SAFETY ASSESSMENT OF YIELDGARD ROOTWORM™ CORN

EXECUTIVE SUMMARY

Corn (*Zea mays* L.) is the world's third leading cereal crop, following wheat and rice. It is grown commercially in over 25 countries. In 2002, worldwide production of corn was approximately 594 million metric tonnes. In the United States (U.S.) its production covered 32 million hectares that yielded 229 million metric tonnes and had a net value of US$21.2 billion.

Corn yields are negatively impacted by a number of insect pests. One of the most pernicious in the U.S. Corn Belt is the corn rootworm (CRW). CRW larvae damage corn by feeding on the roots, reducing the ability of the plant to absorb water and nutrients from soil, and causing harvesting difficulties due to plant lodging. CRW is the most significant insect pest problem for corn production in the U.S. Corn Belt from the standpoint of chemical insecticide usage. Over 14 million acres of corn in the U.S. were treated with organophosphate, carbamate and pyrethroid insecticides to control CRW in 2000. CRW has been described as the billion dollar pest complex (Metcalf, 1986), based on costs associated with the application of soil insecticides and crop losses due to pest damage.

Monsanto Company has developed, through the use of recombinant DNA techniques, corn plants that are protected from damage due to CRW feeding. The tissues of these plants produce a *Bacillus thuringiensis* Cry3Bb1 protein that is selectively toxic to CRW species. A DNA vector containing the *cry3Bb1* gene was introduced into embryonic corn cells by microprojectile bombardment. Transformation event MON 863 was selected for development as *YieldGard Rootworm™ Corn*. Corn varieties containing transformation event MON 863 are afforded a level of protection from CRW feeding damage that is comparable or superior to that offered by currently available conventional insecticides.

Bacillus thuringiensis (B.t.) Cry proteins have a long history of safe and widespread use in agriculture. The Cry3Bb1 protein produced in *YieldGard Rootworm Corn* binds to specific receptors in the midgut of sensitive insects, but exerts no toxicity in species that lack these receptors. Cry3Bb1 protein has been shown to be selectively toxic to specific coleopteran insects such as corn rootworms.

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The food and feed safety of *YieldGard Rootworm Corn* has been established through the long history of safe use for *B.t.* Cry proteins, including members of the Cry3 class, compositional analyses of corn varieties containing event MON 863, Cry3Bb1 rodent toxicity bioassays, and biochemical fate analyses. The results of biochemical analyses of the grain and forage demonstrate the compositional equivalence of *YieldGard Rootworm Corn* to conventional corn varieties. Acute oral administration of Cry3Bb1 protein to laboratory mice was without effect at the highest dose attainable. Subchronic dietary administration of grain containing event MON 863 failed to produce any evidence of adverse health effects in rats. *In vitro* digestive fate studies with the Cry3Bb1 protein demonstrated that the protein is rapidly degraded to small pesticidally inactive fragments in a matter of seconds, the protein is not stable to heat, is not glycosylated, and it has no biologically relevant amino acid sequence similarity to known allergens and toxins. The Cry3Bb1 protein is present at low levels in grain and corn-based food and feed products. Using upper bound estimates of corn consumption for humans and livestock, the margin of safety for Cry3Bb1 in humans is $>5x10^4$ and in livestock is $>1x10^3$. Nutritional equivalence and comparative animal feeding performance of *YieldGard Rootworm* hybrids to conventional corn hybrids have been confirmed in feeding studies with broiler chickens, feedlot steers, dairy cattle and swine.

The environmental safety of *YieldGard Rootworm Corn* has been established through extensive laboratory and field testing of plant tissue or purified Cry3Bb1 protein with a wide range of nontarget species. No adverse effects have been observed in nontarget species exposed to maximum expected environmental concentrations of Cry3Bb1 protein. Furthermore, environmental fate studies demonstrate that Cry3Bb1 protein rapidly degrades in a variety of soil types. Agronomic, morphological and pest susceptibility observations have been recorded in multiple field trials conducted across major corn growing regions of the United States. Results from these trials confirm that *YieldGard Rootworm Corn* is phenotypically equivalent to conventional corn except for its tolerance to CRW and other coleopteran pests.

Collectively, the data summarized in this document support a conclusion that food and feed products derived from corn containing event MON 863 are as safe and nutritious for consumption as those derived from conventional corn varieties and that the use of this product poses no meaningful risk to the environment. In fact, use of this new technology in place of conventional insecticides will dramatically reduce overall environmental exposure. The introduction of *YieldGard Rootworm Corn* will offer U.S. farmers an environmentally sound and effective alternative to the use of chemical insecticides for control of the CRW pest.

Information and data contained within this document have been provided to regulatory authorities for review. Regulatory reviews continue as we update regulatory files and make submissions to additional countries globally.