EXECUTIVE SUMMARY
to
Application to Food Standards Australia New Zealand for the Inclusion of Cotton MON 88702 in *Standard 1.5.2 - Food Derived from Gene Technology*

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EXECUTIVE SUMMARY

Food/Feed Safety and Nutritional Assessment of MON 88702

Monsanto Company has developed insect-protected cotton MON 88702, which produces a modified Cry51Aa2 insecticidal crystal (Cry) protein derived from *Bacillus thuringiensis* (*Bt*) that protects against feeding damage caused by targeted hemipteran and thysanopteran insect pests. The modified Cry51Aa2 protein has been assigned the unique name Cry51Aa2.834_16 (herein referred to as mCry51Aa2).

In recent years, hemipteran and thysanopteran insects have become some of the most economically detrimental pests in U.S. cotton production. In the face of increasing pest pressure, MON 88702 offers cotton growers an additional choice for insect pest management, by providing crop protection against targeted hemipteran and thysanopteran insects including two species of tarnished plant bugs (*Lygus hesperus*, and *Lygus lineolaris*), cotton fleahopper (*Pseudatomoscelis seriatus*), and thrips (*Frankliniella* spp.).

MON 88702 will likely be combined, through traditional breeding methods, with other insect-protection and herbicide-tolerance biotechnology-derived traits that have been approved/ deregulated/ registered. These next-generation cotton products will provide greater crop management choices for growers, to help meet the needs of U.S. and global food, feed and fiber markets.

Molecular Characterization of MON 88702 Verifies the Integrity and Stability of the Inserted DNA

MON 88702 was developed through *Agrobacterium*-mediated transformation of cotton using a two transfer DNA (T-DNA) transformation plasmid vector. The first T-DNA, designated as T-DNA I, contains the *Cry51Aa2.834_16* expression cassette (herein referred to as the *mCry51Aa2* expression cassette), which expresses the mCry51Aa2 protein. The second T-DNA, designated as T-DNA II, contains the *aadA* expression cassette. During transformation, both T-DNAs were inserted into the cotton genome. Subsequently, traditional breeding, segregation, selection, and screening were used to isolate those plants that contained the *mCry51Aa2* expression cassette (T-DNA I) and did not contain the *aadA* expression cassette (T-DNA II).

Characterization of the DNA insert in MON 88702 was conducted using a combination of sequencing, PCR, and bioinformatics. The results of this characterization demonstrate that MON 88702 contains a single copy of the intended transfer DNA (T-DNA I) with the *mCry51Aa2* expression cassette, which is stably inherited over multiple generations and segregates according to Mendelian principles. No additional backbone from the transformation plasmid was detected in the transformed plant. The results of this characterization also confirm that T-DNA II is not present.

mCry51Aa2 is Safe for Consumption in Food or Feed

The mCry51Aa2 protein expressed by MON 88702 was developed through limited modification to the Cry51Aa2 protein sequence derived from *Bt*.

Bt strains and their insecticidal proteins, including Cry proteins, have a more than 50-year history of safe use for insect control in agriculture, and have been safely applied to numerous fruit and vegetable crops, such as grapes, tomatoes, lettuce, spinach, and cabbage, often right up to the point of harvest. Certain *Bt* strains also have a history of safe use in public health settings for controlling mosquitoes and blackflies, and have been very extensively applied to aquatic environments, including locations that serve as sources of drinking water for humans. The mCry51Aa2 protein expressed by MON 88702 shares a similar structure and general mode-of-action with other insecticidal *Bt* Cry proteins, as well as pore-forming proteins identified in organisms with a history of safe human consumption, including common crop plants, vegetables, mushrooms, and fish.

A weight-of-evidence approach, in accordance with guidelines established by the Codex Alimentarius Commission, OECD, and the principles and guidance of the U.S. FDA's 1992 policy on foods from new plant varieties, was used to characterize the mCry51Aa2 protein present in MON 88702. No evidence was observed to indicate that mCry51Aa2 shared relevant similarities between allergens, mammalian toxins, or biologically active proteins of concern. Suscetibility of mCry51Aa2 was observed to pepsin digestion and sequential digestion using pepsin followed by pancreatin, while degradation and loss of functional activity were seen after exposure to elevated temperatures. Additionally, no adverse effects were observed after acute oral exposure of mice to mCry51Aa2 protein.

Additionally, exposure to mCry51Aa2 through food and feed is anticipated to be extremely low, as only highly-refined cotton products (refined, bleached, and deodorized (RBD) oil and linters) are suitable for human consumption, which contain neglible amounts of protein. Additionally, due to the presence of anti-nutrients in cottonseed most monogastric farm animals are not fed cottonseed meal to any appreciable level, while ruminants are able to incorporate only limited amounts of cottonseed into their diets as a protein supplement.

The safety assessment therefore supports the conclusion that dietary exposure to mCry51Aa2 protein derived from MON 88702 poses no meaningful risk to human or animal health.

Analysis Demonstrates that MON 88702 is Compositionally Equivalent to the Conventional Crop

Compositional analysis was conducted on cottonseed harvested from MON 88702 and a conventional control grown at five sites in the United States during 2015. The evaluation of MON 88702 followed considerations relevant to the compositional quality of cotton as defined by the OECD consensus document on compositional considerations (OECD, 2009). Cottonseed samples were analyzed for levels of nutrients, including proximates (protein, total fat, moisture, and ash), amino acids (18 components), fatty acids (22 components), carbohydrates by calculation, fiber (acid detergent fiber (ADF), neutral detergent fiber (NDF) and total dietary fiber (TDF)), minerals (calcium and phosphorus), and vitamin E. Other

components assessed in cottonseed included anti-nutrients (total gossypol, free gossypol, malvalic acid, sterculic acid, and dihydrosterculic acid).

Of the 46 compositional components statistically analyzed for MON 88702, 36 showed no significant differences between MON 88702 and the conventional control. Ten components in cottonseed (protein, myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, arachidic acid, eicosadienoic acid, behenic acid, and calcium) showed a statistically significant difference between MON 88702 and the conventional control at the 5% level ($\alpha = 0.05$). For these 10 components, the mean difference between MON 88702 and the conventional control was less than the range value (maximum value minus the minimum value) of the conventional control; in addition, these MON 88702 mean component values were within the natural variability observed by the range of available values reported in the literature and/or the ILSI Crop Composition Database (ILSI-CCDB) values (note: 20:2 eicosadienoic acid is a low abundance fatty acid for which literature and ILSI Crop Composition Database (ILSI-CCDB) values were not reported. However, the observed mean value for 20:2 eicosadienoic acid in MON 88702 was within the data range reported by (Codex Alimentarius, 1999) in cottonseed oil.

These results support the conclusion that the introduction of the trait into cotton to make MON 88702 was not a major contributor to variation in component levels in cottonseed, and confirm the compositional equivalence of MON 88702 to the conventional control.

Conclusion

The data and information presented in this safety summary support the conclusion that food and feed derived from MON 88702 and its progeny are as safe and nutritious as food and feed derived from conventional cotton.