanine	1.75 (0.017) (1.74 - 1.77)	1.86 (0.017) (1.82 - 1.90)	-0.11 (0.024) (-0.16 - -0.054)	-0.17, -0.042	0.010	1.56, 1.91 (1.59 - 1.86)
Arginine	3.25 (0.053) (3.09 - 3.36)	3.88 (0.053) (3.83 - 3.93)	-0.63 (0.074) (-0.83 - -0.47)	-0.83, -0.42	0.001	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.56 (0.041) (4.45 - 4.63)	4.94 (0.041) (4.90 - 5.01)	-0.38 (0.057) (-0.56 - -0.27)	-0.54, -0.22	0.002	4.04, 5.13 (4.22 - 4.94)
Cystine	0.62 (0.0062) (0.60 - 0.63)	0.59 (0.0062) (0.59 - 0.60)	0.028 (0.0081) (0.0092 - 0.039)	0.0061, 0.051	0.024	0.50, 0.68 (0.53 - 0.66)

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Table E-16 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Glutamic Acid	7.28 (0.081) (7.06 - 7.40)	8.00 (0.081) (7.91 - 8.14)	-0.73 (0.11) (-1.09 - -0.54)	-1.05, -0.41	0.003	6.28, 8.30 (6.69 - 7.92)
Glycine	1.73 (0.015) (1.69 - 1.75)	1.86 (0.015) (1.83 - 1.89)	-0.13 (0.022) (-0.20 - -0.076)	-0.19, -0.066	0.004	1.53, 1.92 (1.58 - 1.84)
Histidine	1.05 (0.0089) (1.02 - 1.06)	1.13 (0.0089) (1.11 - 1.14)	-0.085 (0.013) (-0.12 - -0.053)	-0.12, -0.050	0.002	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.85 (0.026) (1.79 - 1.90)	2.00 (0.026) (1.94 - 2.04)	-0.15 (0.036) (-0.24 - -0.046)	-0.25, -0.051	0.014	1.65, 2.06 (1.68 - 2.02)
Leucine	3.03 (0.027) (2.96 - 3.09)	3.28 (0.027) (3.24 - 3.32)	-0.24 (0.038) (-0.36 - -0.15)	-0.35, -0.14	0.002	2.72, 3.39 (2.80 - 3.27)
Lysine	2.60 (0.023) (2.53 - 2.65)	2.75 (0.023) (2.71 - 2.77)	-0.15 (0.032) (-0.23 - -0.091)	-0.24, -0.060	0.009	2.33, 2.84 (2.38 - 2.74)

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Table E-16 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Amino Acid (% dwt)						
Methionine	0.58 (0.0090) (0.57 – 0.60)	0.58 (0.0090) (0.57 – 0.60)	-0.00056 (0.0072) (-0.0027 – 0.00085)	-0.021, 0.020	0.942	0.50, 0.64 (0.52 – 0.63)
Phenylalanine	2.04 (0.027) (2.00 – 2.07)	2.21 (0.027) (2.16 – 2.27)	-0.18 (0.038) (-0.27 - -0.083)	-0.28, -0.069	0.010	1.80, 2.30 (1.85 – 2.21)
Proline	1.98 (0.024) (1.94 – 2.00)	2.10 (0.024) (2.08 – 2.13)	-0.13 (0.032) (-0.14 - -0.11)	-0.21, -0.038	0.016	1.65, 2.26 (1.74 – 2.16)
Serine	2.04 (0.035) (2.01 – 2.06)	2.16 (0.035) (2.06 – 2.21)	-0.12 (0.050) (-0.19 – 0.0063)	-0.26, 0.018	0.073	1.78, 2.27 (1.90 – 2.18)
Threonine	1.55 (0.015) (1.52 – 1.57)	1.62 (0.015) (1.60 – 1.64)	-0.069 (0.021) (-0.10 - -0.032)	-0.13, -0.011	0.029	1.40, 1.69 (1.47 – 1.64)
Tryptophan	0.47 (0.012) (0.44 – 0.48)	0.46 (0.012) (0.45 – 0.46)	0.010 (0.017) (-0.0098 – 0.023)	-0.036, 0.057	0.567	0.38, 0.52 (0.39 – 0.50)

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Table E-16 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)^1	MON 87708^2 Mean (S.E.)^3 (Range)	Control^4 Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval^5 (Range)
Amino Acid (% dwt)						
Tyrosine	1.35 (0.027) (1.28 – 1.43)	1.49 (0.027) (1.48 – 1.52)	-0.14 (0.032) (-0.20 - -0.088)	-0.23, -0.052	0.011	1.24, 1.50 (1.26 – 1.49)
Valine	1.95 (0.029) (1.89 – 2.00)	2.13 (0.029) (2.05 – 2.17)	-0.17 (0.041) (-0.27 - -0.050)	-0.29, -0.061	0.012	1.72, 2.20 (1.73 – 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.74 (0.12) (11.39 – 12.07)	11.49 (0.12) (11.38 – 11.55)	0.25 (0.15) (-0.15 – 0.52)	-0.17, 0.67	0.169	8.44, 12.56 (9.40 – 11.54)
18:0 Stearic	3.85 (0.12) (3.60 – 4.12)	3.76 (0.12) (3.67 – 3.91)	0.093 (0.14) (-0.078 – 0.42)	-0.30, 0.48	0.544	2.90, 5.19 (3.24 – 4.67)
18:1 Oleic	18.58 (0.31) (17.85 – 19.42)	20.01 (0.31) (19.60 – 20.32)	-1.43 (0.35) (-1.74 - -0.90)	-2.40, -0.45	0.015	15.73, 27.19 (17.88 – 25.31)
18:2 Linoleic	54.89 (0.41) (53.59 – 55.67)	54.68 (0.41) (54.18 – 54.99)	0.21 (0.53) (-0.59 – 0.68)	-1.25, 1.67	0.708	48.61, 59.37 (50.95 – 56.68)

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Table E-16 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.33 (0.21) (9.91 - 10.88)	9.47 (0.21) (9.13 - 9.68)	0.85 (0.16) (0.59 - 1.20)	0.40, 1.31	0.006	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.25 (0.0063) (0.23 - 0.26)	0.24 (0.0063) (0.24 - 0.25)	0.0034 (0.0071) (-0.0079 - 0.020)	-0.016, 0.023	0.652	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.091 (0.015) (0.073 - 0.12)	0.072 (0.015) (0.068 - 0.075)	0.018 (0.022) (-0.0014 - 0.050)	-0.042, 0.078	0.445	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.27 (0.0046) (0.26 - 0.28)	0.27 (0.0046) (0.27 - 0.28)	-0.0067 (0.0034) (-0.012 - 0.0024)	-0.016, 0.0028	0.121	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dwt)						
Vitamin E	1.32 (0.10) (1.21 - 1.54)	1.23 (0.10) (1.11 - 1.40)	0.097 (0.022) (0.049 - 0.14)	0.037, 0.16	0.010	0, 3.49 (0.69 - 2.91)

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[1] dwt = dry weight; fwt = fresh weight; FA = fatty acid.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error)

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-17. Statistical Summary of Site PAHM Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Anti-nutrient (% dwt)						
Lectin (H.U./mg dwt)	2.81 (0.80) (2.08 - 3.34)	3.85 (0.80) (3.28 - 4.45)	-1.03 (1.03) (-1.73 - 0.051)	-3.88, 1.81	0.370	0, 7.73 (0.68 - 8.34)
Phytic Acid	1.35 (0.077) (1.13 - 1.51)	1.50 (0.077) (1.41 - 1.62)	-0.15 (0.092) (-0.28 - -0.054)	-0.40, 0.11	0.179	0.77, 1.91 (1.00 - 1.64)
Raffinose	0.47 (0.047) (0.32 - 0.55)	0.54 (0.047) (0.49 - 0.57)	-0.072 (0.066) (-0.24 - 0.058)	-0.26, 0.11	0.339	0.13, 0.70 (0.26 - 0.59)
Stachyose	3.29 (0.18) (3.19 - 3.47)	3.36 (0.18) (3.07 - 3.90)	-0.075 (0.25) (-0.69 - 0.40)	-0.77, 0.62	0.777	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dwt)	32.53 (4.33) (27.64 - 36.16)	30.39 (4.33) (26.59 - 33.33)	2.14 (5.59) (1.05 - 2.83)	-13.38, 17.66	0.721	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dwt)						
Daidzein	1918.51 (144.27) (1565.54 - 2305.26)	1642.38 (144.27) (1510.07 - 1729.91)	276.14 (204.03) (-121.61 - 795.19)	-290.35, 842.62	0.247	0, 2271.38 (451.33 - 2033.05)

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Table E-17 (continued). Statistical Summary of Site PAHM Soybean Seed Anti-nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Isoflavone (µg/g dwt)						
Genistein	1196.16 (107.80) (976.03 - 1496.78)	1101.98 (107.80) (983.22 - 1162.01)	94.18 (152.45) (-185.98 - 513.56)	-329.09, 517.45	0.570	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	110.37 (7.95) (93.26 - 119.09)	81.44 (7.95) (68.68 - 90.51)	28.93 (11.25) (2.75 - 50.41)	-2.30, 60.16	0.061	31.24, 233.60 (73.61 - 231.75)

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[1] dwt = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-18. Statistical Summary of Site PAHM Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Proximate (% dwt)						
Ash	7.51 (0.26) (7.18 – 8.13)	7.88 (0.32) (7.67 – 8.09)	-0.37 (0.41) (-0.86 - -0.49)	-1.67, 0.94	0.438	3.36, 10.84 (5.20 – 9.81)
Carbohydrates	70.95 (1.04) (69.23 – 73.31)	65.81 (1.16) (65.74 – 66.41)	5.14 (1.03) (3.49 – 6.90)	1.85, 8.43	0.015	60.69, 73.46 (62.73 – 71.72)
Moisture (% fwt)	74.27 (0.63) (73.40 – 75.40)	74.91 (0.63) (73.80 – 74.90)	-0.64 (0.15) (-0.90 - -0.40)	-1.11, -0.18	0.021	62.08, 89.80 (70.40 – 84.10)
Protein	17.47 (1.26) (15.23 – 19.58)	21.96 (1.45) (21.49 – 21.91)	-4.49 (1.45) (-6.26 - -2.34)	-9.10, 0.12	0.053	15.69, 26.63 (18.50 – 25.86)
Total Fat	3.97 (0.26) (3.82 – 4.21)	4.18 (0.31) (4.30 – 4.35)	-0.20 (0.31) (-0.42 - -0.14)	-1.19, 0.78	0.553	0, 10.04 (1.57 – 7.99)
Fiber (% dwt)						
Acid Detergent Fiber	26.97 (1.95) (25.46 – 29.89)	26.02 (2.39) (21.79 – 30.24)	0.96 (3.08) (-4.78 – 8.09)	-8.86, 10.77	0.776	16.54, 41.80 (20.98 – 39.23)

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Table E-18 (continued). Statistical Summary of Site PAHM Soybean Forage Nutrients for MON 87708 (Treated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Commercial Tolerance Interval[5] (Range)
Fiber (% dwt)						
Neutral Detergent Fiber	29.45 (1.01) (27.00 - 32.07)	30.20 (1.24) (30.00 - 30.40)	-0.75 (1.60) (-3.40 - -0.71)	-5.83, 4.34	0.672	20.28, 44.03 (24.81 - 42.80)

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[1] dwt = dry weight; fwt = fresh weight.

[2] MON 87708 was treated with dicamba.

[3] Mean (S.E.) = least-square mean (standard error)

[4] Control refers to the near isogenic conventional soybean control A3525.

[5] With 95% confidence, interval contains 99% of the values expressed in the population of commercial reference soybean varieties. Negative limits set to zero.

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Table E-19. Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)^{1}	MON 87708^{2} Mean (S.E.)^{3} (Range)	Control^{4} Mean (S.E.) (Range)	Difference (MON 87708minus Control)			Conventional Tolerance Interval^{5} (Range)
			Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	
Proximate (% dw)						
Ash	5.35 (0.070)	5.29 (0.070)	0.058 (0.098)	-0.22, 0.33	0.589	4.74, 6.01
	(5.24 - 5.46)	(5.19 - 5.47)	(-0.0028 - 0.16)			(4.93 - 5.88)
Carbohydrates	37.68 (0.56)	37.97 (0.56)	-0.29 (0.55)	-1.83, 1.25	0.628	32.07, 40.08
	(36.27 - 39.10)	(37.17 - 38.45)	(-0.90 - 0.65)			(33.82 - 39.26)
Moisture (% fw)	7.84 (0.28)	6.07 (0.28)	1.77 (0.39)	0.68, 2.86	0.010	4.27, 9.58
	(7.39 - 8.73)	(5.84 - 6.36)	(1.05 - 2.89)			(5.50 - 9.23)
Protein	40.95 (0.27)	41.09 (0.27)	-0.15 (0.16)	-0.60, 0.31	0.420	35.50, 45.19
	(40.72 - 41.20)	(40.69 - 41.74)	(-0.54 - 0.069)			(37.06 - 43.42)
Total Fat	16.03 (0.47)	15.61 (0.47)	0.42 (0.66)	-1.41, 2.25	0.562	12.33, 24.10
	(14.69 - 17.31)	(15.38 - 15.82)	(-0.69 - 1.49)			(15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	13.78 (0.38)	12.60 (0.38)	1.18 (0.54)	-0.33, 2.69	0.096	10.06, 18.04
	(12.82 - 14.36)	(11.92 - 13.17)	(-0.35 - 2.45)			(12.07 - 17.46)

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Table E-19 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Crude Fiber	7.63 (0.33) (6.85 - 8.07)	7.41 (0.33) (7.17 - 7.60)	0.23 (0.46) (-0.60 - 0.90)	-1.05, 1.50	0.650	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	14.50 (0.89) (13.26 - 15.98)	13.27 (0.89) (11.81 - 14.42)	1.22 (1.25) (-0.34 - 4.17)	-2.26, 4.71	0.384	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.75 (0.026) (1.72 - 1.79)	1.74 (0.026) (1.69 - 1.77)	0.0049 (0.036) (-0.028 - 0.030)	-0.096, 0.11	0.900	1.56, 1.91 (1.59 - 1.86)
Arginine	3.35 (0.055) (3.30 - 3.41)	3.45 (0.055) (3.27 - 3.56)	-0.099 (0.061) (-0.19 - 0.037)	-0.27, 0.070	0.177	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.60 (0.060) (4.57 - 4.62)	4.63 (0.060) (4.46 - 4.74)	-0.033 (0.084) (-0.11 - 0.10)	-0.27, 0.20	0.711	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0094) (0.61 - 0.61)	0.59 (0.0094) (0.56 - 0.62)	0.018 (0.013) (-0.0068 - 0.044)	-0.019, 0.054	0.256	0.50, 0.68 (0.53 - 0.66)

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Table E-19 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Glutamic Acid	7.33 (0.10) (7.25 - 7.43)	7.41 (0.10) (7.12 - 7.58)	-0.074 (0.15) (-0.19 - 0.12)	-0.48, 0.34	0.644	6.28, 8.30 (6.69 - 7.92)
Glycine	1.75 (0.024) (1.74 - 1.76)	1.76 (0.024) (1.70 - 1.79)	-0.013 (0.034) (-0.049 - 0.041)	-0.11, 0.081	0.720	1.53, 1.92 (1.58 - 1.84)
Histidine	1.05 (0.014) (1.05 - 1.06)	1.06 (0.014) (1.02 - 1.08)	-0.0055 (0.019) (-0.026 - 0.029)	-0.059, 0.048	0.786	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.87 (0.038) (1.86 - 1.88)	1.88 (0.038) (1.79 - 1.94)	-0.011 (0.054) (-0.068 - 0.085)	-0.16, 0.14	0.851	1.65, 2.06 (1.68 - 2.02)
Leucine	3.05 (0.041) (3.01 - 3.08)	3.07 (0.041) (2.96 - 3.14)	-0.020 (0.058) (-0.065 - 0.055)	-0.18, 0.14	0.746	2.72, 3.39 (2.80 - 3.27)
Lysine	2.62 (0.030) (2.61 - 2.62)	2.62 (0.030) (2.54 - 2.66)	-0.00013 (0.042) (-0.047 - 0.083)	-0.12, 0.12	0.997	2.33, 2.84 (2.38 - 2.74)

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Table E-19 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Methionine	0.58 (0.013) (0.57 - 0.59)	0.56 (0.013) (0.53 - 0.60)	0.019 (0.019) (-0.0030 - 0.056)	-0.034, 0.072	0.376	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.03 (0.036) (1.98 - 2.09)	2.03 (0.036) (1.95 - 2.09)	-0.00029 (0.050) (-0.024 - 0.022)	-0.14, 0.14	0.995	1.80, 2.30 (1.85 - 2.21)
Proline	1.94 (0.035) (1.89 - 1.98)	1.98 (0.035) (1.89 - 2.07)	-0.048 (0.050) (-0.10 - 0.043)	-0.19, 0.091	0.390	1.65, 2.26 (1.74 - 2.16)
Serine	2.02 (0.044) (1.91 - 2.10)	2.00 (0.044) (1.95 - 2.08)	0.017 (0.036) (-0.043 - 0.073)	-0.082, 0.12	0.653	1.78, 2.27 (1.90 - 2.18)
Threonine	1.53 (0.023) (1.49 - 1.57)	1.54 (0.023) (1.51 - 1.58)	-0.0028 (0.023) (-0.026 - 0.033)	-0.067, 0.061	0.909	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.44 (0.0092) (0.41 - 0.46)	0.45 (0.0092) (0.44 - 0.47)	-0.012 (0.013) (-0.053 - 0.018)	-0.048, 0.024	0.405	0.38, 0.52 (0.39 - 0.50)

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Table E-19 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.40 (0.013) (1.38 - 1.40)	1.38 (0.013) (1.37 - 1.42)	0.012 (0.016) (-0.011 - 0.032)	-0.033, 0.057	0.494	1.24, 1.50 (1.26 - 1.49)
Valine	1.98 (0.046) (1.97 - 2.00)	1.99 (0.046) (1.90 - 2.05)	-0.0086 (0.065) (-0.077 - 0.097)	-0.19, 0.17	0.900	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.51 (0.051) (11.39 - 11.63)	11.00 (0.051) (10.92 - 11.08)	0.51 (0.062) (0.41 - 0.59)	0.34, 0.68	0.001	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	3.95 (0.067) (3.75 - 4.06)	4.00 (0.067) (3.99 - 4.01)	-0.052 (0.095) (-0.23 - 0.044)	-0.32, 0.21	0.613	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.28 (0.20) (18.77 - 19.68)	21.67 (0.20) (21.48 - 21.78)	-2.39 (0.28) (-2.71 - -2.07)	-3.17, -1.61	0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.30 (0.33) (53.70 - 55.34)	52.70 (0.33) (52.66 - 52.73)	1.60 (0.46) (1.04 - 2.61)	0.32, 2.89	0.025	48.61, 59.37 (50.95 - 56.68)

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Table E-19 (continued). Statistical Summary of Site IARL Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.38 (0.13) (9.94 - 10.60)	10.04 (0.13) (10.00 - 10.12)	0.34 (0.19) (-0.18 - 0.61)	-0.18, 0.86	0.144	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.25 (0.0038) (0.24 - 0.26)	0.25 (0.0038) (0.25 - 0.26)	-0.0024 (0.0054) (-0.014 - 0.0033)	-0.017, 0.013	0.680	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.071 (0.0020) (0.065 - 0.076)	0.070 (0.0020) (0.069 - 0.071)	0.00087 (0.0028) (-0.0039 - 0.0043)	-0.0070, 0.0087	0.773	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.26 (0.0035) (0.26 - 0.27)	0.28 (0.0035) (0.27 - 0.28)	-0.014 (0.0042) (-0.017 - -0.010)	-0.025, -0.0021	0.030	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	1.26 (0.058) (1.11 - 1.42)	0.94 (0.058) (0.89 - 0.97)	0.32 (0.066) (0.23 - 0.46)	0.13, 0.50	0.008	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-20. Statistical Summary of Site IARL Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	2.98 (0.64) (2.35 - 3.87)	1.53 (0.64) (0.46 - 2.70)	1.46 (0.90) (-0.35 - 2.46)	-1.04, 3.96	0.180	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.43 (0.032) (1.38 - 1.47)	1.53 (0.032) (1.47 - 1.62)	-0.10 (0.045) (-0.18 - -0.040)	-0.23, 0.024	0.088	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.41 (0.022) (0.38 - 0.45)	0.43 (0.022) (0.40 - 0.45)	-0.024 (0.020) (-0.063 - 0.00015)	-0.079, 0.030	0.284	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.30 (0.20) (2.94 - 3.59)	3.89 (0.20) (3.76 - 4.15)	-0.59 (0.28) (-0.82 - -0.18)	-1.37, 0.19	0.101	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	29.97 (2.63) (23.32 - 33.42)	29.67 (2.63) (25.64 - 32.71)	0.30 (3.19) (-2.32 - 2.51)	-8.57, 9.17	0.929	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	1734.44 (145.92) (1522.84 - 2125.56)	1447.97 (145.92) (1404.40 - 1505.77)	286.47 (206.36) (17.08 - 691.83)	-286.47, 859.41	0.237	0, 2271.38 (451.33 - 2033.05)

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Table E-20 (continued). Statistical Summary of Site IARL Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	1099.12 (83.29) (954.54 - 1380.52)	954.99 (83.29) (900.10 - 984.62)	144.13 (117.79) (-22.32 - 400.27)	-182.91, 471.17	0.288	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	110.70 (5.35) (99.92 - 117.72)	106.40 (5.35) (97.49 - 111.71)	4.30 (2.24) (2.43 - 7.73)	-1.92, 10.52	0.127	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-21. Statistical Summary of Site IARL Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Proximate (% dw)						
Ash	8.37 (0.62) (7.23 - 9.45)	8.87 (0.62) (7.58 - 10.46)	-0.50 (0.52) (-1.01 - -0.13)	-1.95, 0.95	0.395	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	62.49 (0.80) (61.64 - 63.41)	65.57 (0.80) (63.58 - 67.74)	-3.08 (1.13) (-6.11 - -0.17)	-6.22, 0.067	0.053	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	83.47 (0.33) (82.70 - 84.10)	81.97 (0.33) (81.40 - 82.70)	1.50 (0.44) (0.90 - 2.70)	0.28, 2.72	0.027	62.08, 89.80 (70.40 - 84.10)
Protein	25.76 (0.54) (24.63 - 27.04)	23.00 (0.54) (22.15 - 24.07)	2.76 (0.76) (1.54 - 4.89)	0.65, 4.88	0.022	15.69, 26.63 (18.50 - 25.86)
Total Fat	3.29 (0.32) (2.61 - 3.91)	2.52 (0.32) (2.01 - 3.27)	0.77 (0.46) (-0.66 - 1.63)	-0.50, 2.04	0.169	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	31.48 (2.83) (29.42 - 34.63)	32.62 (2.83) (28.87 - 38.15)	-1.14 (3.30) (-3.52 - 1.51)	-10.31, 8.04	0.748	16.54, 41.80 (20.98 - 39.23)

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Table E-21 (continue). Statistical Summary of Site IARL Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	37.35 (2.66)	35.01 (2.66)	2.34 (3.76)	-8.11, 12.79	0.567	20.28, 44.03
	(37.11 - 37.80)	(27.47 - 39.42)	(-2.29 - 9.63)			(24.81 - 42.80)

[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-22. Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	5.10 (0.080) (4.94 - 5.27)	5.05 (0.080) (4.88 - 5.22)	0.046 (0.089) (0.025 - 0.059)	-0.20, 0.29	0.632	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	35.98 (0.68) (35.27 - 37.36)	35.77 (0.68) (34.11 - 37.16)	0.21 (0.97) (-1.89 - 3.25)	-2.48, 2.90	0.839	32.07, 40.08 (33.82 - 39.26)
Moisture (% fw)	5.78 (0.20) (5.68 - 5.88)	6.44 (0.20) (6.20 - 6.63)	-0.66 (0.28) (-0.75 - -0.52)	-1.43, 0.11	0.077	4.27, 9.58 (5.50 - 9.23)
Protein	41.07 (0.40) (40.92 - 41.22)	41.72 (0.40) (40.81 - 42.67)	-0.65 (0.55) (-1.60 - 0.42)	-2.17, 0.88	0.305	35.50, 45.19 (37.06 - 43.42)
Total Fat	17.87 (0.45) (16.66 - 18.66)	17.49 (0.45) (16.81 - 18.39)	0.37 (0.63) (-1.73 - 1.46)	-1.39, 2.13	0.588	12.33, 24.10 (15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	14.54 (0.45) (13.36 - 15.72)	14.04 (0.45) (13.47 - 14.57)	0.50 (0.61) (-0.71 - 1.16)	-1.18, 2.19	0.452	10.06, 18.04 (12.07 - 17.46)

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Table E-22 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control)			Conventional Tolerance Interval[5] (Range)
			Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	
Fiber (% dw)						
Crude Fiber	8.08 (0.29) (7.30 - 8.89)	8.38 (0.29) (8.20 - 8.64)	-0.30 (0.41) (-1.33 - 0.60)	-1.44, 0.84	0.508	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	17.05 (0.63) (16.33 - 18.38)	16.85 (0.63) (15.19 - 17.99)	0.20 (0.73) (-1.05 - 1.27)	-1.84, 2.24	0.797	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.78 (0.014) (1.77 - 1.80)	1.81 (0.014) (1.78 - 1.84)	-0.027 (0.020) (-0.067 - -0.0037)	-0.084, 0.030	0.259	1.56, 1.91 (1.59 - 1.86)
Arginine	3.21 (0.053) (3.12 - 3.27)	3.30 (0.053) (3.19 - 3.43)	-0.094 (0.049) (-0.21 - -0.0074)	-0.23, 0.043	0.129	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.69 (0.037) (4.63 - 4.74)	4.76 (0.037) (4.73 - 4.82)	-0.072 (0.034) (-0.12 - 0.0057)	-0.17, 0.022	0.099	4.04, 5.13 (4.22 - 4.94)
Cystine	0.60 (0.0078) (0.59 - 0.61)	0.59 (0.0078) (0.58 - 0.60)	0.013 (0.011) (-0.0016 - 0.030)	-0.018, 0.043	0.322	0.50, 0.68 (0.53 - 0.66)

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Table E-22 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Amino Acid (% dw)						
Glutamic Acid	7.44 (0.073) (7.33 - 7.51)	7.61 (0.073) (7.52 - 7.76)	-0.17 (0.056) (-0.28 - -0.042)	-0.33, -0.014	0.039	6.28, 8.30 (6.69 - 7.92)
Glycine	1.78 (0.013) (1.77 - 1.78)	1.81 (0.013) (1.79 - 1.83)	-0.027 (0.014) (-0.046 - -0.0099)	-0.066, 0.012	0.126	1.53, 1.92 (1.58 - 1.84)
Histidine	1.06 (0.0071) (1.05 - 1.07)	1.08 (0.0071) (1.07 - 1.09)	-0.014 (0.0055) (-0.019 - -0.0059)	-0.029, 0.00090	0.059	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.94 (0.013) (1.91 - 1.95)	1.97 (0.013) (1.97 - 1.97)	-0.035 (0.017) (-0.058 - -0.021)	-0.083, 0.013	0.110	1.65, 2.06 (1.68 - 2.02)
Leucine	3.11 (0.022) (3.08 - 3.13)	3.17 (0.022) (3.14 - 3.19)	-0.058 (0.012) (-0.060 - -0.056)	-0.090, -0.025	0.008	2.72, 3.39 (2.80 - 3.27)
Lysine	2.66 (0.017) (2.62 - 2.67)	2.67 (0.017) (2.65 - 2.69)	-0.012 (0.013) (-0.032 - 0.017)	-0.047, 0.024	0.413	2.33, 2.84 (2.38 - 2.74)

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Table E-22 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Methionine	0.57 (0.012) (0.56 - 0.58)	0.57 (0.012) (0.56 - 0.58)	-0.0026 (0.017) (-0.0052 - -0.00024)	-0.049, 0.044	0.886	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.07 (0.022) (2.05 - 2.08)	2.13 (0.022) (2.09 - 2.19)	-0.064 (0.018) (-0.11 - -0.038)	-0.12, -0.014	0.024	1.80, 2.30 (1.85 - 2.21)
Proline	1.95 (0.019) (1.90 - 1.98)	2.06 (0.019) (2.04 - 2.09)	-0.11 (0.019) (-0.14 - -0.058)	-0.16, -0.058	0.004	1.65, 2.26 (1.74 - 2.16)
Serine	2.06 (0.027) (2.05 - 2.08)	2.08 (0.027) (2.01 - 2.15)	-0.015 (0.025) (-0.069 - 0.037)	-0.084, 0.055	0.593	1.78, 2.27 (1.90 - 2.18)
Threonine	1.58 (0.015) (1.56 - 1.61)	1.59 (0.015) (1.58 - 1.59)	-0.00051 (0.019) (-0.023 - 0.020)	-0.052, 0.051	0.979	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.48 (0.0090) (0.46 - 0.48)	0.48 (0.0090) (0.47 - 0.50)	-0.0026 (0.0084) (-0.015 - 0.017)	-0.026, 0.021	0.770	0.38, 0.52 (0.39 - 0.50)

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Table E-22 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.42 (0.033) (1.35 - 1.48)	1.43 (0.033) (1.39 - 1.51)	-0.0065 (0.045) (-0.075 - 0.098)	-0.13, 0.12	0.892	1.24, 1.50 (1.26 - 1.49)
Valine	2.01 (0.015) (1.99 - 2.04)	2.05 (0.015) (2.05 - 2.06)	-0.043 (0.021) (-0.070 - -0.011)	-0.10, 0.016	0.113	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	12.12 (0.073) (12.10 - 12.15)	11.95 (0.073) (11.73 - 12.08)	0.17 (0.089) (0.067 - 0.37)	-0.076, 0.42	0.127	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	3.94 (0.044) (3.87 - 4.05)	3.93 (0.044) (3.86 - 4.02)	0.0064 (0.062) (-0.13 - 0.19)	-0.16, 0.18	0.922	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	19.85 (0.29) (19.62 - 20.22)	21.57 (0.29) (21.07 - 22.44)	-1.72 (0.41) (-2.82 - -0.85)	-2.86, -0.58	0.013	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.31 (0.25) (53.67 - 54.63)	53.26 (0.25) (52.77 - 53.74)	1.05 (0.35) (-0.064 - 1.85)	0.074, 2.02	0.040	48.61, 59.37 (50.95 - 56.68)

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Table E-22 (continued). Statistical Summary of Site ILCY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	9.09 (0.074) (8.94 - 9.23)	8.58 (0.074) (8.42 - 8.71)	0.51 (0.099) (0.23 - 0.67)	0.23, 0.79	0.006	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0035) (0.26 - 0.27)	0.26 (0.0035) (0.26 - 0.27)	-0.0013 (0.0050) (-0.014 - 0.014)	-0.015, 0.013	0.802	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.15 (0.0016) (0.15 - 0.16)	0.16 (0.0016) (0.16 - 0.17)	-0.0078 (0.0023) (-0.013 - -0.0010)	-0.014, -0.0013	0.028	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.28 (0.0030) (0.28 - 0.28)	0.29 (0.0030) (0.28 - 0.30)	-0.0065 (0.0042) (-0.019 - -0.00002)	-0.018, 0.0052	0.199	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	2.21 (0.077) (2.11 - 2.27)	1.86 (0.077) (1.71 - 2.11)	0.35 (0.089) (0.16 - 0.49)	0.10, 0.60	0.016	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-23. Statistical Summary of Site ILCY Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	3.52 (1.81) (2.56 - 4.82)	5.54 (1.81) (2.14 - 10.38)	-2.02 (2.55) (-7.83 - 1.05)	-9.11, 5.07	0.473	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.08 (0.032) (1.05 - 1.11)	1.16 (0.032) (1.10 - 1.22)	-0.077 (0.045) (-0.17 - 0.015)	-0.20, 0.048	0.163	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.56 (0.013) (0.55 - 0.58)	0.57 (0.013) (0.54 - 0.60)	-0.0071 (0.018) (-0.045 - 0.049)	-0.057, 0.043	0.711	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.56 (0.10) (3.35 - 3.74)	3.64 (0.10) (3.43 - 3.83)	-0.086 (0.14) (-0.32 - 0.30)	-0.48, 0.31	0.576	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	34.71 (1.10) (33.01 - 37.61)	32.78 (1.10) (31.06 - 34.22)	1.93 (1.56) (-0.72 - 6.55)	-2.39, 6.26	0.282	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	1061.06 (72.66) (910.73 - 1156.87)	922.21 (72.66) (762.49 - 1098.08)	138.85 (102.76) (-187.35 - 394.38)	-146.46, 424.16	0.247	0, 2271.38 (451.33 - 2033.05)

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Table E-23 (continued). Statistical Summary of Site ILCY Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	721.38 (45.60) (654.16 - 792.83)	653.27 (45.60) (588.17 - 770.79)	68.12 (64.49) (-116.63 - 204.65)	-110.93, 247.17	0.350	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	125.94 (8.11) (120.06 - 133.73)	113.29 (8.11) (96.25 - 122.09)	12.65 (11.47) (-2.04 - 37.48)	-19.20, 44.51	0.332	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

Table E-24. Statistical Summary of Site ILCY Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	5.45 (0.22) (4.92 - 6.04)	6.27 (0.22) (6.10 - 6.49)	-0.82 (0.32) (-1.57 - -0.054)	-1.70, 0.052	0.059	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	66.21 (0.61) (65.30 - 67.29)	66.38 (0.61) (65.53 - 67.94)	-0.17 (0.87) (-1.89 - 1.62)	-2.58, 2.24	0.855	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	73.27 (0.25) (73.20 - 73.40)	73.53 (0.25) (73.20 - 73.80)	-0.27 (0.35) (-0.60 - 0.20)	-1.24, 0.70	0.488	62.08, 89.80 (70.40 - 84.10)
Protein	22.53 (0.51) (22.29 - 22.65)	21.64 (0.51) (20.88 - 23.03)	0.89 (0.68) (-0.38 - 1.77)	-1.00, 2.79	0.261	15.69, 26.63 (18.50 - 25.86)
Total Fat	5.73 (0.38) (5.34 - 6.04)	5.77 (0.38) (5.15 - 6.72)	-0.040 (0.52) (-1.38 - 0.67)	-1.47, 1.39	0.942	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	28.43 (1.09) (27.35 - 30.49)	28.46 (1.09) (27.05 - 30.90)	-0.027 (1.54) (-0.41 - 0.31)	-4.30, 4.24	0.986	16.54, 41.80 (20.98 - 39.23)

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Table E-24 (continued). Statistical Summary of Site ILCY Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	32.83 (1.65) (30.68 - 34.48)	28.06 (1.65) (23.66 - 32.73)	4.76 (2.33) (0.59 - 10.81)	-1.72, 11.24	0.110	20.28, 44.03 (24.81 - 42.80)

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[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-25. Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control)			Conventional Tolerance Interval[5] (Range)
			Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	
Proximate (% dw)						
Ash	5.30 (0.084) (5.24 - 5.34)	5.23 (0.084) (5.13 - 5.29)	0.068 (0.084) (0.039 - 0.11)	-0.17, 0.30	0.465	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	38.39 (0.44) (37.03 - 39.08)	38.29 (0.44) (38.19 - 38.42)	0.10 (0.45) (-1.17 - 0.83)	-1.15, 1.35	0.835	32.07, 40.08 (33.82 - 39.26)
Moisture (% fw)	6.66 (0.16) (6.34 - 6.83)	6.16 (0.16) (5.79 - 6.41)	0.51 (0.22) (-0.070 - 1.03)	-0.11, 1.12	0.084	4.27, 9.58 (5.50 - 9.23)
Protein	41.96 (0.28) (41.53 - 42.72)	41.99 (0.28) (41.72 - 42.25)	-0.022 (0.38) (-0.46 - 0.47)	-1.07, 1.02	0.956	35.50, 45.19 (37.06 - 43.42)
Total Fat	14.36 (0.38) (13.95 - 15.03)	14.49 (0.38) (14.40 - 14.54)	-0.14 (0.44) (-0.59 - 0.62)	-1.37, 1.10	0.776	12.33, 24.10 (15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	13.71 (0.43) (13.31 - 14.17)	12.96 (0.43) (12.48 - 13.69)	0.75 (0.61) (-0.39 - 1.68)	-0.93, 2.43	0.283	10.06, 18.04 (12.07 - 17.46)

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Table E-25 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Crude Fiber	7.37 (0.52) (6.14 - 8.72)	7.58 (0.52) (7.39 - 7.82)	-0.21 (0.74) (-1.25 - 1.19)	-2.25, 1.83	0.787	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	15.79 (0.72) (15.13 - 16.53)	13.78 (0.72) (13.44 - 14.00)	2.00 (0.94) (1.23 - 3.09)	-0.61, 4.62	0.100	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.77 (0.0076) (1.76 - 1.79)	1.75 (0.0076) (1.75 - 1.76)	0.020 (0.0093) (0.0086 - 0.043)	-0.0057, 0.046	0.096	1.56, 1.91 (1.59 - 1.86)
Arginine	3.52 (0.037) (3.41 - 3.60)	3.57 (0.037) (3.55 - 3.60)	-0.049 (0.040) (-0.14 - 0.051)	-0.16, 0.062	0.288	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.72 (0.017) (4.68 - 4.75)	4.67 (0.017) (4.67 - 4.68)	0.050 (0.020) (-0.0019 - 0.082)	-0.0047, 0.11	0.064	4.04, 5.13 (4.22 - 4.94)
Cystine	0.63 (0.0090) (0.61 - 0.64)	0.61 (0.0090) (0.58 - 0.62)	0.021 (0.0092) (0.0091 - 0.034)	-0.0042, 0.047	0.081	0.50, 0.68 (0.53 - 0.66)

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Table E-25 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Glutamic Acid	7.53 (0.030) (7.49 - 7.56)	7.51 (0.030) (7.49 - 7.53)	0.023 (0.031) (-0.0030 - 0.066)	-0.064, 0.11	0.506	6.28, 8.30 (6.69 - 7.92)
Glycine	1.78 (0.0053) (1.77 - 1.79)	1.77 (0.0053) (1.76 - 1.77)	0.013 (0.0075) (-0.0019 - 0.032)	-0.0078, 0.034	0.155	1.53, 1.92 (1.58 - 1.84)
Histidine	1.08 (0.0032) (1.07 - 1.08)	1.07 (0.0032) (1.06 - 1.07)	0.011 (0.0046) (0.00005 - 0.024)	-0.0016, 0.024	0.071	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.90 (0.012) (1.88 - 1.91)	1.90 (0.012) (1.88 - 1.91)	0.0031 (0.0040) (-0.00070 - 0.0093)	-0.0081, 0.014	0.486	1.65, 2.06 (1.68 - 2.02)
Leucine	3.12 (0.011) (3.10 - 3.13)	3.10 (0.011) (3.09 - 3.13)	0.017 (0.0062) (0.0081 - 0.030)	-0.00030, 0.034	0.052	2.72, 3.39 (2.80 - 3.27)
Lysine	2.68 (0.0062) (2.66 - 2.69)	2.63 (0.0062) (2.62 - 2.64)	0.046 (0.0088) (0.029 - 0.069)	0.022, 0.071	0.006	2.33, 2.84 (2.38 - 2.74)

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Table E-25 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Amino Acid (% dw)						
Methionine	0.59 (0.0074) (0.58 - 0.59)	0.58 (0.0074) (0.56 - 0.59)	0.0067 (0.010) (-0.0018 - 0.017)	-0.022, 0.036	0.553	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.07 (0.019) (2.06 - 2.08)	2.07 (0.019) (2.05 - 2.10)	-0.0031 (0.021) (-0.044 - 0.023)	-0.063, 0.056	0.892	1.80, 2.30 (1.85 - 2.21)
Proline	2.02 (0.020) (1.97 - 2.05)	2.05 (0.020) (2.01 - 2.09)	-0.028 (0.028) (-0.12 - 0.041)	-0.11, 0.049	0.368	1.65, 2.26 (1.74 - 2.16)
Serine	2.10 (0.013) (2.09 - 2.11)	2.06 (0.013) (2.02 - 2.09)	0.043 (0.013) (0.023 - 0.073)	0.0084, 0.078	0.026	1.78, 2.27 (1.90 - 2.18)
Threonine	1.59 (0.0042) (1.58 - 1.60)	1.55 (0.0042) (1.54 - 1.55)	0.044 (0.0049) (0.031 - 0.052)	0.031, 0.058	<0.001	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.48 (0.0083) (0.46 - 0.50)	0.47 (0.0083) (0.45 - 0.48)	0.016 (0.011) (-0.014 - 0.032)	-0.015, 0.046	0.227	0.38, 0.52 (0.39 - 0.50)

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Table E-25 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.40 (0.024) (1.35 - 1.44)	1.36 (0.024) (1.34 - 1.40)	0.032 (0.027) (-0.0023 - 0.084)	-0.044, 0.11	0.305	1.24, 1.50 (1.26 - 1.49)
Valine	2.00 (0.013) (1.97 - 2.02)	2.01 (0.013) (2.01 - 2.02)	-0.011 (0.012) (-0.031 - 0.012)	-0.045, 0.024	0.443	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.13 (0.041) (11.02 - 11.21)	11.04 (0.041) (10.97 - 11.12)	0.085 (0.057) (-0.094 - 0.24)	-0.074, 0.24	0.212	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.47 (0.063) (4.30 - 4.57)	4.25 (0.063) (4.16 - 4.31)	0.23 (0.089) (-0.010 - 0.38)	-0.019, 0.47	0.062	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	20.24 (0.25) (19.52 - 20.73)	21.14 (0.25) (20.78 - 21.55)	-0.89 (0.36) (-2.03 - -0.045)	-1.89, 0.11	0.068	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	52.87 (0.32) (52.18 - 53.74)	52.90 (0.32) (52.33 - 53.20)	-0.024 (0.46) (-0.98 - 1.41)	-1.30, 1.25	0.961	48.61, 59.37 (50.95 - 56.68)

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Table E-25 (continued). Statistical Summary of Site ILWY Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.65 (0.10) (10.37 - 10.90)	10.05 (0.10) (9.89 - 10.14)	0.60 (0.14) (0.25 - 1.01)	0.20, 1.00	0.014	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.28 (0.0041) (0.27 - 0.29)	0.27 (0.0041) (0.26 - 0.27)	0.011 (0.0058) (-0.0031 - 0.022)	-0.0048, 0.027	0.123	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.077 (0.0020) (0.073 - 0.079)	0.076 (0.0020) (0.075 - 0.077)	0.00030 (0.0023) (-0.0037 - 0.0039)	-0.0060, 0.0066	0.901	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.28 (0.0032) (0.28 - 0.29)	0.28 (0.0032) (0.28 - 0.29)	-0.0029 (0.0040) (-0.010 - 0.0054)	-0.014, 0.0081	0.503	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	1.15 (0.037) (1.11 - 1.20)	0.94 (0.037) (0.89 - 0.99)	0.21 (0.053) (0.12 - 0.31)	0.061, 0.35	0.017	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-26. Statistical Summary of Site ILWY Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	1.36 (0.44) (1.18 - 1.63)	2.33 (0.44) (1.34 - 3.68)	-0.97 (0.43) (-2.04 - -0.16)	-2.17, 0.23	0.087	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.43 (0.033) (1.43 - 1.43)	1.55 (0.033) (1.47 - 1.61)	-0.12 (0.044) (-0.19 - -0.045)	-0.24, 0.0051	0.056	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.37 (0.026) (0.34 - 0.41)	0.41 (0.026) (0.41 - 0.41)	-0.038 (0.036) (-0.065 - 0.0072)	-0.14, 0.064	0.361	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.60 (0.19) (3.37 - 3.85)	3.76 (0.19) (3.68 - 3.85)	-0.17 (0.27) (-0.39 - 0.0078)	-0.92, 0.59	0.573	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	38.93 (2.07) (37.89 - 39.49)	29.73 (2.07) (25.43 - 32.22)	9.20 (2.89) (5.67 - 13.97)	1.18, 17.22	0.033	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	1307.12 (35.08) (1291.91 - 1320.17)	1271.60 (35.08) (1196.71 - 1354.96)	35.52 (31.48) (-34.79 - 95.20)	-51.87, 122.92	0.322	0, 2271.38 (451.33 - 2033.05)

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Table E-26 (continued). Statistical Summary of Site ILWY Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	832.43 (28.15) (780.21 - 862.94)	860.58 (28.15) (784.27 - 913.26)	-28.14 (39.82) (-103.98 - 69.88)	-138.69, 82.40	0.518	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	96.96 (2.15) (92.19 - 103.25)	79.70 (2.15) (77.14 - 81.62)	17.26 (2.23) (11.83 - 21.63)	11.06, 23.46	0.001	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-27. Statistical Summary of Site ILWY Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	6.76 (0.23) (6.52 - 7.14)	6.88 (0.23) (6.82 - 6.99)	-0.12 (0.30) (-0.30 - 0.15)	-0.95, 0.71	0.706	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	65.94 (0.77) (64.34 - 67.08)	66.26 (0.77) (65.71 - 66.67)	-0.31 (1.08) (-1.37 - 0.68)	-3.32, 2.69	0.786	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	75.13 (0.55) (74.10 - 75.70)	75.40 (0.55) (75.10 - 75.60)	-0.27 (0.65) (-1.00 - 0.10)	-2.07, 1.54	0.702	62.08, 89.80 (70.40 - 84.10)
Protein	22.27 (0.58) (22.05 - 22.54)	21.97 (0.58) (21.81 - 22.13)	0.30 (0.82) (0.091 - 0.58)	-1.98, 2.59	0.730	15.69, 26.63 (18.50 - 25.86)
Total Fat	5.01 (0.52) (4.25 - 6.52)	4.91 (0.52) (4.50 - 5.63)	0.11 (0.35) (-0.31 - 0.88)	-0.86, 1.08	0.773	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	27.49 (1.73) (23.32 - 29.63)	27.77 (1.73) (25.12 - 31.00)	-0.28 (2.44) (-7.68 - 4.38)	-7.06, 6.49	0.912	16.54, 41.80 (20.98 - 39.23)

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Table E-27 (continued). Statistical Summary of Site ILWY Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	29.89 (1.83) (26.37 - 35.43)	33.25 (1.83) (31.89 - 34.06)	-3.36 (2.59) (-5.93 - 1.37)	-10.55, 3.83	0.264	20.28, 44.03 (24.81 - 42.80)

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[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-28. Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	5.13 (0.11) (5.05 - 5.30)	4.95 (0.11) (4.73 - 5.23)	0.18 (0.15) (-0.18 - 0.41)	-0.24, 0.60	0.295	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	37.64 (0.78) (35.63 - 39.79)	35.95 (0.78) (35.27 - 37.04)	1.69 (1.10) (0.10 - 4.52)	-1.37, 4.75	0.200	32.07, 40.08 (33.82 - 39.26)
Moisture (% fw)	6.67 (0.20) (6.26 - 7.11)	6.53 (0.20) (6.32 - 6.84)	0.13 (0.29) (-0.18 - 0.31)	-0.67, 0.93	0.667	4.27, 9.58 (5.50 - 9.23)
Protein	41.47 (0.53) (40.22 - 43.06)	43.58 (0.53) (43.50 - 43.69)	-2.11 (0.76) (-3.28 - -0.63)	-4.21, -0.014	0.049	35.50, 45.19 (37.06 - 43.42)
Total Fat	15.75 (0.45) (14.93 - 16.26)	15.55 (0.45) (14.52 - 16.10)	0.20 (0.56) (-1.10 - 1.55)	-1.37, 1.77	0.739	12.33, 24.10 (15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	12.89 (0.35) (12.06 - 13.49)	12.77 (0.35) (12.28 - 13.25)	0.12 (0.46) (-0.72 - 1.22)	-1.15, 1.39	0.800	10.06, 18.04 (12.07 - 17.46)

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Table E-28 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Crude Fiber	7.38 (0.18) (7.06 - 7.61)	6.89 (0.18) (6.59 - 7.12)	0.49 (0.25) (0.11 - 0.87)	-0.21, 1.19	0.123	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	14.43 (0.67) (12.91 - 15.21)	14.66 (0.67) (13.24 - 15.56)	-0.23 (0.95) (-2.27 - 1.97)	-2.86, 2.41	0.822	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.79 (0.021) (1.76 - 1.84)	1.84 (0.021) (1.80 - 1.87)	-0.054 (0.022) (-0.10 - -0.027)	-0.12, 0.0067	0.068	1.56, 1.91 (1.59 - 1.86)
Arginine	3.40 (0.044) (3.35 - 3.50)	3.72 (0.044) (3.64 - 3.81)	-0.32 (0.062) (-0.46 - -0.19)	-0.49, -0.14	0.007	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.72 (0.062) (4.59 - 4.90)	4.89 (0.062) (4.80 - 4.95)	-0.17 (0.078) (-0.34 - -0.050)	-0.39, 0.044	0.091	4.04, 5.13 (4.22 - 4.94)
Cystine	0.62 (0.0067) (0.60 - 0.63)	0.59 (0.0067) (0.59 - 0.60)	0.031 (0.0094) (0.0031 - 0.047)	0.0050, 0.057	0.029	0.50, 0.68 (0.53 - 0.66)

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Table E-28 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Glutamic Acid	7.56 (0.11) (7.36 - 7.88)	7.93 (0.11) (7.75 - 8.02)	-0.36 (0.14) (-0.66 - -0.14)	-0.76, 0.035	0.064	6.28, 8.30 (6.69 - 7.92)
Glycine	1.80 (0.020) (1.76 - 1.85)	1.85 (0.020) (1.82 - 1.87)	-0.054 (0.027) (-0.11 - -0.016)	-0.13, 0.020	0.111	1.53, 1.92 (1.58 - 1.84)
Histidine	1.07 (0.012) (1.05 - 1.11)	1.11 (0.012) (1.10 - 1.12)	-0.038 (0.016) (-0.072 - -0.0075)	-0.083, 0.0072	0.079	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.92 (0.042) (1.80 - 2.02)	2.00 (0.042) (1.95 - 2.03)	-0.079 (0.057) (-0.22 - -0.0049)	-0.24, 0.080	0.238	1.65, 2.06 (1.68 - 2.02)
Leucine	3.12 (0.041) (3.03 - 3.24)	3.24 (0.041) (3.20 - 3.26)	-0.12 (0.052) (-0.22 - -0.023)	-0.26, 0.023	0.080	2.72, 3.39 (2.80 - 3.27)
Lysine	2.67 (0.030) (2.60 - 2.76)	2.72 (0.030) (2.68 - 2.76)	-0.053 (0.035) (-0.13 - -0.0027)	-0.15, 0.045	0.205	2.33, 2.84 (2.38 - 2.74)

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Table E-28 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Amino Acid (% dw)						
Methionine	0.59 (0.0086) (0.56 - 0.61)	0.59 (0.0086) (0.58 - 0.60)	0.00055 (0.012) (-0.036 - 0.021)	-0.033, 0.034	0.966	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.08 (0.030) (2.03 - 2.14)	2.20 (0.030) (2.13 - 2.23)	-0.12 (0.040) (-0.17 - -0.090)	-0.23, -0.011	0.037	1.80, 2.30 (1.85 - 2.21)
Proline	2.01 (0.010) (1.99 - 2.04)	2.06 (0.010) (2.05 - 2.07)	-0.054 (0.015) (-0.079 - -0.015)	-0.095, -0.014	0.020	1.65, 2.26 (1.74 - 2.16)
Serine	2.06 (0.028) (1.97 - 2.11)	2.13 (0.028) (2.13 - 2.14)	-0.072 (0.029) (-0.15 - -0.026)	-0.15, 0.0094	0.070	1.78, 2.27 (1.90 - 2.18)
Threonine	1.57 (0.019) (1.51 - 1.61)	1.61 (0.019) (1.60 - 1.62)	-0.040 (0.027) (-0.088 - -0.0061)	-0.11, 0.034	0.206	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.48 (0.013) (0.46 - 0.50)	0.45 (0.013) (0.43 - 0.46)	0.026 (0.018) (0.0012 - 0.044)	-0.025, 0.076	0.231	0.38, 0.52 (0.39 - 0.50)

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Table E-28 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.39 (0.024) (1.37 - 1.40)	1.44 (0.024) (1.38 - 1.47)	-0.055 (0.022) (-0.077 - -0.018)	-0.12, 0.0073	0.070	1.24, 1.50 (1.26 - 1.49)
Valine	2.03 (0.045) (1.90 - 2.13)	2.12 (0.045) (2.06 - 2.16)	-0.097 (0.063) (-0.25 - -0.015)	-0.27, 0.078	0.198	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.45 (0.068) (11.23 - 11.57)	11.19 (0.068) (11.14 - 11.21)	0.27 (0.097) (0.014 - 0.44)	-0.00083, 0.54	0.050	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	4.15 (0.047) (4.07 - 4.24)	4.25 (0.047) (4.16 - 4.31)	-0.096 (0.066) (-0.20 - -0.022)	-0.28, 0.088	0.219	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	18.80 (0.085) (18.63 - 18.96)	20.19 (0.085) (20.12 - 20.23)	-1.39 (0.093) (-1.60 - -1.26)	-1.65, -1.14	<0.001	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	54.94 (0.10) (54.79 - 55.13)	54.43 (0.10) (54.32 - 54.64)	0.51 (0.14) (0.15 - 0.81)	0.11, 0.90	0.024	48.61, 59.37 (50.95 - 56.68)

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Table E-28 (continued). Statistical Summary of Site INRC Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.05 (0.050) (10.00 - 10.10)	9.31 (0.050) (9.26 - 9.40)	0.74 (0.070) (0.60 - 0.84)	0.54, 0.93	<0.001	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.26 (0.0029) (0.26 - 0.27)	0.27 (0.0029) (0.26 - 0.27)	-0.0072 (0.0041) (-0.014 - -0.0026)	-0.019, 0.0043	0.156	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.070 (0.0020) (0.068 - 0.073)	0.071 (0.0020) (0.069 - 0.076)	-0.0014 (0.0025) (-0.0073 - 0.0035)	-0.0083, 0.0056	0.615	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.28 (0.0033) (0.27 - 0.28)	0.29 (0.0033) (0.29 - 0.30)	-0.016 (0.0047) (-0.023 - -0.0045)	-0.029, -0.0032	0.025	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	1.25 (0.054) (1.11 - 1.40)	1.16 (0.054) (1.10 - 1.23)	0.091 (0.067) (0.0086 - 0.17)	-0.094, 0.28	0.244	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-29. Statistical Summary of Site INRC Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	2.94 (0.32) (2.24 - 3.81)	2.56 (0.32) (2.33 - 3.02)	0.39 (0.45) (-0.78 - 1.48)	-0.88, 1.65	0.443	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.24 (0.071) (1.09 - 1.37)	1.19 (0.071) (1.09 - 1.36)	0.052 (0.087) (-0.099 - 0.26)	-0.19, 0.29	0.585	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.45 (0.023) (0.42 - 0.47)	0.40 (0.023) (0.36 - 0.43)	0.049 (0.033) (0.042 - 0.056)	-0.043, 0.14	0.215	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.50 (0.077) (3.35 - 3.62)	3.46 (0.077) (3.33 - 3.67)	0.044 (0.11) (-0.32 - 0.28)	-0.26, 0.35	0.704	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	30.68 (1.79) (28.59 - 32.19)	29.28 (1.79) (25.22 - 31.77)	1.40 (1.83) (0.42 - 3.37)	-3.69, 6.49	0.487	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	1671.09 (67.03) (1485.63 - 1842.13)	1419.40 (67.03) (1416.92 - 1421.55)	251.69 (94.79) (68.71 - 422.41)	-11.48, 514.87	0.056	0, 2271.38 (451.33 - 2033.05)

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Table E-29 (continued). Statistical Summary of Site INRC Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	992.90 (50.59) (842.93 - 1103.14)	862.03 (50.59) (840.10 - 890.94)	130.88 (71.54) (-48.01 - 248.10)	-67.75, 329.51	0.141	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	119.27 (3.23) (113.04 - 124.24)	98.42 (3.23) (89.42 - 103.14)	20.86 (3.31) (17.40 - 23.62)	11.67, 30.05	0.003	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-30. Statistical Summary of Site INRC Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Proximate (% dw)						
Ash	6.20 (0.24) (5.87 - 6.72)	6.95 (0.24) (6.84 - 7.07)	-0.74 (0.26) (-1.20 - -0.22)	-1.47, -0.015	0.047	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	64.35 (0.69) (63.90 - 64.94)	63.82 (0.69) (62.91 - 64.44)	0.53 (0.98) (-0.23 - 0.99)	-2.18, 3.25	0.614	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	72.70 (0.32) (72.30 - 72.90)	72.27 (0.32) (71.60 - 72.70)	0.43 (0.39) (-0.20 - 1.30)	-0.64, 1.50	0.323	62.08, 89.80 (70.40 - 84.10)
Protein	23.46 (0.41) (23.10 - 24.15)	23.33 (0.41) (22.64 - 24.11)	0.13 (0.41) (-0.10 - 0.46)	-1.01, 1.28	0.760	15.69, 26.63 (18.50 - 25.86)
Total Fat	5.98 (0.27) (5.92 - 6.01)	5.88 (0.27) (5.39 - 6.19)	0.10 (0.39) (-0.18 - 0.63)	-0.97, 1.17	0.809	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	25.59 (1.50) (24.69 - 27.00)	23.83 (1.50) (22.93 - 25.53)	1.77 (2.13) (-0.44 - 3.99)	-4.14, 7.67	0.452	16.54, 41.80 (20.98 - 39.23)

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Table E-30 (continued). Statistical Summary of Site INRC Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	26.13 (1.62) (25.38 - 27.64)	26.11 (1.62) (23.91 - 29.42)	0.020 (2.04) (-4.04 - 3.73)	-5.65, 5.69	0.992	20.28, 44.03 (24.81 - 42.80)

[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-31. Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Proximate (% dw)						
Ash	5.20 (0.11) (4.89 - 5.51)	5.05 (0.11) (4.96 - 5.17)	0.16 (0.16) (-0.28 - 0.55)	-0.28, 0.59	0.378	4.74, 6.01 (4.93 - 5.88)
Carbohydrates	36.81 (0.51) (35.36 - 37.56)	35.23 (0.51) (34.49 - 35.75)	1.58 (0.64) (0.87 - 2.06)	-0.20, 3.35	0.069	32.07, 40.08 (33.82 - 39.26)
Moisture (% fw)	9.53 (0.22) (9.21 - 9.91)	10.50 (0.22) (10.40 - 10.60)	-0.97 (0.22) (-1.19 - -0.69)	-1.58, -0.36	0.011	4.27, 9.58 (5.50 - 9.23)
Protein	40.38 (0.41) (39.96 - 40.97)	43.69 (0.41) (43.46 - 43.85)	-3.31 (0.51) (-3.89 - -2.78)	-4.73, -1.88	0.002	35.50, 45.19 (37.06 - 43.42)
Total Fat	17.61 (0.63) (17.32 - 18.17)	16.05 (0.63) (15.64 - 16.85)	1.56 (0.89) (1.32 - 1.70)	-0.90, 4.02	0.153	12.33, 24.10 (15.47 - 21.34)
Fiber (% dw)						
Acid Detergent Fiber	11.96 (0.35) (11.01 - 12.89)	11.96 (0.35) (11.62 - 12.17)	0.0073 (0.43) (-0.61 - 0.72)	-1.18, 1.20	0.987	10.06, 18.04 (12.07 - 17.46)

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Table E-31 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Crude Fiber	7.05 (0.63) (6.81 - 7.28)	6.61 (0.63) (6.05 - 6.98)	0.43 (0.71) (0.064 - 0.76)	-1.55, 2.41	0.578	5.76, 10.76 (6.35 - 11.31)
Neutral Detergent Fiber	14.44 (0.36) (14.21 - 14.87)	13.11 (0.36) (12.63 - 13.62)	1.33 (0.50) (1.12 - 1.62)	-0.064, 2.73	0.056	11.36, 19.38 (11.66 - 19.45)
Amino Acid (% dw)						
Alanine	1.79 (0.017) (1.76 - 1.81)	1.86 (0.017) (1.82 - 1.90)	-0.068 (0.024) (-0.10 - -0.043)	-0.13, -0.0016	0.046	1.56, 1.91 (1.59 - 1.86)
Arginine	3.39 (0.053) (3.35 - 3.44)	3.88 (0.053) (3.83 - 3.93)	-0.49 (0.074) (-0.55 - -0.45)	-0.70, -0.29	0.002	2.55, 3.83 (2.88 - 3.74)
Aspartic Acid	4.66 (0.041) (4.64 - 4.69)	4.94 (0.041) (4.90 - 5.01)	-0.28 (0.057) (-0.35 - -0.22)	-0.44, -0.12	0.008	4.04, 5.13 (4.22 - 4.94)
Cystine	0.61 (0.0062) (0.61 - 0.61)	0.59 (0.0062) (0.59 - 0.60)	0.015 (0.0081) (0.0099 - 0.021)	-0.0078, 0.037	0.144	0.50, 0.68 (0.53 - 0.66)

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Table E-31 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Glutamic Acid	7.42 (0.081) (7.32 - 7.50)	8.00 (0.081) (7.91 - 8.14)	-0.58 (0.11) (-0.70 - -0.46)	-0.90, -0.26	0.007	6.28, 8.30 (6.69 - 7.92)
Glycine	1.77 (0.015) (1.76 - 1.78)	1.86 (0.015) (1.83 - 1.89)	-0.090 (0.022) (-0.13 - -0.068)	-0.15, -0.029	0.014	1.53, 1.92 (1.58 - 1.84)
Histidine	1.07 (0.0089) (1.07 - 1.08)	1.13 (0.0089) (1.11 - 1.14)	-0.061 (0.013) (-0.073 - -0.045)	-0.096, -0.026	0.008	0.93, 1.16 (0.95 - 1.13)
Isoleucine	1.89 (0.026) (1.88 - 1.91)	2.00 (0.026) (1.94 - 2.04)	-0.11 (0.036) (-0.16 - -0.036)	-0.21, -0.013	0.035	1.65, 2.06 (1.68 - 2.02)
Leucine	3.10 (0.027) (3.08 - 3.11)	3.28 (0.027) (3.24 - 3.32)	-0.18 (0.038) (-0.23 - -0.15)	-0.28, -0.074	0.009	2.72, 3.39 (2.80 - 3.27)
Lysine	2.64 (0.023) (2.62 - 2.65)	2.75 (0.023) (2.71 - 2.77)	-0.11 (0.032) (-0.12 - -0.091)	-0.20, -0.023	0.025	2.33, 2.84 (2.38 - 2.74)

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Table E-31 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Methionine	0.57 (0.0090) (0.55 - 0.59)	0.58 (0.0090) (0.57 - 0.60)	-0.017 (0.0072) (-0.036 - -0.0056)	-0.037, 0.0031	0.078	0.50, 0.64 (0.52 - 0.63)
Phenylalanine	2.08 (0.027) (2.03 - 2.11)	2.21 (0.027) (2.16 - 2.27)	-0.13 (0.038) (-0.18 - -0.047)	-0.24, -0.027	0.025	1.80, 2.30 (1.85 - 2.21)
Proline	2.00 (0.024) (1.93 - 2.04)	2.10 (0.024) (2.08 - 2.13)	-0.11 (0.032) (-0.17 - -0.060)	-0.20, -0.019	0.028	1.65, 2.26 (1.74 - 2.16)
Serine	2.08 (0.035) (2.02 - 2.11)	2.16 (0.035) (2.06 - 2.21)	-0.078 (0.050) (-0.19 - 0.054)	-0.22, 0.060	0.191	1.78, 2.27 (1.90 - 2.18)
Threonine	1.57 (0.015) (1.55 - 1.60)	1.62 (0.015) (1.60 - 1.64)	-0.047 (0.021) (-0.077 - 0.0039)	-0.10, 0.010	0.085	1.40, 1.69 (1.47 - 1.64)
Tryptophan	0.48 (0.012) (0.44 - 0.50)	0.46 (0.012) (0.45 - 0.46)	0.021 (0.017) (-0.013 - 0.049)	-0.026, 0.067	0.287	0.38, 0.52 (0.39 - 0.50)

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Table E-31 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Amino Acid (% dw)						
Tyrosine	1.44 (0.027) (1.42 - 1.46)	1.49 (0.027) (1.48 - 1.52)	-0.057 (0.032) (-0.086 - -0.028)	-0.15, 0.033	0.152	1.24, 1.50 (1.26 - 1.49)
Valine	2.00 (0.029) (2.00 - 2.00)	2.13 (0.029) (2.05 - 2.17)	-0.13 (0.041) (-0.17 - -0.049)	-0.24, -0.014	0.035	1.72, 2.20 (1.73 - 2.13)
Fatty Acid (% Total FA)						
16:0 Palmitic	11.79 (0.12) (11.74 - 11.89)	11.49 (0.12) (11.38 - 11.55)	0.31 (0.15) (0.20 - 0.37)	-0.11, 0.72	0.112	8.44, 12.56 (9.40 - 11.54)
18:0 Stearic	3.70 (0.12) (3.55 - 3.93)	3.76 (0.12) (3.67 - 3.91)	-0.056 (0.14) (-0.12 - 0.023)	-0.45, 0.33	0.708	2.90, 5.19 (3.24 - 4.67)
18:1 Oleic	18.45 (0.31) (18.26 - 18.80)	20.01 (0.31) (19.60 - 20.32)	-1.56 (0.35) (-2.02 - -1.31)	-2.53, -0.58	0.011	15.73, 27.19 (17.88 - 25.31)
18:2 Linoleic	55.44 (0.41) (55.13 - 55.62)	54.68 (0.41) (54.18 - 54.99)	0.76 (0.53) (0.26 - 1.43)	-0.70, 2.22	0.223	48.61, 59.37 (50.95 - 56.68)

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Table E-31 (continued). Statistical Summary of Site PAHM Soybean Seed Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fatty Acid (% Total FA)						
18:3 Linolenic	10.03 (0.21) (9.74 - 10.18)	9.47 (0.21) (9.13 - 9.68)	0.56 (0.16) (0.49 - 0.61)	0.11, 1.01	0.026	6.01, 12.58 (7.43 - 11.37)
20:0 Arachidic	0.24 (0.0063) (0.23 - 0.25)	0.24 (0.0063) (0.24 - 0.25)	-0.0067 (0.0071) (-0.011 - -0.0013)	-0.026, 0.013	0.396	0.19, 0.34 (0.20 - 0.30)
20:1 Eicosenoic	0.086 (0.015) (0.066 - 0.13)	0.072 (0.015) (0.068 - 0.075)	0.014 (0.022) (-0.0088 - 0.058)	-0.046, 0.073	0.565	0.022, 0.24 (0.065 - 0.17)
22:0 Behenic	0.26 (0.0046) (0.25 - 0.27)	0.27 (0.0046) (0.27 - 0.28)	-0.013 (0.0034) (-0.018 - -0.0076)	-0.022, -0.0036	0.018	0.24, 0.40 (0.28 - 0.36)
Vitamin (mg/100g dw)						
Vitamin E	1.37 (0.10) (1.26 - 1.59)	1.23 (0.10) (1.11 - 1.40)	0.15 (0.022) (0.10 - 0.19)	0.087, 0.21	0.002	0, 3.49 (0.69 - 2.91)

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[1] dw = dry weight; fw = fresh weight; FA = fatty acid.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-32. Statistical Summary of Site PAHM Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Anti-nutrient						
Lectin (H.U./mg dw)	4.41 (0.80) (1.96 - 6.35)	3.85 (0.80) (3.28 - 4.45)	0.57 (1.03) (-1.85 - 3.07)	-2.28, 3.41	0.610	0, 7.73 (0.68 - 8.34)
Phytic Acid (% dw)	1.44 (0.077) (1.41 - 1.48)	1.50 (0.077) (1.41 - 1.62)	-0.057 (0.092) (-0.21 - 0.034)	-0.31, 0.20	0.569	0.77, 1.91 (1.00 - 1.64)
Raffinose (% dw)	0.53 (0.047) (0.48 - 0.55)	0.54 (0.047) (0.49 - 0.57)	-0.014 (0.066) (-0.022 - -0.0042)	-0.20, 0.17	0.841	0.13, 0.70 (0.26 - 0.59)
Stachyose (% dw)	3.43 (0.18) (3.26 - 3.65)	3.36 (0.18) (3.07 - 3.90)	0.067 (0.25) (-0.64 - 0.53)	-0.63, 0.76	0.800	2.30, 4.07 (2.50 - 3.94)
Trypsin Inhibitor (TIU/mg dw)	40.89 (4.33) (28.31 - 51.50)	30.39 (4.33) (26.59 - 33.33)	10.50 (5.59) (-2.94 - 18.17)	-5.02, 26.01	0.133	22.05, 41.12 (22.81 - 44.56)
Isoflavone (µg/g dw)						
Daidzein	2085.21 (144.27) (1931.40 - 2297.58)	1642.38 (144.27) (1510.07 - 1729.91)	442.84 (204.03) (296.74 - 610.43)	-123.65, 1009.32	0.095	0, 2271.38 (451.33 - 2033.05)

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Table E-32 (continued). Statistical Summary of Site PAHM Soybean Seed Anti-Nutrients for MON 87708 (Untreated) vs. Conventional Control

			Difference (MON 87708 minus Control)			
Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Mean (S.E.) (Range)	95% Confidence Interval	Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Isoflavone (µg/g dw)						
Genistein	1300.54 (107.80) (1209.90 - 1469.13)	1101.98 (107.80) (983.22 - 1162.01)	198.56 (152.45) (61.89 - 307.12)	-224.71, 621.83	0.262	78.36, 1869.48 (533.88 - 1726.03)
Glycitein	99.12 (7.95) (83.25 - 112.67)	81.44 (7.95) (68.68 - 90.51)	17.68 (11.25) (10.93 - 27.53)	-13.55, 48.91	0.191	31.24, 233.60 (73.61 - 231.75)

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[1] dw = dry weight; H.U. = Hemagglutinating Units; TIU = Trypsin Inhibitor Units.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Table E-33. Statistical Summary of Site PAHM Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)¹	MON 87708² Mean (S.E.)³ (Range)	Control⁴ Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval⁵ (Range)
Proximate (% dw)						
Ash	8.26 (0.26) (7.81 - 8.65)	7.88 (0.32) (7.67 - 8.09)	0.38 (0.41) (-0.28 - 0.97)	-0.93, 1.69	0.422	3.36, 10.84 (5.20 - 9.81)
Carbohydrates	68.76 (1.04) (67.19 - 71.05)	65.81 (1.16) (65.74 - 66.41)	2.95 (1.03) (1.45 - 4.64)	-0.35, 6.24	0.065	60.69, 73.46 (62.73 - 71.72)
Moisture (% fw)	74.47 (0.63) (73.40 - 75.60)	74.91 (0.63) (73.80 - 74.90)	-0.44 (0.15) (-0.50 - -0.40)	-0.91, 0.021	0.055	62.08, 89.80 (70.40 - 84.10)
Protein	19.46 (1.26) (16.28 - 21.25)	21.96 (1.45) (21.49 - 21.91)	-2.49 (1.45) (-5.21 - -0.66)	-7.10, 2.12	0.183	15.69, 26.63 (18.50 - 25.86)
Total Fat	3.46 (0.26) (2.69 - 3.87)	4.18 (0.31) (4.30 - 4.35)	-0.72 (0.31) (-0.49 - -0.48)	-1.70, 0.27	0.102	0, 10.04 (1.57 - 7.99)
Fiber (% dw)						
Acid Detergent Fiber	25.62 (1.95) (24.22 - 28.01)	26.02 (2.39) (21.79 - 30.24)	-0.40 (3.08) (-2.23 - 2.83)	-10.21, 9.42	0.905	16.54, 41.80 (20.98 - 39.23)

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Table E-33 (continued). Statistical Summary of Site PAHM Soybean Forage Nutrients for MON 87708 (Untreated) vs. Conventional Control

Analytical Component (Units)[1]	MON 87708[2] Mean (S.E.)[3] (Range)	Control[4] Mean (S.E.) (Range)	Difference (MON 87708 minus Control) Mean (S.E.) (Range)	Difference (MON 87708 minus Control) 95% Confidence Interval	Difference (MON 87708 minus Control) Significance (p-Value)	Conventional Tolerance Interval[5] (Range)
Fiber (% dw)						
Neutral Detergent Fiber	28.70 (1.01) (27.46 - 29.45)	30.20 (1.24) (30.00 - 30.40)	-1.50 (1.60) (-0.95 - -0.83)	-6.59, 3.58	0.415	20.28, 44.03 (24.81 - 42.80)

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[1] dw = dry weight; fw = fresh weight.

[2] MON 87708 plants were not sprayed with dicamba, but received another conventional treatment as was done for the conventional control.

[3] Mean (S.E.) = least-square mean (standard error).

[4] Control refers to the non-biotechnology derived, conventional control (A3525).

[5] With 95% confidence, interval contains 99% of the values expressed in the population of conventional substances. Negative limits set to zero.

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Appendix F: Materials, Methods, and Individual Site Results for the Seed Dormancy and Germination Assessment of MON 87708

F.1. Materials

Seed dormancy and germination characteristics were assessed on seed from MON 87708, the near isogenic conventional soybean control A3525, and commercial reference varieties produced at the Howard County, Iowa; Stark County, Illinois; and Shelby County, Missouri sites in 2008 field trials (Appendix G). The field trial at each site was established in a randomized complete block design with three replications. The seed from MON 87708, conventional control, and the commercial reference varieties were harvested from all three replicated plots at each of the three field sites. In order to provide a representative sample from each field site for dormancy and germination testing, the replicate samples from each field trial were pooled to produce one seed sample (lot) of MON 87708, the conventional control, and each commercial reference variety (Table F-1).

Table F-1. Starting Seed of MON 87708, Conventional Control, and Commercial Reference Varieties Used in the Dormancy and Germination Assessment

Production Site[1]	Material Name[2]	Material Type	Phenotype	Seed Lot #
IA	MON 87708	Test	Dicamba-Tolerant	11222450-001
IA	A3525	Control	Conventional	11222449-001
IA	Garst 3585N	Reference	Conventional	11222451-001
IA	Pioneer 93B15	Reference	Conventional	11222452-001
IA	Crows C37003N	Reference	Conventional	11222453-001
IA	NK S33-A8	Reference	Roundup Ready	11222454-001
IL	MON 87708	Test	Dicamba-Tolerant	11222456-001
IL	A3525	Control	Conventional	11222455-001
IL	Croplan HT3596STS	Reference	Conventional	11222457-001
IL	NK S37-N4	Reference	Roundup Ready	11222458-001
IL	Stewart SB3454	Reference	Conventional	11222459-001
IL	Midland 363	Reference	Conventional	11222460-001
MO	MON 87708	Test	Dicamba-Tolerant	11222462-001
MO	A3525	Control	Conventional	11222461-001
MO	Garst 3585N	Reference	Conventional	11222463-001
MO	Pioneer 93B15	Reference	Conventional	11222464-001
MO	Crows C37003N	Reference	Conventional	11222465-001
MO	NK S33-A8	Reference	Roundup Ready	11222466-001

[1] IA = Howard County, IA; IL = Stark County, IL; MO = Shelby County, MO.

[2] MON 87708, the conventional control, and commercial reference varieties seed used to assess dormancy and germination characteristics were all produced from replicated field trials conducted in 2008 to assess plant phenotypic characteristics and, therefore, were not obtained from commercial sources. The

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commercial reference varieties were all conventional soybean varieties with the exception of NK S33-A8 and NK S37-N4, which were Roundup Ready® soybean varieties.

F.2. Characterization of the Materials

For the MON 87708, conventional control, and the commercial reference varieties starting seed lots, the presence or absence of the *dmo* expression cassette was confirmed by event-specific polymerase chain reaction analyses.

F.3. Germination Testing Facility and Experimental Methods

Seed dormancy and germination evaluations were conducted at BioDiagnostics, Inc. in River Falls, WI. The principal investigator was qualified to conduct seed dormancy and germination testing consistent with the standards established by the Association of Official Seed Analysts, a seed trade association (AOSA, 2000; AOSA, 2006; AOSA, 2007).

Seed lots of MON 87708, the conventional control, and four commercial reference varieties were produced from each of three sites and tested under six different temperature regimes. Six germination chambers were maintained dark under one of the following temperature regimes: constant temperature of approximately 10, 20, or 30°C or alternating temperatures of approximately 10/20, 10/30, or 20/30°C. The alternating temperature regimes were maintained at the lower temperature for 16 hours and the higher temperature for eight hours. The temperature inside each germination chamber was monitored and recorded every 15 minutes throughout the duration of the assessment. For each seed lot, four replicated paper germination towels were prepared per facility SOPs for each temperature regime. Wax coated paper was placed on a large tray followed by a water-moistened germination towel. A target of 100 seeds per seed lot were placed on the germination towel (*i.e.*, one seed lot per towel) using a vacuum planting system. A second water-moistened germination towel was placed on top of the seed. The towels were then rolled up and secured with a rubber band. All rolled germination towels were placed into appropriately labeled buckets that were then covered with ventilated plastic bags attached with rubber bands. The buckets were arranged in the germination chambers in a split-plot design, where the whole-plot treatment was seed production site and the sub-plot treatment was seed material (*i.e.*, MON 87708, the conventional control, or commercial reference varieties).

A description of each germination characteristic evaluated and the timing of evaluations are presented in Table VII-1. The types of data collected depended on the temperature regime. Each rolled germination towel in the AOSA-recommended temperature regime (*i.e.*, 20/30°C) was evaluated periodically during the study for normal germinated, abnormal germinated, hard, dead, and firm-swollen seed as defined by AOSA guidelines (AOSA, 2006; AOSA, 2007). AOSA only provides guidelines (AOSA, 2007) for testing seed under optimal temperatures (20/30°C); however, additional temperature regimes were included to test a range of temperature conditions. Each rolled germination towel in

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the additional temperature regimes (*i.e.*, 10, 20, 30, 10/20, and 10/30°C) was evaluated periodically for germinated, hard, dead, and firm-swollen seed. Emergence and/or development of essential structures of seedlings that otherwise would be categorized as "normal germinated" under optimal temperature conditions may not be so at non-optimal temperatures. Therefore, for the additional temperature regimes, no distinction was made between normal and abnormal germinated seed.

F.4. Statistical Analysis

Analysis of variance was conducted according to a split-plot design with four replications. SAS® (Version 9.2) was used to compare MON 87708 to the conventional control within each seed production site (individual-site analyses) and in a combined-site analysis, in which the data were pooled across all sites, for the following germination characteristics: percent germinated (categorized as percent normal germinated and percent abnormal germinated for the AOSA temperature regime), percent viable hard, percent dead, and percent viable firm-swollen seed. The level of statistical significance was predetermined to be 5% ($\alpha = 0.05$). MON 87708 was not statistically compared to the commercial reference varieties nor were comparisons made across temperature regimes. For each assessed characteristic, the minimum and maximum means were determined from among the commercial reference varieties to provide a range of values that are representative of commercial soybean varieties. The following is a summary of the results from the individual-site analyses. Results from the combined-site analysis are presented in Table VII-2.

F.5. Individual-Site Seed Dormancy and Germination Analysis

In the individual-site analyses, no statistically significant differences were detected between MON 87708 and the conventional control for any of the measured characteristics (*i.e.*, percent germinated, viable hard, dead, or viable firm-swollen seed) in any temperature regime for seed produced at the MO site. Six statistically significant differences in total were detected between MON 87708 and the conventional control for seed produced at the IA and IL sites (Table F-2). MON 87708 had lower percent germinated seed than the conventional control at 10°C for seed produced at the IA (97.5% vs. 99.3%) and IL (99.3% vs. 100.0%) sites and at 10/30°C for seed produced at the IA site (96.8% vs. 99.0%). MON 87708 had lower percent viable hard seed than the conventional control at 10/30°C for seed produced at the IA site (0.0% vs. 0.3%). Percent dead seed was higher for MON 87708 than the conventional control at 10°C (2.0% vs. 0.3%) and 10/30°C (3.3% vs. 0.8%) for seed produced at the IA site.

Statistically significant differences between MON 87708 and the conventional control for germination characteristics in the individual-site analyses were not consistently detected across temperature regimes or seed production sites. While some statistically significant differences were detected in the combined-site analysis, the assessed dormancy and germination characteristics of MON 87708 were within the range of values expected for the commercial reference varieties and therefore are considered not biologically meaningful in terms of increased weediness of MON 87708 compared to the conventional soybean.

