EXECUTIVE SUMMARY
to
Application to Food Standards Australia New Zealand for the Inclusion of Soybean MON 87751 in *Standard 1.5.2 - Food Derived from Gene Technology*

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EXECUTIVE SUMMARY

MON 87751 Product Description

Monsanto Company has developed insect-protected soybean MON 87751 that produces the CrylA.105 and Cry2Ab2 insecticidal (Cry) proteins. Cry1A.105 is a modified Cry1A protein derived from *Bacillus thuringiensis*. Cry2Ab2 is derived from *B. thuringiensis* subsp. *kurstaki*. The CrylA.105 and Cry2Ab2 proteins provide protection from feeding damage caused by targeted lepidopteran insect pests. Studies conducted with MON 87751 demonstrated efficacy against key soybean pests including *Crocidosema aporema* (bean shoot moth), *Rachiplusia nu* (sunflower looper) and *Spodoptera frugiperda* (fall armyworm). Cry1A.105 and Cry2Ab2 are also known to be active against lepidopteran soybean pests such as *Anticarsia gemmatalis* (velvetbean caterpillar), *Chrysodeixis includens* (soybean looper) and *Helicoverpa zea* (corn earworm). The season-long expression pattern of Cry1A.105 and Cry2Ab2 in MON 87751 is expected to control target insects that are heterozygous for resistance genes specific to one of the proteins and provide an effective tool in managing potential insect resistance, thus prolonging the durability of this product. MON 87751 is expected to provide benefits to growers similar to those obtained by use of other lepidopteran-protected crop varieties, including reduced use of broad spectrum insecticides, increased yield protection and increased worker safety.

MON 87751 will be combined, through traditional breeding methods, with other deregulated biotechnology-derived traits to provide additional protection against lepidopteran soybean pests as well as tolerance to multiple herbicides. These next generation combined-trait soybean products will offer the ability to maximize grower choice, improve production efficiency and increase pest control and weed control durability.

History of Use of the Host and Donor Organisms

MON 87751 produces the CrylA.105 and Cry2Ab2 insecticidal (Cry) proteins. Cry1A.105 is a modified Cry1A protein derived from *Bacillus thuringiensis*. Cry2Ab2 is derived from *B. thuringiensis* subsp. *kurstaki*. The CrylA.105 and Cry2Ab2 proteins provide protection from feeding damage caused by targeted lepidopteran insect pests.

MON 87751 is intended primarily for use as a broad-acre commodity (or field) soybean and not for vegetable, garden, or food-grade soybean that are generally used to produce tofu, soybean sprouts, soymilk, green soybean (*e.g.* edamame) or other similar food items. Vegetable and food-grade soybean generally have a different size, flavor, texture and other characteristics than field soybean and are more easily cooked. Other than the introduction of the insect protection trait, MON 87751 is not materially different from conventional field soybeans and can be processed into a wide variety of food products). Field soybean is a blended commodity that is highly processed before being consumed by humans. Thus, most food products derived from MON 87751 would likely be blended with those derived from other commercial soybean varieties before entering the human food supply.

Nature of the Genetic Modification

MON 87751 was produced by *Agrobacterium tumefaciens*–mediated transformation of soybean tissue using the transformation plasmid vector PV–GMIR13196. PV–GMIR13196 contains two separate T–DNAs that are each delineated by left and right border regions. The first T–DNA, designated as T–DNA I, contains the Cry1A.105 coding sequence regulated by the *RbcS4* promoter and *Pt1* terminator; and the Cry2Ab2 coding sequence regulated by the *Act2* promoter and *Mt* terminator. The second T–DNA, designated as T–DNA II, contains the *aadA* coding sequence regulated by the *FMV* enhancer, *EF–1α* promoter and *E9* terminator; and the *splA* coding sequence regulated by the *Usp* promoter and *nos* terminator. During transformation, both T–DNAs were inserted into the soybean genome. Subsequently, traditional breeding, segregation, selection and screening were used to isolate those plants that contain the Cry1A.105 and Cry2Ab2 expression cassettes (T–DNA I) and do not contain the *aadA* and *splA* expression cassettes (T–DNA II), resulting in the production of marker–free MON 87751.

Bioinformatic analysis of next–generation sequence data (comprehensively covering the genome) was used to characterize the insert number of any DNA sequences from the transformation plasmid vector PV–GMIR13196. The data indicated that MON 87751 contains a single integration locus and a single copy of PV-GMIR13196 T–DNA I, is devoid of plasmid backbone or T–DNA II sequence and demonstrated that the DNA insert in MON 87751 was stably maintained across five breeding generations.

Characterisation of Novel Proteins or Other Novel Substances

MON 87751 expresses the Cry1A.105 and Cry2Ab2 proteins to control lepidopteran soy pests. A multistep approach was used to characterise and assess the safety of the CP4 Cry1A.105 and Cr2Ab2 proteins expressed in MON 87751. The expression levels of the Cry1A.105 and Cry2Ab2 proteins in selected tissues of MON 87751 were determined and exposure to humans and animals through diet was evaluated. In addition, the donor organisms for the Cry1A.105 and Cry2Ab2 protein coding sequences, *Bacillus thuringiensis* spp, are ubiquitous in the environment and are not commonly known for human or animal pathogenicity or allergenicity. Bioinformatics analysis determined that the Cry1A.105 and Cry2Ab2 proteins lack structural similarity to known allergens or protein toxins. As has been previously shown in safety assessments of other Cry1A.105 and Cry2Ab2-containing crops, the Cry1A.105 and Cry2Ab2 proteins are rapidly digested in simulated digestive fluids and demonstrate no acute oral toxicity in mice at the levels tested. Hence, the consumption of the Cry1A.105 and Cry2Ab2 proteins from MON 87751 or its progeny poses no meaningful risk to human and animal health or an increased plant pest risk.

