Decision for the Safety Assessment of
Monsanto and Dow AgroSciences' corn MON 89034 x TC507 x NK603,
for Direct Use as food and feed or for processing

Food and Feed Safety

The product dossiers of Monsanto Philippines and Dow AgroSciences' combined trait product corn: MON 89034 x TC1507 x NK603 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the food/feed safety assessment is based on three major issues/concerns regarding stacked genes from different sources namely: a) gene interaction; b) effect on metabolic pathways and c) differential gene expression due to stacking.

A biosafety notification for combined trait product: corn MON 89034 x TC1507 x NK603 and all progenies derived from crosses of the product with any conventionally bred corn and corn containing approved-biotech events for direct use as food, feed or for processing was issued to Monsanto and Dow AgroSciences on the 10th day of December 2010. The notification is valid for five years and shall expire on December 9, 2015 subject to the terms and conditions set forth in DA Administrative Order No. 8 (DA AO8), Series of 2002, and Memorandum Circulars Nos. 6 and 8, Series of 2004. The said combined trait product was included in the Lists of Approval Registry being prepared by the Department of Agriculture – Bureau of Plant Industry.

This approval is for use as Food, Feed and Processing only. This does not include cultivation of combined trait product corn MON 89034 x TC1507 x NK603 in the Philippines. Food and Feed use of combined trait product corn: *MON 89034 x TC1507 x NK603* and *its by-products is therefore authorized as of 10th December 2010. The biosafety notification (No. 10-033) stated that combined trait product corn: MON 89034 x TC1507 x NK603 is as safe for human food, livestock feed and for processing as its conventional counterparts".*

I. Brief Identification of the Genetically Modified Organism (Living Modified Organism)

Designation:	Combined trait product corn: MON 89034 x TC1507 x NK603
Applicant:	Monsanto Philippines, Inc. and Dow AgroSciences
Plant Species:	
Name:	corn (*Zea mays* L.*)*
Parent Material:	Inbred corn lines (and/or isolines) developed and produced by Monsanto and Dow AgroSciences
Center of Origin:	Mexico and Central America
Toxic Factors/Allergen(s):	Corn is not a common allergenic food. Phytic acid raffinose are antinutrients included in corn.
Trait Description:	Insect resistance and herbicide tolerance
Trait Introduction Method:	Conventional breeding

Donor Organisms: *Bacillus thuringiensis* - a source of (Bt) *cry1A.105* and *cry2Ab*2 genes which confers resistance to lepidopteran insects.

Bacillus thuringiensis var. *aizawai* strain PS811, source of *cry1F* gene which confers resistance to lepidopteran pests.

Streptomyces viridochromogenes, source of *pat* genes which confers tolerance to herbicide (glufosinate).

Agrobacterium sp. Strain CP4, source of *cp4 epsps* gene which encodes only for the naturally glyphosate-tolerant EPSPS protein

Pathogenicity: *Bacillus thuringiensis* (Bt) has been used commercially in the US for over four decades to produce microbial pesticides. Cry proteins produced from Bt have a history of safe use since 1958 as active ingredients either in Bt microbial pesticides or in biotechnology derived food and feed crops. The assessment of potential allergenicity and toxicity showed that there was a reasonable certainty of no harm to mammals from exposure to the Cry1A.105 and Cry2Ab2 proteins.

Bacillus thuringiensis var. *aizawai* is found naturally in soil worldwide. No known mammalian health effects have been reported. It has been in commercial use as a microbial pesticide on food crops, including fresh vegetables, for over 30 years.

Streptomyces viridochromogenes is a non-pathogenic microorganism commonly found in the soil environment. There are no known adverse pathogenic or toxicological effects reported.

The *cp4* gene was derived from the common soil bacterium *Agrobacterium* sp. Strain CP4 which encodes only for the naturally glyphosate-tolerant EPSPS protein. No other protein is produced or introduced which may bring about toxicity, allergenicity or may be anti-nutritional in nature. No known pathogenicity in humans and animals because of the absence of the shikimic acid pathway in animals.

Proposed Use: For direct use as food, feed or for processing

II. Background Information

Monsanto Philippines and Dow AgroSciences have filed an application with attached technical dossiers to the Bureau of Plant Industry (BPI) on May 12, 2010 for a biosafety notification for direct use as food, feed and for processing under Administrative Order (AO) No. 8 Part 5 for stacked trait product corn: MON 89034 x TC1507 x NK603 which has been genetically modified for insect resistance and herbicide tolerance.

A safety assessment of combined trait product corn: MON 89034 x TC1507 x NK603 was conducted as per Department of Agriculture Administrative Order No. 8 Series of 2002 and Memorandum Circulars Nos. 6 and 8, Series of 2004. The focus of risk assessment is the gene interactions between the five transgenes**.**

Review of results of evaluation by the BPI Biotech Core Team in consultation with DA-Biotechnology Advisory Team (DA-BAT) completed the approval process.

