

**CONSOLIDATED REPORT OF BAYER CROPSCIENCE INC.'s SOYBEAN FG72 x A5547-127  
APPLICATION FOR DIRECT USE AS FOOD AND FEED, OR FOR PROCESSING**

**EXECUTIVE SUMMARY**

On April 11, 2017, Bayer CropScience Inc. applied the combined trait product soybean FG72 x A5547-127 as an original application under the DOST-DA-DENR-DOH-DILG Joint Department Circular No. 1 Series of 2016 (JDC No.1, S2016).

Under the JDC No.1, S2016, the assessors for Bayer's FG72 x A5547-127 for direct use as food and feed or for processing were the following:

- One (1) member of the Scientific and Technical Review Panel (STRP) – for evaluation of the Applicant's submitted risk assessment report
- Department of Environment and Natural Resources (DENR) – for the determination of the environmental impact of the said application
- Department of Health (DOH) - for the determination of the environmental health impact of the said application
- Bureau of Animal Industry (BAI) – for the determination if the application is in compliance with feed safety standards
- Bureau of Plant Industry- Plant Products Safety Services Division (BPI-PPSSD)- for the determination if the application is in compliance with food safety standards
- Socio-economic, ethical and cultural (SEC) Expert – to evaluate SEC impact of the said application

After reviewing the documents submitted by the applicant, the STRP, BPI-PPSSD and BAI find scientific evidence that the regulated article applied for direct use as food and feed, or for processing, has no evidence of interaction on the resulting gene products while DOH, DENR, and SEC expert recommended for the issuance of Biosafety Permit for soybean A5547-127 x FG72.

**BACKGROUND**

In accordance with Article VII. Section 20 of the JDC, no regulated article, whether imported or developed domestically, shall be permitted for direct use as food and feed, or for processing, unless: (1) the Biosafety Permit for Direct Use has been issued by the BPI; (2) in the case of imported regulated article, the regulated article has been authorized for commercial distribution as food and feed in the country of origin; and (3) regardless of the intended use, the regulated article does not pose greater risks to biodiversity, human and animal health than its conventional counterpart.

The BPI Biotech Office provided the assessors, the complete dossier submitted by Bayer. Upon receipt of the individual reports from the assessors, the BPI Biotech staff prepared this consolidated risk assessment report for the information of the public.

**STRP ASSESSMENT AND RECOMMENDATIONS**

**A. Gene Interaction**

The STRP has concurred that there is no likelihood of interaction among the three proteins (2mEPSPS, HPPD W336 and PAT) that will produce new allergens and new toxins based on their distinct mode of action. The three proteins have specific enzymatic activities using different substrates and via different metabolic pathways

They also concur that the expressed proteins accumulate in the subcellular components i.e., the cytoplasm of the soybean plant cells. However, the possibility of the occurrence of interaction among the 3 enzymes is NIL because they catalyze different reactions in their metabolic pathways.

## B. Metabolic Pathways

The STRP agree that the mode of action of each gene product is adequately described and that the results on the multisite field evaluation in 9 locations (2012) summarized the continuous and categorical parameters and indicated that the protein expression of each single event is similar to that of the stacked product and hence, there are no possible unexpected effects on the metabolism of the soybean plant.

## C. Gene Expression

The STRP has stated that sandwich ELISA was used to analyze the levels of the 3 proteins in different plant parts (leaves, roots, forage, flower and grain matrices) and that the proteins are expressed at low levels in the plant (microgram levels).

The STRP also stated that the bla marker genes were only used for the selection of the plasmids in E.coli and are controlled only in E coli. Also, the vector was digested to disrupt the coding sequence of the marker genes. Hence, there is a distant possibility that the bla marker genes be expressed in the transformed soybean plant.

Lastly, the STRP also agree that there is no likelihood of interaction that might affect the stability and protein expression levels of either one of the three genes involved.

## D. Recommendation

Find scientific evidence that the regulated article applied for direct use has no evidence of interaction on the resulting gene products.