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Table F-2. Dormancy and Germination Characteristics of MON 87708 and Conventional Control Seed Produced at each of Three Field Sites

		Mean % (S.E.)†					
		IA		IL		MO	
Temperature Regime	Germination Category	MON 87708	Control	MON 87708	Control	MON 87708	Control
10°C	Germinated	97.5 (1.0)*	99.3 (0.5)	99.3 (0.3)*	100.0 (0.0)	100.0 (0.0)	99.8 (0.3)
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Dead	2.0 (0.9)*	0.3 (0.3)	0.5 (0.3)	0.0 (0.0)	0.0 (0.0)	0.3 (0.3)
	Viable Firm-swollen	0.5 (0.3)	0.5 (0.3)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
20°C	Germinated	98.0 (0.9)	98.3 (0.6)	99.8 (0.3)	99.8 (0.3)	100.0 (0.0)	100.0 (0.0)
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)
	Dead	2.0 (0.9)	1.8 (0.6)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Viable Firm-swollen	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
30°C	Germinated	96.3 (1.1)	98.3 (0.3)	100.0 (0.0)	100.0 (0.0)	99.8 (0.3)	99.8 (0.3)
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Dead	3.8 (1.1)	1.8 (0.3)	0.0 (0.0)	0.0 (0.0)	0.3 (0.3)	0.3 (0.3)
	Viable Firm-swollen	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)

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Table F-2 (continued). Dormancy and Germination Characteristics of MON 87708 and Conventional Control Seed Produced at each of Three Field Sites

Temperature Regime	Germination Category	Mean % (S.E.)[1]					
		IA		IL		MO	
		MON 87708	Control	MON 87708	Control	MON 87708	Control
10/20°C	Germinated	98.0 (0.4)	97.8 (0.3)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)
	Viable Hard	0.3 (0.3)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Dead	1.8 (0.3)	1.8 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Viable Firm-swollen	0.0 (0.0)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
10/30°C	Germinated	96.8 (0.8)*	99.0 (0.4)	99.0 (0.6)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)
	Viable Hard	0.0 (0.0)*	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Dead	3.3 (0.8)*	0.8 (0.5)	1.0 (0.6)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Viable Firm-swollen	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
20/30°C[2]	Normal Germinated	91.5 (2.1)	92.0 (0.7)	97.5 (1.0)	99.0 (0.4)	98.8 (0.5)	98.8 (0.6)
	Abnormal Germinated	5.8 (1.0)	6.3 (1.0)	1.8 (0.9)	0.8 (0.5)	1.3 (0.5)	1.3 (0.6)
	Viable Hard	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Dead	2.8 (1.3)	1.8 (0.8)	0.8 (0.3)	0.3 (0.3)	0.0 (0.0)	0.0 (0.0)
	Viable Firm-swollen	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)

Note: Seed for the germination study were produced in Howard County, IA; Stark County, IL; and Shelby County, MO in 2008. Seed was arranged in germination chambers in a split-plot design where the whole-plot treatment was seed production site and the sub-plot treatment was seed material (*i.e.*, MON 87708, the conventional control, or commercial reference soybean varieties).

*Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

†No statistical comparisons were made due to lack of variability in the data.

[1] Means based on four replicates (n = 4) of 100 seeds. The total percentage of all germination characteristics of MON 87708 or the conventional control in some temperature regimes is greater than 100.0% due to numerical rounding of the means. S.E. = Standard Error

[2] Germinated seed in the AOSA temperature regime 20/30°C were categorized as either normal germinated or abnormal germinated seed.

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Appendix G: Materials, Methods, and Individual-Site Results from the Phenotypic, Agronomic, and Environmental Interaction Assessment of MON 87708 under Field Conditions

G.1. Materials

The soybean materials for the phenotypic and environmental interactions assessment in the 2008 field included untreated MON 87708, the near isogenic conventional soybean control A3525, and 18 commercial reference soybean varieties. The references included both conventional and Roundup Ready® soybean varieties. The list of the soybean materials planted at each of 18 field sites is presented in Table G-1.

The soybean materials for the phenotypic and environmental interactions assessment in the 2009 field included dicamba-treated MON 87708, the near isogenic conventional soybean control A3525, and 14 conventional, commercial reference soybean varieties. The list of the soybean materials planted at each of 8 field sites is presented in Table G-2.

G.2. Characterization of the Materials

For the MON 87708 and the conventional control starting seed lots, the presence or absence of the *dmo* expression cassette was confirmed by event-specific polymerase chain reaction analyses.

G.3. Field Sites and Plot Design

Data were collected at 16 field sites in the U.S. and two sites in Canada during 2008 (Section VII, Table VII-3). Data were collected at 8 field sites in the U.S. during 2009 (Section VII, Table VII-4). These 26 locations provided a diverse range of environmental and agronomic conditions representative of commercial soybean production areas in North America. The researchers at each field site were familiar with the growth, production, and evaluation of soybean characteristics.

The experiment was established at each of the 18 sites in the 2008 field trials in a randomized complete block design with three replications. Each plot at the IL2, IN1, MI, and MO1 sites consisted of twelve 30 feet long rows spaced approximately 30 inches apart. Rows # 2 and 3 were designated for the collection of phenotypic data. Rows # 5 and 6 were designated for the collection of abiotic stress response, disease damage, and arthropod-related damage data. Rows # 8-10 were designated for the collection of arthropod samples. Rows # 1, 4, 7, 11, and 12 were used as buffer rows. Each plot was surrounded by approximately 5-15 feet of a commercial soybean variety by planting border rows in the alleyways between blocks and around the entire perimeter of the plot area. The purpose of the planted borders was to create a continuous soybean stand across the plot area to ensure collection of more robust arthropod abundance data.

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Each plot at the AR, Can1, Can2, IA1, IA2, IA3, IL1, IN2, IN3, KS, MO2, NE, PA, and WI sites consisted of four 20 feet long rows spaced approximately 30 inches apart. Rows # 2 and 3 were designated for the collection of phenotypic, abiotic stress response, disease damage, and arthropod-related damage data. Rows # 1 and 4 were used as buffer rows. The entire plot area was surrounded by an approximately 10 foot wide, four-row border of a commercial soybean variety.

In the 2009 field trials the experiment was established at each of the sites in a randomized complete block design with four replications. Each plot consisted of eight 20 feet long rows spaced approximately 30 inches apart. Rows 1 and 2 were designated for the collection of plant tissue and harvested seed samples for use in other studies. Rows 4 and 5 were designated for the collection of phenotypic, abiotic stress response, disease damage, and arthropod damage data in this report. Rows 3 and 6 - 8 were used as buffer rows. The plots within each replicate were separated by approximately a two-row buffer of a commercially-available soybean variety, and the entire plot area was surrounded by approximately a four-row border of a commercially-available soybean variety. A minimum of a 15 foot fallow area was established around the perimeter of the study area at each site to clearly isolate the experiment from other soybean.

G.4. Planting and Field Operations

Field and planting information for the 2008 field trials are listed in Table G-3. Field and planting information for the 2009 field trials are listed in Table G-4. Agronomic practices used to prepare and maintain each study site were characteristic of those used in each respective geographic region. All maintenance operations were performed uniformly over the entire trial area.

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Table G-1. Starting Seed for the Phenotypic, Agronomic, and Environmental Interaction Assessment for 2008 Field Trials

Material Name	Material Type	Relative Maturity	Phenotype	Monsanto Seed Lot #	Sites[1]
MON 87708	Test	3.5	Dicamba-Tolerant	10001256	All
A3525	Control	3.5	Conventional	10001257	All
FS 3591	Reference	3.5	Conventional	10001448	AR, IA2, IN1, MI, PA
AG3505	Reference	3.5	Roundup Ready[2]	10001281	AR, IA2, IN1, MI, PA
Wilken 3316	Reference	3.3	Conventional	10001505	AR, IA2, IN1, MI, PA
Stine 3300-0	Reference	3.3	Conventional	10001312	AR, IA2, IN1, MI, PA
Garst 3585N	Reference	3.5	Conventional	10000883	IA3, IN2, MO1, WI
Crows C37003N	Reference	3.7	Conventional	10001508	IA3, IN2, MO1, WI
Garst S33-A8	Reference	3.3	Roundup Ready[2]	10001284	Can1, IA3, IN2, MO1,
Pioneer 93B15	Reference	3.1	Conventional	10001304	Can1, IA3, IN2, MO1,
Dekalb DKB28-53	Reference	2.8	Roundup Ready[2]	10001950	Can1, Can2
Asgrow AG2801	Reference	2.8	Roundup Ready[2]	10001951	Can1, Can2
Pioneer 93M52	Reference	3.5	Conventional	10001311	Can2, IL1, IN3, MO2
NK S38-T8	Reference	3.8	Conventional	10001509	IL1, IN3, MO2
Lewis 3716	Reference	3.7	Roundup Ready[2]	10001278	IL1, IN3, MO2
Hoegemeyer 333	Reference	3.2	Conventional	10001590	Can2, IL1, IN3, MO2
Croplan	Reference	3.5	Conventional	10001450	IA1, IL2, KS, NE
NK S37-N4	Reference	3.7	Roundup Ready[2]	10001286	IA1, IL2, KS, NE
Stewart SB3454	Reference	3.4	Conventional	10000887	IA1, IL2, KS, NE
Midland 363	Reference	3.3	Conventional	10001570	IA1, IL2, KS, NE

[1] MON 87708 and the conventional control were planted at all field sites; the commercial reference varieties were site-specific. Site codes are as follows: AR = Jackson County, AR; Can1 = Norfolk, Ontario, Canada; Can2 = Kent, Ontario, Canada; IA1 = Jefferson County, IA; IA2 = Benton County, IA; IA3 = Howard County, IA; IL1 = Clinton County, IL; IL2 = Stark County, IL, IN1 = Boone County, IN; IN2 = Clinton County, IN; IN3 = Parke County, IN; KS = Pawnee County, KS; MI = Ottawa County, MI; MO1 = Shelby County, MO; MO2 = Macon County, MO; NE = York County, NE; PA = Berks County, PA; WI = Walworth County, WI.

[2] Commercial Roundup Ready soybean variety

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Table G-2. Starting Seed for the Phenotypic, Agronomic, and Environmental Interaction Assessment for 2009 Field Trials

Material Name	Material Type[1]	Relative Maturity	Phenotype[2]	Monsanto Seed Lot #	Site[3]
A3525	Control	3.5	Conventional	11225301	ALL
FS 3591	Reference	3.5	Conventional	10001448	ARNE
Crows C3908	Reference	3.9	Conventional	10001074	ARNE
NK S38-T8	Reference	3.8	Conventional	10001509	ARNE
Croplan HT3596STS	Reference	3.5	Conventional	10001117	IARL
Midland 363	Reference	3.3	Conventional	10001570	IARL
Stewart SB3454	Reference	3.4	Conventional	10001130	IARL
Quality Plus 365C	Reference	3.6	Conventional	10001129	ILCY
Channel Bio 3461	Reference	3.4	Conventional	10001115	ILCY
Pioneer 93M52	Reference	3.5	Conventional	10001128	ILCY
FS 3591	Reference	3.5	Conventional	10001448	ILWY
Stewart SB3454	Reference	3.4	Conventional	10001130	ILWY
NK 32Z3	Reference	3.2	Conventional	10001126	ILWY
Garst 3585N	Reference	3.5	Conventional	10001119	INRC
Channel Bio 37002	Reference	3.7	Conventional	10001116	INRC
Quality Plus 365C	Reference	3.6	Conventional	10001129	INRC
Croplan HT3596STS	Reference	3.5	Conventional	10001117	INSH
Stewart SB3454	Reference	3.4	Conventional	10001130	INSH
Crows C37003N	Reference	3.7	Conventional	10001508	INSH
Pioneer 93M52	Reference	3.5	Conventional	10001128	KSLA
NK S38-T8	Reference	3.8	Conventional	10001509	KSLA
Quality Plus 365C	Reference	3.6	Conventional	10001129	KSLA
Garst 3585N	Reference	3.5	Conventional	10001119	NEYO
Wilken 3316	Reference	3.3	Conventional	10001505	NEYO
Midland 363	Reference	3.3	Conventional	10001570	NEYO
MON 87708[4]	Test		DT	11225299	ALL

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[1] T = Test, C = Control, and R = reference.

[2] Phenotypic abbreviations: NT = non-biotech conventional, Conventional = conventional commercial, DT = dicamba-tolerant.

[3] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[4] Received a mandatory dicamba application.

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Table G-3. Field and Planting Information for 2008 Field Trials

Site	Planting Date[1]	Planting Rate (seeds/ft)	Planting Depth (in)	Plot Size (ft)[2]	Rows/ Plot	Soil Series, Organic Matter, pH	Cropping History	
							2007	2006
AR	05-29-08	8-9	0.75	10 × 20	4	Bosket sandy loam; 1.2%; 6.4	Cotton	Soybean
Can1	05-26-08	9	1.5	10 × 20	4	Norfolk sandy loam; 1.5%; 6.6	Corn	Soybean
Can2	05-27-08	9	1.5	10 × 20	4	Thames clay loam; 3.4%; 7.4	Corn	Soybean
IA1	06-07-08	9	1.25	10 × 20	4	Mahaska silty clay loam; 3.18%; 5.9	Sorghum	Soybean
IA2	06-19-08	9	2.0	10 × 20	4	Tama Muscatine silty clay loam; 3.9%; 6.1	Soybean	Milk thistle
IA3	06-26-08	9	1.0	10 × 20	4	Lawler loam; 7.3%; 7.6	Corn	Soybean
IL1	06-19-08	9	1.25	10 × 20	4	Cisne-Huey Complex silt loam; 1.3%; 7.1	Milo	Soybean
IL2	06-02-08	9	1.25	30 × 30	12	Plano silt loam; 3.5%; 6.4	Corn	Soybean
IN1	05-28-08	9	1.5	30 × 30	12	Crosby silt loam; 2.5%; 7.1	Corn	Soybean
IN2	05-27-08	9	1.5	10 × 20	4	Fincastle silt loam; 2.0%; 7.0	Sweet corn	Soybean
IN3	07-01-08	9	1.0	10 × 20	4	Silty loam; 3%; 6.5	Soybean	Wheat
KS	06-04-08	9	1−1.25	10 × 20	4	Farnum loam; 2.6%; 7.6	Sorghum	Winter wheat

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MI	05-27-08	9	1.5	30 × 30	12	Nester loam; 2.1%; 6.5	Corn	Soybean
MO1	06-18-08	9	1.25	30 × 30	12	Putnam silt loam; 2.1%; 6.6	Corn	Soybean
MO2	06-19-08	9	1.0	10 × 20	4	Gorin silt loam; 4.2%; 6.3	Soybean	Fescue
NE	06-02-08	9	1.0	10 × 20	4	Hastings silt loam; 3.0%; 6.2	Soybean	Soybean
PA	06-03-08	9	1.25	10 × 20	4	Philo/Atkins silt loam; 2.0%; 6.2	Fallow	Tomatoes
WI	05-29-08	9	1.25	10 × 20	4	Radford silt loam; 2.2%; 5.9	Corn	Corn

[1] Month-day-year.
[2] Width × length.

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Table G-4. Field and Planting Information for 2009 Field Trials

Site Code[1]	Planting date[2]	Planting rate (seeds/ft)	Planting depth (in)	Plot size (ft)[3]	Rows/ plot	Soil series, organic matter, pH	Cropping History 2008
ARNE	6/20/2009	9	0.5	20 × 20	8	Bosket sandy loam, 1.0%, 6.0	Cotton
IARL	6/26/2009	9	1.3	20 × 20	8	Taintor/Mahaska silty clay loam, 3.5%, 7.0	Sorghum/Soybean
ILCY	6/29/2009	9	1.4	20 × 20	8	Hoyleton-Darmstadt silt loam, 2.6%, 7.3	Sorghum
ILWY	6/24/2009	9	1.8	20 × 20	8	Flanagan silt loam, 3.8%, 6.5	Corn
INRC	6/30/2009 7/06/2009*	9	1.0	20 × 20	8	Reeseville silt loam, 1.4%, 5.8	Wheat
INSH	6/19/2009	9	1.5	20 × 20	8	Crosby silt loam, 2.3%, 5.6	Corn
KSLA	6/23/2009	9	1.0	20 × 20	8	Silt loam, 2.6%, 7.6	Fallow/Sorghum
NEYO	6/24/2009	9	1.0	20 × 20	8	Hastings silt loam, 3.0%, 6.2	Sorghum

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[1] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[2] Month-day-year.

[3] Width × length.

* Two packets were planted on 7/06/2009 to replace two packets broken on 6/30/2009.

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G.5. Phenotypic Observations

The description of the characteristics measured and the designated developmental stages when observations occurred are listed in Table VII-1.

G.6. Environmental Interaction Observations

Environmental interactions (*i.e.*, interactions between the crop plants and their receiving environment) were used to characterize MON 87708 by evaluating plant response to abiotic stress, disease damage, arthropod-related damage, and pest and beneficial arthropod abundance in the plots using the methods described in G.7 and G.8.

G.7. Abiotic Stress Response, Disease Damage, and Arthropod-Related Damage

MON 87708 and the conventional control were evaluated at all 26 sites for differences in plant response to abiotic stress, disease damage, and arthropod-related damage. Three abiotic stressors, three diseases, and three arthropod pests were evaluated four times during the growing season at the following intervals:

Observation 1: V2 – V4 growth stage[12]
Observation 2: R1 – R2 growth stage
Observation 3: R3 – R5 growth stage
Observation 4: R6 – R8 growth stage

The researcher at each field site chose abiotic stressors, diseases, and arthropod pests that were either actively causing plant injury in the study area or were likely to occur in soybean during the given observation period. Therefore, abiotic stressors, diseases, and arthropod pests assessed often varied between observations at a site and between sites.

Abiotic stress response and disease damage observations were collected from each plot using a continuous 0 – 9 scale of increasing severity. Data were collected numerically and then placed into one of the following categories for reporting purposes:

Rating	Severity of plant damage
0	none (no symptoms observed)
1 – 3	slight (symptoms not damaging to plant development)
4 – 6	moderate (intermediate between slight and severe)
7 – 9	severe (symptoms damaging to plant development)

Arthropod-related damage was assessed from each plot on the upper four nodes of 10 representative plants using the arthropod-specific 0 – 5 rating scales of increasing severity listed below.

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[12] For the 2009 field trials Observation 1 occurred at the V2-V3 growth stage.

Defoliating arthropods (*e.g.*, corn earworm, bean leaf beetle, Japanese beetle, soybean looper)	
Rating	**Severity of plant damage**
0	None
1	1 – 20 % defoliation
2	21 – 40% defoliation
3	41 – 60% defoliation
4	61 – 80% defoliation
5	> 80% defoliation

Pod feeding arthropods (*e.g.*, corn earworm, bean leaf beetle, stink bug, Lygus bug on reproductive plant parts)	
Rating	**Severity of plant damage**
0	None
1	1 – 20 % damaged pods
2	21 – 40% damaged pods
3	41 – 60% damaged pods
4	61 – 80% damaged pods
5	> 80% damaged pods

Leafhoppers (*e.g.*, potato leafhopper)	
Rating	**Severity of plant damage**
0	None
1	1 – 50% of foliage with leaf yellowing; no leaf puckering or leaf margin necrosis
2	1 – 50% of foliage with leaf yellowing, leaf puckering and/or leaf margin necrosis
3	> 50% of foliage with leaf yellowing; no leaf puckering or leaf margin necrosis
4	> 50% of foliage with leaf yellowing, leaf puckering, and/or leaf margin necrosis
5	> 50% of foliage with necrotic leaves (leaves dead due to leafhopper damage)

Aphids (*e.g.*, soybean aphid)	
Rating	**Severity of plant damage**
0	None
1	1 – 100 aphids per plant; no leaf puckering
2	101 – 250 aphids per plant; no leaf puckering
3	≥ 250 aphids per plant with leaf puckering
4	≥ 250 aphids per plant with leaf puckering and leaf yellowing and/or necrosis
5	≥ 250 aphids per plant with plant stunting

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G.8. Arthropod Abundance

Pest and beneficial arthropods were collected at the IL2, IN1, MI, and MO1 sites four times during the growing season at the following intervals:

Collection 1: R1 – R2 growth stage
Collection 2: Approximately two weeks after collection 1
Collection 3: Approximately two weeks after collection 2
Collection 4: Approximately two weeks after collection 3

Arthropods were collected using a beat sheet sampling method (Kogan and Pitre, 1980). The beat sheet was a 36 × 42 inch white, vinyl sheet that was spread between the plants of two adjacent rows. Plants were shaken vigorously along the length of each side of the beat sheet to dislodge arthropods from the plants. A total of four subsamples were collected in this way from each plot. Specifically, two subsamples were collected from rows # 8 and 9 of each plot (subsamples 1 and 3) and two subsamples were collected from rows # 9 and 10 of each plot (subsamples 2 and 4). The subsamples collected from within each pair of rows were at least 10 feet apart and at least 3 feet from the edge of each plot. The four subsamples were combined into one pre-labeled container and placed on freezer ice packs. The samples were then sent overnight to Monsanto Company, St. Louis, MO for arthropod identification and enumeration.

A maximum of six pest and six beneficial arthropods were evaluated for each collection interval. These specific arthropods were then enumerated across all samples from a given collection interval at each individual site. Three of the six pest and three of the six beneficial arthropods were predetermined prior to the collection of samples, namely bean leaf beetle, green cloverworm, and stink bugs for the pests and Araneae (spiders), *Nabis* spp. and *Orius* spp. for the beneficial arthropods, and were evaluated from all collections from all sites. For each specific collection interval at each individual site, up to three additional pest and three additional beneficial arthropods, which were determined to be the most abundant, were evaluated across all samples from the site in addition to the predetermined arthropods. The suite of pest and beneficial arthropods assessed often varied between collections from a site and between sites due to differences in temporal activity and geographical distribution of arthropod taxa.

No arthropod abundance data were collected from the 2009 field trials.

G.9. Environmental Interactions Evaluation Criteria

For the assessments of abiotic stress response and disease damage, MON 87708 and the conventional control were considered different in susceptibility or tolerance to an abiotic stress or disease on a particular observation date at a site if the range of injury severity to MON 87708 did not overlap with the range of injury severity to the conventional control across all three replications. These data are categorical and were not subjected to statistical analysis. For each observation at a site, the range of injury severity across the commercial reference varieties provided data that are representative of commercial

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soybean varieties. Arthropod-related damage and abundance data were quantitatively evaluated and subjected to statistical analysis as appropriate.

G.10. Data Assessment

Experienced scientists familiar with the experimental design and evaluation criteria were involved in all components of data collection, summarization, and analysis. Personnel assessed that measurements were taken properly, data were consistent with expectations based on experience with the crop, and the experiment was carefully monitored. Prior to analysis, the overall dataset was evaluated for evidence of biologically relevant changes and for possible evidence of an unexpected plant response. Any unexpected observations or issues that would impact the evaluation objectives were noted. Data were then subjected to statistical analysis as indicated below.

G.11. Statistical Analysis

Analysis of variance was conducted according to a randomized complete block design using SAS® (Version 9.2). The level of statistical significance was predetermined to be 5% (α=0.05). MON 87708 was compared to the conventional control within each site (individual-site analyses) and in a combined-site analysis, in which the data were pooled across sites, for early stand count, seedling vigor, days to 50% flowering, plant height, lodging, pod shattering, final stand count, seed moisture, 100 seed weight, seed test weight, and yield. Growth stage, flower color, plant pubescence, abiotic stress response, and disease damage data were categorical and not statistically analyzed. Arthropod-related damage and pest and beneficial arthropod abundance data were statistically analyzed only within individual observations/collections and sites due to the variation in temporal activity and geographical distribution of the taxa.

No statistical comparisons were made between MON 87708 and the commercial reference varieties. The reference range for each measured phenotypic characteristic was determined from the minimum and maximum mean values from among the 18 commercial reference varieties planted among the sites. The reference range for the damage from and abundance of each arthropod evaluated from a given observation/collection and site was determined from the minimum and maximum mean damage or abundance values collected from the commercial reference varieties planted at the site.

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G.12. Individual Field Site Plant Growth and Development Results and Discussion

G.12.1. 2008 Untreated MON 87708 Individual Field Site Plant Growth and Development Results and Discussion

In the individual-site analyses, no statistically significant differences were detected between MON 87708 and the conventional control for 153 out of 179 comparisons for the assessed phenotypic characteristics (Table G-5). Lack of variability in the data precluded statistical comparisons between MON 87708 and the conventional control for seedling vigor at the IL2 site; days to 50% flowering at the IN1 site and MI sites; lodging at the Can1, IN3, and MO1 sites; and pod shattering at the Can1, Can2, IA1, IA2, IA3, IL1, IL2, IN1, IN2, IN3, KS, MI, and NE sites. For these data, the means for MON 87708 and the conventional control were the same value, indicating no biological differences (Table G-5).

A total of 26 statistically significant differences were detected between MON 87708 and the conventional control in the individual-site analyses (Table G-5). These differences were distributed among nine phenotypic characteristics. Seedlings of MON 87708 were less vigorous than the conventional control at the Can2 site (6.3 vs. 5.0 rating). MON 87708 flowered one day later than the conventional control at the MO2 site (214 vs. 213 days after Jan. 1, 2008), but one day earlier than the conventional control at the WI site (210 vs. 211 days after Jan. 1, 2008). Plants of MON 87708 were taller than the conventional control at the AR (28.9 vs. 27.1 inches), IA1 (39.1 vs. 34.1 inches), IA2 (37.1 vs. 34.6 inches), IL1 (26.1 vs. 22.3 inches), IN1 (33.6 vs. 30.5 inches), IN2 (39.6 vs. 37.3 inches), MO1 (23.4 vs. 21.1 inches), and MO2 (31.4 vs. 28.7 inches) sites. MON 87708 had more lodging than the conventional control at the IA1 (2.0 vs. 0.7 rating), IL2 (1.0 vs. 0.3 rating), and the WI (1.3 vs. 0.0 rating) sites, but less lodging than the conventional control at the KS site (1.3 vs. 2.0 rating). Final stand count was higher for MON 87708 than the conventional control at the IN3 site (330.3 vs. 298.0 plants/plot). Seed moisture was higher for MON 87708 than the conventional control at the WI site (11.7 vs. 11.2%). The weight of 100 seeds was lower for MON 87708 than the conventional control at the Can1 (15.9 vs. 17.1 g), Can2 (16.9 vs. 18.1 g), IL2 (14.2 vs. 15.0 g), NE (15.4 vs. 15.9 g), and PA (13.4 vs. 15.4 g) sites. Test weight was higher for MON 87708 than the conventional control at the AR site (55.4 vs. 54.0 lb/bu), but lower than the conventional control at the IL1 site (54.2 vs. 55.9 lb/bu). Yield was lower for MON 87708 than the conventional control at the AR (63.3 vs. 70.4 bu/a) and PA (53.9 vs. 65.5 bu/a) sites. Since the statistically significant differences detected in the individual-site analyses for seedling vigor, days to 50% flowering, lodging, final stand count, seed moisture, test weight, and yield were not detected in the combined--site analysis, this suggests these differences were not indicative of a consistent response in the data associated with the trait and are considered not biologically meaningful in terms of increased weediness of MON 87708 compared to the conventional control. While a statistically significant difference was detected for plant height and 100 seed weight in the combined-site analysis, the assessed phenotypic values of MON 87708 for both characteristics in the combined-site analysis were within the range of values observed for the commercial reference varieties.

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G.12.2. 2009 Dicamba-Treated MON 87708 Individual Field Site Plant Growth and Development Results and Discussion

In the individual-site analysis, a total of 88 comparisons were made (Table G-6). Of these comparisons, no numerical differences were observed for 9 comparisons for which p-values could not be generated due to lack of variability. The eight flower color comparisons were categorical and were not statistically analyzed; however, at each site, all plants of treated MON 87708 and the control had purple flowers as expected. For the remaining comparisons, a total of fourteen statistically significant differences were detected out of 71 comparisons between treated MON 87708 and the conventional control. These differences were distributed among eight out of the 11 phenotypic characteristics. Early stand count was lower for treated MON 87708 than the control at the ARNE site (263.0 vs. 300.5 plants/plot) and higher for the ILWY site (338.0 vs. 321.0 plants/plot). Plants of MON 87708 flowered earlier than the control at the ILCY site (215.3 vs. 217.3 days after 1 Jan. 2009), and later than the control at the NEYO site (214.0 vs. 210.0 days after 1 Jan. 2009. Plants of MON 87708 were taller than the control at the ILCY site (26.4 vs. 24.1 inches). MON 87708 had less lodging than the control at the ARNE site (5.3 vs. 6.3 rating) and the NEYO site (1.3 vs. 2.0 rating). Pod shattering was higher for MON 87708 then the control at the NEYO site (1.8 vs. 1.3 rating). Treated MON 87708 had a lower final stand count than the control at the ARNE site (254.3 vs. 290.8 plants/plot). Seed moisture was lower for treated MON 87708 than the control at the ARNE site (10.8 vs. 13.3%). The weight of 100 seeds was lower for MON 87708 than the control at the ARNE site (13.8 vs. 15.2 g), INSH site (15.4 vs. 16.9 g), KSLA site (17.0 vs. 17.8 g), and the NEYO site (14.0 vs. 15.3 g). Considering that the statistical differences detected in the individual-site analyses for early stand count, days to 50% flowering, plant height, lodging, pod shattering, final stand count, and seed moisture were not detected in the combined-site analysis, this suggests these differences were not indicative of a consistent plant response associated with the trait and are unlikely to be biologically meaningful in terms of increased weed potential of MON 87708 when treated with dicamba compared to the control. While a statistical difference was detected for 100 seed weight at three sites and in the combined-site analysis, the assessed phenotypic values of treated MON 87708 was within the expected values for commercial soybean (Section 3.8, step 4, “no” answer). Conventional cultivars seed weight ranges from 0.12 to 0.18 grams per seed (Heatherly and Elmore, 2004).

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Table G-5. 2008 Individual-Site Phenotypic Comparison of Untreated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)							
	Early stand count (#/plot)		Seedling vigor (1-9 scale)		Days to 50% flowering[1]		Flower Color/Plant pubescence[2]	
Site	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708	Control
AR	160.3 (11.3)	142.7 (13.3)	6.0 (0.0)	6.0 (0.0)	183.3 (0.3)	183.0 (0.0)	Purple/hairy	Purple/hairy
Can1	224.7 (2.0)	237.3 (15.1)	3.0 (0.0)	3.0 (0.0)	201.0 (0.6)	200.3 (0.3)	Purple/hairy	Purple/hairy
Can2	327.3 (24.5)	363.0 (13.3)	6.3 (0.3)*	5.0 (0.0)	202.0 (0.0)	202.7 (0.7)	Purple/hairy	Purple/hairy
IA1	281.0 (11.9)	251.7 (16.8)	1.7 (0.7)	1.7 (0.3)	203.7 (0.7)	202.3 (1.3)	Purple/hairy	Purple/hairy
IA2	142.3 (23.0)	111.0 (21.3)	3.3 (0.3)	4.0 (0.6)	221.7 (0.7)	221.7 (0.7)	Purple/hairy	Purple/hairy
IA3	328.3 (13.7)	293.7 (2.7)	1.0 (0.0)	1.0 (0.0)	216.0 (0.0)	216.0 (0.0)	Purple/hairy	Purple/hairy
IL1	317.3 (4.4)	315.3 (5.0)	4.3 (0.3)	4.3 (0.3)	212.0 (0.0)	212.0 (0.0)	Purple/hairy	Purple/hairy
IL2	299.9 (3.5)	309.9 (1.2)	2.0 (0.0) †	2.0 (0.0)	203.3 (0.7)	203.3 (0.3)	Purple/hairy	Purple/hairy
IN1	307.9 (3.7)	305.0 (4.2)	5.7 (0.3)	4.7 (0.3)	206.0 (0.0)†	206.0 (0.0)	Purple/hairy	Purple/hairy
IN2	285.7 (55.4)	304.0 (39.3)	5.0 (1.0)	4.3 (0.7)	202.0 (0.0)	202.0 (0.0)	Purple/hairy	Purple/hairy
IN3	338.0 (5.1)	310.3 (15.5)	3.7 (0.9)	3.3 (0.9)	220.0 (0.0)	220.7 (0.7)	Purple/hairy	Purple/hairy
KS	198.0 (11.2)	175.3 (29.2)	2.7 (0.3)	3.3 (0.7)	198.7 (0.3)	199.0 (0.0)	Purple/hairy	Purple/hairy
MI	333.7 (3.1)	342.8 (3.2)	4.0 (0.0)	3.7 (0.3)	208.0 (0.0)†	208.0 (0.0)	Purple/hairy	Purple/hairy
MO1	195.2 (13.9)	219.4 (14.6)	4.7 (0.3)	4.7 (0.3)	212.7 (0.9)	213.0 (0.0)	Purple/hairy	Purple/hairy
MO2	325.7 (0.9)	318.0 (6.0)	3.3 (0.3)	2.7 (0.3)	214.0 (0.0)*	213.0 (0.0)	Purple/hairy	Purple/hairy
NE	271.3 (9.5)	254.7 (3.3)	2.3 (0.3)	2.3 (0.3)	199.3 (1.3)	198.0 (0.0)	Purple/hairy	Purple/hairy
PA	266.3 (14.3)	262.3 (14.0)	3.0 (0.6)	2.7 (0.3)	201.3 (0.3)	201.0 (0.0)	Purple/hairy	Purple/hairy
WI	277.0 (24.2)	254.0 (0.0)	1.3 (0.3)	1.0 (0.0)	210.0 (0.0)*	211.0 (0.0)	Purple/hairy	Purple/hairy

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Table G-5 (continued). 2008 Individual-Site Phenotypic Comparison of Untreated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)							
	Plant height (inch)		Lodging (0-9 scale)		Pod shattering (0-9 scale)		Final stand count (#/plot)	
Site	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)
AR	28.9 (0.2)*	27.1 (0.1)	2.7 (0.3)	2.0 (0.6)	0.3 (0.3)	0.3 (0.3)	140.3 (8.7)	138.0 (16.0)
Can1	32.1 (0.6)	31.7 (0.5)	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	240.3 (1.7)	248.0 (5.5)
Can2	40.1 (0.7)	38.6 (0.8)	4.0 (0.6)	3.3 (0.9)	0.0 (0.0)†	0.0 (0.0)	309.3 (6.9)	287.7 (2.3)
IA1	39.1 (0.5)*	34.1 (0.3)	2.0 (0.6)*	0.7 (0.3)	0.0 (0.0)†	0.0 (0.0)	242.7 (5.8)	221.3 (15.1)
IA2	37.1 (0.3)*	34.6 (0.4)	2.0 (0.0)	2.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	123.0 (17.7)	102.7 (17.9)
IA3	24.6 (0.5)	23.5 (0.8)	0.7 (0.3)	0.7 (0.3)	0.0 (0.0)†	0.0 (0.0)	293.3 (4.7)	285.7 (5.2)
IL1	26.1 (1.4)*	22.3 (0.2)	1.0 (0.0)	0.3 (0.3)	0.0 (0.0)†	0.0 (0.0)	321.7 (6.1)	317.0 (7.2)
IL2	39.0 (0.3)	37.4 (0.5)	1.0 (0.0)*	0.3 (0.3)	0.0 (0.0)†	0.0 (0.0)	295.9 (4.5)	287.0 (3.5)
IN1	33.6 (2.3)*	30.5 (1.9)	1.3 (0.3)	0.7 (0.3)	0.0 (0.0)†	0.0 (0.0)	223.5 (25.1)	223.9 (29.1)
IN2	39.6 (0.6)*	37.3 (0.4)	1.0 (0.0)	1.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	262.3 (7.0)	264.0 (39.2)
IN3	25.3 (0.3)	24.3 (0.5)	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	330.3 (7.7)*	298.0 (15.9)
KS	40.5 (1.5)	38.2 (1.3)	1.3 (0.3)*	2.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	187.7 (10.5)	167.0 (24.0)
MI	29.5 (2.6)	30.9 (1.8)	0.7 (0.3)	0.3 (0.3)	0.0 (0.0)†	0.0 (0.0)	304.2 (4.5)	308.8 (5.2)
MO1	23.4 (1.0)*	21.1 (0.8)	0.0 (0.0)†	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	186.8 (3.7)	214.8 (9.0)
MO2	31.4 (1.7)*	28.7 (1.1)	0.7 (0.3)	0.3 (0.3)	1.0 (0.0)	1.0 (0.0)	308.3 (1.7)	299.3 (1.9)
NE	40.5 (0.9)	38.9 (1.3)	0.3 (0.3)	1.0 (0.0)	0.0 (0.0)†	0.0 (0.0)	254.0 (7.8)	233.7 (5.9)
PA	32.9 (0.8)	33.3 (0.8)	1.3 (0.3)	0.7 (0.7)	0.0 (0.0)	0.0 (0.0)	260.0 (16.2)	255.0 (11.4)
WI	39.5 (0.7)	37.3 (0.3)	1.3 (0.3)*	0.0 (0.0)	0.0 (0.0)	0.5 (0.5)	235.7 (20.2)	223.0 (1.0)

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Table G-5 (continued). 2008 Individual-Site Phenotypic Comparison of Untreated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)							
	Seed moisture (%)		100 seed weight (g)		Test weight (lb/bu)		Yield bu/a)	
Site	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)
AR	9.5 (0.1)	9.7 (0.3)	16.1 (0.3)	15.1 (1.1)	55.4 (0.4)*	54.0 (0.7)	63.3 (3.7)*	70.4 (3.3)
Can1	12.4 (0.1)	12.1 (0.3)	15.9 (0.5)*	17.1 (0.0)	55.7 (0.4)	55.5 (0.5)	66.7 (3.0)	65.8 (5.0)
Can2	13.3 (0.2)	13.2 (0.1)	16.9 (0.2)*	18.1 (0.2)	57.3 (0.2)	57.4 (0.2)	76.4 (0.1)	78.5 (3.3)
IA1	11.4 (0.2)	11.2 (0.1)	15.0 (0.0)	14.7 (0.3)	55.6 (0.8)	54.5 (0.3)	71.7 (3.3)	75.0 (3.4)
IA2	12.6 (0.1)	12.1 (0.5)	16.5 (0.3)	16.0 (0.2)	57.3 (0.3)	57.3 (0.3)	54.7 (6.7)	45.5 (2.7)
IA3	7.5 (0.1)	7.5 (0.1)	12.0 (0.3)	12.5 (0.2)	58.1 (0.6)	57.2 (0.7)	20.5 (1.1)	20.4 (2.0)
IL1	10.4 (0.0)	10.4 (0.1)	11.7 (0.5)	12.0 (0.5)	54.2 (0.7)*	55.9 (0.2)	46.5 (5.5)	37.2 (1.8)
IL2	12.3 (0.1)	12.3 (0.3)	14.2 (0.1)*	15.0 (0.2)	54.3 (0.3)	54.3 (0.9)	55.3 (0.8)	55.9 (2.8)
IN1	9.2 (0.1)	9.3 (0.1)	14.5 (0.0)	14.6 (0.0)	55.4 (0.9)	54.6 (0.9)	56.0 (2.4)	55.5 (4.1)
IN2	10.9 (0.2)	10.7 (0.3)	14.9 (0.1)	15.0 (0.1)	51.0 (1.1)	50.7 (0.5)	61.9 (4.3)	66.2 (4.8)
IN3	10.0 (0.1)	10.0 (0.2)	16.0 (0.2)	16.4 (0.3)	59.5 (1.3)	59.6 (1.5)	48.7 (2.6)	45.8 (0.6)
KS	17.7 (0.2)	17.9 (0.3)	15.0 (0.0)	15.7 (0.3)	56.2 (0.4)	55.4 (0.3)	66.0 (2.9)	60.0 (6.0)
MI	15.5 (0.0)	14.8 (0.2)	18.2 (0.7)	18.8 (0.3)	56.6 (0.3)	56.2 (0.2)	42.9 (4.7)	44.2 (2.6)
MO1	11.9 (0.4)	12.1 (0.4)	14.3 (0.3)	15.0 (2.0)	55.8 (0.2)	55.7 (0.3)	35.1 (2.4)	31.6 (5.2)
MO2	12.0 (0.0)	11.8 (0.2)	15.3 (0.3)	15.7 (0.3)	54.0 (0.3)	53.5 (1.2)	43.5 (1.4)	40.0 (2.2)
NE	13.1 (0.1)	13.4 (0.3)	15.4 (0.2)*	15.9 (0.3)	59.2 (0.1)	59.1 (0.2)	69.3 (1.3)	71.5 (1.2)
PA	10.4 (0.2)	10.5 (0.2)	13.4 (0.3)*	15.4 (0.2)	57.2 (0.3)	57.5 (0.3)	53.9 (1.3)*	65.5 (2.1)
WI	11.7 (0.1)*	11.2 (0.1)	14.2 (0.2)	15.4 (0.4)	58.0 (0.6)	58.3 (0.3)	65.0 (2.7)	66.4 (1.3)

Note: The experimental design at each site was a randomized complete block with three replications. S.E. = Standard Error

[1] Calendar day number when approximately 50% of the plants in each plot were flowering.

[2] Flower color and plant pubescence data were categorical and were not statistically analyzed.

*Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

†No statistical comparisons were made due to lack of variability in the data.

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Table G-6. 2009 Individual-Site Phenotypic Comparison of Dicamba Treated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)							
	Early stand count (#/plot)		Seedling vigor (1-9 scale)		Days After 1 Jan 2009 to 50% flowering		Flower color^{2}	
Site^{1}	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean(S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)
ARNE	263.0* (13.73)	300.5 (5.42)	5.8 (0.25)	5.3 (0.48)	203.8 (0.25)	204.0 (0.41)	Purple	Purple
IARL	290.8 (3.42)	285.0 (12.88)	4.8 (1.18)	5.8 (0.48)	220.3 (0.48)	220.3 (0.25)	Purple	Purple
ILCY	337.0 (2.35)	328.3 (6.70)	1.0 (0.00)	1.8 (0.25)	215.3* (0.48)	217.3 (0.25)	Purple	Purple
ILWY	338.0* (5.00)	321.0 (3.03)	1.0† (0.00)	1.0 (0.00)	216.0 (0.00)	216.0 (0.00)	Purple	Purple
INRC	276.5 (5.07)	293.3 (7.34)	3.3 (0.75)	2.3 (0.48)	224.3 (0.85)	225.3 (0.25)	Purple	Purple
INSH	300.8 (8.19)	287.8 (6.94)	2.0 (0.41)	1.5 (0.29)	217.0 (0.00)	217.0 (0.00)	Purple	Purple
KSLA	276.3 (9.41)	285.3 (6.80)	3.3 (0.25)	3.3 (0.25)	207.0 (0.00)	207.3 (0.25)	Purple	Purple
NEYO	309.0 (2.35)	307.8 (4.52)	3.0† (0.00)	3.0 (0.00)	214.0* (0.00)	210.0 (0.00)	Purple	Purple

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Table G-6 (continued). 2009 Individual-Site Phenotypic Comparison of Dicamba Treated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)							
	Plant Height (in)		Lodging (1-9 scale)		Pod Shattering (1-9 scale)		Final Stand Count (#/plot)	
Site[1]	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)
ARNE	32.9 (1.07)	32.3 (0.77)	5.3* (0.48)	6.3 (0.25)	1.0† (0.00)	1.0 (0.00)	254.3* (12.02)	290.8 (5.48)
IARL	33.6 (0.60)	32.7 (0.43)	3.3 (0.63)	3.5 (0.65)	1.0 (0.00)	1.5 (0.50)	280.5 (1.32)	271.3 (5.92)
ILCY	26.4* (0.99)	24.1 (0.26)	1.0† (0.00)	1.0 (0.00)	1.0† (0.00)	1.0 (0.00)	231.8 (37.47)	242.5 (11.21)
ILWY	35.2 (0.18)	35.3 (0.33)	2.0 (0.00)	2.0 (0.00)	1.0† (0.00)	1.0 (0.00)	300.5 (7.71)	294.3 (8.80)
INRC	23.1 (0.74)	21.7 (0.72)	1.0† (0.00)	1.0 (0.00)	1.0† (0.00)	1.0 (0.00)	226.3 (9.54)	223.3 (7.47)
INSH	33.3 (0.97)	33.4 (0.56)	1.5 (0.50)	1.0 (0.00)	1.0† (0.00)	1.0 (0.00)	270.0 (15.87)	255.8 (8.61)
KSLA	35.1 (0.82)	35.1 (0.30)	2.3 (0.25)	2.5 (0.29)	1.0 (0.00)	1.0 (0.00)	260.8 (5.44)	257.3 (10.58)
NEYO	33.4 (0.42)	35.4 (1.45)	1.3* (0.25)	2.0 (0.00)	1.8* (0.25)	1.3 (0.25)	295.8 (2.50)	299.0 (5.55)

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Table G-6 (continued). 2009 Individual-Site Phenotypic Comparison of Dicamba Treated MON 87708 to Conventional Control

	Phenotypic Characteristic (units)					
	Seed Moisture (%)		100 Seed Weight (g)		Yield (bu/ac)	
Site[1]	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)	MON 87708 Mean (S.E.)	Control Mean (S.E.)
ARNE	10.8* (0.38)	13.3 (0.76)	13.8* (0.23)	15.2 (0.18)	48.5 (2.96)	47.9 (2.33)
IARL	11.7 (0.05)	11.5 (0.16)	13.0 (0.41)	14.0 (0.41)	37.3 (1.52)	35.6 (1.25)
ILCY	12.9 (0.14)	13.1 (0.25)	14.9 (0.27)	15.7 (0.25)	52.0 (8.22)	51.6 (1.58)
ILWY	17.7 (0.14)	17.8 (0.20)	15.1 (0.21)	15.4 (0.24)	49.7 (1.97)	52.9 (2.74)
INRC	12.5 (0.27)	12.7 (0.31)	13.8 (0.15)	14.2 (0.30)	29.6 (2.75)	31.3 (2.00)
INSH	12.6 (0.04)	12.5 (0.13)	15.4* (0.31)	16.9 (0.22)	58.2 (2.56)	57.7 (2.48)
KSLA	11.9 (0.34)	11.5 (0.38)	17.0* (0.00)	17.8 (0.25)	65.5 (1.63)	66.0 (1.54)
NEYO	15.0 (0.13)	15.0 (0.09)	14.0* (0.41)	15.3 (0.25)	33.2 (1.58)	31.7 (0.55)

Note: The experimental design was a randomized complete block with four replications.

* Statistically significant differences (α=0.05) between MON 87708 and the conventional soybean control.

† No statistical comparisons were made due to lack of variability in the data.

[1] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[2] Flower color data were categorical and were not statistically analyzed.

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Table G-7. Growth Stage Monitoring of Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Assessment Date and Range of Growth Stages Observed[2]									
Site[1]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10
AR		06/18/2008	07/6/2008	07/23/2008	08/06/2008	08/23/2008	09/02/2008	9/24/2008	—	—	—
	MON 87708	V2	R2	R3	R5	R6	R6	R8	—	—	—
	Control	V2	R2	R3	R5	R6	R6	R8	—	—	—
	References	V2-V3	R2	R3	R5	R6	R6	R8	—	—	
Can1		06/11/2008	06/24/2008	07/08/2008	07/25/2008	08/11/2008	08/25/2008	09/08/2008	09/23/2008	10/10/2008	10/18/2008
	MON 87708	VE	V1-V2	V3-V4	R2	R3-R4	R4-R5	R5-R6	R6-R7	R7-R8	R8
	Control	VE	V1-V2	V3-V4	R2	R3-R4	R4-R5	R5-R6	R6-R7	R7-R8	R8
	References	VE	V1-V2	V3-V4	R2	R3-R4	R4-R5	R5-R6	R6-R7	R7-R8	R8
Can2		06/10/2008	06/25/2008	07/10/2008	07/21/2008	08/06/2008	08/23/2008	09/03/2008	09/20/2008	10/15/2008	
	MON 87708	VE	V2-V3	V5	R2	R3	R5	R6	R7	R8	—
	Control	VE	V2-V3	V5-V6	R2	R3	R5	R6	R7	R8	—
	References	VE	V2-V3	V5-V6	R2	R3	R5	R6	R7	R8	—
IA1		07/01/2008	07/16/2008	08/06/2008	08/27/2008	09/15/2008	10/1/2008				
	MON 87708	V1-V2	V6-V7	R2	R4	R6	R7-R8	—	—	—	—
	Control	V2	V6	R2-R3	R4	R6	R7-R8	—	—	—	—
	References	V1-V2	V6-V7	R2-R3	R4	R6	R7	—	—	—	—
IA2		07/17/2008	08/05/2008	08/20/2008	09/10/2008	09/29/2008	10/15/2008	11/04/2008			
	MON 87708	V3	R2	R3	R5	R6	R7	R8	—	—	—
	Control	V3	R2	R3	R5	R6	R7	R8	—	—	—
	References	V3	R2	R3	R5	R6	R7	R8	—	—	—

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Table G-7 (continued). Growth Stage Monitoring of Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Assessment Date and Range of Growth Stages Observed[2]									
Site[1]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10
IA3		07/10/2008	07/20/2008	08/04/2008	08/24/2008	09/13/2008	09/30/2008				
	MON 87708	VC-V1	V1-V2	R2	R4	R5	R6	—	—	—	—
	Control	V1	V2	R2	R4	R5	R6	—	—	—	—
	References	VC-V1	V1-V2	R2-R3	R3-R4	R4-R6	R6	—	—	—	—
IL1		07/07/2008	07/22/2008	08/12/2008	09/01/2008	09/19/2008	10/06/2008				
	MON 87708	V1	R1	R2-R3	R6	R6	R8	—	—	—	—
	Control	V1	R1	R2	R5-R6	R6-R7	R8	—	—	—	—
	References	V1	R1	R2-R3	R5-R6	R6-R7	R8	—	—	—	—
IL2		06/25/2008	07/16/2008	08/07/2008	08/27/2008	09/17/2008	10/08/2008				
	MON 87708	V2	V6	R3	R5	R7	R7-R8	—	—	—	—
	Control	V2	V6	R3	R5	R7	R7-R8	—	—	—	—
	References	V2	V6	R3	R5	R7	R7-R8	—	—	—	—
IN1		06/25/2008	07/14/2008	07/25/2008	08/13/2008	08/28/2008	09/18/2008	10/01/2008			
	MON 87708	V2-V3	R1	R2	R5	R6	R7	R8	—	—	—
	Control	V2-V3	R1	R2	R4-R5	R6	R7	R8	—	—	—
	References	V2-V3	R1	R2	R4-R5	R6	R7-R8	R8	—	—	—
IN2		06/25/2008	07/14/2008	07/21/2008	08/11/2008	08/26/2008	09/10/2008	10/01/2008			
	MON 87708	V3	R1	R2	R5	R6	R6	R8	—	—	—
	Control	V2-V3	R1	R2	R5	R6	R6-R7	R8	—	—	—
	References	V2-V3	R1	R2	R4-R5	R6	R6-R7	R8	—	—	—

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Table G-7 (continued). Growth Stage Monitoring of Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Assessment Date and Range of Growth Stages Observed[2]									
Site[1]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10
IN3		07/15/2008	08/08/2008	08/27/2008	09/11/2008	09/25/2008	10/07/2008	10/20/2008			
	MON 87708	V2	R1-R2	R4	R5	R6	R7	R8	—	—	—
	Control	V2	R1-R2	R4	R5	R6	R7	R8	—	—	—
	References	V2	R1-R2	R4	R5	R6	R7	R8	—	—	—
KS		06/27/2008	07/08/2008	07/23/2008	08/04/2008	08/18/2008	08/29/2008	09/10/2008	09/26/2008	10/10/2008	
	MON 87708	V2	V5-V6	R2	R3	R5	R5	R6	R8	R8	—
	Control	V2	V5-V6	R2	R3	R5	R5	R6	R8	R8	—
	References	V2	V5-V6	R2	R3	R4-R5	R5	R6	R7	R8	—
MI		06/24/2008	07/08/2008	07/22/2008	08/05/2008	08/18/2008	09/02/2008	09/17/2008	10/02/2008	10/13/2008	
	MON 87708	V2	V4-V5	V8-V9	R3	R5	R6	R6	R7	R8	—
	Control	V2	V4-V5	V8-V9	R3	R5	R6	R6	R7	R8	—
	References	V2	V4-V5	V8-V9	R3	R5	R6	R6	R7	R8	—
MO1		07/16/2008	07/30/2008	08/19/2008	09/09/2008	09/23/2008	10/07/2008	10/21/2008	10/31/2008		
	MON 87708	V2-V3	V5-R2	R4	R5	R6	R8	R8	R8	—	—
	Control	V3	R1	R4	R5	R6	R8	R8	R8	—	—
	References	V2-V3	R1-R2	R4	R5	R6	R7-R8	R8	R8	—	—
MO2		07/14/2008	08/02/2008	08/14/2008	08/20/2008	09/10/2008	09/24/2008	10/07/2008	10/31/2008		
	MON 87708	V2	R2	R3	R4	R6	R6	R8	R8	—	—
	Control	V2	R2	R3	R4	R6	R6	R8	R8	—	—
	References	V2-V3	R1-R2	R2-R3	R4	R5-R6	R6	R7-R8	R8	—	—

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Table G-7 (continued). Growth Stage Monitoring of Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Assessment Date and Range of Growth Stages Observed[2]									
Site[1]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10
NE		06/26/2008	07/17/2008	08/07/2008	08/28/2008	09/23/2008	10/08/2008				
	MON 87708	V2	R1-R2	R4	R6	R7	R8	—	—	—	—
	Control	V2	R2	R4	R6	R7	R8	—	—	—	—
	References	V2	R1-R2	R4	R6	R7	R8	—	—	—	—
PA		06/20/2008	07/10/2008	07/24/2008	08/12/2008	08/29/2008	09/16/2008	09/30/2008	10/15/2008		
	MON 87708	V1	V4	R2	R4	R5-R6	R7	R8	R8	—	—
	Control	V1	V4	R2	R4	R5	R7	R7-R8	R8	—	—
	References	V1	V4-V5	R2-R3	R4-R5	R5-R6	R6-R7	R7-R8	R8	—	—
WI		07/01/2008	07/16/2008	08/08/2008	08/29/2008	09/16/2008	09/30/2008				
	MON 87708	V3	V5*	R3	R5	R6	R7	—	—	—	—
	Control	V3	V4	R3	R5	R6	R7	—	—	—	—
	References	V3	V4-V5	R3	R5	R6	R7	—	—	—	—

*Indicates that MON 87708 and the conventional control were not within the same range of plant growth stages on this observation date.

[1] Site codes are as follows: AR = Jackson County, AR; Can1 = Norfolk, Ontario, Canada; Can2 = Kent, Ontario, Canada; IA1 = Jefferson County, IA; IA2 = Benton County, IA; IA3 = Howard County, IA; IL1 = Clinton County, IL; IL2 = Stark County, IL; IN1 = Boone County, IN; IN2 = Clinton County, IN; IN3 = Parke County, IN; KS = Pawnee County, KS; MI = Ottawa County, MI; MO1 = Shelby County, MO; MO2 = Macon County, MO; NE = York County, NE; PA = Berks County, PA; WI = Walworth County, WI.

[2] Obs. = Observation number; dates in month/day/year format.

Dash (—) indicates information not available or plants had already reached full maturity (R8).

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Table G-8. Growth Stage Monitoring of Dicamba Treated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2009 Field Trials

		Assessment Date and Range of Growth Stages Observed[1]											
Site [2]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10	Obs. 11	Obs. 12
ARNE		7/10/2009	7/25/2009	8/12/2009	9/02/2009	9/22/2009	10/08/2009						
	MON 87708[3]	V2	R1-R2	R4-R5	R6	R6	R8						
	Control	V2	R1-R2	R5	R6	R6	R8						
	References	V2	V6-R2	R4-R5	R6	R6	R8						
IARL		7/17/2009	7/23/2009	7/27/2009	7/29/2009	8/12/2009	8/14/2009	8/21/2009	8/28/2009	9/7/2009	9/14/2009	9/28/2009	10/29/2009
	MON 87708[3]	V2	V3	V3	V4	R1	R2	R2-R3	R4	R5	R5	R6	R8
	Control	V2	V3	V3	V3-V4	R1	R2	R2-R3	R4	R5	R5	R6	R8
	References	V2	V3	V3	V3-V4	R1	R2	R2-R4	R4	R5	R5	R6	R8
INRC		7/30/2009	8/6/2009	8/22/2009	8/26/2009	9/3/2009	9/15/2009	10/5/2009	10/12/2009	10/29/2009	—	—	—
	MON 87708[3]	V2	V3	R2	R3	R5	R5	R6	R7	R8	—	—	—
	Control	V2	V3	R2	R3	R5	R5	R6	R7	R8	—	—	—
	References	V2	V3	R2	R2-R3	R5	R5	R6	R7	R8	—	—	—

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Table G-8 (continued). Growth Stage Monitoring of Dicamba Treated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2009 Field Trials

		Assessment Date and Range of Growth Stages Observed[1]											
Site[2]	Material	Obs. 1	Obs. 2	Obs. 3	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9	Obs. 10	Obs. 11	Obs. 12
INSH		7/14/2009	8/11/2009	9/1/2009	10/5/2009	11/6/2009	—	—	—	—	—	—	—
	MON 87708[3]	V3	R2	R4	R7	R8	—	—	—	—	—	—	—
	Control	V3	R2	R4	R7	R8	—	—	—	—	—	—	—
	References	V3	V10-R2	R4	R7	R8	—	—	—	—	—	—	—
KSLA		7/9/2009	7/27/2009	8/6/2009	8/20/2009	9/3/2009	9/16/2009	10/1/2009	10/16/2009	10/28/2009	—	—	—
	MON 87708[3]	V2	R1	R1	R3-R4	R5	R6	R7	R8	R8	—	—	—
	Control	V2	R1	R1	R4	R5	R6	R7	R8	R8	—	—	—
	References	V2	R1	R1	R3-R4	R4-R5	R6	R6-R7	R8	R8	—	—	—
NEYO		7/17/2009	8/7/2009	8/26/2009	—	—	—	—	—	—	—	—	—
	MON 87708[3]	V3	R1	R4	—	—	—	—	—	—	—	—	—
	Control	V3	R1	R4	—	—	—	—	—	—	—	—	—
	References	V3	R1	R4	—	—	—	—	—	—	—	—	—

Obs. = Observation number

[1] Month-day-year.

[2] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[3] Received a mandatory dicamba application.

— Dashes indicate information not provided. Growth stage data from the ILWY and ILCY site were not collected properly and are not presented.

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Table G-9. Abiotic Stress Response Evaluations of Untreated MON 87708 and Conventional Control from 2008 Field Trials Using an Observational Severity Scale

Abiotic Stressor	Number of observations across all sites	Number of observations where no differences were observed between MON 87708 and conventional control
Total	194	193
Cold	6	6
Compaction	9	9
Crusting	1	1
Drought	27	27
Excess moisture	20	20
Flooding	18	18
Frost	3	3
Hail	30	30
Heat damage	21	21
Mineral Toxicity	1	1
Nutrient deficiency[1]	28	28
Wind	30	29*

Note: The experimental design was a randomized complete block with three replications. Observations were conducted at four crop developmental stages: Observation 1 at V2-V4; Observation 2 at R1-R2; Observation 3 at R3-R5; Observation 4 at R6-R8.

*Indicates a difference observed between MON 87708 (slight damage observed) and the conventional control (no damage observed) for wind damage during Observation 4 at the WI site. Data were not subjected to statistical analysis.

[1] Includes iron deficiency.

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Table G-10. Disease Damage Evaluations of Untreated MON 87708 and Conventional Control from 2008 Field Trials Using an Observational Severity Scale

Disease stressor	Number of observations across all sites	Number observations where no differences were observed between MON 87708 and conventional control
Total	215	215
Alternaria leaf spot	7	7
Anthracnose	10	10
Asian rust	4	4
Bacterial blight	16	16
Brown stem rot	5	5
Cercospora[1]	3	3
Charcoal rot	4	4
Downy mildew	7	7
Frogeye leaf spot	24	24
Phytophthora[2]	13	13
Pod and stem blight	1	1
Powdery mildew	20	20
Pythium	7	7
Rhizoctonia	10	10
Septoria brown spot[3]	39	39
Soybean cyst nematode	2	2
Soybean mosaic virus	1	1
Soybean rust[4]	14	14
Stem canker	2	2
Sudden death syndrome[5]	14	14
White mold	11	11
Yellow mosaic virus	1	1

Note: The experimental design was a randomized complete block with three replications. Observations were conducted at four crop developmental stages: Observation 1 at V2-V4; Observation 2 at R1-R2; Observation 3 at R3-R5; Observation 4 at R6-R8.

[1] Includes *Cercospora* leaf blight and *Cercospora* leaf disease.

[2] Includes *Phytophthora* root rot.

[3] Includes *Septoria*.

[4] Includes rust.

[5] Includes sudden death.

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Table G-11. Arthropod–Related Damage Evaluations of Untreated MON 87708 and Conventional Control from 2008 Field Trials Using an Observational Severity Scale

Arthropod	Number of observations across sites[1]	Number of observations where no differences were detected between MON 87708 and conventional control[2]	Statistically Significant Differences[4]				
			Site[3]	Observation Number	Arthropod-Related Damage Rating (0-5 scale)		
					MON 87708 (S.E.)	Control (S.E.)	Reference Range
Aphid	33	31	IA2	3	0.3 (0.06)	0.5 (0.07)	0.3-0.5
			IA3	2	0.8 (0.03)	0.9 (0.06)	0.8-1.0
Armyworm	2	2	–	–	–	–	–
Bean leaf beetle	48	48	–	–	–	–	–
Blister beetle	5	4	MO1	2	0.1 (0.03)	0.4 (0.12)	0.0-0.2
Cabbage looper	1	1	–	–	–	–	–
Corn rootworm beetle	3	3	–	–	–	–	–
Cutworm	1	1	–	–	–	–	–
Fall armyworm	3	3	–	–	–	–	–
Grasshopper	29	29	–	–	–	–	–
Green cloverworm	10	10	–	–	–	–	–

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Table G-11 (continued). Arthropod-Related Damage Evaluations of Untreated MON 87708 and Conventional Control from 2008 Field Trials Using an Observational Severity Scale

Arthropod	Number of observations across sites[1]	Number of observations where no differences were detected between MON 87708 and conventional control[2]	Statistically Significant Differences[4]				
			Site[3]	Observation Number	Arthropod-Related Damage Rating (0-5 scale)		
					MON 87708 (S.E.)	Control (S.E.)	Reference Range
Japanese beetle	27	25	IN1	2	0.6 (0.03)	0.9 (0.12)	0.7-0.9
			PA	4	0.6 (0.07)	0.4 (0.03)	0.3-0.5
Leafhopper[5]	5	4	PA	1	1.1 (0.07)	0.6 (0.23)	0.4-1.3
Seedcorn maggot	1	1	−	−	−	−	−
Soybean looper	7	7	−	−	−	−	−
Spider mite	8	8	−	−	−	−	−
Sting bug	24	24	−	−	−	−	−
Thistle caterpillar	3	3	−	−	−	−	−
Thrips	2	2	−	−	−	−	−
Yellow woollybear	4	4	−	−	−	−	−

Note: The experimental design was a randomized complete block design with three replications. Observations were conducted at four crop developmental stages: Observation 1 = V2-V4, Observation 2 = R1-R2, Observation 3 = R3-R5, and Observation 4 = R6-R8.

[1] Statistical comparisons were made between MON 87708 and the conventional control for 95 of the observations. Lack of variability in the data precluded statistical comparisons for 121 of the observations.

[2] No statistically significant difference (α = 0.05) or numerical difference.

[3] Site codes IA2 = Benton County, IA; IA3 = Howard County, IA; IN1 = Boone County, IN; MO1 = Shelby County, MO; PA = Berks County, PA.

[4] Means, standard errors (S.E.), and reference ranges for differences between MON 87708 and the conventional control that were statistically different (α=0.05). Reference ranges were determined from the minimum and maximum mean values from among the commercial reference varieties.

[5] The difference detected in leafhopper damage during the first observation at the PA site was for damage caused by potato leafhoppers.

Dash (−) indicates no statistically significant difference between MON 87708 and the conventional control (α = 0.05).

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Table G-12. Abundance of Pest Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Pest Arthropod[2]								
		Aphid			Bean Leaf Beetle			Grape Colaspis		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	–	–	–	13.7 (4.8)	13.7 (4.1)	6.3 - 13.3	0.7 (0.3)	1.3 (1.3)	0.3 - 2.7
	IN1	–	–	–	0.3 (0.3)	0.3 (0.3)	0.7 - 1.0	0.0 (0.0)	0.3 (0.3)	0.0 - 0.0
	MI	–	–	–	0.0 (0.0)[†]	0.0 (0.0)	0.0 - 0.0	–	–	–
	MO1	–	–	–	0.0 (0.0)	0.0 (0.0)	0.3 - 0.7	–	–	–
2	IL2	–	–	–	4.3 (2.6)	5.7 (3.5)	2.7 - 5.0	–	–	–
	IN1	–	–	–	1.3 (0.9)	2.0 (0.6)	0.3 - 1.7	–	–	–
	MI	816.7 (252.2)	383.3 (116.7)	600.0 - 1366.7	0.0 (0.0)[†]	0.0 (0.0)	0.0 - 0.0	–	–	–
	MO1	–	–	–	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	0.0 (0.0)	0.3 (0.3)	0.0 - 0.0
3	IL2	–	–	–	0.3 (0.3)	1.3 (0.9)	0.7 - 1.3	–	–	–
	IN1	–	–	–	0.3 (0.3)	0.7 (0.3)	0.0 - 1.3	–	–	–
	MI	93.3 (78.4)	33.3 (16.7)	3.3 - 60.0	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	–	–	–
	MO1	13.3 (3.3)	16.7 (3.3)	6.7 - 33.3	1.0 (1.0)	0.0 (0.0)	0.0 - 1.3	–	–	–
4	IL2	–	–	–	14.0 (3.5)	14.3 (4.7)	5.7 - 10.3	–	–	–
	IN1	–	–	–	2.0 (0.6)	2.3 (1.2)	0.3 - 2.0	–	–	–
	MI	–	–	–	0.0 (0.0)[†]	0.0 (0.0)	0.0 - 0.0	–	–	–
	MO1	–	–	–	5.0 (2.6)	3.3 (0.9)	3.3 - 4.7	–	–	–

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Table G-12 (continued). Abundance of Pest Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Pest Arthropod[2]								
		Garden Flea-hopper			Green Clover-worm			Japanese Beetle		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	-	-	-	0.0 (0.0) *	2.0 (0.0)	0.3 - 2.7	0.3 (0.3)	0.0 (0.0)	0.0 - 0.7
	IN1	-	-	-	0.0 (0.0)	0.3 (0.3)	0.0 - 1.3	9.0 (4.6)	12.0 (7.6)	0.7 - 11.7
	MI	-	-	-	1.7 (0.9) *	0.0 (0.0)	0.0 - 1.7	2.3 (1.9) *	8.0 (4.2)	1.7 - 5.7
	MO1	-	-	-	2.3 (1.9)	5.0 (2.1)	1.0 - 3.7	–	–	–
2	IL2	-	-	-	16.0 (5.0)	14.7 (2.8)	7.3 - 17.7	–	–	–
	IN1	-	-	-	6.3 (0.3)	3.7 (0.9)	3.7 - 7.3	1.3 (0.7)	0.7 (0.7)	0.5 - 2.7
	MI	-	-	-	1.7 (0.7)	2.7 (1.7)	1.0 - 3.0	2.7 (0.3)	5.3 (2.9)	1.0 - 5.0
	MO1	0.3 (0.3)	1.0 (0.6)	0.0 - 1.0	7.0 (2.3)	7.7 (0.3)	0.7 - 8.3	–	–	–
3	IL2	-	-	-	6.3 (2.8)	6.3 (2.4)	7.7 - 15.7	–	–	–
	IN1	-	-	-	7.0 (1.7) *	11.3 (2.2)	8.0 - 13.0	2.3 (0.3)	0.3 (0.3)	0.5 - 5.7
	MI	-	-	-	1.0 (0.6)	2.0 (0.6)	0.3 - 2.3	1.3 (0.9)	5.3 (1.8)	0.7 - 4.3
	MO1	-	-	-	1.3 (0.9)	1.3 (0.9)	0.0 - 1.3	–	–	–
4	IL2	-	-	-	1.0 (1.0)	1.0 (0.0)	0.3 - 2.0	–	–	–
	IN1	-	-	-	1.7 (0.9)	2.3 (1.2)	1.0 - 3.7	0.0 (0.0)	0.0 (0.0)	0.0 - 1.3
	MI	-	-	-	0.0 (0.0) *	0.7 (0.3)	0.0 - 0.0	0.0 (0.0)	0.3 (0.3)	0.0 - 1.3
	MO1	0.3 (0.3)	0.0 (0.0)	0.0 - 0.3	0.0 (0.0)	0.7 (0.7)	0.0 - 0.7	–	–	–

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Table G-12 (continued). Abundance of Pest Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

Coll.	Site[1]	Pest Arthropod[2]								
		Potato Leafhopper			Stink Bug			Tarnished Plant Bug		
		MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	13.0 (10.1)	28.7 (12.3)	15.7 - 43.3	0.0 (0.0)	0.0 (0.0)	0.0 - 2.7	–	–	–
	IN1	–	–	–	0.0 (0.0)	0.3 (0.3)	0.0 - 0.3	–	–	–
	MI	–	–	–	0.0 (0.0)	0.3 (0.3)	0.0 - 0.3	1.3 (1.3)	0.3 (0.3)	0.3 - 1.0
	MO1	0.0 (0.0)	0.3 (0.3)	0.0 - 1.0	0.3 (0.3)	1.0 (0.6)	0.0 - 0.7	–	–	–
2	IL2	–	–	–	0.3 (0.3)	0.3 (0.3)	0.3 - 1.3	–	–	–
	IN1	–	–	–	0.7 (0.3)	0.0 (0.0)	0.3 - 0.7	–	–	–
	MI	–	–	–	0.3 (0.3)	1.0 (0.6)	1.0 - 6.3	1.3 (1.3)	3.0 (2.5)	0.7 - 4.0
	MO1	–	–	–	0.3 (0.3)	0.0 (0.0)	0.0 - 1.3	–	–	–
3	IL2	–	–	–	0.0 (0.0) *	1.3 (0.9)	0.0 - 0.7	0.0 (0.0)	0.0 (0.0)	0.0 - 1.0
	IN1	–	–	–	2.0 (1.5) *	0.0 (0.0)	0.0 - 0.7	–	–	–
	MI	–	–	–	2.0 (1.2)	2.3 (0.9)	1.7 - 3.7	6.0 (1.5)	12.3 (0.3)	6.0 – 13.0
	MO1	–	–	–	0.3 (0.3)	0.7 (0.7)	0.3 - 1.3	–	–	–
4	IL2	–	–	–	2.3 (0.3)	2.0 (1.5)	1.7 - 5.0	0.7 (0.7)	2.3 (0.7)	0.3 - 1.3
	IN1	–	–	–	1.3 (0.9)	1.0 (0.6)	1.0 - 5.0	–	–	–
	MI	–	–	–	3.7 (0.7)	3.0 (0.6)	1.7 - 4.7	2.0 (1.2)	1.7 (0.3)	1.3 - 1.3
	MO1	–	–	-	1.3 (0.9)	1.0 (0.6)	0.3 - 4.0	–	–	–

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Table G-12 (continued). Abundance of Pest Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Pest Arthropod[2]					
		Velvet-bean Caterpillar			Wooly-bear Caterpillar		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	–	–	–	–	–	–
	IN1	–	–	–	–	–	–
	MI	–	–	–	–	–	–
	MO1	–	–	–	–	–	–
2	IL2	–	–	–	–	–	–
	IN1	–	–	–	–	–	–
	MI	–	–	–	–	–	–
	MO1	–	–	–	–	–	–
3	IL2	–	–	–	–	–	–
	IN1	0.7 (0.7)	1.3 (0.3)	0.0 - 1.5	–	–	–
	MI	–	–	–	–	–	–
	MO1	–	–	–	–	–	–
4	IL2	–	–	–	–	–	–
	IN1	–	–	–	2.3 (0.9)	3.0 (1.2)	0.7 - 3.0
	MI	–	–	–	0.7 (0.3)	0.3 (0.3)	0.3 - 1.0
	MO1	–	–	–	0.0 (0.0)	0.0 (0.0)	0.0 - 0.7

Note: The experimental design was a randomized complete block with three replications. Arthropod collection (Coll.) 1 was conducted at the R1-R2 growth stage, and the three subsequent collections were conducted at approximately two week intervals thereafter.

* Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

† No statistical comparisons were made due to lack of variability in the data.

[1] Site codes are as follows: IL2 = Stark County, IL; IN1 = Boone County, IN; MI = Ottawa County, MI; MO1 = Shelby County, MO.

[2] MON 87708 and the conventional control values represent mean number of arthropods collected from three replications. S.E. = Standard Error Reference ranges were determined from the minimum and maximum mean values from among the commercial reference varieties at the site.

Dash (−) indicates arthropod not evaluated.

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Table G-13. Abundance of Beneficial Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Beneficial Arthropod[2]								
		Araneae (spiders)			Big eyed bug			Carabidae		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	1.0 (1.0)	0.0 (0.0)	0.0 - 1.0	–	–	–	–	–	–
	IN1	0.0 (0.0)	0.0 (0.0)	0.0 - 0.7	–	–	–	–	–	–
	MI	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	–	–	–	–	–	–
	MO1	0.0 (0.0)	0.0 (0.0)	0.3 - 1.0	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	–	–	–
2	IL2	0.7 (0.3)	1.0 (0.0)	0.0 - 1.3	–	–	–	–	–	–
	IN1	0.3 (0.3)	0.7 (0.7)	0.3 - 0.7	–	–	–	–	–	–
	MI	1.3 (0.3)	0.7 (0.3)	0.0 - 1.0	–	–	–	–	–	–
	MO1	3.7 (2.7)	1.0 (0.0)	0.7 - 2.3	0.0 (0.0)	0.3 (0.3)	0.0 - 0.3	–	–	–
3	IL2	0.0 (0.0)	0.3 (0.3)	0.0 - 0.3	–	–	–	0.3 (0.3)	0.0 (0.0)	0.0 - 0.7
	IN1	0.0 (0.0)	0.3 (0.3)	0.0 - 0.3	–	–	–	–	–	–
	MI	0.3 (0.3)	0.3 (0.3)	0.0 - 0.0	–	–	–	–	–	–
	MO1	7.7 (0.9)	7.7 (0.9)	4.3 - 7.7	–	–	–	–	–	–
4	IL2	0.3 (0.3)	0.7 (0.7)	0.3 - 1.3	–	–	–	–	–	–
	IN1	0.3 (0.3)	0.0 (0.0)	0.0 - 1.0	–	–	–	–	–	–
	MI	0.0 (0.0)*	3.0 (0.6)	0.7 - 1.0	–	–	–	–	–	–
	MO1	0.3 (0.3)	0.3 (0.3)	1.0 - 2.0	–	–	–	–	–	–

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Table G-13 (continued). Abundance of Beneficial Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Beneficial Arthropod[2]								
		Lacewings			Ladybird beetles			Micro-parasitic wasps		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	–	–	–	–	–	–	–	–	–
	IN1	–	–	–	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	–	–	–
	MI	0.7 (0.7)	0.0 (0.0)	0.0 - 0.7	0.0 (0.0)	0.7 (0.3)	0.3 - 1.0	–	–	–
	MO1	–	–	–	1.0 (0.6)	0.7 (0.7)	0.3 - 1.7	–	–	–
2	IL2	–	–	–	–	–	–	–	–	–
	IN1	–	–	–	–	–	–	–	–	–
	MI	4.7 (1.7)	5.7 (1.2)	2.3 - 8.0	0.7 (0.7)	0.7 (0.7)	1.7 - 5.0	–	–	–
	MO1	1.0 (0.6)	0.7 (0.3)	0.0 - 1.7	1.7 (0.3)	2.3 (0.9)	0.0 - 1.0	–	–	–
3	IL2	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	0.0 (0.0) †	0.0 (0.0)	0.0 - 0.0	–	–	–
	IN1	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3	–	–	–	–	–	–
	MI	8.7 (1.2)	6.0 (3.1)	5.3 - 6.0	13.7 (6.7)	5.7 (0.7)	5.3 - 14.0	–	–	–
	MO1	6.3 (5.4)	2.0 (0.6)	2.0 - 6.0	8.3 (0.9)	9.7 (4.3)	4.7 - 12.7	0.7 (0.7)	1.7 (0.9)	0.0 - 2.0
4	IL2	0.7 (0.3)	0.7 (0.3)	0.0 - 2.0	0.0 (0.0)	0.7 (0.3)	0.0 - 0.7	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3
	IN1	–	–	–	–	–	–	–	–	–
	MI	4.0 (0.6)	2.0 (1.2)	1.3 - 6.0	3.7 (0.9)	4.0 (1.5)	2.7 - 7.3	1.0 (0.6)	1.3 (0.7)	0.3 - 1.3
	MO1	1.7 (1.7)	1.3 (0.9)	0.7 - 3.0	7.3 (0.3)	4.7 (1.2)	2.0 - 8.3	–	–	–

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Table G-13 (continued). Abundance of Beneficial Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Beneficial Arthropod[2]								
		Nabis spp.			Opiliones			*Orius* spp.		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	1.7 (0.7)	1.0 (0.6)	0.7 - 2.7	0.7 (0.3)	0.3 (0.3)	0.0 - 0.3	0.7 (0.7)	2.3 (0.9)	0.7 - 3.3
	IN1	0.0 (0.0) †	0.0 (0.0)	0.0 - 0.0	0.3 (0.3)	0.3 (0.3)	0.0 - 0.7	0.0 (0.0) †	0.0 (0.0)	0.0 - 0.0
	MI	0.0 (0.0)	0.3 (0.3)	0.0 - 0.7	–	–	–	0.0 (0.0) †	0.0 (0.0)	0.0 - 0.0
	MO1	0.0 (0.0)	0.0 (0.0)	0.0 - 1.0	–	–	–	0.3 (0.3)	0.7 (0.7)	0.0 - 0.7
2	IL2	1.3 (0.3)	1.3 (0.9)	1.0 - 2.0	–	–	–	0.0 (0.0)	0.7 (0.7)	0.0 - 1.0
	IN1	0.0 (0.0)	0.3 (0.3)	0.0 - 1.3	0.3 (0.3)	0.7 (0.3)	0.0 - 1.0	0.0 (0.0)	0.3 (0.3)	0.0 - 0.0
	MI	2.3 (1.2)	4.0 (1.5)	1.7 - 2.3	–	–	–	7.7 (1.3)	7.0 (1.5)	4.7 - 6.7
	MO1	0.3 (0.3)	0.0 (0.0)	0.0 - 1.0	–	–	–	1.7 (0.9)	2.0 (1.2)	1.3 - 2.0
3	IL2	0.3 (0.3)	0.7 (0.3)	0.3 - 1.3	–	–	–	0.0 (0.0) †	0.0 (0.0)	0.0 - 0.0
	IN1	0.3 (0.3)	0.0 (0.0)	0.0 - 0.3	0.0 (0.0)	0.0 (0.0)	0.0 - 0.7	0.0 (0.0)	0.0 (0.0)	0.0 - 0.3
	MI	3.3 (0.9)	1.3 (0.7)	2.0 - 4.0	–	–	–	4.7 (1.2)	4.7 (1.8)	2.3 - 12.0
	MO1	1.3 (1.3)	2.0 (1.5)	0.3 - 3.3	–	–	–	4.7 (0.9)	2.3 (1.3)	3.7 - 6.7
4	IL2	0.0 (0.0)	1.0 (0.6)	1.0 - 2.7	–	–	–	3.3 (0.3)	1.3 (0.9)	0.3 - 3.3
	IN1	0.0 (0.0)	0.7 (0.7)	0.0 - 0.7	1.0 (0.0)	1.3 (0.3)	0.3 - 1.0	0.7 (0.7)	0.0 (0.0)	0.0 - 0.3
	MI	4.7 (0.7)*	1.7 (1.7)	2.0 - 6.3	–	–	–	1.0 (0.6)	2.7 (0.9)	0.7 - 2.0
	MO1	0.7 (0.7)	0.3 (0.3)	0.3 - 3.0	–	–	–	0.0 (0.0)	3.0 (1.5)	0.7 - 6.0

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Table G-13 (continued). Abundance of Beneficial Arthropods in Beat Sheet Samples Collected from Untreated MON 87708, Conventional Control, and the Commercial Reference Varieties from 2008 Field Trials

		Beneficial Arthropod[2]		
		Syrphid larvae		
Coll.	Site[1]	MON 87708 (S.E.)	Control (S.E.)	Reference range
1	IL2	−	−	−
	IN1	−	−	−
	MI	−	−	−
	MO1	−	−	−
2	IL2	−	−	−
	IN1	−	−	−
	MI	1.7 (1.2)	3.0 (1.0)	1.0 - 4.3
	MO1	−	−	−
3	IL2	−	−	−
	IN1	−	−	−
	MI	1.3 (0.7)	0.7 (0.7)	0.0 - 2.3
	MO1	−	−	−
4	IL2	−	−	−
	IN1	−	−	−
	MI	−	−	−
	MO1	−	−	−

Note: The experimental design was a randomized complete block with three replications. Arthropod collection (Coll.) 1 was conducted at the R1-R2 growth stage, and the three subsequent collections were conducted at approximately two week intervals thereafter.

* Indicates a statistically significant difference between MON 87708 and the conventional control (α=0.05).

† No statistical comparisons were made due to lack of variability in the data.

[1] Site codes are as follows: IL2 = Stark County, IL; IN1 = Boone County, IN; MI = Ottawa County, MI; MO1 = Shelby County, MO.

[2] MON 87708 and the conventional control values represent mean number of arthropods collected from three replications. S.E. = Standard Error. Reference ranges were determined from the minimum and maximum mean values from among the commercial reference varieties at the site.

Dash (−) indicates arthropod not evaluated.

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Table G-14. Abiotic Stress Response Evaluations of Dicamba-Treated MON 87708 and Conventional Control from 2009 Field Trials Using an Observational Severity Scale

Abiotic Stressor	Number of observations across all sites[1]	Number of observations where no differences were observed between MON 87708 and control
Total	89	89
Cold	1	1
Compaction	3	3
Drought[2]	21	21
Flood[3]	17	17
Frost damage	4	4
Hail damage	13	13
Nutrient deficiency	10	10
Wind damage	20	20

Note: The experimental design was a randomized complete block with four replications. Observations were made at approximately the following four crop developmental stages: Observation 1 at V3 –V5; Observation 2 at R1 - R2; Observation 3 at R3 - R5; Observation 4 at R6 - R8.

Data were not subjected to statistical analysis.

[1] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[2] Includes heat and dry.

[3] Includes wet soil, excess moisture.

