

Determination of the Safety of Pioneer's and Dow Agro Sciences
Combined trait product corn: 1507 x NK603
For Direct Use as Food, Feed, and Processing

Food and Feed Safety:

The product dossiers on Pioneer's and Dow Agro Sciences combined trait product corn: 1507 x NK 603 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: 1507 x NK 603 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 were issued to Pioneer Hi-Bred Inc. and Dow Agro Sciences of the Philippines on February 17, 2006. The notification is valid for five years and shall expire on February 16, 2011 subject to the terms and conditions set forth in DA Administrative Order No. 8, 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 (Delisting) 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: 1507 x NK 603 in the Philippines. Food and Feed use of combined trait product corn: 1507 x NK603 its by-products is therefore authorized as of February 17, 2006. The biosafety notification (No. 06-008) stated that combined trait product corn: 1507 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: 1507 x NK 603

Applicant: **PIONEER HI-BRED INC.**
24F Antel Global corporate Center
Dona Julia Vargas Avenue
Ortigas Center, Pasig City

and

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

Plant Species:

Name: Corn (*Zea mays*)

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|-----------------------------------|--|
| Parent Material: | Maize developed and produced by Pioneer Hi-Bred and DowAgro Sciences |
| 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)- one (DIMBOA) a potential toxicant but declines rapidly as the plant grows |
| Trait Description: | Insect resistance and herbicide tolerance |
| Trait Introduction Method: | Conventionally breeding |
| Donor Organisms: | <p><i>Bacillus thuringiensis</i> var. <i>aizawai</i> strain PS811, source of <i>cryIF</i> gene which confers resistance to specific lepidopteran insects</p> <p><i>Streptomyces viridochromogenes</i>, source of <i>pat</i> genes which confers tolerance to herbicidal active ingredient glufosinate-ammonium.</p> <p><i>Agrobacterium tumefaciens</i> strain CP4, source of <i>cp4epsps</i> genes which confers tolerance to herbicidal active ingredient glyphosate.</p> |
| Pathogenicity: | <p><i>Bacillus thuringiensis</i> var. <i>aizawai</i> (PS811), source of <i>cryIF</i> gene, is non-pathogenic to humans, plants and animals. Its toxicity is limited only to certain species of insects belonging to the Lepidopteran order. The Cry1F protein also does not possess or exhibit any allergic properties.</p> <p><i>Streptomyces viridochromogenes</i>, a source of <i>pat</i> gene, has no known adverse environmental or toxicological effects and has no known record toxicity, allergenicity or infectivity to human beings and animals.</p> <p><i>Agrobacterium tumefaciens</i>, strain CP4, source of <i>cp4epsps</i> gene which encodes a glyphosate-tolerant form of the enzyme EPSPS, is a common soil bacterium that is responsible for causing crown gall diseases in susceptible plants. There have been no reports of adverse effects on humans and animals</p> |
| Proposed Use: | For direct use as food, feed or for processing |

II. Background Information

Pioneer Hi-Bred Inc. and Dow AgroSciences of the Philippines have filed an application with attached technical dossiers to the Bureau of Plant Industry on July 11, 2005 for a biosafety notification for direct use as food, feed and for processing under Administrative Order (AO) No. 8 Part 5 for combined trait product corn: 1507 x NK603 which has been genetically modified for insect resistance and herbicide tolerance.

A safety assessment of combined trait product corn: 1507 x NK 603 was conducted as per Department of Agriculture Administrative Order No. 8 Series of 2002. The focus of risk assessment is the gene interactions between the two 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

The 1507 x NK 603 maize has been obtained from traditional breeding methods between progeny of two genetically modified maize. The two GM maize events are DAS-Ø15Ø 7-1, referred to as 1507 maize, and MON- ØØ6Ø3-6, referred to as NK603. No new genetic modification has been introduced in 1507 x NK 603 maize.

The 1507 maize has been genetically modified to express the proteins Cry1F and phosphinotricin – N-acetyltransferase (PAT). Expression of the Cry1F protein confers resistance against certain lepidopteran pests, and expression of the PAT protein confers tolerance to the application of glufosinate-ammonium herbicide. The NK 603 maize has been genetically modified to express a 5-enolpyruvyl-shikimate-3-phosphate synthase (*cp4epsps*) gene isolated from the *Agrobacterium* sp strain, CP4, which encodes for the CP4EPSPS protein.

Safety of the Expressed Proteins

There is no known interaction between the cry1F, pat and cp4epsps genes as observed in the western blots. The Cry1F, PAT and CP4EPSPS proteins expressed in 1507x NK 603 maize do not present the characteristics associated with allergenic proteins. Therefore, 1507x NK 603 maize is unlikely to pose any significant allergenic risk or toxicity to humans and animals. The mode of action of each gene product is different the possibility of unexpected effects of the genes on the metabolism of the plant is very minimal. The expression levels of the proteins in grain from 1507x NK 603 maize are comparable.

There are no unexpected effects of the stacked genes on the metabolism of the plant since the 1507 x NK 603 maize has been obtained from traditional breeding methods between progeny of two genetically modified maize. All proteins within the combined trait product are expressed in the individual 1507 and NK603 maize hybrids. There is no known interaction between the *cry1F*, *pat* and *cp4epsps* genes that would affect the stability and expression level of the individual genes.

IV. Nutritional Composition (Compositional Analysis)

The World Health Organization (1995) stated that two plants that are substantially equivalent to conventional varieties are crosses by conventional breeding techniques, the combined trait product is expected to be substantially equivalent to the single event products. In accordance with OECD guideline (OECD, 2002) substantial equivalence was evaluated by comparing a) mean analyte values

of the test maize to an appropriate control of similar genetic background, and b) mean proximate values of the test maize entry to analyte ranges available in the published literature.

V. Anti-Nutritional Factors

No known anti nutritional factors for individual events. Thus, 1507 x NK 603 maize has no known antinutritional factors.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the stacked trait corn 1507 x NK 603 application of Pioneer Hi-Bred Inc. (PHI) and Dow Agro Sciences (DAS) of the Philippines, 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. PHI and DAS 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.