

Decision for the Safety Assessment of  
Bayer Crop Science's Soybean A2704-12  
For Direct use as Food and Feed or for Processing

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**Food and Feed Safety:**

The product dossier on Soybean A2704-12 was reviewed for safety and nutritional differences compared with the conventional soybean. 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 soybean. At the end of the safety assessment, a conclusion was made that the Soybean A2704-12 is as safe as the conventional soybean taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Soybean A2704-12 and all progenies derived from crosses of the product with any conventionally-bred soybean and soybean containing approved-biotech events for direct use as food, feed or for processing were issued to Bayer CropScience, Inc. on January 23, 2009. The said Soybean A2704-12 will be included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture.

This approval is for use as Food and Feed or for Processing only. This does not include cultivation of Herbicide tolerant soybean A2704-12 in the Philippines. Food and Feed use of soybean A2704-12 its by-products is therefore authorized as of January 23, 2009. The Biosafety Permit (No. 09-044) stated that "Herbicide tolerant soybean A2704-12 is as safe for human food, livestock feed and for processing as its conventional counterparts".

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

Designation:	Soybean A2704-12
Applicant:	Bayer CropScience 3/F Bayer House Canlubang Industrial Estate Calamba, Laguna
Plant Species:	
Name:	Soybean (Glycine max L.)
Parent Material:	A2704
Center of Origin:	USA

Toxic Factors/Allergen(s):	Soybeans naturally contain multiple endogenous antinutrients: trypsin inhibitors, raffinose and stachyose, lectins, phytic acid and phytoestrogens.
Trait Description:	Phosphinothricin (PPT) herbicide tolerance, specifically glufosinate ammonium.
Trait Introduction Method:	Microparticle bombardment of plant cells or tissue
Donor Organisms:	The <i>pat</i> gene was isolated from <i>Streptomyces viridochromogenes</i> , not known to be a human pathogen. A synthetic coding sequence of the <i>pat</i> gene was constructed for improved expression in plant. It encodes for a protein identical to the native protein of <i>Streptomyces viridochromogenes</i> .
Pathogenicity:	<i>Streptomyces viridochromogenes</i> organism, source of <i>pat</i> gene, is a common soil saprophytic bacterium, not known to be pathogenic, toxic or allergenic to humans and animals.
Proposed Use:	For direct use as food and feed or for processing

## **II. Background Information**

Bayer CropScience Inc. has developed Soybean A2704-12 that contains the *pat* gene from *Streptomyces viridochromogenes*. The *pat* gene encodes the phosphinothricin acetyltransferase (PAT) enzyme, which confers tolerance to glufosinate ammonium herbicides. AgrEvo first provided some background information on the new soybean varieties (derived from events A2704-12 and A5547-127) on March 21, 1998. The food and feed uses of this new soybean variety are no different than those varieties currently in the market.

On April 28, 2008, Bayer Crop Science Inc. submitted an application to the Bureau of Plant Industry requesting for a biosafety permit under Administrative Order (AO) No. 8 Part 5 for Soybean A2704-12 which has been genetically modified for herbicide tolerance

Bayer CropScience. Inc. has provided data on the identity of Soybean A2704-12, a detailed description of the transformation method, data and information on the gene insertion sites, copy number 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 and non-target organisms. Relevant scientific publications were supplied.

Soybean A2704-12 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 soybean.

The petitioner/applicant published the said application on two widely circulated newspapers: Malaya and Daily Tribune on July 3, 2008 respectively for public comment/review. BPI received no comment 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**

The Glufosinate resistant soybean event A2704-12 contains the *pat* gene derived from *Streptomyces viridochromogenes* introduced through the vector plasmid transferred to the soybean genome using the particle acceleration method. Stable insertion of the *pat* gene into the soybean genome results in the expression of the PAT enzyme.

Analytical tests demonstrate the equivalence of the PAT protein produced in *E. coli* and soybean event A2704-12. The results show that the PAT protein produced in *E. coli* is representative of the PAT protein produced in soybean event A2704-12.

