

Determination of the Safety of Pioneer Hi-Bred's and Dow AgroSciences'
Corn 59122 (Insect resistance and herbicide tolerance corn)
for Direct Use as Food, Feed and for Processing

Food and Feed Safety:

The product dossier on Corn 59122 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the review was on any new or altered expression trait and changes in composition and nutritional content or value relative to the conventional corn. At the end of the safety assessment, a conclusion was made that the Corn 59122-7 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Corn 59122 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 and for processing was issued to Pioneer Hi-Bred Inc. and Dow Agro Sciences of the Philippines on August 9, 2006. The permit is valid for five years and shall expire on August 8, 2011 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002. The said corn event was included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture-Bureau of Plant Industry.

This approval is for direct use as food, feed and for processing only. This does not include cultivation of Corn 59122 in the Philippines. Food and Feed use of Corn 59122 and its by-products is therefore authorized as of August 9, 2006. The Biosafety Permit (No. 06-025) stated that Bacillus thuringiensis (B.t.) Cry34/35/Ab1 insect-resistant, glufosinate-tolerant maize line containing transformation event 59122 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: Corn 59122-7

Applicant: **PIONEER HI-BRED PHILIPPINES, INC. (PHI)**
Anthel Global Bldg., Julia Vargas St.,
Ortigas Center, Pasig, Metro Manila
Philippines
and

DOW AGRO SCIENCES (DAS)
2nd Floor Bank of Commerce Building
J. Catolico Sr. Avenue, Lagao
General Santos City, South Cotabato
Philippines

Plant Species:

Name: Corn (*Zea mays*)

Parent Material: Inbred corn lines (and/or isolines) developed and produced by Pioneer Hi Bred and Dow AgroSciences.

Center of Origin: Mexico, Central America, and South America

Toxic Factors/Allergen(s):	Trypsin inhibitor, phytic acid, and secondary metabolites such as raffinose, ferulic acid and p-coumaric acid are present in low amount, 2,4-dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-1 (DIMBOA) is a potential toxicant but declines rapidly as the plant grows.
Trait Description:	Insect-resistance and herbicide (glufosinate) tolerance
Trait Introduction Method:	<i>Agrobacterium</i> mediated transformation
Donor Organism:	<i>Bacillus thuringiensis</i> strain PS149B1, source of <i>cry34Ab1</i> , <i>cry35Ab1</i> which produces crystal protein effective as insecticide against specific group of insects. <i>Streptomyces viridochromogenes</i> , source of <i>pat</i> genes which confers tolerance to herbicidal active ingredient glufosinate-ammonium.
Pathogenicity:	The Bt genes <i>cry34Ab1</i> and <i>cry35Ab1</i> originated from <i>Bacillus thuringiensis</i> strain PS149B1 which comes from a diverse group of gram-positive, spore-forming microorganisms which produces insecticidal proteins that are very selective in toxicity to specific organisms. Decades of safety testing on Bt proteins demonstrate the lack of toxicity to humans and animals, and the absence of adverse effects on non-target organisms and environment. The <i>pat</i> gene is a synthetic version based on the native <i>pat</i> gene derived from <i>Streptomyces viridochromogenes</i> , a non-pathogenic organism. The PAT protein does not confer pesticidal activity and there are no known adverse environmental or toxicological effects. Both donor organisms have no known record toxicity, allergenicity or infectivity to human beings and animals.
Proposed Use:	For direct use as food, feed of for processing

II. Background Information

PHI and DAS have submitted an application to the Bureau of Plant Industry (BPI) in order to obtain approval for the importation for direct use as food, feed of processing of *B.t.* Cry34/35Ab1 insect-resistant, glufosinate-tolerant maize line containing transformation event DAS-59122-7 (referred to as B.t.Cry34/35Ab1 maize line 59122).

PHI and DAS have developed maize plants that contain a plant-incorporated-protectant that effectively controls certain corn rootworm (CRW) pests. The tissues of these maize plants have been genetically modified, via recombinant DNA techniques, to express insecticidal crystal proteins (ICP) from *Bacillus thuringiensis* strain PS149B1 which are selectively toxic to CRW.

In addition to the *B.t.* genes, the *pat* gene, which encodes the enzyme phosphinothricin acetyltransferase, is also present in event DAS-59122-7. The *pat* gene is a synthetic version based on the native *pat* gene from *Streptomyces viridochromogenes*, a non-pathogenetic microorganism. The inclusion of the *pat* gene enables plant selection of the *B.t.* lines and provides tolerance to glufosinate-ammonium herbicides.