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Table G-15. Disease Damage Evaluations of Dicamba-Treated MON 87708 and Conventional Control from 2009 Field Trials Using an Observational Severity Scale

Disease stressor	Number of observations across all sites[1]	Number observations where no differences were observed between MON 87708 and control
Total	93	92
Anthracnose	1	1
Bacterial blight[2]	7	7
Bacterial leaf spot	2	2
Brown stem rot	3	3
Cercospora[3]	5	5
Charcoal rot	1	1
Downy mildew	13	13
Frogeye leaf spot[4]	8	8
Leaf spot[5]	21	21
Phytophthora root rot	7	7
Powdery mildew	5	5
Pythium	2	2
Rhizoctonia	3	3
Soybean mosaic virus	1	1
Soybean rust	1	1
Stem canker	1	1
Sudden death	9	9
White mold[6]	3	2

Note: The experimental design was a randomized complete block with four replications. Observations were made at approximately the following four crop developmental stages: Observation 1 at V3 –V5; Observation 2 at R1 - R2; Observation 3 at R3 - R5; Observation 4 at R6 - R8.

[1] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[2] Includes *Pseudomonas*.

[3] Includes *Cercospora* leaf blight and *Cercospora* leaf disease.

[4] Includes eye spot.

[5] Includes *Septoria* and *Alternaria*.

[6] Indicates a difference observed between MON 87708 and the control for white mold at the ILWY site (Observation 2; slight vs. none). The damage rating for MON 87708 was outside of the reference range (no white mold was observed in the references). Data were not subjected to statistical analysis.

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Table G-16. Arthropod–Related Damage Evaluations of Dicamba-Treated MON 87708 and Conventional Control from 2009 Field Trials Using an Observational Severity Scale

Arthropod	Number of observations across sites[1]	Number of observations where no differences were detected between MON 87708(N) and the control[2]	Statistically Significant Differences[4]				
			Site[3]	Observation Number	Arthropod Damage Rating (0-5 scale)		
					MON 87708(N) (S.E.)	Control (S.E.)	Reference Range
Aphids[5]	10	10	–	–	–	–	–
Bean leaf beetle	23	22	KSLA	3	0.00(0.00)	0.08(0.05)	0.00-0.03
Blister beetle	1	1	–	–	–	–	–
Cabbage looper	1	1	–	–	–	–	–
Corn earworm	1	1	–	–	–	–	–
Fall armyworm	1	0	–	–	–	–	–
Grasshopper	18	16	INRC	3	0.45(0.09)	0.10 (0.06)	0.23-0.28
			KSLA	3	0.20(0.00)	0.03(0.03)	0.10-0.20
Green cloverworm	7	7	–	–	–	–	–
Japanese beetle	10	10	–	–	–	–	–

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Table G-16 (continued). Arthropod–Related Damage Evaluations of Dicamba-Treated MON 87708 and Conventional Control from 2009 Field Trials Using an Observational Severity Scale

Arthropod	Number of observations across sites[1]	Number of observations where no differences were detected between MON 87708 and the control[2]	Statistically Significant Differences[4]				
			Site[3]	Observation Number	Arthropod Damage Rating (0-5 scale)		
					MON 87708 (S.E.)	Control (S.E.)	Reference Range
Potato leaf hopper	3	3	–	–	–	–	–
Soybean looper	2	2	–	–	–	–	–
Stink bugs[6]	9	9					
Three cornered alfalfa hopper	3	3	–	–	–	–	–
Velvet bean caterpillar	4	4	–	–	–	–	–

Note: The experimental design was a randomized complete block design with four replications. Observations were conducted at approximately the following four crop developmental stages: Observation 1 = V3-V5, Observation 2 = R1-R2, Observation 3 = R3-R5, and Observation 4 = R6-R8.

[1] A total of 93 arthropod damage observations were made across sites. Lack of variability in the data precluded statistical comparisons for 34 of the observations. Statistical comparisons could be made between MON 87708 and control for 59 of the observations.

[2] No statistically significant differences were detected (α=0.05) or numerical differences between MON 87708 and the conventional soybean control where p-values could not be generated due to lack of variability in the data.

[3] Site codes are as follows: ARNE = Jackson County, AR; IARL = Jefferson County, IA; ILCY = Clinton County, IL; ILWY = Stark County, IL; INRC = Parke County, IN; INSH = Boone County, IN; KSLA = Pawnee County, KS; NEYO = York County, NE

[4] Means, standard errors (S.E.), and reference ranges are reported for a statistically significant difference that was detected (α=0.05) between MON 87708 and the conventional soybean control. Reference range = minimum and maximum mean values among the commercial reference varieties.

[5] Aphids include soybean aphids.

[6] Stink bugs include green stink bugs.

− indicates that there were no statistically significant differences were detected (α=0.05) between MON 87708 and the conventional soybean control.

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Appendix H: Materials and Methods for Pollen Morphology and Viability Assessment

H.1. Plant Production

MON 87708, the near isogenic conventional soybean control A3525, and four commercial reference varieties were grown under similar agronomic conditions in a field trial in Clinton County, IL (Table G-1; IL1 site). The trial was arranged in a randomized complete block design with three replications. Each plot consisted of four rows approximately 20 feet in length.

H.2. Flower Collection

When the soybean plants were flowering, twenty whole flowers were collected from the fourth row of each plot. Four flowers were taken from each of five representative plants per plot. All flowers from a plot were placed into a single, clean container that was labeled with the plot number from which the sample originated. The containers were kept on ice for ≤ 8 hours until the pollen was prepared and stained.

H.3. Pollen Sample Preparation

Pollen samples were prepared in a laboratory. Clean microscope slides were labeled with the plot number. A circle of approximately one centimeter in diameter was drawn in the center of the slide with a pap hydrophobic barrier pen. Tweezers and a dissecting needle were used to open each of the collected flowers from a plot and brush the pollen into the circle on the slide. The utensils were cleaned between extractions. Approximately 20 µl of Alexander’s stain (Alexander, 1980) was added to the center of the circle containing the pollen. The pollen was stained at ambient temperature for at least ten minutes prior to examination. Pollen samples from all plots within a replicate were stained and evaluated on the same day.

H.4. Data Collection

Pollen characteristics were assessed by viewing samples under an Olympus Provis AX70 light/fluorescence microscope equipped with an Olympus DP70 digital color camera. The microscope and camera were connected to a computer running Microsoft Windows 2000 Professional and installed with associated DP Controller v1.2.1.108 and DP Manager v1.2.1.107 camera software and Image-Pro Plus v6.2.1.491 imaging software.

H.4.1. Pollen Viability

When exposed to the staining solution, viable pollen grains stained red to purple due to the presence of living cytoplasmic content. Nonviable pollen grains stained blue to green and may have appeared round to collapsed in shape, depending on the degree of hydration. The number of viable and nonviable pollen grains in each pollen sample was counted from a random field of view under the microscope. A minimum of 75 pollen grains were counted in each sample. Dense clusters of pollen or pollen grains adhering to

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flower parts were not counted because they may not have absorbed the staining solution uniformly.

H.4.2. Pollen Diameter

Micrographs of ten representative pollen grains from each plot were taken at 400× magnification and imported into the imaging software. The software was used to measure pollen grain diameter along two perpendicular axes for each selected pollen grain. Mean pollen diameter for each plot was calculated from the 20 total measurements.

H.4.3. General Pollen Morphology

General pollen morphology was observed from micrographs of MON 87708, the conventional control, and commercial reference varieties that were also used for pollen diameter measurements.

H.5. Statistical Analysis

An analysis of variance was conducted according to a randomized complete block design using SAS® (Version 9.2). The level of statistical significance was predetermined to be 5% (α=0.05). MON 87708 was compared to the conventional control for percent viable pollen and pollen diameter. No statistical comparisons were made between MON 87708 and the commercial reference varieties. Instead, a reference range for each measured characteristic was determined from the minimum and maximum mean values from among the four commercial reference varieties. General pollen morphology was qualitative; therefore, no statistical analysis was conducted on these observations.

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Alexander, M.P. 1980. A versatile stain for pollen fungi, yeast and bacteria. Stain Technology 55:13-18.

SAS Software Release 9.2 (TS1M0). ©2002-2008 by SAS Institute Inc., Cary, North Carolina.

Appendix I: Materials and Methods for Symbiont Assessment

I.1. Materials

The soybean materials for the symbiont interaction assessment included MON 87708, the near isogenic conventional soybean control A3525, and six commercial reference varieties (Table I-1). Nodules, root tissue, and shoot tissue collected from MON 87708, the conventional control, and the commercial reference varieties were evaluated.

Table I-1. Starting Seed of MON 87708, Conventional Control, and Commercial Reference Varieties Used in the Symbiont Assessment

Material Name	Material Type	Phenotype	Monsanto Seed Lot #
MON 87708	Test	Dicamba-tolerant	11225299
A3525	Control	Conventional	10001822
A2553	Reference	Conventional	10000961
LG C3884N	Reference	Conventional	11226859
Stewart SB3454	Reference	Conventional	11242910
Garst 3585N	Reference	Conventional	10001517
Hartz H5218	Reference	Conventional	10001410
A5560	Reference	Conventional	10001114

I.2. Characterization of the Materials

For the MON 87708 and conventional control starting seed lots, the presence or absence of the *dmo* expression cassette was confirmed by event-specific polymerase chain reaction analyses.

I.3. Greenhouse Phase and Experimental Design

Eight replicate 6-inch pots were prepared for each soybean material (MON 87708, the conventional control, and commercial reference varieties). The pots contained nitrogen deficient potting medium (Sunshine® Mix #2 Basic/LB2) composed of primarily peat, vermiculite, and perlite. At planting, each seed was inoculated with approximately 1×10^7 cells of *Bradyrhizobium japonicum* (VAULT® NP, Becker Underwood) in phosphate-buffered saline. Three seeds were planted in each pot. The soybean plants were grown in a greenhouse where temperatures ranged from approximately 17 to 35°C. Once pots were thinned to a single plant per pot, the pots were arranged in eight replicated blocks using a randomized complete block design.

Replicates 1, 2, and 3 were planted on September 8, 2009; replicates 4, 5, and 6 were planted on September 9, 2009; and replicates 7 and 8 were planted on September 10, 2009. In all cases, replicate pots had a minimum of one plant emerge within one week. A nitrogen-free nutrient solution (approximately 250 ml) was added weekly after plant emergence.

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I.4. Plant Harvesting/Data Collection

Six weeks after emergence, plants were excised at the surface of the potting medium and shoot and root plus nodule material were removed from the pots. The shoot material was cut into smaller pieces and placed in labeled bags. The plant roots with nodules were separated from the potting medium by washing with water. Excess moisture was removed using absorbent paper towels, and the roots with nodules were placed in labeled bags. On the same day that plants were harvested, nodules were removed by hand from the roots of each plant, enumerated, and weighed to determine the fresh weight of the nodules.

The remaining root and shoot mass were determined for each plant. Nodules as well as root and shoot material were placed in a drying oven on the same day as collected or stored for up to four days at approximately 4°C before being placed in the drying oven. The plant material was dried for at least 72 hours at approximately 65°C to determine dry weight. The shoot tissue was ground after drying with a Harbil 5G high-speed paint shaker prior to total nitrogen analysis. Shoot total nitrogen was determined by combustion using a nitrogen analyzer (rapid N cube, Elementar Americas, Inc.).

I.5. Statistical Analysis

An analysis of variance was conducted according to a randomized complete block design using SAS® (Version 9.2). The level of statistical significance was predetermined to be 5% ($\alpha=0.05$). MON 87708 was compared to the conventional control for nodule number, nodule dry weight (g), shoot dry weight (g), root dry weight (g), and shoot total nitrogen (% and g/plant). No statistical comparisons were made between MON 87708 and the commercial reference varieties. Instead, a reference range for each measured characteristic was determined from the minimum and maximum mean values from among the six commercial reference varieties.

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References for Appendix I

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Appendix J: Petitioner's Environmental Report

J.1. Background

This appendix provides information regarding four key areas to be covered in an environmental assessment: Purpose and Need, Alternatives, the Affected Environment, and Potential Environmental Impacts. This environmental report has been prepared by Monsanto to facilitate APHIS's compliance with the National Environmental Policy Act (NEPA), including compliance with the Council on Environmental Quality's (CEQ) regulations that implement NEPA[13].

Monsanto has produced dicamba-tolerant soybean plants (hereafter referred to as MON 87708) by inserting a gene that was discovered in a naturally occurring microorganism. The gene produces a dicamba mono-oxygenase (DMO) protein (referred to as the MON 87708 DMO) in the plant that inactivates the herbicide dicamba, thus rendering the plant tolerant to applications of the herbicide. Other broadleaf plants, including weeds in soybean fields, do not naturally contain the gene or exhibit tolerance to dicamba and when treated with dicamba do not survive. Numerous field trials conducted in the U.S. under APHIS notifications since 2005 have included MON 87708. Information has been collected from field trials, laboratory and greenhouse studies, and the literature to assess whether the tolerance to dicamba through production of the MON 87708 DMO protein and/or the gene insertion process has altered MON 87708 in any way that would make these plants more of a plant pest compared to conventional soybean or cause significant environmental impacts, including cumulative impacts. The purpose of this report is to provide relevant information regarding the potential for reasonably foreseeable, significant environmental impacts of widespread cultivation of MON 87708.

MON 87708 will enable an expanded application window of dicamba in soybean, allowing for preemergence application through crop emergence (cracking), and postemergence in-crop applications through the R1/R2 growth stage. The current maximum allowable dicamba use pattern allowed on soybean, the proposed maximum allowable dicamba use pattern on MON 87708, and the maximum annual allowable dicamba rates are summarized in Table J-1. The anticipated use rates for dicamba on MON 87708, however, are expected to be less than the proposed maximum allowabable use rates. Section VIII.H.2 of the petition describes in detail the anticipated use rates and patterns for dicamba on MON 87708.

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[13] Title 40 of the Code of Federal Regulation (40 CFR) Parts 1500-1508.

Table J-1. Summary of Dicamba Uses on Soybean

Application Timing	Current Approved Uses		Proposed Uses on MON 87708	
	Maximum Single Application Rate (lbs a.e./acre)	**Maximum Annual Application Rate (lbs a.e./acre)**	**Maximum Single Application Rate (lbs a.e./acre)**	**Maximum Annual Application Rate (lbs a.e./acre)**
Preemergence	**0.50**[a]	**2.0**	**1.0**[b]	**2.0**
Post-emergence	**Not labeled**		**0.50** (V3) + **0.50** (R1/R2)[c]	
Pre-harvest (7 days prior to harvest)	**1.0**		**Not labeled**	

[a] 14-28 day planting interval based on product application rate

[b] No planting interval

[c] In-crop application through V3 with a sequential application through R1/R2 growth stage as needed. Total of all in-crop applications from emergence up to R1/R2 is 1.0 lb a.e./acre.

An analysis of the potential impact from deregulation of MON 87708 on current soybean agronomic production systems, and related activities such as soybean processing, food and feed uses as well as marketing of soybean and soybean products is presented in this Environmental Report. Factors evaluated as part of the assessment include potential impacts to:

- land use patterns, climate, water, soil and air quality, non-agricultural lands, farming practices, commodity and specialty soybean production,
- marketability of soybean seed for planting and seed for specialty and commodity markets, and
- public health, non-target organisms, threatened or endangered species, and biodiversity.

The analysis conducted considers current and reasonably foreseeable conditions, the potential for deregulation of MON 87708 to impact these conditions, and potential cumulative impacts. In most cases, there are no impacts to current conditions (*e.g.*, no differences between deregulation of MON 87708 versus continuing to regulate). Where differences are noted, these differences are described and their significance evaluated.

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J.2. Purpose and Need for the Action

APHIS' mission is to protect the health and value of American agriculture and natural resources.[14] Under the authority of the Plant Protection Act (PPA), APHIS' Biotechnology Regulatory Services (BRS) regulates the introduction (importation, interstate movement, or release into the environment) of certain genetically engineered (GE) organisms and products that may pose a risk to plant health.[15] An organism is no longer subject to these regulations when APHIS determines that it is unlikely to pose a plant pest risk. A GE organism is considered a regulated article if APHIS has reason to believe it could pose a plant pest risk. A person may petition the agency to evaluate submitted data and determine that a particular regulated article is unlikely to pose a plant pest risk, and, therefore, should no longer be regulated as a potential plant pest.[16] The petitioner is required to provide information related to plant pest risk that the USDA may use to assist in determining whether the regulated article is unlikely to present a plant pest risk.[17] If, based on this information, as well as other sources of information, the USDA determines that the article is unlikely to pose a plant pest risk, the article may be granted nonregulated status.

Monsanto Company (Monsanto) has submitted a petition (designated as 10-188-01p) to APHIS seeking the determination of nonregulated status in whole for MON 87708 soybean plants genetically engineered to produce the MON 87708 DMO which is not typically found in soybean. Monsanto researchers have found that when soybean plants produce the MON 87708 DMO, they are tolerant to the broadleaf herbicide dicamba.

Due to the unique broad spectrum herbicide properties of glyphosate, growers may use only glyphosate for their total weed management. As a result, in certain cropping and cultural systems (e.g., common corn and-soybean rotations), an increase in the number of crop acres with glyphosate resistant weed populations has occurred over the last decade and, recently, the number of growers incorporating other weed management practices has also grown over time. A prominent strategy to delay the development of herbicide-resistant weeds is to increase the diversity of weed management options in agriculture, including use of herbicides with different modes-of-action, in a grower's weed management program (Duke and Powles, 2009). MON 87708 has been developed to provide an effective and efficient method to incorporate another herbicide mode-of-action into the Roundup Ready soybean system (dicamba tolerance will be integrated into the Roundup Ready soybean system). This combination of herbicide-tolerance traits will allow the preemergence (including pre-plant) and postemergence use of both dicamba and glyphosate herbicides in an integrated weed management program to control a broad spectrum of grass and broadleaf weed species (Johnson et al., 2010). Increasing postemergence herbicide options is important, especially in conservation tillage situations, where the performance and consistency of postemergence herbicides has generally been greater than that of soil active residual products. Dicamba will improve the control of broadleaf weeds that are hard-to-control with glyphosate (*e.g.*, common

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[14] Souce is website: http://www.aphis.usda.gov/index.shtml.

[15] Source is 7 U.S.C. § 7701–7772, 7 CFR Part 340.

[16] Source is 7 CFR § 340.6 "Petition for Determination of Nonregulated Status".

[17] Source is 7 CFR § 340.6(c)(4).

lambsquarters, hemp sesbania, morningglory species, nightshade, Pennsylvania smartweed, prickly sida¸ and wild buckwheat) and also offer an effective control option for glyphosate-resistant broadleaf weed species, namely marestail, common ragweed, giant ragweed, palmer pigweed, and waterhemp (Johnson et al., 2010). Dicamba will also offer an effective control option for broadleaf species resistant to ALS and PPO chemistries. In the case of PPO herbicides which are currently being heavily relied upon for control of glyphosate resistant *amaranthus* species, a primary dicamba benefit will be to provide options for delaying the further evolution and spread of PPO resistant *amaranthus* species (University of Tennessee, 2010).

Upon integration of MON 87708 into the Roundup Ready soybean system, growers will have the ability to continue to use established soybean production practices including crop rotation, tillage systems, labeled herbicides, and other cultural practices such as row spacing, thereby using the same planting and harvesting machinery currently being used. Growers will also continue to have the flexibility and simplicity in weed control provided by glyphosate that will allow growers to continue to reap the environmental benefits associated with the use of conservation-tillage that is facilitated by the use of glyphosate for postemergence weed control in the Roundup Ready soybean system (CTIC, 2011; CTIC, 2004).

Monsanto has requested that APHIS make a determination that these soybean plants and their progeny will no longer be considered regulated articles under 7 CFR Part 340. APHIS' action in this case is the determination whether or not to grant nonregulated status to MON 87708. APHIS' purpose and need in making this determination is to fulfill its responsibilities under the PPA as defined under 7 CFR Part 340.

While APHIS must consider impacts associated with the use of dicamba on the quality of the human environment as part of its determination to grant nonregulated status of MON 87708, the use of the pesticide is regulated at the federal level by the U.S. Environmental Protection Agency (U.S. EPA), not APHIS. APHIS's authority under the Plant Protection Act does not allow it to specify conditions for the use of herbicides. Instead, EPA specifically approves labeling for any herbicide use including uses on agricultural crops. Before any dicamba product could be used over MON 87708 it must first be approved by the EPA as required by the Federal Insecticide Fungicide and Rodenticide Act (FIFRA); EPA must approve the pesticide (herbicide) product labeling for that specific use. Nevertheless, this environmental report examines the potential impact of dicamba use on MON 87708 on the human environment.

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J.3. Affected Environment

This section describes the affected environment as it relates to soybean, *Glycine max* (L.) Merr., its uses and where soybean is grown. Related agricultural practices such as tillage, crop rotation, pesticide use, weed management, irrigation practices, and non-agricultural lands are also considered part of the affected environment, as is specialty soybean production, including organic soybean production and seed production. The information in this section, with minor exceptions as noted, is based upon information from Sections

II through IX of the petition, with those sections more specifically referenced throughout this section.

J.3.1. Commercial Soybean Production and Uses

Commercial soybean production and uses are discussed in Section VIII.B of the petition and summarized here; refer to the petition for more detail. Soybean is grown as a commercial crop in over 35 countries and is one of the most valued agricultural commodities because of its high protein and oil content. In 2008, soybean represented 56% of world oilseed production, and approximately 33% of those soybean were produced in the U.S. In 2008, the U.S. exported 1.16 billion bushels (31.6 million metric tons) of soybean, which accounted for 40% of the world's soybean exports and was valued at $[redacted] (ASA, 2009).

Approximately 94% of the world's soybean seed supply was crushed to produce soybean meal and oil in 2008 (Soyatech, 2010), and the majority was used to supply the feed industry for livestock use or the food industry for edible vegetable oil and soybean protein isolates.

The U.S. soybean acreage in the past 10 years has varied from approximately 64.7 to 75.7 million acres. Average soybean yields have varied from 33.9 to 43.3 bushels per acre over this same time period. According to data from USDA-NASS (2009a), soybean was planted on approximately 75.7 million acres in the U.S. in 2008, producing 2.96 billion bushels of soybean with a value of $[redacted] (USDA-NASS, 2009b,c).

In the U.S., soybean production occurs in three major soybean growing regions accounting for 99.1% of the soybean acreage: Midwest region (IL, IN, IA, KS, KY, MI, MN, MO, NE, ND, OH, SD, and WI), Southeast region (AL, AR, GA, LA, MS, NC, SC, and TN) and the Eastern Coastal region (DE, MD, NJ, NY, PA, and VA). Table J-1 shows the relative productivity of the three regions in 2008.

Table J-2. 2008 Soybean Productivity by Region

Region	% 2008 U.S. Soybean Acreage	2008 Average Yield (bushels per acre)	Range of Average State Yields (bushels per acre)
Midwest/Great Plains	82.1	38.6	28.0 – 47.0
Southeast	14.3	34.4	30.0 – 40.0
Eastern Coastal	2.7	34.1	27.5 – 46.0

Source: USDA-NASS (2009a,b).

J.3.2. Specialty Soybean Production

Specialty soybean are grown on fewer acres than commercial or commodity soybean and are typically grown, harvested and handled differently than commodity soybean, and premiums and incentives are paid for delivering a product that meets purity and quality

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standards for the soybean variety. This category includes certified seed, organic production, soybean with specialty oil profiles, food grade soybean, and others.

J.3.2.1. Certified Seed Production

Certified seed production is discussed in Section VIII.B.2 of petition #10-SY-210U and summarized here; refer to the petition for more detail. Standardized seed production practices are responsible for maintaining high-quality seed stocks, an essential basis for U.S. agriculture. The value of seed quality (including genetic purity, vigor, and minimizing presence of weed seed, seed-borne diseases, and inert materials, such as dirt) has been identified as a major factor in determining crop yields.

Soybean seed has four classes: 1) breeder, 2) foundation, 3) registered, and 4) certified (Association of Official Seed Certifying Agencies (AOSCA), 2009). Breeder seed is seed directly controlled by the originating or sponsoring plant breeding organization or firm. Foundation seed is first-generation seed increased from breeder seed and is handled to maintain purity and identity of a specific variety. Registered seed is the progeny of foundation seed that is handled to maintain satisfactory variety purity and identity. Certified seed is the progeny of breeder, foundation or registered seed, and is typically two generations from foundation seed. Not all soybean seed sold is officially certified; however, commercial soybean seed sold and planted for commodity soybean production typically meets or exceeds certified seed standards.

Seed certification programs were initiated in the early 1900s in the U.S. to preserve the genetic identity and variety purity of seed. There are special land requirements, seed stock eligibility requirements, field inspections and seed labeling standards for seed certification. Seed certification services are available through various state agencies affiliated with the AOSCA.

Soybean seed is produced throughout most of the U.S. soybean-growing regions by companies that produce and sell seed, and by toll seed producers, or tollers, which are companies that produce certified seed for other companies pursuant to a contract. Seed companies and tollers in turn contract acreage with growers to produce the required amount of soybean seed. Production or processing plants at these seed companies clean, condition, and bag the harvested soybean seed as well as monitor and inspect all the processes at the plant.

The entire seed production process at the majority of the seed companies and tollers operates under standards established by the International Organization for Standardization (ISO), and includes internal and external audits (ISO, 2009). Field inspections are conducted on seed production fields throughout the soybean growing season to evaluate variety purity and ensure soybean plants are developing properly. Management practices are designed with the intent to keep the fields free of weeds, insects, and diseases, and to prevent mechanical mixing with other soybean varieties. The fields are also mapped to ensure the seed field has the minimum isolation requirement to prevent potential outcrossing. Isolation distances are agreed to by the

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seed companies based on topography, varieties, volunteers, weeds, insects and weather patterns (AOSCA, 2009; ASTA, 2011).

The field operations and management practices for producing soybean seed are similar to normal soybean production. However, special attention is needed in certain production practices to produce seed with high quality, high germination rates, and high genetic purity (Helsel and Minor, 1993).

J.3.2.2. Organic Soybean Production

Organic soybean production occurred on 125,600 acres in 2008 across Midwest and Southeast regions. Iowa, Minnesota, Michigan and Arkansas combined for over half the U.S. organic soybean acres. Over the past decade, organic soybean production peaked at 174,500 acres in 2001 and ranged from 100,000 to 125,600 acres since 2000 (USDA-ERS, 2008a). Organic farming operations as described by the National Organic Program, which is administered by USDA's Agricultural Marketing Service (AMS), requires organic production operations to have distinct, defined boundaries and buffer zones to prevent unintended contact with prohibited substances or products of excluded methods from adjoining land that is not under an organic production management plan. Organic production operations must also develop and maintain an organic production system plan approved by an accredited certifying agent. This plan enables the production operation to achieve and document compliance with the National Organic Standards, including the prohibition of the use of excluded methods.[18] Excluded methods include a variety of methods used to genetically engineer organisms or influence their growth and development by means that are not possible under natural conditions or processes. The use of biotechnology such as that used to produce MON 87708 is an excluded method under the National Organic Program.[19]

Organic certification involves oversight by an accredited certifying agent of the materials and practices used to produce or handle an organic agricultural product. This oversight includes an annual review of the certified operation's organic system plan and on-site inspections of the certified operation and its records. Although the National Organic Standards prohibit the use of excluded methods, they do not require testing of inputs or products for the presence of excluded methods. The presence of a detectable residue of a product of excluded methods alone does not necessarily constitute a violation of the National Organic Standards (USDA-AMS, 2011). The unintentional presence of the products of excluded methods will not affect the status of an organic product or operation when the operation has not used excluded methods and has taken reasonable steps to avoid contact with the products of excluded methods as detailed in an approved organic system plan. Organic certification indicates that organic production and handling processes have been followed, not that the product itself is "free" from any particular substance.

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[18] Title 7 of the Code of Federal Regulation (7 CFR) Part 205.

[19] Source is 7 CFR § 205.2.

Organic soybean producers use production practices designed to prevent commingling of their crop with neighboring crops treated with herbicides and other pesticides (spray drift), or that may be using plant varieties produced by excluded methods (pollen movement). These well established practices include isolation zones, use of buffer rows surrounding the organic crop, adjusted planting dates, and varietal selection.[20] The implementation of management practices to avoid pollen from a biotechnology-derived crop in organic or conventional soybean production operations is facilitated by the nature of soybean pollination. Soybean is a highly self-pollinated species and exhibits a very low level of outcrossing (see Section IX.D). Outcrossing is the genetic transmission of a defined heritable characteristic from one group of individuals (population, crop variety) to another. Outcrossing most commonly results from cross-pollination. Since soybean is highly self-pollinating, organic or conventional soybean producers can and have effectively implemented practices (*e.g.*, isolation during the growing season, equipment cleaning during harvest, and post-harvest separation of harvested seed) that allow them to reasonably avoid biotechnology-derived soybean and maintain organic or conventional production status (Brookes and Barfoot, 2004). Information about the National Organic Program, organic standards, and practices can be viewed on line (USDA-AMS, 2011).

J.3.3. Agricultural Practices for Soybean

J.3.3.1. Tillage

Tillage is performed to prepare the soil for seed bed preparation and also serves as a weed control method because it uproots established plants and smothers them. Tillage in soybean production is discussed in Sections VIII.C.1 and VIII.C.2 of the petition and summarized here; refer to the petition for more detail. The benefits of conservation tillage or no-till systems relative to conventional tillage are well documented and include reduced soil erosion, reduced fuel and labor costs, conservation of soil moisture, improvement of soil structure, reduction of soil compaction and improvement of soil organic matter content. In 2007, approximately 27.5 million acres (39.6%) of soybean were planted in a no-till system (CTIC, 2007). In 2011 over 65% of U.S. soybean acres used some form of conservation tillage (USB, 2011a). The decision to plant soybean in a conservation tillage or no-till system is made long before planting as it may require special equipment. In addition, this decision is usually a long-term commitment, provided the system is successful.

Slow soybean emergence and growth, plus lower yields, have been some of the concerns associated with adoption of conservation tillage systems in soybean, especially no-till. Research in Wisconsin and Minnesota shows that soil temperatures can be four to five degrees colder in no-till systems than in conventional tillage systems, which can slow emergence, but have little effect on soybean yield (Pedersen, 2008). Improved planters for establishment of good soybean populations and planting Roundup Ready® soybean varieties to effectively control weeds in no-till fields have made no-till a more viable

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[20] Source is at website: http://attra.ncat.org/attra-pub/PDF/cropsfarmplan.pdf [Accessed on May 26, 2010].

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production system for soybean. In 1995, before the introduction of Roundup Ready soybean, approximately 27% of the U.S. soybean acres used no-till production. In 2004, nine years after the introduction of Roundup Ready soybean system, no-till acreage increased to 36% of the total soybean acres (Sankula, 2006). The most recent surveys indicate that 39% of the soybean acres are produced using no-till methods (CTIC, 2007). Researchers still recommend some spring tillage on fine-textured and poorly drained soils for proper seedbed preparation (Pedersen, 2008).

J.3.3.2. Crop Rotation

The use of crop rotation in soybean production is discussed in Section VIII.I of petition #10-SY-210U and summarized here; refer to the petition for more detail. The well-established farming practice of crop rotation is still a key management tool for soybean growers. The purposes of growing soybean in rotation include:

- improving yield and profitability of one or both crops over time;
- decreasing the need for nitrogen fertilizer on the crop following soybean;
- mitigating or breaking disease, insect, and weed cycles;
- improving soil tilth and soil physical properties;
- increasing residue cover;
- reducing soil erosion;
- increasing soil organic matter; and
- reducing runoff of nutrients, herbicides, and insecticides (Boerma and Specht, 2004; Al-Kaisi et al., 2003).

According to USDA Economic Research Service, 95% of the soybean-planted acreage has been in some form of a crop rotation system since 1991 (USDA-ERS, 2001). Corn- and wheat-planted acreage has been rotated at a slightly lower level of 75% and 70%, respectively. Although the benefits of crop rotations can be substantial, the grower must make cropping decisions by evaluating both the agronomic and economic returns of various cropping systems. Crop rotations also afford growers the opportunity to diversify farm production in order to minimize market risks.

Agronomic practices such as rotation patterns for soybean vary from state to state. However, there are similarities among states within certain growing regions. The majority of the U.S. soybean acreage (68.6%) is rotated to corn with approximately 14.5% of the soybean acreage rotated back to soybean the following year. Wheat follows soybean on approximately 11.2% of the U.S. soybean acreage (see Table VIII-22 in the petition).

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Continuous soybean production is uncommon in the Midwest. Soybean extension specialists encourage growers to avoid the practice as a way to reduce the risk of damage from diseases and nematodes (Hoeft et al., 2000; Al-Kaisi et al., 2003). Corn and soybean occupy more than 80% of the farmland in many of the Midwestern states, and the two-year cropping sequence of soybean-corn is used most extensively in this region. However, a soybean crop sometimes is grown after soybean and then rotated to corn in a 3-year rotation sequence (soybean-soybean-corn) in the Midwest. Compared to corn, soybean shows a greater yield response to being grown after a number of years without soybean. The yield of both corn and soybean is approximately 10% higher when grown in rotation than when either crop is grown continuously (Hoeft et al., 2000).

A combination of conservation tillage practices and crop rotation has been shown to be very effective in improving soil physical properties. Long-term studies in the Midwest indicate that the corn-soybean rotation improves yield potential of no-till systems compared to continuous corn production (Al-Kaisi, 2001).

J.3.3.3. Irrigation

The use of irrigation in soybean production is discussed in Section VIII.B of the petition and summarized here; refer to the petition for more detail. The productivity of soybean is highly dependent upon soil and climatic conditions. In the U.S., the soil and climatic requirements for growing soybean are very similar to corn. The soils and climate in the Midwestern, Eastern and portions of the Great Plains regions of the U.S. provide sufficient water under normal climatic conditions to produce a soybean crop. The general water requirement for a high-yielding soybean crop is approximately 20 inches of water during the growing season (Hoeft et al., 2000). Soil texture and structure are key components determining water availability in soils, where medium-textured soils hold more available water, allowing soybean roots to penetrate deeper in medium-textured soils than in clay soils. Irrigation is used on approximately 9% of the soybean acreage in the U.S. to supplement the water supply during dry periods in the Western and Southern soybean growing regions (USDA-ERS, 2008b).

J.3.3.4. Management of Insects

The management of insects in soybean production is discussed in Section VIII.D of the petition and summarized here; refer to the petition for more detail. Although insects are rated as less problematic than weeds in U.S. soybean production, management of insect pests during the growth and development of soybean is important for protecting the yield of soybean (Aref and Pike, 1998). Understanding the impact of insects on soybean growth is essential for proper management (Higley and Boethel, 1994). It is important to understand the way that insects injure soybean as well as how the soybean plant responds to insect injury. Insect injury can impact yield, plant maturity, or seed quality. The ultimate impact of injury is damage, as a measurable reduction in plant growth development or reproduction. Insect injury in soybean seldom reaches levels to cause an economic loss in the primary soybean production areas, as indicated by the low percentage (16%) of soybean acreage that receives an insecticide treatment (USDA-NASS, 2007b).

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Characterizing soybean responses to insect injury is essential in establishing economic injury levels (Higley and Boethel, 1994). Most often, soybean insects pests are categorized or defined by the plant parts they injure, namely root-feeding, stem-feeding, leaf-feeding, or pod-feeding insects. The root- and stem-feeding insect groups are often the hardest to scout and typically are not detected until after they have caused their damage. The leaf-feeding insects comprise the biggest group of soybean insect pests, but not necessarily the most economically damaging insects. Recent research on defoliation has determined that a major effect of leaf injury is to reduce light interception by the soybean canopy which in turn can have a significant effect on yield (Higley and Boethel, 1994). Soybean has an extraordinary capacity to withstand considerable defoliation early in the season without significant yield loss. By contrast, defoliation during the flowering and pod filling stages poses a greater threat to yield, because the soybean plant has less time to compensate for injury compared to other growth stages. Research indicates that the soybean plant can sustain a 35% leaf loss prior to the pre-bloom period without lowering yield (NDSU, 2002). However, from pod-set to maturity, the plant can tolerate only a 20% defoliation level before yield is impacted.

J.3.3.5. Management of Diseases and Other Pests

The management of diseases and other pests in soybean production is discussed in Section VIII.E of the petition and summarized here; refer to the petition for more detail. More than 100 pathogens are known to affect soybean, of which 35 are considered to be of economic importance (Heatherly and Hodges, 1999). The estimated yield losses to soybean diseases in the U.S. were 12.5, 13.2, and 13.0 million metric tons in 2008, 2009, and 2010, respectively (Wrather and Koenning, 2011), which equates to 15.5%, 14.4% and 14.4% losses of total soybean production, respectively (ASA, 2011). Pathogens can affect all parts of the soybean plant, resulting in reduced quality and yield. The extent of losses depends upon the pathogen, the state of plant development and health when infection occurs, the severity of the disease on individual plants, and the number of plants affected (Heatherly and Hodges, 1999).

According to field surveys conducted in fifteen soybean-producing states during 1996 to 2010, soybean cyst nematode (*Heterodera glycines*) caused the greatest soybean yield losses (Wrather and Koenning, 2011). Phytophthora root and stem rot (*Phytophthora sojae*), brown spot (*Septoria glycines*), charcoal rot (*Macrophomina phaseolina*), sclerotinia stem rot (*Sclerotinia sclerotiorum*), seedling diseases, and sudden death syndrome (*Fusarium solani f.sp. glycines*) followed in economical importance. As expected, yield losses vary by region (Wrather et al., 2001).

Selecting resistant varieties is the primary tool growers have for disease control (Heatherly and Hodges, 1999). Resistant varieties may have morphological or physiological characteristics that provide immunity, resistance, tolerance or avoidance to certain pathogens. Cultural practices can also play an important role in disease management by reducing initial inoculums or reducing the rate of disease development (Heatherly and Hodges, 1999).

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Preplant tillage can bury crop residue, which encourages the decomposition of fungal-resting structures. Crop rotation is often recommended as a disease-management strategy. Rotating crops interrupts the disease cycle and allows time for the decomposition of inoculums. One exception is *Rhizoctonia*, a soil-inhabitant pathogen that grows on a wide variety of crops and can survive sufficiently in the soil to make crop rotation an impractical means of controlling this pest. Row spacing, plant population, and planting date can also be changed to manage soybean diseases.

Soybean cyst nematode (SCN), *Heterodera glycines*, is one of the most damaging pathogens of soybean throughout the soybean growing regions of the U.S. with losses estimated to be about $[redacted] (Pedersen, 2008). The simplest, least expensive method to reduce populations of this pest is to rotate soybean with a non-host crop such as corn, small grains, or sorghum. However, planting resistant varieties is regarded as the best and most effective management practice to prevent losses from this pest (Wrather and Mitchum, 2010).

High-quality seed is essential for controlling seedling diseases. The most important seedling diseases in soybean are *Phytophthora*, *Pythium*, *Rhizoctonia*, and *Fusarium* (Pedersen, 2008). Many soybean varieties demonstrate resistance to specific taxonomic races of *Phytophthora*. Treating soybean seed with a fungicide (*e.g.*, metalaxyl or mefenoxam) is effective against damping-off disease (seedling blight) caused by common soil fungi, such as *Phytophthora* and *Pythium*. Fungicide seed treatments are recommended where there is a history of these seedling diseases.

Asian soybean rust is a foliar fungal disease that typically infests soybean during reproductive stages of development and can cause defoliation and reduce yields significantly in geographies such as Brazil (Dorrance et al., 2007). Soybean rust is caused by the fungus *Phakopsora pachyrhizi*. This disease in the U.S. was first detected in Louisiana in 2004 (LSU, 2009). At this time, foliar application of fungicides is the standard disease-management practice to limit yield losses due to soybean rust.

J.3.3.6. Management of Weeds

The management of weeds in soybean production is discussed in Section VIII.F of petition #10-SY-210U and summarized here; refer to the petition for more detail. Annual weeds are perceived to be the greatest pest problem in soybean production, followed by perennial weeds (Aref and Pike, 1998). Weed control in soybean is essential to optimizing yields because weeds compete with soybean for light, nutrients, and soil moisture. Weeds can also harbor insects and diseases, and also can interfere with harvest, causing extra wear on harvest equipment (Pedersen, 2008).

Foxtail spp. (*Setaria* spp.), pigweed (*Amaranthus* spp.), velvetleaf (*Abutilon theophrasti*), lambsquarters (*Chenopodium album*), and cocklebur (*Xanthium strumarium*) are common weeds in Midwest corn and soybean fields. However, growers consider giant ragweed (*Ambrosia artemisiifolia*), lambsquarters, Canada thistle (*Cirsium arvense)*, cocklebur, and velvetleaf to be the top five most problematic weeds in corn and soybean because of the difficulty to control these weeds (Nice and Johnson, 2005).

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The primary weed competition factors that affect a potential yield loss in soybean from weed competition are the weed species, weed density, and the duration of the competition. When weeds are left to compete with soybean for the entire growing season, yield losses can exceed 75% (Dalley et al., 2001). Generally, the competition between crops and weeds increases with increasing weed density. The time period that weeds compete with the soybean crop influences the level of yield loss. In general, the later the weeds emerge, the less impact the weeds will have on yield. Soybean plants withstand early-season weed competition longer than corn, and the canopy generally closes earlier in soybean than corn (*i.e.*, plants in adjacent rows grow to a sufficient size such that their foliage touches between the rows blocking the sunlight from reaching the ground). In addition, canopy closure is much sooner when soybean is planted in narrow rows.

The most effective weed management programs in soybeans use a combination of cultural, mechanical, and/or herbicide control practices, hereafter called diversified weed management practices. Herbicide practices include the use of several herbicides with different modes-of-action, either within or across seasons, applying herbicides at the labeled rate at the correct timing, and proper application of the herbicide. Cultural and mechanical weed control practices can also be important components of an effective diversified weed management program (Loux et al., 2009). Cultural practices such as crop rotation, narrow row spacing and planting date are a few of the crop management practices that are implemented to provide the crop with a competitive edge over weeds. Mechanical methods of weed control including tillage have been used for centuries to control weeds in crop production. Spring or fall preplant tillage and in-crop shallow cultivation can effectively reduce the competitive ability of weeds by burying the plants, disturbing or weakening their root systems, or causing sufficient physical injury to kill the plants. A consequence of in-crop cultivation for weed control is that it can injure crop roots and cause moisture loss. The planting of winter cover crops is another cultural practice that can also be utilized. The planting of cover crops, such as grasses, legumes or small grains, can protect and improve soil quality, help reduce erosion, and can serve as surface mulch in no-till cropping practices (Mannering et al, 2007). However the planting of a cover crop incurs additional costs to the grower and therefore cover crops are not a major weed management practice in major soybean growing areas (Iowa State University, 2006).

The use of herbicides has become an important part of managing weeds in soybean. In 2006, approximately 98% of the soybean acreage received an herbicide application (USDA-NASS, 2007b). Over 35 different herbicide active ingredients are registered and available for use by soybean growers to control weeds (Tables VIII-7 and VIII-8). Herbicide weed control programs in conventional soybean consist of preemergence herbicides used alone or in mixtures with other preemergence herbicides. Mixtures of two preemergence herbicides are used to broaden the spectrum of control to both grasses and broadleaf weed species. Preemergence herbicides are followed by postemergence applications to control weeds that emerge later in the crop. Total postemergence weed control programs were seldom used in conventional soybean prior to 1995. Prior to Roundup Ready soybean, soybean planted in a no-till system would receive a preplant burndown herbicide application for broad-spectrum control of existing weeds at time of

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planting, followed by different multiple soil residual herbicides at planting and possibly still other herbicides applied postemergence to the crop and the weeds. In conventional soybeans the typical herbicide program consisted of multiple soil residual herbicides applied preemergence to the crop and weeds and, possibly, other herbicides applied postemergence to the crop and weeds. Therefore, multiple herbicides and/or multiple applications were generally made in conventional and no-till non-Roundup Ready soybean. The average number of herbicide applications per acre in soybean rose from 1.5 in 1990 to 1.7 applications in 1995 reflecting the use of at-plant and postemergence applications or two postemergence applications (Gianessi et al., 2002).

Selective herbicides are designed to kill specific types of plants, usually grasses or broad leaf weeds, and have proved effective to reduce in-crop tillage or cultivation to control weeds in soybean production. The development of selective herbicides has progressed since the introduction of the first herbicide (2,4-D) for weed control in corn in early 1940s. Although the primary purpose of tillage is for seedbed preparation, tillage still is used to supplement weed control with selective herbicides in soybean production.

The availability of herbicide-tolerant soybean products are an important aspect of weed management in U.S. soybean production, as discussed in Section VIII of the petition and summarized here; refer to the petition for more detail. Herbicide-tolerant soybean was introduced to provide growers with additional options by improving crop safety (no herbicide damage to the crop) and improving weed control. In 2006, herbicide-tolerant soybean (glyphosate-tolerant) was planted on 89% (67.2 million acres) of the of soybean acres (USDA-NASS, 2007a). The percentage of herbicide-tolerant soybean subsequently increased to 91% in 2009. With the high percentage of glyphosate-tolerant soybean and the use of glyphosate for preplant burndown and postemergence in-crop applications, it is not surprising that glyphosate was used on 97% of the total soybean acres in 2006.

Because of the unique broad spectrum herbicide activity of glyphosate, it is possible for growers to choose to use only glyphosate for their total weed management. Some growers made this choice, choosing not to utilize diversified weed management practices and instead relying only on glyphosate for total weed management. As a result of these practices, there has been an increase in the number of crop acres with glyphosate resistant weed populations over the last decade. However, recently the number of growers incorporating other weed management practices along with the use of glyphosate, such as other herbicide modes-of-action or cultivation practices, has grown over time in part in response to the evolution of glyphosate resistant weeds and based upon recommendations from Monsanto, academics, and the pesticide industry. Academics and university extension services recommend growers use diversified weed management practices, as described above, as the guiding principle for managing resistance and shifts in weed population. The specific practices to be recommended by area or by farm will be communicated by local experts versed in the best methods for both proactive and reactive management of resistance. Since many soybean farmers practice conservation tillage and some may chose to plant soybeans repeatedly on the same land, the use of multiple herbicide modes-of-action with overlapping effectiveness on the targeted weed spectrum will be the primary method employed. Studies have demonstrated that using the same combination of herbicides with multiple modes-of-action and overlapping effectiveness

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over multiple seasons is an effective way to proactively manage resistance (Beckie and Reboud, 2009).

The incorporation of additional weed management practices has been most pronounced in Roundup Ready corn and Roundup Ready cotton but a growing trend in Roundup Ready soybeans has also occurred. In a 2005 grower survey, 15 to 21% of growers applied non-glyphosate herbicides in addition to glyphosate for weed control in glyphosate-tolerant soybean (Givens et al., 2009). These non-glyphosate herbicides were applied prior to planting, at planting and/or postemergence in soybean (see Section VIII.F.1 of the petition). In another grower survey conducted at the end of the 2009 growing season, the percent of growers applying non-glyphosate herbicides rose to 33% for those growing continuous Roundup Ready soybeans, and to 33% and 52% for growers growing Roundup Ready soybeans in rotation with Roundup Ready corn and Roundup Ready cotton, respectively (personnel communication from [redacted] December 2011). These data indicate a trend towards increased diversification of weed management practices in glyphosate-tolerant crops.

Further evidence of increased adoption of diversified weed management practices, including incorporation of multiple herbicide modes-of-action, across Roundup Ready corn, cotton and soybeans is presented by Prince et. al, (2011). This study reported that between 46% and 54% of surveyed Roundup Ready growers (corn, cotton and soybeans) who responded that they did not have glyphosate-resistant weeds on their farm used either a non-glyphosate residual and/or postemergence herbicide in the 2009 growing season. For growers indicating they have on-farm herbicide-resistant weed populations to other herbicides, the percentage of growers was higher at 72% to 75%. Furthermore, researchers report that approximately 40 to 50% of the growers utilizing glyphosate-tolerant crops indicate that rotating herbicides or tank mixing glyphosate with other herbicides is an effective management practice to minimize the development of glyphosate resistance (Powles et al., 1996; Diggle et al., 2003; Beckie, 2006; Beckie and Reboud, 2009). Indeed, as described in detail below, a prominent strategy to delay the development of herbicide-resistant weeds is to increase the diversity of weed management options in agriculture, including use of herbicides with different modes-of-action in a grower's weed management program (Duke and Powles, 2009).

Herbicide-resistant Weeds

The use of any herbicide results in the potential for the selection of weeds resistant to that herbicide particularly when the herbicide is not used as part of a diversified weed management program. Within a weed species, individuals may possess an inherent ability to withstand the effects of a particular herbicide. Repeated use of that herbicide will expose the weed population to a "selection pressure," which may lead to an increase in the number of surviving resistant individuals in the population (HRAC, 2010). The increased and repeated use of glyphosate over glyphosate-tolerant crops without incorporation of diversified weed management practices, such as crop rotation, cultivation or use of multiple herbicide modes-of-action, has resulted in the selection of glyphosate-resistant weeds. Glyphosate-resistant weed biotypes found in soybean fields include Palmer pigweed (*Amaranthus palmeri*), tall waterhemp (*Amaranthus*

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tuberculatus), common ragweed (*Ambrosia artemisiifolia*), giant ragweed (*Ambrosia trifida*), hairy fleabane (*Conyza bonariensis*), horseweed (*Conyza canadensis*), kochia (*Kochia scoparia*), goosegrass (*Eleusine indica*), Italian ryegrass (*Lolium multifloru*), rigid ryegrass (*Lolium rigidum*), Johnsongrass (*Sorghum halepe*) (Heap, 2011). As with other herbicide resistant weeds that have developed, the emergence of glyphosate resistant weed biotypes over the past decade represents a need for growers to adapt and implement improved weed management strategies.

Weed resistance is common in the major non-glyphosate soybean herbicide groups. Table J-2 and Table J-3 summarize known resistance among the major weed species present in soybean within each of the key soybean herbicide groups and herbicide classes active on broadleaf weeds (Heap, 2011). Resistance to the ALS group of herbicides is present in most of the major broadleaf weed species commonly found in soybeans. For common ragweed and waterhemp there is known resistance to at least one member for several of the major soybean herbicide chemistry classes. While there are still effective options for managing common ragweed, waterhemp, palmer pigweed and other key broadleaf weeds, there is a need for additional herbicide modes-of-action to combat future resistance in soybeans and continued management of existing herbicide-resistant weed populations. Similarly, there has been an increase in the detection of weed populations with multiple resistance (i.e., resistance to multiple herbicide modes-of-action) in some weed species, for example, *Amaranthus* spp. (Tranel et al, 2010). The emergence of these resistant biotypes and continued need to utilize diverse weed management practices supports the need for additional herbicide modes-of-action in major crops such as soybeans.

Monsanto and academics recommend the use of multiple herbicide modes-of-action in the Roundup Ready soybean system regardless of whether glyphosate-resistant or hard-to-control broadleaf weeds are present. Monsanto specifically recommends the use of a soil residual as part of the weed management system. Growers may also choose to switch to other weed management systems in their soybean. APHIS has approved other herbicide-tolerant soybean including phosphinothricin-tolerant and ALS-tolerant soybean events (Table J-4). For growers who choose to use the Roundup Ready soybean system, Monsanto and university extension agents provide recommended control options for glyphosate-resistant weeds. These options include the use of residual and postemergent herbicides such as synthetic auxins (2,4-D), ACCase inhibitors (clethodim, sethoxydim), PPO inhibitors (lactofen, fomesafen), and ALS inhibitors (cloransulam).[22] These herbicides alone or combinations of these herbicides as well as traditional tillage methods are and will continue to be used to control glyphosate-resistant or hard-to-control broadleaf weeds.

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[22] Monsanto Technology Use Guide; www.weedresistancemanagement.com.

Table J-3. Known Weed Resistance in the Southern U.S.[1]

Most Common Broadleaf Weeds (# states where listed as a top weed)	Resistance Group[2]	ALS (Group 2)			PPO (Group 14)		PS II (Group 5)	Glycine (Group 9)	Phenoxy (Group 4)	
	Chemistry Class[2]	Sulfonyl Urea	Imidazol inones	Triazoles	Diphenyl ether	N-phenyl thalimide	Triazinones	-	Phenoxy	Benzoic acid
	Example	chlorimuron	imazapyr	chloransulam	lactofen fomesafen	flumioxazin	metribuzin	glyphosate	2,4 D	dicamba
Morning glory (5)										
Sida (prickly sida (5)			X							
Sicklepod (4)										
Hemp sesbania (3)										
Pigweed spp.[3] (3)		X	X	X	X					
Palmer pigweed (2)		X	X	X				X		
Cocklebur (1)		X	X	X						
Horseweed (marestail) (1)		X		X				X		

[1] Source: www.weedscience.org

[2] Cross resistance is possible within a resistance group and/or chemistry class

[3] Includes redroot pigweed and smooth pigweed

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Table J-4. Known Weed Resistance in the Midwest U.S.[1]

Most Common Broadleaf Weeds (# states where listed as a top weed)	Resistance Group[2]	ALS (Group 2)			PPO (Group 14)		PS II (Group 5)	Glycine (Group 9)	Phenoxy (Group 4)	
	Chemistry Class[2]	Sulfonyl Urea	Imidazolinones	Triazoles	Diphenyl ether	N-phenyl thalimide	Triazinones	-	Phenoxy	Benzoic acid
	Example	chlorimuron	imazapyr	chloransulam	lactofen fomesafen	flumioxazin	metribuzin	glyphosate	2,4 D	dicamba
Pigweed spp.[3] (12)		X	X	X	X					
Velvetleaf (11)										
Lambsquarters (10)		X	X				X			
Cocklebur (9)		X	X	X						
Common ragweed (7)		X	X	X	X	X		X		
Smartweed spp. (6)										
Morning glory (5)										
Waterhemp (5)		X	X	X	X			X	X	
Horesweed (marestail) (3)		X		X				X		
Giant ragweed (3)		X	X	X				X		
Kochia (2)		X	X					X		X

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[1] Source: www.weedscience.org
[2] Cross resistance is possible within a resistance group and/or chemistry class
[3] Includes redroot pigweed and smooth pigweed

J.3.3.7. Dicamba Herbicide Use in the U.S.

Dicamba use in the U.S. is discussed in Section VIII.G of the petition and summarized here; refer to the petition for more detail. Dicamba is a broadleaf selective herbicide that was approved by the Environmental Protection Agency (U.S. EPA) for agricultural application uses in 1967 (U.S. EPA, 2009b). Dicamba herbicide is currently labeled for weed control in corn, soybean, cotton, sorghum, wheat, barley, oats, millet, pasture, rangeland, asparagus, sugarcane, and turf, grass grown for seed, conservation reserve programs, and fallow croplands. Dicamba treated acreage has ranged from 17.4 to 36.3 million acres between 1990 and 2008. Usage of dicamba peaked during the period of 1994 through 1997, where 1994 was the peak year when 36 million acres were treated with 9.4 million pounds of dicamba. Since 1994, the use of dicamba has steadily declined to 20.2 million treated acres with 2.67 million pounds applied in 2008. The decline is due to the competitive market introductions of sulfonylurea herbicides (chlorsulfuron, metsulfuron-methyl, and thifensulfuron-methyl) in wheat, new broadleaf herbicide active ingredients in corn, and glyphosate-tolerant corn. Usage in cotton is one exception, where dicamba-treated acres (preplant applications) have increased from 140,000 to 590,000 acres from 2004 to 2008. Dicamba is formulated as a standalone herbicide product and marketed by several companies under various trade names such as Banvel®, Clarity®, Diablo®, Rifle®, Sterling®, and Vision. These dicamba products can also be tank mixed with one or more active ingredients depending on the treated crop. For example, Clarity can be tank mixed with over 75 herbicide products in labeled crops. Additionally, dicamba is formulated as a premix product with one or more other herbicide active ingredients such as glyphosate, 2,4-D, diflufenzopyr, atrazine, nicosulfuron, metsulfuron, primsulfuron, triazulfuron, rimsulfuron and halosulfuron.

Based on USDA-NASS (2004, 2006b, 2007b, 2008) statistics, dicamba application rates ranged from 0.03 to 0.25 pounds per acre with the average number of applications ranging from 1 to 1.2 applications per cropping season. Dicamba rates are the lowest in barley, wheat, and oats, where typically more than one application is made in these crops per cropping season. The average application rate in corn is 0.19 pounds of dicamba per acre with slightly over one application per season.

Dicamba is currently labeled for use in conventional or Roundup Ready soybean, although dicamba use is extremely limited because applications are restricted to preplant and/or preharvest applications due to crop tolerance concerns. The dicamba-treated acreage in 2008 soybean production was approximately 530,000 acres representing 0.7% of the total soybean acreage.

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J.3.4. Human Health and Worker Safety

Soybean is a highly versatile crop which can be processed into a wide variety of food products. Soybean protein is used to enhance nutrition in a wide variety of food products, such as breakfast cereals and pasta. Soybean protein is also an important component in baked goods, alternative meat products, soups, energy bars, nutritional beverages infant formula and dairy replacement products (USB, 2011b). Soybean oil constitutes the majority (68%) of consumed edible fats and oils in the U.S. (ASA, 2011). It is present in numerous food products including cooking oils, shortening, margarine, mayonnaise, salad dressings and a wide variety of fat or oil-based products (USB, 2011b).

Humans consume soybean and have done so for thousands of years. Soybean improved with new traits produced by biotechnology pose no unique risks relative to other soybean developed using traditional breeding methods. Biotechnology-derived soybean is evaluated extensively prior to commercial introduction. All biotechnology-derived soybean products on the market today have satisfactorily completed the FDA consultation process established to review the safety of foods and feeds derived from biotechnology-derived crops for human and animal consumption. Biotechnology-derived soybean crop varieties that have been deregulated or are under consideration for deregulation are shown in Table J-5.

Pesticides have been used extensively in the production of soybean (see Section J.3.3.6). The use of these pesticides is regulated by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of the active ingredient, as well as a review of all data submitted to the EPA. During the reregistration process, EPA thoroughly reviews the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential risks arising from the currently registered uses of a pesticide, to determine the need for additional data on health and environmental effects, and to determine whether or not the pesticide continues to meet the "no unreasonable adverse effects" criteria of FIFRA.

In order to comply with FIFRA, EPA evaluates potential risks to humans and the environment, and may require applicants to submit more than 100 different scientific studies conducted according to EPA guidelines. The data required by EPA are used to evaluate whether a pesticide has the potential to cause adverse effects on humans (including chronic, reproductive and cancer risk), wildlife, fish, and plants (including endangered species and other non-target organisms, *i.e.*, organisms that the pesticide is not intended to act against). If the pesticide may be used on food or feed crops, EPA also sets tolerances (maximum pesticide residue levels) for the amount of the pesticide residue that can legally remain in or on foods. EPA undertakes this analysis under the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), and must conclude that such tolerances will be safe, meaning that there is a reasonable certainty that no harm will result from aggregate (food, water and non-occupational residential/recreational) exposure to the pesticide residues.

EPA has evaluated dicamba and concluded that is has a complete and comprehensive regulatory database (toxicity, environmental fate, and ecological toxicity) that has been evaluated by the EPA. EPA completed the reregistration process for dicamba and a Registration Eligibility Decision (RED) was issued in 2006 and subsequently amended in 2008 and 2009 (U.S. EPA, 2009b). EPA concluded the available data submitted for dicamba are complete and adequate to support the continued registration of dicamba products and uses. EPA also considered toxicity data and available information concerning the variability of sensitive subpopulations, including infants and children.

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The EPA concluded there is reasonable certainty that no harm will result to the general population, or to infants and children, as a result of aggregate exposure to dicamba residues. Thus, all then-current dicamba uses were eligible for reregistration (U.S. EPA, 2009b). See Appendix M, Section M.2 and M.3 for additional details about the EPA registration process and the reregistraiton of dicamba.

In the agricultural production of soybean, growers and workers may be exposed to pesticides applied to soybean by mixing, loading, or applying chemicals, or by entering a previously treated site. EPA conducts a comprehensive occupational worker safety evaluation and risk assessment of pesticides to assess the risk to agricultural workers during mixing, loading, and applying. EPA evaluated occupational risk to workers as a part of the dicamba RED and concluded that worker exposure to dicamba for all registered agricultural uses, including exposures associated with the current preemergence and postemergence pre-harvest soybean uses, meet the "no unreasonable adverse effects" criteria of FIFRA (U.S. EPA, 2009b). The use of dicamba on MON 87708 does not pose any new exposure considerations for workers. Therefore the use of dicamba on MON 87708 will not pose a risk to agricultural workers. See Appenidx M, Section M.2.2 for additional details on applicator exposure.

In addition, the Worker Protection Standard (WPS) provides additional protections to agricultural workers and pesticide applicators. The WPS contains requirements for pesticide safety training, notification of pesticide applications, use of personal protective equipment (PPE), restricted-entry intervals (REI) after pesticide application, decontamination supplies, and emergency medical assistance. Under the WPS, EPA requires the pesticide label to specify PPE and REI, based on the properties of the pesticide product, that will provide an appropriate level of protection[23].

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[23] www.epa.gov/pesticides/health/worker.htm

Table J-5. Deregulated or Submitted Biotechnology-derived Soybean Products

Phenotype	Event	Institution	Date Deregulated
High Oleic Acid, Low Saturated Fat	MON 87705	Monsanto	December 16, 2011
Omega 3 Fatty Acid	MON 87769	Monsanto	Submitted
Lepidopteran Resistant	MON 87701	Monsanto	June 28, 2011
Herbicide-tolerant (*2,4-D*)	DAS-68416-4	Dow AgroSciences	Submitted
Herbicide-tolerant (*Glyphosate*/*Isoxaflutole*)	FG72	Bayer Crop Sciences	Submitted
Herbicide-tolerant (*Imidazolinone*)	BPS-CV127-9	BASF Plant Science	Submitted
High Oleic Acid	DP-305423-1	Pioneer	June, 2010
Glyphosate- and ALS-tolerant	DP-356043-5	Pioneer	July, 2008
Glyphosate-tolerant	MON 89788	Monsanto	February, 2007
Phosphinothricin-tolerant	GU262	AgrEvo	October, 1998
Phosphinothricin-tolerant	A5547-127	AgrEvo	May, 1998
Altered Oil Profile	G94-1, G94-19, G-168	DuPont	May, 1997
Phosphinothricin-tolerant	W62, W98, A2704-12, A2704-21, A5547-35	AgrEvo	August, 1996
Glyphosate-tolerant	40-3-2	Monsanto	May, 1994

Source is website: http://www.aphis.usda.gov/brs/not_reg.html

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J.3.5. Animal and Plant Communities, Soil Microorganisms and Biodiversity

J.3.5.1. Animal Communities

Soybean production systems in agriculture are host to many animal species including deer, groundhogs, rabbits, raccoons, geese and small rodents (USDA-APHIS, 2011b). Mammals and birds, including migratory mammals and birds, may seasonally consume grain (Galle et al., 2009), and invertebrates can feed on the plant during the entire growing season.

Animals that feed primarily on soybean are seed-feeding insects and rodents found in agricultural fields. Crop pest insects are considered less problematic than weeds in U.S. soybean production as indicated by the low percentage (14%) of soybean acreage that receives insecticide treatment (USDA-NASS, 2006). Management of insects in soybean production fields is discussed in Section VIII.D of the petition. Some rodents, such as mice or squirrels, may seasonally feed exclusively on soybean seeds. Thus, these animals may have a diet containing significant amounts of soybean seeds. Deer may also browse in soybean fields on the forage and on seed left after harvest.

Animals that feed outside soybean fields are also considered in this section. The environment surrounding a soybean field, which may vary in plant composition depending on the region, may serve as a food source and habitat for mammals, birds, fish and insects. In certain areas, soybean fields may be bordered by other soybean, corn, or other crops; soybean fields may also be surrounded by woods and/or pasture/grassland areas, as well as aquatic environments. Therefore, the types of vegetation, including weeds, around a soybean field depend on the area where the soybean is planted. Fertilizers and/or water containing pesticides may run off into adjacent lands, pesticides may also move outside of the agroecosystem from drift and offsite movement. Regardless of the agricultural operation, animals and insects outside the field may be impacted directly from the use of fertilizers, pesticides, and erosion caused from agricultural operations, or indirectly, both positively and negatively, from effects on the plant community outside the soybean field.

J.3.5.2. Plant Communities

The affected environment for growing soybean plants can generally be considered the agroecosystem (managed agricultural fields) plus some area extending beyond the intended plantings that might be affected by agricultural operations. Plants, extraneous to the crop, which grow in planted fields can be considered weeds and are dealt with in section J.3.3.6 of this document.

Plants growing outside soybean fields are considered in this section. The environment surrounding a soybean field varies in plant composition depending on the region. In certain areas, soybean fields may be bordered by other soybean, corn, or other crops; fields may also be surrounded by woods and/or pasture/grassland areas, as well as aquatic environments. Therefore, the types of vegetation, including weeds, around a soybean field depend on the area where the soybean is planted. A variety of weeds dwell in and

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around soybean fields; those species may also vary depending on the region where the soybean is planted. These plants may be found in ditches, hedge rows, fence rows, wind breaks, yards, and other uncultivated areas, and may be annuals, biennials or perennials. Regardless of the agricultural operation, these plants may be impacted, both positively and negatively, by agricultural operations. Fertilizers and/or water may run off into adjacent lands, resulting in increased plant growth outside the agroecosystem. Negative impacts on plants adjacent to production fields can occur from herbicide runoff and drift.

Finally, soybeans infrequently occur as a volunteer when soybean seeds remain in a field following harvesting and may be considered a weed in the subsequent crop. Volunteer soybean in rotational crops is not a concern in the Midwest region because the soybean seed is typically not viable after the winter period (Carpenter et al., 2002; OECD, 2000). In southern soybean growing areas of the U.S. where the winter temperatures are milder, it is possible for soybean seed to remain viable over the winter and germinate the following spring. If volunteer soybean should emerge after planting, shallow cultivation and/or use of another herbicide will control volunteers and effectively reduce competition with the crop. Several postemergence herbicides are also available to control volunteer soybean (conventional or glyphosate-tolerant soybean, and by extension dicamba-tolerant soybean) in each of the major soybean rotational crops (Section VIII.J. of petition #10-SY-210U). Therefore, volunteer soybean normally is not a concern in rotational crops, such as corn, cotton, rice and small grains (e.g., wheat, barley, sorghum and oats), which are the primary rotational crops following soybean due to the availability of adequate control measures for volunteer soybean (Carpenter et al, 2002; OECD, 2000).

J.3.5.3. Soil Microorganisms

Soil microbial communities are highly complex and are often characterized by high microbial diversity (Tiedje et al., 1999). The occurrence and abundance of soil microorganisms are affected by 1) soil characteristics like tilth, organic matter, nutrient content, and moisture capacity, 2) typical physico-chemical factors such as temperature, pH, and redox potential, and 3) soil management practices. Agricultural practices such as fertilization and cultivation may also have profound effects on soil microbial populations, species composition, colonization, and associated biochemical processes (Buckley and Schmidt, 2001; 2003). Consequently, significant variation in microbial populations is expected in agricultural fields.

Members of the bacterial family *Rhizobiaceae* and *Bradyrhizobiaceae* form a highly complex and specific symbiotic relationship with leguminous plants, including soybean (Gage, 2004). The nitrogen-fixing plant-microbe symbiosis results in the formation of root nodules, which provide an environment in which differentiated bacteria called bacteroids are capable of reducing or “fixing” atmospheric nitrogen. The product of nitrogen fixation, ammonia, can then be utilized by the plant. As a result of this relationship, nitrogen inputs are typically not necessary for agricultural production of soybeans.

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J.3.6. Biodiversity

Biodiversity refers to all plants, animals, and microorganisms interacting in an ecosystem. Among other benefits, biodiversity provides valuable genetic resources for crop improvement (Harlan, 1975) and also provides other functions beyond food, fiber, fuel, and income. These include pollination, genetic introgression, biological control, nutrient recycling, competition against natural enemies, soil structure, soil and water conservation, disease suppression, control of local microclimate, control of local hydrological processes, and detoxification of noxious chemicals (Altieri, 1999). The loss of biodiversity results in a need for costly external inputs in order to provide these functions to the crop (Altieri, 1999). Agricultural land subject to intensive farming practices, such as that used in crop production, generally has low levels of biodiversity compared with adjacent natural areas.

The use of broad spectrum insecticides and herbicides is one of the most severe constraints for biological diversity in crops. Tillage, seed bed preparation, planting of a monoculture crop, pesticide use, fertilizer use, and harvest may all limit the diversity of plants and animals (Lovett, Price, & Lovett, 2003). Herbicide use in agricultural fields is likely to indirectly impact biodiversity by decreasing weed species present in the field and those insects, birds and mammals that utilize these weeds.

Conservation tillage practices can have a positive impact on wildlife, including beneficial arthropods (Altieri, 1999; Landis et al., 2005; Towery and Werblow, 2010). Conservation tillage practices benefit biodiversity due to decreased soil erosion improves surface water quality, retention of vegetative cover, crop residues serve as a food source,; and increased populations invertebrates which can serve as food sources to other organisms (Landis et al. 2005; Sharpe, 2010)

J.3.7. Physical Environment

J.3.7.1. Land Use

In 2008, soybean was grown as a commercial crop on over 75 million acres in at least 27 states in the U.S. (USDA-NASS, 2009a). Soybean acreage in the past five years has been relatively stable varying from 64.7 million to 75.7 million acres with a 10-year average of 73.3 million acres (Table VIII-1). Soybean fields are typically highly managed agricultural areas that can be expected to be dedicated to crop production for many years. Fluctuations in soybean acreage are due to environmental, agronomic and economic factors, as well as government programs such as the conservation reserve program (CRP).

Currently, biotechnology-derived herbicide tolerant soybean is planted on 91% of the soybean acreage (USDA-NASS, 2009a) and the Roundup Ready soybean system has become the standard weed control program in U.S. soybean production. There is no indication that the introduction and widespread adoption of biotechnology-derived crops in general has resulted in a significant change to the total U.S. acreage devoted to agricultural production. The cumulative land area in the U.S. planted to principal crops, which include corn, sorghum, oats, barley, winter wheat, rye, durum, spring wheat, rice, soybean, peanuts, sunflower, cotton, dry edible beans, potatoes, canola, proso millet, and

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sugar beets, has remained relatively constant over the past 27 years. From 1982 to 1995, the average yearly acreage of principal crops was 323 million. This average is essentially unchanged at 326 million acres since the introduction of biotechnology-derived crops in 1996 (USDA-NASS, 1984, 1988, 1990, 1992, 1995, 1998, 2000, 2003, 2006a, 2009a).

J.3.7.2. Water Resources

The soils and climate in the Midwestern, Eastern and portions of the Great Plains regions of the U.S. provide sufficient water under normal climatic conditions to produce a soybean crop. Irrigation is used on approximately 9% of the soybean acreage in the U.S. to supplement the water supply during dry periods in the Western and Southern soybean growing regions (USDA-ERS, 2008b). More information on water management in soybean production can be found in Sections VIII.B and J.3.3.3 of the petition.

Groundwater may be impacted from soybean production by the movement of pesticides and fertilizers vertically through soil. Surface water may also be impacted from soybean production by runoff from soybean fields that carries soil particles and herbicides or other pesticides to streams, rivers, lakes, wetlands and other water bodies. As discussed below, based on existing data, the soil component of runoff is a much more important contributor to surface water impacts than is the pesticide component.

Tillage causes widespread soil disturbance. Thus, erosion, topsoil loss and the resulting sedimentation and turbidity in streams are likely to increase with increased tillage. In 2009, based on the states' water quality reports, EPA identified sedimentation and turbidity as two of the top 10 causes of impairment to surface water in the U.S. in general; in 2007, EPA identified sedimentation/siltation as a leading cause of impairment to rivers and streams in particular (U.S. EPA, 2009a; EPA, 2007a). EPA has projected conservation tillage to be "the major soil protection method and candidate best management practice for improving surface water quality" (U.S. EPA, 2002). EPA identifies conservation tillage as the first of its CORE4 agricultural management practices for water quality protection (U.S. EPA, 2008a).

Based on the states' water quality reports to EPA, which EPA makes available through its National Assessment Database, pesticides in general and herbicides in particular are a relatively minor contributor to impairment of surface water in the U.S., compared to sedimentation/siltation and turbidity (U.S. EPA, 2008b). Pesticides accounted for less than one percent of reported causes of surface water impairment in all but four of the 17 leading U.S. soybean-producing states. In those four states, pesticides accounted for two to eight percent of reported causes of impairment. Of the pesticides that were reported as contributing to impairment among the 17 leading soybean-producing states, almost all are highly persistent chemicals that are no longer registered for use in the U.S. (U.S. EPA, 2008b). Dicamba is not included on this list.

Water resources (Ground and surface water) may also be impacted from the use herbicides used to control weeds. Dicamba has been widely used in agriculture over the last four decades with dicamba's peak use occurring in 1994 (see Section VIII.G of the petition). In the dicamba Reregistration Eligibility Decision (RED) document, EPA

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considered potential risks associated with dicamba use, and its degradate DCSA when appropriate, due to surface or ground water using screening level (high-end exposure) models to estimate environmental concentrations. The EPA then compared these exposure estimates to appropriate endpoints from mammalian and aquatic animal and plant ecotoxicity studies to determine potential impacts on human health and the environment. The EPA used the models PRZM/EXAMS and SCIGROW to estimate levels of dicamba in surface and ground water, respectively, using the physical, chemical, and environmental fate properties, and approved high-end use patterns of dicamba (see Appendix M, Section M.3.2 of the petition).

For drinking water resources, estimated surface water concentrations using the simulated sugarcane crop scenario for both ground and aerial applications of 2.8 lbs a.e./acre ranged from 9.7 to 13 µg/L dicamba a.e. and 0.66 to 0.81 µg/L for DCSA (U.S. EPA, 2005a). For environmental-ecological water quality, estimated surface water concentrations for a simulated soybean crop scenario for ground and aerial applications of 2.0 lbs a.e./acre ranged from 33.3 to 36.1 µg/L dicamba a.e. The U.S. Geological Survey National Water Quality Assessment (NAWQA) monitoring program also analyzed surface water in a 1993-2003 survey of surface waters of the United States, which included geographical areas where dicamba use has historically been most intense. Dicamba had a low incidence of detections (approximately 3% of samples) and the highest levels detected were approximately 2 µg/L (U.S. EPA, 2005a).

For groundwater, estimated concentrations using the simulated sugarcane crop scenario for both ground and aerial applications of 2.8 lbs dicamba a.e. per acre were 0.016 µg/L dicamba and 0.008 µg/L for DCSA, dicamba's major environmental degradate (U.S. EPA, 2005a). The EPA also analyzed groundwater in a 1971-1991 national monitoring study. The frequency of dicamba detection was less than 2.5% based on 3172 samples analyzed, and dicamba was detected at levels from less than 0.01 to 44µg/L (U.S. EPA, 1992), and peak dicamba detections occurred between 1985 and 1990. Dicamba also had a low incidence of detections (less 3% of samples) in the 1993-2003 NAWQA monitoring program where the highest detections were approximately 2.5 µg/L (U.S. EPA, 2005a).

J.3.7.3. Soil Quality

Soybean is cultivated across a wide variety of soils in the U.S. Cultivation and tillage practices can directly impact the attributes of soil, including its physical and biological properties. Microbial populations and associated biochemical processes are critical to maintaining soil health and quality. Additionally, maintaining soil pH in the range of 6.0 to 7.0 will enhance the availability of inherent and fertilizer nutrients, reduce the availability of toxic elements, particularly aluminum and manganese, and enhance microbial activity (Hoeft, 2000). The increased microbial activity that is associated with the optimum pH level results in oxidation of organic matter and increased release of nutrients from the organic matter.

Conservation tillage and no-till systems enhance soil quality relative to conventional tillage. Benefits of conservation tillage are well documented and include reduced soil

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erosion, conservation of soil moisture, improvement of soil structure, reduction of soil compaction and improvement of soil organic matter content. In 2010, approximately 27.5 million acres (39.6%) of soybean were planted in a no-till system (CTIC, 2010). In 2011 over 65% of U.S. soybean acres used some form of conservation tillage (USB, 2011a).

J.3.7.4. Air Quality and Climate

Many agricultural activities affect air quality including tillage, farm equipment, and nitrous oxide emissions from the use of nitrogen fertilizer. These agricultural activities individually have potential adverse environmental impacts on air quality and climate and may be impacted, positively or negatively, by changes in agricultural practices. Issues of concern include, but are not necessarily limited to, atmospheric emission of carbon dioxide, nitrogen oxide, sulfur oxide, and particulate matter. Agricultural practices have the potential to directly and indirectly impact air quality and contribute emissions which could lead to climate change.

Tillage contributes to the release of greenhouse gases (GHG) because of the loss of carbon dioxide to the atmosphere and the exposure and oxidation of soil organic matter (Baker, et al., 2005). Emissions released from agricultural equipment (e.g., irrigation pumps and tractors) include carbon monoxide, nitrogen oxides, particulate matter, and sulfur oxides. Nitrous oxide may also be released following the use of nitrogen fertilizer. Agriculture, including land-use changes for farming, is responsible for an estimated 17 to 32% of all human-induced GHG emissions (USDA-APHIS, 2011b). Generation of GHGs may have long term impacts on climate change as they function as retainers of solar radiation. The U.S. agricultural sector has been identified as the second largest contributor to GHG emissions (USDA-APHIS, 2011b). Herro (2008) proposes that if agriculture practices were modified, significant reductions in the release of GHGs could be achieved.

J.3.8. Adjacent-Agricultural Crop and Non-Agricultural Plants

Soybean is widely grown throughout the U.S. on land devoted to agricultural use. The biology of soybean is discussed in Section II of the petition and summarized here; refer to the petition for more detail. Soybean does not have any related wild relatives in the U.S. with which it can hybridize. Soybean does not survive outside of cultivation and is not invasive or weedy. Soybean is grown adjacent to large acre crops such as corn, wheat, and alfalfa, near vegetables, orchards, pastures, and adjacent to non-agricultural lands, such as forests, grasslands, streams, lakes, rivers and occasionally near urban lands.

Herbicides are commonly used in the production of soybean and a detailed discussion of their use can be found in Section VIII.F.1 of the petition; refer to the petition for more detail. Impacts on adjacent agricultural crops and non-agricultural plants can occur from offsite movement of any herbicide, and these impacts are actively managed by farmers and applicators specially trained to use such products consistent with product labels and other state or local restrictions. Depending upon the herbicide, factors for managing the potential for drift and offsite movement include the selectivity and sensitivity of the

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herbicide, local weather conditions at the time of application (wind, temperature, humidity, inversion potential), droplet size distribution, application volume, boom height (height of the application equipment above the crop canopy), sprayer speed, and distance from the edge of the application area (SDTF, 1997; Felsot et al., 2010). A variety of measures can be employed to control the potential for spray drift and offsite movement, including nozzle selection and application techniques and restrictions.

The potential for offsite movement of an herbicide is regulated at a federal level by EPA. EPA considers possible effects from offsite movement as part of the pesticide registration process required under FIFRA. Specifically, in order to approve the use of a pesticide (herbicide), EPA must conclude that no unreasonable adverse effects on non-target vegetation will result from potential offsite movement when the pesticide is used according to the product label. When pesticides are applied in accordance with label instructions, offsite impacts can be avoided. EPA reassessed the potential risks to non-target plants in its analysis in the dicamba RED, concluding that no specific additional drift mitigations were needed to support the continued registration of all dicamba uses, including use in conventional soybean with applications at early preemergence prior to planting and late postemergence prior to harvest (U.S. EPA, 2009b). A detailed discussion of the use of dicamba herbicide in the U.S. can be found in Section VIII.G of the petition.

J.3.9. Animal Feed

Soybean meal is the most valuable component obtained from processing soybean, accounting for roughly 50-75% of its overall value (USDA-ERS, 2005). The majority of soybean meal is used by the animal feed industry as a cost-effective protein and amino acid source to animal diets. Soybean meal can serve as a excellent protein source that can complement the limited amino acid profile of feeds derived from corn (Kerley and Allee, 2003). In 2009, approximately 36 million tons of soybean meal was produced, 27 million tons of which was marketed for animal feed with the largest volumes consumed by poultry (48%), swine (26%), and beef (12%) (ASA, 2010).

Dairy and livestock producers use soybean forage as feed. Soybean forage is an inexpensive, readily available, on-farm source of high-quality, high-protein forage adapted to growth during the summer months when other forage legume species typically are restricted in growth (USDA-ARS, 2006). Soybean forage can be used as hay or to produce silage (MAFRI, 2004). An additional use of soybean for feed can be full-fat (whole) soybean for dairy cattle and swine, but for swine it is limited due to the high oil content to a maximum of 20% of the total diet (Yacentiuk, 2008).

Monsanto has completed the biotechnology consultation process with FDA for the safety and nutritional assessment of food and feed derived from MON 87708 soybean on October 11, 2011 (BNF No. 00125, Monsanto, 2011). As a part of its evaluation, FDA reviewed information on the identity, function, and characterization of the genes, including expression of the gene products in MON 87708 soybean, as well as information on the safety of the MON 87708 DMO and MON 87708 including a dietary risk assessment.

