January 2020

Safety Assessment of Dicamba and Glufosinate-Tolerant Cotton MON 88701

Monsanto Company has developed dicamba and glufosinate-tolerant cotton, MON 88701, which will allow over-the-top applications of dicamba herbicide for the control of broadleaf weeds from preemergence to seven days preharvest and glufosinate herbicide for broad spectrum weed control from emergence through early bloom growth stage. MON 88701 provides a wider dicamba window of application beyond the current preplant cotton uses and glufosinate application rates and timings that are equivalent to current commercial glufosinate-tolerant cotton. The combination of these two unique herbicide modes-of-action provides an effective weed management system for cotton production. Dicamba provides effective control of over 95 annual and biennial weed species, and suppression of over 100 perennial broadleaf and woody plant species. Glufosinate, a broad-spectrum contact herbicide, provides nonselective control of approximately 120 broadleaf and grass weeds. Additionally, dicamba and glufosinate provide control of herbicide-resistant weeds, including glyphosate-resistant biotypes of Palmer amaranth (*Amaranthus palmeri*), marestail (*Conyza canadensis*), common ragweed (*Ambrosia artemisiifolia*), giant ragweed (*Ambrosia trifida*) and waterhemp (*Amaranthus tuberculatus*). MON 88701 contains a demethylase gene from *Stenotrophomonas maltophilia* that expresses a dicamba mono-oxygenase (DMO) protein to confer tolerance to dicamba herbicide. DMO protein rapidly demethylates dicamba to the herbicidally inactive metabolite 3,6-dichlorosalicylic acid (DCSA). DCSA has been previously identified as a metabolite of dicamba in cotton, soybean, livestock, and soil. Furthermore, the use of dicamba on MON 88701 does not promote any new environmental exposure scenarios not previously evaluated and deemed acceptable by U.S. EPA

MON 88701 also contains a bialaphos resistance (bar) gene from *Streptomyces hygroscopicus* that expresses the phosphinothricin N-acetyltransferase (PAT) protein to confer tolerance to glufosinate herbicide. PAT (bar)1 protein acetylates the free amino group of glufosinate to produce non-herbicidal N-acetyl glufosinate, a well-known metabolite in glufosinate-tolerant plants. The use pattern and rate of glufosinate on MON 88701 will follow the existing glufosinate-tolerant cotton uses outlined on the glufosinate herbicide label. The glufosinate residues in MON 88701 treated with commercial glufosinate rates are below the established pesticide residue tolerances for both cottonseed and gin by-products. Therefore, Monsanto will not seek any changes in the glufosinate label or the established tolerances for its use on MON 88701 cotton. MON 88701 will be combined, through traditional breeding methods, with other deregulated herbicide-tolerant (e.g., glyphosate-tolerant) events. The in-crop use of dicamba and glufosinate herbicides, in addition to glyphosate herbicide, provides improved weed management options in cotton to control a broad spectrum of grass and broadleaf weed species and effective control of weeds resistant to several herbicide families. Successful integration of MON 88701 into glyphosate-tolerant cotton systems will provide: 1) an opportunity for an efficient, effective weed management system for hard-to-control and herbicide-resistant weeds; 2) a flexible system for two additional herbicide modes-of-action for in-crop application in current cotton production systems as recommended by weed science experts to manage future weed resistance development; 3) an option to delay or prevent further resistance to glyphosate and other critically important cotton herbicides; in particular, herbicides in the acetolactate synthase inhibitor (ALS) and protoporphyrinogen oxidase inhibitor (PPO) class of chemistry; 4) crop tolerance to dicamba, glufosinate, and glyphosate; and 5) additional weed management tools to enhance weed management systems necessary to maintain yield and quality to meet the growing needs of the food, feed, and industrial markets.

MON 88701 was intensively tested in the laboratory and across multiple field sites in the USA. Data from those studies were used to conduct the product safety assessment and achieve government regulatory approvals. The product safety was based on the following:

- A detailed molecular characterization of the inserted DNA demonstrated a single, intact copy of the T-DNA insert in a single locus within the cotton genome.
- Extensive evaluation of the introduced proteins expressed in MON 88701, dicamba monooxygenase (MON 88701 DMO) and phosphinothricin acetyltransferase [PAT (bar)], confirmed they are unlikely to be toxins or allergens. In addition, PAT proteins are in several other commercially-available crops that have been reviewed and previously deregulated by USDA, including those in cotton, corn, soy, canola, sugarbeet, and rice.
- A compositional assessment of cottonseed confirmed that MON 88701 is compositionally equivalent to commercially cultivated cotton.
- An extensive evaluation of phenotypic, agronomic, and plant mapping characteristics, as well as environmental interactions of MON 88701, demonstrated no increased plant pest potential compared to commercially cultivated cotton.
- An assessment of potential impact on non-target organisms (NTOs) indicated that, under anticipated agricultural conditions, MON 88701 is unlikely to have adverse effects on these organisms compared to commercially cultivated cotton.
- Evaluation of MON 88701 using current agronomic management practices for cotton concluded that deregulation of MON 88701 is not likely to impact cotton agronomic practices or land use, with the exception of the expanded window of dicamba application.

These studies establish the food, feed and environmental safety of MON 88701 cotton by demonstrating the safety to humans and animals, establishing equivalent nutritional composition and wholesomeness compared to conventional cotton varieties, and confirming that the potential impact on the environment is no different than conventional cotton varieties.