On December 5, 2005, PHI and DAS of the Philippines submitted an application to the Bureau of Plant Industry (BPI) requesting for Biosafety Permit under Administrative Order Number 8 (AO#8) Part 5 for Corn 59122 which has been genetically modified for herbicide resistance.

PHI and DAS has provided data on the identity of the corn 59122, a detailed description of the modification method, data and information on the gene insertion sites, copy numbers and levels of expression in the plant, the role of the inserted genes and regulatory sequences in donor organisms, and full nucleotide sequences. The novel proteins were identified, characterized, and compared to the original bacterial proteins, including an evaluation of their potential toxicity to livestock. Relevant scientific publications were also supplied.

Corn 59122 has been evaluated according to BPI's safety assessment by concerned agencies {(Bureau of Animal Industry (BAI), Bureau of Agriculture, Fisheries and Product Standards (BAFPS)) and a Scientific Technical Review Panel (STRP). The process involves an intensive analysis of the nature of the genetic modification together with a consideration of general safety issues, toxicological issues and nutritional issues associated with the modified corn.

The petitioner/applicant published the Public Information Sheet (PIS) of the said application on two widely circulated newspapers: Malaya and Manila Times, on January 30, 2006 for public comment/review. BPI received no comments on the petition during the 30-day comment period.

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

Cry34Ab1 and Cry35Ab1 proteins are from *Bacillus thuringiensis* PS149B1 and have activity against certain beetles.

B.t.Cry 34/35Ab1 corn was produced by *Agrobacterium tumefaciens*-mediated transformation of a corn line with T-DNA from plasmid PHP17662, which contains cry34Ab1, cry35Ab1, pat, and regulatory sequences necessary for the expression of the genes. The cry34Ab1 and cry35Ab1 transgenes were optimized for expression in maize, but the amino acid sequence of the expressed proteins is identical to the native proteins from B.t. Characterization of the DNA isolated from Bt. Cry34/35Ab1 corn using resistant enzyme digests and Southern blot analysis indicated that the T-DNA from plasmid PHP17662 inserted as a single, intact copy into the corn genome. In addition, DNA analysis indicated stability and inheritance of the inserted DNA within and across several generations.

Studies on the mode of action of Cry34Ab1 and Cry35Ab1 indicate that similar to other *B.t.* delta-endotoxins, Cry34Ab1 and Cry35Ab1 appear to target midgut epithelial cells in susceptible larvae. Cry34Ab1 appears to cause pore formation in phospholipid membranes, and addition of Cry35Ab1 resulting in pores remaining open longer and improved membrane permeability. Ribosomal inhibition activity was also investigated. The results demonstrated that the insecticidal activity of Cry34Ab1 and Cry35Ab1 is not associated with the inhibition of protein synthesis.

Safety of Expressed Proteins

Based on the available data submitted by the applicants, food and feed derived from *B.t.* Cry3435Ab1 maize line 59122 are substantially equivalent to existing food and feed based on information provided on the genetic material, the history of human consumption, the nutrient

and anti-nutrient components, and the similarities between the usage of conventional maize and *B.t.* Cry34/35Ab1 maize line 59122.

No nucleic acid sequences that code for a protein toxic to humans or antibiotic resistance were introduced into *B.t.* Cry34/35Ab1 maize line 59122.

IV Nutritional Composition (Compositional Analysis)

Proximate analysis of maize forage and grain showed no statistically significant differences observed for mean crude protein, crude fat, crude fiber, ADF or NDF values. Mineral analysis, fatty acid composition, amino acid composition and vitamin analysis also showed no significant differences and is comparable to conventional maize hybrids.

V. Anti-Nutritional Factors

The levels of key nutrients in grain and whole plant forage samples from *B.t.* Cry34/35Ab1 maize line 59122. No statistically significant differences were observed for inositol, raffinose, p-coumaric acid, ferulic acid, phytic acid, or trypsin inhibitor. All mean values for anti-nutrients in grain for *B.t.* Cry34/35Ab1 maize line 59122 and the control line were within reported literature ranges.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Pioneer Hi-Bred and Dow Agro Sciences of the Philippines, it is concluded that Corn 59122 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 or feed or for processing is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, or feed or for processing. PHI and DAS shall duly inform the public of this approval by way of publishing in any one (1) of the top three (3) leading newspapers in the country that imports of this product is covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.