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EPA has responsibility to regulate the use of pesticides (herbicides) that may be used on feed crops, and must establish pesticide tolerances (maximum pesticide residue levels) for the amount of pesticide residue that can legally remain in or on the feed crop. EPA undertakes this analysis under the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), and must conclude that such tolerances will be safe, meaning that there is a reasonable certainty that no harm to human health will result from the use of the pesticide. EPA reassessed all dicamba pesticide tolerances (food and feed tolerances) as part of the dicamba RED, including the 10 ppm soybean seed tolerance supporting the existing use in conventional soybean for early postemergence applications up to 0.5 pound a.e. per acre and late postemergence prior to harvest up to 1.0 pound a.e. per acre (U.S. EPA, 2009b). A complete listing of dicamba feed tolerances can be found at 40 CFR § 180.227. Monsanto has also petitioned (Pesticide Petition # 0F7725) the EPA to establish new feed tolerances on soybean forage (45 ppm) and soybean hay (70 ppm). Tolerances for soybean forage and hay for current dicamba uses in conventional soybean were not previously established because the current preharvest application is made past the stage where the crop would be useful as forage or hay.

J.4. Alternatives

The action of deregulation is governed by 7 CFR § 340.6 (d)(3)(i) which states that APHIS may approve the petition in whole or in part, resulting in three possible Agency actions in response to the petition:

- No action

  MON 87708 would remain a regulated article

- Approval in part

  MON 87708 would be granted deregulated status with some restrictions or conditions (*e.g.*, geographic)

- Approval in whole

  MON 87708 would be granted full deregulated status

J.4.1. No Action Alternative

Under the "no action" alternative, MON 87708 would remain a regulated article under 7 CFR Part 340. MON 87708 could be grown under USDA notification or permit and confined release conditions. MON 87708 would not have unrestricted availability to commercial soybean growers. Under this alternative, growers will likely continue to use biotechnology-derived soybean that are commercially available and herbicides to control weeds in soybean fields. In 2009, 91% of the U.S. soybean was produced with herbicide-tolerant biotechnology-derived soybean. In 2006, 98% of soybean fields received an herbicide application for weed control. Over 35 different herbicide active ingredients are available for use by soybean growers (Tables VIII-7 and VIII-8) and it is reasonably foreseeable that new herbicide active ingredients may be discovered or existing

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herbicides used in other crops may be adapted for use on soybean in the future under this alternative. Growers may continue to use agronomic practices they currently use for production of soybean, including the Roundup Ready soybean system. Residual herbicides will continue to be recommended for use in the Roundup Ready soybean system to provide a second herbicide mode-of-action for weed resistance management. In areas where glyphosate-resistant or hard-to-control broadleaf weeds are present, growers may continue to choose to use the Roundup Ready soybean system and incorporate herbicides with other modes-of-action, including residual herbicides. Recommended control options for glyphosate-resistant broadleaf weeds include the use of residual herbicides, preemergent herbicides such as synthetic auxins (2,4-D), and postemergent herbicides such ACCase inhibitors (clethodim, sethoxydim), PPO inhibitors (lactofen, fomesafen), and ALS inhibitors (cloransulam).[24] Under the no action alternative, these herbicides alone and combinations of these herbicides, as well as tillage, could be used to control glyphosate-resistant and hard-to-control broadleaf weeds. Because of existing resistance to currently available soybean herbicides and in the absence of new herbicide options, the number of weed populations and species with multiple resistance in soybean production areas may continue to increase as well as resistance to herbicide classes that are currently being relied on to manage current levels of resistance to glyphosate and other herbicides (e.g., use of PPO herbicides to manage glyphosate resistant palmer pigweed and waterhemp). In the event new resistant biotypes to key herbicides in the PPO group evolve and increase, there will be fewer options available for herbicide control of key weed species such as in the *Amaranthus* genus.

Under the no action alternative, growers may choose to use other biotechnology-derived herbicide-tolerant soybean products that have been deregulated by APHIS, including glyphosate-tolerant, ALS-tolerant (DP356043-5), or phosphinothricin-tolerant (*e.g.*, A2704-12 and other events) soybean. Three other herbicide-tolerant soybean products are currently under consideration for deregulation by APHIS including: 2,4-D-tolerant (DAS-68416-4), glyphosate-tolerant and isoxaflutole-tolerant (FG72), and imidazolinone-tolerant (BPS-CV127-9). Thus, it is reasonably foreseeable that growers may choose these options and use of their companion herbicides under the no action alternative.

Currently, 91% of the U.S. soybean crop is produced with herbicide-tolerant (principally glyphosate-tolerant) soybean (USDA-NASS, 2009a), indicating growers are using non-glyphosate based herbicides and/or traditional tillage methods for weed control on about 10% of soybean acreage. Growers may choose to use the non-glyphosate based weed control systems and/or traditional tillage methods under the no action alternative.

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J.4.2. Alternatives Considered but Eliminated from Detailed Evaluation

Approval in part based on plant pest risk

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[24] Monsanto Technology Use Guides can be found at: http://www.monsanto.com/SiteCollectionDocuments/Technology-Use-Guide.pdf
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Based on APHIS' regulatory authority, MON 87708 could be granted "approval in part" dependent upon a finding of a plant pest risk in certain geographies or under certain conditions. APHIS may impose restrictions upon the cultivation or use of MON 87708 in specific geographies or circumstances to mitigate an identified plant pest risk. MON 87708 has been thoroughly characterized, and extensive information presented in Sections I through IX of petition #10-SY-210U demonstrates that MON 87708 does not present a plant pest risk under any circumstance. Therefore, from a plant pest risk perspective, there is no basis for imposing geographic or other restrictions on MON 87708.

The safe use of dicamba for agricultural purposes was first established in 1967, and EPA recently reaffirmed its human and environmental safety for agricultural uses, including soybean production, with the reregistration in 2006 (U.S. EPA, 2009b). The decisions regarding the safe use of dicamba belong solely with EPA. APHIS has no regulatory authority to restrict the use of pesticides or impose measures to mitigate their risk. Monsanto has applied for a label for use of dicamba on MON 87708, and requested the establishment of new feed tolerances for soybean forage and hay. EPA will review the proposed label amendment and assess if the requested use pattern and use instructions meet its statutory standard of no unreasonable adverse effects.

On the basis of this analysis demonstrating that there is no plant pest risk consideration or other risks that would lead USDA to consider approval in part, and because EPA has authority to regulate the herbicide dicamba, these alternatives were not further considered in this report.

J.4.3. Approval in Whole Alternative

Under the "approval in whole" alternative, MON 87708 would no longer be a regulated article under 7 CFR Part 340 and would be widely available for planting. Growers would have the option of treating their soybean crop with dicamba using an expanded window of herbicide application. MON 87708 will allow for preemergent applications up to crop emergence (cracking) and in-crop postemergent applications up to R1/R2 growth stage, compared to existing uses which permit only early preemergence applications 14-28-days prior to planting and late postemergence applications prior to harvest. With the approval by the EPA for the use of dicamba on MON 87708 and the integration of MON 87708 into the Roundup Ready soybean system through traditional breeding, the combined crop-tolerances to both glyphosate and dicamba would allow growers to utilize glyphosate and dicamba herbicides in their weed management systems, as well as other herbicides currently registered for use in soybean. Monsanto is requesting approval in whole or full deregulated status for MON 87708. Information and assessments presented throughout this environmental report demonstrate that MON 87708 does not present a significant environmental impact when approved in whole.

J.5. Potential Environmental Impacts

The Council on Environmental Quality (CEQ) regulations require that significance be evaluated in terms of context (affected environment) and intensity (the severity of the

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impact).[25] Analysis of these factors considered the "no action" and the "approval in whole" alternatives. The differences between the two alternatives address the relevant issues in considering whether deregulation of MON 87708 results in a significant impact to the quality of the human environment. In most cases, there are no differences between the two alternatives. Where differences are noted, these differences are described and their significance evaluated. Factors evaluated as part of the assessment of significance include: potential impacts to land use patterns, farming practices, specialty and organic soybean production; potential impacts to non-agricultural lands; potential impacts to the marketability of soybean seed for planting and harvested seed for commodity markets; potential impacts to public health; and potential impacts to non-target organisms and threatened or endangered species, and biodiversity. Finally, cumulative impacts are considered in light of this action combined with past and reasonably foreseeable future actions.

J.5.1. Methodology and Assumptions

MON 87708 is intended to be a trait that will have utility across all of the acreage upon which soybean is currently grown and widely available in soybean varieties sold to growers. It is impossible to determine the exact amount of acreage on which MON 87708 may be grown if deregulated. However, for the purposes of this assessment, it is assumed that MON 87708 will occupy 40% of the U.S. soybean acreage at peak penetration (see Section VIII.H.2 of the petition). Over the past decade, glyphosate-tolerant soybean varieties have been widely adopted in the marketplace. In most cases, glyphosate was applied to control narrowleaf and broadleaf weeds in U.S. soybean fields, where glyphosate provided excellent control of most weeds. In recent years, the development of glyphosate-resistant weeds and shifts in broadleaf weed populations to species that are inherently more tolerant to glyphosate have increased the use of additional herbicides that work through a different mode-of-action to achieve an acceptable level of weed control. As a result of the ongoing need to control the majority of weed species present in soybean fields, additional herbicides are being used, and multiple herbicide-tolerance traits are being developed to provide growers with additional weed control options that will compete with MON 87708. These herbicides and traits will likely be available at the time MON 87708 is introduced to the marketplace; thus, MON 87708 will compete for market share with established products, like Roundup Ready soybean 40-3-2 first introduced in 1996, and new herbicide-tolerance traits that will be available in the foreseeable future. Growers will ultimately select weed control systems that fit the needs for their individual farming operation, such that some proportion of growers will choose to use MON 87708 integrated into the Roundup Ready soybean system.

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It is EPA's regulatory authority under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) to register pesticide products for their intended uses, see Section J.3.4 for additional detail. Potential impacts of dicamba use associated with MON 87708 are a connected activity under the deregulation in whole alternative, and while pesticide use is regulated by EPA, dicamba use will also be discussed in order to assess potential impacts to the quality of the human environment. Monsanto has submitted to EPA an application to amend EPA Reg. No. 524-582 to register a new use pattern for dicamba. On the basis of Monsanto's assessment of EPA registration decisions and approved labels for alternative herbicides, the use of dicamba on MON 87708 poses less risk potential to human health and the environment than some existing alternative non-glyphosate herbicides (see Appendix L). The primary basis for this assertion is that the introduction of MON 87708 and the associated use of dicamba when compared to other non-glyphosate herbicides registered for use on soybean will: 1) reduce human health risk potential for applicators, bystanders, and consumers; 2) reduce risk potential to aquatic organisms in the environment; 3) positively impact the sustainability of soybean production in the U.S. due to the addition of a second mode-of-action into the Roundup Ready soybean system, thereby potentially delaying further development of glyphosate-resistant broadleaf weed populations, and to broadleaf weed herbicides in general; and 4) support the continued use of conservation tillage with its well known environmental benefits.

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[25] CEQ regulations are available in 40 CFR §1508.27.

J.5.2. Physical Impacts; Land Use, Water Quality, Climate, Soil Quality and Air Quality

J.5.2.1. Land Use Impacts

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Herbicide-tolerant soybean has been deregulated and grown in the U.S. since 1996. Roundup Ready soybean currently occupies greater than 90% of total soybean acres. Fluctuations in total soybean acreage before and after herbicide-tolerant soybean was commercialized (USDA-NASS, 2011) indicates that factors unrelated to the availability of the herbicide-tolerant trait play a role in total soybean acres planted. Agricultural land use, and consequently crop production is dictated by many factors, the most significant of which are commodity prices. Accordingly, growers may increase acres dedicated to soybean production to meet increased demand, but they do so in response to commodity prices and market demand, not in response to availability or adoption of biotechnology-derived traits.

With the exception of tolerance to dicamba, MON 87708 is phenotypically and agronomically unchanged from conventional soybean. Phenotypic and agronomic information collected from field trials conducted in 2008 using the same agricultural inputs showed no meaningful changes between MON 87708 and the conventional control (see Section VII.D of the petition). Information presented in the petition demonstrates that compared to conventional soybean, MON 87708 does not display increased

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susceptibility to pests or diseases, and is not changed regarding crop emergence, growth development or yield. Additional laboratory and greenhouse-based experiments reached the same conclusion; MON 87708 was unchanged compared to the conventional control for seed germination and symbiotic relationship parameters. Therefore, production management practices (*e.g.*, planting and harvest timing, fertilizer inputs, and pesticide use other than dicamba) are not expected to change with the introduction of MON 87708. Similarly, because there are no changes in growth and development or yield, there is no expectation that the introduction of MON 87708 and its use in development of soybean varieties will significantly alter the geographical range of commercial soybean cultivation. Thus, the introduction of MON 87708 is not anticipated to facilitate production of soybean in areas where it is not currently grown or have significant impact on total soybean production acres. Therefore, the approval in whole and no action alternatives are the same regarding their potential impact on land use.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative dicamba herbicide would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use pattern in soybean. As discussed above, full deregulation of MON 87708 is not expected to result in changes to land use. Similarly, land use changes would not be expected with the no action alternative. As discussed, relatively minor fluctuations in soybean acreage would be expected with either alternative, resulting from environmental, agronomic, economic and governmental influences. Therefore, the no action and approval in whole alternatives are the same regarding their potential impact on land use.

J.5.2.2. Water Quality Impacts

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Impacts associated with MON 87708

Water quality could be impacted either directly by MON 87708 via plant material impacts on water resources, or indirectly via impacts from the use of dicamba or tillage practices associated with the planting of MON 87708. Conservation tillage, a system that leaves 30% or more of the previous crop residue covering the soil when planting another crop has been increasingly employed in commercial soybean acres, and helps minimize any impacts of soybean production on water quality by reducing soil erosion.

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In terms of potential direct impacts on water quality, MON 87708 has been shown to be compositionally, agronomically and phenotypically equivalent to conventional soybean and is therefore unlikely to have any significant impact on surface water quality. The DMO protein contained in MON 87708 is a member of the larger family of oxygenase proteins that are ubiquitous in plants and microbes in the environment. The mode of action of this family of proteins is well known, and the introduced DMO protein itself was derived from a common soil bacterium (*Stenotrophomonas maltophilia*). MON 87708 DMO has been shown to have a high level of substrate specificity, and characterization data provided in Section V of petition #10-SY-210U demonstrate the safety of the DMO protein. Therefore, it is unlikely that the presence of DMO protein in MON 87708 will have a significant impact on water quality.

Under full deregulation of MON 87708, there will be a decreased need for farmers employing conventional tillage practices in order to manage certain weed situations. There is a potential impact to soil conservation in those situations where tillage has been employed to manage resistant weeds (CAST, 2011). Dicamba's complementary and supplementary postemergence activity to glyphosate will provide improved postemergence weed management options and thus support more sustainable conservation tillage practices because postermergence herbicide options are generally preferred by growers (Fawcett and Towery, 2002). Tillage causes widespread soil disturbance causing erosion and topsoil loss, impacting the sedimentation and turbidity of streams. EPA identified sedimentation and turbidity as two of the top 10 causes of impairment to surface water in the U.S.; similarly in 2007, EPA identified sedimentation/siltation as a leading cause of impairment to rivers and streams in particular (U.S. EPA, 2007a; 2009a;). EPA has projected conservation tillage to be "the major soil protection method and candidate best management practice for improving surface water quality" (U.S. EPA, 2002). EPA identifies conservation tillage as the first of its CORE4 agricultural management practices for water quality protection (U.S. EPA, 2008a). Therefore, the approval in whole and no action alternatives are not significantly different regarding the impact of the cultivation of MON 87708 on water quality.

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Impacts from use of dicamba on MON 87708

Under full deregulation, dicamba would be an additional weed management tool for managing hard-to-control and herbicide-resistant broadleaf weeds found in soybean fields. The use of dicamba on soybean would be expected to increase relative to current and historical levels of use, up to 2.6 times the maximum historical annual level in 1994. However, potential impacts associated with any increased use of dicamba from the cultivation of MON 87708 have been adequately assessed by EPA as part of the dicamba Reregistration Eligibility Decision (RED), therefore it is reasonably foreseeable that EPA will register this specific use of dicamba under FIFRA. EPA considered potential risks associated with dicamba use, including its degradate DCSA when appropriate, on surface or ground water using screening level (high-end exposure) models to estimate environmental concentrations. The EPA then compared these exposure estimates to appropriate endpoints from mammalian, aquatic animal and plant ecotoxicity studies, and concluded dicamba meets the FIFRA standard for no unreasonable adverse effects on human health and the environment (see Section J.3.7.2 and Appendix M.5.2 of the petition for additional detail on the EPA analysis). The EPA analysis, based on use patterns that exceed the proposed single and annual maximum use rates for dicamba on MON 87708, does not take into account normal variation in environmental concentrations that can occur, and assumes that greater than 85% of the water shed is treated with the herbicide at the maximum labeled rate on the same day. In addition, the EPA examined and considered available monitoring data as part the dicamba RED, where concentrations of dicamba in ground and surface water were detected at levels up to 44 µg/L and 1.76 µg/L, respectively. Furthermore, potential impacts on ground and surface water from dicamba use on MON 87708 will be considered by EPA as part of Monsanto's pending application to register the use of dicamba on MON 87708, and must meet the FIFRA standard for no unreasonable adverse effects on human health or the environment prior to approval.

It is foreseeable that the frequency of dicamba detections in ground and surface water could increase as a result of the cultivation of MON 87708, however levels of dicamba in water are not expected to increase above the levels already evaluated and considered by EPA. Existing monitoring data provides additional support that water resources will not be impacted from any potential increase in dicamba use. Monsanto has compiled publicly available surface and ground water monitoring data from across the United States from 1990 through 2010, including sampling sites in areas where soybean and corn are grown (Upper Midwest, see Figure VIII-1 of the petition) and where dicamba use has historically been most intense (See Figure VIII-2 of the petition). Maximum labeled use rates during most of this timeframe (2.8 lb a.e. per acre single maximum and 7.7 lb a.e. per acre annual maximum) were much higher than presently allowed rates (1.0 lb a.e. per acre single maximum and 2.0 lb a.e. per acre annual maximum) and the rates proposed on Monsanto's dicamba label for use on MON 87708. Therefore, an examination of available surface and groundwater monitoring data in these areas during the mid-1990s would be indicative of the anticipated levels of dicamba that may occur from the use on MON 87708.

An evaluation of the compiled surface water data from 1994 through 1998 for the major soybean areas during the primary dicamba application months of April through July indicates that detected levels of dicamba (90th percentile concentration for all samples where dicamba was detected[26]) were less than 1 µg/L. Monitoring data from April through July were evaluated because these are the months where the majority of dicamba applications are made to soybean (preemergence) and corn (pre- and postemergence), and when surface water concentrations from with these applications would be expected to peak. The maximum level of dicamba in surface water during this same timeframe was 9.4 µg/L. Similarly, the evaluation of the groundwater data for major soybean growing areas from 1994 through 1998 indicates that detected levels of dicamba (90th percentile concentration of all samples where dicamba was detected) were 0.25 µg/L or less. The maximum level of dicamba in groundwater during this same timeframe was 2.2 µg/L.

Considering the available monitoring data for ground and surface water during the period of dicamba's most intensive use and when application rates were significantly higher than

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[26] EPA uses the 90th percentile as the relevant high-end endpoint when analyzing water monitoring data

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the rates proposed for us on MON 87708, it is reasonable to assume that levels in ground and surface water that may result from the use of dicamba on MON 87708 would be below the levels (high-end exposure modeling and monitoring data) considered by the EPA in the dicamba RED, and where EPA concluded would no unreasonable adverse effects on human health or the environment. Therefore, the approval in whole and no action alternatives are similar regarding their potential impact on surface and ground water quality from the use of dicamba on MON 87708.

No action alternative

Surface water may be impacted from soybean production by runoff from soybean fields that carries soil particles and herbicides or other pesticides to streams, rivers, lakes, wetlands and other water bodies. As discussed above, based on existing data, the soil component of runoff is a much more important contributor to surface water impacts than is the pesticide component. Similarly, ground water may be impacted from soybean production due to the use of herbicides or other pesticides for weed management.

Under full deregulation, growers' use of dicamba for managing hard-to-control and herbicide-resistant broadleaf weeds in soybean fields would be expected to increase. Under the no action alternative, growers would need to use other practices for dealing with hard-to-control and herbicide-resistant broadleaf weeds. These practices would likely consist of some combination of herbicide use and traditional tillage method. However, the specific combination of herbicides used would likely be different than with full deregulation, as dicamba would not be able to be used late preemergence or postemergence with MON 87708. Growers would likely use some combination of herbicides currently in use for soybean (discussed in Section VIII of the petition).

If the no action alternative resulted in increased use of conventional tillage practices for weed control, overall adverse surface water impacts may be greater with the no action alternative than under full deregulation alternative. Tillage causes widespread soil disturbance. Thus, erosion, topsoil loss and the resulting sedimentation and turbidity in streams are likely to increase with increased tillage. Based on the states' water quality reports to EPA, which EPA makes available through its National Assessment Database, pesticides in general and herbicides in particular are a relatively minor contributor to impairment of surface water in the U.S., compared to sedimentation/siltation and turbidity (U.S. EPA, 2008b). Pesticides accounted for less than one percent of reported causes of surface water impairment in all but four of the 17 leading U.S. soybean-producing states. In those four states, pesticides accounted for 2% to 8% of reported causes of impairment. Of the pesticides that were reported as contributing to impairment among the 17 leading soybean-producing states, almost all are highly persistent chemicals that are no longer registered for use in the U.S. Only one currently used herbicide, atrazine, was reported (U.S. EPA, 2008b).

In summary, based on EPA data, herbicides in general are minor contributors to surface water impairment in the U.S., while sedimentation/siltation and turbidity are major contributors. The no action alternative, compared to full deregulation of MON 87708, would likely result in a different combination of alternative herbicides being used and

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may result in increased tillage to obtain effective weed control. Weed management is a primary reason for tillage and reduced herbicide options due to existing herbicide resistance, in some cases, may increase the need for tillage (CAST, 2011). Increased tillage could contribute to adverse surface water impacts through increased runoff of soil particles to surface water bodies. Therefore, the no action and approval in whole alternatives are not significantly different regarding their impact on water quality from the cultivation of MON 87708 and associated use of dicamba.

J.5.2.3. Air Quality and Climate Impacts

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be the integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Agricultural activities have the potential to impact air quality. These activities include emissions from farming equipment, burning, nitrous oxide associated with the use of nitrogen fertilizer, and pesticide applications (Aneja et al., 2009; USDA-NRCS, 2006). Mechanical tillage practices also have the potential to impact air quality through the suspension of soil particulates in the air (USDA-NRCS, 2005; CTIC, 2011; Baker et al, 2005).

Agricultural practices are not expected to change significantly with the introduction of MON 87708. A discussion of the agricultural practices associated with soybean production in the U.S. is provided in Section VIII of the petition, and includes discussion of cultural, mechanical and herbicide practices for weed management. Deregulation of MON 87708 is expected to facilitate the trend toward increased adoption of conservation tillage methods by soybean growers because conservation tillage (specifically no-till) relies on the use of herbicides to control weeds that emerge in a field prior to or after planting the soybean seed into the previous crop stubble, thus avoiding disturbance of the soil. MON 87708 would help to maintain existing conservation tillage practices and facilitate the adoption of conservation tillage practices by simplifying weed control options for growers utilizing a non-glyphosate herbicide or where there are glyphosate-resistant or hard-to-control broadleaf weeds present. Soybean represents the greatest number of acres of the major field crops utilizing conservation tillage and the highest percentage of total crop acres devoted to conservation tillage practices (CTIC, 2007). Considerable benefits to the physical environment, including those related to air quality, are obtained from use of conservation tillage methods including (CTIC, 2011; USDA-NRCS, 2005):

- Dramatic reduction in soil erosion from wind and water;

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- Less herbicide, water, and soil runoff from soils improving the quality of streams and lakes;
- Overall healthier soils;
- Increased carbon sequestration leading to reduced greenhouse gases;
- Decreased fuel emissions due to reduced use of tractors to plow fields;
- Reduced nitrogen applications (much of which is made from fossil fuels); and
- Less overall water usage for agricultural purposes.

While approval in whole of MON 87708 may facilitate some trend towards increasing conservation tillage, it is not expected to significantly impact climate or air quality. Therefore approval in whole and no action alternatives are not significantly different regarding their impacts on climate and air quality.

No action alternative

As discussed above, compared with full deregulation of MON 87708, the no action alternative may result in increased tillage, and decreases in conservation tillage. EPA reports conservation tillage as an agricultural practice that "increases carbon storage through enhanced soil sequestration" and that "may reduce energy-related CO_2 emissions from farm equipment" (U.S. EPA, 2010). When carbon is stored, it is not available to be emitted in the form of carbon dioxide (CO_2), a greenhouse gas. Thus, the no action alternative may result in increased tillage, which could cause some adverse, but probably not significant climate and air quality impacts compared with full deregulation.

Under the no action alternative growers would still likely practice conservation tillage, and in certain situations they would rely on tillage and/or other soybean herbicides. Other herbicide-tolerant soybean events have been deregulated by APHIS or have been submitted to APHIS for deregulation. These events and their companion herbicides may be used to promote conservation tillage practices under the no action alternative. Therefore, the no action and approval in whole alternatives are not significantly different regarding their potential impact on air quality.

J.5.2.4. Soil Quality Impacts

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

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Other than changes associated with herbicide use, MON 87708 will not alter the agronomic practices typically utilized in the cultivation of soybean. MON 87708 has been found to be compositionally, agronomically and phenotypically equivalent to conventional soybean. Therefore microbial populations and associated biochemical processes in soil are not expected to change with the introduction of MON 87708. The MON 87708-produced protein DMO demonstrates a high level of substrate specificity and is not expected to persist in the environment (see Section V.E in the petition). Studies have shown no impact to the symbiont interactions of MON 87708 (see Section VII.C.4 of the petition), or to NTOs such as beneficial and pest arthropods when exposed to MON 87708 DMO in the field (see Section VII.C.2.4). Based on these data, the cultivation of MON 87708 is not expected to impact microbial populations and associated biochemical processes.

Multiple herbicides are already used in soybean production. Agricultural fields are purposefully managed to be weed-free resulting in greater economic benefit to the grower. A discussion of weed management practices is provided in Section VIII.F.1 of the petition. In the U.S., 98% of soybean acreage was treated with an herbicide in 2006 (USDA-NASS, 2007b). Therefore, introduction of MON 87708 and treatment with dicamba is unlikely to affect soil quality in commercial soybean production systems differently than those herbicides already used in soybean. Dicamba has been registered by the EPA for use on a wide range of agricultural uses since 1967 (see Appendix M, Section M.1 of the petition). The EPA evaluated the environmental safety of dicamba and its metabolites as part of the RED (U.S. EPA, 2005b), and concluded that dicamba may accumulate with frequent and intensive use (2.0 and 2.8 lb per acre a.e. single application and 7.7 lb per acre a.e. annually). The EPA mandated reductions in dicamba use rates as part of dicamba's continued registration to effect these and other potential impacts (U.S. EPA, 2009b). Based on the reduced application rates (1.0 lb per acre a.e. with a maximum annual rate of 2.0 lb a.e. per acre) dicamba is unlikely accumulate or persist in the environment. In addition, results of standardized tests with dicamba and dicamba formulations indicate no long-term effects on functional processes of soil microorganisms (carbon respiration and nitrogen transformation) at rates proposed for dicamba on MON 87708 (European Commission, 2007a). Based on this analysis, the approval in whole and no action alternatives are not significantly different regarding their impact on soil quality.

No action alternative

Under the no action alternative agronomic practices currently utilized in the cultivation of soybean would not be altered. However, some combination of herbicides already used in soybean production acres and possibly increased tillage may be used more frequently to control problematic weeds. Under the no-action alternative, an increase in tillage may occur, and would negate many of the benefits of conservation tillage to soil including improvement of soil structure, reduction of soil compaction, conservation of soil moisture, reduction of soil erosion and improvement of soil organic matter content. Overall, the no action and approval in whole alternatives are similar regarding the potential impacts on soil quality.

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J.5.3. Potential Impacts to Agricultural Practices

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

MON 87708 has been shown to be no different from conventional soybean in its agronomic and ecological characteristics (see Sections VII, VIII, IX and X of the petition), and has the same levels of tolerance to insects and diseases as conventional soybean. A summary of agronomic practices currently used for soybean production is presented in Section VIII of the petition. Except for weed management relative to dicamba use, the majority of agricultural practices, including tillage, insect and disease management, crop rotation practices, irrigation and volunteer management, will not change under full deregulation.

For weed management under full deregulation growers would have the option of a wider window for treating their soybean crop with dicamba and the number of acres upon which dicamba is used will likely increase under this alternative. An estimate of the increase in treated acres can be made using the following assumptions. If dicamba-treated acres reach 40% of the 75 million U.S. soybean acres, approximately 30 million acres of soybean would be treated with dicamba. Currently dicamba is used on 20.2 million acres in all crops including soybean (soybean accounts for 0.53 million acres) and has historically been used on up to 36.3 million acres across all uses at its peak (see Table VIII-11 of the petition). The potential use of dicamba on MON 87708 would result in a total of 50.2 million acres treated with dicamba. Similarly, the total amount of dicamba applied in overall agriculture would also increase. Based upon an upper-end estimation of the anticipated commercial use pattern for dicamba in MON 87708 as described in Section VIII.H, an additional 22 million pounds of dicamba is estimated (high-end) to be added to U.S. soybean fields each season. According to NASS statistics (USDA-NASS, 2007b), approximately 103 million pounds of herbicides were used on soybean in 2006 (Table VIII-8 of the petition), and recently the trend has been towards increasing herbicide use for the management of problematic weeds including resistant populations as well as the incorporation of diversified weed management practices in soybean growing areas (see Section J.3.3.6 for additional details regarding recent trends). As discussed previously, dicamba will displace in part the use of some existing soybean herbicides.

Dicamba use presents a relative reduction of risk potential in comparison to some of the alternative non-glyphosate herbicides currently available to soybean growers. The rationale and supporting information for the comparative alternative analysis is provided in Appendix L and summarized below:

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- Dicamba has a more favorable toxicity profile and poses a lower health risk potential to applicators and consumers compared to some alternative herbicides (Appendix L, Table L-25);

- Dicamba has lower toxicity to aquatic animals and plants and poses lower risk potential to aquatic organisms compared to some alternative herbicides (Appendix L, Table L-25);

- Dicamba when used in conjunction with MON 87708 integrated into the Roundup Ready soybean system provides growers with a more flexible and reliable weed management system (Peterson et al., 2011).

Dicamba tolerance would allow growers to utilize an expanded application window of dicamba in their weed management systems, while still allowing alternative herbicides currently registered for use in soybean to be applied. Breeding MON 87708 with glyphosate-tolerant soybean, such as Roundup Ready 2 Yield soybean, would allow for in-season application of glyphosate and dicamba, thereby improving the sustainability of weed efficacy for glyphosate, dicamba and other soybean herbicides.

A reasonably foreseeable impact under full deregulation is the delay in the evolution and development of glyphosate- and dicamba-resistant broadleaf weeds as well as weeds resistant to other soybean herbicide classes, such as PPO herbicides, in soybean producing areas. This is because growers will likely use dicamba together with glyphosate on the combined dicamba- and glyphosate-tolerant soybean product because of the excellent crop tolerance and compatibility of the two herbicides. In addition, other herbicides will be recommended and used by growers especially in cases where the grower is managing a weed population already resistant to glyphosate. This will further assist in delaying resistance to dicamba and other herbicides used in the MON87708 system.

Dicamba is an excellent option to delay resistance to other herbicides because of its broad activity on broadleaf weeds and low level of weed resistance, specifically on the summer spectrum of weeds known to infest soybean acres. A prominent strategy to delay the evolution and development of herbicide-resistant weeds is to increase the diversity of weed management practices used in a particular cropping system. Diversified weed management practices use a combination of cultural (e.g., crop rotation), mechanical (e.g., cultivation), and herbicide control practices, including use of herbicides with different modes-of-action (Duke and Powles, 2009). See Section J.3.3.6 of the petition for additional details on diversified weed management practices. Thus, MON 87708 integrated into the Roundup Ready soybean system provides the opportunity to increase the diversity of in-crop herbicide control options for growers and, in turn, supports the long term sustainability of the Roundup Ready soybean system with its established benefits.

In summary, no significant changes in common agricultural practices are anticipated from to the cultivation of MON 87708 and the associated use of dicamba. Shifts in herbicide use will occur, with dicamba displacing some of the alternative herbicides. A decrease in

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tillage practices may occur in some circumstances, and a delay in the development of glyphosate- and dicamba-resistant broadleaf weeds may be possible. Overall, the approval in whole and no action alternatives are similar regarding their impact on soybean agricultural practices.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative dicamba herbicide would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use pattern in soybean. Growers would continue to use the Roundup Ready soybean system for broad spectrum weed control, other registered alternative herbicides alone or in combination with other herbicide-tolerant soybean for targeted hard-to-control weeds, and/or incorporate tillage into their practices.

Integration of MON 87708 into the Roundup Ready soybean system has the potential to delay or prevent development of dicamba- and glyphosate-resistant weeds (see Appendix K of petition for additional detail). For soybean, the use of dicamba in conjunction with glyphosate provides growers with an herbicide system with two different modes of action. Thus, it is foreseeable that under the no action alternative, the inability to integrate MON 87708 into the Roundup Ready soybean system could increase the potential for glyphosate resistant weed populations to evolve and spread in soybean producing areas. In addition, the potential for resistance to evolve and spread for other soybean herbicides could also increase in these areas where growers do not use multiple modes-of-action.

Also under the no action alternative, increased use of other non-glyphosate alternative herbicides, some with higher risk potential for human health and environmental characteristics compared to dicamba, and reduced flexibility for the grower (*e.g.*, restricted plant-back intervals, rotational crop restrictions) would be expected. A number of weeds commonly found in the Midwestern and southern portions of the U.S. already display resistance to many of these alternative herbicides (Tables J-3 and J-4), while only four broadleaf weed species have been confirmed to be resistant to dicamba in the U.S., even though dicamba has been widely in use for over 40 years. Increasing the number of weed management options available to soybean growers, including other herbicide-tolerant traits pending deregulation (see Table J-5), is an important element to delay and prevent further development of resistant weed populations. Given these observations, the no action alternative and corresponding lack of effective alternative modes of action may lead to an increase in weed resistant populations for these alternative herbicides.

Herbicides are a critical element of conservation tillage practices. Since weed management is a primary reason for tillage, herbicides are the primary tool to replace tillage and thus are critical to the sustainability of conservation tillage practices. Under the no action alternative increased use of traditional tillage methods for the control of problematic weeds may occur in some situations and result in the potential loss of many of the benefits of conservation tillage.

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Overall herbicides are widely used in production of a soybean crop. Information presented in Section VIII.F.1 of the petition highlights the dynamics of herbicide use in soybean. Considerable shifts in use patterns of herbicides occur over time based upon many factors including availability of new herbicides and herbicide-tolerant crops, herbicide efficacy, convenience and economics. Yet, herbicides in general remain a critical element of soybean production.

From this analysis it is concluded that overall use of herbicides in soybean production is unlikely to be significantly different between the approval in whole and the no action alternatives although shifts in use patterns of herbicides may occur based on the decision to deregulate MON 87708. Additionally, an increase in tillage may occur in some circumstances under the no action alternative. Therefore, the no action and approval in whole alternatives are similar regarding potential impacts on soybean agricultural practices.

J.5.3.1. Potential Impacts on Weed Resistance

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present, where application of an herbicide with a different mode-of-action would aid in weed control, or for grower implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

A potential impact with the increased use of any herbicide is the development of herbicide-resistant weeds. A comprehensive discussion concerning the potential development of dicamba-resistant weeds may be found in Appendix K of the petition. The potential for the development of weed resistance to an herbicide is a function of the duration and frequency of herbicide use in the absence of other methods of weed control. Initially, resistant weed populations are localized at the field level, however resistant populations can become more widespread and effect larger areas as a result of the development of additional resistant populations occurring from selection pressure, or from gene flow and/or seed movement from existing resistant populations combined with inadequate management practices. In either case, the use of diversified weed management practices are essential to effectively manage weed resistance.

Dicamba has been used for over 40 years and some resistant weeds have developed due to use of the herbicide and the selection pressure applied with continued use of this herbicide. The introduction of MON 87708 will likely result in limited additional selection pressure for the development of dicamba-resistant weeds for several reasons: 1) dicamba, as a broadleaf herbicide, would primarily be used in combination with glyphosate on MON 87708 integrated into the Roundup Ready soybean system because dicamba does not control narrowleaf weeds and broad spectrum control of broadleaf and narrowleaf weeds is the objective of all weed control systems; 2) the use of glyphosate plus dicamba would provide multiple modes-of-action on key broadleaf weeds which

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would diminish the chance for selection of dicamba-resistant broadleaf weeds; 3) in cases where glyphosate plus dicamba will be applied to soybean fields with a known presence of glyphosate-resistant broadleaf weeds, a third herbicide mode of action will be recommended to growers that also has activity on the glyphosate-resistant broadleaf weed thereby providing two effective modes-of-action to control the glyphosate-resistant weed; and 4) the proposed dicamba herbicide label for MON 87708, existing glyphosate herbicide labels and separate Monsanto weed management recommendations (e.g., Monsanto's annual TUG[27] and publically available websites[28]) will specify the effective rate and timing of dicamba and glyphosate applications for optimal weed control, thereby reducing selection pressure for dicamba as well as glyphosate.

Furthermore, in the unlikely case that broadleaf weeds were to evolve or develop with resistance to dicamba, existing cultivation and alternative herbicide tools (see Section VIII.F.1 for description of alternative herbicides) would remain potential options to provide effective control. Additionally, as discussed above in Section J.5.3, it is reasonably foreseeable that under full deregulation a delay in development and spread of glyphosate- and dicamba-resistant broadleaf weeds, as well as weeds resistant to other soybean herbicide classes such as PPO herbicides, will occur due to the likely use of dicamba and glyphosate on fields planted with the combined dicamba and glyphosate tolerance product.

In summary, there is a low probability that additional dicamba resistant weed species or populations will evolve or develop as a result of the cultivation of MON 87708 and the use of dicamba and glyphosate in the weed management systems, and a delay in the development of glyphosate- and dicamba-resistant broadleaf weeds may be possible. Overall, the approval in whole and no action alternatives are similar regarding their impact on herbicide weed resistance.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative dicamba herbicide would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use pattern in soybean. Growers would continue to use the Roundup Ready soybean system for broad spectrum weed control, other registered alternative herbicides alone or in combination with other herbicide-tolerant soybean, and/or incorporate tillage into their practices. There is a potential for glyphosate-resistant weed populations to increase and spread in soybean cultivation areas, as well as the potential for the development and spread of resistant populations to other alternative soybean herbicides.

Integration of MON 87708 into the Roundup Ready soybean system has the potential to delay or prevent development of dicamba- and glyphosate-resistant weeds in soybean cultivation areas (Appendix K of petition). For soybean, the use of dicamba in

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[27] http://www.monsanto.com/SiteCollectionDocuments/Technology-Use-Guide.pdf

[28] http://www.monsanto.com/weedmanagement/Pages/default.aspx

conjunction with glyphosate provides growers with an efficient, effective and flexible herbicide system with two different herbicide modes-of-action with overlapping activity on many broadleaf weeds. Thus, it is foreseeable, under the no action alternative and the inability to integrate MON 87708 into the Roundup Ready soybean system, that there is an increased potential for glyphosate resistant weed populations in soybean growing areas to evolve and spread, as well as an increased potential for resistance to evolve and spread for other soybean herbicides where growers do not effectively use multiple modes-of-action. However, existing alternative soybean herbicides will continue to be available. Therefore, the no action and approval in whole alternatives are similar regarding potential impacts on weed resistance.

J.5.4. Potential Impact to Commercial Soybean Production

Approval in whole alternative

Soybean is a globally traded commodity with the U.S. being the top global producer (Soyatech, 2010). An overview of U.S. soybean production is provided in Section VIII.B.1 of the petition. Biotechnology-derived crops are subject to regulation in many countries. In order to support free trade in soybean, Monsanto will seek regulatory approval for MON 87708 and stacked products (i.e., products combined using traditional breeding techniques) with other biotechnology-derived soybean, where required, in all key soybean import countries with a functioning regulatory system to support the flow of international trade. As described in Section VIII.L of the petition, Monsanto adheres to the BIO Product Launch Policy[30] including: 1) conducting a market and trade assessment, 2) securing regulatory approvals in key export countries prior to full commercial launch, 3) following generally accepted best seed management practices to prevent unintended low level presence of the event in seed, 4) providing reliable detection methods to growers, processors and buyers prior to commercialization, and 5) communicating to stakeholders the company's product launch stewardship policies. These actions protect against adverse impacts to trade of soybean due to the introduction of a new biotechnology-derived soybean.

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Soybean is primarily a self-pollinated crop with minimal gene movement (see Section IX of the petition). Due to the biology of soybean flowers which results in low cross pollination potential, pollen movement between soybean fields is minimal. Thus the introduction of MON 87708 is not expected to effect commodity soybean production, due to low potential gene movement to neighbouring soybean crops. In 2009, 91% of the

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[30] BIO's Product Launch guidelines can be found at: http://www.excellencethroughstewardship.org/LinkClick.aspx?fileticket=ppgyTABguQs%3d&tabid=84.

U.S. soybean acres were planted to biotechnology-derived herbicide-tolerant soybean (USDA-NASS, 2009a). Thus, growers are accustomed to the presence of biotechnology-derived soybean in proximity to production fields and have developed practices to allow for production of a crop to meet customer expectations. Therefore, the approval in whole and no action alternatives are similar regarding potential impacts on commercial soybean production.

No action alternative

Under the no action alternative, MON 87708 would remain a regulated article and would not be available to growers. Growers could continue to use the Roundup Ready soybean system for broad spectrum weed control. Therefore, the no action and approval in whole alternatives are not different in their impact to commercial soybean production, because the majority of soybean grown in the U.S. is already biotechnology-derived and due to company stewardship policies accompanying the introduction of new biotechnology-derived products, as described above. Technology providers maintain a dialogue with stakeholders to communicate global approval status for biotechnology-derived soybean to avoid potential market disruption. Commodity and specialty soybean growers and handlers are accustomed to a diversity of soybean types in the marketplace, including soybean with modified oil profiles, food grade, clear hilum, and others. They have demonstrated an ability to provide soybean that meet their customers' expectations. MON 87708 represents another biotechnology-derived soybean in the marketplace adding to the diversity of soybean available to growers and the market. Therefore the no action and approval in whole alternatives are expected to be the same regarding potential impacts on commercial soybean production.

J.5.5. Potential Impact to Certified Seed Production

Approval in whole alternative

Certified seed production is a carefully managed process (see Section VIII.B.2 of petition for additional detail). MON 87708 is not expected to impact certified seed production practices or production of specialty soybean seed for reasons described in this section.

If MON 87708 is deregulated, seed production would occur within production systems already developed by seed producers for certified soybean seed. MON 87708 has been thoroughly characterized and (with the exception of its tolerance to dicamba) is not agronomically or phenotypically different from commercial soybean. The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers. However, the implementation of management practices to avoid pollen from a biotechnology-derived soybean in organic, specialty or conventional soybean seed or commodity seed production operations is dictated by the nature of soybean pollination (see Section

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VIII.B.2), and MON 87708 has been shown in field testing to not differ from commercial soybean varieties regarding pollen characteristics. Soybean is a highly self-pollinated species that exhibits very low levels of outcrossing. Numerous evaluations on soybean cross-pollination have been conducted, and the published results are summarized in Table IX-1 of the petition. Under typical soybean planting and cultivation conditions, cross-pollination among adjacent plants in a row or among plants in adjacent rows ranged from 0 to 6.3%. In experiments where supplemental pollinators (usually bees) were added to the experimental area, cross-pollination ranged from 0.5 to 7.74% in adjacent soybean plants or adjacent rows (Abrams et al., 1978; Chiang and Kiang, 1987). However, cross-pollination even at the low levels observed in these controlled trials does not occur over long distances. Cross-pollination rates decrease to less than 1.5% beyond one meter from the pollen source, and rapidly decrease with greater distances from the source. The following cross-pollination rates at extended distances have been reported: 0.02% at 8.2 m of separation (Caviness, 1966), 0.05% at 5.4 m (Ray et al., 2003), and 0% at 6.5 m (Abud et al., 2003).

The low potential for cross pollination in soybean is recognized in certified seed regulations for foundation seed in the U.S., which require no measured isolation between different soybean cultivars in the field as long as there is adequate separation between the fields to prevent mechanical mixing (USDA-APHIS, 2006). Hence, certified soybean seed producers can and have effectively implemented practices (*e.g.*, isolation distances during the growing season, equipment cleaning during harvest, and post-harvest separation of harvested seed) that allow them to maintain commercially acceptable levels of varietal purity. Because MON 87708 has been shown to be no different from conventional soybean relative to pollen morphology and viability, the cultivation of MON 87708 will not impact the ability to implement production practices required for the production of certified seed. Therefore, the approval in whole and no action alternatives are the same regarding the potential impact on certified seed production practices.

No action alternative

Under the no action alternative, MON 87708 would not be propagated to any extent by seed producers because there would be no commercial demand for seed containing MON 87708. Seed production practices would be the same as those described above for the deregulation in whole alternative and in Section VIII.B.2 of the petition. Seed producers already produce numerous varieties of soybean, the vast majority of which include a biotechnology-derived trait. Therefore, the no action and approval in whole alternatives are the same regarding the potential impacts on certified seed production.

J.5.6. Potential Impacts to Organic Soybean Production

Approval in whole alternative

Organic soybean production is a carefully managed and regulated process. MON 87708 and biotechnology-derived soybean in general, including those currently grown commercially, are not allowed for use in organic production systems because they were

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developed through the use of excluded methods as defined by the National Organic Production (NOP) program standards (7 CFR § 205.2). With the exception of its tolerance to dicamba, MON 87708 has been shown to be no different from conventional soybean in its agronomic and ecological characteristics including characteristics of the pollen produced by MON 87708. Thus, MON 87708 is expected to be no different from other soybean in its ability to cross pollinate with other soybean and, therefore, no additional means beyond those already used to produce biotechnology-derived and organic soybean will be needed if MON 87708 were grown commercially.

Similar to the exclusion of biotechnology-derived products in organic production, the use of synthetic herbicides, such as dicamba, are also excluded under the NOP. Dicamba is presently registered for early preemergence (early pre-plant) and late postemergence (pre-harvest) applications in soybean, and in other crops (corn, sorghum and wheat) commonly grown in rotation with soybean. It is likely that dicamba herbicide will be applied to MON 87708. As mentioned previously, herbicides are used extensively for production of soybean and the potential increased use of dicamba, along with its concurrent replacement of some alternative herbicides used to control glyphosate's hard-to-control and resistant weeds, is minimal considering the amount of herbicides (103M lbs and trending higher, see Table VIII-8 and discussion in J.5.3 of the petition) currently applied in commodity soybean production each year. For these reasons, production systems and practices in place now (discussed below) are sufficient to mitigate any impacts from the introduction of MON 87708 to organic soybean production.

Currently, biotechnology-derived herbicide-tolerant soybean is planted on over 90% of the soybean acreage (USDA-NASS, 2009a). Despite the high adoption rates of biotechnology-derived soybean by growers, organic and conventional soybean production remains an option for growers who choose to produce soybean using these production practices. The decision to grow organic, conventional, or biotechnology-derived soybean is typically an economic one based on market dynamics. Organic soybean producers and those growing conventional soybean for non-biotechnology markets typically receive a market premium offsetting the additional production and record-keeping costs. While the widespread demand for Roundup Ready soybean has reduced the number of conventional soybean varieties that seed companies choose to sell, conventional and organically produced soybean seed is currently available from numerous seed suppliers (Table J-6). Additional information on organic seed sources is provided though the U.S. Agricultural Marketing Service (AMS). Thus, growers have a choice in the soybean they plant, and this is not expected to change with the introduction of MON 87708.

Production systems designed prior to the introduction of MON 87708 or even prior to the introduction of biotechnology-derived soybean have allowed for production of soybean to meet varied customer demands. In addition to the market segments that produce organic or conventional soybean, distinct identity-preserved specialty soybean with such traits as clear hilum or high protein have also been grown and successfully marketed for specific food uses in domestic and export markets for many years (Cui et al., 2004). The NOP requires organic soybean producers utilize production practices designed to specifically avoid the presence of soybean products using conventional herbicide or other pesticide

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treatments, as well as avoiding the use of biotechnology-derived crops. These well established practices to avoid the use of "excluded methods" will continue with the commercial introduction of MON 87708 integrated into the Roundup Ready system. They include isolation zones, use of buffer rows surrounding the organic crop, adjusted planting dates and varietal selection.[31] The implementation of management practices to avoid pollen from a biotechnology-derived crop in organic or conventional soybean production operations is facilitated by the nature of soybean pollination. As noted previously in the petition, soybean is a highly self-pollinated species and exhibits a very low level of outcrossing. Hence, organic or conventional soybean producers can and have effectively implemented practices (*e.g.*, isolation during the growing season, equipment cleaning during harvest, and post-harvest separation of harvested seed) that allow them to avoid the presence of biotechnology-derived soybean and maintain organic or conventional production status.[32]

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. There is potential for cultivation of soybean containing the MON 87708 trait to provide weed control solutions for problematic weeds and proactively manage and prevent the development of herbicide resistant weeds. However, the presence of a biotechnology-derived product like MON 87708 is unlikely in instances where producers utilize production practices designed to avoid biotechnology-derived products. Although the USDA's National Organic Standards prohibit the use of excluded methods, the presence of products of an excluded method alone does not necessarily constitute a violation of the Standard or a loss of organic certification (USDA-AMS, 2011). While the NOP does not set specific thresholds for the allowable presence of products of excluded methods, there may be some specifications in buyer allowances that permit between 0.1 to 5% biotechnology-derived soybean in organic soybean.[33] Similarly, international regulatory authorities have set allowable tolerances for the presence of biotechnology-derived material in conventional products to support food labeling and traceability laws. These tolerances allow from 0.9% (European Union) up to 5% (Japan) of the food to be biotechnology-derived in products considered "conventional." Levels above the threshold may trigger special labeling.

Given that allowances for minor amounts of biotechnology derived material are allowed in soybean exported to key markets and that systems are in place for production of soybean that meet buyer expectations and the prevalence of biotechnology-derived soybean already on the market, the introduction of a new biotechnology-derived soybean product is unlikely to have an effect on organic soybean production. This conclusion is supported by USDA-ERS (2010) data that show the organic soybean market share was 0.17% in 1995, the year prior to the introduction of Roundup Ready soybean, and was at 0.2% in 2008; indicating availability of biotechnology-derived soybean has not significantly impacted the organic soybean industry. Therefore, the approval in whole

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[31] Information on isolation methods can be found at: www.attra.ncat.org [Accessed on June 2, 2010].

[32] Source is website: http://attra.ncat.org/attra-pub/PDF/cropsfarmplan.pdf [Accessed on June 2, 2010].

[33] Source is website: http://attra.ncat.org/attra-pub/PDF/marketingorganicgrains.pdf [Accessed on May 27, 2010].

and no action alternatives are the same regarding the potential impact on organic soybean production.

No action alternative

The majority of soybean is currently produced using biotechnology-derived soybean. Growers have come to rely on biotechnology-derived soybean and their benefits. Given that several biotechnology-derived soybean have previously been deregulated by USDA and other events are under consideration for deregulation, the use of biotechnology-derived soybean is expected to remain relatively constant for the foreseeable future. Similarly, herbicide use is also expected to remain a key agronomic practice in production of commodity soybean. Thus, organic growers will continue to manage their production fields to avoid excluded methods and drift of pesticides under the no action alternative, and growers would continue to utilize the same practices they use now to produce their organic crop. Thus, the no action and approval in whole alternatives are the same regarding the potential impact to organic soybean production.

Table J-6. Organic and Conventional Soybean Seed Sources

Organic Soybean Seed Sources[1]:	Conventional Soybean Seed Sources
Albert Lea Seed House	AgVenture Seeds (modified oil)
Blue River Hybrids	Campbell Seed (modified oil)
Golden Grains	Becks Hybrids (food grade)
Great Harvest Organics	Monsanto (Asgrow)
Greis Seed Farm	Schillinger Seed
Lancaster Ag Products	Pioneer
Lawler Farm Center	Soy Genetics
Prairie Gold Seeds	Stewart Seed (modified oil)
Superior Organic Grains, Ltd	Stine Seed
Walter Seed and Honey Co	Syngenta - multiple brands
	Terral Seed
	Various State Crop Improvement Organizations

[1] Source is: www.organicgrains.ncsu.edu.

J.5.7. Potential for Adjacent Agricultural Crop and Non-agricultural Impacts

Approval in whole alternative

Soybean (*Glycine max*) does not grow in the wild in North America (Hymowitz, 1987). Soybean does not grow and persist in unmanaged habitats and would not be expected to invade and/or persist in the natural environment, including streams, lakes, oceans or other aquatic environments. With the exception of the production of MON 87708 DMO that

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confers tolerance to dicamba, MON 87708 is similar to other commercial soybean currently grown in the U.S. It is expected that under the approval in whole alternative MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers. MON 87708 displays no altered plant pest characteristics compared to conventional soybean and is no more susceptible to insects or diseases that commonly infest soybean. On the basis of the information presented in petition #10-SY-210U on phenotypic and agronomic characteristics of MON 87708, and based upon the biology of soybean, MON 87708 is unlikely to effect adjacent vegetation. Therefore, the approval in whole and no action alternatives are the same regarding potential impacts on adjacent agricultural crops and non-agricultural areas.

Herbicides are extensively used in U.S. soybean production, and their historic and current uses are described in Section VIII.F.1 of the petition. Herbicide drift and offsite movement are regulated by the U.S. EPA and actively managed by farmers and applicators specially trained to use such products consistent with product labels and other state or local restrictions. Depending upon the herbicide employed, relevant factors in managing the potential for spray drift include the selectivity and sensitivity of the herbicide, local weather conditions at the time of application (wind, temperature, humidity, inversion potential), droplet size distribution, application volume, boom height (height of the application equipment above the crop canopy), sprayer speed, and distance from the edge of the application area (SDTF, 1997; Felsot et al., 2010). A variety of measures can be employed to control the potential for spray drift and offsite movement, including nozzle selection and application techniques and restrictions.

The approval in whole alternative would result in an increase in dicamba use in soybean compared to its current use. The U.S. EPA considers possible effects from offsite movement as part of the pesticide registration process. APHIS's authority under the Plant Protection Act, on the other hand, does not authorize it to specify conditions or in any way regulate the use of herbicides. As a result, before any dicamba formulation could be employed over MON 87708, EPA's approval of a FIFRA label for that specific use would be required. Such a label would address not only application rates, but as appropriate, could also include other measures to address the potential for offsite movement. EPA considers possible effects from offsite movement as part of the pesticide registration process. Specifically, in order to approve the use of a pesticide (herbicide) under FIFRA, EPA must conclude that no unreasonable adverse effects on non-target vegetation will result from offsite movement when the pesticide is used according to the product label, and when herbicides are applied according to the label requirements, offsite impacts can be avoided. EPA employed this analysis of offsite impacts in the dicamba RED, and concluded that no specific additional drift mitigations were needed to support the continued registration of all dicamba uses (U.S. EPA, 2009b). Since the proposed use pattern for dicamba on MON 87708 is consistent with use patterns evaluated in the dicamba RED, it would be reasonable to conclude that dicamba use on MON 87708 meets existing FIFRA standards related to drift and offsite movement.

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The use of dicamba on MON 87708 in accordance with the FIFRA approved label does not pose any greater risk to non-target vegetation over existing dicamba agricultural uses approved by EPA. Nevertheless, Monsanto has already taken additional steps to manage dicamba offsite movement even though such steps are not required by EPA as stated in the RED. In the pending application to EPA, Monsanto requested the use of dicamba on MON 87708 on the low volatility DGA salt formulation (U.S. EPA Reg. No. 524-582) and limited dicamba application to ground application equipment as additional stewardship measures. Monsanto plans to further address the use of dicamba on MON 87708 with US EPA to evaluate whether any additional measures may be appropriate to further address potential drift and offsite movement.

Monsanto will also implement a robust stewardship program to reinforce the EPA label requirements, including a strong emphasis on grower and applicator training by working with American Association of Pesticide Safety Educators (AAPSE) and other stakeholders in applicator training to further facilitate proper use of dicamba. Furthermore, as part of Monsanto's stewardship program, Monsanto will encourage growers and applicators to consult with available sensitive crop registries prior to making dicamba applications to MON 87708. Many state lead agriculture agencies (IA, IL, IN, KS, MI, MN, MO, NE, OK, WI) have developed tools and resources to assist the applicator in the location of sensitive areas, such as vegetable or organic production fields, in an effort to minimize commercial impacts associated with herbicide offsite movement.

Herbicides are widely used now in soybean production, and growers and commercial herbicide applicators have over 40 years experience in making dicamba applications in numerous crops including preemergence applications on conventional soybean. Alternative herbicides will continue to be used, as needed, for weed management or to implement weed resistance management practices, however it is anticipated that dicamba will displace in part the use of some alternative herbicides. EPA regulates the use of herbicides and has concluded that dicamba offsite movement from uses consistent with those proposed for MON 87708 does not pose unreasonable adverse effects to non-target vegetation. Furthermore, as indicated above, when herbicides are applied in accordance with the FIFRA label application use instructions, potential impacts on adjacent agricultural crops and non-agricultural plants can be avoided. Thus, potential impacts to these adjacent areas due to deregulation of MON 87708 and use of dicamba are similar when compared to the no action alternative (discussed below). Therefore, the approval in whole and no action alternatives are similar regarding potential impacts on adjacent agricultural and non-agricultural areas.

No action alternative

Under the no action alternative, MON 87708 would not be widely available and growers would continue to use other practices for control of weeds in soybean fields. These practices would likely consist of some combination of herbicide use and tillage. However, the combination of herbicides used would likely be different than with full deregulation, as dicamba would only have a limited use pattern on soybean. Growers would likely use some combination of the herbicides currently in use for soybean

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(discussed in Section VIII.F.1 of the petition). It is reasonably foreseeable that new herbicides will be invented, or that existing herbicides will be adopted for use on soybean or herbicides associated with soybean events under consideration for deregulation may be used (*e.g.*, other auxin type herbicides like 2,4-D) (Table J-5). Offsite impacts to adjacent plants from these alternative herbicides would vary, depending on active ingredients, weather conditions, formulations, application methods and other factors. Because herbicides are currently used extensively in soybean production and will be for the foreseeable future, it is likely that the effects to adjacent crops and non agricultural plants would be similar under the no action and approval in whole alternatives.

J.5.8. Potential Impacts to Raw or Processed Agricultural Commodities

Approval in whole alternative

It is expected that under the approval in whole alternative MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Within petition #10-SY-210U, extensive data have been presented relating to plant growth parameters, disease susceptibility, insect susceptibility, and forage and seed composition of MON 87708 compared to conventional soybean. These data indicate that there are no biologically relevant differences between MON 87708 and conventional soybean, except for its tolerance to dicamba. Biotechnology-derived crops used for food or feed undergo a voluntary food and feed consultation process with the FDA prior to release on the market. Monsanto will complete this consultation process with FDA prior to commercial introduction of MON 87708.

Soybean compositional data on MON 87708 and conventional soybean are presented in Section VI of the petition. Information from this evaluation shows that soybean produced from MON 87708 is of comparable quality to soybean commercially produced in the U.S. for commodity markets. Dicamba residue levels in soybean seed harvested from MON 87708 treated with dicamba (1.0 lb a.e. per acre preemergent followed by two, sequential 0.5 lb a.e. per acre postemergent applications) at more than twice the anticipated commercial in-crop application rate were low, less than 0.1 ppm, and well below the established 10 ppm pesticide residue tolerance[34] supporting dicamba use on commercial soybean (see Appendix M, Section M.4.1.1 of the petition). Monsanto is also petitioning the agency for the establishment of new tolerances on forage (45 ppm) and hay (70 ppm).

Due the established safety of dicamba and allowable residues in food and feed, there is no evidence that the deregulation of MON 87708 would cause any impacts on either raw or

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[34] EPA established tolerances for dicamba can be found at 40 CFR § 180.227. Dicamba residue is defined as dicamba, DCSA and 5-hydroxy dicamba. Analysis of MON 87708 included quantification of these defined dicamba residues, in addition to the minor metabolite DCGA.

processed soybean commodities resulting from the deregulation of MON 87708. EPA will evaluate any potential risks associated with the pending application for the new use of dicamba on MON 87708 and the establishment of new feed tolerances on soybean forage and hay as a part their review, and will conclude a reasonable certainty of no harm to human health when it approves the pending new use application.

No action alternative

MON 87708 would not be widely available or grown commercially under this alternative. Under this alternative, other herbicides and other biotechnology-derived soybean products or traditional tillage practices would be used instead of MON 87708 with its associated dicamba treatment. Therefore, the no action and approval in whole alternatives are similar regarding their impacts to raw and processed agricultural commodities.

J. 5.9. Potential Impacts to Human Health and Safety

It is expected that under the approval in whole alternative MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Prior to the introduction of a biotechnology-derived crop product into the marketplace, Monsanto conducts tests to assure that the products are safe for their intended use and are appropriately labeled. For MON 87708, impacts on human health are considered for exposure to the biotechnology-derived soybean (MON 87708) and the associated dicamba herbicide. As mentioned previously, biotechnology-derived crops for food and feed use undergo a voluntary consultation process with the FDA prior to release onto the market. Although a voluntary process, Monsanto routinely completes a consultation with the FDA prior to placing a new biotechnology-derived crop product on the market. The consultation process with FDA on MON 87708 (BNF No. 125) was completed on October 11, 2011 (see Section I.C.I of the petition).

Herbicide use and resulting residues associated with herbicide-tolerant crops improved through biotechnology are regulated under the Federal Food, Drug, and Cosmetic Act (FFDCA) by the EPA. Under the FFDCA (21 USC 301 et seq.), pesticide residues in or on raw agricultural commodities or processed foods are considered to be safe after a tolerance or exemption from tolerance has been established. The FDA enforces the tolerances set by the EPA. Currently, a pesticide residue tolerance exists for residues of dicamba on soybean seed at 10 ppm (40 CFR § 180.227), which is based on the approved late season postemergence (prior to harvest) use of dicamba on commercial soybean. As previously mentioned, Monsanto has submitted an application to EPA to register a new use pattern for dicamba on MON 87708 that will allow for preemergence and up to two postemergence in-crop applications of dicamba. Residue data generated on MON 87708 to support this new dicamba use pattern using maximum label rates, show low levels of

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dicamba residues on soybean seed (< 0.1 ppm dicamba a.e.; see Appendix M, Section M.4.1.1 of the petition) and confirm the current soybean seed tolerance is sufficient to support the new use on MON 87708. Monsanto has also petitioned the EPA to establish new tolerances for dicamba on soybean forage (45 ppm) and hay (70 ppm) to allow soybean commodities to be fed to or grazed by livestock. Existing dicamba tolerances for animal foodstuffs (*e.g.*, meat, milk) are sufficient to address potential incremental dietary exposure to livestock from dicamba-treated MON 87708 forage and hay, as discussed in Section J.5.9.2.

J.5.9.1. Human Health (MON 87708)

Approval in whole alternative

Under full deregulation, MON 87708 could be grown broadly across the U.S. Soybean and forage produced from MON 87708 would enter the food and feed chain and would be consumed by humans and animals. Agricultural workers would be exposed to MON 87708 and its associated agricultural practices. The potential human health impacts associated with the introduction of MON 87708 and increased applications of dicamba are separately discussed below.

MON 87708 was developed through *Agrobacterium*-mediated transformation of soybean meristem tissue using the binary transformation plasmid PV-GMHT4355 (Section III; Figure III-1 and Table III-1). MON 87708 contains one copy of the insert at a single integration locus. No additional genetic elements from the transformation vector were detected in the genome of MON 87708, including backbone sequence from plasmid PV-GMHT4355. Additionally the data confirm the organization and sequence of the insert, and demonstrate the stability of the insert over several generations. On the basis of these data, it is concluded that only the MON 87708 DMO is produced from the inserted DNA.

For MON 87708, the available data demonstrate that harvested seed is as safe as conventional soybean for food and feed uses; thus it is safe and wholesome for consumption. To assess the impact of MON 87708 DMO on food and feed safety, bioinformatic analyses were used to establish the lack of both structurally and immunologically-relevant similarities between MON 87708 and allergens or toxins, based on the amino acid sequence of MON 87708 DMO. Furthermore, digestive fate experiments conducted with MON 87708 DMO demonstrate rapid digestion in simulated gastric fluid (SGF), a characteristic shared among many proteins with a history of safe consumption. Rapid digestion of MON 87708 DMO in SGF indicates that it is highly unlikely that MON 87708 DMO will reach absorptive cells of the intestinal mucosa. This, combined with the history of safe consumption of mono-oxygenases (the class of enzymes to which MON 87708 DMO belongs) and the lack of homology of the amino acid sequence to known allergens and toxins, supports a conclusion that MON 87708 DMO has low allergenic and toxic potential. Finally, a high dose of MON 87708 DMO in a mouse acute oral toxicity evaluation demonstrated that it is not acutely toxic, and does not cause any adverse effect. The safety assessment supports the conclusion that exposure to MON 87708 DMO poses no meaningful risk to human or animal health.

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Extensive analysis of the composition of MON 87708 seed and forage demonstrated that no biologically relevant changes were detectable. A detailed compositional assessment of soybean harvested seed and forage is presented in Section VI of petition #10-SY-210U. The levels of key nutrients, anti-nutrients, and other components in MON 87708 were examined and compared to that of the near-isogenic conventional soybean control, A3525, a conventional soybean variety with background genetics representative of MON 87708, but without the genetic modification. Additionally, tolerance intervals representing 99% of the values of each analyte for a commercial soybean population were established. Results demonstrate that the levels of key nutrients, anti-nutrients, and other components of MON 87708 are compositionally equivalent to the conventional control and within the range of variability of commercial soybean that were grown concurrently in the same trial. Furthermore, FDA completed its consultation on the food, feed and nutritional safety assessment on MON 87708 on October 11, 2011, confirming Monsanto's conclusion on the safety of MON87708-derived food and feed.

On the basis of the characteristics of MON 87708 DMO and the extensive compositional characterization of MON 87708 harvested seed, no impacts to human health are expected from the approval in whole alternative. Thus, the approval in whole and no action alternatives are similar regarding the potential impacts of MON 87708 on human health.

No Action Alternative

Under the no action alternative, MON 87708 would continue to be a regulated article. Human exposure to existing conventional and GE soybean would remain unchanged. Growers and consumers exposed to MON 87708 would be limited to individuals involved in the cultivation of MON 87708 under the conditions of regulation. Therefore, the no action and approval in whole alternatives are similar regarding the potential impacts of MON 87708 to human health.

J.5.9.2. Human Health (Dicamba)

Approval in whole alternative

The toxicology or safety profile of dicamba has been extensively reviewed (U.S. EPA, 2009b). Dicamba does not pose any unusual toxicological concerns and is not carcinogenic (U.S. EPA, 2009b; Durkin and Bosch, 2004; PMRA, 2008; European Commission, 2007b). EPA completed the reregistration of dicamba in 2006. The Reregistration Eligibility Decision (RED) document for dicamba and its associated salts concluded a high level of confidence exists for the dicamba hazard data base and the reliability of these data necessary to support the required safety finding for continued registration, including the pre-harvest use on commercial soybean. The dicamba RED document, and the related Health Effects Division (HED) of the EPA chapter (U.S. EPA, 2005a), provide a detailed overview of the toxicological properties of dicamba. A summary of dicamba's toxicity profile is presented in Section L.3.1 of Appendix L of the petition.

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EPA evaluated the potential risks to humans from the use of dicamba as a part of the dicamba RED, concluding that aggregate exposure to dicamba, defined as dietary (food and water) and non-occupational (residential and recreational) exposures, meet the FIFRA determination of no unreasonable adverse effects and the FFDCA determination for reasonable certainty of no harm to human health (see Section M.4.1 of the petition for more detail). EPA has conducted acute and chronic dietary (food and water) risk assessments for dicamba based on a theoretical worst case exposure estimate. For food, this estimate assumes that dicamba is used on 100 percent of all the crops on which the pesticide is currently approved for use. It further assumes that the resulting pesticide residues found on all harvested food and feed crops and derived animal food commodities (e.g., meat and milk) are at the level of the legally established tolerance (i.e., the maximum allowable pesticide residue level). Residues of dicamba are defined as dicamba and its metabolites 5-hydroxy dicamba and 3,6-dichlorosalicylic acid (DCSA) in soybean commodities, and as dicamba and DCSA in animal food commodities, as currently regulated in 40 CFR § 180.227. For water, EPA assumed that dicamba could potentially move offsite to adjacent surface water bodies as a result of drift or runoff, or move through soil to groundwater. Since the estimated concentrations in groundwater were significantly lower compared to surface water, surface water estimates were used in the worse case dietary assessments (see Section J.5.2.2 and Section M.5.2 of the petition for details on dicamba levels in water resources). Based on the worst-case assumptions outlined above, acute and chronic dietary exposure was well below the Agency's level of concern to satisfy the FIFRA and FFDCA standards (U.S. EPA, 2009b).

Characterization of the nature of dicamba residues in MON 87708 confirms no additional residues of concern are created in MON 87708, and the current soybean seed dicamba residue definition is applicable for MON 87708. Residue levels in soybean seed harvested from MON 87708 treated with dicamba at the proposed maximum allowable application use pattern (1.0 pound a.e. per acre preemergence and two 0.5 pound a.e. per acre postemergence applications) were less than 0.1 ppm, well below the established 10 ppm tolerance supporting the current use of dicamba on conventional soybean. These dicamba residue data for MON 87708 were submitted to the U.S. EPA on April 28, 2010 (OPP Decision Number: D-432753, Registration Number 524-582), along with a proposed label for the use of dicamba on MON 87708.

Presently, dicamba is applied to less than 1% of soybean acres using pre-plant and pre-harvest burn down applications (see Table VIII-12 in petition #10-SY-210U). Under the approval in whole alternative, dicamba will be used on more soybean acres and a higher percentage of soybean and soybean-derived foods will contain dicamba residues; however, dicamba residue levels in MON 87708 harvested seed or processed foods will be significantly lower compared to levels originating from the current pre-harvest soybean use (approximately 100-fold lower, based on <0.1 ppm. residue in MON 87708 seed compared to established 10 ppm tolerance (see Appendix M, Section M.4.1.1 for residue levels in seed). It is difficult to determine the exact impact on actual dietary exposure from the expanded use of dicamba on MON 87708; however, the EPA concluded that residues of dicamba up to 10 ppm in soybean seed are safe (reasonable certainty of no harm as defined by FFDCA) for human and animal consumption, based on the EPA's Tier 1 dietary and aggregate (dietary plus other non-occupational) exposure

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assessments which assume 100% of soybean foods contain dicamba residues at the 10 ppm tolerance level.

Additionally, Monsanto has petitioned the EPA to establish new feed tolerances for soybean forage and hay to allow MON 87708 forage and hay to be fed to livestock, a practice that is presently prohibited for dicamba-treated commercial soybean (see Appendix M, Section M.4.1.1 for residue levels in forage and hay). This practice is presently not allowed because the current preharvest application is made past the stage where the crop would be useful as forage or hay. Thus, there has been no reason for pursuing these tolerances until earlier in-crop applications of dicamba were possible, as with MON 87708. Dietary exposure to livestock from the feeding of MON 87708 soybean forage and hay does not result in an exceedance of the livestock maximum theoretical dietary burden established by the EPA, which is used to establish animal by-product commodity tolerances (*e.g.*, meat and milk). Therefore, the approval of soybean forage and hay tolerances does not result in a change to the current animal by-product commodity (food) tolerances and as a result does not increase potential dietary exposure of dicamba.

Since no changes to the current dicamba food tolerances (soybean seed and animal by-products) are needed, the dietary and aggregate risk assessments conducted in the RED are inclusive of the incremental exposure resulting from the use of dicamba on MON 87708. Therefore, the deregulation of MON 87708 would not present a significant impact to human health, and the approval in whole and no action alternatives are the similar regarding potential impacts on human health.

No Action Alternative

Under the no action alternative, MON 87708 would remain a regulated article and would not be commercially available to growers. It is likely that growers will continue to use herbicides in soybean production, and use the Roundup Ready soybean system. Growers will continue to use additional herbicides where needed or recommended to control hard-to-control or glyphosate-resistant weeds. Growers may also choose to use other herbicide-tolerant soybean events, use a combination of alternative herbicides registered for use in soybean, or use traditional tillage practices to control weeds. In addition, dicamba will continue to be used on a small number of soybean acres (refer to Section VIII.G in the petition). Consumers will be exposed to residues of dicamba and the alternative herbicides through consumption of soybean and soybean-derived foods, and from residues on other food crops such as corn and wheat. On the basis of the analysis above, the approval in whole and no action alternatives involve the continued use of herbicides for production of soybean. Thus, the no action and approval in whole alternatives are similar regarding potential impacts to human health.

J.5.9.3. Worker Safety

Approval in whole alternative

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It is expected that under the approval in whole alternative MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

There is no notable worker safety issue related directly to exposure to MON 87708. As described elsewhere, MON 87708 is as safe as conventional soybean for use as food or feed. MON 87708 DMO has no safety concerns that would result in adverse effects to workers exposed to MON 87708 plant tissues.

Agricultural workers can be exposed to dicamba during the herbicide application or upon re-entry into treated MON 87708 fields. Under the proposed label, dicamba can be applied as a preemergent treatment on MON 87708 at rates up to 1 lb a.e. per acre and then again in two sequential 0.5 lb a.e. per acre postemergent treatments up to the R1/R2 growth stage using a ground application method. The EPA conducted a comprehensive occupational exposure assessment as part of the dicamba reregistration in 2006 and concluded no unreasonable risk to agricultural workers from ground and aerial dicamba applications to soybean at rates up to 2 lb a.e. per acre when required personal protective equipment is worn (U.S. EPA, 2009b). See Section M.4.2 of the petition for additional detail. The application scenario evaluated by EPA encompasses the application method and rates for dicamba applied to MON 87708. Therefore, the deregulation of MON 87708 does not present a significant impact to the health of agricultural workers.

No Action Alternative

Under the no action alternative, MON 87708 would remain a regulated article and would not be commercially available to growers. It is likely that growers will continue to use herbicides in soybean production, and use the Roundup Ready soybean system and utilize additional herbicides where needed or recommended to control hard-to-control or glyphosate-resistant weeds. Growers may also choose to use other herbicide-tolerant soybean events, use a combination of alternative herbicides registered for use in soybean, or use traditional tillage practices. The continued use of dicamba on a small number of soybean acres would also be expected. Therefore, agricultural workers will be exposed to residues of dicamba and the alternative herbicides. On the basis of the analysis above, the deregulation in whole and no action alternatives involve the continued use of herbicides for production of soybean. Thus the impacts to agricultural worker health for either alternative are not considered different.

J.5.10. Potential Impacts to Plant and Animal Communities Including Threatened or Endangered Species, Soil Microorganisms and Biodiversity

Under the approval in whole alternative it is expected that MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode of action would aid in weed control or the

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implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

The potential for MON 87708 to harm plant, animal and microbial communities as well as threatened and endangered species (TES) was evaluated by considering the biology of soybean, biochemical information and experimental data. Soybean does not have any sexually-compatible relatives in the U.S. Therefore, any effect due to movement of the dicamba tolerance trait is confined to soybean (*Glycine max*). The biochemical information and experimental data included product characterization information, information from the MON 87708 DMO safety assessments, the history of environmental exposure to mono-oxygenases (the class of enzymes to which MON 87708 DMO belongs), results from the environmental assessment described in the petition, and the demonstration of compositional, agronomic and phenotypic equivalence to conventional soybean. An analysis of the effects of MON 87708 on plant, animal and microbial communities as well as threatened and endangered species is found below.

J.5.10.1. Gene Movement

Approval in whole alternative

In assessing the potential impact to plant and animal communities, the potential for gene movement and introgression from MON 87708 was evaluated because movement and establishment of the gene and trait to related species could have indirect impacts to plant and animal communities that extend beyond the original recipient organism. Additional discussion of the potential environmental impact due to gene movement may be found in Section IX.D of the petition. Monsanto considered two primary issues: 1) the potential for gene flow and introgression, and 2) the potential impact of introgression. The genus *Glycine* has approximately nine species, with commercial soybean (*G. max*) being placed in the subgenus *Soja* along with one other species, *G. soja*. *G. max* is sexually compatible only with *G. soja* and no other *Glycine* species. *G. max* is the only *Glycine* species located in the United States. Therefore, the probability of gene flow and introgression of MON 87708 into other species in the U.S. is essentially zero (Stewart et al., 2003); thus, the potential impact of MON 87708 introgression to sexually compatible relatives on plant and animal communities is nonexistent if MON 87708 were approved in whole. The approval in whole and no action alternatives are the same regarding potential impacts on gene movement.

No action alternative

As discussed above under the approval in whole alternative, soybean is not sexually compatible with any other plant species in the U.S. Therefore, the no action and approval in whole alternatives are the same regarding potential impacts on gene movement.

J.5.10.2. Animal Communities

Approval in whole alternative

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Soybean production systems in agriculture are host to many animal species. Mammals and birds, including migratory mammals and birds, may seasonally consume grain in the field, and invertebrates can feed on the plant during the entire growing season. Animals that feed primarily on soybean are seed-feeding insects and rodents found in agricultural fields. Rodents, such as mice or squirrels, may seasonally feed exclusively on soybean seeds. Thus, these animals may have a diet containing significant amounts of soybean seeds. Deer may also forage in soybean fields on forage and seed left after harvest (see Section IX.B.3.5 of the petition).

Under the approval in whole alternative, the cultivation of MON 87708 is not expected to impact soybean agronomic practices, with the exception of a change in dicamba use pattern. Cultivation of MON 87708 would not alter agronomic inputs or the number of soybean acres under cultivation, and may have a small positive effect on tillage cultivation practices. Potential impacts to animals from widespread cultivation of MON 87708 would be primarily based on the possible effects of the introduced MON 87708 DMO that provides tolerance to dicamba and a broadened application window of dicamba to MON 87708. For instance, if MON 87708 is deregulated, MON 87708 and MON 87708 DMO will be present in soybean consumed by animals. As discussed previously, there is no meaningful risk to animal or human health from dietary exposure to MON 87708 DMO. There are no known toxic properties associated with MON 87708 DMO. Furthermore, the composition of the seed and forage produced by MON 87708 is compositionally equivalent to conventional soybean. This information on the safety of MON 87708 DMO and composition of MON 87708 soybean seed, as detailed in petition, indicate that there would be no negative effects to mammals that consume MON 87708 seed and forage. Similarly, it is expected that there would be no impact to birds or other animals, including migratory birds and animals, that may consume soybean forage or soybean seed from MON 87708. During field trials with MON 87708, no biologically relevant changes in insect feeding damage were observed (see Section VII of the petition) indicating similar insect susceptibility for MON 87708 compared to conventional soybean. As MON 87708 exhibits no toxic effects on animals or insects, it is concluded that they will not be affected. In addition, the cultivation of MON 87708 does not impact the nutritional quality, safety or availability of animal feed (see Section J.5.11 of the petition).

Dicamba is currently registered for early season preemergence (early preplant) and late season postemergence (pre-harvest) soybean applications. Upon deregulation, dicamba could also be applied late preemergence (up to cracking) and in-season postemergence applications up to R1/R2 growth stage. Therefore, with the exception of late preemergent and in-season applications of dicamba, the agronomic practices used to produce MON 87708 will be the same as those used to produce commercially available soybean. Animals may be affected by dicamba runoff and/or herbicide spray drift. However, a comprehensive safety evaluation and risk assessment conducted by EPA concluded that dicamba has low toxicity to mammals, is not a carcinogen, does not adversely affect reproduction and development, and does not bioaccumulate in mammals (U.S. EPA, 2009b). An ecotoxicological risk assessment concluded that the use of dicamba does not pose an unreasonable risk of adverse effects to non-target species, such as birds and fish, when used according to label directions, nor does it pose an unreasonable risk of adverse effects to insects outside of the application area (U.S. EPA, 2009b). Furthermore, outside the cultivated soybean field, dicamba is unlikely to affect forbs and beneficial arthropods that are dependent on plants for survival. On the basis of this analysis, approval in whole of MON 87708 will not result in significant impacts on animals, including insects and beneficial arthropods that live in or near soybean fields containing MON 87708, and the approval in whole and no action alternatives are the same regarding potential impacts on animals and animal communities.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative dicamba tolerance trait would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use pattern in soybean. Adding other herbicides with different modes-of-action into the Roundup Ready system to mitigate development of glyphosate resistant weeds and control glyphosate resistant weeds would continue to remain an option. Additionally, conventional tillage may increase in some instances as an additional means to control problematic weeds.

In order to manage weeds, growers would continue to use available herbicides, some of which may pose greater potential risks to animals or insects than dicamba; and cultivation practices may increase. Therefore, the no action and approval in whole alternatives are similar regarding their effects to animals and animal communities.

J.5.10.3. Plant Communities

Approval in whole alternative

Soybean production systems in agriculture are host to many plant species. Likewise, the environment surrounding a soybean field varies in plant composition depending on the region. In certain areas, soybean fields may be bordered by other soybean, corn or other crops; fields may also be surrounded by wooded and/or pasture/grassland areas, as well as aquatic environments. Therefore, the types of vegetation, including weeds, around a soybean field depend on the area where the soybean is planted. A variety of weeds dwell in and around soybean fields; those species will also vary depending on the region where the soybean is planted.

If MON 87708 is approved in whole, it will not compete with plants found outside of agricultural production, because, like commercially available soybean, MON 87708 does not exhibit characteristics associated with weedy growth. Weeds within fields of MON 87708 will be managed using existing agricultural practices, including mechanical, cultural, and chemical control measures. This will include in-season (up to R1/R2 growth stage) applications of dicamba.

