

# Safety Assessment of Roundup Ready® Flex Cotton, MON 88913

## Executive Summary

Since the commercialization of the first cotton varieties with biotechnology-derived traits in the mid-1990s, one of the most successful products, in terms of farmer adoption, has been Roundup Ready® cotton. This product, MON 1445, is tolerant to glyphosate, the active ingredient in the Roundup® family of agricultural herbicides. Roundup Ready cotton has been rapidly adopted by U.S. cotton farmers (95% grower satisfaction<sup>1</sup>) and has been a significant part of U.S. annual cotton production since its market introduction. Cotton with the Roundup Ready trait is currently cultivated on approximately 59% of the U.S. cotton acres (USDA-NASS, 2003). However, a constraint within that Roundup Ready cotton system was the limitation of in-crop, over-the-top herbicide application to cotton plants after the four true leaf stage. Applications at the fifth true leaf stage and beyond required specialized spray equipment to apply the herbicide between the rows and away from the cotton plant.

Monsanto Company has developed a second-generation glyphosate-tolerant cotton product, Roundup Ready Flex cotton, MON 88913 (OECD Unique Identifier MON-88913-8), that provides increased tolerance to glyphosate during the critical reproductive phases of growth compared to the first generation Roundup Ready cotton product. Use of MON 88913 enables the application of a Roundup agricultural herbicide over the top of the cotton crop at later stages of development than is possible with MON 1445. This allows for effective weed control during crop production, because Roundup agricultural herbicides are highly effective against the majority of annual and perennial weeds that can be problematic during the later stages of crop development, with minimal risk of crop injury.

The data and information presented in this summary demonstrate that MON 88913, and the feeds and foods derived from it, are as safe and nutritious as commercial conventional varieties of cotton and the comparable feeds and foods derived from these varieties. This is based on three categories of analysis. The first is a detailed molecular characterization of the inserted DNA and a detailed biochemical characterization of the CP4 EPSPS protein produced in MON 88913. The second is a direct assessment of the toxicity and allergenic potential of the CP4 EPSPS protein produced in MON 88913, and the potential for environmental interactions. The third is a safety and nutritional assessment that demonstrates MON 88913 is compositionally equivalent to commercial conventional cotton varieties.

MON 88913 produces the same CP4 EPSPS protein (5-enolpyruvylshikimate-3-phosphate synthase from *Agrobacterium sp.* strain CP4) that provides tolerance to the action of Roundup agricultural herbicides. The CP4 EPSPS protein produced in MON 88913 is derived from the common soil bacterium, *Agrobacterium*.

The amino acid sequence of the CP4 EPSPS protein produced in MON 88913 is identical to the CP4 EPSPS protein made in Roundup Ready cotton 1445. It is also identical to, or greater than 99% identical to the CP4 EPSPS proteins in other Roundup Ready crops, such as soybean, corn (NK603), and canola, which have nearly a decade of safe human and farm animal consumption. The CP4 EPSPS protein produced in MON 88913 is structurally homologous to EPSPSs naturally present in plants, including food crops (*e.g.*, soybean and corn), and in fungal and microbial food sources such as Baker's yeast (*Saccharomyces cerevisiae*), which have a history of safe use in human consumption (Padgett et al., 1996; Harrison et al., 1996). These data taken together demonstrate a long history of safe consumption by humans and farm animals of EPSPS proteins, including CP4 EPSPS protein, that occur in crops and microbially-based foods. Additionally, bioinformatic analyses, feeding studies, and acute toxicity studies demonstrate that CP4 EPSPS protein is unlikely to be an allergen or toxin. Only low levels of CP4 EPSPS protein are present in MON 88913 seed, representing less than 0.12% of the total protein on a dry weight basis, and there is no significant human consumption of cottonseed protein. The only significant sources of food from cotton are oil and linters, neither of which contains significant levels of protein.

An assessment of the nutritional and compositional equivalence of MON 88913 to a negative segregant control and to 16 commercial conventional cotton varieties was performed on 53 components of cottonseed, 41 components of cottonseed meal, and 13 components of refined, bleached cottonseed oil. These analyses included an assessment of protein, ash, moisture, total fat, carbohydrates, calories, minerals, fiber, amino acids, fatty acids, cyclopropanoid fatty acids, and gossypol levels. Results of these extensive compositional analyses demonstrated that the levels of important nutrients, anti-nutrients, and natural toxicants in MON 88913 were comparable to the control, and not outside the expected values for conventional cotton varieties or published ranges for conventional cotton varieties. Based on these data, and the principle of substantial equivalence as articulated by the World Health Organization, Organization for Economic Cooperation and Development as well as the United Nations Food and Agriculture Organization, MON 88913 cottonseed and its processed products are as safe and nutritious as conventional cotton varieties and their processed food and feed products on the market today.

Independent product safety reviews were conducted for Roundup Ready Flex cotton, MON 88913, by governmental regulatory agencies responsible for the safety assessment of products of modern plant biotechnology. Several of these assessments are listed in Table 1. These assessments include environmental, food, and feed safety; the results of all assessments support the safety and nutritive value of Roundup Ready Flex cotton, MON 88913.

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