Cry1A.105 and Cry2Ab2 are Safe for Consumption in Food and Feed

Safety assessments had been conducted on MON 87751 resulting in USDA deregulation on October 17, 2014 and approval by Canadian Food Inspection Agency and Health Canada on October 31, 2014. Both Cry1A.105 and Cry2Ab2 proteins produced in MON 87751 are also present in MON 89034 maize, which received FSANZ approval under Application A595 in 2008. MON 89034 and data demonstrating its safety were also satisfactorily reviewed by

U.S. agencies in accordance with the review responsibilities under the Coordinated Framework, resulting in full approval of the product in the U.S. The safety of these proteins as expressed in MON 89034 has also been reviewed and approved in numerous other countries (*e.g.* Argentina, Canada, China, the European Union, Japan, Korea, Mexico, Philippines, Taiwan).

The Cry1A.105 and Cry2Ab2 proteins belong to a family of Cry proteins from *B. thuringiensis* that has been used commercially in the U.S. to produce microbial-derived products with insecticidal activity. There are at least 180 registered microbial *B. thuringiensis* products and over 120 microbial products in the European Union. Applications of sporulated *B. thuringiensis* have a long history of safe use for pest control in agriculture, especially in organic farming. The consumption of agricultural food crops sprayed with commercial *B. thuringiensis* microbial pesticides has a 50-year history of safe use and crops expressing proteins derived from *B. thuringiensis* have been commercially cultivated since 1996.

Cry1A.105 in MON 87751 is a protein consisting of a single polypeptide of 1181 amino acids containing three domains with an apparent molecular weight of approximately 133 kDa. The Cry1A.105 protein expressed in MON 87751 is targeted to chloroplasts through the addition of a chloroplast transit peptide (CTP) coding sequence at the 5′ end of the coding sequence. Experimental analysis of the N-terminus of MON 87751-produced Cry1A.105 protein indicated the presence of four additional amino acids at the N-terminus compared to the Cry1A.105 protein in MON 89034. The additional four amino acids are cysteine (C), methionine (M), glutamine (Q), and alanine (A). With the exception of the four additional CTP-derived amino acids, the deduced sequence of the Cry1A.105 protein that accumulates in MON 87751 shares 100% amino acid identity with the deduced sequence of the Cry1A.105 protein present in MON 89034. The presence of these four additional amino acids at the N-terminus of the MON 87751-produced Cry1A.105 protein are unlikely to impact protein specificity because they are not within the trypsin-resistant core that is responsible for target organism specificity and efficacy. Accordingly, this small difference is not expected to result in unanticipated adverse impacts on humans, livestock or NTOs.

Cry2Ab2 protein in MON 87751 is a protein consisting of a single polypeptide of 619 amino acids with an apparent molecular weight of approximately 62 kDa. Experimental analysis of the N-terminus of MON 87751-produced Cry2Ab2 protein (described below) indicated that the conjunction of the CTP sequence with the Cry2Ab2 sequence resulted in CTP cleavage at a position 15 amino acids within the Cry2Ab2 protein sequence, likely as a result of the processing of the N-terminal CTP by a general stromal processing peptidase (SPP). This deletion results in an amino acid sequence for the MON 87751-derived Cry2Ab2 protein that is 18 amino acids shorter than the MON 89034-derived Cry2Ab2 protein because the MON 89034-derived protein is three amino acids longer than wild type Cry2Ab2. With the exception of the deletions, the deduced sequence of the Cry2Ab2 protein that accumulates in MON 87751 shares 100% amino acid identity with the deduced sequence of the Cry2Ab2 protein present in MON 89034. The deletion of these amino acids at the N-terminus of the MON 87751-produced Cry2Ab2 protein are unlikely to impact protein specificity because

they are not within the trypsin-resistant core that is responsible for target organism specificity and efficacy. Accordingly, this small difference is not expected to result in unanticipated adverse impacts on humans or livestock.

Compositional Analyses of the GM Food

Compositional analysis was conducted on seed and forage of MON 87751 and a conventional control grown at eight sites in the United States during a 2012 field production. The compositional analysis, based on the OECD consensus document for soybean, also included measurement of nutrients, anti-nutrients and other components in all varieties, including the conventional reference soybean varieties, to provide data on the natural variability of each compositional component analyzed.

Of the 50 components statistically assessed for MON 87751 only eight components (protein, glycine, proline, phosphorus, vitamin E, and raffinose in seed, and total fat and NDF in forage) showed a significant difference between MON 87751 and the conventional control. For these eight components, the mean difference in component values between MON 87751 and the conventional control was less than the range of the conventional control values and the reference variety values. The MON 87751 mean component values were within the 99% tolerance interval, the values observed in the literature, or the ILSI-CCDB values.

These results support the overall conclusion that MON 87751 was not a major contributor to variation in component levels in soybean seed and forage and confirmed the compositional equivalence of MON 87751 to the conventional control in levels of these components. These data indicated that the components with statistically significant differences were not compositionally meaningful from a food and feed safety perspective

Conclusion

The data and information presented in this safety summary, supported by current tolerance exemptions and approval for use for Cry1A.105 and Cry2Ab2, demonstrate that the food and feed derived from MON 87751 and its progeny are as safe and nutritious as food and feed derived from conventional soy.