Plants on adjacent land have the potential to be affected by dicamba runoff and offsite movement (spray drift and volatility), but when herbicides are applied according to the FIFRA label application instructions, offsite impacts can be avoided. EPA concluded in the dicamba RED (U.S. EPA, 2009b) that existing label language to mitigate offsite

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movement was sufficient to reduce the potential risk of damage to adjacent vegetation. Since the proposed use pattern for dicamba on MON 87708 is consistent with the uses evaluated by EPA as part of the RED and the proposed label contains the offsite movement mitigation language, it is reasonable to conclude that the use of dicamba on MON 87708 also meets the FIFRA no unreasonable effects standard for drift and offsite movement. Nevertheless, Monsanto has taken additional steps to manage dicamba offsite movement as stewardship measures. In the pending application to EPA, Monsanto requested the use of dicamba on MON 87708 on the low volatility DGA salt formulation (U.S. EPA Reg. No. 524-582) and limited dicamba applications to ground application equipment. Monsanto also plans to further address the specific use of dicamba on MON 87708 with US EPA to evaluate whether additional measures, may be appropriate to address potential drift and offsite movement.

Therefore, the presence of the dicamba tolerance trait in MON 87708 and the use of dicamba is not expected to have a significant impact on surrounding plant communities, and the approval in whole and no action alternatives are similar regarding potential impacts on plant communities.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative dicamba tolerance trait would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use pattern in soybean. Adding other herbicides with different modes-of-action into the Roundup Ready system to mitigate development of glyphosate resistant weeds and control glyphosate resistant weeds would continue to remain an option. Growers will continue to use existing soybean herbicides to control glyphosate-resistant or hard-to-control weeds in soybean production fields. In addition, approximately 60% of soybean acres in the U.S. do not use conservation tillage practices, and it is anticipated that conventional tillage may increase in some instances as an additional means to control hard-to-control or resistant weeds. Therefore, the no action and approval in whole alternatives are similar regarding potential impacts to plants and plant communities.

J.5.10.4. Threatened and Endangered Species

Congress passed the Endangered Species Act (ESA) of 1973, as amended, to prevent extinctions facing many species of fish, wildlife, and plants. The purpose of the ESA is to conserve endangered and threatened species and the ecosystems on which they depend as key components of America‘s heritage. To implement the ESA, the U.S. Fish and Wildlife Service (USFWS) works in cooperation with the National Marine Fisheries Service (NMFS); other Federal, State, and local agencies; Tribes; non-governmental organizations; and private citizens. Before a plant or animal species can receive the protection provided by the ESA, it must first be added to the Federal list of threatened and endangered wildlife and plants.

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A species is added to the list when it is determined by the USFWS/NMFS to be endangered or threatened because of any of the following factors:

- The present or threatened destruction, modification, or curtailment of its habitat or range;
- Overutilization for commercial, recreational, scientific, or educational purposes;
- Disease or predation;
- The inadequacy of existing regulatory mechanisms; and
- The natural or manmade factors affecting its survival.

Once an animal or plant is added to the list, in accordance with the ESA, protective measures apply to the species and its habitat. These measures include protection from adverse effects of Federal activities. Section 7 (a)(2) of the ESA requires that Federal agencies, in consultation with USFWS and/or the NMFS, ensure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. It is the responsibility of the Federal agency taking the action to assess the effects of their action and to consult with the USFWS and NMFS if it is determined that the action "may affect" listed species or critical habitat. To facilitate APHIS' ESA consultation process, APHIS has met with the USFWS from 1999 to 2003 to discuss factors relevant to APHIS' regulatory authority and effects analysis for petitions for nonregulated status, and developed a process for conducting an effects determination consistent with the Plant Protection Act of 2000 (Title IV of Public Law 106-224). This process is described in a decision tree document, which have been included in recent Environmental Assessments (USDA-APHIS, 2011a) . APHIS has used this process to help fulfill its obligations and responsibilities under Section 7 of the ESA for biotechnology regulatory actions.

The potential impact of MON 87708 on federally listed Threatened or Endangered Species (TES) and species proposed for listing has been evaluated. In this analysis, the biology of MON 87708 and the agricultural practices associated with the cultivation of MON 87708 have been considered for potential adverse impact on TES and their critical habitats. Additionally, the potential indirect effects of dicamba applications due to either the introduction or non-introduction of MON 87708 on TES are discussed. While APHIS does not have statutory authority to authorize or regulate the use of herbicides, APHIS considers the evaluation of potential impacts on TES from the application of dicamba, as conducted by the EPA, as part of its environmental analysis under NEPA. APHIS' regulatory authority over GE organisms under the PPA is limited to those GE organisms for which it has reason to believe it may be a plant pest or those for which APHIS does not have sufficient information to determine that the GE organism is unlikely to pose a plant pest risk (7 CFR § 340.1).

Approval in whole alternative

It is expected that under the approval in whole alternative MON 87708 will be integrated into the Roundup Ready soybean system using traditional breeding techniques. For those

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acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode-of-action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers. Monsanto intends to make MON 87708 available for cultivation across all soybean growing regions in the U.S. The cultivation of MON 87708 is not expected to change the agronomic practices or expand soybean production acres beyond levels and geographies of current commercial soybean varieties. Several lines of evidence can be used to assess the potential for MON 87708 to have adverse effects on TES. The first line of evidence is based on the characteristics and evaluation of MON 87708 DMO and natural constituents present in MON 87708. The second line of evidence is the potential for TES species to interact with MON 87708. The third line of evidence is based on the biology and competitiveness of MON 87708 compared to conventional soybean. Finally, as the introduction of MON 87708 may result in increased use of dicamba in soybean (see Section VIII.H of the petition for additional details), potential indirect effects of dicamba on TES are also discussed, although it is the EPA's statutory obligation to comply with the ESA in the registration of this use.

J.5.10.4.1. Evaluation of MON 87708 and MON 87708 DMO

As previously noted, (see Section V.F.), bioinformatics analysis determined that MON 87708 DMO does not share amino acid sequence similarities with known allergens, gliadins, glutenins, or protein toxins. MON 87708 DMO was rapidly digested in *in vitro* assays using simulated gastric and intestinal fluids and did not show any adverse effects when administered to mice via oral gavage at levels far in excess of that reasonably expected to be consumed by humans or animals. Compared to conventional soybean, MON 87708 does not express any additional proteins or natural toxicants that are known to directly or indirectly affect a listed TES or species proposed for listing by the U.S. Fish and Wildlife Service. Compositional analysis of MON 87708 for nutrients and anti-nutrients indicated that the harvested seed and forage from MON 87708 were compositionally equivalent to conventional soybean. Thus, MON 87708 would not be expected to have any impacts on TES that would differ from conventional soybean.

J.5.10.4.2. Potential Interactions of TES with MON 87708

The only TES animal listed that occupies habitat that is likely to include soybean fields and that might feed on soybean is the Federally Endangered Delmarva Peninsula Fox Squirrel, *Sciurus niger cinereus*, found in areas of the mid-Atlantic Eastern seaboard.[35] It is known to utilize certain agricultural lands readily, and its diet includes acorns, nuts/seeds of hickory, beech, walnut, and loblolly pine, buds and flowers of trees, fungi, insects, fruit, and an occasional bird egg. Given its varied diet, the safety of MON 87708 DMO, and the demonstrated compositional, agronomic and phenotypic equivalence of MON 87708 to conventional soybean, it is concluded that no biologically significant changes to the habitat or diet of the Delmarva Peninsula Fox Squirrel are

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[35] Source is from website: http://ecos.fws.gov/tess_public/SpeciesReport.do; [Accessed May 14, 2009].

expected. Consequently, the planting of MON 87708 is not expected to impact the Delmarva Peninsula Fox Squirrel.

Additionally, MON 87708 has demonstrated no characteristics that would allow it to expand agricultural production into new natural areas where other TES animal species could be found. Consequently, the planting of MON 87708 is not expected to affect any TES animal species.

J.5.10.4.3. Potential Hybridization or Competition of MON 87708 with TES

Soybean is not native to the U.S., and MON 87708 is not sexually compatible with any federally listed TES or a species proposed for listing. Like other *G. max*, MON 87708 will likely be a poor competitor with native vegetation and will not survive outside of cultivation (Baker, 1965). Thus, MON 87708 is not expected to interbreed with any plant species or displace natural vegetation in the U.S.

J.5.10.5. Potential Impact of Dicamba on TES

As a result of joint discussions between USFWS and APHIS officials on June 15, 2011, the Agencies have agreed that it is not necessary for APHIS to perform an ESA effects analysis for the herbicide use associated with a biotechnology-derived crop. This is because EPA has both regulatory authority over the labeling of pesticides and the necessary technical expertise to assess pesticide effects on the environment under FIFRA. Similarly for MON 87708, since APHIS has no regulatory jurisdiction to authorize or regulate the use of dicamba by growers and the EPA has an application pending for the use of dicamba on MON 87708, the EPA will also have the obligation to conduct an ESA effects analysis for the use of dicamba on MON 87708. However, APHIS does consider the evaluation of potential impacts on TES from the application of dicamba as part of its environmental analysis.

In order to register a pesticide under FIFRA, the EPA must reach a conclusion that the pesticide will not cause an unreasonable adverse effect when used as intended. Thus, the current and future proposed uses of dicamba on soybean must meet this standard to be registered by the EPA. Monsanto has requested approval of the use of dicamba on MON 87708 by amending the label for EPA Registration Number 524-582 (as described in Appendix L, Section L.2.4). In the EPA's review of this registration request, they will apply the same statutory-based regulatory requirements as they do to all pesticides.

In the 2006 dicamba RED (U.S. EPA, 2009b), EPA discussed the changes in the registered use pattern of dicamba that were required to assure that dicamba meets the FIFRA regulatory standards of no unreasonable adverse effects for pesticides in the U.S. Accordingly, EPA reduced the maximum single application rate to 1.0 lb a.e. per acre with a maximum annual rate of 2.0 lb a.e. per acre (reduced from 2.8 lb a.e. per acre single and 7.7 lb a.e. per acre maximum annual rate, respectively). EPA went further in the RED to state that no specific additional mitigations for offsite movement were needed (U.S. EPA, 2009b).

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The EPA's new application rates, among other measures implement by EPA as part of the dicamba RED, provide protection to non-target organisms. Because the proposed use of dicamba on MON 87708 falls within the use rate limits established by EPA in the 2006 RED, it can be concluded that risks to non-target organisms from the use of dicamba on MON 87708 have been assessed.

Furthermore, Monsanto has conducted a species-specific analysis on threatened and endangered (TE) birds, mammals, amphibians, reptiles, terrestrial invertebrates, and non-moncotyledonous terrestrial and semi-aquatic plants. This refined analysis utilized dicamba- and species-specific information, in accordance with guidance and procedures outlined in the *Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency, Endangered and Threatened Species Effects Determinations*, published in 2004 (U.S. EPA, 2004), and methods utilized in more recent threatened and endangered species effects determinations conducted by the EPA (U.S. EPA, 2007b; 2008c). This analysis concluded that TE birds, mammals, amphibians, reptiles, terrestrial invertebrates, and monocotyledonous plants will not be adversely affected from environmental exposure to dicamba at levels anticipated from the use on MON 87708. A summary of the refined species analysis may be found in Appendix N of the petition. The summary and supporting detailed analyses have been provided to EPA ([redacted] 2011 and 2012; [redacted] 2012; [redacted] 2010; [redacted] 2012; [redacted] 2012).

For the remaining federally listed TE non-monocotyledonous terrestrial plants, less than one percent of potential soybean production acres (defined as all cultivated crop acres listed in the 2001 National Land Coverage database in states with reported soybean production [36]) are conservatively estimated to be in proximity to a TE non-monocotyledonous terrestrial plant species.[37] For the limited areas where a federally listed TE non-moncotyledonous terrestrial plant is in proximity to a MON 87708 field where dicamba may be applied, Monsanto has already undertaken steps to manage the offsite movement of dicamba (described in Section J.5.7) to further reduce potential impacts on these plant species. These measures include registering the use on MON 87708 on the low volatility DGA salt formulation of dicamba and limiting dicamba use on MON 87708 to ground application only. Monsanto will also consult with U.S. EPA in coming months to evaluate whether additional measures may be appropriate to address potential drift and offsite movement. Finally, upon commercialization of MON 87708, Monsanto will implement a web-based endangered species mitigation system, similar to PreServe.org, to further mitigate potential impacts of dicamba on TE non-monocotyledonous terrestrial plants. Therefore, the approval in whole and no action alternatives are similar regarding potential impacts on threatened or endangered species from dicamba use on MON 87708.

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[36] Potential soybean production acres include all land of Class 81 (cultivated crops) and Class 82 (pasture/hay) from the 2001 National Land Cover Database, in counties reporting soybean production in the 1997, 2002, and 2007 Ag Census.

[37] Based on species location information available from the FIFRA Endangeres Species Task Force (FESTF) Multi-Jurisdictional Database (MJD) and other state and federal information sources.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be widely grown. Under this alternative MON 87708 would not become integrated into the Roundup Ready soybean system and dicamba use would likely remain similar to today's use in soybean. Adding other herbicides with different modes-of-action into the Roundup Ready system to mitigate development of glyphosate resistant weeds and to control glyphosate resistant weeds would continue to remain an option. Alternatively, tillage may increase in some instances as an additional means to control problematic weeds.

Since other herbicides are currently available and used in soybean production, and would likely be used instead of dicamba, tillage practices would likely continue as a method of weed control. Therefore, the approval in whole and the no action alternatives are similar regarding their effects to TES.

J.5.10.6. Soil Microorganisms

Approval in whole alternative

Potential impacts to soil microorganisms can arise from the exposure to the introduced gene and expressed protein in the GE crop product. In addition, agricultural practices such as pesticide applications and tillage are known to impact soil microbial populations, species composition, colonization, and associated biochemical processes.

Soil microorganisms in general and symbiotic microbes associated with soybean roots are discussed in Section VII.C.4 and Appendix J, Section J.3.5.3 of the petition, and summarized here. The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. MON 87708 is not expected to alter the current agronomic practices for soybean cultivation. No adverse effects on soil microorganisms are associated with MON 87708 or its cultivation, nor do the characteristics of the MON 87708 DMO pose any concern to soil microorganisms. The *B. japonicum*-soybean symbiosis of MON 87708 was not changed either as a result of the introduction of the dicamba tolerance trait or as a result of the MON 87708-produced DMO.

Dicamba was registered as an agricultural herbicide in 1967 (U.S. EPA, 2009b) and has a long history of use. Impacts on soil microorganisms have not been raised as a significant concern, and results of standardized tests with dicamba and dicamba formulations did not indicate any long term effects on soil microorganisms (see Section M.5.6.3 of the petition). Results of standardized tests with dicamba and dicamba formulations indicate no long-term effects on functional processes of soil microorganisms (carbon respiration and nitrogen transformation) at rates proposed for dicamba on MON 87708 (European Commission, 2007a).

On the basis of these observations and in conjunction with related phenotypic measurements for MON 87708, no impact on soil microorganisms is expected from the

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cultivation of MON 87708. Therefore, the approval in whole and no action alternatives are the same regarding potential impacts on soil microorganisms.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles, would not be commercially grown and use of dicamba herbicide would likely remain similar to today's use pattern in soybean.

Adding other herbicides with different modes-of-action into the Roundup Ready system to mitigate development of glyphosate resistant weeds and control glyphosate resistant weeds would continue to remain an option. Additionally, conventional tillage may increase in some instances as an additional means to control problematic weeds.

Agricultural practices such as pesticide applications and tillage are known to impact soil microbial populations, species composition, colonization, and associated biochemical processes. However, alternative herbicides are already available and are used in soybean, and would likely be used instead of dicamba under the no action alternative. Similarly, approximately 40% of the U.S. soybean acres use conservation tillage and would likely continue to do so. Therefore, the no action and approval in whole alternatives are similar regarding potential impacts to microorganisms.

J.5.10.7. Biodiversity

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system with the potential for cultivation of soybean seed containing the MON 87708.

As confirmed in trials to evaluate plant growth and phenotypic characteristics, MON 87708 exhibits no traits that would cause increased weediness of soybean. Since soybean is not sexually compatible with any other plant species in the U.S., its unconfined cultivation would not lead to increased weediness of other sexually compatible relatives. Therefore, it is unlikely to have effects on non-target organisms common to agricultural ecosystems or TES recognized by the U.S. Fish and Wildlife Service and National Marine Fisheries Service, or to colonize adjacent non-agricultural ecosystems thereby compromising their biodiversity.

MON 87708 DMO originates from *S. maltophilia*, an organism that is ubiquitous in the environment. MON 87708 DMO shares sequence identity and many catalytic and domain structural similarities with a wide variety of oxygenases present in bacteria and plants currently widely consumed, establishing that animals and humans are extensively exposed to these types of enzymes. Bioinformatics analysis determined that MON 87708 DMO does not share amino acid sequence similarities with known allergens, gliadins, glutenins, or protein toxins. MON 87708 DMO was rapidly digested in *in vitro* assays using simulated gastric and intestinal fluids and did not show any adverse effects when administered to mice via oral gavage at levels that resulted in large margins of exposure.

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MON 87708 DMO demonstrates a high level of substrate specificity. Additionally, studies have shown no impact to NTOs such as beneficial and pest arthropods when exposed to MON 87708 DMO in the field. Taken together these data indicate low probability that MON 87708 DMO will have a significant impact on biodiversity.

The use of herbicides in agricultural fields is likely to indirectly impact biodiversity by decreasing weed species present in the field. Agricultural fields are purposefully managed to be weed-free resulting in greater economic benefit to the grower. In the U.S., 98% of soybean acreage was treated with an herbicide in 2006 (USDA-NASS, 2007b). Therefore, introduction of MON 87708 and treatment with dicamba is unlikely to affect the animal or plant communities found in commercial soybean production systems differently than those already occurring due to the use of herbicides in soybean fields. Dicamba has an established history of safe use in agriculture. For an overview of the environmental safety of dicamba, see Appendix M of the petition. Based on this analysis, it is concluded that the potential effect of approval in whole of MON 87708 on biodiversity would not differ from impacts associated with current agricultural practices used for production of soybean. Therefore, the approval in whole and no action alternatives are similar regarding potential impacts on biodiversity.

No action alternative

Under the no action alternative MON 87708 and its progeny would continue to be regulated articles and would not be commercially grown. Use of dicamba herbicide would likely remain similar to today's use pattern in soybean, and growers would likely continue to use alternative herbicides or incorporate more tillage in soybean production to manage hard to control weeds. Thus, the approval in whole and the no action alternatives are similar regarding potential impacts on biodiversity.

J.5.11. Animal Feed

The majority of the soybean cultivated in the U.S. is grown for animal feed and primarily fed as soybean meal. Soybean forage may also be used as feed for dairy cattle and livestock. Biotechnology-derived products may undergo a voluntary consultation process with the FDA prior to commercialization. Monsanto has completed the biotechnology consultation process with FDA for the safety and nutritional assessment of food and feed derived from MON 87708 soybean on October 11, 2011 (BNF No. 00125, Monsanto, 2011). As a part of its evaluation, FDA reviewed information on the identity, function, and characterization of the genes, including expression of the gene products in MON 87708 soybean, as well as information on the safety of the MON 87708 DMO and MON 87708 soybean.

Approval in whole alternative

The difference between the approval in whole and the no action alternative is expected to be integration of MON 87708 into the Roundup Ready soybean system using traditional breeding techniques. Under the approval in whole alternative, there is potential for cultivation of soybean seed containing the MON 87708 trait to proactively manage and

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prevent the development of herbicide resistant weeds. For those acres where glyphosate resistant weeds may already be present or where application of an herbicide with a different mode-of-action would aid in weed control or the implementation of weed resistant management practices, the cultivation of soybean containing the MON 87708 trait would be an option for growers.

Potential impacts to the safety of animal feed from widespread cultivation of MON 87708 would be primarily based on the possible effects of the introduced MON 87708 DMO that provides tolerance to dicamba and a broadened application window of dicamba to MON 87708. Upon deregulation, MON 87708 containing MON 87708 DMO and dicamba residues from the application of dicamba will be present in animal feed. As discussed previously, there is no meaningful risk to animal health from dietary exposure to MON 87708 DMO. There are no toxic properties associated with MON 87708 DMO. Furthermore, the composition of the seed and forage produced by MON 87708 is equivalent to conventional soybean. This information on the safety of MON 87708 DMO and composition of MON 87708 soybean seed as detailed in petition #10-SY-210U indicate that there would be no negative impact on the safety or nutritional quality of animal feed from the cultivation of MON 87708. The cultivation of MON 87708 will not change the number of soybean acres cultivated in the U.S., the extent in which soybean acres are cultivated will continue to be based on the same market-based drivers that exist today

As discussed previously, dicamba is presently applied to less than 1% of soybean acres using pre-plant and pre-harvest burn down applications. Under the approval in whole alternative, dicamba will be used on more soybean acres and a higher percentage of soybean-derived animal feeds will contain dicamba residues. However, dicamba residue levels in MON 87708 harvested seed or processed meal will be significantly lower compared to levels originating from the current pre-harvest soybean use (approximately 100-fold lower, based on <0.1 ppm residue in MON 87708 seed compared to established 10 ppm tolerance - see Appendix M, Section M.4.1.1 for residue levels in seed). As part of the pesticide tolerance setting process for dicamba (40 CFR 180.227), the EPA concluded that residues of dicamba up to 10 ppm in soybean seed are safe (reasonable certainty of no harm as defined by FFDCA) for animal consumption. Additionally, as discussed in detail in Section J.5.9.2, Monsanto has petitioned the EPA to establish new feed tolerances for soybean forage and hay to allow MON 87708 forage and hay to be fed to livestock. Dietary exposure to livestock from the feeding of MON 87708 soybean forage and hay does not result in an increase in the maximum dietary (feed) exposure of dicamba evaluated and deemed safe by EPA.

MON 87708, MON 87708 DMO and dicamba residues in MON 87708-derived feed components do not effect on the safety or nutritional quality of animal feed, therefore the deregulation of MON 87708 will not result in a significant impact on animal feed, and consequently to animal health. Therefore, the approval in whole and the no action alternatives are the same regarding their effects an animal feed.

No action alternative

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The no action alternative would not allow the widespread planting of MON 87708, and the use of dicamba herbicide would remain unchanged including the pre-harvest treatments which result dicamba residues in soybean seed up to the 10 ppm tolerance. Other herbicides are available and would be used in soybean as need to control weeds in conventional and herbicide-tolerant soybean. The availability of safe and nutritional animal feed from existing soybean crops, including crops containing dicamba or other herbicide residues from currently established uses, will continue. Therefore, the no action and approval in whole alternatives are similar regarding their potential impacts on animal feed.

J.6. Socioeconomic Effects

Approval in whole alternative

The decision to deregulate MON 87708 would allow for breeding of this product with conventional and previously deregulated biotechnology-derived soybean products of diverse genetic backgrounds. These varieties will include soybean with glyphosate tolerance (MON 89788; Roundup Ready 2 Yield soybean), to deliver products that enhance growers ability to manage weeds. It is expected that breeders and certified seed producers would use MON 87708 to develop varieties and to supply seed for planned commercial markets in the U.S. Monsanto anticipates that commercial use of MON 87708 will include export of soybean and soybean products, and has described import approval submission plans in Section I of petition #10-SY-210U. Monsanto's pre-launch stewardship plan for this product is described in Section VIII-L of the petition.

An extensive analysis of the socioeconomic impacts of herbicide-tolerant crops can be found in a recent series of articles published in the on-line journal AgBioForum.[38] Much of the information below has been summarized from this series of articles.

The adoption of herbicide-tolerant (Roundup Ready) soybean has been unprecedented since its commercialization in 1996. The technology was rapidly adopted by growers. Four years after being introduced, approximately 60% of U.S. soybean acreage was planted to Roundup Ready soybean; by 2005 over 80% of the soybean acres were planted to Roundup Ready soybean, and most recently in 2009 approximately 91% of soybean acres were planted to Roundup Ready varieties. Herbicide-tolerant crops have had a profound impact on agricultural production globally and similar adoption profiles have occurred in other geographies where herbicide-tolerant crops have been introduced (*e.g.*, Argentina, Brazil, Canada). Early efforts to understand the reason Roundup Ready soybean and other herbicide-tolerant crops achieved such rapid adoption focused on profitability, yield and costs (Carpenter and Gianessi, 2001). Information from recent grower surveys cite other advantages such as simplicity, convenience, flexibility and safety as some of the primary reasons for using Roundup Ready crops (Hurley et al., 2009). One of the most significant advantages of Roundup Ready cropping systems has

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[38] The source of information can be found at: http://www.agbioforum.org/v12n34/v12n34a00-frisvold.htm [Accessed May 19, 2010].

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been the reduction in labor. The reduction in labor allowed growers more free time to pursue other activities and freed up farm management time for non-farm income.

As with all herbicides, the intensive use of glyphosate in the absence of diverse weed management practices (i.e., other herbicide modes-of-action, mechanical cultivation, crop rotation or other cultural practices) has led to increased selection pressure and has contributed to weed shifts for the hard-to-control broadleaf weeds and/or the development of glyphosate-resistant weeds. Diversified weed management is recognized by Monsanto, academics and other weed science experts as the guiding principle for managing resistance and shifts in weed populations. Diversified weed management is the cornerstone of our stewardship messaging and weed management recommendations for Monsanto's product portfolio, including MON 87708 soybean. It is well recognized that in situations where there is diversity in weed control methods, few to no resistant weeds develop (Dukes and Powles, 2009; Beckie and Reboud, 2009). One strategy recommended by experts to prevent or delay the development of resistant weed populations is to diversify herbicide weed control methods.

MON 87708 was developed to provide soybean growers with a simple and flexible option to manage existing glyphosate-resistant weeds and better control of other hard-to-control weeds as well as delay or prevent further development of glyphosate-resistant broadleaf weeds and preserve the use of glyphosate in soybean production. Through traditional breeding methods, integration of MON 87708 into the Roundup Ready soybean system will allow for effective weed control through the application of glyphosate and dicamba. While either herbicide can be applied independently, it is envisioned that both glyphosate and dicamba will be tank mixed to simplify the application. Growers may also choose to treat or not treat with either herbicide depending on the unique situation for each farm and their overall diversified weed management plan.

Monsanto considered the properties of herbicides available for use in soybean in developing a second herbicide-tolerance trait to complement the glyphosate tolerance trait. Dicamba was selected because it is very complementary to glyphosate in terms of the spectrum of broadleaf weeds controlled, its postemergence activity and because very few weeds have developed resistance to dicamba over many decades of use. Dicamba adds another postemergence herbicide mode-of-action for growers to use in their weed control system, thus diversifying the spectrum of weed control options and providing better overall weed control superior to current practices.

The socio-economic benefits of MON 87708 are expected to complement and help maintain the benefits growers have realized using the Roundup Ready system. These include time and labor savings to growers through the simplicity and flexibility of the dicamba/glyphosate weed control system over alternative herbicides that are authorized for use in soybean production. In addition, the ability to use dicamba in combination with glyphosate will further preserve the benefits the Roundup Ready system has provided in the form of increasing adoption of conservation tillage acres. Monsanto and academics recommend the use of a third herbicide mode-of-action with soil residual activity as part of a comprehensive weed resistance management program to assure that

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at least two effective modes-of-action are always used in the cultivated soybean field. The cultivation of MON 87708 provides an efficient and effective method to delay or prevent the development of glyphosate- or dicamba-resistant weeds, as well as weeds resistant to other herbicide class of chemistries, and is expected to outweigh additional costs of controlling resistant weeds through the dicamba/glyphosate weed control system.

No action alternative

Under the no action alternative, MON 87708 would not be available to commercial growers. Alternative herbicides would remain available for control of broadleaf weeds in soybean fields, and these herbicides will likely be used instead of dicamba. Monsanto, university extension services and other weed science organizations such as HRAC promote the use of integrated, diversified weed management systems with soybean growers; these recommendations include the rotation of herbicides with different modes-of-action or herbicide mixtures containing multiple modes-of-action in their weed management program. Growers have increasingly adopted these diversified weed management practices, specifically use of multiple modes-of-action, in major corn and soybean geographies of the U.S. (see Section J.3.3.6). Thus it is anticipated that the cost of the weed management to the soybean grower will not significantly change as a result of the cultivation of MON 87708. Technology providers are developing other herbicide-tolerant crops that will likely be combined with glyphosate-tolerant crops to simplify weed control which may provide similar socioeconomic benefits to growers as those described above for MON 87708. On the basis of the above analysis, the approval in whole and no action alternatives are similar regarding potential increased costs and complexity in weed control for soybean growers. However, the no action alternative would not provide as many options to prevent or delay the development of herbicide-resistant weeds, and not take advantage of MON 87708 to help sustain the long-term agronomic, environmental and socioeconomic value and benefits of the Roundup Ready soybean system.

J.7. Cumulative Effects

A cumulative impact may be an effect on the environment which results from the incremental impact of the proposed action when added to other past, present, and reasonably foreseeable future actions.

J.7.1. Conventional Breeding with Other Biotechnology-derived or Conventional Soybean

The potential effects associated with a determination of nonregulated status of a biotechnology-derived crop in combination with the future production of crop varieties with different GE traits that are no longer subject to the regulatory requirements of 7 CFR part 340 (i.e., "stacked" traits) would be considered a cumulative impact.

Approval in whole alternative

As previously mentioned, several biotechnology-derived soybean products have been deregulated or are under consideration for deregulation, and a list of the events

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deregulated by USDA is presented in Table J-4. Once deregulated, MON 87708 may be bred with these deregulated biotechnology-derived soybean products as well as with conventional soybean, creating new improved varieties. APHIS has determined that none of the individual biotechnology-derived soybean products it has previously deregulated displays increased plant pest characteristics or creates potentially significant impacts on the human environment. APHIS has also concluded that any progeny derived from crosses of these deregulated biotechnology-derived soybean products with conventional or previously deregulated biotechnology-derived soybean are unlikely to exhibit new plant pest properties. This presumption that combined trait biotechnology products are unlikely to exhibit new characteristics that would pose new plant pest risks or potential environmental impacts not observed in the single event biotech product is based upon several facts. Namely 1) stability of the genetic inserts is confirmed in each single event product across multiple generations; 2) stability of each of the introduced traits is continually and repeatedly assessed as new combined trait varieties are created by plant breeders and tested over multiple seasons prior to commercial release; 3) combined trait products are developed using the well established process of conventional breeding that has been safely used for thousands of years to generate new varieties; and 4) in both principle and practical application in the field, it has been shown that two unrelated biotechnology traits combined together by conventional breeding, do not display new characteristics or properties distinct from those present in the single event biotech products.

Demonstrated Genetic and Phenotypic Stability

An assessment of the stability of the genetic insert in MON 87708 is discussed in Section IV of petition #10-SY-210U and summarized here; refer to the petition for more detail. Generational stability analysis was assessed by Southern blot analysis and demonstrated that the genetic insert present in MON 87708 was maintained across the five breeding generations evaluated. These data demonstrate that MON 87708 is stable in its progeny. Having established that the genetic material is stable and inherited in a Mendelian fashion, and based on experience with MON 87708 in Monsanto's plant breeding program over the course of many generations and many field seasons[39], it is concluded that the phenotype of MON 87708 is likewise stable. There are numerous examples in the literature that confirm that GE events and their associated phenotypes and overall characteristics are stably inherited across generations and across genetic backgrounds, including when they are combined by conventional breeding to produce combined trait products (McCann et al., 2005, Ridley et al., 2011, Zhou et al., 2011).

Combined Trait Product Performance in Principle and in Practice

Conventional plant breeding is routinely used to improve crop performance and is specifically employed to develop plant varieties that fit particular environments and production practices (Powell et al., 2003). The same biological and selective principles used for conventional and single GE event variety development are used to combine previously approved GE events. When conventional breeding is used to generate varieties with combined GE events, these varieties are screened over multiple generations

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[39] Field trials have been conducted with MON 87708 since 2005.

and across diverse growing environments. Typically, product performance and agronomic features are evaluated and crop characteristics such as yield, field performance, and disease resistance are measured and tested to ensure that the traits are stable, heritable, and express the desired phenotype under a wide range of environmental conditions. The phenotypic characteristics evaluated during the screening of new combined GE event candidate varieties are the result of the plant's genotype and are the culmination of the complex metabolic pathways that are activated in response to environmental conditions. The evaluation of phenotypic characteristics allows breeders to assess and screen for potential unintended effects produced as a result of the various traits (both GE traits and other inherent traits) combined in the variety. Selection during the conventional breeding process is valuable in removing undesirable characteristics and thereby helps to maintain the safety and quality of the food and/or feed product (Cellini et al., 2004; NRC, 2004; WHO, 1995).

When assessing the safety of combined GE events, it is important to consider international guidance regarding conventional breeding and assessments of the substantial equivalence of GE events combined by conventional breeding. For example, the World Health Organization concludes that a substantial equivalence conclusion can be maintained in a combined GE trait variety if substantial equivalence had been demonstrated for each of the single event parents. Specifically, they argue that ''...if substantial equivalence has been demonstrated both for a [genetically engineered] tomato with a gene producing a delayed ripening phenotype and for a [genetically engineered] tomato with a gene for herbicide resistance, then crossing these two varieties would result in a new variety that would be expected to be substantially equivalent to the parents'' (WHO, 1995). Additional international groups, including the Food and Agriculture Organization/World Health Organization (FAO, 1996), International Seed Federation (ISF, 2005), and CropLife International (CLI, 2005) similarly advocate basing the safety of combined GE events on the safety of the parental GE events. The FDA has stated that ''narrow crosses are unlikely to result in unintended changes to foods that raise safety or other regulatory questions'' – ''including narrow crosses between different rDNA-modified [GE] lines'' (U.S. FDA, 2001).

Thus, the data packages that are developed for single GE events are useful in establishing the safety of the combined GE event product. Accordingly, single GE events previously assessed to be as safe as their conventional counterparts should continue to be safe when combined through conventional plant breeding. As a result, the rigorous safety assessments and plant pest risk assessments conducted on single GE events, which were deemed to pose no more risk than their conventional counterparts, also can be used to predict the safety and potential risk of the combined GE event product. As described below, this assertion is supported by direct experience gained through the commercial planting and utilization of combined GE event products as well as a body of information collected to support authorizations where combined GE event products require additional assessment.

There are many examples of combined trait biotech products that have been produced commercially on millions of acres without incident over the past decade in both the US

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and in other countries[40]. In the US, there are over 30 combined trait products that have been made commercially available. In 2011, 49% of the total corn acres planted (92 M acres) and 58% of total cotton planted (13M acres) contained multiple (2 or more) GE events (USDA-ERS, 2011)[41]. Combined trait biotech products were planted on 40 million hectares or 25% of the global biotech area of 160 million hectares in 2011[42]. The safety of commercially available combined trait biotech products has been well-demonstrated in multiple independent reports that document the continually increasing acceptance and use of these products by farmers globally (Brookes and Barfoot, 2009; James, 2009; Lemaux, 2008; Sankula, 2006).

In addition, regulatory agencies in some countries request additional characterization of combined GE events and comparisons to single event parental controls and conventional comparators. These additional studies may include analysis of phenotype, molecular characteristics, protein characteristics, morphology and compositional evaluation. Analyses of combined GE events compared to parental controls have consistently revealed the following: no phenotypic differences from parental events; molecular characteristics that are the same as parental events with all events inherited stably; levels of introduced proteins comparable to the single event parents; no morphological differences compared to parental events; compositional equivalence based on nutrient and anti-nutrient evaluations, and no pleiotropic or toxic effects compared to the conventional non-GE crop (Pilacinski et al., 2011).

Summary

Traditional soybean breeding has an established history of safe use, and use of MON 87708 in breeding programs is expected to behave in a manner similar to other conventional traits and biotechnology-derived traits. Given that there have been no plant pest characteristics associated with MON 87708, or with any of the previously deregulated events listed in Table J-5, no significant impacts are expected to other soybean through the use of MON 87708 in breeding programs and in combination with any of the previously deregulated biotechnology-derived soybean products.

All biotechnology-derived soybean products on the market today have satisfactorily completed the FDA consultation process established to review the safety of foods and feeds derived from biotechnology-derived crops for human and animal consumption (see Table J-5). As mentioned previously, MON 87708 is intended to be combined with MON 89788 (Roundup Ready 2 Yield soybean) through traditional breeding. MON 87708 is expected to be utilized broadly in future additional combined trait soybean products, and thus will likely be bred with other biotechnology-derived soybean products that have been deregulated or have deregulation petitions pending before APHIS (*e.g.*, MON 87701, MON 87705, MON 87769; see Table J-4 for current status). No impacts to public health (*e.g.*, food or feed safety) are expected due to combination of these events through conventional breeding because the deregulated events have or will

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[40] See http://www.biotradestatus.com for list of combined trait products that have previously been commercialized.

[41] See http://www.ers.usda.gov/data/biotechcrops/adoption.htm

[42] http://www.isaaa.org/resources/publications/briefs/43/executivesummary/default.asp

have completed a safety consultation with FDA and on the basis of knowledge of the type of modifications made to each of the deregulated events, and to the events under review, the biochemical pathways are unrelated to the trait introduced in MON 87708 and therefore not expected to interact or result in the production of novel properties or constituents.

The decision to approve in whole MON 87708 would also allow for breeding of this product with conventional soybean of diverse genetic background. No impacts to public health (*e.g.*, food or feed safety) or environmental safety are expected due to the breeding of MON 87708 with these other soybean because these varieties have an established history of safe use.

Based on the above analysis, the approval in whole and no action alternatives are similar regarding potential cumulative impacts associated with the conventional breeding of MON 87708 with other conventional or biotechnology-derived soybean products.

No action alternative

Under the no action alternative, MON 87708 would not be used to produce new soybean varieties or in the commercial production of soybean because the trait would remain regulated. There are no effects that have been identified from combining MON 87708 with other Monsanto biotechnology-derived soybean that have been deregulated by USDA; therefore, the no action and approval in whole alternatives are similar regarding their potential cumulative impacts associated with conventional breeding with other soybean products.

J.7.2. Conservation Tillage

Approval in whole alternative

The single most damaging effect on land due to agriculture is loss of soil caused by tillage. Tillage is primarily performed for seed bed preparation and has the added benefit as a weed control measure. Roundup Ready crops, with Roundup Ready soybean being the most widely adopted, have enabled significant implementation/adoption of no-till or reduced tillage methods for weed control (Duke and Powles, 2009).

In 1995, before the introduction of Roundup Ready soybean, approximately 27% of the U.S. soybean acres used no-till production. By 2004, no-till acreage increased to 36% of the total soybean acres (Sankula, 2006). The most recent surveys indicate that 39% of the soybean acres are produced using no-till methods (CTIC, 2007). A few states provide statistics on the adoption of no-till acres in their state. In 2006 in Illinois, no-till farming was used on 51% of the soybean acres. The University of Illinois Extension Service attributed that figure to the fact that 90% of the state's soybean acres were planted to Roundup Ready soybean varieties, along with other factors, such as high fuel prices, improved equipment, higher yields using no-till practices, and better grower awareness of the advantages to soil and water quality from no-till farming. Approval in whole would allow for continued adoption and preservation of conservation tillage methods resulting

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in positive cumulative environmental impacts. Therefore, the approval in whole and no action alternative are similar regarding the potential cumulative impacts on conservation tillage practices

No action alternative

Under this alternative, MON 87708 would not be grown commercially and growers would not be able to utilize dicamba to the same extent as they would if APHIS granted approval in whole to MON 87708. This alternative would limit grower's options regarding the selection of herbicides available for use in conservation tillage. This option could potentially result in an increased use of tillage over time and potential loss of no-till acres in some soybean fields, thus decreasing the use of conservation tillage methods and environmental benefits associated with conservation tillage. Overall, the no-action and approval in whole alternatives are similar regarding the potential cumulative impacts on conservation tillage practices.

J.7.3. Resistant Weeds

Approval in whole alternative

Another cumulative effect includes the potential for development of herbicide-resistant weeds, including weed populations with multiple resistance. Integration of MON 87708 into the Roundup Ready soybean system has the potential to delay or prevent development of dicamba- and glyphosate-resistant weeds, as well as resistance to other herbicide classes such as PPO herbicides. These issues have been discussed in Section J.5.3.1 and in Appendix K of petition #10-SY-210U, but warrant additional discussion under the assessment of cumulative effects. The development of resistant weed populations occurs over a period of time (Heap, 2009), and is an foreseeable consequence of herbicide use in the absence of diverse weed management practices as is discussed in additional detail in Section J.3.3.6. One of the strategies recommended by experts to prevent or delay the development of resistant weed populations is to diversify weed control methods. The use of herbicides such as dicamba in conjunction with glyphosate provides growers with an herbicide system with two different modes-of-action. Thus, it is foreseeable that integration of MON 87708 into the Roundup Ready soybean system with the use of dicamba and glyphosate together would have a low probability for increases in new weed populations developing resistance to either glyphosate or dicamba. In addition there would be the potential for fewer new species to evolve or develop resistance for either herbicide compared to a glyphosate or dicamba herbicide system alone. In the MON 87708 weed management system the use of glyphosate is not expected to increase. Even thought there will be an increase in the use of dicamba, it is clear that in situations where there is diversity in weed control methods, there will be a low probability for resistant weeds to develop (Dukes and Powles, 2009; Beckie and Reboud, 2009). In the unlikely case that broadleaf weeds were to develop with resistance to dicamba or with accumulated resistance to both glyphosate and dicamba, existing cultivation and alternative herbicide tools (see Section VIII.F.1 for description of alternative herbicides) would remain potential options to provide effective control.

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Therefore, the approval in whole and no action alternatives are similar regarding potential cumulative impacts on weed resistance.

No action alternative

Other herbicide options for weed resistance management are available to growers. Under the no action alternative, grower's options regarding the selection of herbicides available for use to control weeds in soybean and specifically herbicides with different modes-of-action would be more limited than the approval in whole alternative as a result of the inability to use dicamba in the weed management system for soybean. Other soybean herbicides are available to growers to use either with or without the dicamba-glyphosate tolerant soybean system, and will remain available to growers in the future. However, herbicide weed management systems under the no action alternative are not as efficient and effective for managing resistant weeds and incorporating additional herbicide modes-of-action. Thus, it is reasonable foreseeable that some increase in the development of additional herbicide-resistant weed populations or development of new herbicide resistant weed species compared to the approval in whole alternative will result. Therefore, the no action and approval in whole alternatives are similar regarding the potential cumulative effects on weed resistance.

J.8. Summary

MON 87708 has been thoroughly characterized and the extensive body of information presented in Sections I through IX of the petition demonstrate that MON 87708 does not present a plant pest risk, has no significant impact on threatened and endangered species or biodiversity, and will not impact the commercial interests of soybean growers or those involved in the marketing and sale of soybean and soybean products. The amount of land devoted to farming (specifically to soybean) has not changed with the introduction of biotechnology-derived crops. Similarly, no significant change in the use of agricultural land or amount of land devoted to farming would be expected to occur with the commercial introduction of MON 87708 integrated into the Roundup Ready soybean system. MON 87708 integrated into the Roundup Ready soybean system will offer growers the opportunity to expand the use of dicamba to late preemergence (up to cracking) and postemergence in-crop applications and, thereby, potentially delay or prevent the development of dicamba- and glyphosate-resistant weeds as well as resistance to other soybean herbicides in U.S. soybean fields. Other cultivation practices typically employed for production of commodity soybean, and management practices will remain unchanged. Growers are accustomed to the use of herbicides in their soybean production systems. For these reasons, the proposed action to grant nonregulated status to MON 87708 does not represent a significant impact to the environment.

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Appendix K: Herbicide Resistance

K.1. Introduction

Based upon theory of natural selection, plant populations can develop resistance to an herbicide due to the selection of individuals that carry specific genes that can render those individuals unaffected by the typical lethal effects of an herbicide. The application of an herbicide to the plant does not, itself, cause a mutation in subsequent generations. Rather, over time, those few plant biotypes containing resistant gene(s) become dominant in the population with repeated use of the herbicide in the absence of other control methods, such as use of other herbicides and/or use of cultural control methods. The development of resistant populations is common to all herbicides. The probability for resistance to develop is a function of: frequency of resistant allele(s)[43], mechanism of resistance, dominance or recessive nature of the resistant allele(s), relative fitness of the resistant biotype, and frequency or duration of herbicide use in the absence of other control methods (Beckie, 2006; Jasieniuk, et al.,1996; Sammons et al., 2007). The probability of resistance is not the same for all herbicides, with some herbicides (*e.g.*, ALS and ACCase classes) exhibiting resistance more quickly than other herbicides (*e.g.* auxin class , glyphosate, dinitroanilines class).

Herbicide resistance can become a limiting factor in crop production if the resistant weed population cannot be controlled with other herbicides or cultural practices. In general, this has not been the case for any herbicide. In most crops, there are multiple herbicide options for growers to use. However, good management practices to delay the development of herbicide resistance have been identified and are being actively promoted by the public and private sectors (HRAC, 2010) and are being implemented by growers.

Monsanto considers product stewardship to be a fundamental component of customer service and business practices. Stewardship of the dicamba herbicide to preserve its usefulness for growers is an important aspect of Monsanto's stewardship commitment. Although herbicide resistance may eventually occur in weed species when an herbicide is widely used, resistance can be postponed, contained and managed through research, education and good management practices. These are the key elements of Monsanto's approach to providing stewardship of dicamba used on MON 87708 integrated into the Roundup Ready soybean system. Monsanto will invest in research, and grower/retailer education and training programs to provide information on best practices to manage dicamba weed resistance in soybean production. This appendix provides an overview of Monsanto's approach to the development of best management practices to mitigate dicamba weed resistance. Monsanto works closely with weed scientists in academia and with other companies to research and develop best management practices and to uniformly communicate such practices to growers. Evidence of this cooperative effort is the recent development and posting of herbicide resistant training modules on the WSSA website (www.wssa.net) and the publication of guidelines by the Herbicide Resistance Action Committee (HRAC) on their website (www.hracglobal.com).

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[43] An allele is any of several forms of a gene, usually arising through mutation, that are responsible for hereditary variation.

K.2. The Herbicide Dicamba

Dicamba (3,6-dichloro-2-methoxybenzoic acid) is classified as a benzoic acid herbicide belonging to the synthetic auxin group of herbicides (HRAC, 2010). The herbicides in this group act as growth regulators similar to endogenous indole acetic acid (IAA) but are structurally diverse. The synthetic auxin group includes five chemical families (benzoic acid, pyridine-carboxylic acid, quinoline carboxylic acid, phenoxy-carboxylic acid and a separate class which includes one herbicide, benazolin ethyl). In addition to dicamba, specific herbicides in this group include 2,4-D, 2,4-DB, mecoprop, MCPA, clopyralid, picloram, quinclorac and several other active ingredients. Dicamba and other synthetic auxin herbicides are classified in Herbicide Group 4 by the Weed Science Society of America (HRAC, 2009). Most herbicides in this group are active on broadleaf weeds only, but a few have significant activity on grasses, *e.g.*, quinclorac. The specific site of action among the different chemistry families may be different. Dicamba provides preemergence and postemergence control of over 95 annual and biennial broadleaf weed species and control or suppression of over 100 perennial broadleaf and woody species[44]. Dicamba is not active on grass weeds and is often used in combination with other herbicides to provide broad spectrum weed control.

Dicamba herbicide was commercialized in the U.S. for agricultural use in 1967 and is currently labeled for preemergence and/or postemergence weed control in corn, soybean, cotton, sorghum, small grains (wheat, barley and oats), millet, pasture, rangeland, asparagus, sugarcane, turf, grass grown for seed, conservation reserve program land, and fallow cropland (U.S. EPA, 2009). Dicamba is sold as standalone formulation which can be tank mixed with one or more active ingredients depending upon the crop and the weed spectrum. Dicamba is also sold as a premix formulation with other herbicides.

Dicamba kills plants by mimicking naturally-occurring plant growth hormones called auxins, thereby destroying tissue through uncontrolled cell division and growth (Ahrens, 1994). Ahrens (1994) further states that dicamba has been found to affect cell wall integrity and nucleic acid metabolism whereas in other cases it has been found to increase cell wall permeability, leading to cell enlargement. At low concentrations, dicamba has been found to increase synthesis of DNA, RNA, and proteins, resulting in altered cell division and growth. At high concentrations, inhibition of cell division and growth occur. In general dicamba and other synthetic auxin herbicides have been found to affect multiple plant physiological systems. The molecular mechanism of auxin action is still not known in detail nor completely understood (Devine et al., 1993, Jugulam et al. 2011). However, Grossmann (2010) in a review of auxin herbicides, outlined a proposed mechanism and mode of action for auxin herbicides and IAA at supraoptimal endogenous concentrations in dicot plant species. The proposal was based upon recent identification of receptors for auxins and hormone interaction in signaling between auxin, ethylene and the upregulations of abscisic acid biosynthesis which would account for a large part of the various auxin-herbicide-mediated responses that are seen in sensitive dicots. In addition research has indicated that there is a high level of redundancy in auxin receptors

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[44] Clarity product label http://www.cdms.net/LDat/ld797002.pdf

which may account for the lack of development of widespread resistance to this herbicide group (Walsh et al., 2006).

Dicamba is taken up by plants through the roots, stems, and foliage (Ahrens, 1994; NPIC, 2002). Dicamba translocates to all plant tissues but accumulates in growing tissues. Translocation of dicamba is typically slower in tolerant plants such as grasses compared to broadleaf plants. Dicamba has a relatively low soil-binding coefficient.

K.3. Herbicide-Resistant Weeds and Resistance Management Strategies

The development of herbicide-resistant weeds is not a new phenomena and resistance is not limited to certain select herbicides. In 1957, the first U.S. herbicide-resistant weed, a spreading dayflower biotype resistant to 2,4-D, was identified in Hawaii (Heap, 2010). Currently, there are 73 individual weed species that have known herbicide-resistant biotypes to one or more herbicides in the U.S. For example, there are 42 weed species resistant to ALS herbicides, 15 to ACCase inhibitors, 24 to photosystem II inhibitors, and 10 to glycine herbicides (Heap, 2010). Growers have been managing herbicide-resistant weeds for decades with the use of alternative herbicides and/or cultural methods such as tillage or crop rotation.

The occurrence of an herbicide-resistant weed biotype does not end the useful lifespan or preclude the effective use of the herbicide in question as part of an overall diversified weed management system. The three herbicide classes with the highest number of resistant species, ALS, ACCase and triazine herbicides, are still effectively used by growers today.

It is important to distinguish herbicide resistance from herbicide tolerance. A herbicide-tolerant weed species is one that is naturally tolerant to a herbicide, for example a grass species is not killed by the application of a broadleaf herbicide. Furthermore, certain weed species, while neither resistant nor tolerant, are inherently difficult to control with a particular herbicide, requiring more careful herbicide use and weed management practices.

Since the first confirmed cases of herbicide resistance, research has been directed at determining which practices are best for managing existing resistance situations and how best to reduce the development of herbicide resistance. Resistant management practices most often recommended by University/Cooperative Extension Service (CES) and industry are: 1) use of multiple herbicide modes-of-action in mixture, sequence, or in rotation, 2) crop rotation, 3) use of cultural control measures such as tillage and time of planting, and 4) use of the labeled herbicide rate at the recommended timing of application (Gressel and Segel, 1990; Beckie, 2006). Recent research by Beckie and Reboud (2009) indicates that in some cases herbicide mixtures offer a better management option than rotating herbicides. Simultaneously using two herbicides with different modes-of-action significantly reduce the probability of weeds developing resistance to either or both herbicides (Beckie and Reboud, 2009). Crop rotation is also an effective method for resistance management due to the fact that it fosters the use of additional herbicide modes- of-action and, potentially, use of additional cultural practices to manage weeds over time. The use of multiple methods of weed control in a single location is the technical basis for developing management programs to delay the development of resistance. This general concept has been referred to as applying "diversity" within a crop or across a crop rotation (Beckie, 2006; Powles, 2008).

It is generally accepted that conservation tillage practices (minimum-till and no-till) create environments where herbicide resistance is more likely to develop (Beckie, 2006). This is probably due to selection pressure put on weeds by herbicides in these non-diverse environments and the absence of tillage as a cultural weed management practice to supplement herbicide use. However, this is not always the case. Legere et al. (2000) found that an increase in the use of ACCase inhibitors in a conservation tillage system (*e.g.* aryloxyphenosy propionates and phenylpyrazolines herbicide families) did not result in an increased incidence of wild oat populations resistant to ACCase inhibitors. In conclusion, conservation tillage practices should not be considered a primary contributing factor to the development of resistance in all cases

K.4. Characteristics of Herbicides and Herbicide Use Influencing Resistance

While the incidence of weed resistance is often associated with repeated applications of an herbicide, the actual probability for the development of resistant populations is related, in part, to the specific herbicide active ingredient, chemical family and the herbicide group. Some herbicides are more prone to the development of resistance than others (Heap, 2010). The graph in Figure K-1 illustrates the global instances of weed resistance to various herbicide groups. The different slopes of observed resistance are largely due to the factors described above, which relate to the specific herbicide active ingredient as well as to the group and herbicide family and its function.

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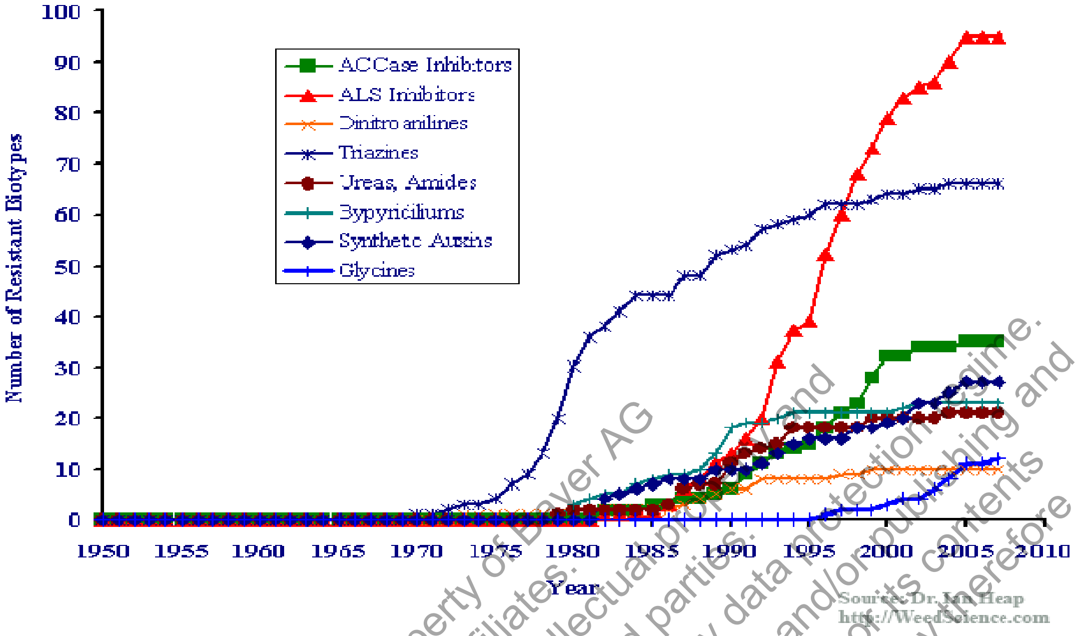

Figure K-1. Weed Resistance to Various Herbicide Families[1]

As can be seen in Figure K-1, weed resistance to the synthetic auxin group of herbicides has been slower to develop than for other herbicide groups even though these were the first synthetic herbicides discovered and used commercially. Possible reasons for this are discussed below.

[1] Global number of resistant biotypes

K.5. Mechanisms of Resistance and Inheritance of Resistance

To date, the three known basic mechanisms by which weed species develop resistance to a herbicide have been identified: 1) target site alteration (target site), 2) enhanced metabolism of the herbicides (metabolism), and 3) reduced absorption and/or translocation of the herbicide such that the herbicide does not get to the site of action within the plant cell (exclusion) (Sammons et al., 2007).

Herbicide resistance via target site alteration is the most common resistance mechanism among the various herbicide groups and chemical families. It has been found that a target site mechanism is the most common mechanism for ALS inhibitors, ACCase inhibitors, and triazines, but is less common for other herbicide groups, such as glyphosate (Powles and Yu, 2010). The most common type of target site alteration is one where amino acid substitution(s) in the protein that is the target of the herbicide occurs such that the alteration prevents the binding of the herbicide to the protein and as a result the activity of the targeted protein is not altered and the plant grows normally.

In the case of synthetic auxin herbicides, resistance has been speculated to be due to mutation(s) in genes encoding an auxin-binding protein causing reduced herbicide binding (Zheng and Hall, 2001; Goss and Dyer, 2003). In several studies, differential

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herbicide absorption, translocation, and metabolism were ruled out as possible mechanisms of resistance in kochia (Cranston et al., 2001) and in wild mustard (Zheng and Hall, 2001). However, current research has not presented convincing evidence for a single mechanism of resistance and this inability to elucidate the mechanism of resistance may be due to a lack of thorough understanding of auxin mechanism of activity (Jasieniuk et al., 1996). Walsh et al. (2006) identified seven alleles at two distinct genetic loci that conferred significant resistance to picolinate auxins (picloram) in *Arabidopsis*, yet had minimal cross-resistance to 2,4 D and IAA.

Multiple mechanisms for inheritance of dicamba resistance have been reported in the literature. Jasieniuk et al. (1995) reported results indicating that inheritance of dicamba resistance in wild mustard is determined by a single, completely dominant nuclear allele. However, Cranston et al. (2001) reported results indicating that dicamba resistance in kochia is determined by a quantitative trait (two or more genes).

In summary, the slow development of weed resistance to synthetic auxin herbicides may in part be due to their proposed multiple sites of physiological action in plants (Jasieniuk et al., 1996) and to the possibility that inheritance, at least in some species, is determined by a quantitative trait (Cranston et al., 2001).

K.6. Weeds Resistant to Dicamba

As noted earlier, like other herbicides, the use of dicamba may lead to the development of dicamba-resistant weed species. To date there are four species with known resistant biotypes to dicamba in the U.S./Canada after over 40 years of use; common hempnettle (*Galeopsis tetrahit*), kochia (*Kochia scoparia*), prickly lettuce (*Lactula serriola*) and wild mustard (*Sinapis arvensis*) (Heap, 2010). Additionally, a population of lambsquarters (*Chenopodium album*) has been confirmed to be resistant in New Zealand for a total of five species worldwide with confirmed resistant biotypes to dicamba. For the synthetic auxin group of herbicides there is a total of 29 species globally with biotypes having confirmed resistance to at least one member of this group but only eight species in the U.S. and four species in Canada (Heap, 2010). All of these populations are, but for two (wild carrot in OH and MI and waterhemp in Nebraska), found in western states or western Canadian provinces. In some species, cross-resistance between different herbicides within the auxin group has been confirmed (cross-resistance is a plant's resistance to another herbicide as a result of exposure to a similarly acting herbicide). Therefore, consideration has to be given to the possibility that dicamba resistance could extend to some of the other broadleaf species listed as resistant to other synthetic auxin herbicides (Miller et al., 2001; Jasieniuk et al., 1995; Cranston et al., 2001). However, because of differences in sites of action among chemistries within this group (*i.e.*, benzoic acids compared to pyridine-carboxylic acids) cross resistance between the herbicide groups is not a certainty (Monaco et al., 2002).

With the introduction of MON 87708 into the Roundup Ready soybean system, where dicamba will be applied in combination with glyphosate, it is important to note that kochia is the only broadleaf species with resistant biotypes to either synthetic auxins or glyphosate. There are no known kochia biotypes resistant to both of these herbicides.

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The development of a dicamba-glyphosate biotype is unlikely because both dicamba and glyphosate, each with two distinct modes-of-action, will likely be applied in the same season to MON 87708 in the Roundup Ready soybean system. If populations with resistance to multiple herbicides were to occur, there are other herbicide options for managing the weed in soybean (*e.g.*, clomazone and flumioxazin) and in its rotational crops (*e.g.*, atrazine and isoxaflutole in corn) (Table K-1). In addition, kochia is a weed found primarily in the western soybean growing regions where soybean would be rotated with corn and wheat for which there are multiple options for kochia control (Casey, 2009). The glyphosate-resistant kochia biotype is also found in western soybean growing areas, but it is isolated to small areas where soybean is grown in limited acreage.

K.7. Sustainable Use of Dicamba as a Weed Management Option in Soybean

Dicamba is a broadleaf herbicide that does not provide control of grass weeds. For that reason, MON 87708 will be sold only in soybean varieties that also contain other herbicide-tolerant traits, such as with the Roundup Ready soybean system (*e.g.*, MON 89788). Soybean varieties containing both MON 87708 and MON 89788 will enable dicamba to be applied with glyphosate or other soybean herbicides in an integrated weed management program, ideally as a mixture, to control a broad spectrum of grass and broadleaf weed species. Dicamba applications on MON 87708 will provide effective control of glyphosate-resistant broadleaf weeds and improve the control of annual and perennial broadleaf weed species, some of which are difficult to control with glyphosate. Dicamba will also help delay development and/or combat existing weed resistance issues that can limit the use of the PPO- and ALS-inhibiting herbicide groups by providing an additional mode of action for management of certain broadleaf species that are known to be prone to resistance to many of the current options for weed management (i.e. *Amarathus* spp.). MON 87708 will foster the adoption of Integrated Pest Management (IPM) practices in soybeans by allowing growers to continue to primarily focus on postemergence in-crop weed control, as they have practiced with the Roundup Ready soybean system. This will allow growers to delay some herbicide treatments until field scouting indicates a need for additional postemergence weed control which is consistent with the principles of IPM. Increasing postemergence herbicide options in soybeans is important, especially in conservation tillage situations, where consistency of postemergence herbicides has generally been greater than that of soil active residual products and thus a driving factor in the adoption of conservation tillage systems in the U.S.

Upon the inclusion and integration of MON 87708 into the Roundup Ready soybean system and approval of the use of dicamba on MON 87708 (Monsanto has submitted to EPA an application to amend Registration Number 524-582 to register a new use pattern for dicamba on MON 87708), preplant/preemergence applications of dicamba can be made up to 1.0 lb a.e./A up through crop emergence (cracking) followed by two in-crop postemergence applications up to 0.5 lb a.e./A through the R1/R2 growth stage in soybean. However, the majority of weed control scenarios in MON 87708 will not require the use of the maximum labeled rate, and the anticipated commercial pre-plant/preemergence and in-crop use rates are between 0.25 to 0.375 lb a.e./A (based on established weed control rates for soybean weeds), with an average application rate of

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0.35 lb a.e./A as described in Section VIII.H). Residual herbicides also will be recommended for use, in addition to glyphosate and dicamba, to provide early season weed control and to supplement dicamba activity on certain hard-to-control and glyphosate-resistant weed biotypes, such as glyphosate-resistant palmer amaranth where weed populations can be very substantial. See section K.8.1 for specific weed management recommendations.

Dicamba, as a complementary herbicide to glyphosate, will provide new weed control options in soybean that strengthen the utility and sustainability of glyphosate as a weed control tool in the Roundup Ready soybean system. Likewise, glyphosate, as a complementary herbicide to dicamba, would strengthen the utility and sustainability of dicamba as a weed control tool for MON 87708 to be integrated into the Roundup Ready soybean system.

In the event there is known or suspected presence of a dicamba-resistant weed, it will be possible to provide the affected grower(s) with options for managing the dicamba-resistant biotype. There are multiple preemergence (including soil residuals) and postemergent herbicide options for managing broadleaf weed populations that are resistant or may potentially develop resistance to dicamba in soybean as well for crops grown in rotation with soybean. These options are noted in Table K-1.

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Table K-1. Management Recommendations for Control of Dicamba- and Other Synthetic Auxin-Resistant Weeds

		Rotational Crops / Other Uses			
Weed Species	Primary Crop Soybean	Corn	Wheat	Pastures/Roadsides	Rice
Kochia (***Kochia scoparia***)	Saflufenacil[a] Clomazone[a] Flumioxazin[a] Glyphosate[a] Paraquat[a]	Atrazine[a] Saflufenacil[a] Isoxaflutole[a] Mesotrione[a] Glyphosate[a]	Saflufenacil[a] Glyphosate[a] Bromoxynil/MCPA[a]		
Prickly Lettuce (***Lactuca serriola***)	Saflufenacil[a] Chlorimuron/metribuzin[a] Glyphosate + imazethapyr[a]	Saflufenacil[a] Atrazine[a] Carfentrazone + atrazine[a] Isoxaflutole + atrazine[a]	Saflufenacil[a] Triasulfuron[a] Metsulfuron + thifensulfuron[a]		
Wild Carrot (***Daucus carota***)	Glyphosate[c] Chlorimuron[c] Chlorimuron/metribuzin[c]	Glyphosate[c] Atrazine[c] Primisulfuron[c] Nicosulfuron[d] Halosulfuron[d]			
Field Bindweed (***Convolvulus arvensis***)	Glyphosate[a]	Glyphosate[a] Glyphosate + imazethapyr[a] Glyphosate + Imazamox[a]	Glyphosate[a]		

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Table K-1 (continued). Management Recommendations for Control of Dicamba- and Other Synthetic Auxin- Resistant Weeds

			Rotational Crops / Other Uses		
Weed	Primary Crop Soybean	Corn	Wheat	Pastures/Roadsides	Rice
Yellow Starthistle (*Centaurea solstitialis*)				Chlorsulfuron Aminopyralid[e]	
Spreading Dayflower (*Commelina diffusa*)					Bentazon halosulfuron penoxsulam bispyribac[f]
Lambsquarters (*Chenopodium album*)[g]	Metribuzin[b] Cloransulam[b] Saflufenacil[a] Imazamox[b] Glyphosate[b]	Isoxaflutole[a] Atrazine[a] Saflufenacil[a] Mesotrione[a] Bromoxynil[b]	Bromoxynil[a] Chlorsulfuron/Metsulfuron[a] Glyphosate[a] Saflufenacil[a]		

[a] Bernards et al., 2010.

[b] Loux et al., 2010.

[c] Michigan State University Extension, 2010.

[d] Kells and Stachler, 1997.

[e] PNWE, 2010.

[f] University of Arkansas CES, 2010.

[g] Resistance to lambsquarters has only been confirmed in New Zealand.

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K.8. Stewardship of Dicamba Use on MON 87708

In order to steward the use of agricultural herbicides and herbicide-tolerant cropping systems such as MON 87708 integrated into the Roundup Ready soybean, Monsanto has conducted investigations and worked extensively with academics and other herbicide manufacturers to understand and recommend best practices to manage herbicide resistance. These investigations have demonstrated that one of the major factors contributing to the development of resistant weed biotypes has been poor weed control management practices. The lack of adequate management includes: 1) application of herbicides at rates below those indicated on the product label for the weed species, and 2) sole reliance on a particular herbicide for weed control without the use of other herbicides or cultural control methods (Beckie, 2006; Peterson et al., 2007).

K.8.1. Weed Control Recommendations

The pending label for dicamba use on MON 87708 is based on the maximum allowable use rates and patterns. Prior to launch of MON 87708 in the Roundup Ready soybean system, Monsanto, in cooperation with academics, will conduct trials to confirm the optimum rate and timing for dicamba alone and in combination with glyphosate and other herbicides. Recommendations to growers will be developed from this information and will be provided in herbicide product labels, Monsanto's Technology Use Guide (TUG), and in other education and training materials to be broadly distributed. Specifically, current research conducted by Monsanto to define the optimum weed management systems indicate the following: 1) in the absence of glyphosate resistant populations, the recommendation will be to apply a soil active residual herbicide followed by a postemergence application of glyphosate plus dicamba to control weed escapes, and 2) in the presence of glyphosate resistant populations, the same system will be recommended with a potential second application of glyphosate plus dicamba if needed. In this latter case, the preemergence herbicide to be recommended will be one with activity against the targeted glyphosate resistant species. This will ensure more than one mechanism of action against the targeted species, which is a fundamental component of a good weed resistance management program. These management systems will reduce the potential for further resistance development to glyphosate, dicamba as well as other critical soybean herbicides. In conservation tillage systems, a preplant application of glyphosate plus dicamba may be recommended in some situations in addition to the in-crop applications described above. This is not expected to increase selection pressure on either product since the preplant weed spectrum is generally different from the in-crop spectrum.

K.8.2. Dispersal of Technical and Stewardship Information

Monsanto will use multiple methods to distribute technical and stewardship information to growers, academics and grower advisors. Monsanto's TUG will set forth the requirements and best practices for the cultivation of MON 87708 including recommendations on weed resistance management practices. Growers who purchase varieties containing MON 87708 will be required to enter into a limited use license with

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Monsanto and must sign and comply with the Monsanto Technology Stewardship Agreement (MTSA), which requires the grower to follow the TUG.

The weed resistance management practices that will be articulated in the TUG will also be broadly communicated to growers and retailers in order to minimize the potential for the development of resistant weeds. These practices will be communicated through a variety of means, including direct mailings to each grower purchasing a soybean variety containing MON 87708, a public website[45], and reports in farm media publications. The overall weed resistance management program will be reinforced through collaborations with U.S. academics who will provide their recommendations for appropriate stewardship of dicamba in soybean production, as well as by collaboration with crop commodity groups who have launched web-based weed resistance educational modules. Finally, Monsanto will urge growers to report any incidence of repeated non-performance of dicamba on weeds in fields planted with MON 87708, and Monsanto will investigate cases of unsatisfactory weed control to determine the cause as defined in K.9.

The EPA is the U.S. federal regulatory agency that administers the federal law governing pesticide sale and use under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). EPA encourages pesticide manufacturers to provide growers with information regarding an herbicide's mode-of-action to aid growers in planning herbicide use practices and to foster the adoption of effective weed resistance management practices as specified by EPA in Pesticide Registration (PR) Notice 2001-5 (U.S. EPA, 2001). In that document EPA states that "this approach to resistance management is sound and would be highly beneficial to pesticide manufacturers and pesticide users." EPA approves all pesticide label use instructions based on its evaluation of supporting data supplied by the pesticide registrant or manufacturer. By approving a label, EPA has concluded that the product will not cause unreasonable adverse effects to the environment when used in accordance with the label's directions. After EPA approves a pesticide label, it is a violation of federal law to use the pesticide for a use or in a manner not in accordance with the label directions. Monsanto incorporates EPA's guidelines for pesticide resistance management labeling on its agricultural herbicide labels, and will continue to do so in the future. Monsanto will adopt a similar approach to pesticide resistance management guidance on its dicamba product labels.

In summary, Monsanto will require weed resistance management practices through the MTSA and TUG for its biotechnology-derived herbicide-tolerant products, such as MON 87708 integrated into the Roundup Ready soybean system, and to promote these practices through product labeling and educational outreach efforts as an effective means to manage weed resistance development for both dicamba and glyphosate.

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K.8.3. Weed Resistance Management Practices

Monsanto will provide information to growers and grower advisors on best management practices to delay the development of resistance to dicamba. The weed resistance management recommendations for the use of dicamba in conjunction with soybean varieties containing MON 87708 will be consistent with the Herbicide Resistance Action Committee's guidelines for prevention and management of herbicide resistance (HRAC, 2010)[46]. These guidelines recommend an integrated approach to weed resistance management including crop management (*i.e.*, row spacing, etc), cultivation techniques, and the use of multiple herbicide modes-of-action to manage a weed population.

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[45] http://www.monsanto.com/weedmanagement/Pages/default.aspx

In cases where resistance is confirmed for dicamba in soybean producing areas, Monsanto and University/Cooperative Extension Service (CES) personnel will provide recommendations for alternative herbicide control methods to growers. These recommendations would be made available through Monsanto supplemental labels, Monsanto and university publications, and internet sites to growers, consultants, retailers and distributors. For all existing cases of dicamba-resistant weeds in the U.S. and globally today, alternative herbicides and cultural methods are available to growers to effectively control these biotypes. Examples of recommended alternative herbicides from University/CES personnel that are applicable to weed species known to be resistant to dicamba and other synthetic auxin herbicides are found in Table K-1. It is important to note that there are many alternative options in each situation.

K.9. Monsanto Weed Performance Evaluation and Weed Resistance Management Plan

An important part of a weed resistance management plan is the timely acquisition of information regarding product performance. Monsanto has an extensive technical, sales and marketing presence in the soybean markets where MON 87708 will be grown. Through our relationships with farm advisors, key University/CES personnel, and growers using our seeds and traits products, Monsanto will acquire important and timely information regarding product performance. This will allow the timely recognition of performance issues that could arise related to weed resistance or other means. Field employees and hired consultants are trained and provided processes for responding to product performance inquiries. Individual performance issues that could be related to potential resistance are promptly handled. In addition performance inquiries are periodically reviewed by Monsanto for trends that could indicate the need for follow up action on a broad scale.

If resistance is confirmed, the scientific and grower communities will be notified and a weed resistance mitigation plan will be implemented by Monsanto in cooperation with the University/CES. The mitigation plan will be designed to manage the resistant biotype through effective and economical weed management recommendations implemented by the grower. The scope and level of intensity of the mitigation plan may vary depending on a combination of the following factors: 1) biology and field characteristics of the weed (seed shed, seed dormancy, etc.), 2) importance of the weed in the agricultural system, 3) resistance status of the weed to other herbicides with alternate modes-of-action, and 4) availability of alternative control options. These factors are analyzed by Monsanto and

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[46] The Herbicide Resistance Action Committee (HRAC) is an international body founded by the agrochemical industry for the purpose of supporting a cooperative approach to the management of herbicide resistance and the establishment of a worldwide herbicide resistance database.

University/CES personnel in combination with economic and practical management considerations to develop a tailored mitigation strategy. The plan considers what is technically appropriate for the particular weed and incorporates practical management strategies that can be implemented by the grower.

After a mitigation plan is developed, Monsanto communicates the plan to the grower community through the use of supplemental labeling (labeling which includes newly approved use directions, or other instructions), informational fact sheets, retailer training programs, agriculture media and/or other means, as appropriate.

In addition to the grower inquiry initiated process, Monsanto, alone and/or in cooperation with University/CES, will conduct field studies to understand the potential for weed resistance and weed shifts as the result of various weed management programs implemented for MON 87708 integrated into the Roundup Ready soybean system. These studies will allow researchers to better track specific factors that can influence the development of resistance to specific weeds.

K.10. Summary

Development of weed resistance is a complex process that can be difficult to accurately predict. Multiple methods for managing weed resistance are available and no single option is best. No single agronomic practice will mitigate resistance for all herbicides or all weeds. As a result, weed resistance needs to be managed on a case-by-case basis and tailored for the particular herbicide and weed in order to meet grower needs. Using good weed management principles, built upon achieving high levels of control through proper application rate, choice of cultural practices, and appropriate companion weed control products will allow dicamba herbicides to continue to be used effectively. In cases where weed populations have developed resistance to dicamba, effective management options are available and experience has shown that growers will continue to find value in using dicamba in their weed control programs.

The key principles for effective stewardship of dicamba use, including the integration of MON 87708 in the Roundup Ready soybean system, include: 1) basing weed management and weed resistance management practices on local needs and using the tools necessary to optimize crop yield, 2) using proper rate and timing of application, 3) not relying solely on one herbicide weed control option across a cropping system, 4) responding rapidly to instances of unsatisfactory weed control, and 5) providing up-to-date weed management and weed resistance management training.

Overall, there is a low potential for dicamba-resistant broadleaf weed populations to arise from the use of dicamba applied to MON 87708 integrated into the Roundup Ready soybean system. The reasons are as follows:

Dicamba will be used in combination with glyphosate in a majority of cropping situations, and weed recommendations will also include the concurrent use of residual herbicides for complementary weed control and different modes-of-action. These use patterns mean

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that there will be multiple modes-of-action against the major broadleaf species present in soybean production. This is a primary way to delay the development of resistance.

The development of resistance to auxin herbicides has been found to be relatively slow. This observation is hypothesized to be due to multiple sites of action within plants and evidence suggesting that resistance is determined by multiple genes (quantitative traits), at least in some species.

Only four broadleaf weed species have been confirmed to be resistant to dicamba in the U.S., and relatively low numbers of broadleaf species have been confirmed to be resistant to synthetic auxin herbicides even though dicamba has been widely in use for over 40 years.

Known resistant broadleaf populations to dicamba and other auxin herbicides are primarily found in the western U.S. and, thus, are not present in the major soybean geographies. In addition, the known dicamba-resistant biotypes are not major weed species present in the U.S. soybean crop.

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Appendix L: Comparative Analysis of Dicamba and Alternative Soybean Herbicides

L.1. Introduction

Dicamba is a selective broadleaf herbicide belonging to the auxin agonist class, the oldest known class of synthetic herbicides, and is a member of the benzoic acids sub-group. Dicamba mimics the action of the plant hormone indole acetic acid and causes rapid uncontrolled cell division, and growth leading to plant death. Dicamba has been registered for agricultural uses in the U.S. since 1967 and has been widely used in agricultural production for over forty years. Dicamba is presently approved for use on asparagus, corn, cotton, grass seed production, pasture and rangeland grasses, small cereals including barley, oats, rye, and wheat, sorghum, soybean, and sugarcane. Dicamba is also used for industrial vegetation management (*e.g.*, forestry and roadsides), professional turf management (*e.g.*, golf courses, sports complexes), and residential turf (U.S. EPA, 2009b).

Monsanto Company has developed biotechnology-derived soybean MON 87708 that is tolerant to dicamba (3,6-dichloro-2-methoxybenzoic acid) herbicide. MON 87708 offers growers expanded use of dicamba in soybean production. The excellent crop tolerance of MON 87708 to dicamba facilitates a wider window of application in soybean, allowing a preemergence application up to emergence (cracking) and in-crop postemergence applications through the R1/R2 stage of growth. Dicamba provides effective control of over 95 annual and biennial weed species, and control or suppression of over 100 perennial broadleaf and woody plant species. MON 87708 will be combined with MON 89788 (Roundup Ready 2 Yield® soybean) utilizing traditional breeding techniques. The combination of herbicide-tolerance traits allows the use of dicamba and glyphosate herbicides in an integrated weed management program to control a broad spectrum of grass and broadleaf weed species, such that the two herbicides can be used in sequence or tank-mixed. Monsanto has submitted an application to the Environmental Protection Agency (U.S. EPA) to register this new use pattern for dicamba on MON 87708 OPP Decision Number D-432752).

The availability of MON 87708 integrated into the Roundup Ready soybean system will result in a simple and effective dual mode-of-action herbicide system that will control hard-to-control broadleaf weeds, assist in the management of resistant broadleaf weeds, including glyphosate-resistant biotypes, and subsequently displace some soybean herbicides currently in use today (also referred to as alternative herbicides).

The intent of this comparative analysis is to define current herbicide use in U.S. soybean production, and to compare dicamba's human health and environmental properties to herbicides currently used by growers for weed control. In order for a pesticide (herbicide) to be registered by EPA it must meet the FIFRA and FFDCA standards for

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safety to human health and the environment. The EPA must conclude that the herbicide when used according to the label does not pose an unreasonable risk to humans or the environment, and, in order to establish a tolerance for the use of a herbicide on a food or feed crop, find there is a reasonable certainty of no harm to human health from non-occupational (food, water and residential/recreational) exposures to the herbicide. Consequently all alternative soybean herbicides can be used safely, and do not pose a risk to humans or the environment.

Nonetheless, in some instances dicamba offers a reduction in risk potential compared to some alternative herbicides, in the same risk category (e.g., acute human risk, aquatic plant risks). In other instances dicamba presents a similar risk potential compared to the some alternatives. In some instances, dicamba presents a greater risk potential compared to some alternatives.

Overall, the use of dicamba on MON 87708 incorporated into the Roundup Ready soybean system will offer a benefit compared to alternative soybean herbicides. For human health, aquatic plants and animals, and preemergence application flexibility. dicamba use on MON 87708 provides an overall reduction of potential risk (combination of "Yes" and "No" entries in Table L-17) compared to the alternatives except for flumiclorac-pentyl. Specifically,:

- Formulations based on the diglycolamine salt of dicamba, such as Clarity® or M1691 herbicide, have favorable acute toxicity profiles that reduce the risk of acute adverse effects for applicators, agricultural workers and bystanders compared to six alternative herbicide products (Section L.5.1.1).

- The active ingredient (a.i.) dicamba has favorable chronic, reproduction, carcinogenicity and developmental toxicity characteristics, which reduce the potential for risks from exposure to applicators, agricultural workers and consumers, compared to exposure from eight alternative herbicide products (Section L.5.1.2).

- Dicamba has very low toxicity to fish and aquatic invertebrates, and based on EPA high end exposure screening level assessment methodology will not affect listed and non-listed aquatic plants and animals, which reduces the potential risk to aquatic organisms as compared to seven alternative products(Section L.5.2.1 and L.5.2.2).

- Dicamba use on MON 87708 will strengthen and extend the benefits of glyphosate-based weed control in soybean, which has many well-known and recognized environmental and human health benefits as acknowledged in previous EPA Office of Pesticide Programs (OPP) decisions to grant reduced risk status to multiple glyphosate-tolerant crop uses, *i.e.*, corn, canola, and sugar beet.[47] Additionally, the use of glyphosate-based weed control in soybean has provided growers with more profit opportunities than conventional soybean by reducing input costs (Gianessi, 2005). By utilizing both active ingredients, which have different herbicidal modes-of-

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[47] http://www.epa.gov/opprd001/workplan/completionsportrait.pdf

action, the risk to soybean production posed by weeds that are hard-to-control with glyphosate alone, or have developed resistant to glyphosate, is reduced. Hard-to-control weeds generally require a higher rate and/or application at a smaller growth stage in order to consistently achieve commercially acceptable control, and includes copperleaf, hemp sesbania, morningglory, prickly sida, velvetleaf, waterhemp, and a number of other broadleaf and grassy weeds. Refer to the Roundup WeatherMax label (U.S. EPA Reg. No. 524-537) for a listing of these weeds.