Event A2704-12 contains the vector pB2/35SacK plasmid containing the right border fragment from the *Agrobacterium tumefaciens*, Ti plasmid and the synthetic *pat* gene fused to the 35S promoter and 35S terminator from the Cauliflower Mosaic Virus.

### **IV. Safety of the Expressed Proteins**

*Streptomyces viridochromogenes* (source of gene) is non-pathogenic and the *pat* gene as well as its encoded PAT protein is not toxic to mammals. PAT also does not possess characteristics associated with food allergens. Based on this information, there is a reasonable certainty of no harm resulting from the inclusion of the PAT protein (encoded by the *pat* gene) in human food and in animal feed.

The history of safe use of the *pat* and *bar* genes and their bacterial sources include a long-term human and animal exposure to the *Streptomyces* bacteria through roots and vegetable consumption, and consequently to the *pat* gene and the PAT protein, without any recorded adverse effects, a well-known and very specific mode of action of the PAT protein for its substrate L-PPT and absence of any adverse effects

observed in toxicity studies and in a human allergenicity study with different PAT-transformed varieties.

Based on amino acid homology comparisons to known toxins and allergens using public databases, determination of N-glycosylation consensus sequences, stability of the PAT protein to heat and digestive fluids, and intravenous injection to mouse – the PAT protein is not toxic and/or allergenic to humans and animals. Scientific data and procedures were to be found in the document entitled “Assessment of the Toxicity and Allergenicity of the PAT Protein”.

## **V. Nutritional Composition (Compositional Analysis)**

Soybean event A2704-12 is found to be compositionally and nutritionally equivalent to its non-transgenic counterpart and to other current commercial soybean varieties. Most of the analyzed values for protein, fiber, fat, ash and carbohydrates were inside the literature range except for ADF wherein deviations were demonstrated. The deviations were not found to be biologically significant.

Samples of hay, forage, seed, hulls, and toasted and non-toasted defatted soy meal from transgenic soybean were subjected to proximate analyses (moisture, crude protein, crude fat, ash, acid detergent fiber, neutral detergent fiber, carbohydrate). Seed samples were subjected to fatty acid analysis, amino acid analysis, and analyses of minerals (calcium, phosphorous, and potassium). Except in one case, there were no statistically significant differences between the values determined for transgenic plant samples and corresponding samples obtained from non-transgenic control plants. Statistical differences were seen in the levels of some amino acids between A2704-12 soybeans and non-transgenic soybean, but that the values were still within the normal range reported by the USDA for soybean.

## **VI. Anti-Nutritional Factors**

Soybeans contain anti-nutrients including trypsin inhibitors, isoflavones, stachyose, raffinose and phytic acid, but they have not posed much concern. Soybeans have a long history of safe use. Isoflavones or phyto estrogens have been reported to have anti cancer activity in humans, and refute somewhat the anti-nutrient notion attached to it.

The compounds such as Daidzin, Daidzein, Genistin, Genistein, Glycitin and Glycitein may also exist as the glucoside, acetylglucoside, or malonylglucoside analogues. Total isoflavone results are built from the sum of all single data (glucosides, esters and aglycones). Processing is not expected to affect the level of isoflavones. There is no significant difference in the endogenous soy allergens of the genetically modified extract as compared to the parental extract. The levels of these compounds were not statistically different between samples from non-transgenic and transgenic soybeans.

The low potential for allergenicity of the PAT protein has previously been established through amino acid sequence comparisons with known protein allergens and digestability studies using simulated gastric and intestinal fluids. Additionally, soybean seed extracts from line A2704-12 and from non-transgenic control plants were screened against a panel of sera from 16 soy-allergic individuals using the radioallergosorbent test (RAST). The results of this study did not reveal any qualitative or quantitative difference in endogenous soybean allergen content between transgenic and non-transgenic soybean.

## **VII. Regulatory Decision**

After reviewing the scientific data and information relevant to the application of Bayer CropScience, Inc., it is concluded that Soybean A2704-12 and all progenies derived from crosses of the product with any conventionally-bred soybean, and soybean 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. Bayer CropScience 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 import of this product is covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.