## **BPI-PPSSD ASSESSMENT AND RECOMMENDATION**

### *Gene Interaction*

FG72 x A5547-127 contains hppdPf W336 gene encoding HPPD W336 protein, 2mepsps gene encoding 2mEPSPS protein and pat gene encoding PAT protein. Both HPPD W336 protein and PAT protein accumulates in the cytoplasm while 2mEPSPS protein are designed to accumulate in the plastids (Capt, 2011; Herouet et al., 2005; Herouet-Guicheney et al., 2009). However the gene products are not likely to interact to produce new allergen or toxins due to their different mode of actions, metabolic pathways and enzymatic activities.

### *Metabolic Pathways*

The 4-hydroxyphenylpyruvate dioxygenase (HPPD) is involved in the biosynthesis of homogentisate in plants (Capt, 2011). It catalyzes the second step in the pathway for the catabolism of tyrosine and are responsible for the transformation of p-hydroxyphenylpyruvate into homogentisic acid. In order to reduce the sensitivity of the HPPD enzyme to the herbicide isoxaflutole, a single amino acid substitution has been made in the wt hppdPf gene that resulted in the introduction of a glycine at position 336.

The phosphinothricin acetyltransferase (PAT) enzyme acetylates L-phosphinothricin, the active isomer of the glufosinate-ammonium herbicide, thereby conferring tolerance to glufosinate-ammonium herbicide (Herouet et al. 2005).

The 5-enol-pyruvylshikimate-3-phosphate synthase (EPSPS) protein is the 6th enzyme of the shikimate pathway, the metabolic pathway for the biosynthesis of aromatic compounds found in microorganisms and in plants (Herouet-Guicheney, 2009). The 2mepsps coding sequence was produced by introducing two point mutations to the wild-type epsps gene cloned from corn (*Zea mays*) through in vitro DNA technologies. The resultant 2mEPSPS protein has a lower binding affinity for glyphosate, thus allowing sufficient enzyme activity for the plants to grow in the presence of glyphosate herbicide.

Based on the documents provided by the developer, there is no possible unexpected effect of the stacked genes on the metabolism of the plant. This was being supported by the expression of the

proteins in soybean plant tissue from FG72 x A5547-127 which is equivalent to the single events, FG72 and A5547-127 (Dharmasri et al., 2015).

#### *Gene Expression*

The expression level of HPPD W336, 2mEPSPS and PAT proteins in different plant parts of FG72 x A5547-127 was determined through Enzyme-linked Immunosorbent Assay (ELISA). Results of the analysis indicated that the levels of expression of the proteins in FG72 x A5547-127 is equivalent to the corresponding single events, FG72 and A5547-127. The marker gene, bla, was also not transferred and expressed in FG72 x A5547-127.

Based on the documents provided by the developer, there is no possible interaction that could affect the stability and expression level of either one of the genes (Dharmasri et al., 2015; Dreesen, 2014). The genes in the stacked trait are expressed properly and similar to parental line, thus, there is no gene interaction.

#### *Conclusion*

After a thorough and scientific evaluation of the documents provided by Bayer CropScience, Inc. and other related literatures, scientific evidence indicates that the Combined Trait Product, FG72 x A5547-127 applied for direct use as food and feed or for processing has no evidence of interaction on the resulting gene products and as safe as it's conventional counterpart.

### **BAI ASSESSMENT AND RECOMMENDATIONS**

#### **A. Gene Interaction**

BAI has agree in the information provided by the applicant that there is no known interaction between 2mEPSPS, HPPD W336 AND PAT proteins and that the 2mEPSPS, HPPD W336 and PAT proteins are targeted to the cytoplasm.

