Safety Assessment of Bollgard II® Cotton Event 15985

Executive Summary

Bollgard II cotton event 15985 was developed by Monsanto Company to produce the Cry2Ab2 insect control protein, which provides effective season-long control of key lepidopteran insect pests. This product was produced by re-transformation of Bollgard® cotton event 531, which produces the CrylAc insect-control protein and the NPTII selectable marker protein. Therefore, Bollgard II cotton produces two proteins for effective control of the major lepidopteran insect pests of cotton, including the cotton bollworm, tobacco budworm, pink bollworm, and armywonn. Bollgard II cotton also produces the P-D-glucuronidase (GUS) marker protein. In addition, Bollgard II cotton provides a more effective insect resistance management program compared to single gene products.

Bollgard cotton has been grown globally on more than 32 million acres since commercial introduction in 1996 (James, 2002). The primary benefits that have resulted from the use of Bollgard cotton are reduced insecticide use, improved control of target insect pests, improved yield, reduced production costs, and improved profitability for cotton growers (Edge *et al.*, 2001; Carpenter and Gianessi, 2001; Betz *et al.*, 2000; Economic Research Service/USDA, 2000; Falck-Zepeda *et al.*, 1998; Falck-Zepeda *et al.*, 2000; Fernandez-Cornjeo and McBride, 2000; Klotz-Ingram *et al.*, 1999; Traxler and Falck-Zepeda, 1999; Xia *et al.*, 1999). With the addition of a second insect protection protein, Bollgard II cotton provides increased control of cotton bollworm, as well as certain secondary insect pests of cotton, including annyworm (U.S. EPA, 2002). Furthermore, along with the other components of Monsanto's insect resistance management program, combining the Cry2Ab2 and CrylAc proteins in a single product provides an additional tool to delay the development of insect resistance to Cry proteins in cotton.

The Cry2Ab2 protein produced in Bollgard II cotton event 15985 is derived from the naturally occurring soil bacterium *Bacillus thuringiensis* ***(B. t.).*** Microbial formulations of *Bacillus thuringiensis*, which include the Cry2A class of proteins, have been registered in numerous countries worldwide and have been safely used for control of lepidopteran insect pests for more than 40 years (Luthy *et aL,* 1982; Baum *et aL,* 1999; IPCS, 1999; Betz *et aL,* 2000). *B. t.* microbial formulations have been shown to be specific to the target insect pests and do not have deleterious effects to non-target organisms such as beneficial insects, birds, fish, and mammals, including humans (U.S. EPA, 1988; U.S. EPA, 1998). Therefore, there is a history of safe dietary and occupational exposure to Cry proteins derived from *B. t.*, including those of the Cry2A class.

The GUS protein present in Bollgard II cotton was used as a marker to facilitate the selection of Cry2Ab2-producing plants. The GUS protein served no other purpose and has

no known insect control properties. The history of safe use of the GUS protein is extensive. Human exposure to the GUS protein is commonplace through intestinal epithelial cells and intestinal microflora, bacterial exposure, and numerous foods containing the GUS protein with no known harmful effects (Gilissen *et al.*, 1998).

The Cry2Ab2 and GUS proteins in Bollgard II cotton event 15985 are present at very low levels in cottonseed and are expected to be absent or inactivated in highly processed cotton food and feed products. The safety of the introduced proteins has been assessed through the confirmation of a history of safe food and feed use of the proteins or highly similar proteins, the determination of no significant allergenic potential of the introduced proteins, and the determination of no significant toxic potential of the introduced proteins. Furthermore, there will be no significant consumption of these proteins in foods derived from Bollgard II cotton due to the extensive processing and refinement of cottonseed oil and cotton-derived food products.

An assessment of the nutritional and compositional equivalence of Bollgard II cotton to conventional cotton varieties was performed on 48 components of cottonseed, oil, and meal. These analyses included protein, fat, moisture, calories, minerals, amino acids, cyclopropenoid fatty acid, and gossypol levels. Results of these extensive compositional analyses demonstrated that the levels of the important nutritional and anti-nutritional components in Bollgard II cotton event 15985 are comparable to the parental variety and are within established ranges for commercial cotton varieties. It is concluded that Bollgard II cotton event 15985 is not materially different in composition, safety, or any relevant parameter from cotton now grown, marketed, and consumed.

The following summary provides information on the methods used to develop Bollgard II cotton event 15985 and a summary of the food, feed, and environmental safety studies performed. On the basis of these evaluations, Bollgard II cotton and its processed fractions were found to be substantially equivalent to conventionally bred cotton, taking into consideration the natural variation observed among cotton varieties, with the exception of the production of the CrylAc, Cry2Ab2, NPTII, and GUS proteins. Previous studies established the food, feed, and environmental safety of the CrylAc and NPTII proteins produced in Bollgard cotton, and more recent studies have confirmed that the Cry2Ab2 and GUS proteins produced in Bollgard II cotton are also safe for human and animal consumption and to the environment.

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