- Dicamba use on MON 87708 will also provide growers with the option to use an herbicide with a different mode-of-action to manage weed species (*e.g.*, Pigweed) where certain biotypes have demonstrated resistance to herbicide classes other than glyphosate, such as protoporphyrinogen oxidase (PPO) or acetolactate synthase (ALS) inhibitors (Section L.5.3.3). Herbicide resistant weeds are those listed on the International Survey of Resistant Weeds website (www.weedscience.org).

- Dicamba use on MON 87708 will reduce the risk to soybean production that ensues when growers utilize alternate herbicides that have long rotation restriction periods or pose potential for substantial crop injury and loss of yield (Section L.5.3.2.1).

- Planting glyphosate tolerant soybean thereby allowing the use of glyphosate to effectively control weeds in no-till fields has made no-till a viable production system for soybean (Pedersen, 2008). The use of dicamba on MON 87708 will reduce the risk of growers reverting back to conventional tillage practices from conservation tillage practices due to concerns over weed control or resistance and thereby foster continued adoption of conservation tillage practices, which is an important goal for the agro-ecosystem and the long term sustainability of U.S. agriculture. The integration of MON 87708 into the Roundup Ready soybean system will allow the flexibility to incorporate a second herbicide and mode-of-action in preemergent or postemergent applications and support the continued use of conservation tillage production (Section L.5.3.3).

In conclusion, dicamba provides a similar and in some cases a more favorable comparative risk profile compared to other alternative herbicide products; the use of dicamba on MON 87708 will positively impact integrated pest management practices and sustainability of soybean production in the United States by providing a valuable weed management tool for this important agricultural crop that imparts greater flexibility and weed control options, and will help to slow the selection for herbicide-resistant weed biotypes for all herbicide modes-of-action *(i.e.*, ALS, HPPD, PPO, glyphosate) currently registered for use in soybean; and will continue to support adoption of no-till and conservational tillage practices.

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L.2. Background

L.2.1. Chemical Name and Structure

Dicamba (3,6-dichloro-2-methoxybenzoic acid) is a carboxylic acid that can form salts in aqueous solution. The chemical structure is provided in Figure L.1. Dicamba products registered for agricultural uses are formulated with various dicamba salts. The formulated products Clarity and M1691 contain the diglycolamine salt of dicamba at a nominal level of 56.8% by weight, which is equivalent to 38.5% by weight dicamba acid (also referred to acid equivalents or a.e.).

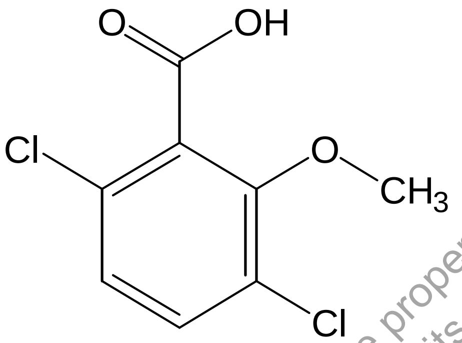

Figure L-1. Structure of Dicamba

L.2.2. Herbicide Class and Herbicidal Mode-of-Action

Dicamba belongs to the "benzoic acid class" of herbicides. The Weed Science Society of America (WSSA) places dicamba in herbicide group number 4.[48] It is an auxin agonist; it is a plant hormone (indole acetic acid, IAA) mimic that causes rapid uncontrolled cell division and growth, leading to plant death. Dicamba is mainly used to control broadleaf weeds and woody plants.

L.2.3. Current U.S. Uses and Established Tolerances

Dicamba is a selective herbicide labeled for control of certain broadleaf weeds and woody plants. It was first registered for agricultural use in the U.S. in 1967 and is widely used today in agricultural, industrial, and residential settings. Dicamba salts have approved uses on asparagus, corn, cotton, grass seed production, pasture and rangeland grasses, small cereals including barley, oats, rye, and wheat, sorghum, soybean, and sugarcane. Dicamba is also used for industrial vegetation management (*e.g.*, forestry and roadside right-of-ways), professional turf management (*e.g.*, golf courses, sports complexes), and residential turf (U.S. EPA, 2009b; Durkin and Bosch, 2004).

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[48] There are several systems of herbicide mode-of-action classification. Among the most widely used are those of the Herbicide Resistance Action Committee (HRAC) and the WSSA. The classifications are compared in a chart at: http://www.plantprotection.org/HRAC/Bindex.cfm?doc=MOA.html. Accessed May 27, 2010

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Established food and feed tolerances are listed at 40 CFR 180.227, and in addition to the crop plants, they include residue limits for meat, milk, and meat by-products that may arise when livestock consume dicamba-treated commodities.

L.2.4. Proposed use pattern for dicamba on MON 87708

Monsanto has submitted to the EPA an application to amend EPA Reg. No. 524-582 to register a new use pattern for dicamba. The new use pattern allows for sequential applications of dicamba, formulated as the diglycolamine salt, to MON 87708:

- Preplant / preemergent applications, totaling up to 1 pound per acre of dicamba a.e.
- One or two postemergent in-crop applications (up to 0.5 pounds a.e./acre each), timed between soybean emergence (cracking) and early flowering (the R1/R2 growth stage) of the soybean.

The proposed use pattern for dicamba on MON 87708 is within the maximum single and annual application rates that have previously been assessed by EPA. Once approved by EPA, this label will become a legally-binding constraint on the use of dicamba on MON 87708.

Residue analyses conducted by Monsanto, in which MON 87708 was treated at the proposed maximum application rates, were found to produce total dicamba-derived residues in soybean seeds at a median level of <0.065 ppm (range of <0.041 to 0.471 ppm). These levels are substantially less than the current established food tolerance; the highest measured residue from the MON 87708 residue study (0.471 ppm) was only 4.7% of the established 10 ppm dicamba soybean tolerance. Therefore, the proposed maximum dicamba treatments to MON 87708 (allowing up to 1 lb a.e. of dicamba per acre applied at a preemergent timing plus up to two postemergent in-crop applications of up to 0.5 lb a.e./acre each), will not increase dietary exposure to dicamba residues in soybean seed beyond that which is already permitted within the existing legal food tolerance.

Residues were also measured in soybean forage and hay of treated MON 87708. Monsanto is seeking the establishment of feed tolerances for soybean forage and hay to allow feeding of these dicamba-treated MON 87708 commodities to livestock. However, these dicamba residues will not increase the livestock dietary burden used to establish the current animal commodity food tolerances, so all dietary exposures from the proposed new dicamba use on MON 87708 have already been accounted for within the existing dicamba food tolerances.

L.3. Properties of Dicamba Herbicide

L.3.1. Human Health

MON 87708, treated with preemergent and over-the-top applications of dicamba herbicide has the opportunity to reduce risks to human health by:

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- Replacing, in part, currently used or foreseeable future alternative herbicide products with less favorable risk profiles, and
- Providing an effective tool to manage hard-to-control broadleaf weeds or broadleaf weeds that are resistant to glyphosate, PPO inhibitors, or ALS inhibitors, thereby preserving the ability of growers to manage broadleaf weed problems and maximize yields in a less risky manner, recognizing the human health benefits offered by the superior toxicity and reduced risk profile of glyphosate and the risk profile demonstrated by dicamba.

Both dicamba, as the Clarity or the M1691 formulation, and glyphosate, as various Roundup-branded formulations, have "CAUTION!" signal words (CAUTION is the most favorable of three possible label signal words that can be required by EPA) and favorable chronic toxicity profiles. In a comparative analysis with other alternative soybean weed control products, dicamba products offer better, or at least equivalent, human health safety profiles, as discussed below.

In 2006, EPA issued the Reregistration Eligibility Decision (RED) document for dicamba and its associated salts (U.S. EPA, 2009b). The RED document, and the related Health Effects Division (HED) chapter (U.S. EPA, 2005b), presented an overview of the toxicological properties of dicamba, which is summarized below.

The measurement of human health is the result of conventional laboratory testing against standard indicator species (generally rats, mice, and dogs) and is required for the registration of a pesticide by the EPA. Results are presented using standard toxicity indices, such as the concentration or dose required for 50% lethality (LC_{50} or LD_{50}), the highest dosing level that produced No Observable Adverse Effects (NOAEL), or the lowest dosing level that produced an Observable Adverse Effect (LOAEL). The results of the acute (single exposure) toxicity studies for dicamba are presented in Table L-1. Results for developmental, reproduction, mutagenic and neurotoxicological studies are presented in Table L-2. Subchronic, chronic and carcinogenicity study results are presented in Table L-3.

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Table L-1. Dicamba Acid Acute Toxicity Study Findings

Study	Endpoint	EPA Category[1]
Acute oral (rat) LD_{50}	2740 mg/kg	III
Acute dermal (rat) LD_{50}	2000 mg/kg	III
Acute inhalation (rat) LC_{50}	5.3 mg/L	IV
Primary eye irritation (rabbit)	Irritant	II
Primary dermal irritation (rabbit)	Irritant	II
Dermal sensitization (guinea pig)[2]	Negative	NA

[1] EPA acute toxicity categories range from I (worst) to IV (best).

[2] Determination of the potential to cause or elicit skin sensitization reactions (allergic contact dermatitis) is an important element in evaluating a substance's toxicity.

Table L-2. Dicamba Acid Reproductive, Developmental, Mutagenic, and Neurotoxicologic Findings

Study	Systemic Toxicity Endpoint (mg/kg body wt/day)	Offspring Toxicity Endpoint (if any) (mg/kg body wt/day)
Developmental (rat)	Maternal NOAEL 160; LOAEL 400. Clinical signs: decreased food consumption and weight gain, increased mortality.	Developmental NOAEL 400 (HDT[1]).
Developmental (rabbit)	Maternal NOAEL 62.5; LOAEL 150. Clinical signs: decreased motor activity, ataxia, increased abortion.	Developmental NOAEL 62.5; LOAEL 150. Clinical signs: Increased abortion.
Developmental Neurotoxicity	Not Required	
Reproduction, multigeneration (rat)	Parental NOAEL 122/136 (M/F[2]); LOAEL 419/450 (M/F). Clinical signs: reduced righting reflex. Reproductive NOAEL 122; LOAEL 419. Delayed F1 male maturation.	Offspring NOAEL 45; LOAEL 136. Clinical signs: Decreased pup weights, all generations.
Acute Neurotoxicity (rat)	NOAEL not established; LOAEL 300. Clinical signs: Impaired gaits and righting reflex, impaired respiration, rigidity.	
Subchronic Neurotoxicity (rat)	NOAEL 401/472 (M/F); LOAEL 768/1029 (M/F). Clinical signs: Rigidity, slightly impaired gait and righting reflex.	
Gene Mutation – Salmonella	Not mutagenic.	
Chromosome aberration (CHO[3])	Aberrations not induced at any tested concentration with or without S9 activation.	
Unscheduled DNA Synthesis (UDS)	No Evidence of UDS up to 3000 µg/mL	

[1] HDT stands for the highest dose tested.
[2] M/F stands for males/females.
[3] Chinese hamster ovaries.

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Table L-3. Dicamba Acid Subchronic, Chronic and Cancer Findings

Study	Toxicity Endpoints (mg/kg body weight/day)
Subchronic Oral (rat)	NOAEL 479/536 (M/F[1]); LOAEL 1000/1065 (M/F). Clinical signs: decreased weight gains, liver effects.
28-day dermal (rat)	NOAEL 1000 (HDT[2]).
Chronic / Carcinogenicity (rat)	NOAEL 107/127 (M/F; HDT). Not carcinogenic.
Chronic (dog)	NOAEL 52 (HDT).
Carcinogenicity (mouse)	NOAEL 358/354 (M/F); (HDT). Not carcinogenic.

[1] M/F stands for males/females.

[2] HDT stands for the highest dose tested.

The EPA has classified dicamba as "Not Likely to Cause Cancer in Humans" (the most favorable among EPA's cancer categories), and concluded that dicamba is not mutagenic and is not a developmental toxin. There was no evidence of behavioral or neurological effects on offspring and, therefore, a developmental neurotoxicity study was not required by the EPA.

In the human health risk assessments for dicamba, the EPA employed a chronic Population Adjusted Dose (cPAD) of 0.45 mg/kg/day, based on a 100-fold safety factor applied to the offspring NOAEL in the multigeneration rat study. For evaluating acute exposures to dicamba, the EPA employed an acute Population Adjusted Dose (aPAD) of 1 mg/kg, based on a 300-fold safety factor (for use of the LOAEL rather than the NOAEL) applied to the LOAEL in the rat acute neurotoxicity study (U.S. EPA 2008a).

Using a dietary exposure model to estimate combined exposures from all presently approved uses, including both food and water exposure routes, and assuming that 100% of all labeled crops are treated with dicamba and that the resulting foods have tolerance-level residues, total dietary exposure reached only 4.4% of the aPAD level and 2.7% of the cPAD level for the general U.S. population; and 11% of the aPAD and 6.8% of the cPAD for the most highly exposed subpopulations of children 1-2 years old (U.S. EPA 2008a). The proposed dicamba use on MON 87708 does not require an increase in the soybean seed food tolerance. Monsanto has requested new tolerances for soybean forage and hay; however, these do not increase the livestock dietary burden utilized in the RED assessment, so all dietary exposures from the proposed new dicamba use on MON 87708 are already accounted for in these assessments.

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L.3.2. Toxicology of Dicamba Plant and Animal Metabolites

MON 87708 has been genetically enhanced to express a dicamba metabolizing enzyme (dicamba mono-oxygenase). The enzyme catalyzes a mono-oxygenation reaction resulting in an oxidative demethylation of dicamba, forming 3,6-dichloro-2-hydroxybenzoic acid, also known as 3,6-dichlorosalicylic acid (DCSA). In the dicamba-treated MON 87708, glucoside conjugates of DCSA were the major plant metabolites.

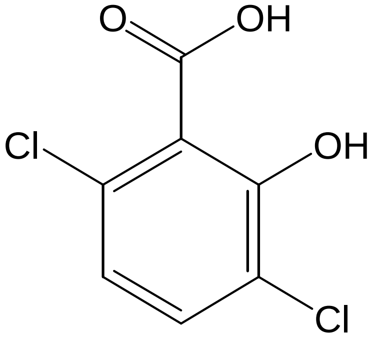

Figure L-2. Structure of DCSA

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DCSA is a known metabolite of dicamba in soil, plants, and livestock. It is presently included in the residue expression specified in the food and feed tolerance for dicamba in 40 CFR 180.227(a)(3). Therefore, the existing food tolerance for soybean seed includes DCSA residues.

In the RED, EPA considered that DCSA has structural similarity to dicamba, and concluded that it would have similar toxicity to the parent dicamba. Monsanto has conducted and submitted additional toxicity studies involving direct dosing with DCSA (U.S. EPA OPP Decision Number D432752) to further substantiate the conclusion reached by the EPA in the RED. The results of these studies, summarized in Table L-4, can be compared to those of dicamba (Tables L-1 through L-3). Monsanto has submitted these studies to the EPA in support of our application to register the use of dicamba on MON 87708.

Table L-4. Summary of Toxicological Findings from Testing of DCSA

Study	Systemic Toxicity Endpoint (mg/kg body wt/day)	Offspring Toxicity Endpoint (if any) (mg/kg body wt/day)
Acute oral (rat) LD_{50}	2641 (Category III)	NA
Developmental (rat)	Maternal NOAEL 100	Developmental NOAEL 100
Developmental (rabbit)	Maternal NOAEL 25	Developmental NOAEL 65 (HDT)
Reproduction, multigeneration (rat)	Parental NOAEL 42 (M/F[1] combined)	Offspring NOAEL 42
Gene mutation – *S. typhimurium* & *E. coli*	Not mutagenic	NA
In vitro chromosome aberration (CHO)	Aberrations not induced	NA
Micronucleus (mouse)	Negative	NA
Subchronic (90-day) oral (Rat)	NOAEL 362/222 (M/F)	NA
Chronic (12-month)(rat)	NOAEL 171/206 (M/F).	NA
Subchronic (90-day) (dog)	NOAEL 50	NA
In Vitro cytogentics (human lymphocytes)	Weakly positive with S9 activation	NA
In Vivo cytogenetics (rat)	Negative	NA
Carcinogenicity	Ongoing	NA

NA denotes Not Applicable.

[1] M/F stands for males/females.

Smaller amounts of a glucoside of another known metabolite, 5-dichloro-3,6-dihydroxybenzoic acid (3,6-dichlorogentisic acid, DCGA) were also identified in the soybean metabolism study. Levels of the DCGA glucoside were less than 10% of total MON 87708 soybean-contained radioactivity. Monsanto conducted a limited set of toxicity studies on DCGA; and has provided these studies to EPA to support our application to register dicamba on MON 87708.

The results of the DCSA and DCGA toxicity studies substantiate the EPA conclusion that dicamba metabolites will have similar toxicity to parent dicamba.

L.3.3. Dicamba Ecological Effects – Non-target Species

The following tables summarize the hazard potency of dicamba to non-target species. These data were taken from the Environmental Fate and Effects Division (EFED) Chapter of the dicamba RED (U.S. EPA, 2005a). These measures are the result of conventional laboratory testing against standard indicator species of fish, birds, mammals, and plants as required for EPA registration. Results are presented using

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standard toxicity indices, such as the concentration or dose required for 50% lethality (LC_{50} or LD_{50}) or the concentration required for a 25 or 50% reduction in growth or biomass (EC_{25} or EC_{50}). In some cases the "No Observable Effect Concentration" (NOEC) or "No Observable Adverse Effect Level" (NOAEL) is also listed. A summary of the findings of the ecotoxicity studies conducted on dicamba acid is provided in Tables L-5 through L-7. Ecotoxicity studies have also been conducted on the diglycolamine (DGA) salt of dicamba and are summarized in Table L-8.

Table L-5. Dicamba Acid Ecotoxicity Findings on Mammals, Birds and Fish (U.S. EPA. 2005a)

Study	Toxicity Endpoint	Comment
Mammals		
Dicamba acid acute oral (rat) LD_{50}	2740 mg/kg body wt	
Multigeneration reproduction (rat) NOAEL/LOAEL	45 /136mg/kg/day	
Birds		
Dicamba acid acute oral (quail) LD_{50}	188 mg/kg body wt	
Dicamba acid acute oral (duck) LD_{50}	1373 mg/kg body wt	
Dicamba acid sub-acute oral (quail) LC_{50}	>10,000 mg/kg diet	
Dicamba acid sub-acute oral (duck) LC_{50}	2009 mg/kg diet	
Dicamba acid sub-acute oral (duck) LC_{50}	>10,000 mg/kg diet	Replicate
Dicamba acid reproduction (quail) NOEC/LOEC	1390 (HDT[1]) mg/kg diet	
Dicamba acid reproduction (duck) NOEC/LOEC	695/1390mg/kg diet	
Fish		
Dicamba acid (trout) LC_{50}	28 mg/L	
Dicamba acid (trout) LC_{50}	135 mg/L	Replicate
Dicamba acid (trout) LC_{50}	153 mg/L	Replicate
Dicamba acid (Bluegill) LC_{50}	135 mg/L	
Dicamba acid (Bluegill) LC_{50}	>50 mg/L	Replicate
Dicamba acid (Sheepshead) LC_{50}	>180 mg/L	
Dicamba acid fish early life stage	NA	
Dicamba acid fish life cycle	NA	

NA denotes Not Applicable.

NOEC stands for No Observable Effect Concentration.

LOEC stands for Lowest Observable Effect Concentration.

[1] HDT stands for the Highest Dose Tested.

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Table L-6. Dicamba Acid Ecotoxicity Findings on Aquatic and Terrestrial Invertebrates (U.S. EPA. 2005a)

Study	Toxicity Endpoint	Comment
Aquatic Invertebrates		
Dicamba acid (Daphnia) LC$_{50}$	111 mg/L	
Dicamba acid (Daphnia) LC$_{50}$	>100 mg/L	Replicate
Dicamba acid (Sowbug) LC$_{50}$	>100 mg/L	
Dicamba acid (Scud) LC$_{50}$	>100 mg/L	
Dicamba acid (Grass Shrimp) LC$_{50}$	>132 mg/L	
Dicamba acid (Fiddler Crab) LC$_{50}$	>173 mg/L	
Dicamba acid (Oyster) LC$_{50}$	>1 mg/L	
Dicamba acid (Glass Shrimp) LC$_{50}$	>56 mg/L	
Invertebrate life cycle	NA	
Terrestrial Invertebrates		
Honeybee LD$_{50}$	>90.6 µg/bee	

NA denotes Not Applicable.

Table L-7. Dicamba Acid Ecotoxicity Results on Aquatic and Terrestrial Plants (U.S. EPA. 2005a)

Study	Toxicity Endpoint	Comment
Aquatic Plants		
Dicamba acid duckweed EC$_{50}$ / NOEC	>3.25 / 0.2 mg/L	
Dicamba acid green alga EC$_{50}$ / NOEC	>3.7 / 3.7 mg/L	
Dicamba acid marine diatom EC$_{50}$ / NOEC	0.49 / 0.011 mg/L	
Dicamba acid blue-green alga EC$_{50}$ / NOEC	0.061 / 0.005 mg/L	
Dicamba acid freshwater diatom EC$_{50}$ / NOEC	2.3 / 0.5 mg/L	
Terrestrial Plants		
Dicamba acid seedling emergence monocot EC$_{25}$ / NOEC	0.004 / <0.032 lb/a	Onion
Dicamba acid seedling emergence dicot EC$_{25}$ / NOEC	0.0027 / < 0.0022 lb/a	Soybean
Dicamba acid vegetative vigor monocot EC$_{25}$ / NOEC	0.15/ 0.13 lb/a	Onion
Dicamba acid vegetative vigor dicot EC$_{25}$ / NOEC	0.0068 / <0.004 lb/a	Soybean

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Table L-8. Dicamba, Diglycolamine (DGA) Salt Ecotoxicity Findings (U.S. EPA. 2005a)

Study	Toxicity Endpoint	Comment
Birds		
Dicamba DGA salt acute oral (quail) LD_{50}	262 mg a.e./kg body weight	
Dicamba DGA salt sub-acute oral (quail) LC_{50}	>1522 mg a.e./kg diet	
Dicamba DGA salt sub-acute oral (duck) LC_{50}	>1522 mg a.e./kg diet	
Fish		
Dicamba DGA salt (trout) LC_{50}	>270mg a.e./L	
Dicamba DGA salt (bluegill) LC_{50}	>270mg a.e./L	
Aquatic Invertebrates		
Dicamba DGA salt (Daphnia) LC_{50}	>270 mg a.e./L	

- As a part of the reregistration evaluation under FIFRA, EPA conducted an ecological screening assessment for dicamba. This assessment compared the results from toxicity tests with dicamba conducted with various plant and animal species to conservative (high end) estimates of the concentration of dicamba to which an organism might be exposed in the environment. These estimates, called the Estimated Environmental Concentrations (EECs), are point estimates for specific types of exposure (*e.g.*, aquatic or dietary) that assume constant high concentrations throughout the lifespan of the organism. These estimates do not take into account normal variation in environmental concentrations, the dilution or dissipation of those concentrations, or the frequency of exposure of wildlife to the pesticide. Such assumptions provide a screening level of assessment where conclusions of no harm can be drawn with high confidence; however, it is also possible to reach a conclusion of no harm with more refined exposure assumptions. EPA derived exposure estimates for a number of use patterns (U.S. EPA, 2005a), including two that are reasonably close to the proposed use pattern of dicamba on MON 87708. These use patterns are: 1) for wheat, with two 1.0 lb a.e./acre applications; and 2) for sorghum, with two 0.5 lb a.e./acre applications. For both crops, the two applications were considered to occur on May 1st and June 1st. Based on these highly conservative screening level assessments, EPA's Environmental Fate and Effects Division (EFED) identified the concerns for non-target species effects (terrestrial plants, Risks to terrestrial plants; acute risks to birds, and chronic risk to mammals in their risk assessment for the 2006 Dicamba RED (U.S. EPA, 2009b), however EPA concluded in the final reregistration decision document that no specific additional drift mitigations were needed to support the continued registration of all dicamba uses.

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L.3.4. Environmental – Soil, Air, and Water Quality

The following tables summarize the physical and chemical properties of dicamba that can influence its mobility and persistence in the environment. These measures are the result of conventional laboratory testing, as required for EPA registration. Results are presented using standard environmental fate indices, such as the time required for 50% degradation (half-life) of the initial concentration.

Table L-9. Environmental Fate and Physical Properties of Dicamba Acid

Environmental Physical Properties	Results
Dicamba acid vapor pressure	3.4×10^{-5} torr (25° C)
Dicamba acid acidity (pKa)	1.87
Dicamba acid water solubility	6100 mg/L
Dicamba acid octanol / water partition coefficient	0.1
Dicamba acid K_{oc} (Freundlich soil-binding constant)	3.5 – 21.1 mL/g
Dicamba acid field dissipation half-life (conducted with salt formulations)	3 – 19.8 days
Dicamba acid aerobic soil half-life, Laboratory	6 days
Dicamba acid anaerobic soil half-life, Laboratory	141 days
Dicamba acid aerobic aquatic half-life, Laboratory	20.2 – 24.3 days
Dicamba acid aqueous photolysis half-life	38.1 days
Dicamba acid soil photolysis degradation rate	~20% after 30 days
Hydrolysis half-life	Stable

L.3.4.1. Risks of Leaching and Runoff

The high water solubility, relatively low soil-binding coefficient, and a pKa that requires dicamba to exist primarily as an anion at normal soil pH suggest that dicamba may have risk of leaching or runoff. These indicators of low soil-binding are largely offset by the rapid soil microbial breakdown of both dicamba and its DCSA metabolite under aerobic conditions, leading overall to only a low to moderate risk of leaching or runoff. Using the Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS[51]) and Screening Concentration in Ground Water (SCI-GROW[52]) models, EPA estimated potential drinking water concentrations originating from ground and surface water for use in the dicamba dietary risk assessment. Model results indicated potential dicamba ground and surface water concentrations of 0.016 µg/L and 13.8 µg/L, respectively (U.S. EPA,

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[51] PRZM-EXAMS Model Description. Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. http://www.epa.gov/oppefed1/models/water/models4.htm#przm. Accessed May 28, 2010

[52] SCI-GROW Model Description. Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. http://www.epa.gov/oppefed1/models/water/scigrow_description.htm. Accessed May 28, 2010.

2008). Surface water modeling using PRZM-EXAMS described in the EFED RED Chapter (U.S. EPA, 2005a) predicted levels ranging from 4.9 to 18 µg/L for a one lb per acre dicamba a.e. application rate to soybean (the highest single proposed application rate for MON 87708). Dicamba has been in use for many years on a significant number of acres in the corn belt, with approximately 36 million treated-acres in 1994 alone (Table VIII-11), so that data from groundwater monitoring studies provide additional evidence pertaining to the potential for dicamba to leach. There has been a low incidence of dicamba detections (approximately 3% of sites) in the U.S. Geological Survey National Water Quality Assessment (NAWQA) monitoring program (U.S. EPA, 2005b). The highest detection levels were approximately 2 µg/L. Altogether, the modeling predictions and the NAWQA monitoring results show that dicamba concentrations that might occur in drinking water are very low, and it confirms that the potential risk of dicamba leaching or runoff does not threaten human health or acceptable water quality. The lifetime Health Advisory Level (HAL)[53] for dicamba is 4,000 µg/L (U.S. EPA, 2011).

L.3.4.2. Other Hazards

Dicamba does not include any fluorine atoms, which are characteristic of ozone depletion risk. Based on the vapor pressure presented in Table L-9, dicamba is not sufficiently volatile to be present in the stratosphere at ozone-threatening levels. Dicamba acid, nor its water soluble salts or derived formulation, does not have the properties of explosiveness, flammability, or corrosion.

L.3.4.3. Efficacy and Weed Management Practices for Dicamba on MON 87708

Since the introduction of the Roundup Ready® soybean crop product in 1996, glyphosate herbicides have become the predominant weed control tool in soybean production. That has been beneficial for growers, because glyphosate use in the Roundup Ready soybean system offers unmatched flexible weed control at a relatively low price; the high adoption rate of the Roundup Ready soybean system by growers is a testament to its ease of use and ability to provide full spectrum weed management. The adoption of the Roundup Ready soybean system has provided additional benefits from a risk perspective, because glyphosate is widely-recognized as an herbicide that has a favorable profile in terms of human health, non-target animal species, and ground and surface water. A significant step that can be taken toward minimizing future potential risk from herbicides is to strengthen and support the continued sustainability of glyphosate use in soybean production by providing a complementary tool to manage hard-to-control weeds and, as a result, optimize soybean yield. As stated earlier, EPA has acknowledged the value of the glyphosate-based weed control system and the need to have other herbicide modes of action available for IPM purposes, including weed resistance management, particularly in

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[53] The concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenetic effects for a lifetime of exposure.

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its decision to continue registration of herbicides in cotton (U.S. EPA, 2009a). In this revised RED decision on MSMA (an organic arsenic herbicide), EPA reversed it decision on continued registration of this active ingredient in cotton based in part on the aforementioned IPM benefits.

According to 2006 market data 75.59 million acres of soybeans were planted in 2006, and 74.6 million acres were harvested (USDA-NASS, 2007a). Soybean-growing acres received approximately 2.0 herbicide treatments (AgroTrak, 2009), leading to approximately 149 million herbicide treated acres. Based on the most recently available USDA-NASS figures from 2006, 97% of the herbicide total treated acres were made with glyphosate herbicides, and the remaining 32% of treatments were made with more than 25 other active ingredients (USDA-NASS 2007b).

In 2008, dicamba-treated soybean acres only accounted for 0.53 million acres, or 0.7% of the soybean acres (Table VIII-12). This is primarily because current commercial soybean varieties are not tolerant to dicamba, and therefore dicamba is only labeled for application at timings that avoid contact with the growing plant or when some level of injury is acceptable: (1) preplant treatments 2 to 4 weeks prior to planting, depending on rate and rainfall, or (2) preharvest treatments after the seeds have matured, at least 14 days before harvest.

As a consequence of the intensive use of glyphosate for weed control in Roundup Ready soybean over the past 13 seasons, certain problematic weeds (glyphosate hard-to-control and-resistant) have become more common, although glyphosate is still considered to provide very broad spectrum weed control. Since the registration and market introduction of glyphosate, it has been known that certain weeds are more difficult to control than others at any given herbicide rate and timing of application. Glyphosate, as with any herbicide, when used repeatedly season-after-season without other weed management practices, can select for those weeds that fall in this “difficult-to-control” category, including weeds such as morning glory, nightshade, and wild buckwheat, so that their populations can increase if the correct rate and application timing are not practiced. For some weed species biotypes, selection and resistance have occurred in some geographical locations. In addition, resistance has developed for some populations of weeds that were formerly well-controlled by glyphosate in soybean; these include glyphosate-resistant waterhemp, Palmer amaranth, horseweed, common ragweed, and giant ragweed. As a group, the glyphosate hard-to-control and glyphosate-resistant weeds are generally broadleaf dicotyledonous weeds. Accordingly, in Roundup Ready soybean fields where these problem weeds are widespread, affecting yield and complicating harvest, growers have begun to use a variety of broadleaf herbicides sequentially or as a mixture with glyphosate.

Monsanto, and other companies, have recognized this weed control need, and now recommend the incorporation of multiple modes-of-action for weed control. Companies are also searching for a companion herbicide for use with glyphosate to manage these populations of problematic broadleaf weeds. A complementary herbicide would provide new weed control options that strengthen the utility and sustainability of glyphosate as a weed control tool in the Roundup Ready soybean system. In the absence of MON 87708

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integrated into the Roundup Ready soybean system, growers will need to rely on multiple herbicide applications at different timings to gain similar weed control. Dicamba is considered an optimum herbicidal companion to glyphosate in control of broadleaf weeds, since soybean injury can be eliminated through the introduction of MON 87708, because it: 1) has a different mode-of-action from glyphosate; 2) dicamba has shown little propensity toward resistance development; 3) is very effective in controlling the problematic broadleaf weed spectrum described above; 4) has a short soil half-life, without the potential for carry-over problems or plant-back restrictions; 5) can offer superior crop safety relative to other postemergent herbicides available for use in soybean; 6) is available at a cost appropriate to its benefit; and 7) is compatible in mixtures with glyphosate and other herbicides.

Monsanto has developed MON 87708 by introducing a gene that encodes an enzyme to catalyze the breakdown of dicamba. The dicamba mono-oxygenase enzyme cleaves a specific carbon-oxygen bond and converts the aromatic methoxyl moiety into a hydroxyl group, to form the non-herbicidal metabolite 3,6-dichlorosalicylic acid (DCSA). The rate of dicamba breakdown in MON 87708 is sufficiently rapid to provide complete protection from herbicidal symptoms, thereby allowing dicamba applications anytime up to crop emergence (cracking) as well as two postemergent in-crop applications between cracking and the R1/R2 growth stage. Monsanto seeks to offer growers soybean varieties that include both the glyphosate- and dicamba tolerance traits (MON 89788 × MON 87708), allowing use of either herbicide alone or together in sequence or as a mixture, to provide wide flexibility to meet diverse and specific weed control needs in individual fields.

L.4. Properties of Alternative Herbicide Products

As discussed in L.3.4, ninety-seven percent (97%) of soybean treated acres receive an application of glyphosate; the remaining acres are treated with more than 25 other active ingredients. In some of the soybean acres, these other active ingredients are applied on acres that also receive a glyphosate application. The ten most widely used herbicides are shown in Table L-10. Integration of MON 87708 into the Roundup Ready soybean system and the subsequent use of dicamba will result in the displacement of some currently used, or foreseeable future use herbicides, and therefore the properties of these alternative herbicides are summarized in this section to provide a baseline for comparison to dicamba use on MON 87708.

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Table L-10. Ten Most Widely Used Alternative Herbicides in U.S. Soybean Production

Herbicide	Treated acres (millions)[1]
2,4-D (acid, salts, and esters, combined)	6.32
flumioxazin	3.45
imazethapyr	3.35
cloransulam-methyl	2.90
chlorimuron-ethyl	2.66
fomesafen	2.26
clethodim	2.16
pendimethalin	2.15
tribenuron	2.05
flumiclorac-pentyl	1.32

[1] AgroTrak, 2009

Table L-11 also summarizes key information from alternate herbicide product labels that are included in the comparative analysis in Section L.5. Table L-12 lists the eighteen active ingredients that make up the products in Table L-11. 2,4-D, being used primarily as a pre-plant application, is the most widely-used herbicide in this alternate herbicide list, representing about 10% of treated acres; whereas acifluorfen, carfentrazone-ethyl, and flufenacet are the least used among these, representing <0.5% of treated acres. Mesotrione has not been used in soybean production previously; the use on soybean was only recently registered by the EPA (2009d). Table L-12 also lists general regulatory information about each herbicide. Note that only paraquat is classified as a Restricted Use pesticide among this group, on the basis of acute toxicological concern.

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Table L-11. Alternative Registered Soybean Herbicides

Brand (U.S. EPA Reg. No.)	Active Ingredient	Signal Word[1]	Active Ingredient Content	Re-entry Interval (REI)[2]	Max. Soybean lb/a (single treatment)[3]	Max. Soybean lb/a (season)	Label Warnings or Special Directions[4]
Aim® (279-3241)	Carfentrazone-ethyl	Caution	2 lb/gal	12 hr	0.008 [5]	0.023	"toxic to fish";"toxic to algae"; V3 - V10; do not feed foliage; some burn injury
Authority® First DF (279-3246)	Sulfentrazone Cloransulam-methyl	Caution	0.62 lb/lb 0.08 lb/lb	12 hr	0.31 0.04	0.31 0.04	"known to leach"; "toxic to marine / estuarine invertebrates.";65-day PHI; crop rotation restrictions, up to 30 mts; soil O.M. limits (sands <1% organic matter)
Authority MTZ (279-3340)	Sulfentrazone Metribuzin	Caution	0.18 lb/lb 0.27 lb/lb	12 hr	0.028 0.042	0.046 0.07	"known to leach"; "toxic to marine / estuarine invertebrates. 120-day PHI (not Over The Top); sensitive varieties, injury possible
Basagran® (7969-45)	Bentazon	Caution	4 lb/gal	48 hr	1	2	"known to leach";30-day PHI for feeding treated forage and hay; minor injury
Butoxone® 7500 (71368-49)	2,4-DB	Caution	0.75 lb/lb	48 hr	0.375		soil type limits
Butyrac® 200 (42750-38)	2,4-DB DMA salt	Danger	2 lb/gal	48 hr	0.4	0.4	"toxic to fish";60-day PHI; injury may occur, especially with tank mixtures
Cadet® (279-3338)	Fluthiacet-methyl	Warning	0.91 lb/gal	12 hr	0.0065	0.009	do not feed foliage; minor injury
Callisto® (100-1131)	Mesotrione	Caution	4 lb/gal	12 hr	0.1875	0.1875	"high potential for runoff"; crop rotation restrictions up to 18 mts; "transient bleaching" may occur; pre-emergence use only, no in crop use

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Table L-11 (continued). Alternative Registered Soybean Herbicides

Brand (U.S. EPA Reg. No.)	Active Ingredient	Signal Word[1]	Active Ingredient Content	Re-entry Interval (REI)[2]	Max. Soybean lb/a (single treatment)[3]	Max. Soybean lb/a (season)	Label Warnings or Special Directions[4]
Classic® (352-436)	Chlorimuron-ethyl	Caution	0.75 lb/lb	12 hr	0.14	0.14[6]	60-day PHI; crop rotation restrictions up to 30 mts and complicated description of 3 different intervals specific to US regions and soil pH; do not feed foliage; soil type limits; "temporary leaf yellowing"
Cobra® (59369-34)	Lactofen	Danger	2 lb/gal	12 hr	0.2	0.4[6]	"toxic to fish"; Do not apply past soybean growth stage R6 / 45-day PHI; minor injury
Extreme® (241-405)	Imazethapyr Glyphosate-IPA	Warning	0.17 lb/gal 2 lb/gal	48 hr	0.064[6] 0.75	0.064[6] 0.75	"properties & characteristics associated with chemicals detected in ground water"; crop rotation limits
FirstRate (62719-275)	Cloransulam-methyl	Caution	0.84 lb/lb	12 hr	0.04	0.055	65-day PHI; crop rotation restrictions up to 30 mts; soil types; 14-day forage and hay feeding restriction
Flexstar® (100-1101)	Fomesafen	Warning	1.88 lb/gal	24 hr	0.35	0.375[6]	"cause tumors"; "known to leach"; 45-day PHI; do not feed foliage; crop rotation limits
Gangster® Co-pack (59639-131)	Flumioxazin Cloransulam-methyl	Caution	51% 84%	12 hr	0.096 0.032	0.096 0.032	"toxic to aquatic invertebrates."; "Preemergent only. "properties & characteristics Associated with chemicals detected in ground water"; "toxic to invertebrates."
Gramaoxone Inteon® (100-1217)	Paraquat dichloride	Danger	2 lb/gal (cation basis)	12 hr	1.5	2.9	"toxic to wildlife"; Restricted Use; no Over-the-Top use

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Table L-11 (continued). Alternative Registered Soybean Herbicides

Brand (U.S. EPA Reg. No.)	Active Ingredient	Signal Word[1]	Active Ingredient Content	Re-entry Interval (REI)[2]	Max. Soybean lb/a (single treatment)[3]	Max. Soybean lb/a (season)	Label Warnings or Special Directions[4]
Ignite® (264-829)	Glufosinate-ammonium	Warning	2.34 lb/gal	12 hr	0.66	0.8	"runoff potential"; "toxic to vascular plants"; 70-day PHI; some crop rotation limits up to 180 days; only Over-the-Top to Liberty Link soybean
Liberty® (264-660)	Glufosinate-ammonium	Warning	1.67 lb/gal	12 hr	0.44	0.8	"runoff potential"; "toxic to vascular plants"; 70-day PHI; do not feed foliage; crop rotation limits up to 120 days;
Phoenix® (59639-118)	Lactofen	Caution	2 lb/gal	12 hr	0.3	0.4 [6]	"toxic to fish"; Do not apply past crop growth stage R6 / 45-day PHI; minor injury
Pursuit® (241-310)	Imazethapyr	Caution	2 lb/gal	4 hr	0.063	0.063	"properties & characteristics associated with chemicals detected in ground water"; 85-day PHI; do not feed forage and hay
Pursuit® Plus (241-331)	Pendimethalin	Caution	2.7 lb/gal	24 hr	0.84	0.84	"properties & characteristics associated with chemicals detected in ground water"; "toxic to fish"; 85-day PHI; crop rotation limits up to 40 months
	Imazethapyr		0.2 lb/gal		0.063	0.063	
Raptor ® (241-379)	Imazamox-ammonium	Caution	1 lb/gal	4 hr	0.04	0.04	"phytotoxic to all plants"; plantback / crop rotation limits up to 26 months, two regions with complicated warnings

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Table L-11 (continued). Alternative Registered Soybean Herbicides

Brand (U.S. EPA Reg. No.)	Active Ingredient	Signal Word[1]	Active Ingredient Content	Re-entry Interval (REI)[2]	Max. Soybean lb/a (single treatment)[3]	Max. Soybean lb/a (season)	Label Warnings or Special Directions[4]
Reflex® (100-993)	Fomesafen	Danger	2 lb/gal	24 hr	0.375	0.375[6]	"known to leach"; 45-day PHI; crop rotation limits up to 18 mts; minor injury, significant geographical restrictions (5 regions each with different rate structure)
Resource® (59639-82)	Flumiclorac-pentyl	Warning	0.86 lb/gal	12 hr	0.081	0.11	"toxic to shrimp"; 60-day PHI; do not feed forage or hay to livestock; temporary spotting or burn to soybean
Scepter ®70 DG (241-306)	Imazaquin	Caution	0.7 lb/lb	12 hr	0.123	0.123[6]	"properties & characteristics associated with chemicals detected in ground water"; 90-day PHI; do not feed forage or hay to livestock; crop rotation limits up to 40 mts; regional limitations (3 regions)
Sencor® (DF 75%) (264-738)	Metribuzin	Caution	0.75lb/lb	12 hr	0.66[6]	1.3[6]	"can seep or leach"; 70-day grain PHI; 40-day PHI on feeding forage to livestock; no Over-the-Top application, directed spray OK; injury in high pH or low O.M. soils or on certain crop varieties, crop rotation limits up to 18 mts
Synchrony® XP (352-648)	Thifensulfuron	Caution	0.069 lb/lb	12 hr	0.013	0.013	45-day planting restriction applied prior to soybean planting / emergence; 60-day PHI; complicated crop rotation restrictions (3 regions, 4 intervals) with limits up to 30 mts; do not feed forage or hay to livestock; soil types; injury if adjuvants or tank mixed
UltraBlazer (70506-60)	Acifluorfen sodium	Danger	2 lb/gal	48 hr	0.374	0.5	50-day PHI; minor injury
	Chlorimuron-ethyl		0.215 lb/lb		0.04	0.04	

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Table L-11 (continued). Alternative Registered Soybean Herbicides

Brand (U.S. EPA Reg. No.)	Active Ingredient	Signal Word[1]	Active Ingredient Content	Re-entry Interval (REI)[2]	Max. Soybean lb/a (single treatment)[3]	Max. Soybean lb/a (season)	Label Warnings or Special Directions[4]
Valor® SX (59639-99)	Flumioxazin	Caution	0.51 lb/lb	12 hr	0.096	0.096	"runoff potential"; "toxic to aquatic invertebrates."; preemergence use only, no in crop use; do not feed forage or hay to livestock; crop rotation limit up to 18 mts. & soil type limits; injury under cool wet conditions or poorly drained soil; restrictions on use with flufenacet, alachlor, metolachlor, or dimenthenamid
Valor® XLT (59639-117)	Flumioxazin	Caution	0.3 lb/lb	12 hr	0.094	0.094	"toxic to aquatic invertebrates."; preemergence only, no in crop use; do not feed forage or hay to livestock; crop rotation limits up to 30 mts; injury under cool wet conditions or poorly drained soil
	Chlorimuron-ethyl		0.103 lb/lb		0.032	0.032	
Weedone® (650, 638, LV4, LV6) and other 2,4-D brands (71368-3, -6, -10, -11, -14, -19)	2,4-D; 2,4-D salts; 2,4-D esters	Varies	Varies		0.93	0.93	Weedone 650 as an example: "toxic to aquatic invertebrates."; do not use on sandy soils (<1% O. M.); preplant to emerged weeds only , no in crop use; do not feed forage or hay to livestock.

[1] The EPA-required statement to convey to applicators the overall acute toxicity hazard posed by the product. Caution is more favorable than Warning, which is more favorable than Danger.

[2] The period of time following application during which worker reentry into the treated area is restricted, according to EPA's Worker Protection Standard (WPS).

[3] The highest single-treatment and seasonal rates that can be applied to soybean according to the product Directions for Use label.

[4] Lists specific statements extracted from the product label that represent specific hazards or limitations that may reduce the utility of the product for soybean weed control

[5] Higher rates with directed / hooded sprayers.

[6] Regional or soil type limitations may lower this rate.

[7] Soybean label not yet publically available. Corn label comments are cited

PHI – preharvest interval, O. M. – organic matter, mts - months.

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Table L-12. Active Ingredients Contained in Alternative Herbicides

Active Ingredient	First Registered[1]	2006 Treated Soybean Acreage (%)[2]	Registration Review Status[3]	RED Date[4]	Max. Soybean lb/a (single treatment)[5]	Max. Soybean lb/a (season)	Tolerances (40 CFR 180)[6]	Restricted Use[7]
glyphosate salts	3-May-76	97	open 2009	Sep-93	1.5	6	364	No
dicamba-diglycolamine salt	2-Feb-56	<0.5	NA	Jun-09, corrected	1[9]	2[9]	227	No
2,4-D acid, salts, and esters	3-Jun-52	10	2013	Jun-05	0.93	0.93	142	No
flumioxazin	12-Apr-2001	3	unscheduled	NA	0.096	0.096	568	No
imazethapyr	30-Jan-87	3	2014	Jun-06	0.064[8]	0.064[8]	447	No
cloransulam-methyl	29-Oct-1997	1	2011	NA	0.04	0.055	514	No
chlorimuron-ethyl	4-Apr-86	4	2011	Sep-04 TRED	0.14	0.14[8]	429	No
fomesafen	10-Apr-87	2	open 2007	TRED Aug-07	0.375	0.375[8]	433	No
flumiclorac-pentyl	23-Mar-94	1	open 2009	Aug-05 TRED	0.081	0.11	477	No
sulfentrazone	22-Nov-93	1	open 2009	NA	0.31	0.31	498	No
thifensulfuron	25-Apr-86	1	2011	NA	0.013	0.013	439	No
imazaquin	20-Mar-86	1	2014	TRED Dec-05	0.123	0.123[8]	426	No
imazamox-ammonium	17-Apr-95	<0.5	2014	NA	0.04	0.04	1223	No
paraquat dichloride	8-Jan-80	1	2012	Aug-97	1.0	2.9	205	**Yes**
lactofen	1-Apr-87	<0.5	open 2007	TRED Sep-03	0.3	0.4	432	No
glufosinate-ammonium	29-May-91	<0.5	open 2008	NA	0.66	0.8	473	No
2,4-DB	30-Jun-66	<0.5	2014	Jan-05	0.4	0.4	331	No
fluthiacet-methyl	14-Apr-99	<0.5	unknown	NA	0.0065	0.009	551	No
acifluorfen sodium	29-May-81	<0.5	unscheduled	Sep-09	0.374	0.5	383	No
Mesotrione	4-Jun-01	0.0	unscheduled	NA	0.1875	0.1875	571	No

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TRED denotes Tolerance Reregistration Eligibility Decision

[1] The date the herbicide was first approved for any use (*e.g.*, industrial) by U.S. EPA.
[2] The percentage of the herbicide-treated soybean acres that were treated with each herbicide in AR, IA, IL, IN, KS, KY, LA, MI, MN, MS, MO, NE, NC, ND, OH, SD, TN, VA, and WI in 2006 (USDA-NASS, 2007b) .
[3] The herbicide's progress in the ongoing EPA program named as Registration Review. Year indicates when the official docket was or will be opened. EPA is required by law to re-evaluate pesticides periodically, generally every 10-15 years.
[4] The date when EPA issued a Reregistration Eligibility Decision document. Reregistration was an earlier re-evaluation program designed to ensure that supporting data are up-to-date for a.i.s first registered before 1984. TRED means Tolerance Reassessment Eligibility Decision, which refers to an alternative review path that some post-1984 a.i.s followed.
[5] The maximum amount of the herbicide that can be applied to soybean in a single treatment or during the entire season, according to product labels.
[6] The number of the paragraph in the Code of Federal Regulations where that herbicide's food and feed tolerances are listed.
[7] An EPA pesticide classification that restricts a product, or its uses, to use by a certificated pesticide applicator or under the direct supervision of a certified applicator. See 40 CFR 152.160.
[8] Regional or soil type limitations may lower this rate.
[9] Maximum treatment rates for the proposed dicamba label.

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L.4.1. Human Health Effects of Alternative Herbicide Products

Table L-13 provides information concerning human health parameters for each alternative herbicide compared to dicamba. The listed parameters include:

- Acute Toxicity Categories for the herbicide.
- Cancer Classification of the herbicide.
- FQPA (Food Quality Protection Act) safety factor employed in EPA's risk assessment process for the herbicide.
- Level of Exposure representing the acceptable safe range for acute (acute population adjusted dose, aPAD) and chronic (chronic population adjusted dose, cPAD) exposures.
- Extent to which all presently approved uses exhaust the acceptable safe exposure range (% aPAD and % cPAD utilized for the most highly exposed population subgroups), according to recent Federal Register Rules or other public risk assessment documents.

A variety of chemical-specific public data sources were used to compile this comparison. Columns 9 to 11 in Table L-13 (to the right of the vertical gray bar) pertain specifically to the use of the herbicide in soybean:

- The established soybean seed food tolerance in 40 CFR 180 that supports the uses in soybean.
- The Theoretical Maximum Residue Concentration (TMRC) arising from this soybean tolerance using the DEEM dietary exposure software, assuming that residues are at tolerance levels and that 100% of the crop has been treated.
- The percentage of the acceptable chronic exposure (cPAD) that is contributed by the soybean TMRC dietary exposure.

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Table L-13. Human Health Risk Parameters for Alternative Herbicides

Active Ingredient	Acute (Oral, Dermal, Inhalation, Eye Irr., Skin Irr., Sens.)[1]	Cancer Classification[2]	cPAD mg/kg/day[3]	% cPAD Utilized[4,5]	aPAD mg/kg/day[6]	% aPAD Utilized [6,5]	FQPA SF[7]		Soy Seed Tol. (ppm)[8,9]	Soybean diet exposure µg/kg/day[5,8,10]	% Soybean diet exposure / cPAD[8,11]
glyphosate acid / potassium salt	IV / IV / NA / II / IV / N; IV / IV / III / III / IV / N	E	1.75	7	NA	NA	1X		20	33.24	1.90%
dicamba acid diglycolamine salt[12]	III / III / IV / II / II / N; III / III / IV / III / III / N	not likely	0.45	6.6	1	11	1x		10	16.62	3.69%
2,4-D acid /salts / esters	III / III / III/ **I** / III-IV / N; III / III / IV / III / IV / N	D	0.005	38	0.067	58	1X		0.02	0.03	0.66%
flumioxazin	IV/III/IV/III/IV/N	not likely	0.02	18	0.03	8	1X		0.02	0.03	0.17%
imazethapyr	IV / III / IV / IV / III / N	not likely	2.5	< 1	NA	NA	1X		0.1	0.17	0.01%
cloransulam-methyl	IV / III / III / III / IV / N	not likely	0.1	<1	NA	NA	1X		0.02	0.03	0.03%
chlorimuron-ethyl	IV / III / IV / III / IV / N	not likely	0.09	0	NA	NA	1X		0.05	0.08	0.09%
fomesafen	III / II /III / **I** / II-III / Y	not likely	0.0025	31	NA	NA	1X		0.05	0.08	3.32%
flumiclorac-pentyl	IV / III/ IV/ IV/ II/ Y	no evidence	1	< 0.01	NA	NA	1X		0.01	0.02	0.00%
sulfentrazone	III/ III / IV / **I** / IV / Y	not likely	0.14	<1	0.25	1	1X		0.05	0.08	0.06%
thifensulfuron	IV / III / IV / IV / III / N	not likely	0.07	<1	1.59	<0.1	1X		0.1	0.17	0.24%
imazaquin	IV / III / III / IV / IV / N	no evidence	0.25	<1	NA	NA	1X		0.05	0.08	0.03%
imazamox-ammonium	IV / III / IV / III / IV / N	not likely	NA	NA	NA	NA	1X		ex '03	NA	NA
paraquat dichloride	II / III / **I** /II / IV / N	E	0.00045	26	0.0042	66	1X		0.7	1.16	**258.53%**

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Table L-13 (continued). Human Health Risk Parameters for Alternative Herbicides

Active Ingredient	Acute (Oral, Dermal, Inhalation, Eye Irr., Skin Irr., Sens.)[1]	Cancer Classification[2]	cPAD mg/kg/day[3]	% cPAD Utilized[4,5]	aPAD mg/kg/day[6]	% aPAD Utilized [6,5]	FQPA SF[7]		Soy Seed Tol. (ppm) [8,9]	Soybean diet exposure µg/kg/day [5,8,10]	% Soybean diet exposure / cPAD [8,11]
lactofen	IV / III / IV / III / IV / N	likely/unlikely	0.008	<0.1	0.17	<0.1	**3X (A)**		0.01	0.02	0.21%
glufosinate-ammonium	III / III / III / III / IV / N	no evid. of	0.006	27	0.0063	48	1X		2	3.32	**55.40%**
2,4-DB	III / III / IV / III / IV /	not likely	0.03	2	0.6	<1	1X		0.5	0.83	2.77%
fluthiacet-methyl	IV / III / IV / IV / IV /N	**likely ($7.5x10^{-7}$)**	0.001	<1	NA	NA	1X		0.01	0.02	1.66%
acifluorfen sodium	III / III / IV / **I** / II / N	likely/unlikely	0.013	<1	0.02	<1	**1X/3X /10X**		0.1	0.17	1.28%
mesotrione	IV / III / IV / III / IV / N	not likely	0.007	5.8	NA	NA	**3X**		0.01	0.02	0.23%

Sources of the information summarized in this table are listed in the Alternative Herbicide Specific References Section.

N denotes negative for dermal sensitization

NA stands for not applicable.

[1] EPA categories for the standard six acute toxicity tests of the active ingredient. Categories I and IV denote the least and most favorable findings, respectively. Category I findings are highlighted in **bold** font.

[2] The conclusion reached by the EPA Office of Pesticide Programs Cancer Assessment Review Committee. The system of classification has changed over the years, resulting in a combination of different terminology. Generally, Group E, "not likely" or "no evid." are the most favorable conclusions, Group D indicates some uncertainty, and "likely/not likely" or "likely" indicate that a potential to induce cancer exists. More information can be found at http://www.epa.gov/opp00001/health/cancerfs.htm. |Accessed March 26, 2010| "Likely" findings are highlighted in bold font.

[3] The EPA-determined chronic Population Adjusted Dose, against which chronic exposure, primarily from combined food and water residues, are compared for human health risk assessment. This key risk assessment parameter is derived from consideration of all the chronic toxicity studies, and includes all necessary safety factors. Higher values indicate herbicides with less severe chronic toxicity effects.

[4] The percentage of the cPAD that is represented by all presently approved uses of that herbicide for the most highly-exposed population subgroup. It is calculated by summing estimated chronic exposures from dietary and water, and dividing by the level of exposure that is considered safe (*i.e.*, cPAD). Lower percentages indicate that current estimated exposure is a smaller proportion of the safe level, and therefore implies a greater margin of safety. EPA presents this calculation when new risk assessments are conducted, such as when a new food tolerance is petitioned.

[5] Most highly exposed population subgroup.

[6] The acute risk assessment parameters correspond to those described above for chronic exposure. In some cases, EPA's review of the acute toxicity testing does not result in an acute effect of concern, and no aPAD is needed, indicated in the table as NA.

[7] The Safety Factor EPA has utilized according to the requirements of the Food Quality Protection Act. FQPA that requires EPA utilize an additional 10-fold (10x) safety factor to protect infants and children, unless the scientific results indicate that a different level is protective. If the database is complete, and the reproductive

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and developmental toxicity studies do not indicate that pre- and postnatal exposure results in increased sensitivity, EPA often reduces the FQPA SF to 1x. If there is indication of increased sensitivity, or the necessary data are lacking, SFs of 3X or 10X are sometimes used. These higher safety factors are considered in this analysis to denote higher risk to infants and children, and such cases are highlighted in bold font.

[8] The 3 columns to the right of the gray bar pertain to the use of each herbicide on soybean only, other current uses are excluded from this analysis.

[9] The soybean seed food tolerance established in the relevant numbered paragraph in 40 CFR 180.

[10] The Monsanto-calculated theoretical maximum dietary exposure to the most highly-exposed U.S. population subgroup if 100% of all soybean were treated with that herbicide, and residues were at tolerance levels. This theoretical exposure does not occur in real life, but allows a consistent comparison for all alternate herbicides. The calculation is made using the same DEEM dietary exposure model that EPA routinely uses http://www.durango-software.com/software/deem.html. |Accessed March 26, 2010|.

[11] The ratio of the prior column divided by the cPAD. It denotes the percentage of the safe exposure level that is attributed to soybean residues, as a soybean risk index. High numbers are less favorable. Any value above 100% requires further risk refinement to be deemed acceptable, such as that for paraquat. Values greater than 10-times that of dicamba are highlighted in bold font.

[12] Dicamba diglycolamine data are for Clarity (U.S. EPA Reg. No. 7969-137) and M1691 formulations (U.S. EPA Reg. No. 524-582).

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L.4.2. Ecological Effects of Alternative Herbicide Products – Non-target Species

L.4.2.1 Fish and Aquatic Invertebrates.

Table L-14 provides information about the hazards, exposures, and risks of dicamba and each of the eighteen alternative herbicides to fish and aquatic invertebrates (considering 2,4-D acid, salts, and esters as one alternative herbicide). The listed parameters include:

- LC_{50} endpoints from acute fish toxicity studies, as reported in EPA's one-liner database[55], published in a RED or Registration Review risk assessments. The highest and lowest available LC_{50} values for any fish study are listed, regardless of species, including both fresh and marine species together. The purpose is to define a range of concentrations that spans the expected fish-toxic levels.

- EC_{50} endpoints from acute aquatic invertebrate studies, as reported from the same sources cited above. The highest and lowest available EC_{50} values for any invertebrate study are listed, regardless of species, including both fresh and marine species together. The purpose is to define a range of concentrations that spans the expected aquatic invertebrate-toxic levels.

- Estimated environmental exposure concentrations (EECs) in surface water for each of the eighteen alternative herbicides. The third column in Table L-14, identified as "Calculated EEC", provides a simple standard estimate based on the maximum single application rate in soybean, using EPA's standard field-farm pond scenario. This scenario examines a 1-acre pond in a 10-acre field in which (1) 5% of the application drifts into the 6-foot-deep pond and (2) 5% of the application onto the 10 acres runs off into the same pond. The fourth column in Table L-14 lists other model estimates of surface water concentrations as provided by one or more modeling programs, as cited by EPA in public documents, such as Federal Register final tolerance rule drinking water assessments. The purpose is to define a range of concentrations that spans available estimates of potential aquatic exposure levels.

- Calculated Risk Quotients (RQs) for aquatic animals, comprised of fish and aquatic invertebrates combined together. Rather than calculate a single RQ for each species, Monsanto has calculated a range of potential RQs for each herbicide, bracketed by the best- and worst-case values. The "best" RQ is derived from the ratio of the lowest reported EEC concentration divided by the highest LC_{50} or EC_{50} for any aquatic animal. Conversely, the "worst" RQ is derived from the ratio of the highest EEC concentration divided by the lowest LC_{50} or EC_{50} for any aquatic animal. (Note: the RQ figures are rounded to two decimal places, so that entries that appear as "0.00" mean that the specific RQ is less than 0.005.) The purpose is to define a range of RQs that span and describe the risk posed by

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[55] National Information System – Regional IPM Centers. OPP Pesticide Ecotoxicity Database. http://www.ipmcenters.org/Ecotox/index.cfm [Accessed May 27, 2010].

the alternative herbicide to aquatic animals. The RQs that exceed the EPA's Level of Concern (LOC) of 0.5 are marked in bold font.

Using the worst case risk quotient, ten of 18 alternative herbicides have risk quotients greater than or equal to 0.01, while the worst case risk quotient for dicamba and seven other herbicide is <0.01. Only three of these 10 herbicides have risk quotients greater than 0.05 or 0.1, the levels of concern for threatened or endangered species and acute restricted use, respectively. Two of these 10 herbicides have RQ values greater than 0.5, the highest acceptable level of concern. Monsanto believes that based on risk quotients, dicamba offers a lower risk to aquatic animals relative to three of the 18 alternative herbicides: 2,4-D esters, flumioxazin, and lactofen. This conclusion is tabulated in Table L-17.

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Table L-14. Aquatic Toxicity Parameters for Fish and Aquatic Invertebrates for Alternative Herbicides

Active Ingredient	Maximum Soybean lb/acre (single treatment)[1]	Calculated EEC (ppm) [2,3]	FIRST, GENEEC or PRZX/EXAMS Surface Water ppm (RED or Tolerance Rule)[4]	Fish LC_{50} Range (ppm)[5]		Aquatic Invertebrate LC_{50} or EC_{50} Range (ppm)[f]		Risk Quotient for Aquatic Animals Range[6]		Label Warnings[7]
				low	high	low	high	best	worst	
glyphosate salts	1.5	0.050	0.0008 - 0.021	45	>1000	55	780	0.00	0.00	
dicamba /DGA salt	1	0.034	0.01 - 0.036	28	> 270	>100	>270	0.00	0.00	
2,4-D acid + salts	0.93	0.031	0.064 - 0.118	>80	2244	25	820	0.00	0.00	
2,4-D esters	0.93	0.031	0.064 - 0.118	>0.15	14.5	2.2	12	0.00	**< 0.79**	
flumioxazin	0.096	0.003	0.018 - 0.034	2.3	21	0.23	5.5	0.00	0.15	"toxic to invertebrates"
imazethapyr	0.064	0.002	0.006	> 112	423	> 109	> 1000	0.00	0.00	
cloransulam-methyl	0.04	0.001	0.002	> 86	> 154	> 111	> 121	0.00	0.00	"toxic to invertebrates"
chlorimuron-ethyl	0.14	0.005	0.003 - 0.005	> 2	8.4	>10[a]	> 10	0.00	0.00	
fomesafen	0.375	0.013	0.006 - 0.012	126	> 163	25	376	0.00	0.00	
flumiclorac-pentyl	0.081	0.003	0.00024	>0.189	> 24	>0.189	>38	0.00	0.02	"toxic to shrimp"
sulfentrazone	0.31	0.010	0.004 - 0.016	94	> 120	1	60.4	0.00	0.02	"toxic to invertebrates"
thifensulfuron	0.013	0.000	0.0003 - 0.004	>100	> 100	>1000	> 1000	0.00	0.00	

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Table L-14 (continued). Aquatic Toxicity Parameters for Fish and Aquatic Invertebrates for Alternative Herbicides

Active Ingredient	Maximum Soybean lb/acre (single treatment)[1]	Calculated EEC (ppm) [2,3]	FIRST, GENEEC or PRZX/EXAMS Surface Water ppm (RED or Tolerance Rule)[4]	Fish LC_{50} Range (ppm)[5]		Aquatic Invertebrate LC_{50} or EC_{50} Range (ppm)[5]		Risk Quotient for Aquatic Animals Range[6]		Label Warnings[7]
				low	high	low	high	best	worst	
imazaquin	0.123	0.004	0.004 - 0.008	280	420	280[a]	280	0.00	0.00	
imazamox-ammonium	0.04	0.001	0.002	> 94.2	> 122	>94.3	> 122	0.00	0.00	
paraquat dichloride	1.0	0.033	0.0015	>1	156	1.2	1.2	0.00	< 0.05	
lactofen	0.3	0.011	0.000008 - 0.4	0.46	0.46	0.02	4.85	0.00	**20**	"toxic to fish"
glufosinate-ammonium	0.66	0.022	0.043 - 0.094	> 320	> 1000	8	668	0.00	0.01	
2,4-DB	0.4	0.013	0.013 - 0.015	2	18	25[a]	25	0.00	0.01	"toxic to fish"
fluthiacet-methyl	0.0065	0.000	0.0005 - 0.0008	0.043	0.16	0.3	>2.3	0.00	0.02	
acifluorfen sodium	0.374	0.013	0.0024 - 0.010	31	204	28.1	> 1000	0.00	0.00	
mesotrione	0.1875	0.011	0.004 - 0.02	> 114	520	3.3	840	0.00	0.01	

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[1] The highest single-treatment rate permitted by the herbicide's product labels. This rate is used to calculate potential acute exposure to aquatic non-target species via spray drift or runoff.

[2] Based on the maximum single treatment rate, with 5% spray drift and 5% runoff from 10 treated acres into a 1-acre 6-foot-deep pond.

[3] The Estimated Environmental Concentration in surface water. It was calculated by Monsanto using the EPA's "standard field-farm pond scenario" http://www.epa.gov/oppefed1/models/water/geneec2_description.htm |Accessed May 28, 2010|. In this scenario, it is assumed that the herbicide is applied to a 10 acre farm field containing a 1 acre pond that is six feet deep. The pond experiences 5% of the application rate by spray drift and 5% of the application on the soil enters the pond via runoff. This concentration estimation is a simple, conservative Tier 1 procedure that utilizes only the application rate to estimate aquatic

exposures, and allows quick comparison of many different herbicides. Other more increasingly-detailed computer models can be used to obtain more refined EEC estimates, but these require the user to input various physical chemical parameters and weather data for each product to be modeled. Examples of these methods are listed in the next column.

[4] Modeling estimates of potential aquatic exposure levels. When EPA conducts risk assessments, it uses computer models to obtain estimates of potential surface water concentrations. These are published in the RED for each herbicide, or in tolerance rules in the Federal Register. The range of estimates is listed, which can be compared to the single number in the prior column. Sources of these estimates are listed in the "ALTERNATIVE HERBICIDE-SPECIFIC REFERENCES" section.

[5] "Fish LC$_{50}$ Range (ppm)" and "Aquatic Invertebrate LC$_{50}$ or EC$_{50}$ Range (ppm)". These four columns describe the range of hazard data found in public data sources representing the toxicity of each herbicide versus freshwater and marine animals. The LC$_{50}$ or EC$_{50}$ means the water concentration needed to kill or immobilize half of the test species, which is a standard potency descriptor. The highest and lowest values found for any fish species (trout, bluegill, sheepshead, etc.) were tabulated. Likewise, the highest and lowest values found for any aquatic invertebrate species (Daphnia, shrimp, crab, etc.) were included. Sources of these data are listed in the "ALTERNATIVE HERBICIDE-SPECIFIC REFERENCES" section and in available public databases (National Information System – Regional IPM Centers. OPP Pesticide Ecotoxicity Database. http://www.ipmcenters.org/Ecotox/index.cfm) |Accessed May 28, 2010|.

[6] EPA's EFED uses a Risk Quotient (RQ) method for ecological risk assessment. The RQ equals the potential exposure level divided by the hazard level. Higher exposures or more potent hazard findings lead to higher RQs. EFED has established Levels of Concern (LOCs) for various non-target species categories. When the RQ exceeds the LOC, further refinement is needed to determine whether risk mitigation might be needed. For non-listed aquatic animals, the LOC for acute risk is 0.5, for acute risk restricted use is 0.1, and for threatened or endangered species it is 0.05. In this analysis, Monsanto calculated best-case RQs by dividing the lowest EEC estimate by the highest hazard (LC$_{50}$ or EC$_{50}$) value, and calculated the worst-case RQ from the highest EEC and lowest hazard value. The purpose was to bracket a range that typified the aquatic animal risk presented by each herbicide. When neither the worst-case nor the best-case RQs exceed a LOC of 0.05, Monsanto concluded that risk to aquatic animals is minimal. Instances where the LOC threshold of 0.5 is exceeded are highlighted in bold font.

[7] Lists instances where the product label includes warning statements about aquatic animal exposure.

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L.4.2.2. Aquatic Plants

Table L-15 provides information about the hazards, exposures, and risks of dicamba and each of the eighteen (18) alternative herbicides to aquatic plant species, specifically duckweed and aquatic algae species (considering 2,4-D acid, salts, and esters as one alternative herbicide). The data format, sources, and methods of Estimated Environmental Exposure Concentration (EEC) calculation are identical to those described above for the aquatic animals (Table L-14). A Level of Concern (LOC) value of 1.0 has been used for judging RQ exceedances in the case of aquatic plants, consistent with EPA EFED's normal practices.

The assessment and comparison summarized in Table L-15 establishes that dicamba poses little acute risk to aquatic plants at use rates of 0.05 – 1.0 lb dicamba a.e./acre, which is consistent with EFED's assessment published in the RED EFED Chapter. Monsanto was unable to identify aquatic plant hazard data for three of the alternative herbicides (imazaquin, chlorimuron-ethyl, and flumiclorac-pentyl). For nine (9) of the eighteen (18) alternative herbicides, the range of RQs is < 0.005 to 0.75; that is, none of these nine a.i.s present an aquatic plant risk, which even in the worst-case calculation, reach EFED's Level of Concern (LOC) for aquatic plants. However, for seven of the alternative herbicides, the worst-case RQs did exceed EFED's LOC of 1.0. It is not surprising that some herbicides are quite toxic to aquatic plants, and the worst-case RQs for three of the alternate herbicides (flumioxazin, lactofen, and paraquat dichloride) exceeded the LOC by a factor of more than 50-fold.

Monsanto believes that dicamba offers a lower risk to aquatic plants relative to seven of the 18 alternative herbicides (2,4-D, flumioxazin, sulfentrazone, thifenslufuron, paraquat dichloride, lactofen, and mesotrione). This conclusion is tabulated in Table L-17.

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Table L-15. Aquatic Toxicity Parameters for Aquatic Plants for Alternate Herbicide Active Ingredients

Active Ingredient	Maximum Soybean lb/acre (single treatment)[1]	Calculated EEC (ppm)[2,3]	FIRST, GENEEC or PRZX/EXAMS Surface Water ppm (RED or Tolerance Rule)[4]	Duckweed and Algae EC_{50} Range (ppm)[5]		Risk Quotient for Aquatic Plants Range[6]	
				low	high	best	worst
glyphosate salts	1.5	0.050	0.0008 - 0.021	0.77	38.6	0.00	0.06
dicamba /DGA salt	1	0.034	0.01 - 0.036	0.06	> 3.7	0.00	0.60
2,4-D acid + salts	0.93	0.031	0.064 - 0.118	0.29	156	0.00	0.41
2,4-D esters	0.93	0.031	0.064 - 0.118	0.066	>19.8	0.00	**1.79**
flumioxazin	0.096	0.003	0.018 - 0.034	0.0005	0.019	0.16	**68.00**
imazethapyr	0.064 *	0.002	0.006	0.008	59.2	0.00	0.75
cloransulam-methyl	0.04	0.001	0.002	0.003	135	0.00	0.67
chlorimuron-ethyl	0.14	0.005	0.003 - 0.005	NA	NA	NA	NA
fomesafen	0.375	0.013	0.006 - 0.012	0.09	71	0.00	0.14
flumiclorac-pentyl	0.081	0.003	0.00024	NA	NA	NA	NA
sulfentrazone	0.31	0.010	0.004 - 0.016	0.002	0.033	0.12	**8.0**
thifensulfuron	0.013	0.000	0.0003 - 0.004	0.0016	> 0.026	0.02	**2.50**
imazaquin	0.123	0.004	0.004 - 0.008	NA	NA	NA	NA
imazamox-ammonium	0.04	0.001	0.002	0.011	> 0.038	0.03	0.18
paraquat dichloride	1.0	0.033	0.0015	0.00055	2.84	0.00	**90.9**
lactofen	0.3	0.011	0.000008 - 0.4	0.001	0.001	0.00	**400**
glufosinate-ammonium	0.66	0.022	0.043 - 0.094	1.5	7.8	0.00	0.06
2,4-DB	0.4	0.013	0.013 - 0.015	>0.932	>0.932	<0.01	<0.02
fluthiacet-methyl	0.0065	0.000	0.0005 - 0.0008	0.0022	>0.018	<0.01	0.36
acifluorfen sodium	0.374	0.013	0.0024 - 0.010	> 0.26	0.38	0.01	<0.05
mesotrione	0.1875	0.011	0.004 - 0.02	0.018	132	0.00	**1.11**

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The first three columns in this table are identical to- those in Table L-14.

[1] The highest single-treatment rate permitted by the herbicide's product labels. This rate is used to calculate potential acute exposure to aquatic non-target species via spray drift or runoff.

[2] Based on the maximum single treatment rate, with 5% spray drift and 5% runoff from 10 treated acres into a 1-acre 6-foot-deep pond.

[3] The Estimated Environmental Concentration in surface water. It was calculated by Monsanto using the EPA's "standard field-farm pond scenario" http://www.epa.gov/oppefed1/models/water/geneec2_description.htm |Accessed May 28, 2010|. In this scenario, it is assumed that the herbicide is applied to a 10 acre farm field containing a 1 acre pond that is six feet deep. The pond experiences 5% of the application rate by spray drift and 5% of the application on the soil enters the pond via runoff. This concentration estimation is a simple, conservative Tier 1 procedure that utilizes only the application rate to estimate aquatic exposures, and allows quick comparison of many different herbicides. Other more increasingly-detailed computer models can be used to obtain more refined EEC estimates, but these require the user to input various physical chemical parameters and weather data for each product to be modeled. Examples of these methods are listed in the next column.

[4] Modeling estimates of potential aquatic exposure levels. When EPA conducts risk assessments, it uses a computer models to obtain estimates of potential surface water concentrations. These are published in the RED for each herbicide, or in tolerance rules in the Federal Register. The range of estimates is listed, which can be compared to the single number in the prior column. Sources of these estimates are listed in the "ALTERNATIVE HERBICIDE-SPECIFIC REFERENCES" section.

[5] These two columns describe the range of hazard data found in public data sources representing the toxicity of each A.I. versus freshwater and marine plants. The EC_{50} means the water concentration needed to kill or prevent growth of half of the test species, which is a standard potency descriptor. The highest and lowest values found for any aquatic plant species (diatom, duckweed, alga, etc.) were tabulated. Sources of these data are listed in the "ALTERNATIVE HERBICIDE-SPECIFIC REFERENCES" section of this document and in available public databases cited in footnote 37 (National Information System – Regional IPM Centers. OPP Pesticide Ecotoxicity Database. http://www.ipmcenters.org/Ecotox/index.cfm |Accessed May 28, 2010|)

[6] As described above for Table L-15, EPA's EFED uses a Risk Quotient (RQ) method for ecological risk assessment. For non-listed aquatic plants or for threatened or endangered species the LOC is 1.0. In this analysis, Monsanto calculated best-case RQs by dividing the lowest EEC estimate by the highest hazard (EC_{50}) value, and calculated the worst-case RQ from the highest EEC and lowest hazard value. The purpose was to bracket a range that typified the aquatic plant risk presented by each herbicide. When neither the worst-case nor the best-case RQs exceed a LOC of 1.0, Monsanto concluded that risk to aquatic plants is minimal. Instances where the LOC threshold of 1.0 is exceeded are highlighted in bold font.

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L.4.3. Looking Toward the Foreseeable Future

As noted, weeds that are difficult to control with glyphosate and weeds that are glyphosate-resistant, PPO-resistant, or ALS-resistant represent an opportunity for improved weed control in soybean. To address this need, Monsanto is seeking to commercialize MON 87708, which will allow dicamba to be used as a weed control tool in this important U.S. crop. Monsanto is also aware that other companies are developing biotechnology-derived soybean enhanced with other herbicide-tolerant traits.

Biotechnology-derived soybean developed to be tolerant to applications of 2,4-D has been submitted to USDA-APHIS for deregulation.[56] Monsanto proposes that 2,4-D presents more relative risk than dicamba in the area of acute human health and chronic exposure risk, and for 2,4-DB relatively more ecological risk for aquatic animals. Applications of 2,4-D will also require management of offsite movement.

In addition, biotechnology-derived soybean enhanced to be tolerant to herbicides that inhibit 4-hydroxyphenylpyruvate dioxygenase (HPPD) is one such trait that Monsanto believes is in development, based on public announcements from companies other than Monsanto; evidence of these developments is apparent in the recent EPA approval of mesotrione for use on mesotrione-tolerant soybean (U.S. EPA, 2009e). HPPD-tolerance allows use of these broadleaf herbicides in soybean production, which is a good technical fit as highlighted by Table L-16 which shows many of the troublesome soybean weeds are effectively controlled by HPPD herbicide products such as Balance Pro (active ingredient: isoxaflutole), Laudis (active ingredient: tembotrione) or Callisto Herbicide (active ingredient: mesotrione). Since some of these products are not yet registered for soybean use, and the label for Callisto defining application parameters in soybean is not yet commercially available, it is not possible to undertake a rigorous application-rate-based risk comparison with dicamba, but it is possible to make a hazard comparison, using isoxaflutole and tembotrione as typical examples (mesotrione is included above in the discussion of alternate herbicides, since has been approved by EPA).

Inhibition of HPPD in plants results in a disruption of carotenoid biosynthesis, which leaves the plant's chlorophyll pigments unprotected from rapid degradation via photooxidation, and results in a very characteristic white bleached symptomology of plant parts that are normally green. HPPD is also an animal liver enzyme involved in the catabolic breakdown of tyrosine, and its inhibition in laboratory animals results in elevated tyrosine plasma concentrations (tyrosinemia), which can cause adverse ocular, developmental, liver, and kidney effects. Stated simply, the mechanism of herbicidal efficacy based on HPPD inhibition is inherently linked to a potential for negative human health effects.

Publicly available study results show that isoxaflutole and tembotrione both caused ocular and liver effects in test animals, and both caused developmental toxicity at non-

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[56] Dow Agrosciences press release, December 15, 2009. http://www.dowagro.com/newsroom/corporatenews/2009/20091215a.htm. [Accessed March, 26, 2010].

maternally toxic levels. Because of the potent toxic effects, EPA has calculated cPADs for isoxaflutole and tembotrione that are lower than that of dicamba by factors of 225 and 1125, respectively. EPA is also considering the need for a cumulative risk assessment approach for these two chemicals, along with mesotrione and other HPPD-inhibiting herbicides, because they share a common toxic mechanism (U.S. EPA, 2009d, e). In addition, both isoxaflutole and tembotrione had carcinogenic effects in long-term testing summarized by EPA. For tembotrione, carcinogenicity was limited to rats only, but isoxaflutole was found to have carcinogenic effects in two species, and was categorized by EPA as a B2 carcinogen in 1998 when first registered. Isoxaflutole products, such as Balance Pro, are Restricted Use pesticides because of a very high level of concern about damage to non-target plants caused by spray drift, and isoxaflutole labels also bear warning statements about the likelihood of persistence and leaching. There have also been concerns about isoxaflutole use leading to levels of herbicidally-active isoxaflutole metabolites in surface water utilized for irrigation purposes. Because of these properties of HPPD chemicals, Monsanto believes that dicamba offers a lower risk relative to these potential future soybean herbicides.

L.4.4. Efficacy and Weed Management Practices of Alternative Herbicide Products

Table L-16 provides weed control effectiveness of formulated products containing dicamba, glyphosate and alternate herbicides. Weed control less than 70% is considered insufficient (white), control between 70 and 85% is considered as marginal effectiveness (black-white), and control of more than 85% is considered commercially acceptable (black). The data presented in Table L-16 are derived by combining state and dealer[57] herbicide guidance for soybean production across major soybean-producing states (Ohio and Indiana[58], Iowa[59], Tennessee[60], North Dakota[61]). Weed control herbicide recommendations provided by University Extension scientists to control specific weeds were converted to a common scale and combined to reflect an average herbicide weed control rating across geographies. Weed control ratings specific to resistant weeds were based mainly on recommendations from Ohio and Indiana. Monsanto weed scientists applied their own expert scientific judgment during the conversion of University Extension recommendations into a common scale. The weeds chosen for inclusion in Table L-16 represent current problem weeds in soybean, either because they exhibit herbicide resistance or because they are generally hard-to-control species.

As Table L-16 shows, the alternative herbicides can be used in preemergent applications, postemergent applications, or, like dicamba and glyphosate, as both pre- and

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[57] 2009 Crop Protection Guide - Information for Dealers http://www.agrisolutionsinfo.com/ *Accessed May 28, 2010*

[58] 2010 Ohio and Indiana Weed Control Guide (Bulletin 789; Pub. WS16) www.btny.purdue.edu/Pubs/WS/WS-16/ *Accessed May 28, 2010*

[59] 2009 Herbicide Guide for Corn and Soybean Production - http://www.weeds.iastate.edu [Accessed May 28, 2010]

[60] 2010 Weed Control Manual for Tennessee http://www.utextension.utk.edu/publications/pbfiles/pb1580.pdf *Accessed may 28, 2010*

[61] 2010(a) NDSU Weed Control Guide - http://www.ndsu.edu/weeds *Accessed May 28, 2010*

postemergent applications. Several herbicides, such as 2,4-D, 2,4-DB, sulfentrazone and paraquat, do not have sufficient soybean safety for application in-crop, so their use is limited to control of existing weeds and preemergent control of later emerging weeds via soil residual activity, if any. Others, such as the protoporphyrinogen oxidase (PPO) inhibitors acifluorofen, lactofen, and fomesafen, are most effective as postemergent treatments, even though they may cause some soybean leaf injury. Acetolactate synthase (ALS) inhibitors like chlorimuron-ethyl and cloransulam-methyl can be used at either timing. Glufosinate, like glyphosate and dicamba, does not have intrinsic soybean selectivity and can only be used as a postemergent application over soybean that is genetically enhanced to provide glufosinate tolerance (*i.e.*, Liberty Link).