III. Description of Novel (Introduced) Traits

Corn MON 89034 was developed though *Agrobacterium*-mediated transformation to produce the Bt insecticidal proteins Cry1A.105 and Cry2Ab2. The introduction of corn MON 89034 is expected to provide enhanced benefits for the control of lepidopteran insects pests such as *Ostrinia furnacalis* (ACB) and *Spodoptera frugiperda* (FAW) and *Helicoverpa zea* (CEW) compared to existing products.

Corn TC1507 was produced via microparticle bombardment of corn cells which contains two expression cassettes; the *cry1F* gene from *Bacillus thuringiensis var. aizawai* conferring resistance to lepidopteran insects and the *pat* gene from *Streptomyces viridochromogenes,* as a selectable marker conferring tolerance to glufosinate-ammonium.

Corn NK603 contains a 5 enolpyruvylshikimate-3-phosphate synthase (*epsps*) gene from *Agrobacterium* sp, strain CP4 (*cp4 epsps*) into the corn genome using particle acceleration method. Corn NK603 expresses a form of EPSPS protein that confers tolerance to glyphosate.

The transgenic traits from Event MON 89034, Event TC1507 and Event NK603 were combined through conventional breeding to produce the MON 89034 x TC1507 x NK603 corn. This stacked hybrid produces the five (Cry1A.105, Cry2Ab2, Cry1F, PAT, CP4 EPSPS) transgenic proteins present in MON89034 x TC1507x NK603 corn plants.

Safety of the Expressed Proteins

Corn MON 89034 x TC1507 x NK603 expresses the Cry1A.105, Cry2Ab2, Cry1F, PAT and CP4 EPSPS proteins at low level, throughout the development of MON 89034 x TC1507 x NK603 corn plants. The safety of the said proteins for animal and human health has been demonstrated as part of the safety evaluation of MON 89034, TC1507 and NK603 corn plants.

Based on the modes of action of the Cry1A.105, Cry2Ab2, Cry1F, PAT and CP4 EPSPS proteins, and location of these proteins' accumulation in the plant cells, there is no known mechanism of interaction among the gene products that could lead to adverse effects in human and animals

The protein expressed by the *cry*1F gene is non-toxic to plants, animals and humans. Its toxicity is limited only to a certain species of insects belonging to the Lepidopteran order. The protein expressed by the *pat* is an enzyme which is also non-toxic to plants, animals and humans. It specifically modifies certain herbicides making them inactive.

The protein products of the inserted genes (*cry*1F and *pat*) are not in any way, proteins that regulate the normal metabolic pathways of plants and therefore will not interfere with the plant's normal growth and development. No nucleic acid sequences that code for a protein toxic to humans or antibiotic resistance were introduced into maize line TC1507. Similarly, no significant homology was demonstrated for the *cry*1F and *pat* with known allergens and neither protein was stable in a simulated gastric fluid. Both proteins have little probability of being allergenic. The corn allergenic responsible for food - induced allergic reactions were identified as a lipid transfer protein present only in the pollen.

CP4 EPSPS proteins are not homologous to known protein allergens included in the available genetic databases. Furthermore, these proteins are present at very low levels in Roundup Ready corn and are from a family of proteins with long history of safe consumption.

Each protein is not designed to alter the corn plant's metabolism and has been shown in the evaluation of each single event (MON 89034, TC1507, NK603) to be equivalent to conventional corn. Having different modes and/or mechanisms of action and binding sites involved for each protein, production of the Cry1A.105, Cry2Ab2, Cry1F, PAT and CP4 EPSPS proteins in the combined trait product does not produce any adverse effects (interactive or synergistic) on plant metabolism.

Furthermore, because there were no synergistic or antagonistic interactions identified in the combined trait product corn, MON 89034 x TC1507 x NK603, it is anticipated that there will be no biologically significant interactions in the dual event combinations that could occur in the grain derived from this combined trait product.

IV. Nutritional Composition (Compositional Analysis)

Based on the modes of action of the Cry1A.105, Cry2Ab2, Cry1F, PAT and CP4 EPSPS proteins expressed in MON89034 x TC1507 x NK603, there is no known mechanism of interaction among the gene products that could lead to adverse effects in human and animals. There were no synergistic or antagonistic interactions identified in this combined trait product corn, the prior safety assessment of these individual events are directly applicable to the combined trait product. Compositional assessments of the corn from MON 89034, TC1507 and NK603 demonstrated that they are nutritionally and biologically equivalent to their conventional counterpart.

V. Anti-Nutritional Factors

There were no synergistic or antagonistic interactions identified in MON89034 x TC1507 x NK603, the prior safety assessment of these individual events are directly applicable to the combined trait product. Compositional assessments for the antinutrients in the corn from MON 89034, TC1507 and NK603 demonstrated that they are nutritionally and biologically equivalent to their conventional counterpart.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the combined trait product corn MON 89034 x TC1507 x NK603 application of Monsanto Philippines and Dow AgroSciences, it is concluded that no interaction found between/among the combined traits. Hence, this plant product was found to be as safe as its conventional corn and can substitute for its traditional counterpart for direct use as food, feed and for processing and is therefore approved for direct use as food, or feed or for processing. Monsanto Philippines and Dow AgroSciences are hereby notified that it may proceed with the activities for the above product for direct use as food and feed or for processing following all existing rules and regulations consistent with DA AO #8.