Table L-16 also highlights expected weed efficacy trends. Glyphosate does not provide commercial control of glyphosate-resistant weed biotypes such as common ragweed or horseweed, but does control the wild type plants of these species. Similarly, ALS-inhibiting herbicides provide poor control of ALS-resistant weeds, and PPO inhibitors do not adequately control PPO-resistant weeds. Table L-16 focuses on problem weeds found in soybean and does not include any weeds with auxin resistance, although 2,4-D provides good control of many herbicide-resistant broadleaf weed biotypes in this group. Extreme, which contains two modes-of-action (glyphosate and imazethapyr), provides better control of this target weed spectrum than most of the herbicide products having only a single mode-of-action.

Further discussion of the comparative effectiveness of dicamba versus alternative herbicide products against herbicide-resistant and hard-to-control weeds can be found in L.5.3.

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Table L-16. Herbicide Efficacy Comparison: Herbicide Resistant Weeds and Hard-to-Control Weeds in Soybean

●	>85% control
◐	70% - 85% control
○	< 70% control

			Resistant Weeds[1]														Hard-to-Control Weeds[2]													
Herbicide	Herbicide Brand	Class	GR Waterhemp	GR Palmer amaranth	GR Horseweed	GR C. ragweed	GR G. ragweed	GR Johnsongrass	ALS C. ragweed	ALS+PPO C. ragweed	ALS+GR C. ragweed	ALS G. ragweed	ALS+GR G. ragweed	ALS+GR Horseweed	ALS Kochia	TRI Lambsquarters	A. Morningglory	B. Nightshade	Cocklebur	C. Ragweed	G. Ragweed	Hemp sesbania	Kochia	Lambsquarters	Horseweed	Palmer Amaranth	Prickly Sida	Sicklepod	Velvetleaf	Waterhemp
Glyphosate	Roundup	EPSPS	○	○	○	○	○	○	●	●	○	●	○	○	●	◐	○	◐	●	●	◐	○	●	◐	●	●	○	●	◐	◐
Dicamba	Clarity	auxin	●	●	●	●	●	○	●	●	●	●	●	●	●	●	●	◐	●	●	●		●	●	◐	●	●	●	◐	●
PREEMERGENCE/BURNDOWN[3]																														
2,4-D	2,4-D	auxin	●	◐	●	●	●	○	●	●	●	●	●	●	●	●	●	○	●	●	●		○	●	◐	◐	◐	◐	◐	◐
2,4 DB	Butyrac 200	auxin	○	○	○	○	○	○	○	○	○	○	○	○	○	●	◐		◐	○		○				◐	○	○		
Chlorimuron + Metribuzin	Canopy DF	ALS/PSII	○	◐	●	◐	◐	○	○	○	○	○	○	○	○	●	○		◐	◐	◐	◐	◐	●	●	◐	◐	○	◐	○
Chlorimuron + Tribenuron	Canopy EX	ALS	◐		●	●	◐	○	○	○	○	○	○	○	○	●	◐		◐	●	◐		◐	●	●		◐		◐	
Imazaquin	Scepter	ALS	○	○	○	◐	◐	○	○	○	○	○	○	○	○	●	○	●	●	◐	◐	○	○	●	○	○	◐	◐	○	
Sulfentrazone + Imazethapyr	Authority Assist	PPO/ALS	●	●	◐	○	○	◐	○	○	○	○	○	◐	◐	●		●	○	○			◐	●	◐	●			◐	●
Sulfentrazone + Metribuzin	Authority MTZ	PPO/PSII	●	●	◐	◐	◐	○	○	○	○	○	○	◐	◐	◐	◐	◐	◐	◐			◐	●	◐	●			◐	●
Sulfentrazone + Cloransulam	Authority First / Sonic	PPO/ALS	●	●	◐	●	●	○	○	○	○	○	○	○	◐	●	●	●	◐	●	◐		◐	●	●	●			●	●
Flumioxazin	Valor	PPO	◐	●	●	◐	○	○	◐	○	○	○	○	◐	◐	●	◐	●	○	◐	○	◐	◐	●	◐	●	◐	○	◐	◐
Flumioxazin + Chlorimuron	Valor XLT	PPO/ALS	◐	●	●	●	◐	○	◐	○	○	○	○	◐	○	●	◐	●	◐	●	◐	●		●	●	●	◐	○	●	◐
Flumioxazin + Cloransulam	Gangster	PPO/ALS	●	●	●	●	●	○	◐	○	○	○	○	◐	○	●	◐	●	○	●	◐	◐	◐	●	●	●	◐	○	◐	●
Cloransulam	Firstrate	ALS	○	○	●	●	●	○	◐	○	○	○	○	○	○	●	◐	○	◐	●	◐		◐	●	●		◐		◐	
Paraquat	Gramoxone Inteon	PSI	◐	◐	○	◐	◐	○	◐	◐	◐	◐	◐	○	●	◐				◐	◐			○	○		○			
HPPD PREEMERGENCE[4]																														
Isoxaflutole	Balance PRO	HPPD	◐	●	●	●	○	◐	●	●	●	○	○	●	◐	●	○	●	○	●	○		◐	●	●	●	◐		●	◐
Mesotrione	Callisto	HPPD	●	●	●	◐	○	○	◐	◐	◐	○	○	●	○	●	○	●	○	◐	○		○	●	●	●	◐		●	●
HPPD POSTEMERGENCE[5]																														
Mesotrione	Callisto	HPPD	●	●	●	◐	◐	○	◐	◐	◐	◐	◐	●	◐	●	◐	●	◐	◐	◐		◐	●	●	●	◐	○	●	●
Tembotrione	Laudis	HPPD	●	●	◐	●	●	◐	◐	●	●	●	●	◐	●	●	◐	●	◐	◐	◐		◐	●	●	●	◐	◐	●	●
Topramezone	Impact	HPPD	●	◐	●	◐	◐	◐	◐	◐	◐	◐	◐	●	●	●	◐	●	◐	◐	◐		◐	●	●	◐	○	○	●	●

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Table L-16 (continued). Herbicide Efficacy Comparison: Herbicide Resistant Weeds and Hard-to-Control Weeds in Soybean

●	>85% control
◑	75% - 85% control
○	< 75% control

			Resistant Weeds[1]														Hard-to-Control Weeds[2]													
Herbicide	Herbicide Brand	Class	GR Waterhemp	GR Palmer amaranth	GR Horseweed	GR C. ragweed	GR G. ragweed	GR Johnsongrass	ALS C. ragweed	ALS+PPO C. ragweed	ALS+GR C. ragweed	ALS G. ragweed	ALS+GR G. ragweed	ALS+GR Horseweed	ALS Kochia	TRI Lambsquarters	A. Morningglory	B. Nightshade	Cockelbur	C. Ragweed	G. Ragweed	Hemp sesbania	Kochia	Lambsquarters	Horseweed	Palmer Amaranth	Prickly Sida	Sicklepod	Velvetleaf	Waterhemp
Glyphosate	Roundup	EPSPS	○	○	○	○	○	○	●	●	○	●	○	○	●	◑	○	◑	●	●	◑	○	●	◑	●	●	○	●	◑	◑
Dicamba	Clarity	auxin	●	●	●	●	●	○	●	●	●	●	●	●	●	●	●	◑	●	●	●		●	●	◑	●	●	●	◑	●
POSTEMERGENCE[5]																														
Imazethapyr + Glyphosate	Extreme	ALS/EPSPS	◑	●	○	●	●	●	●	●	○	●	○	○	●	●	◑	●	●	●	●		●	●		●	◑		●	◑
Fomesafen	Flexstar	PPO	●	●	○	●	●	○	●	○	●	●	●	○	○	○	◑	◑	◑	●	●	◑	○	○		●	○	○	○	●
Imazethapyr	Pursuit	ALS	○	○	○	○	○	●	○	○	○	○	○	○	○	○	◑	●	◑	○	○	○	◑	○		○	○	○	◑	○
Cloransulam	Firstrate	ALS	○	○	◑	●	●	○	○	○	○	○	○	○	○	○	◑	○	●		●	○	○	○		○	○	◑	◑	○
Flumiclorac	Resource	PPO	○	○	○	◑	○	○	◑	○	◑	○	○	○	○	○	○	○	○		○	◑	○	○		○	◑	◑	●	○
Chlorimuron	Classic	ALS	○	○	◑	◑	○	○	○	○	○	○	○	○	○	○	◑	○	●		○	●	○	○		○	○	◑	◑	○
Imazamox	Raptor	ALS	○	●	○	○	◑	●	○	○	○	○	○	○	◑	○	◑	●	◑	○	◑		◑	○		●	○	○	●	○
Lactofen	Cobra / Phoenix	PPO	●	●	○	●	●	○	●	○	●	●	●	○	○	○	◑	◑	◑	●	●	●	○	○		●	○	○	○	●
Fomesafen	Reflex	PPO	●	●	○	●	●	○	●	○	●	●	●	○	○	○	◑	◑	◑	◑	●	●	○	○		●	○	○	○	●
Acifluorfen	Ultra Blazer	PPO	●	●	○	●	◑	○	●	○	●	◑	◑	○	○	○	◑	◑	◑	●	◑	●	○	○		●	○	○	○	●
Glufosinate	Ignite	Glu	◑	◑	◑	●	●	○	●	●	●	●	●	◑	●	◑	●	●	●	●	●		●	◑		◑	◑	●	◑	◑
Chlorimuron + Thifensulfuron	Synchrony XP	ALS	○	●	◑	◑	◑	○	○	○	○	○	◑	○	○	◑	◑	○	●	◑	◑		○	◑		●			◑	○
Fluthiacet	Cadet	PPO	◑	○	○	○	○	○	○	○	○	○	○	○	○	◑	◑	◑	○	○			○	◑		○			●	◑

Horseweed is synonymous to marestail.
GR = Glyphosate resistant
ALS = Acetolactate synthase
Tri = Triazine
PPO = protoporphyrinogen oxidase

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Note: This table was based primarily on State University Extension weed control recommendations for soybean growing areas, Table L-16 indicates the degree to which each product controls the targeted weeds in soybean. The legend describes the meaning of the symbols. See L.5.3 for additional detail.

[1] The section of the table describes control of populations (biotypes) of weeds that are known to have genetic resistance to specific herbicidal modes-of-action

[2] This section describes control of weeds that are difficult to control in soybean with existing herbicide treatments. Generally these are broadleaf weeds whose removal would require herbicide rates that would severely damage the crop.

[3] This section describes weed control by herbicides that are applied prior to soybean emergence. The weeds may or may not be emerged.

[4] This section describes foreseen use of herbicides that are not yet approved for use in soybean that have inhibition of 4-hydroxyphenylpyruvate dioxygenase.

[5] The section describes weed control by herbicides that are applied after the soybean emergence, generally over-the-top of the crop.

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L.5. Comparison of Dicamba Use in the Dicamba-Tolerant Soybean System (MON 87708) to Alternative Herbicides

The intent of the comparative analysis is to define current herbicide use in U.S. soybean production, and to compare dicamba's human health and environmental properties to herbicides currently used by growers for weed control. In order for a pesticide (herbicide) to be registered by EPA it must meet the FIFRA and FFDCA standards for safety to human health and the environment. The EPA must conclude that the herbicide when used according to the label does not pose an unreasonable risk to humans or the environment; and in order to establish a tolerance for the use of an herbicide on a food or feed crop, find there is a reasonable certainty of no harm to human health from non-occupational (food, water and residential/recreational) exposures to the herbicide. Consequently all alternative soybean herbicides can be used safely, and do not pose a risk to humans or the environment.

L.5.1. Comparisons for Human Health Risks

Table L-13 provides information concerning human health parameters for dicamba and the alternative herbicide products. These data allow a comparison of the relative human health safety among the optional weed control products on the basis of:

- Acute toxicity.
- Chronic toxicity.
- Cancer risks and classification.
- Risk to infants and children.
- Magnitude of potential exposure that is considered to be within the acceptable safe range.
- Extent to which all presently approved uses exhaust the acceptable safe acute and chronic dietary exposure ranges for the most highly exposed population subgroups.
- The proportion of present dietary exposure that arises through use on soybean.

A compilation of Monsanto's comparative determinations of the risks posed by the 18 alternate herbicides compared to dicamba in the four basic human health risk categories (acute, cancer, chronic and infants/children) is tabulated in Table L-17. A "Yes" entry indicates a benefit for dicamba compared to that alternative herbicide. Entries not indicated with a "Yes" mean that dicamba is either comparable or less favorable than the alternative herbicide. A "Neutral" entry means that dicamba and the alternative herbicide have similar risks, and a "No" entry denotes alternative herbicides that have a benefit compared to dicamba. Table L-17 is intended as a 1-page scorecard summary of these

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benefit comparisons. Monsanto has concluded that dicamba use on MON 87708 will provide benefits compared to the alternate herbicides used for soybean weed control.

L.5.1.1. Acute Health Risks

Dicamba acid has a Category II classification for eye and skin irritation, but once the acid is neutralized to form the DGA or other salt forms used in herbicide product formulations, all acute Categories are III or IV. These classifications are the most favorable acute toxicity categories in EPA's acute hazard paradigm. Several alternative herbicides (acifluorfen, sulfentrazone, and some forms of 2,4-D) have high risk of eye irritation (Category I). Principal formulations of fomesafen, paraquat, lactofen, 2,4-DB (DMA salt), and acifluorfen have a "DANGER!" signal word (Table L-11). The 18 alternate herbicide actives, as a group, also have relatively low acute (oral, dermal or inhalation) toxicity. For eight of the eighteen, EPA determined that an acute dietary risk assessment is not needed because there are no relevant acute toxicological effects. One notable exception is paraquat, which has high risk (Category I) of acute toxicity by the inhalation route, and present uses occupy 66% of the aPAD (the safe exposure level). 2,4-D and glufosinate have relatively low aPADs compared to their dietary residues, and present uses occupy 58% and 48% of their respective aPADs. Overall, Monsanto concludes that dicamba has a lower acute toxicity risk compared to six of the eighteen alternate herbicides and their formulated products (paraquat, 2,4-D, glufosinate, acifluorfen, sulfentrazone, and fomesafen). These six are indicated by a "Yes" in the "Acute Toxicity Risk" column of Table L-25. Flumioxazin and 2,4-DB were judged to have similar acute toxicity risk as dicamba, and are marked as "Neutral" in Table L-17. Ten herbicides, which either did not have relevant acute toxicological effects or which utilized 1% or less of the allowable acute exposure (aPAD), were judged to have less acute toxicity risk than dicamba, and are marked as "No" in Table L-17.

L.5.1.2. Chronic Risk

Chronic dietary risk can be evaluated by consideration and comparison of the percentage of the safe exposure level (chronic population adjusted dose: cPAD) that is used up by all currently registered uses of an active ingredient. Table L-17summarizes the % cPAD utilized for each alternative herbicide, according to recently published Federal Register Final Rule information. A number of the alternative herbicides have very low use rates, and result in very low residues in treated food or feed and, accordingly, utilize only a small percentage of the cPAD. For dicamba and twelve of the alternate herbicides, the percentage of the cPAD utilized for all approved uses is <10%, so that this group has at least an added 10-fold margin of safety beyond that which EPA has determined is protective of human health. For imazamox, EPA has determined that residues in food or feed are not likely to approach levels of concern, and exempted it from the requirement of food and feed tolerances. The remaining five herbicides (2,4-D, flumioxazin, fomesafen, paraquat, and glufosinate) utilize a somewhat higher portion of the cPAD, ranging from 18% to 38%. Although the 10% cutoff is an arbitrary one, and the increased risk of even the worst-case alternative herbicide for chronic risk is only 6-fold greater than that of dicamba, Monsanto concludes that dicamba offers a lower chronic toxicity risk compared to 2,4-D, flumioxazin, fomesafen, paraquat and glufosinate.

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Another way to compare chronic dietary risk would be to focus directly on the soybean seed residues and their contribution to cPAD utilization. In Table L-13, columns 9 to 11 (those to the right of the gray bar) present the established soybean seed tolerance for each herbicide. Using DEEM (a computer dietary exposure model used commonly by EPA,) and a theoretical worst-case approach (assume 100% of soybean is treated with a given herbicide that results in residues at the tolerance level), Monsanto calculated the theoretical maximum residue contribution (TMRC, a standard Tier 1 dietary risk method) to dietary exposure of each herbicide via soybean seed in µg/kg/day and as a percentage of the cPAD, as shown in Table L-13. This analysis highlighted paraquat and glufosinate as alternative herbicides with notably higher cPAD utilization by the soybean residue component, both herbicides were considered to present more relative risk than dicamba in the previous comparative method as well. The TMRC soybean calculation for paraquat yields a number that is 2.6-fold higher than the cPAD, because the EPA's risk assessment methodology for paraquat assumes a market penetration in soybean of <5%. If this market share were increased, the risk attributed to soybean residue could become a substantial portion of the cPAD.

Based on this reasoning, Monsanto concluded that dicamba offers lower chronic toxicity risk than five alternative herbicides (2,4-D, flumioxazin, fomesafen, paraquat and glufosinate), and these a.i.s are marked with a "Yes" in the chronic toxicity column of Table L-17. Imazamox-ammonium was considered by EPA to have such low toxicity that no food or feed tolerances were required by EPA, and therefore imazamox-ammonium was judged by Monsanto to have lower chronic toxicity risk than dicamba, indicated by a "No" in Table L-17. The alternate herbicide other a.i.s under consideration were judged to have similar chronic toxicity risk as dicamba, and are marked "Neutral" in Table L-17.

L.5.1.3. Cancer Risk

EPA classified dicamba as "not likely" for human carcinogenicity. Fourteen of the alternative herbicides are classified similarly – "not likely", "no evidence", or "Group E (Evidence of Non-Carcinogenicity for Humans)". 2,4-D is classified as "D", meaning that although the studies are acceptable, the evidence is unclear and some uncertainty remains. Two of the alternative herbicides (lactofen and acifluorfen) are classified as "not likely" at low doses but "likely" at high doses, due to liver and other effects. A peroxisome proliferation mechanism is established for acifluorfen. Since acifluorfen is a metabolite of lactofen, the similarity in toxicology and cancer classification is appropriate. One alternative herbicide, fluthiacet-methyl, is categorized as a "likely" human carcinogen, due the occurrence of dose-related tumors in both rats and mice; a Q* of 7.5×10^{-7} has been calculated, which is a measure of carcinogenic potency that EPA utilizes in risk assessment. Overall, Monsanto concludes that dicamba has a cancer risk benefit compared to four of the alternative herbicides (2,4-D, lactofen, acifluorfen, and fluthiacet-methyl), and this judgment is indicated by a "Yes" in the Cancer Risk column of Table L-17. Four alternative herbicide a.i.s (flumiclorac-pentyl, glufosinate, imazaquin, and paraquat) have been categorized by EPA as Group E or "no evidence", and Monsanto judges that these four have lower cancer risk than dicamba, and are marked as "No" in Table L-17. The other alternate herbicide a.i.s that are in the "not

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likely" category have similar cancer risk to dicamba, and are marked as "Neutral" in table L-17.

L.5.1.4. Risks to Infants and Children

The Food Quality Protection Act (FQPA) requires that EPA take special care in its risk assessments to establish that infants and children do not have increased sensitivity to pesticides and thereby experience greater risks from residues in food than the general U.S. population. EPA's implementation of this requirement is embodied in the additional FQPA safety factor, which is established by the statute at 10-fold, unless there is evidence that another level is protective. When making determinations about the magnitude of the FQPA safety factor, the EPA considers the completeness of the database and specifically the findings from the developmental and reproductive toxicity studies to determine if there is evidence that infants and children are more sensitive than adults. Therefore, the magnitude of the FQPA safety factor (usually 1X, 3X, or 10X) is a comparative parameter that may be used as an indication of the potential risks to infants and children and for overall developmental and reproductive toxicity findings.

Dicamba risk assessments for both acute and chronic effects utilize an FQPA safety factor of 1X. This is also the case for 15 of the 18 alternate herbicides, although in some cases, an acute dietary risk assessment was not necessary due to a lack of acute toxicity effects. For lactofen, acifluorfen, and mesotrione a 3X or 10X FQPA safety factor was used for the acute and/or chronic assessments, indicating a higher level of risk or uncertainty. Therefore, Monsanto concludes that dicamba offers an improved risk profile for infants and children compared to these three alternative herbicides, which are marked with a "Yes" in the Infants & Children Risk column in Table L-17. All other alternate herbicide a.i.s which have an FQPA safety factor of 1X are judged to have similar potential risk as dicamba, and are marked with "Neutral" in Table L-17.

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Table L-17. Summary of Comparative Analysis of Dicamba and Alternative Herbicides

Active Ingredient	Mode-of-Action (WSSA Group[1])	Human Health Risk Measures[2]				Aquatic Non-Target Species Risk Measures[3]		Known Resistant Weed Species[4]	Herbicidal Efficacy[5] (< 50% of dicamba)	Long Rotational Crop Restriction[6]	Serious Crop Injury Potential[7]	Number of "Yes" Entries[8]	Number of "No" Entries[9]
		Acute Toxicity Risk	Cancer Risk	Chronic Risk	Infants & Children Risk	Aquatic Animal Risk	Aquatic Plant Risk						
2,4-D acid / esters	Aux (4)	**Yes**	**Yes**	**Yes**	Neutral	**Yes**	**Yes**	28	Neutral	Neutral	Neutral	**6**	**0**
2,4-DB		Neutral	Neutral	Neutral	Neutral	Neutral	Neutral		**Yes**	Neutral	Neutral	**2**	**0**
imazethapyr	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	Neutral	107 **(Yes)**	**Yes**	**Yes**	Neutral	**3**	**1**
cloransulam-methyl	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	Neutral		**Yes**	**Yes**	Neutral	**4**	**1**
chlorimuron-ethyl	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	NA		**Yes**	**Yes**	Neutral	**3**	**1**
thifensulfuron	ALS (2)	No	Neutral	Neutral	Neutral	Neutral	**Yes**		**Yes**	**Yes**	Neutral	**4**	**1**
imazaquin	ALS (2)	No	No	Neutral	Neutral	Neutral	NA		**Yes**	**Yes**	Neutral	**3**	**2**
imazamox-ammonium	ALS (2)	No	Neutral	No	Neutral	Neutral	Neutral		**Yes**	**Yes**	Neutral	**4**	**2**
flumioxazin	PPO (14)	Neutral	Neutral	**Yes**	Neutral	**Yes**	**Yes**	5	**Yes**	**Yes**	Neutral	**5**	**0**
fomesafen	PPO (14)	**Yes**	Neutral	**Yes**	Neutral	Neutral	Neutral		Neutral	**Yes**	**Yes**	**4**	**0**
flumiclorac-pentyl	PPO (14)	No	No	Neutral	Neutral	Neutral	NA		**Yes**	Neutral	Neutral	**1**	**2**
sulfentrazone	PPO (14)	**Yes**	Neutral	Neutral	Neutral	Neutral	**Yes**		**Yes**	Neutral	Neutral	**4**	**0**
lactofen	PPO (14)	No	**Yes**	Neutral	**Yes**	**Yes**	**Yes**		Neutral	Neutral	**Yes**	**5**	**1**
fluthiacet-methyl	PPO (14)	No	**Yes**	Neutral	Neutral	Neutral	Neutral		**Yes**	Neutral	**Yes**	**3**	**1**
acifluorfen sodium	PPO (14)	**Yes**	**Yes**	Neutral	**Yes**	Neutral	Neutral		**Yes**	Neutral	**Yes**	**5**	**0**
paraquat dichloride	BiPyr (22)	**Yes**	No	**Yes**	Neutral	Neutral	**Yes**	24	**Yes**	Neutral	Neutral	**4**	**0**
glufosinate-ammonium	Glu (10)	**Yes**	No	**Yes**	Neutral	Neutral	Neutral	No reports	Neutral	Neutral	Neutral	**3**	**0**
mesotrione	HPPD (28)	**No**	Neutral	**Neutral**	Yes	Neutral	Yes	No reports	Yes	Yes	Neutral	**4**	**1**

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Table L-17 is intended to be a 1-page scorecard to track the benefits of dicamba use on MON 87708 according to the different listed criteria. Each “Yes” entry signifies that Monsanto has concluded that dicamba represents a benefit versus the relevant alternative herbicide on the basis of the risk factor in that column’s heading. The basis for entering a “Yes” under each risk factor is further explained in the relevant portions of this document. ”Neutral” entries indicate similar risks exist for dicamba and the alternative herbicide. “No” means the alternative herbicide offers a risk benefit compared to dicamba

[1] The herbicidal biochemical mechanism of weed-killing activity, according to the Weed Science Society of America. www.plantprotection.org/HRAC/Bindex.cfm?doc=MOA.html |Accessed May 27, 2010|

[2] A tally of the benefits dicamba use on MON 87708 offers over the alternative herbicide in the four categories of human health risk, according to the criteria described in L.5.1.

[3] A tally of the benefits dicamba use on MON 87708 offers over the alternative herbicides in the two categories of aquatic non-target species risk, according to the criteria described in L.5.2.

[4] A listing of the worldwide numbers of known resistant weeds for each herbicide based on its mode-of-action group. Dicamba has 5 known resistant spp worldwide. A “Yes” indicates that the number of resistant weeds in this herbicide class is many more than the known five dicamba resistant species biotypes. A comparison of each individual herbicide in the class is not provided. See L.5.3.3. www.weedscience.org/summary/MOASummary.asp |Accessed May 28, 2010|

[5] Alternative herbicides that provide commercial control of fewer than 50% of targeted problem weeds in soybean compared to dicamba, according to the data in Table L-16, where commercial control is considered to be >85%, as indicated by a fully-black circle symbol. See L.5.3.1.

[6] Alternative herbicides that require long waiting periods between application and subsequent planting of a crop other than soybean. This constraint is a disadvantage to growers. See Table L-18 and L.5.3.2.

[7] “Alternative herbicides that can substantially injure the soybean crop when applied for weed control, potentially reducing soybean yield. See L.5.3.2.

[8] Tabulation of the number of “Yes” entries in each row, indicating a total score for improved risk profile for dicamba use on MON 87708 offers versus an alternative herbicide. This summation is not presented as a net value (*i.e.*, subtracting where an alternative herbicide has a benefit over dicamba).

[9] Tabulation of the number of “No” entries in each row, indicating a total score for worse risk profile for dicamba use on MON 87708 offers versus an alternative herbicide. This summation is not presented as a net value (*i.e.*, subtracting where an alternative herbicide has a benefit over dicamba).

NA – not available.

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L.5.2. Comparisons for Ecological Effects

MON 87708 can be treated with preemergence and postemergence in-crop applications of dicamba. Such a weed control treatment regime has the opportunity to reduce risks to aquatic fish and invertebrates by:

- Replacing currently-used or foreseeable future alternative herbicide products that have higher aquatic toxicity risk profiles, and

- Addressing hard-to-control broadleaf weeds or broadleaf weeds that are resistant to glyphosate, PPO inhibitors, or ALS inhibitors, thereby preserving the ability of growers to manage weed problems and maximize soybean yield in the least risky manner, recognizing the ecological benefits offered by the superior hazard and reduced risk profile of glyphosate and the favorable profile of dicamba compared to some of the alternative herbicides..

L.5.2.1. Aquatic Animals

As mentioned, Table L-14 provides information concerning hazards, potential exposures, and risks to fish and aquatic invertebrates for each alternate herbicide and for dicamba. These data allow a comparison of the relative aquatic animal safety among the optional weed control products on the basis of:

- Potency against the indicator species.

- Estimates of potential exposure to aquatic animals.

- Calculated RQs for aquatic animals, by combining the hazard and exposure parameters. The RQs that exceed the EPA's LOC for non-listed aquatic animal species of 0.5 are marked in bold font.

The assessment and comparisons summarized in Table L-17 establish that dicamba poses little acute risk to aquatic animals, which is consistent with EFED's assessment published in the RED EFED Chapter and described in more detail in L.3.3. Furthermore, for 16 of the 18 alternate herbicides, aquatic animal RQs range from < 0.005 to 0.05, and do not present a risk to aquatic animals even using a worst-case upper bound exposure estimation. Only 2,4-D (the esters form) and lactofen exceed the LOC of 0.5 using conservative "worst-case" exposure estimates. These are highlighted in bold font. Monsanto notes that EPA considers the LOC for aquatic animals that are listed as endangered or threatened species to be 0.05 and the LOC for acute restricted use to be 0.1. If the 10-fold to 5-fold lower level of concern were applied, flumioxazin would also exceed the LOC based on this "worst-case" exposure estimate.

In addition to the calculated RQs, product labels for five of the alternative herbicides bear EPA-required warning statements for toxicity to fish or invertebrates, based on the hazard values (low LC_{50} or EC_{50}) of those herbicides. These are flumioxazin, cloransulam-methyl, flumiclorac-pentyl, lactofen, and 2,4-DB.

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Therefore, Monsanto concludes that dicamba presents a risk benefit for aquatic animals compared to three of the 18 alternate herbicides: 2,4-D, flumioxazin, and lactofen. This conclusion is tabulated in the Table L-17 scorecard by a “Yes” in the relevant column. The alternative herbicide a.i.s that have a “worst-case” RQ < 0.05 are similar to dicamba in regards to aquatic animal risk, and are marked “Neutral” in Table L-17.

L.5.2.2. Aquatic Plants

As mentioned, Table L-15 provides information concerning hazards, potential exposures, and risks to aquatic plants for each alternate herbicide and for dicamba. These data allow a comparison of the relative aquatic plant safety among available weed control products on the basis of:

- Potency against the indicator species.
- Estimates of potential exposure to aquatic plants.
- Calculated RQs for aquatic plants, by combining hazard and exposure parameters. The RQs that exceed the EPA’s LOC for non-listed aquatic plant species of 1.0 are marked in bold font.

The data format, sources, and methods are identical to those described above for the aquatic animals (Table L-14). A Level of Concern (LOC) value of 1.0 has been used for judging RQ exceedances in the case of aquatic plants, consistent with EPA EFED’s normal practices.

The assessment and comparison summarized in Table L-17 establishes that dicamba poses little acute risk to aquatic plants, which is consistent with EFED’s assessment published in the RED EFED Chapter (U.S. EPA, 2005a) and discussed above. Monsanto was unable to locate public aquatic plant hazard data for three of the alternate herbicides (imazaquin, chlorimuron-ethyl, and flumiclorac-pentyl). For 9 of the 18 alternatives, the worst case RQs ranged between < 0.02 and 0.75; and do not present a risk to aquatic plants even using a worst-case upper bound exposure estimation. However, for seven alternative herbicides, the worst-case RQs did exceed EFED’s LOC of 1.0. It is not surprising that some herbicides are quite toxic to aquatic plants. The worst-case RQs for three of the alternate herbicides (flumioxazin, paraquat dichloride, and lactofen) exceeded the LOC by a factor of more than 50-fold.

Therefore, Monsanto concludes that dicamba presents less risk to aquatic plants compared to seven of the 18 alternative herbicides: 2,4-D (ester form), flumioxazin, sulfentrazone, thifensulfuron, paraquat dichloride, lactofen, and mesotrione. This conclusion is tabulated in the Table L-17 scorecard by a “Yes” in the relevant column. The other alternative herbicide a.i.s, for which RQs are less than EPA’s LOC have similar non-target aquatic plant risk as dicamba, and are marked in Table L-17 with “Neutral”. The three herbicides for which no relevant data were available are marked as “NA”.

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L.5.3. Comparison for Efficacy and Weed Management, Including Weed Resistance

L.5.3.1. Comparison of Weed Management Efficacy

As mentioned, Table L-16 compares weed control effectiveness of formulated products containing dicamba and the alternative herbicides. The various products' overall effectiveness can be compared using the simple method of counting the fully-black circle symbols, which identify instances of commercial level weed control. Dicamba provides commercial control for 23 of the listed weeds (primarily broadleaf species), which is the most of any of the herbicides in the table; dicamba offers commercial control for 13 of the herbicide-resistant biotypes and 10 of the hard-to-control species. After dicamba, preemergent treatments with 2,4-D, or postemergent treatments with glufosinate, tembotrione, and imazethapyr plus glyphosate are the next most effective herbicides against this target group of weeds. The least effective herbicides in this analysis against these targeted weeds and resistant biotypes are 2,4-DB, paraquat, imazethapyr alone, flumiclorac-pentyl, chlorimuron-methyl and fluthiacet. To summarize the comparative herbicidal effectiveness in this analysis, the scorecard in Table L-16 contains a column in which those herbicides that provide commercial control of 50% or fewer weeds compared to the number of weeds controlled by dicamba (i.e., eleven or fewer fully-black circles in Table L-16) are marked with a "Yes", to denote a clear dicamba advantage. Alternative herbicide a.i.s that provide commercial control of greater than 50% of the number of weeds controlled by dicamba (i.e., 12 or more fully-black circles in Table L-16) are marked in Table L-17 with "Neutral", meaning are judged similar to dicamba. The 50% threshold criterion is Monsanto's arbitrary choice that is intended to identify herbicide options that are expected to provide substantially poorer weed control compared to dicamba.

L.5.3.2. Comparison for Weed Management Practices

Beyond direct efficacy against the key weeds, other advantages of MON 87708 treated with dicamba exist.

L.5.3.2.1. Increased Weed Control Flexibility

MON 87708 will allow more flexibility for control of weeds just prior to or at planting of the crop, due to elimination of preplant intervals or plant back restrictions on present dicamba labels. These restrictions were in place due to concern over potential soybean injury, which is not a concern for MON 87708. Current common practice is to use 2,4-D for preemergent burndown treatment. When applied too close to soybean planting, 2,4-D can potentially reduce crop stands and cause injury to new seedlings (Thompson et al., 2007). Restrictions have been implemented for most products and are as follows: rates up to 0.5 lb a.i. per acre must be applied at least seven days prior to planting; rates between 0.5 and 1 lb a.i. per acre must be applied at least 30 days prior to planting. Additionally, several sulfonylurea herbicides can also be utilized for preemergent burndown weed control in soybean. For example, Canopy herbicide can be applied prior to planting with the following restrictions: rates of 2.2 oz per acre or less should be

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applied at least seven days prior to planting; rates of 2.2 to 3.3 oz per acre should be applied at least 14 days before planting.

Current recommendations to control glyphosate-resistant biotypes of waterhemp and Palmer amaranth include the use of a residual herbicide treatment and postemergent applications of PPO-inhibiting herbicides such as Cobra (lactofen), Ultra Blazer (acifluorfen), or Cadet (fluthiacet). It is commonly known that these postemergent herbicides can cause excessive injury to soybean, especially under hot and sunny conditions. Soybean injury, caused by acifluorfen from early (V2 to V3 growth stage) or late postemergence (V5 to V6) applications, was seen as increased chlorosis and stunting that translated into yield reduction (Young et al., 2003). Furthermore, Legleiter et al. (2009) illustrated the effectiveness of preemergent herbicides for the control of resistant waterhemp populations and demonstrated inconsistent control with PPO-inhibiting herbicides or herbicide combinations for the control of waterhemp populations with multiple resistance to glyphosate and PPO-inhibiting herbicides. The introduction of MON 87708 will provide an effective management option for herbicide-resistant biotypes of waterhemp and Palmer amaranth that is not expected to cause either crop injury or yield loss.

Residual herbicides containing herbicides including sulfentrazone, dimethenamid, pendimethalin, metribuzin, or metolachlor have been shown to control waterhemp and Palmer amaranth; however, such products can present other challenges. Limitations include the need of adequate soil moisture for activation, potential crop injury, crop rotation restrictions, and use restrictions based on soil type. As an example, metribuzin should not be used on sands, loamy sands, and sandy loams with less than 1% organic matter[62], and pendimethalin applied after crop-emergence can result in soybean injury[63].

For some residual herbicides there are extensive rotational crop restrictions, ranging from four to 40 months after application, to avoid subsequent crop injury to the rotated crop caused by herbicide remaining in the soil. These limitations reduce the choice of crops that can be planted in case the soybean crop is destroyed by weather or even the following growing season. Examples of planting limitations among the alternate herbicides are shown in Table L-18.

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[62] Product label for Metribuzin 75 DF (http://www.cdms.net/LabelsMsds/LMDefault.aspx?pd=7614&t=). [Accessed 5/14/2010]

[63] Product label for Pendimax 3.3 (http://aesop.rutgers.edu/~plantbiopath/links/bbcpestweb/GrapeLabels/pendimax33.pdf). [Accessed 5/14/2010]

Table L-18. Planting Restrictions (months) for Alternative Herbicide Products

	Herbicide Product (Active Ingredient)			
CROP	Authority MTZ (sulfentrazone + metribuzin)	Pursuit (imazethapyr)	CANOPY EX (chlorimuron + tribenuron)	Raptor (imazamox)
Field corn	4	8.5	8	8.5
Wheat	4	4	4	9
Cotton	12	18	8	9
Peanut	12	0	15	9
Sorghum	12	18	9	3
Onions	18	40	30	9

Dicamba does not have rotational restrictions for such extended time periods, and provides a substantial advantage in flexibility. For the majority of crops, no rotational restrictions apply after 120 days following dicamba applications. Specifically, there are no rotational restrictions for planting corn following a dicamba application. For cotton, a rotational restriction of 21 days is recommended. To summarize this advantage, Table L-17 includes a column in which a "Yes" is marked for those alternative herbicides that include substantial rotational or replanting restrictions. Entries for alternative herbicide a.i.s that do not require long rotation intervals are judged similar to dicamba, and are marked in Table L-17 with a "Neutral" in the relevant column.

Furthermore, in situations where sequential herbicide applications were employed to control common waterhemp populations, reduced soybean yields have been reported. Yield reductions up to 19% compared to a non-treated control were reported when acifluorfen or fomesafen was the postemergent herbicide (Soltani et al., 2009). These reduced yields were associated with crop injury (chlorosis and stunting) following postemergent applications of certain herbicides, especially PPO inhibitors (Baumann et al., 2010; Loux et al., 2009).

Dicamba treatments in MON 87708 provide excellent crop safety. Table L-17 includes a column in which the crop injury potential versus dicamba is summarized; a "Yes" entry indicates a substantial potential for visible soybean injury. Entries for alternative herbicide a.i.s with good soybean crop safety are judged to be similar to dicamba, and are marked with a "Neutral" in the relevant column of Table L-17. In conclusion, the introduction of MON 87708 will provide an additional mode-of-action for postemergent weed control with excellent crop safety.

L.5.3.2.2. Weed Spectrum Benefits

Dicamba provides control of over 95 annual and biennial weed species, and control or suppression of over 100 perennial broadleaf and woody species. Dicamba provides more effective preemergent weed control than 2,4-D on cutleaf evening primrose, clover, and chickweed (Loux et al., 2009). Furthermore, dicamba provides excellent control compared to 2,4-D on summer annuals including those with a prostrate growth habit such

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as knotweed and purslane. With regard to perennial weeds, research conducted at North Dakota State University indicates that dicamba is more effective in controlling Canada thistle compared to 2,4-D and effectively controls field bindweed (Zollinger, 2000; NDSU, 2010b).

Dicamba also provides excellent control of wild buckwheat while 2,4-D has only limited activity and provides inadequate control (Zollinger et. al, 2006). Other preemergent or postemergent herbicides often provide incomplete control of wild buckwheat including dinitroanilines or PPO inhibitors. The most effective herbicides for buckwheat are dicamba, and some sulfonylurea products; however, some of the sulfonylurea herbicides may persist and carry over for more than one growing season, especially in high pH soils.

Dicamba has been valued as more efficacious on lambsquarters than fomesafen or acifluorfen based on university weed control guidelines (Moechnig et al., 2010; University of Illinois, 2008; Legleiter et al., 2009; Loux et al., 2009). In addition, dicamba exhibits improved control of sicklepod (Loux et al., 2009), kochia and common ragweed (Legleiter et al., 2009), and waterhemp (Soltani et al., 2009) compared to fomesafen and acifluorfen.

L.5.3.3. Comparison for Herbicide-Resistant Weeds

The development of weed resistance reduces the effectiveness of all major herbicide classes used in soybean production today, including glyphosate, thereby jeopardizing soybean yields and requiring the introduction of new tools to control populations of resistant weeds. It is widely recognized that utilizing herbicides with different modes-of-action in conjunction with established products is especially effective combating further weed resistance development and to provide control of existing populations (Beckie, 2006). Preplant / preemergent or early-postemergent in-crop applications of dicamba in MON 87708 will introduce a new mode-of-action; thus the introduction of dicamba use on MON 87708 holds great promise for addressing current and future weed management needs in soybean. The primarily basis for this promise is the wide spectrum of activity of dicamba on broadleaf weed species, which are the most common hard-to-control species and resistant weed biotypes in soybean production today.

Dicamba belongs to the auxin agonist class of herbicides, which is the oldest class of known synthetic herbicides. This class includes 2,4-D, 2,4-DB, mecoprop, MCPA, clopyralid, and several other active ingredients, and is WSSA Herbicide Group Number 4.[64] On the basis of their structural and chemical properties, auxinic herbicides have been classified into several sub-groups, *i.e.*, phenoxyalkanoic acids (*e.g.*, 2,4-D, MCPA), benzoic acids (*e.g.*, dicamba, chloramben), pyridines (*e.g.*, picloram, clopyralid), and quinolinecarboxylic acids (*e.g.*, quinclorac, quinmerac). Generally, auxinic herbicides are effective against broadleaf (dicotyledonous) plant species, allowing them to be used in production of narrow leaf (monocotyledonous) crops such as corn and wheat. The

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[64] There are several systems of herbicide mode-of action classification. Among the most widely used are those of the Herbicide Resistance Action Committee (HRAC) and the Weed Science Society of America. The classifications are compared in a chart at http://www.plantprotection.org/HRAC/Bindex.cfm?doc=MOA.html [Access May 28, 2010]

relative occurrence of herbicide-resistant weeds differs between the different sub-groups of auxinic herbicides. The largest number of resistant weed biotypes has been found for 2,4-D. Considering that auxinic herbicides have been widely used in agriculture for more than 60 years, the occurrence of weed resistance to this class is relatively low (28 species worldwide, to date) and its development has been slow especially when compared to the speed of appearance of resistance to ALS inhibitors (107 species) or triazine-resistant populations (68 species).[65] The relatively low incidence of auxinic herbicide resistance is believed to be attributable to the fact that there are multiple mechanisms of action for these herbicides (Gressel et al., 1982; Morrison and Devine, 1994).

Only five weed species have been reported to date to be resistant to dicamba worldwide: kochia (*Kochia scoparia*)[66], lambsquarters (*Chenopodium album*)[67], prickly lettuce (*Lactuca serriola*), common hempnettle *(Galeopsis tetrahit*) and wild mustard (*Brassica caber*)[68]. Of these five species, resistant populations of lambsquarters have only been reported in New Zealand. Regarding the two species with resistant populations in the U.S. (kochia, prickly lettuce) and Canada (common hempnettle and wild mustard), all were common to cereal production areas in the Western U.S. and Canada. No dicamba-resistant populations have been reported in the main soybean production areas, including the Midwest, the South and the East coast of the U.S. Table L-17 shows the number of U.S. weed species known to have resistance to each of the major herbicide groups (or sub-groups within groups, as appropriate) to which the alternative herbicides belong. It also contains a "Yes" marker for those herbicides that have many more known resistant weed biotypes than the five known for dicamba, indicating a potential lower risk for weed resistance development for dicamba compared to alternative herbicides. Entries not indicated with a "Yes" mean that dicamba is either comparable or less favorable than the alternative herbicide. A comparison of each individual herbicide in the class is not provided.

Although dicamba resistance exists, weed populations that are resistant to dicamba in U.S. soybean cropping areas have not been overly problematic to date, possibly because selection pressure on summer annual weeds has been low. Dicamba has seen very limited use in soybean (0.7% of treated soybean acres as a preplant and pre-harvest applications) and currently has relatively low usage in the crops that are commonly rotated with soybean (9.4% of corn acres as preplant and in-crop applications, 6.3% of cotton acres as a preplant application, and 8.4% of wheat acres, respectively) (Table VIII-12), although historically dicamba was used more extensively in corn. In addition, there are over 20 commercially-available pre-mixed multiple-herbicide formulations that contain dicamba, so dicamba is often used in combination with other

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herbicide modes-of-action. It is expected that selection pressure favoring the development of dicamba-resistant weeds will continue to be low even after in-crop use of dicamba on MON 87708 is approved. Monsanto believes this is because dicamba will predominantly still be used in combination with other herbicides exhibiting different modes-of-action, principally glyphosate, but also with other soil-active herbicides. The presence of multiple herbicides in the weed management system greatly diminishes the likelihood of weed resistance to dicamba developing to a level of predominance in weed populations. Dicamba is an excellent complement to the weed control spectrum of glyphosate, and it has a relatively low cost and low potential for crop injury to MON 87708 relative to other broadleaf weed options. Taken together, these factors will help to ensure that more fields receive weed-control treatments using multiple herbicide modes-of-action, in a proactive way, aimed at slowing the evolution of resistance. In general, this will serve to further reduce the development of weed resistance problems to all herbicides targeting broadleaf weeds in soybean production, and in crops rotated with soybean.

As part of the projected role of dicamba as a companion herbicide for glyphosate, dicamba will provide growers with a new mode-of-action for use in-crop against summer annual broadleaf weeds. Dicamba will help prevent and/or combat existing weed resistance issues that can limit effectiveness of the PPO- and ALS-inhibiting herbicide classes. Herbicides from these two herbicide classes have historically dominated the non-glyphosate broadleaf weed control tools available in soybean (13 of the 18 alternative herbicides considered here are PPO- or ALS-inhibiting herbicides (Table L-17)), and were the predominant modes-of-action used for weed control in soybean production prior to the introduction of the Roundup Ready soybean system; and remain the primary options recommended for management of glyphosate-resistant or hard-to-control broadleaf weeds in soybean. For example, fomesafen and flumioxazin, both PPO Inhibitors, are the primary herbicides recommended for control of glyphosate-resistant Palmer amaranth (pigweed) in soybean.

Dicamba will foster the adoption of IPM practices in soybean by allowing growers to continue to primarily focus on postemergent in-crop weed control, as they have practiced with Roundup Ready soybean, and will make current practices more effective by providing an additional mode-of-action herbicide. This will allow growers to delay some herbicide treatments until field scouting indicates a need for additional weed control which is consistent with the principles of Integrated Pest Management. Dicamba, as a companion product to glyphosate, will also continue to foster adoption of and maintain the use of conservation tillage practices, because of grower preference to use postemergent products, such as dicamba on MON 87708, compared to reliance on soil-active preemergent products

In summary, the ability to use dicamba as part of a weed management program in U.S. soybean production will provide significant benefits for managing broadleaf weed resistance not only relative to glyphosate but also to other herbicides such as those included in PPO- and ALS-inhibitor classes. There is evidence in the scientific literature from data generated in field studies and from model simulations that the application of multiple herbicides, each effective in controlling a weed spectrum, with more than one

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mode-of-action can significantly delay the evolution of resistant populations within a field (Powles et al., 1996; Beckie, 2006). In addition, there is evidence that resistance would be delayed longer by use of herbicide mixtures than by using an herbicide rotation strategy (Diggle et al., 2003; Beckie and Reboud, 2009). Based on this general information on resistance, Monsanto believes that application of dicamba on MON 87708 integrated into the Roundup Ready soybean system will reduce the development of herbicide-resistant broadleaf populations to glyphosate and other herbicides. This conclusion is based on the following: 1) the efficacy and broad spectrum of glyphosate and weed control spectrum of dicamba, 2) the low level of dicamba-resistant broadleaf weeds in the major soybean production areas, 3) the low number of species resistant to glyphosate, 4) the expected use of dicamba applied to MON 87708, and 5) the fact that dicamba will be used in combination with glyphosate, and other alternative herbicides as necessary to control problematic weeds. Using available information, Monsanto conservatively estimates that dicamba use on MON 87708 could reduce the growth of resistant weed populations on five to ten percent of the expected 75 million U.S. planted soybean acres (Table VIII-1), which is equal to approximately 3.6 to 7.2 million acres.

Furthermore, Monsanto believes the opportunity for dicamba use on MON 87708 will foster continued adoption of conservation tillage practices, an important goal for the agro-ecosystem and the long term sustainability of U.S. agriculture. Presently, 41.5% of an estimated 74 million acres of U.S. soybean acres, or 30.6 million acres, employ no-till or conservation tillage production systems (CTIC, 2007). The introduction of MON 87708 into the Roundup Ready soybean system would allow the flexibility to incorporate an additional herbicide mode-of-action in both pre- or postemergent applications, and support the continued use of conservation tillage production systems. The benefits of conservation tillage are well known and demonstrated including soil and water conservation, improved environmental (*e.g.*, water) quality, and a reduced carbon footprint (Arriaga and Balkcom, 2005; Reicosky, 2008). These conservation tillage acres will represent a significant portion of the 30 million total acres projected for MON 87708 planting, in turn representing a significant number of acres where a delay in the development of glyphosate-resistant biotypes could be expected to occur.

L.6. Statement of Benefits for Dicamba-Tolerant Soybean MON 87708

Monsanto intends to commercialize MON 87708 in combination with the Roundup Ready 2 Yield soybean platform (glyphosate-tolerant soybean), so that both herbicide tolerance traits occur in the same soybean plant. The addition of MON 87708 to the Roundup Ready 2 Yield soybean platform enables the use of dicamba withglyphosate or other herbicides as a mixture or sequential applications for pre-plant burndown and in-season weed control, resulting in a highly effective weed management system for soybean growers. Combined use of dicamba plus glyphosate will provide excellent grass and broadleaf weed control, including those broadleaf weeds that are hard–to-control or glyphosate-resistant. The use of dicamba and glyphosate should deter the spread of existing glyphosate-resistant broadleaf weeds, and possibly delay the development of new resistant populations through use of multiple modes-of-action. The decision by growers to adopt MON 87708 x Roundup Ready 2 Yield soybean system and to include a dicamba herbicide treatment, either preemergent or in-crop, will be dependent up on three factors: weed spectrum in a grower's field, efficacy of dicamba against broadleaf weeds, and costs and flexibility versus alternative herbicide programs.

The use of dicamba in combination with glyphosate for burndown treatments prior to planting on no-till acres will provide growers with a more flexible weed management tool than is presently available. MON 87708 (in combination with application of dicamba) will provide growers with greater flexibility in timing of application of burndown treatments, eliminating the need for any interval between dicamba application and planting, and improving overall efficacy on hard-to-control and larger broadleaf weeds. In addition, dicamba is an effective complement to glyphosate in cropping systems where glyphosate-resistant weeds such horseweed (*Conyza canadensis)* have developed. Approximately 40% of the total soybean acres in the United States are produced in a no-till system (CTIC, 2007). In these cropping systems, it is anticipated that dicamba will displace other herbicides, such as 2,4-D, because a preplant interval is not needed with MON 87708 to avoid potential crop injury, and because dicamba has a better weed spectrum profile, as discussed previously. However, the potential future introduction of 2,4-D-tolerant soybean will likely allow for a decreased preplant interval for soybean containing this trait.

In addition to soybean production under no-till cropping systems, MON 87708 offers an effective solution for improving weed control in conventional tillage cropping systems. Herbicides with soil residual and postemergent efficacy are frequently used in combination with glyphosate to control weeds that are hard-to-control, resistant to glyphosate, or are capable of producing multiple flushes. Examples include, but are not limited to, the following species: *Amaranthus tuberculatus* (tall waterhemp), Palmer amaranth (*Amaranthus palmeri*), giant ragweed (*Ambrosia trifida*) and lambsquarters (*Chenopodium album*). In these cropping situations, it could be assumed that dicamba would replace some of the less effective PPO inhibitors (such as acifluorfen and lactofen) that have greater potential for crop injury. The opportunity to use dicamba as yet a third mode-of-action in these situations would also reduce the potential for selection pressure for resistance to any single herbicidal mode-of-action.

Assuming that the U.S. soybean crop is grown on approximately 75 million acres (Table VIII-1), it is estimated that dicamba herbicides could be used for weed control on a total of approximately 30 million acres. There are currently 11 active ingredients that account for 90% of the herbicide usage (based on expenditure) in soybean production today (AgroTrak, 2009). The estimated percentage of treated soybean acreage by active ingredient is presented in Table L-12 based on the latest USDA-NASS use data from 2008. The use of dicamba as a preplant burndown or in-crop application has the potential to reduce the rates, acreage, and/or the number of applications of these alternative herbicides in soybean production.

There are widely varying estimates of the current number of soybean acres that have populations of weeds that are resistant to one or more of the classes of herbicides currently registered for use in soybean. It is difficult to determine the validity and comparability of these estimates, as different regions and weed scientists have a different approach or method for deriving these estimates. Regardless of the accuracy of these

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estimates of the current state of herbicide resistance in soybean production, the application of dicamba on MON 87708 will provide a benefit in broadleaf weed resistance management for all the herbicide modes-of-action currently used in soybean for the following reasons: 1) the broad spectrum of broadleaf weed control provided by dicamba, 2) the limited number of dicamba-resistant biotypes present after decades of dicamba use, 3) the projected soybean acreage (40%) adopting MON 87708 into the Roundup Ready soybean system and the combination with other herbicide modes-of-action on these acres, and 4) the compatibility of dicamba end-use products with herbicides having other modes-of-action.

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Appendix M: Potential Impact of Dicamba on Human Health and the Environment

M.1. Overview

Dicamba use is regulated at the federal level by EPA, not APHIS. APHIS's authority under the Plant Protection Act does not allow it to specify conditions for the use of herbicides. Instead, EPA specifically approves labeling for any herbicide use including uses on agricultural crops. Before any dicamba product could be used over MON 87708 it must first be approved by the EPA as required by the Federal Insecticide Fungicide and Rodenticide Act (FIFRA); EPA must approve the pesticide (herbicide) product labeling for that specific use. Nevertheless, Appendix M examines the potential impact of dicamba use on MON 87708 on human health and the environment. It first provides a background discussion of U.S. EPA's authority to regulate pesticides. Next, Appendix M addresses the regulatory background for dicamba, including the proposed use on MON87708. Appendix M then discusses the potential impact of dicamba on human health, including impacts on pesticide applicators. Appendix M concludes with a discussion of drift and offsite movement aspects associated with dicamba use.

M.2. Regulation of Pesticides in U.S.

M.2.1. Pesticide Registration, Reregistration and Tolerance Setting

FIFRA requires that before the sale or distribution of a new pesticide or a new use of a registered pesticide, a company must obtain a registration, or license, from EPA. The EPA must ensure that the pesticide, when used according to its label directions, will not cause unreasonable adverse effects on human health and the environment. In order to address this standard, EPA evaluates potential risks to humans and the environment, and may require applicants to submit more than 100 different scientific studies conducted according to EPA guidelines. According to EPA, more than 1000 active ingredients are currently registered as pesticides in the U.S., which are, in turn, formulated into many thousands of pesticide products that are available in the marketplace (U.S. EPA, 2010).

Pesticide registration is a scientific, legal, and administrative procedure through which EPA examines the ingredients of the pesticide; the particular site or crop on which it is to be used; the amount, frequency, method and timing of application, and other conditions of its use; and storage and disposal practices. In evaluating a pesticide registration application, EPA assesses a wide variety of data indicating the potential human health and environmental effects associated with use of the pesticide product. The data required by EPA are used to evaluate a wide array of potential impacts, including whether a pesticide has the potential to cause adverse effects on humans, wildlife, fish, and plants (including endangered species and other non-target organisms, *i.e.*, organisms that the pesticide is not intended to act against). The registration applicant must also supply data on the pesticide's potential impact on surface water and ground water, should leaching or runoff occur. The potential human health and safety risks assessed range from short-term toxicity to long-term effects such as cancer and reproductive system disorders.

Pesticide label directions are considered as part of EPA's evaluation to determine whether a pesticide can be used safely, as required by FIFRA, and the language that appears on each pesticide label has been expressly approved by EPA. A pesticide product can only be used

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legally according to the directions for use on the labeling accompanying the product at the time of sale.

The registration of a new pesticide is not EPA's only opportunity to evaluate the product's safety. EPA has recently completed a program to review older pesticides (those initially registered before November 1984) under FIFRA to ensure that they meet current scientific and regulatory standards. Reregistration, like the initial registration process, considers the human health and ecological effects of pesticides and results in actions to reduce risks that are of concern.

Where pesticides may be used on food or feed crops, EPA also sets pesticide tolerances, i.e., maximum pesticide residue levels that can legally remain in or on foods. EPA undertakes this analysis under the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA). Under the FFDCA, EPA must find that such tolerances will be safe, meaning that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide residue. This finding must be made and the appropriate tolerance established before a pesticide can be registered for use on the particular food or feed crop in question. EPA must consider several factors before a tolerance can be established, including:

- the aggregate, non-occupational exposure from the pesticide (exposure through diet, from using pesticides in and around the home, and from drinking water);
- the cumulative effects from exposure to different pesticides that produce similar effects in the human body;
- evidence of increased susceptibility to infants and children, or other sensitive subpopulations, from exposure to the pesticide; and
- evidence that the pesticide produces an effect in humans similar to an effect produced by a naturally occurring estrogen or produces other endocrine-disruption effects.

M.2.2. Pesticide Human Risk Assessment

The process EPA uses for evaluating the health impacts of a pesticide, under either FIFRA or FFDCA, is called risk assessment. EPA uses the National Research Council's four-step process to assess potential human health risks. This process involves hazard identification, dose-response assessment, exposure assessment and risk characterization. Each of these steps is discussed below.

The first step in the risk assessment process is hazard identification to identify potential health effects, or hazards, which may occur from different types of pesticide exposure. EPA considers the full spectrum of a pesticide's potential health effects. Hazards are identified through a battery of studies that examine the potential toxicity of the pesticide in various tests including, where appropriate, tests with laboratory animals.

To assess human health risk of the pesticide, pesticide companies conduct many toxicity studies based on EPA guidelines and the Good Laboratory Practice (GLP) standards. Results are evaluated for acceptability by EPA scientists. EPA evaluates pesticides for a wide range of

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effects, from eye and skin irritation to cancer and birth defects. EPA may also consult the public literature or other sources of information on any aspect of the chemical.

The next step of the risk assessment is dose-response assessment which considers the levels at which the pesticide produces adverse effects. Dose levels at which adverse effects were observed in test animals are then translated into equivalent doses for humans.

Step three of the process involves an exposure assessment. People can be exposed to pesticides in three ways:

1. Inhaling pesticides (inhalation exposure),
2. Absorbing pesticides through the skin (dermal exposure), and
3. Ingesting pesticides (oral exposure).

Depending on the situation, pesticides could enter the body by any one or all of these routes. Typical sources of pesticide exposure include food (following agricultural uses); home and personal use pesticides; pesticides applied to lands that make their way into the drinking water; or occupational exposure for agricultural workers or pesticide applicators.

Risk characterization is the final step in assessing human health risks from pesticides. It is the process of combining the hazard, dose-response and exposure assessments to describe the overall risk from the use of a pesticide. It explains the assumptions used in assessing exposure as well as the uncertainties that are built into the dose-response assessment. The strength of the overall database is considered, and broad conclusions are made. EPA's role is to evaluate both toxicity and exposure and to determine the risk associated with use of the pesticide.

The risk to human health from pesticide exposure depends on both the toxicity of the pesticide and the likelihood of people coming into contact with it, *i.e.*, the probability of exposure. At least some exposure and some toxicity are required to result in a risk. For example, if the pesticide is found to have a high level of toxicity, but people are not exposed to the pesticide, there is no risk. Likewise, if there is ample exposure but the pesticide is nontoxic, there is no risk. Typically, however, there is some toxicity and exposure, which results in a potential risk.

EPA recognizes that effects vary between animals of different species and from person to person. To account for this variability, a 100-fold uncertainty factor is built into the risk assessment with a 10X factor to account for differences between test species and humans, and a 10X factor to account for differences between people. This uncertainty factor creates an additional margin of safety for protecting people who may be exposed to the pesticides. The Food Quality Protection Act (FQPA) requires EPA to use an additional, up to a 10-fold safety factor, if necessary, to protect special subpopulations if they show potential increased susceptibility to effects of the pesticide, typically infants, children or women of child-bearing age.

Once EPA completes the risk assessment process for a pesticide, the Agency uses this information to determine if there is a reasonable certainty of no harm to human health as a result of the use of the pesticide according to label directions as required by FIFRA. Using the conclusions of a risk assessment, EPA can then make an informed decision regarding whether to

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approve a pesticide chemical or use, as proposed by the product label, or whether additional protective measures are necessary to limit exposure to a pesticide. For example, EPA may prohibit pesticide use on certain crops because consuming the treated commodity may result in an unacceptable risk to consumers. Another example of protective measures is requiring workers to wear personal protective equipment (PPE) such as a respirator or chemical resistant gloves, or not allowing workers to enter treated crop fields until a specific period of time has elapsed (Restricted Reentry Interval or REI). If, after considering all appropriate risk reduction measures, the pesticide still does not meet EPA's safety standard, the Agency will not allow the proposed chemical or use. Regardless of the specific measures enforced, EPA's primary goal is to ensure that legal uses of the pesticide are protective of human health, especially the health of children, and the environment.

M.3. Dicamba Regulatory Status in U.S.

M.3.1. Dicamba – Registration History

Dicamba is a selective broadleaf herbicide belonging to the auxin agonist class, the oldest known class of synthetic herbicides, and is a member of the benzoic acids sub-group. Dicamba mimics the action of the plant hormone indole acetic acid, and causes rapid uncontrolled cell division and growth, leading to plant death. Dicamba has been registered in the U.S. for use on food crops since 1967 (U.S. EPA, 2009) and has been widely used in agricultural production for over forty years. Dicamba is presently approved for use on asparagus, corn, cotton, grass seed production, pastures and rangelands, small cereals (including wheat), sorghum, soybean, and sugarcane. Dicamba is also used for industrial vegetation management (*e.g.*, forestry and roadsides), professional turf management (*e.g.*, golf courses, sports complexes), and residential turf (U.S. EPA, 2009; Durkin and Bosch, 2004).

Dicamba has a complete and comprehensive regulatory database (toxicity, environmental fate, and ecological toxicity) that has been evaluated by the United States Environmental Protection Agency (U.S. EPA). A Registration Eligibility Decision (RED) for dicamba was completed by EPA in 2006 and subsequently amended in 2008 and 2009 (U.S. EPA, 2009), as required for continued registration of all pesticides originally registered prior to 1984. EPA concluded the available data submitted for dicamba are complete and adequate to support the continued registration of dicamba products. EPA has evaluated the available toxicity data and concluded that a high level of confidence exists in the quality of the dicamba data base and in the reliability of the dicamba toxicity endpoints for risk assessment. EPA also considered toxicity data and available information concerning the variability of sensitive subpopulations, including infants and children. The EPA concluded there is reasonable certainty that no harm will result to the general population, or to infants and children, as a result of aggregate (all) exposure to dicamba residues. Thus, all current dicamba uses were eligible for reregistration (U.S. EPA, 2008a; U.S. EPA, 2008b; U.S. EPA, 2008c). In 2008, dicamba also successfully completed reevaluation by the Pest Management Regulatory Agency of Health Canada (PMRA, 2008) and the European Commission Health and Consumer Protection Directorate-General (European Commission, 2008). Dicamba has been approved by the EPA for a number of food and feed uses, including the major agricultural crops of corn, soybean and small grains (*e.g.*, wheat or barley). Dicamba presently has 68 food and feed pesticide tolerances (40 CFR §180.227) established in support of these uses.

Dicamba is presently registered for preemergence (early pre-plant) applications up to 0.5 pound acid equivalence per acre (lb a.e./A) and late postemergence (pre-harvest) applications to soybean at rates up to 1.0 lb a.e./A, and a pesticide tolerance is established for residues of dicamba on soybean seed (10 ppm) in support of these uses.

M.3.2. Dicamba – Proposed New Use on MON 87708

An application has been submitted to the EPA to amend Registration Number 524-582 (a diglycolamine (DGA) salt formulation) to register a new use pattern for dicamba on MON 87708. In support of the new use of dicamba on MON 87708, mammalian toxicity data on the dicamba metabolites DCSA (3,6-dichlorosalicylic acid) and DCGA (3,6-dichlorogentisic acid), and crop metabolism and residue data on dicamba-treated MON 87708 have been generated. These data confirm that existing dicamba food tolerances are sufficient to address any incremental exposure to dicamba resulting from its use on MON 87708. Furthermore, the proposed use pattern for dicamba on MON 87708 maintains the presently established maximum single and annual application rates. Therefore the existing ecological risk assessment conducted by EPA as part of the dicamba RED is sufficient to address any incremental ecological effects resulting from this new use.

M.4. Potential Impact of Dicamba on Human Health

M.4.1. Dicamba Safety Evaluations for Consumers

On the basis of the risk assessments summarized below, EPA has concluded that there is a reasonable certainty that the existing uses of dicamba will not pose a risk to consumers, including infants and children.

Dicamba presently has 68 established food and feed pesticide tolerances in the U.S. (40 CFR § 180.227). Each time EPA reviews an application to add a new food or feed use to the dicamba label, the EPA is required by FFDCA to conduct an aggregate risk assessment. This assessment considers potential exposure from the proposed new use with all other existing exposures, including non-occupational sources of exposure to the pesticide, and must conclude that aggregate exposure to the pesticide will be safe as defined by the statute and regulations. Risks associated with potential occupational exposure for each new use are considered under the FIFRA standard of no unreasonable adverse effects to the environment, which includes humans and workers (hereafter referred to as FIFRA unreasonable risk standard). Over the course of numerous reviews, the toxicology of dicamba has been extensively studied. Dicamba does not pose any unusual toxicological concerns (U.S. EPA, 2009; Durkin and Bosch, 2004; European Commission, 2007a) and is classified by EPA as "Not likely to be Carcinogenic to Humans" (U.S. EPA, 2009). PMRA and the European Commission have also classified dicamba as non-carcinogenic (PMRA, 2007, 2008; European Commission, 2007a).

Dietary exposure, as previously stated, is included in the aggregate exposure assessment, and considers pesticide residues that may remain on food from crops on which the pesticide is applied (pre- or postemergence), as well as any residue in drinking water as a result of pesticide use. Non-dietary exposure is also included in this assessment, and includes exposure to the pesticide through residential use, such as on lawns, as well as exposure in a recreational context,

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such as from a golf course or sports field. Based on these data, EPA must be able to make a determination of reasonable certainty of no harm to human health as required by the FFDCA. At the time that dicamba was undergoing reregistration review, occupational exposure was not considered as part of the aggregate exposure and is evaluated separately under the FIFRA unreasonable risk standard.

In making a determination of whether a reasonable certainty of no harm to human health exists, dietary risk assessments are performed that consider both the potential exposure and toxicity of a given pesticide. The dietary risk is then described as a percentage of a level of concern. The level of concern, which is also referred to as the population adjusted dose (PAD), is the dose (level of exposure) predicted to result in no adverse health effects to any human population subgroup, including sensitive subgroups, such as infants and children. The PAD may be expressed based on acute (aPAD, one day or less) or chronic exposures (cPAD, lifetime exposure). The PAD is the reference dose (RfD) for the compound but with any additional safety/uncertainty factors to protect sensitive subpopulations, or to address the completeness, quality or reliability of the toxicity data. The PAD is an estimate of the amount of daily pesticide exposure to the human population that can occur acutely (less than one day) or over a lifetime with a reasonable certainty of no harm to human health.[69] An estimated exposure less than 100% of the PAD is below the level of concern for the EPA.

The EPA evaluated the potential risks to human health associated with all then-registered dicamba uses as part of the reregistration of dicamba, and published the results and conclusion in the dicamba RED (U.S. EPA, 2009). Since reregistration, the EPA has approved an additional use on sweet corn, and as part of the approval included this new use in an updated dietary risk assessment. Since the sweet corn use pattern was within that reviewed during reregistration, EPA determined that the ecological and environmental fate assessments did not need to be updated and utilized the drinking water concentration from the RED in the updated sweet corn dietary risk assessment. The sweet corn use did not result in any noticeable increase in dietary exposure compared to the assessment from the RED; therefore, the risk assessment conduced for the dicamba RED is representative of all current registered uses of dicamba. EPA has conducted acute and chronic dietary (food and water) risk assessments for dicamba based on a theoretical worst case exposure estimate. For food, this estimate assumes that dicamba is used on 100 percent of all the crops on which the pesticide is currently approved for use. It further assumes that the resulting pesticide residues found on all harvested food crops and derived animal food commodities (*e.g.*, meat and milk) are at the level of the legally established tolerance (*i.e.*, the maximum allowable pesticide residue level). Residues of dicamba are defined as dicamba and its metabolites 5-hydroxy dicamba and 3,6-dichlorosalicylic acid (DCSA) in soybean commodities, and as dicamba and DCSA in animal food commodities, as currently regulated in 40 CFR § 180.227 (U.S. EPA, 2005a; U.S. EPA, 2005b). For water, EPA assumed that dicamba could potentially move offsite to adjacent surface water bodies as a result of drift or runoff. EPA also assumed dicamba could move through soil to groundwater; however, estimated concentrations in groundwater were significantly lower and therefore surface water estimates were used in the worse case dietary assessments. Surface water estimates were generated with the conservative screening level models SCIGROW and PRZM/EXAM using an exaggerated

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[69] RfD is the current terminology used by EPA; however, earlier EPA risk assessment terminology used the term Acceptable Daily Intake (ADI). RfD and ADI are synonymous.

application rate that is 2.8 times higher than the current 1.0 lb a.e./A maximum single application rate established in the dicamba RED (U.S. EPA, 2009, U.S. EPA, 2005b), and the maximum single application rate proposed for MON 87708. EPA mandated reductions in dicamba use rates as part of the dicamba RED (1 lb a.e./A and 2 lb a.e./A for a single application and for annual application, respectively).

The acute PAD for dicamba is 1 mg per kg body weight per day (mg/kg/day), based on an acute neurotoxicity study in rats (U.S. EPA, 2009). Based on the worst-case assumptions outlined above, the result of the dietary assessment gave a conservative, high-end (95th percentile) estimate of risk, which was well below the Agency's level of concern for both the U.S. population in general and for all population subgroups. As shown in Table M-1, when both food and water are combined, infants were the most highly exposed subgroup with 11% of the aPAD, or acute level of concern, consumed. Because even this most highly exposed subgroup consumes a small percentage of the acute level of concern for dicamba, EPA concluded there is a reasonable certainty that acute dietary exposure to dicamba will not pose a risk to human health, including that of infants and children (U.S. EPA, 2009).

The chronic PAD for dicamba is 0.45 mg/kg/day, based on a two-generation reproduction study in rats (U.S. EPA, 2009). Based on worst-case assumptions outlined above, EPA developed exposure estimates for the general U.S. population and the 8 other subpopulations of consumers evaluated by EPA, the major subpopulations are summarized in Table M-1. EPA determined that the most highly exposed subgroup for chronic dietary exposure (including both food and water) was children aged 1-2 years old, which consumed 6.6% of the cPAD, or chronic level of concern. Since even the most highly exposed subgroup consumes a small percentage of the chronic level of concern, EPA concluded there is a reasonable certainty that chronic dietary exposure to dicamba will not pose a risk to human health, including that of infants and children (U.S. EPA, 2009).

Table M-1. Summary of Dietary Exposure and Risk for Dicamba: Food and Water

	Acute dietary (95th percentile)		Chronic dietary	
Population subgroup	Dietary exposure (mg/kg/day)	% aPAD	Dietary exposure (mg/kg/day)	% cPAD
General U.S. population	0.0435	4.4	0.0118	2.6
All infants (<1 year old)	0.108	11	0.0199	4.4
Children 1-2 years old	0.0756	7.6	0.0297	6.6

Source: EPA 2005b.

The EPA also conducted an aggregate risk assessment which included dietary exposure (food and water) as well as other non-occupational exposures (*e.g.*, from residential uses such as lawns and recreational uses such as golf courses or sports fields). For acute and chronic aggregate risk assessment, the aggregate exposure is the same as the dietary exposure. EPA does not typically aggregate acute dietary exposures with acute non-occupational exposures because it is unlikely that high end dietary exposure will occur on the same day as maximum non-occupational

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exposures (U.S. EPA, 2005b). Current residential uses of dicamba do not result in long term residential exposure scenarios, so chronic aggregate exposure/risk is equal to chronic dietary exposure/risk. Therefore, the acute and chronic dietary exposure and risk summarized in Table M-1 also represents the acute and chronic aggregate exposure and risk.

For short-term aggregate risk assessment of dicamba, EPA considered exposures from food, water, and residential handling and post-application. As shown in Table M-2, the highest exposed individuals in this assessment were adult males mixing, loading and applying dicamba using a hose-end sprayer, resulting in an aggregate exposure of 5.1% of the cPAD, and toddlers playing on treated turf which results in an aggregate exposure of 9.7% of cPAD. This short-term risk aggregate risk assessment was also considered to be protective of intermediate and long term exposures to dicamba. A large margin of safety exists for exposure to dicamba, even considering all the approved food, feed and non-crop uses of dicamba.

Table M-2. Aggregate (Short-term) Exposure Assessment for Dicamba

Population	Food + Water Exposure mg/kg/day	Incidental Oral Exposure, mg/day	Dermal Dose, mg/kg/day	Combined Exposure, mg/kg/day	%PAD
Adult Male - Handler	0.0128	0	0.0102	0.023	5.1
Adult Male – Post Application	0.0128	0	0.0037	0.0165	3.7
Child – 1-2 years	0.0297	0.0078	0.0062	0.0437	9.7

Source: EPA, 2005b.

In summary, based on the EPA risk assessments discussed above, there is a reasonable certainty that the existing uses of dicamba will not pose a risk to consumers, including infants and children.

M.4.1.1. Dicamba Safety Evaluation for Use on MON 87708

Monsanto has submitted to EPA an application to register the use of dicamba on MON 87708 (U.S. EPA OPP Decision Number D-432752). The proposed use of dicamba on MON 87708 will not result in measurable increases in the exposure to dicamba or significant changes in the human health risk assessment. Plant metabolism studies have shown that the majority of the dicamba residue found in MON 87708 is DCSA, with lesser amounts of 3,6-dichlorogentisic acid (DCGA), 5-hydroxydicamba (5-OH dicamba) and parent dicamba (Table M-3). Toxicology studies submitted to EPA have demonstrated that the toxicology profiles for both DCSA and DCGA are comparable to that of parent dicamba, and that the existing hazard endpoints (RfDs and PADs) for dicamba are adequate to assess the potential human health risks from the metabolites as well. Studies have shown that the total dicamba residues in soybean seed following application of dicamba to MON 87708 will be well below the current 10 ppm soybean seed tolerance, an exposure level which has been determined as acceptable by EPA. In addition, Monsanto is proposing to establish new feed tolerances for soybean forage (45 ppm) and hay (70 ppm), which will allow the feeding of forage and hay to livestock. This practice is not

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presently allowed because the preharvest application occurs after the stage where the crop would be useful as forage and hay. Note that the maximum residue for forage at 51.2 ppm is above the proposed MRL of 45 ppm. This is due to the way the data are distributed and the use of the NAFTA MRL calculator, which is the standard method used by EPA to calculate pesticide tolerance levels (U.S. EPA, 2011a). The EPA will perform its own calculations based on the data summarized in the table below to establish an appropriate feed tolerance for dicamba on soybean forage and hay.

Table M-3. Residues of Dicamba, DCSA, 5-Hydroxydicamba and DCGA in Dicamba-Tolerant Soybean Forage, Hay and Seed

Commodity	PPM (Expressed as Each Analyte per se)				PPM (Dicamba Acid Equivalents)
	Dicamba	**DCSA**	**5-OH dicamba**	**DCGA**	**Total as current definition of residue (dicamba + DCSA + 5-OH dicamba)**
Forage					
Mean	0.342	15.8	<0.006	2.04	17.3
Median	0.068	14.0	<0.005	1.95	15.2
Minimum	<0.021	8.34	<0.005	0.359	10.0
Maximum	2.62	47.9	0.010	5.95	51.2
Hay					
Mean	0.130	30.1	<0.014	2.68	32.3
Median	0.051	29.8	<0.014	2.02	31.9
Minimum	<0.014	11.4	<0.014	0.169	12.2
Maximum	1.16	57.1	<0.014	7.33	61.1
Seed					
Mean	<0.013	0.055	<0.021	0.032	<0.091
Median	<0.013	0.031	<0.021	0.017	<0.065
Minimum	<0.013	0.009	<0.021	<0.011	<0.041
Maximum	<0.013	0.411	<0.021	0.136	0.471

Human dietary exposure will not increase beyond what has already been evaluated and determined acceptable by the EPA because established tolerances for animal food commodities (*e.g.*, meat or milk) are sufficient to address livestock consumption of soybean forage or hay. This is because the proposed soybean forage and hay tolerances (residues) are lower than existing livestock dietary constituents that could potentially be replaced with soybean forage or hay in the livestock diet (*e.g.*, grass forage at 125 ppm could be replaced with soybean forage at 45 ppm). Soybean forage and hay are also not common livestock dietary constituents, as concluded by the EPA in its policy to permit label restrictions for livestock feeding of soybean forage and hay (U.S. EPA, 1996).

Furthermore, since existing dicamba food tolerances (soybean seed and animal by-products) are inclusive of dicamba exposures arising from its use on MON 87708, the most recent EPA dietary and aggregate risk assessments for dicamba also address exposure from the proposed use in MON 87708. Therefore, these risk assessments demonstrate that there is a reasonable certainty that the use of dicamba on MON 87708, together with all other approved uses of dicamba, will

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not pose a risk to human health, including that of infants and children. While the use of dicamba is expected to increase as a result of the availability of MON 87708 integrated into the Roundup Ready® soybean system, the risk associated with the new use has been adequately assessed by EPA through the risk assessment conducted as part of the dicamba RED. Lastly, EPA will review and confirm the acceptability of dietary exposure of dicamba residues on MON 87708 as part of the review of our pending application.

M.4.2. Dicamba Safety Evaluation for Applicator

Other potential impacts considered by EPA in its human health assessment are occupational exposure of the pesticide handler/applicator, and post-application exposure resulting from re-entry to treated fields or areas. The occupational exposure scenarios evaluated by the EPA as a part of the dicamba RED are also applicable to the proposed use of dicamba on MON 87708 (U.S. EPA, 2005b; U.S. EPA, 2005d).

Using exposure data from the Pesticide Handler Exposure Database (PHED), Outdoor Residential Exposure Task Force (ORETF), and California Department of Pesticide Regulations, the EPA assessed short-term and intermediate-term occupational handler and post-application exposures. Handler exposure scenarios included mixer-loader, applicator and flagger activities. When exposure assumptions included the wearing of chemical resistant gloves during mixer/loader operations involving liquids required by dicamba product labeling, all occupational handler and post-application re-entry scenarios exhibited margins of exposure greater than 100 and did not exceed the EPA level of concern (U.S. EPA, 2009). The use of dicamba on MON 87708 does not pose any new exposure considerations for workers beyond those which have been previously evaluated by EPA as part of the dicamba RED. Therefore the use of dicamba on MON 87708 will not pose a risk to agricultural workers.

M.5. Potential Impact of Dicamba on the Environment

As discussed above, environmental effects are carefully considered as a part of the FIFRA pesticide registration process. Prior to the approval of a new pesticide or a new use (including a change in pesticide application rates and/or timing) and before reregistering an existing pesticide, EPA must consider the potential for environmental effects and conclude no unreasonable adverse effects to the environment will result from the new pesticide, new use or continued use.

To make this determination, EPA requires a comprehensive set of environmental fate and ecotoxicology data on the pesticide active ingredient (40 CFR Part 158). EPA uses these data to assess the pesticide's potential environmental risk (risk = hazard × exposure). The required data include both short and long-term hazard data on representative organisms that are used to predict hazards to terrestrial animals (birds, non-target insects, and mammals), aquatic animals (freshwater fish and invertebrates, estuarine and marine organisms), and non-target plants (terrestrial and aquatic).

EPA reevaluated the environmental safety of dicamba in 2006 as part of the FIFRA-required reregistration of all pesticides. At the end of this evaluation, EPA concluded that all then-

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registered uses of dicamba were eligible for reregistration, including single terrestrial (*i.e.*, land-based) applications up to 1.0 lb a.e./A dicamba, and annual terrestrial applications up to 2.0 lb a.e./A. (U.S. EPA, 2009). This EPA assessment fully supports the use of dicamba on MON 87708 as the proposed use pattern is within that assessed in the RED assessment.

M.5.1. Persistence of Dicamba in the Soil

Dicamba's fate in soil has been evaluated to determine the extent of its persistence in soil. While dicamba is stable to hydrolysis and photodegrades slowly on soil, dicamba is readily degraded in soil by aerobic soil microorganisms (U.S. EPA, 2009). Both laboratory and field studies demonstrate that dicamba dissipates quite rapidly in soil and has a low potential for accumulation.

In a laboratory aerobic soil metabolism study, dicamba was rapidly metabolized to the non-persistent degradate DCSA with a half-life of six days. DCSA was rapidly degraded at a rate comparable to that of dicamba producing carbon dioxide and being incorporated into biological natural products (U.S. EPA, 2005c). Other laboratory aerobic soil studies (Krueger et al., 1991) have been conducted for dicamba. In these studies, conducted in a number of different soils under various moisture and temperature conditions, dicamba degraded with half-lives ranging from 17 to 45 days. The European Union did not consider these half-lives indicative of the degradation rate of dicamba after evaluating the Krueger and other aerobic soil degradation studies (European Commission, 2007b).

Field dissipation studies conducted with dicamba formulations also demonstrate rapid dissipation of dicamba in soil. Application of dicamba formulated as various salts (diglycolamine, dimethylamine and sodium salts corresponding to commercial products) to bare-ground plots at labeled rates (1 or 2 lb a.e./A) resulted in half-lives for dicamba of 3-20 days. Results also confirmed low vertical mobility under the conditions of the studies as demonstrated by only low concentrations (<20 ppb) of dicamba and its major degradate DCSA present in soil segments deeper than 10 cm (U.S. EPA, 2005c). The proposed maximum use rates of dicamba on MON 87708 (single application rate of 1 lb a.e./A dicamba, total annual application rate of 2 lbs a.e./A) are within the rates investigated in these dissipation studies. In addition, dicamba applications, which can be applied prior to planting up through the R1/R2 reproductive stage to MON 87708, should occur when soil temperatures are favorable for aerobic microbial degradation of dicamba.

As with many chemicals, dicamba is metabolized somewhat slowly under anaerobic conditions, degrading with a half-life of 141 days (U.S. EPA, 2005c). However, under conditions amenable to aerobic degradation of dicamba and where retention of dicamba in aerobic soil layers is adequate for microbial degradation to occur, movement of dicamba to anaerobic soil layers would be minimal. Under normal soybean growing conditions of adequate soil temperatures and soil moisture, dissipation of dicamba through aerobic degradation would be rapid and it is unlikely that significant amounts of dicamba would reach anaerobic soil layers.

Based on these data, EPA concluded that dicamba and DCSA (the primary environmental degradate) are "somewhat persistent" under aerobic and anaerobic conditions (U.S. EPA, 2009). This statement reflects the difference in degradation rates under aerobic conditions (non-persistent) and anaerobic conditions (persistent). As discussed above, applications of dicamba

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on MON 87708 are likely to occur when environmental conditions are conducive to rapid aerobic microbial degradation; therefore, dicamba is not expected to persist in soil as a result of the use on MON 87708. Furthermore, EPA concluded, based on the registered use patterns of dicamba and product label mitigation statements, no unreasonable adverse effects to the environment would result from the (all) registered uses of dicamba.

M.5.2. Surface Water and Groundwater

The EPA evaluated potential risks to surface and groundwater from the approved uses of dicamba as part of the 2006 Reregistration Eligibility Decision (RED). The EPA estimated levels of dicamba in surface and ground water using screening level (high-end exposure) models PRZM/EXAMS and SCIGROW, respectively, which estimate concentrations based on the physical, chemical and environmental fate properties of dicamba, and high-end use patterns. These conservative estimates do not take into account normal variation in environmental concentrations that can occur from dilution and dissipation. Based on simulated sugarcane crop scenarios for both ground and aerial applications of 2.8 lbs dicamba a.e./A (2.5 to 5 times the proposed maximum single application rate for MON 87708),estimated groundwater concentrations were 0.016 µg/L dicamba and 0.008 µg/L for DCSA, the major environmental degradate (U.S. EPA, 2005b). In addition, EPA measured dicamba as part of its 1971-1991 pesticides ground water survey. Dicamba was detected at a low level of incidence, less than 3% of the 3172 samples, at levels ranging from trace to 44 µg/L(U.S. EPA, 1992). Dicamba also had a low incidence of detections in groundwater (less than 3% of the 6571 samples) in the U.S. Geological Survey National Water Quality Assessment (NAWQA) monitoring program during 1993-2003, where dicamba was detected at levels ranging from 0.008 to 2.50 µg/L (U.S. EPA, 2005b). Only parent dicamba and not the DCSA metabolite was analyzed in these water monitoring surveys.

For drinking water derived from surface water, estimated concentrations (1 in 10 year annual mean) using the simulated sugarcane crop scenario for both ground and aerial applications of 2.8 lbs dicamba a.e./A, ranged from 9.7 to 13 µg/L dicamba a.e. and 0.66 to 0.81 µg/L for DCSA (U.S. EPA, 2005b) Estimated surface water concentrations considered for aquatic organism risk assessment using simulated soybean crop scenario for ground and aerial applications of 2.0lb dicamba a.e./A ranged from 33.3-36.1 µg/L dicamba a.e. (U.S. EPA, 2005c). The NAWQA program also analyzed for dicamba in surface water samples in the 1993-2003 survey, where dicamba was detected at a low incidence (3% of the 6614 samples) at levels ranging from 0.009 to 1.76 µg/L (U.S. EPA, 2005b).

Measured dicamba concentrations in ground and surface water were also evaluated from a collection of publicly-available water monitoring data assembled by Monsanto Company from across the U.S. during 1990-2010. Data sources include the U.S. EPA (Pesticide Data Program, Safe Drinking Water Information System, Storage and Retrieval Data Warehouse and Unregulated Contaminant Monitoring Regulation data), the U.S. Geological Survey (NAWQA, National Water Information System), and various state water quality databases. From this collection of water monitoring data, relevant dicamba samples for ground and surface water were identified. First, data were restricted to the major soybean production states in the Midwest (IA, IL, IN, KS, KY, MI, MN, MO, ND, NE, NM, OH, SD and WI) and Arkansas. Second, the following samples types were excluded from the evaluation: finished drinking water, quality

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control samples, urban stream monitoring samples, and alternative purpose sampling (e.g., contaminated site investigation). Records for which a sampling date or location was not reported were also excluded from the evaluation. Finally, for surface water, the data were limited to those samples collected during the months of April – July, which is considered the typical period when dicamba would be applied for agricultural uses, and for which maximum concentrations of dicamba in surface water would be expected.

Dicamba concentrations in ground water are presented in Table M-4 for several year ranges and for the entire dataset evaluated. Overall, traces of dicamba were detected in less than 6% of the samples. For samples with detected dicamba levels, the minimum, median, 90th percentile and maximum concentrations are provided. The maximum level of dicamba detected in groundwater between 1990 and 2010 was 2.2 µg/L. However the 90th percentile of dicamba detections during 1994-1998, corresponding to the peak dicamba usage period (see Table VIII-11), and across the entire monitoring period was 0.25 µg/L.

Table M-4. Dicamba Concentrations (µg/L) in Groundwater in Major Soybean Growing States

		1990-1993	**1994-1998**	**1999-2004**	**2005-2010**	**1990-2010**
Number of Detects & Non-detects	*n*	1796	2781	2558	2568	9703
Number of Detects	*n*	121	413	1	3	538
Dicamba Concentration (µg/L) in Ground Water Based on Detects Only	Min	0.01	0.01	0.73	0.1	0.01
	Median	0.25	0.25	n/a	0.1	0.25
	90th Percentile	0.25	0.25	n/a	0.18	0.25
	Max	1	2.2	0.73	0.2	2.2

n/a: not applicable due to single data point

The geographical coverage of the groundwater sampling sites is provided in Figure M-1, which shows the locations of the sampling sites associated with all samples (detects and non-detects) and for detects only. The location of sampling sites during the 1994-1998 timeframe, which corresponds to dicamba's peak historical use period, provide a geographical representation of the areas of dicamba historical agricultural use intensity (see Figure VIII-1) and the major areas of soybean cultivation (see Figure VIII-2).

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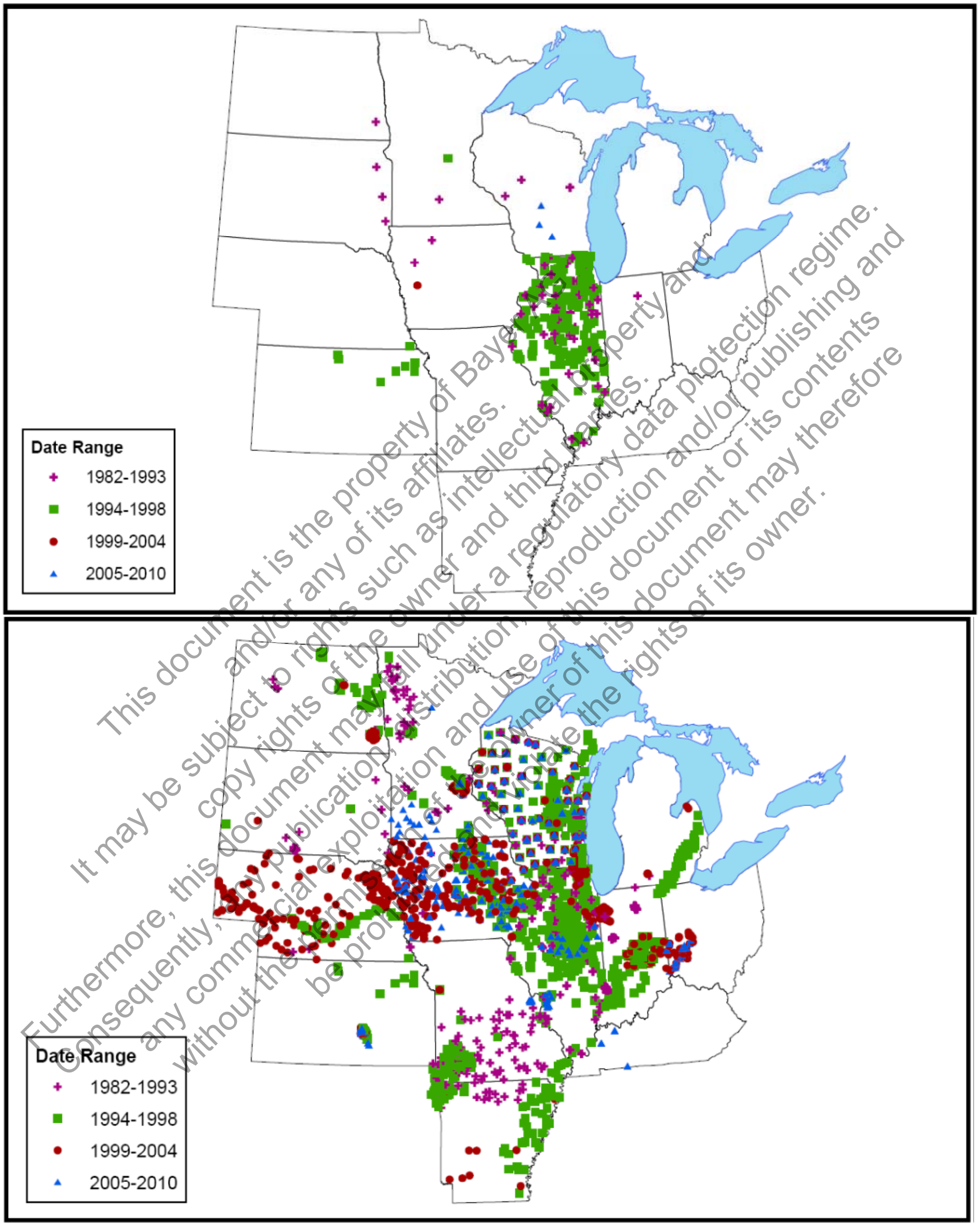
Figure M-1. Ground Water Sampling Sites for Dicamba (Top: Detects only; Bottom: detects and non-detects)


Date Range
1982-1993
1994-1998
1999-2004
2005-2010
Date Range
1982-1993
1994-1998
1999-2004
2005-2010

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Dicamba concentrations in surface water are presented in Table M-5 for several year ranges and for the entire dataset evaluated. Overall, traces of dicamba were detected in less than 11% of the samples. For samples with detected dicamba levels, the minimum, median, 90th percentile and maximum concentrations are provided. The maximum level of dicamba detected in surface water between 1990 and 2010 was 17 µg/L. However the 90th percentile of dicamba detections during 1994-1998, corresponding to the peak dicamba usage period (see Table VIII-11), and across the entire monitoring period was 0.74 and 0.883 µg/L, respectively.

Table M-5. Dicamba Concentrations (µg/L) in Surface Water in Major Soybean Growing States

		1990-1993	**1994-1998**	**1999-2004**	**2005-2010**	**1990-2010**
Number of Detects & Non-detects	*n*	588	1,362	2,443	1,033	5,426
Number of Detects	*n*	146	206	222	14	588
Dicamba Concentration (µg/L) in Surface Water Based on Detects Only	Min	0.01	0.008	0.01	0.03	0.008
	Median	0.2	0.25	0.29	0.2935	0.25
	90th Percentile	1.39	0.74	0.944	0.497	0.883
	Max	17	9.4	3.3	0.94	17

The geographical coverage of surface water sampling sites is provided in Figure M-2, which shows the locations of the sampling sites associated with all samples (detects and non-detects) and for detects only. The location of sampling sites during the 1994-1998 timeframe, which corresponds to dicamba's peak historical use period, represent a segment of the areas of dicamba historical agricultural use intensity (see Figure VIII-1) and the major areas of soybean cultivation (see Figure VIII-2).

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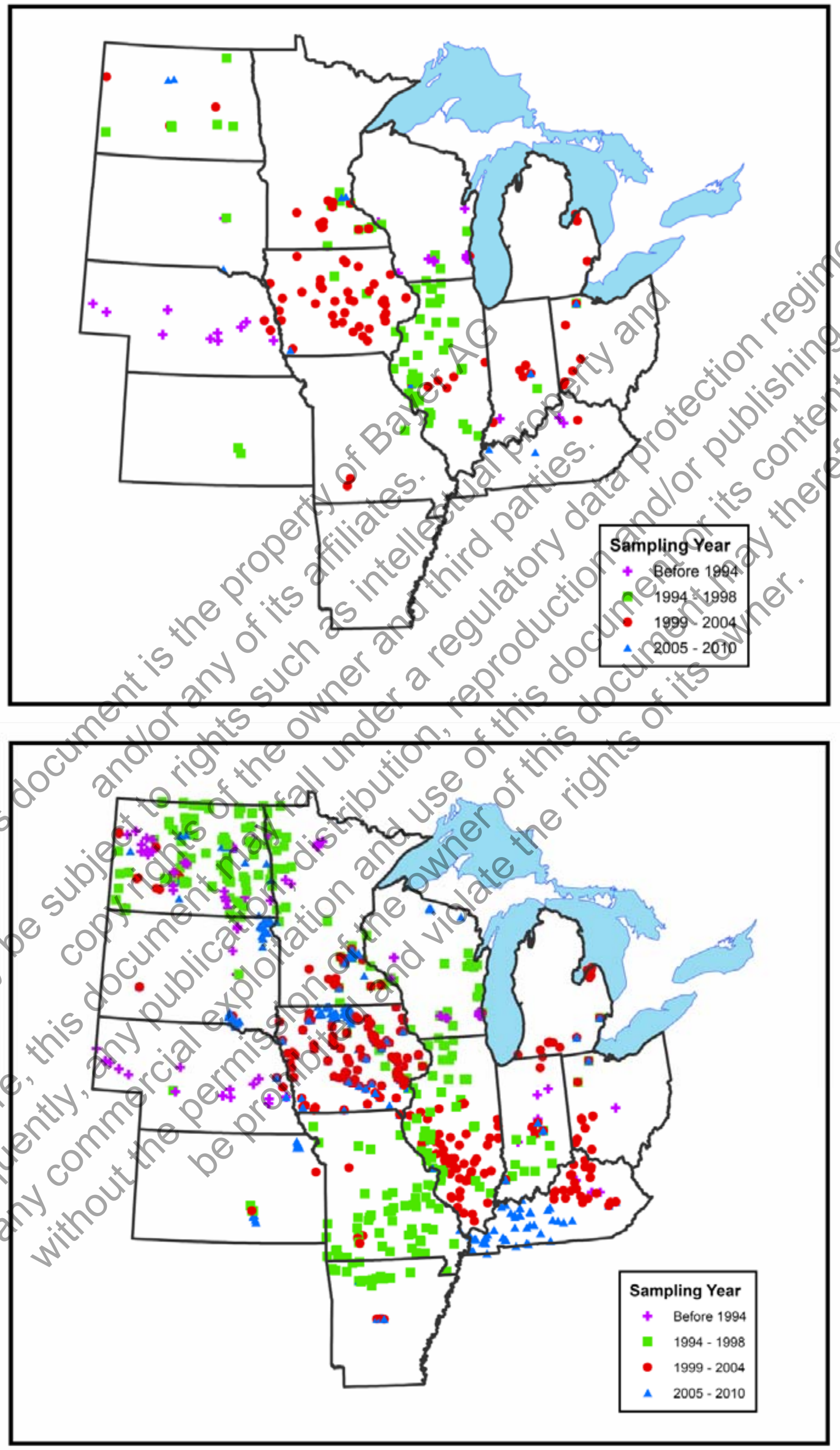
Figure M-2. Surface Water Sampling Sites for Dicamba (Top: Detects only; Bottom: detects and non-detects)


Sampling Year
Before 1994
1994 - 1998
1999 - 2004
2005 - 2010
Sampling Year
Before 1994
1994 - 1998
1999 - 2004
2005 - 2010

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Altogether, the modeling estimates, based on high-end exposure assumptions, and monitoring results show that concentrations of dicamba in potential drinking water resources as a result of its use are very low, and are well below the lifetime Health Advisory Level (HAL) for dicamba of 4 mg/L (U.S. EPA, 2011b). Similarly, the estimated and monitoring levels of dicamba in surface water are low and do not exceed the EPA level of concern for aquatic plants[70] and animals (U.S. EPA, 2005c). Therefore, the potential risk of dicamba from leaching or runoff as a result of incremental exposure from the use of dicamba associated with the planting of MON 87708 is very low and is unlikely to adversely affect human health or aquatic plants or animals.

M.5.3. Wildlife

M.5.3.1. Animals

As a part of the reregistration evaluation under FIFRA, EPA conducted an ecological screening assessment for dicamba. This assessment compared the results from toxicity tests with dicamba conducted with various plant and animal species to conservative (high end) estimates of the concentration of dicamba to which an organism might be exposed in the environment. These estimates, called the Estimated Environmental Exposure Concentrations (EECs), are point estimates for specific types of exposure (*e.g.*, aquatic or dietary) that assume constant high concentrations throughout the lifespan of the organism. These estimates do not take into account normal variation in environmental concentrations, the dilution or dissipation of those concentrations, or the frequency of exposure of wildlife to the pesticide. Such assumptions provide a screening level of assessment where conclusions of no harm can be drawn with high confidence; however, it is also possible to reach a conclusion of no harm with more refined exposure assumptions. During the reregistration process for dicamba and associated salts, the EPA derived exposure estimates for a number of use patterns (U.S. EPA, 2005c), including two scenarios that are reasonably close to the proposed use pattern for dicamba on MON 87708. These use patterns are: 1) wheat, with two 1.0 lb a.e./A applications; and 2) sorghum, with two 0.5 lb a.e./A applications. For both cropping scenarios, the two applications were considered to occur on May 1st and June 1st.

Based on the EPA screening-level analysis for relevant use patterns (wheat and sorghum) described above, no acute or chronic risk to aquatic animals was identified. Also, no chronic risk to birds or acute risk to mammals was identified. Considering maximum and mean residue levels assumed from the Kenaga nomogram (Fletcher et al., 1994)[71], and application at rates of 1.0 lb a.e./A and 0.5 lb a.e./A, the screening assessment did determine that the risk quotient (RQ) exceeded the Level of Concern (LOC= 0.5) for acute risk to some non-endangered bird species based on size and diet (U.S. EPA, 2005c). Using the toxicity endpoints from the avian oral gavage[72] study, i.e., a study which forces a single high dose of dicamba directly into the birds's crop and is not representative of realistic exposure scenarios for birds, EPA concluded acute exposure risks exceeded their level of concern for small (20 g) and medium (100 g) size birds.

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[70] Currently there are no federally listed threatened or endangered nonvascular aquatic plants, so only risk to non-listed aquatic nonvascular plants is considered.

[71] The Kenaga nomogram was developed by the U.S. Environmental Protection Agency (U.S. EPA) to predict the maximum potential pesticide residue levels in the food chain of wildlife for use in risk assessment.

[72] Forcing a single high concentration of dicamba directly into the bird's crop, and is not representative of realistic exposure scenarios for birds.

Despite these predictions of potential effects, no incident reports have been filed with EPA for adverse effects on birds from dicamba use (U.S. EPA, 2005c). Furthermore, when exposure via the avian diet (the most relevant and realistic route of exposure of birds to dicamba) is considered, the EPA classified dicamba acid and its salts as practically non-toxic to birds (U.S. EPA, 2005c). Avian toxicity to dicamba (as the DGA salt) via dietary exposure is significantly less (> 5-fold) than toxicity from exposure via oral gavage. Therefore, it is unlikely that dicamba will pose an acute risk to birds when a more realistic dietary exposure is considered where dicamba residues are mixed with other food components and eaten over the entire day as would occur in the natural environment.

The screening level assessment predicts that there will be no chronic risk (RQ < 1) to mammals regardless of size or dietary habits when mean residues resulting from application at a maximum rate of 1.0 lb a.e./A are utilized in the assessment (U.S. EPA, 2009). Mean initial residues, rather than maximum initial residues, provide a more realistic, but still conservative, dietary exposure estimate for a chronic exposure which would occur over days to weeks of duration.

The EPA has classified dicamba as practically nontoxic to honey bees based on an acute contact LD50 value of >90.65 µg/bee (the honeybee is used to assess effects on non-target insects in general), and practically nontoxic to birds from dietary exposure. Dicamba presents a low hazard to aquatic organisms. Consequently, aquatic animals were predicted not to be at risk from rates of dicamba up to 2.8 lbs a.e./A, the highest rate assessed (U.S. EPA, 2005c). Dicamba has a low octanol-water coefficient (Log P < 3), indicating that it has a tendency to remain in the water phase rather than move from the water phase into fatty substances; therefore, dicamba is not expected to bioaccumulate in fish or other animal tissues (U.S. EPA, 2005c).

In conclusion, no acute or chronic risk to aquatic or terrestrial animals, as defined above, is anticipated to result from potential incremental exposure of dicamba associated with the use of MON 87708.

M.5.3.2. Plants

Dicamba is a selective herbicide with more activity on dicotyledonous (dicot) plants than monocotyledonous plants (Ashton and Crafts, 1981). The EFED Reregistration Chapter for Dicamba / Dicamba Salts concluded that listed and non-listed terrestrial plants are potentially at risk from runoff and drift associated with all uses, but no risk to listed and non-listed aquatic plants (vascular or non-vascular) is expected as result of dicamba use at single application rates up to 1.0 lb a.e./A (U.S. EPA, 2005c).

In the Reregistration Eligibility Decision (U.S. EPA, 2009), EPA concluded that a reduction in the maximum rate for a single application to 1.0 lb a.e./A and reduction in the total annual application rate to 2.0 lb a.e./A reduced the risk to terrestrial plants, and further determined that all currently registered uses of dicamba were eligible for reregistration provided that these rate mitigation measures were adopted on product labels.

In conclusion, since the application rates for use of dicamba on MON 87708 fall within the reduced application rates mandated by the RED, the use of dicamba on MON 87708 will not pose a risk to non-target aquatic plants. Further, risks to non-target terrestrial plants are

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adequately managed through appropriate application of dicamba as directed on the pesticide label and any effects will be mostly limited to non-lethal, temporary visible effects.

M.5.4. Endangered and Threatened Species

In the dicamba RED EPA discussed the changes in the registered use pattern of dicamba that were required to assure that dicamba meets the regulatory standards for pesticides in the United States. The primary use restriction that EPA determined was necessary to provide adequate protection of the environment, including non-target species, was the reduction of the maximum single dicamba application rate to 1.0 lb a.e./acre and the maximum annual rate of 2.0 lb a.e./A. EPA went further in the RED to state that no specific additional mitigations of off-target movement due to spray drift were needed (U.S. EPA, 2009). Because these limits were mandated by EPA to provide protection to non-target organisms, and because the proposed use of dicamba on MON 87708 falls within these limits, the risks to these non-target organisms from the use of dicamba on MON 87708 has also been addressed.

As stated earlier, because the maximum single and annual application rates for the proposed use pattern for dicamba on MON 87708 are within the range of maximum application rates implemented as the primary use restriction mandated by the dicamba RED, the same conclusion can be reached for this use. Monsanto has requested approval of the use of dicamba on MON 87708; in its review of this registration request, EPA will address this use of dicamba under applicable statutory and regulatory requirements for pesticides.

In addition, Monsanto has gone beyond the existing restrictions in place for dicamba use under FIFRA in order to assure adequate protection of endangered and threatened species under the proposed use of dicamba on MON 87708. Specifically, Monsanto's registration submission for dicamba use on MON 87708 requested use only for a low volatile salt form of dicamba (diglycolamine or DGA) and requested only ground applications be allowed (*i.e.*, no aerial application).

M.5.5. Potential Effects on Endangered Animal Species Identified in Litigation

In response to litigation brought by the Washington Toxics Coalition, the EPA conducted an assessment for dicamba and its impact on the endangered Pacific anadromas salmonids and their critical habitat. In this analysis, the EPA concluded that dicamba does not impact the endangered salmonids or their critical habitat (U.S. EPA, 2003). EPA also considered risks to endangered species as part of the reregistration of dicamba in 2006. Using an extremely conservative deterministic screening level ecological risk assessment (U.S. EPA, 2004), the EPA concluded that use of dicamba would have no effect on threatened or endangered freshwater fish, estuarine fish, and aquatic invertebrates (U.S. EPA, 2009).

The EPA has also evaluated the potential effect of dicamba on salmon in eleven areas of California and Southern Oregon[73] in response to the consent agreement reached in the Washington Toxics lawsuit.[74] The conclusion of EPA's risk assessment is as follows:

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[73] These areas are called Evolutionarily Significant Units based on the salmonid populations present in these areas.

[74] Washington Toxics Coalition v. Environmental Protection Agency, 413 F.3d 1024 (9th Cir. 2005).

"Regardless of the specific dicamba compounds, I conclude that dicamba compounds with currently registered uses will have "no effect" on listed Pacific salmon and steelhead and their critical habitat…" (U.S. EPA, 2003).

Since the use rates of dicamba proposed for MON 87708 are within the currently registered and evaluated use rates, no further consideration of the risk to Pacific salmon or steelhead is needed. This conclusion is consistent with EPA's determination of no risk to fish or other aquatic animals in the dicamba screening assessment in the dicamba RED (U.S. EPA, 2005c). Furthermore, soybean production is not commonly practiced in the Pacific Northwest. However, based on the analysis above, risk to endangered Pacific salmon or steelhead is not expected from the use of dicamba on MON 87708.

M.5.6. Other Potential Environmental Impacts Associated with Dicamba Use on MON 87708

M.5.6.1. Potential Offsite Movement of Dicamba

Herbicide drift and offsite movement are actively managed by farmers and applicators specially trained to use such products consistent with product labels and other state or local restrictions. Depending upon the herbicide being used, factors for managing the potential for spray drift include the selectivity and sensitivity of the herbicide, local weather conditions at the time of application (wind, temperature, humidity, inversion potential), droplet size distribution, application volume, boom height (height of the application equipment above the crop canopy), sprayer speed, and distance from the edge of the application area (SDTF, 1997; Felsot et al., 2010). A variety of measures can be employed to control the potential for spray drift and offsite movement, including nozzle selection and application techniques and restrictions.

The potential for offsite movement is regulated at the federal level by EPA. As indicated, EPA specifically approves product labeling for all crop uses of the herbicides. Before any dicamba formulation could be used on MON 87708, EPA is required to approve the pesticide label for that respective use, including specific directions for the use and application of the herbicide on the proposed crop. Label use directions would address not only application rates and timing, but as appropriate, could also include other measures to address the potential for offsite movement. EPA considers possible effects from offsite movement as part of the pesticide registration process required under FIFRA. Specifically, in order to approve the use of a pesticide (herbicide), EPA must conclude that no unreasonable adverse effects on non-target vegetation will result from potential offsite movement when the pesticide is used according to the product label.

EPA reassessed the potential risks to non-target plants in its analysis in the dicamba RED, concluding that no specific additional drift mitigations were needed to support the continued registration of all dicamba uses (U.S. EPA, 2009). Since the proposed use pattern for dicamba on MON 87708 is consistent with use patterns evaluated and deemed eligible for reregistration in the dicamba RED, it is reasonable to conclude that dicamba use on MON 87708 meets the FIFRA standards related to drift and offsite movement. Thus, when herbicides are applied in accordance with the application instructions on the FIFRA label, offsite impacts can be avoided.

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The use of dicamba on MON 87708 does not pose any greater risk to non-target vegetation over existing dicamba agricultural uses approved by EPA. Nevertheless, Monsanto has already taken additional steps to manage dicamba offsite movement even though EPA stated in the RED that no specific drift mitigation measures were needed. In the pending application to EPA, Monsanto requested the use of dicamba on MON 87708 on the low volatility DGA salt formulation (U.S. EPA Reg. No. 524-582) and limited dicamba applications to ground application equipment. Monsanto also plans to further address the specific use of dicamba on MON 87708 with US EPA, to evaluate whether additional measures may be appropriate to address potential drift and offsite movement.

In addition, Monsanto will implement a robust stewardship program that will include a strong emphasis on grower and applicator training by working with American Association of Pesticide Safety Educators (AAPSE) and other stakeholders in applicator training to further facilitate on-target applications of dicamba. There is an extensive pesticide education system within the United States as evidenced by the existence of the AAPSE. Members of this organization train and certify 500,000 applicators in agriculture and other pesticide use areas, working in land-grant university cooperative extension services and tribal, state, trust, territory, and federal agencies across the nation. Furthermore, EPA actively supports pesticide applicator training by funding the pesticide safety education program (PSEP). Since 1975, EPA has had an interagency agreement with USDA to distribute funds to the state cooperative extension service for the purpose of training pesticide applicators.

M.5.6.2. No-Till Practices

Conservation (no-till and minimum-till) production practices are used on approximately 40% of the U.S. soybean acres (CTIC, 2007). The increase in the number of resistant weed biotypes to soybean herbicides, including glyphosate, could adversely affect the sustainability of conservation production acres. The availability of MON 87708 and the flexibility to use dicamba for both preemergent and postemergent control of resistant and hard-to-control broadleaf weeds will provide a tool to help maintain this important agricultural practice. Furthermore, the use of dicamba on MON 87708 integrated into the Roundup Ready soybean system will help to delay the development of new resistant weed biotypes as a result of a second mode-of-action in the weed management system.

The benefits of conservation tillage are well known and demonstrated, and include soil and water conservation, improved water quality and a reduced carbon footprint (CTIC, 2011). No-till production is the practice of establishing an agricultural seed bed and controlling weeds without mechanically tilling the soil. Instead, the only tillage of the soil is done at the time of planting, with the crop being seeded directly into the previous year's crop residue. Among other environmental benefits, no-till production reduces soil erosion and the use of petroleum-based fuels for tractors. The practice has been shown to minimize surface water runoff and to improve soil quality by increasing the soil organic matter that helps bind soil nutrients and prevent their loss to runoff, erosion and leaching (Arriaga and Balkcom, 2005; Leep et al., 2003). Less soil erosion into surface waters would positively impact stream dynamics (McVay et al., 2005; Reicosky, 2008).

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No-till agriculture can provide benefits to water bodies as well. No-till practices reduce soil erosion to surface water bodies, decreasing the amount of sediment in rivers and streams. Sedimentation increases the turbidity (cloudiness) of surface water bodies, reducing light penetration, impairing photosynthesis and altering oxygen levels, which cause a reduction of food sources for some aquatic organisms. Sediment can also cover spawning beds and impact fish populations. Phosphorus (a major component of fertilizer) bound to soil particles can be transferred to rivers and lakes via soil erosion, giving rise to high levels of phosphorus in surface waters, which may lead to algae blooms that can impact desirable fish populations (Hill and Mannering, 1995).

No-till practices have also been shown to reduce the carbon footprint from agricultural production by decreasing carbon emissions due to fewer cultivation activities. In addition, deposits of crop residue on the soil surface are converted to organic matter and humus through carbon cycling, preserving soil carbon reserves and increasing fertility and nutrient cycling (Reicosky, 2008).

M.5.6.3. Soil Microorganisms

Results of standardized tests with dicamba and dicamba formulations performed for submission to regulatory agencies indicate no long-term effects on functional processes of soil microorganisms (carbon respiration and nitrogen transformation) when exposed to dicamba at rates up to 3.8 pound a.e./A. These levels exceed the current maximum single and annual dicamba use rates of one lb a.e./A and two lbs a.e./A, respectively (European Commission, 2007b).

M.5.6.4. Impact on Beneficial Arthropods

Dicamba is a broadleaf herbicide that controls a range of dicot plants in the presence of monocots and other crops. Its effects primarily arise from direct applications in the field to reduce the plant mass and reproductive potential of susceptible weeds. Indirect effects outside of the treated areas as a result of spray drift would be significantly less since the amount of dicamba that can drift offsite at the field margins is typically less than 1% of the amount directly applied to the field (U.S. EPA,2005c). Dicamba has little or no effect on monocot plants and is considered by EPA to be practically non-toxic to insects, including honeybees and other arthropods (U.S. EPA, 2005c). Most available studies on the effects of herbicide treatment on arthropod communities are done with direct applications, and potential indirect effects from dicamba outside of the treated area are extrapolations from the direct effects at high exposure levels. Within the application area, the expected effects would be reduction in food sources (foliage, nectar, seeds) and cover for insects due to the intended weed control in the crop provided by dicamba application.

Indirect effects of dicamba and related herbicides have been studied as potential effects on community structure, impacts to butterfly communities and other insect communities in areas adjacent to agricultural fields, and in the treated fields themselves. Fuhlendorf et al. (2002) studied the impact of direct application of selective broadleaf herbicides on forb[78] community

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[78] Forbs are herbaceous flowering plants that are not graminoids (grasses, sedges and rushes). Examples of forbs are clover, sunflower and milkweed.

richness and arthropod composition in a tall grass prairie. The authors reached the following conclusions: “This study demonstrates that the application of a selective herbicide can reduce the abundance and species richness of forbs that may serve as critical hosts to some arthropod species. However, analysis of these tallgrass communities did not yield significant differences in arthropod abundance or richness between grasslands treated with an herbicide and grasslands not treated with an herbicide… These results suggest that a single application of herbicide in tallgrass prairies of North America, although reducing the abundance and richness of forbs, neither eradicates the forb growth form nor substantially changes forb composition in the grassland community. Hence, neither does the arthropod community change. Relationships between forb cover and the arthropod community suggest that single applications of broadleaf herbicides may only have an effect on arthropods when forb abundance is dramatically reduced (below 5% cover). This study is incapable of concluding that herbicides targeted at forbs do not always influence the forb and arthropod communities, because herbicides are applied typically to native grasslands on southern Great Plains at 3–5 year intervals (Vallentine, 1989; New, 1997; Hanselka et al., 1990).” (Fuhlendorf et al., 2002).

Longley and Sotherton (1997) also reviewed the literature regarding effects of pesticides on butterfly populations in agricultural areas. Excerpts from this review follow: “The main impact on butterfly populations is accidental drift or intentional direct spraying of broad-spectrum herbicides onto field boundaries to reduce certain pernicious perennial weeds (Marshal and Smith, 1987). However, the production of annual grass species is encouraged by these herbicide applications leading to a species-poor community (Smith and Macdonald, 1992). Consequently, herbicides may affect butterfly populations through the direct mortality of their larval food plants and flowering-nectar sources such as bramble (*Rubus fruticosus*), mayweed (*Matricaria perforata*), marjoram (*Origanum vulgare)* and thistle-like *Compositae*. The removal of host plants or premature senescence of plant parts can lead to larval starvation or the exclusion of less-fit adults (Courtney, 1981)”. Later in the review, Longley and Sotherton indicate that species vulnerability depends on larval food plants utilized by the species. “With the various factors influencing the extent of spray deposition on plants, the degree of pesticide (herbicide) exposure encountered by different butterfly families, and hence their vulnerability, will depend upon their choice of larval food plants. Members of the *Hesperiidae* and *Satyridae* families feed mainly on a range of coarse, densely tufted perennial grass species which are commonly found growing within many field boundaries”. Application of broadleaf selective herbicides such as dicamba that allow for selective growth of grasses would increase the food source for these species. Indirect exposures from spray drift at greatly reduced rates would result in substantially less impact to plant and arthropod communities surrounding the agricultural fields since exposures at drift rates are usually insufficient to reduce the survivability and reproductive potential of plants (Al-Khatib and Tamhane, 1999; Auch and Arnold, 1978; Behrens and Lueschen, 1979; Andersen et al., 2004). Since control of vegetation other than soybeans within the field is a component of soybean production, and since dicamba is anticipated to have little effect on forbs outside the field, the use of dicamba on MON 87708 is anticipated to have little or no effects on arthropod communities that are dependent on plants for their survival.

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Appendix N: Overview of Evaluation of Potential Exposure and Biological Effects on Endangered Species for Dicamba Use in MON 87708

N.1. Introduction

This overview report provides a summary of a multi step approach that has been utilized to evaluate the potential effects on federally listed threatened and endangered ("listed") species from the use of the herbicide dicamba on dicamba-tolerant (DT) soybean. This analysis follows the procedures described in the Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency (U.S. EPA), Endangered and Threatened Species Effects Determinations, published in 2004 (U.S. EPA, 2004), as well as methods utilized in more recent threatened and endangered species effects determinations conducted by the U.S. Environmental Protection Agency (USEPA) for atrazine (U.S. EPA, 2007), and for a number of active ingredients in assessing their potential effects on the California red legged frog (U.S. EPA, 2008a). A four step process is described in more detail below.

N.2. Endangered Species Exposure and Effects Analysis

N.2.1. Screening Level Analysis

An initial analysis of the potential for exposure and effects to all taxa from dicamba use in dicamba-tolerant soybean based on the use pattern pending at EPA was conducted ([redacted] 2011) using the EPA deterministic risk quotient approach (U.S. EPA, 2004).[79] The use pattern for dicamba utilized in this analysis was a pre-emergence application at a rate of 1.0 lb dicamba acid equivalents per acre (a.e/A) followed by two post-emergence applications each at a rate of 0.5 lb a.e./A with a 6-day interval between the pre-emergence application and the first post-emergence application, and a 6-day interval between the two post-emergence applications, with all applications being made using ground application equipment.[80] The 6-day application intervals utilized in this analysis are expected to be shorter than the intervals actually used in practice, since a grower is expected to wait at least 7 days before deciding to make a subsequent application in order to allow evidence of dicamba efficacy to develop.

Initial exposure estimates using the above described use pattern were based on standard EPA exposure models and default assumptions; toxicity effects endpoints were taken from the EPA Environmental Fate and Effects Division (EFED) Science Chapter for the Reregistration Eligibility Decision for dicamba (U.S. EPA, 2005) or from more recent EPA guideline studies conducted by BASF under an EPA data call-in (Porch et al.,

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[79] This approach calculates a risk quotient (RQ) by dividing the Estimated Environmental Concentration (EEC) by the appropriate toxicity endpoint, and then compares that value with the appropriate Level of Concern (LOC). The LOC is established by EPA policy as the criteria used by EPA in comparison to the calculated risk quotient (RQ) to assess the potential for a pesticide use to cause adverse effects to non-target organisms.

[80] The dicamba label for DT soybeans will not permit aerial application.

2009[81]), when these endpoints were more consistent with current EPA guidelines. The conclusion from this initial analysis, based on risk quotients (RQs) being less than the EPA Levels of Concern (LOCs), is that dicamba use on dicamba-tolerant soybean would not affect threatened and endangered species in the following taxa:[82]

- Fish, aquatic phase amphibians, and aquatic invertebrates (acute or chronic exposure)
- Birds, terrestrial-phase amphibians, and reptiles (chronic exposure)
- Mammals (acute exposure)
- Insects, aquatic vascular plants and monocotyledonous terrestrial plant species[83,84]

Although the RQ for aquatic nonvascular plants exceeded the LOC additional analysis was not conducted because there are no federally listed nonvascular aquatic plants.

These conclusions for aquatic plants and animals, birds, mammals and insects are consistent with the risk conclusions presented in the EFED science chapter for dicamba reregistration (U.S. EPA, 2005; 2006).

The conclusion for monocots is based on more recent nontarget plant studies with a typical dicamba end use product that were required by EPA during the reregistration process (Porch et al., 2009).[85] Using the no-observed-effect endpoints from these 2009 studies and the EPA model TerrPlant to calculate exposure and risk quotients, the RQs for monocots were below the LOC, and thus result in a conclusion of no effect. The levels of concern considered by EPA for threatened and endangered (listed) species risk assessments are given in Table N-1.

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[81] New studies were required by EPA because previous studies did not meet current regulations requiring the use of formulated product for these studies. This new testing resulted in a more conservative endpoint for the vegetative vigor study and confirmed field observations of relative sensitivity for the seedling emergence study.

[82] "If assumptions associated with the screening level action area result in RQs that are below the listed species LOCs, a "no effect" determination conclusion is made with respect to listed species in that taxa, and no further refinement of the action area is necessary." EFED Reregistration Chapter for Dicamba/Dicamba Salts,.

[83] According to EPA methodology (U.S. EPA, 2004), risk to non-target plants is assessed only outside the application area.

[84] Exposure for insects and plants is not divided into acute and chronic durations.

[85] The new study was conducted under the OPPTS 850.4225 draft guideline which is very similar to the current OECD nontarget plant guideline, and the results are considered to be more representative of effects that would be expected to occur in the field because of an improved study design.

Table N-1. EPA Levels of Concern for Threatened and Endangered Species

Risk Presumption	Calculation for Risk Quotient	Level of Concern
Birds:		
Acute Risk	EEC/LC_{50} (application of a liquid) or LD_{50}/ft^2 or LD_{50}/day (application as a granule, bait, or treated seed)	0.1
Chronic Risk	EEC/NOAEC	1.0
Wild Mammals		
Acute Risk	EEC/LC_{50} (application of a liquid) or LD_{50}/ft^2 or LD_{50}/day (application of a granule, bait, or treated seed)	0.1
Chronic Risk	EEC/NOAEC	1.0
Aquatic Animals		
Acute Risk	EEC/LC_{50} or EC_{50}	0.05
Chronic Risk	EEC/MATC or NOAEC	1.0
Terrestrial and Semi-Aquatic Plants		
Acute Risk	EEC/EC_{05} or NOAEC	1.0
Aquatic Plants		
Acute Risk	EEC/EC_{05} or NOAEC	1.0

Source: U.S. EPA, 2004

N.2.2. Refinement to the Screening Level Analysis - Use of Dicamba-specific Foliar Residue Values

Consistent with EPA guidance found in the Overview Document (U.S. EPA, 2004), if screening-level assessments do not result in a "no effect" determination, EPA does not then conclude that an herbicide "may affect" threatened and endangered species; rather, more refined assessments must be conducted to ascertain if any effects are expected to occur. Accordingly, for threatened and endangered animal species and the exposure durations for which the risk quotient exceeded the LOC in the screening level analysis (acute exposure for birds, amphibians and reptiles, and chronic exposure for mammals), refined exposure estimates were developed utilizing measured dicamba residues on pasture grasses and soybean forage[86] (as representative residues for short grass and broadleaf foliage[87] components of animal diets) ([redacted] 2011). These data were from residue

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[86] Residue values from these studies were converted to values expressed as parts per million per pound dicamba acid from residues values for application rates of 0.5, 1.0, and 2.0 lb a.e./A for grasses and 0.5 and 1.0 lb a.e./A for soybeans.

[87] EPA assumes that broadleaf foliage and small insects have the same residue values, so these dicamba-specific values were used both for broadleaf foliage and small insects.

studies conducted under Good Laboratory Practices by dicamba registrants and by Monsanto, respectively, and are used to provide dicamba-specific residues for components of animal diets, instead of using the EPA default residue values based on the Kenega nomogram (Hoerger and Kenega, 1972) as revised by Fletcher (1994). Both the soybean residue study and one of the grass residue studies, as well as a wheat residue study, included sites with several sampling points for forage which occurred soon after application so that the rate of decline of dicamba residues on soybean, grass, and wheat foliage could be determined, and the time required for dissipation of fifty percent of the residues (DT50) calculated.[88] The Overview Document (U.S. EPA, , 2004)[89]) indicates that chemical-specific foliar dissipation values can be used for multiple application exposure modeling for wildlife; accordingly, as a conservative assumption, the longest of the representative dicamba-specific foliar DT50 values for these three crops (5.63 days, for pasture grass) was used in the calculation of the dicamba-specific residues for chronic exposure. For grass and broadleaf dietary items, both mean and upper bound residue values[90] were considered in the evaluation; these levels are suitable to estimate realistic (mean) and worst case (upper bound) levels of exposure. A comparison of the default upper bound residue values and dicamba-specific upper bound residue values is given in Table N-2.

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[88] For the pasture grass and wheat residue studies, there were over 50 treatments per study for which a DT_{50} value could be calculated. With such a large number of data points, the 90th percentile upper confidence limit of the mean DT_{50} value was selected as an appropriate DT_{50} value to use for calculation of residue decline for these crops. For the soybean residue study with only six treatments available to calculate DT_{50} values, the maximum value was considered representative of residue decline in soybean forage.

[89] Overview Document (U.S. EPA, 2004),

[90] A 90th centile value was used for pasture grass and the maximum residue value was used for soybean forage due to the difference in numbers of residue values available to calculate the upper bound residue.

Table N-2. Comparison of Default Kenaga Residues and Dicamba-specific Residues in Food-Items

	Maximum dicamba residues in food items (ppm a.e.) based on a 1 lb a.e./A pre-emergence application followed by two sequential post-emergence 0.5 lb a.e./A applications			
	Short Grass	Tall Grass	Broadleaf Plants/ Small Insects	Fruits/Pods/Seeds/ Large Insects
Using upper bound Kenaga residues & default foliar half-life (35 days)				
Day 0 (after 1st application)	240.0	110.0	135.0	15.0
Maximum residue[a] (after 3rd application)	415.8	190.6	233.9	26.0
Using Dicamba-specific residues & foliar half-life (5.63 days)				
Day 0 (after 1st application)	131.0	60.0	103.9	15.0
Maximum residue[a] (after 1st application)	131.0	60.0	103.9	15.0

[a] Using the default foliar half-life, the highest residue occurs immediately after the third application. Using the dicamba-specific half-life, the highest residue occurs immediately after the first application

These refined residue values for dietary items were considered when using the EPA model T-REX (v1.4.1) for the calculation of risk quotients and subsequent comparison to LOCs for acute exposures to birds, terrestrial amphibians, and reptiles, and for chronic exposures to mammals.[91] Figure N-1 describes the process for identifying the taxa that had risk quotients exceeding the EPA's LOC after the screening level analysis.

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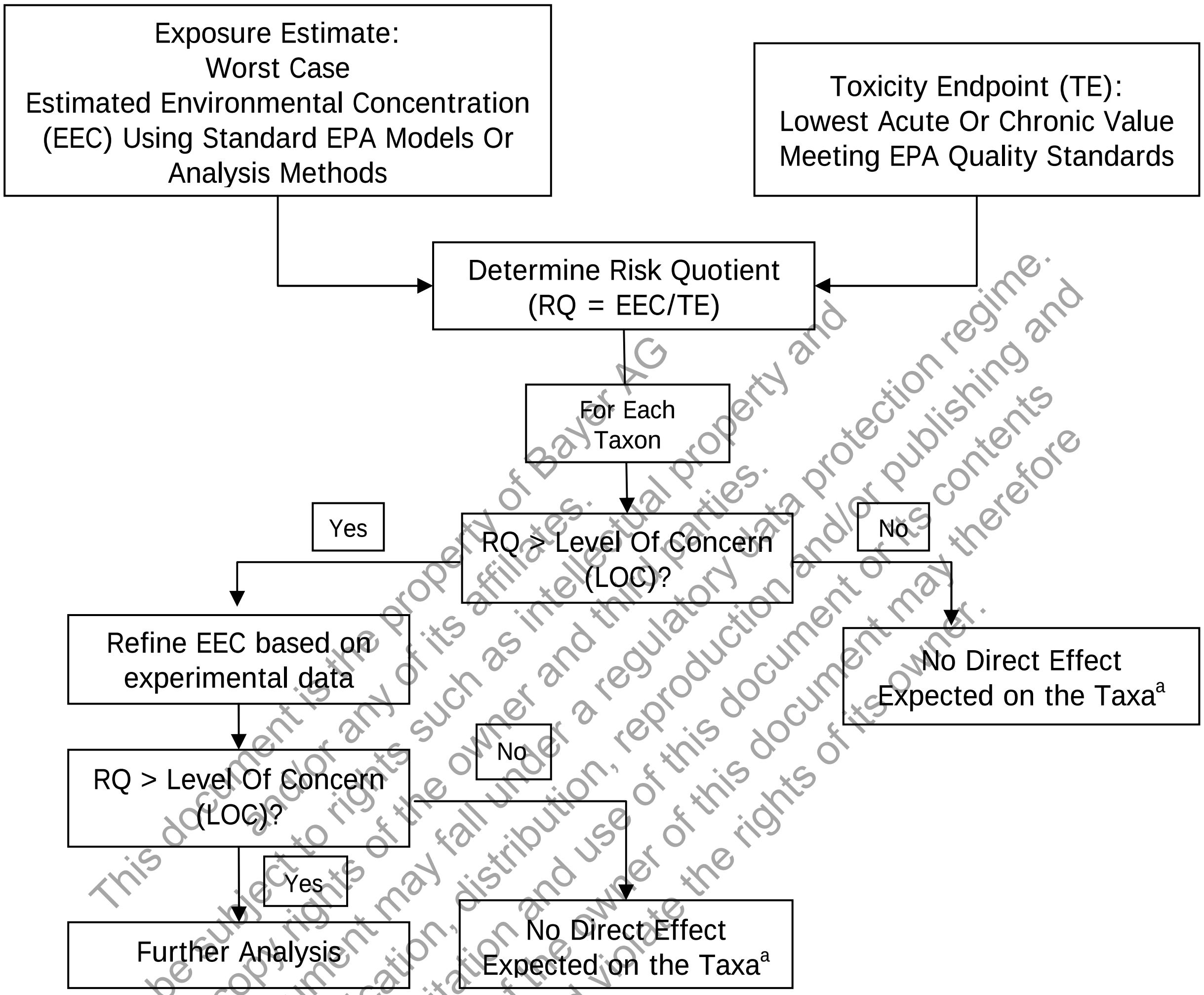
[91] The T-REX model is not designed to allow modification of the dietary food item residues. Thus, the dicamba-specific residues reported in Table N-2 were considered in the risk quotient calculations by applying a correction factor to the estimated environmental concentrations (EEC) values computed using the standard T-REX model for a single 1-lb/A application.

Figure N-1. Identification of Taxa Exceeding Endangered Species Levels of Concern


Exposure Estimate:
Worst Case
Estimated Environmental Concentration (EEC) Using Standard EPA Models Or Analysis Methods
Toxicity Endpoint (TE):
Lowest Acute Or Chronic Value Meeting EPA Quality Standards
Determine Risk Quotient (RQ = EEC/TE)
For Each Taxon
RQ > Level Of Concern (LOC)?
Yes
No
Refine EEC based on experimental data
No Direct Effect Expected on the Taxa[a]
RQ > Level Of Concern (LOC)?
No
Yes
Further Analysis
No Direct Effect Expected on the Taxa[a]

[a] The basis for this conclusion is described in U.S. EPA, 2004. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency, Endangered and Threatened Species Effects Determinations

Risk quotients for chronic exposure to mammals calculated using upper bound residues slightly exceed the LOC for small and medium-sized mammals consuming short grass; however, utilizing mean residue values as a further refinement, risk quotients are all below the LOC (Table N-3) leading to a conclusion of no effect on the species. This is consistent with the finding in the EFED Science Chapter for dicamba (U.S. EPA, 2005) and the revised RED (U.S. EPA, 2006) for a single application rate of 1.0 lb a.e./A. Because there will be at most only three applications per year and dicamba dissipates rapidly, an individual small or medium-sized mammal will not chronically consume foliage containing maximum residue levels from dicamba-treated fields. Therefore,

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reliance on dicamba-specific Day 0 mean residue values is also a conservative dietary exposure estimate for chronic exposure that is expressly countenanced by EPA.[92]

Table N-3. Risk Quotients for Chronic Exposure a for Mammalian Species Based on Dicamba-Specific Residue Values and DT_{50}.

Diet	Mammal Size (g)	Risk Quotient using Upper Bound Residues[a,b]	Risk Quotient using Mean Residues
Short Grass	15	**1.26**	0.75
	35	**1.08**	0.64
	1000	0.58	0.34
Tall Grass	15	0.58	0.32
	35	0.49	0.27
	1000	0.27	0.15
Broadleaf Foliage / Small Insects	15	1.00	0.75
	35	0.86	0.64
	1000	0.46	0.34
Fruits/Pods/Seeds/Large Insects	15	0.14	0.07
	35	0.12	0.06
	1000	0.07	0.03
Grain	15	0.032	0.015
	35	0.027	0.013
	1000	0.015	0.007

[a] Dicamba-specific refined residue values based on a 1 lb a.e./A application rate were 131, 60.0, 103.9, and 15.0 mg a.e./kg diet, respectively, for upper bound values for short grass; tall grass; broadleaf foliage / small insects; and fruits/ pods/ seeds/ large insects, and 77.9, 33.0, 77.7, and 7.0 mg a.e./kg, respectively, for mean residues. The dicamba-specific residue decline half-life (DT_{50}) of 5.63 days instead of the EPA default value of 35 days was also used in determining the peak residue value resulting from the three sequential applications.

[b] Numbers with Bold font indicate the RQ exceeds the LOC (1.0).

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With respect to birds, analyses were performed using measured dicamba residue values (Table N-2) for RQ calculations for acute exposure. The following could be excluded from concern (and, therefore, no effects would be expected to occur): birds of all sizes consuming only grain or fruits/pods/seeds/large insects, and large birds consuming broadleaf foliage/small insects or tall grass. Small and medium-sized birds consuming broadleaf foliage/small insects or grasses and large birds consuming short grass required further analysis. RQ values are presented in Table N-4. Because birds are the surrogate species for terrestrial phase amphibians and reptiles, further analysis was also conducted to ensure that amphibians and reptiles could be excluded from concern for adverse effect.

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[92] Overview Document (USEPA, 2004)

Table N-4. Risk Quotients for Acute Exposure to Birds Using Measured Dicamba Residue and Residue Decline Values

Diet	Acute RQs: (Dose-based EEC/adjusted LD50)[a]		
	Upper Bound Residues		
	20 g Small	100 g Medium	1000 g Large
Short grass	**0.79**	**0.35**	**0.11**
Tall grass	**0.36**	**0.16**	0.05
Broadleaf plants/small insects	**0.63**	**0.28**	0.09
Fruits/pods/seeds/large insects	0.09	0.04	0.01
Granivore	0.02	0.01	0.003

[a] Bold numbers indicate the RQ exceeds the LOC (0.1).

N.2.3. Refined Analysis Considering Species County-Level Locations

Certain sizes of threatened and endangered birds, amphibians, reptiles, and mammals had risk quotients exceeding the LOC as a result of the use of dicamba on dicamba-tolerant soybean based on a default exposure analysis or an analysis using refined residues. Consistent with guidance set forth in the EPA Overview Document, a more detailed evaluation of the locations of these threatened and endangered species relative to potential areas of soybean production was undertaken.

First, the co occurrence of threatened and endangered species of these remaining taxa[93]and the production of soybeans was determined at the county level. Listing status[94],, species habitat and proximity data to soybean production at the county level were evaluated for these identified species to determine which species in which counties can be excluded from further evaluation and which require further evaluation. This process is referred to as the "county-level analysis" ([redacted] 2012) and is discussed in more detail in Section N.3 below.

Next, the Overview Document provides that – for those threatened and endangered species (avian, reptilian, amphibian (terrestrial-phase), and mammalian) that require further evaluation – each species be considered individually to determine whether it can

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[93] For completeness, all threatened and endangered avian, amphibian, reptilian, and mammalian species were included in the county-level analysis.

[94] Listing status refers to whether the species is classified as threatened, endangered, no longer considered threatened or endangered (delisted), etc.

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be excluded from concern for potential effects based on body weight or dietary considerations. Accordingly, for these animal species, refined risk quotient calculations were performed considering individual species body weight, food type and food intake rate, as described in Section N.4 and in [redacted] (2012), and consistent with EPA guidance found in the Overview Document (U.S. EPA, 2004). Based on these refined county-level analyses, as discussed below, animal species were excluded from concern, and, therefore, would not be affected by dicamba use on DT-soybean.

N.3. County-level Analysis: Co-occurrence of Listed Species in Crop Production Areas

The procedures used in the county-level analysis to identify counties containing threatened or endangered species that require further evaluation are depicted as a flow chart in Figure N-2 and are described in detail in [redacted] (2012).[95]. The U.S. counties where soybean production was reported were identified using available data from the U.S. Census of Agriculture. Census data from 1997, 2002 and 2007 were utilized to identify these counties. This information was supplemented with soybean production data available from the California Department of Pesticide Regulation. Counties without soybean production, but adjacent to counties with soybean production were also identified. In total, there were 2,728 counties considered in this analysis (2,198 soybean counties, 530 adjacent counties). The counties considered at the beginning of county-level analysis are shown graphically in Figure N-3.

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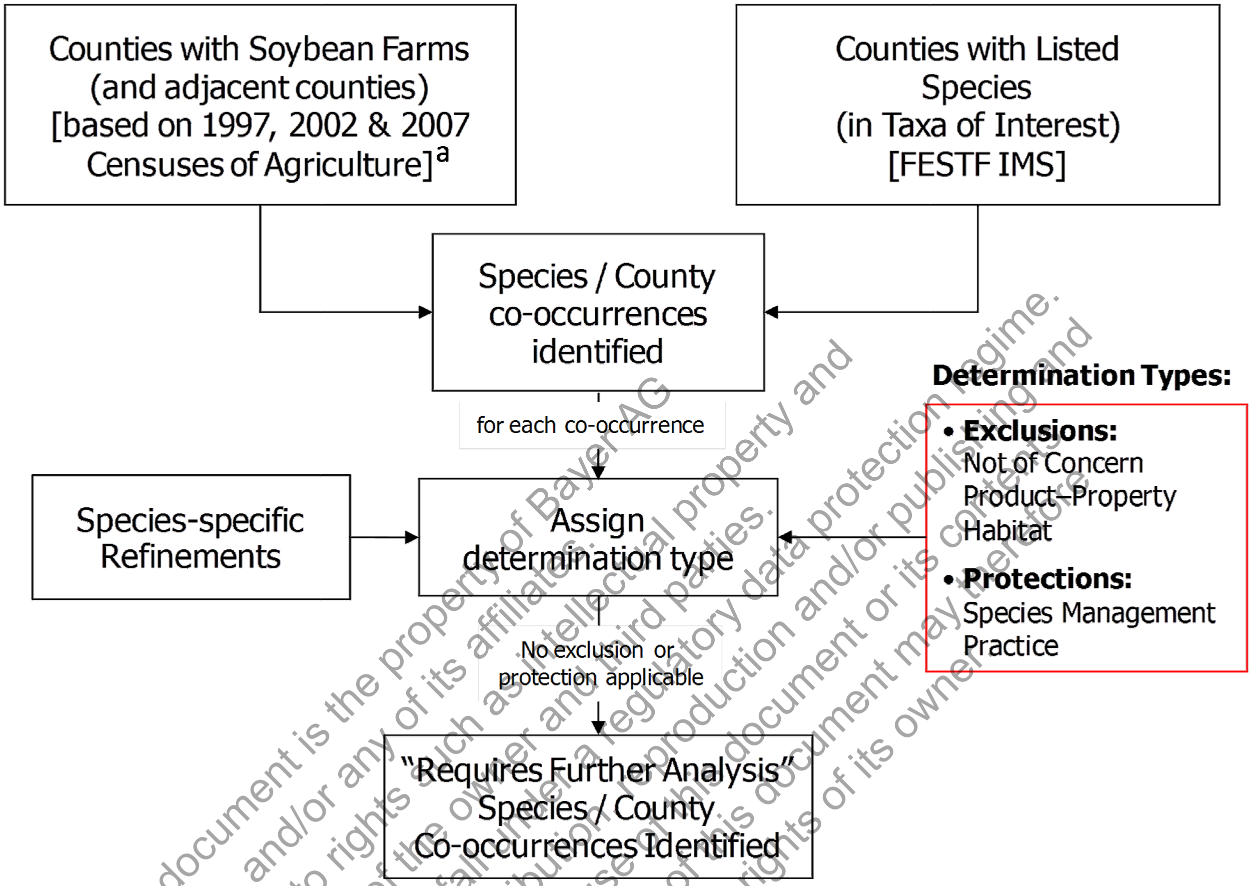
[95] Overview Document (US EPA, 2004)

Figure N-2. County-Level Analysis Process


Counties with Soybean Farms (and adjacent counties) [based on 1997, 2002 & 2007 Censuses of Agriculture]a
Counties with Listed Species (in Taxa of Interest) [FESTF IMS]
Species / County co-occurrences identified
for each co-occurrence
Species-specific Refinements
Assign determination type
Determination Types:
• Exclusions:
Not of Concern
Product–Property
Habitat
• Protections:
Species Management Practice
No exclusion or protection applicable
"Requires Further Analysis" Species / County Co-occurrences Identified

[a] Information from the California Pesticide Use Reporting database was also used to identify counties with herbicide applications to soybean fields in California.

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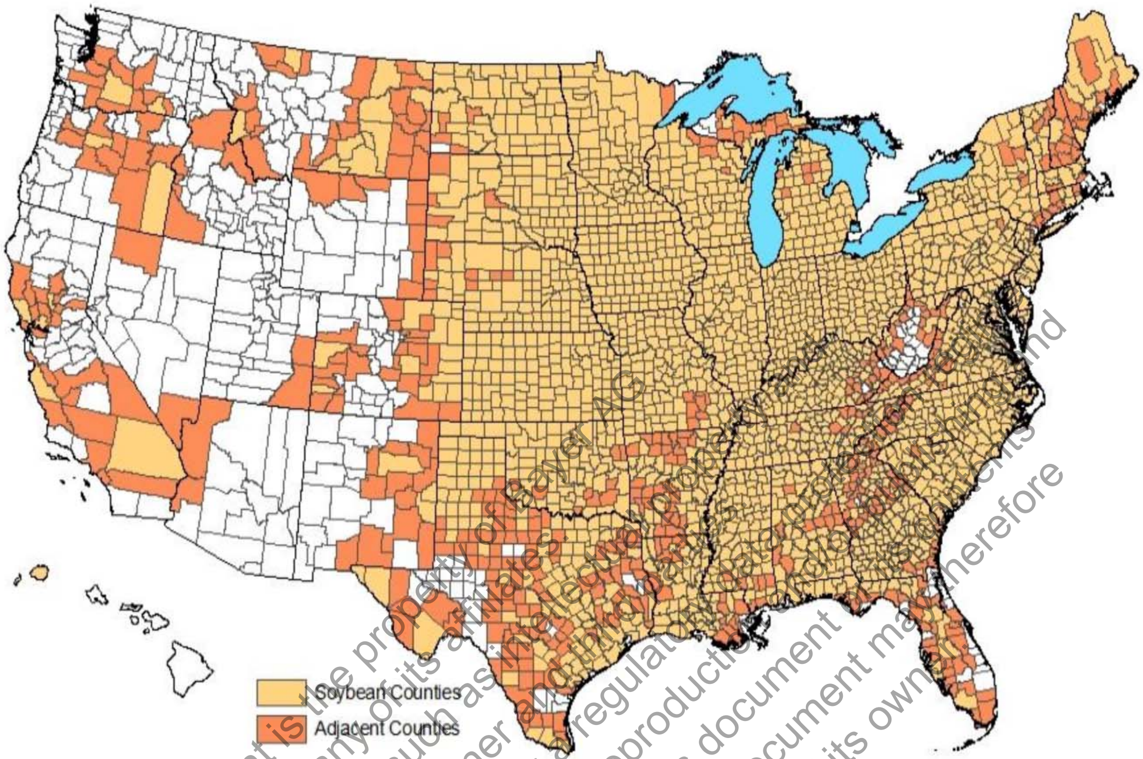
Figure N-3. Counties with Soybean Farms and Adjacent Counties



In the identified counties, available county-level presence information for threatened or endangered avian, reptilian, amphibian, and mammalian species was evaluated, using county-level location information compiled by the FIFRA Endangered Species Task Force (FESTF) in the FESTF Information Management System (IMS).[96] Of the 2,728 counties initially considered, there were 2505 counties with listed species in the taxa of concern and where soybeans are produced (including counties adjacent to counties where soybeans are produced). These counties are depicted graphically in Figure N-4 and contain 140 distinct species in 49 states (all states except Alaska) and the District of Columbia. There were 7,048 species/county co-occurrence records considered across all animal taxa evaluated. In these counties, each species was evaluated with respect to the current listing status, county-level locations, species biology, and species habitat requirements, in order to determine whether exposure to dicamba from use on DT-soybean could potentially result in adverse effects to the species. Some listed species could be removed from concern for adverse effects based on exclusions that currently

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[96] The FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) Endangered Species Task Force (FESTF) Information Management System 2.7 (IMS) (referred to as the "FESTF IMS") was developed in order to meet the legal obligations of its member companies to submit data required by EPA/OPP under FIFRA (as described in Pesticide Registration Notice 2000-2) in support of the members' registration and re-registration actions. The purpose of the IMS is to meet the data requirements in a manner that significantly improves the consistency, quality, availability and use of existing information on threatened and endangered species and pesticide use. http://www.festf.org/visitors/default.asp

exist and are documented. Exclusions that have been employed include change in species listing status, not present due to extirpation[97], habitat not in proximity to agriculture, product properties[98], and species not in proximity to agriculture for other reasons.

For animal species that have been identified in the county-level analysis as requiring further analysis, species-specific refinements as described in Section N.4 have been considered. T-HERPS was utilized to calculate risk quotients for amphibians of similar body weight as the California red-legged frog. Diet information was utilized for individual species of birds, reptiles, and mammals to determine if actual diet considerations can justify removing a species from concern.

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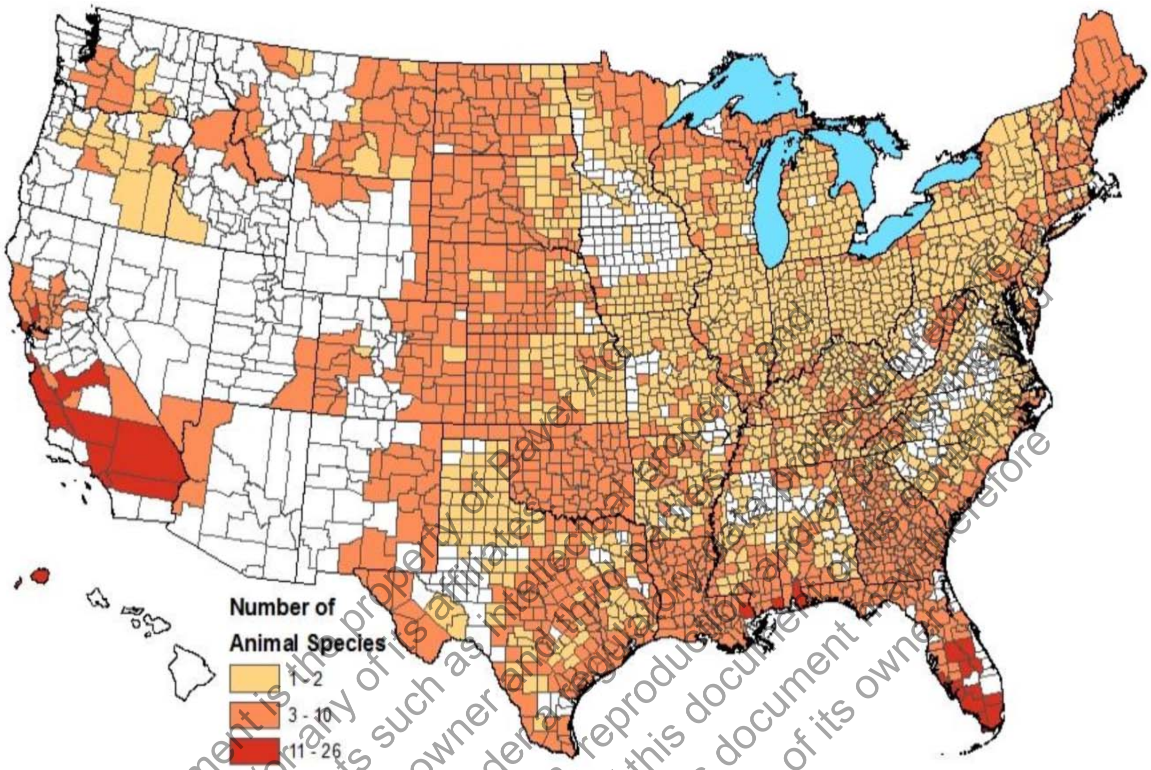
[97] An extirpated species is defined as “a species no longer surviving in regions that were once part of its range” (http://www.fws.gov/midwest/endangered/glossary/index.html).

[98] A product properties exclusion is based on a quantitative analysis of dicamba properties beyond the screening level analysis in the EFED Science Chapter. Specifically, this analysis involves assessing use of measured foliar residues and foliar decline rates following dicamba applications, adjusted to reflect the use pattern for DT-soybeans. The size and diet of the animal species are also considered. (See Sections 2 and 4)

Figure N-4. Counties with Soybean Farms (or Adjacent Counties) with Listed Species in the Taxa of Interest



N.4. Species-specific Risk Quotient Calculations

Consistent with EPA's Overview Document, species-specific dietary exposure was assessed considering animal body weight and diet ([redacted] 2012) for birds and mammals of certain sizes because risk quotients exceeded the level of concern after the initial refinements described above. A similar assessment was conducted for amphibians and reptiles because birds serve as the surrogate for terrestrial phase amphibians and reptiles. Biological information was gathered from a number of sources, including U.S. Fish and Wildlife Service (USFWS) species recovery plans, primary literature, and other technical sources (e.g., NatureServe[99])

Mammals

For mammals, 38 species were examined for the potential for chronic adverse effects based on biological characteristics (i.e., dietary preferences and body size). The analysis progressed in a step-wise fashion:

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[99] NatureServe is a non-profit conservation organization that collects detailed local information on plants, animals, and ecosystems. NatureServe has a public website available at http://www.natureserve.org.

1) From the baseline analysis, assuming the maximum-use pattern (as described Section N.2.1.) and using the upper bound dicamba-specific foliar residue and foliar half-life values, the LOC for wild mammals was exceeded only for chronic exposures to small and medium sized mammals consuming short grasses (Section N.2, Table N-3).

2) Using species-specific information, 27 species were given product property exclusions based on size (e.g. >1kg, large-sized mammals) and/or diet (e.g. carnivorous, frugivorous, etc.).

3) The remaining 11 mammals, small and medium-sized species that consume grasses, were examined using the U.S. EPA T-REX model with species-specific weights used for the model input parameters. The predicted EECs were determined based on the upper bound dicamba- specific foliar residue and half-life values, as described in Section N.2.2.

4) For 4 of these 11 species, RQs were below the LOC considering upper bound dicamba-specific residues and species-specific body weights. For another 3 of the 11 species, examination of the diet indicated that seeds were the primary constituent of the diet with grasses or other items being a very small component, and with this consideration RQs were below the LOC. For the remaining 4 species, considering the rapid rate of dicamba foliar residue dissipation, chronic RQ's calculated with upper bound residues exceed the RQ for such a short exposure duration (*i.e.*, < 1 day to < 4 days) that it should not be considered a chronic exposure.

Furthermore, all mammalian species can be excluded from further consideration based on chronic RQ's being below the LOC when RQs are calculated with initial mean residues. As indicated earlier, initial mean residues are considered more appropriate for assessing chronic risk. Thus, for these 38 species of mammals, chronic exposure to dicamba from application to DT-soybean can be excluded from concern and, therefore, would not affect these species.

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Birds

For birds, of the 43 species evaluated in this refined analysis:

1) Using species-specific information, 24 species were excluded from the need for further consideration because their refined T-REX acute RQs were less than the LOC based on characteristics of diet and body weight considering dicamba-specific residues.

2) The 19 remaining species were excluded from the need for further consideration because the upper bound EECs calculated for these species were lower than dose-based No Observed Effect Levels (NOELs) calculated from acute dietary exposure studies.

The potential for acute adverse effects as determined in the analysis in Table N-4 is based on an oral gavage, a route of administration that can overestimate the expected exposure compared to more environmentally relevant methods with a slower rate of delivery (e.g., dietary exposure). Therefore, the use of the acute oral gavage toxicity test to predict the potential for adverse effects to birds from dicamba use on DT-soybean should be considered a screening-level approach that is expected to overestimate the actual potential for effects. A more appropriate method to determine the acute risk to birds from consuming prey or food items containing dicamba residues is to estimate the dose-based effect levels from dietary toxicity studies (Durda and Preziosi, 2000). This approach is consistent with the EPA Overview Document (U.S .EPA, 2004) which indicates that for avian risk assessments, dietary residues are compared with dietary toxicity endpoints based on dietary concentrations (e.g. LC$_{50}$s for acute effects)[100]. This method was used for the 19 remaining species described above, with the conservative assumption that the avian species under evaluation are passerine species (highest metabolic/ingestion rates; U.S. EPA, 1993), and the toxicity endpoint selected from the dietary studies was the NOEL value rather than a LD50 value. Even with the high ingestion rate relative to body weight, these birds cannot ingest enough food to achieve doses that would exceed the NOEL (highest dose tested). Also, it is likely that the birds will not be in soybean fields actively foraging, but rather foraging in the adjacent habitats (e.g., tree canopy) outside of the fields. Threatened and endangered species are "strongly associated" with their specific habitat type and, therefore, it is improbable that 100% of the bird's diet will consist of dietary items exposed in the field. Thus, for these 43 species of birds, acute exposure to dicamba from application to DT-soybean can be excluded from concern and, therefore, would not affect these species.

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Amphibians and Reptiles

For amphibians and reptiles, a total of 25 species (10 amphibians and 15 reptiles) were evaluated. The allometric equations used in the T-REX model assume that the ingestion rates for amphibians and reptiles are equal to those of birds, when in fact they are lower. Thus, the dose-based estimates of exposure calculated by T-REX are an over-estimation of exposure for amphibians and reptiles. Therefore, the risk evaluation for amphibians and reptiles for dicamba from dietary exposure was refined using the U.S. EPA T-HERPS model Version 1.0. Following U.S. EPA guidance, the T-HERPS model is to be used only after the RQs exceed the LOC for endangered species using the standard T-REX model (U.S. EPA, 2008b). T-HERPS is currently approved for use for terrestrial-phase amphibian and reptile species with diets similar to the federally threatened California red-legged frog, since the exposure values are considered more representative of potential exposure to herpetofaunal species.

The T-HERPS model was used to generate upper bound EECs resulting from the maximum application scenario using refined residue and half-life data (Section N.2). The avian acute and chronic toxicity data was used as a surrogate for the amphibian and reptilian species. A default scaling factor of 1.0 was used in the model calculations, as the relationship between body weight and toxicity has not been examined for amphibian and reptile species (U.S. EPA, 2008b). Given the limited availability of morphometric data for many species, similar species were analyzed collectively as a group (e.g., frogs and toads) using the weight data from a single representative species as a proxy for all species within the group. The exposure analysis only considered dicamba residues within prey items typical for each species group and animal size. With these considerations, the T-HERPS model was used to calculate RQs for frogs, toads, salamanders, lizards and skinks. For these species, the acute, subacute, and chronic RQ values based on refined residue and half-life values do not exceed the LOC for endangered species. Thus, for frogs, toads, salamanders, lizards, and skinks, exposure resulting from the dicamba maximum use pattern can be excluded from concern and, therefore, would not affect these species.

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[100] Overview Document (U.S. EPA, 2004) p. 40.

For snakes, turtles and tortoises, a species-specific exposure analysis was conducted using allometric equations for each specific dietary component (U.S. EPA, 1993). Exposure estimates based on refined dicamba-specific residue data and residue decline data were compared to acute and chronic avian toxicity values, and the calculated risk quotients were all determined to be below the level of concern, indicating that these species can be excluded from concern and, therefore, would not be affected.

After considering species-specific body sizes and dietary components, all the amphibian and reptilian species evaluated were determined to have risk quotients below the level of concern resulting in the conclusion that dicamba use on DT-soybean will not affect these species.

N.5. Indirect effects on Threatened and Endangered Species of Other Taxa resulting from Direct Effects on Plant Species

To assess the potential for indirect effects on threatened and endangered species, the U.S. EPA evaluates the risk of direct effects on non-endangered species from relevant taxonomic groups to make inferences concerning the potential for indirect effects upon threatened or endangered species that rely on non-endangered species in that category for critical resources (U.S. EPA, 2004). The RQ values used to assess the potential for indirect effects from dicamba applications to DT-soybean indicate that indirect effects to other taxa resulting from effects on monocot plant species from application of dicamba at rates up to 1.0 lb a.e./A would not occur. Further, indirect effects to other taxa as a result of effects on dicot plant species from a combination of sheet runoff and spray drift to soil would also not occur ([redacted] 2011). In addition, utilizing a refined exposure assessment, indirect effects to other taxa resulting from effects on dicot plant species exposed via a combination of channelized runoff and spray drift to soil would not occur ([redacted] 2011). When RQ values are calculated for all six of the dicot species tested in the vegetative vigor study, RQs exceed the LOC for only two of the six species indicating that habitat and food sources from dicot plants will be present adjacent to areas treated with dicamba ([redacted] 2011). Furthermore, field studies demonstrate that even very sensitive plants at the edge of a field sprayed with dicamba are not affected to the extent that impacts on habitat would result. Additionally, effects from drift can be further minimized through the use of best management practices such as drift reducing technologies (e.g., low drift spray nozzles, boom height, deposition aides). Considering

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these factors, indirect effects on threatened and endangered animals resulting from spray drift onto nontarget plants can be excluded from concern.

N.6. Conclusions

In the EFED ecological risk assessment conducted for dicamba reregistration (U.S. EPA, 2005), using a screening level assessment, EPA scientists concluded that a “no effect” determination can be made for all dicamba uses for listed fish, aquatic invertebrates, and vascular aquatic plant species. The potential for adverse effects to listed birds and mammals, non-vascular aquatic plants and terrestrial and semi-aquatic plants could not be excluded based on the EPA screening level assessment, the initial phase of analysis. However, since there are currently no listed nonvascular aquatic plants, this taxon does not require further investigation at this time. Recognizing that screening level analysis is only the first step in evaluating impacts on threatened and endangered species, the EFED Science Chapter (U.S. EPA, 2005) indicates that “additional information on the biology of listed species, the locations of these species, and the locations of the use sites … could be considered along with available information on the fate and transport properties of the pesticide to determine the extent to which screening assumptions regarding an action area apply to a particular listed organism.”

This report summarizes the conclusions of three other reports ([redacted] 2011; [redacted] [redacted] 2012, and [redacted] 2012) that utilize some of the refinements described by EPA in the previous paragraph to evaluate the potential for adverse effects to listed birds and mammals as well as amphibians, reptiles, and terrestrial invertebrates. When the properties of dicamba and species-specific information are taken into account, these reports demonstrate that listed birds, mammals, amphibians, reptiles and terrestrial invertebrates would not be affected by dicamba use in DT-soybean. In addition, based on non-target plant studies conducted as a requirement of dicamba reregistration, monocotyledonous terrestrial and semi-aquatic plants outside the treated area also would not be affected ([redacted] 2011).

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March 28, 2012

[redacted]
Director, Environmental Risk Analysis Programs
USDA-APHIS/Biotechnology Regulatory Services
4700 River Road, Unit 146
Riverdale, MD 20737

RE: Submission of revised petition and waiver of Confidential Business Information (CBI) Claim for Petition 10-188-01p for the Determination of Deregulated Status of Dicamba-Tolerant Soybean MON 87708

Dear [redacted]

In preparation for the posting of the #10-188-01p petition for public comment, Monsanto has made minor modifications to the March 1, 2012 petition. These changes are outlined below and do not substantively alter the content of the petition dated March 1, 2012.

- Removed sentences that refer to supplemental submissions which will be made in support of APHIS' NEPA analysis, and are not necessary to deem the plant pest petition complete under 7 CFR 340.6(b) and (c). These changes were made on pages 207, 209, 218, 546, 557 and 696 of the enclosed petition dated March 26, 2012.
- Modifications to address grammatical errors or correct minor inconsistencies. These changes were made on pages 208, 217 and 643 of the enclosed petition dated March 26, 2012.

Monsanto does not object to APHIS publishing for public comment the attached un-redacted version of Monsanto's petition for the determination of non-regulated status for MON 87708. As we explained in our letter and supporting analysis provided to APHIS on March 1, 2012, Monsanto's Confidential Business Information (CBI) claim for certain information in our draft petition extends until such time as: 1) APHIS determines the petition to be "complete"; and 2) APHIS makes the final petition available for public comment. Therefore, we hereby waive all prior CBI claims related to this petition upon APHIS' publication of the same for public comment.

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Monsanto is providing two printed copies and an electronic pdf version of the revised #10-188-01p petition dated March 26, 2012. The enclosed petition is intended to replace, in its entirety, the previous petition dated March 1, 2012.

Should you have any questions concerning this letter or the revised petition, or wish to set up a meeting for further discussion, please contact [redacted] U.S. Agency Regulatory Affairs Lead, Washington DC, at [redacted] or myself at [redacted] or at [redacted].

Sincerely,
[redacted]
Regulatory Affairs Manager

cc: [redacted] USDA
[redacted] USDA
[redacted] Monsanto
Regulatory files/10-SY-210U

Enclosure/ Attachment
- Revised Petition #10-188-01p dated 3/26/2012
- CBI Justification

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