#### **B. Metabolic Pathways**

BAI has concurred that (a) 2mEPSPS protein has lower binding affinity for glyphosate and so confers tolerance to glyphosate herbicides. The protein provides the plant's need for aromatic amino acids the production of which is prevented by the inhibition of the EPSPS enzyme in the Shikimic Acid Pathway in glyphosate-treated plants,(b) HPPD enzyme catalyzes the second step in the pathway for the catabolism of tyrosine and is responsible for the transformation of p-hydroxyphenylpyruvate into homogentisic acid. The modified HPPD W336 is tolerant to isoxaflutole (IFT) herbicide, and (c) PAT enzyme metabolizes glufosinate to an inactive acetylated derivative thereby conferring tolerance to glufosinate-ammonium.

They also concur that all the gene products have different modes of action, the gene products do not share the same metabolic pathway and that comparative analysis of agronomic and phenotypic characteristic show no unexpected adverse effects on the metabolism of FG72 x A5547-127.

#### **C. Gene Expression**

BAI stated that overlapping ranges of expression levels were observed between treated and untreated single-trait plant samples and treated and untreated stacked-trait plant samples. Based on this, 2mEPSPS, HPPD W336 and PAT are similarly expressed in the single- and stacked-trait events and that the proteins are expressed at low levels.

They also stated that there were no marker genes transferred in the stacked hybrid and that Gene interaction is not expected to occur. Stability of the genes in FG72 x A5547-127 and the protein expression levels were confirmed by Southern blot analyses and protein expression studies.

#### **D. Recommendation**

Find scientific evidence that the regulated article applied for direct use has no evidence of interaction on the resulting gene products.

### **DENR ASSESSMENT AND RECOMMENDATION**

After a thorough and scientific review and evaluation of the documents provided by the Bureau of Plant Industry (BPI) on the application of Bayer CropScience Inc. for direct use as food and feed or for processing of soybean FG72 x A5547-127. I/We,

Find scientific evidence that the regulated article applied for Direct Use as Food and Feed, or for processing is as safe as its conventional counterpart and is not expected to pose any significant risk to the environment. The following are the observations and recommendations:

1. Upon extensive review and evaluation of the application submitted by the proponent, including scientific evidences from the provided references, literature, and other related studies, the Committee accepts that the direct use of the regulated article whether for food, feed, and/or processing will not cause any significant adverse effect on the environment (land, air and soil) and non-target organisms, to wit:
  - a. before planting, the genetic stability in the transgenic crop is ensured such that no unintended horizontal gene transfer shall occur to unrelated species.
  - b. the protein product produced by the transgenic crop will immediately degrade upon exposure to natural environment
  - c. Characterization of the inserted gene has shown that the protein product will not increase the weediness potential of the transgenic crop.

The data evaluated support the conclusion that the regulated article is as safe as its conventional counterpart.

2. The Project Description Report (PDR) discusses the specified environmental management plan indicating the possible risk and harm to the environment and non-target organisms as well as the mitigating measures and contingency plan of the proponent. Upon evaluation of the submitted PDR, the Committee notes that the chances of unintended release or planting of the regulated article is very minimal and will not cause any damaging and lasting effects to the environment.

3. The Committee would like to suggest that the BPI ensure the proper and secure packaging of the regulated article for transport and the safety and durability of the transport vehicle, for prevention of any possible spillage or unintended release during transport/import as per BPI's inspection in the port area.

4. Based on the above considerations and with the submitted sworn statement and accountability of the proponent, we hereby submit our recommendation relative to the biosafety permit application of Bayer CropScience, Inc., for direct use as food, feed, or processing of Soybean FG72 x A5547-127.

### **DOH ASSESSMENT AND RECOMMENDATION**

After a thorough review and evaluation of the documents provided by the proponent, Bayer CropScience Inc., through the Bureau of Plant Industry, in support of their application for approval for Direct Use for food and feed, or for processing of soybean FG72 x A5547-127. I/We, Find that the regulated article applied for Direct Use for food and feed, or for processing (FFP) is as safe as its conventional counterpart and shall not pose any significant risk to human and animal health and environment.

The following are the observations and recommendations:

1. Find that the regulated article applied for direct use for food and feed, or for processing does not require changes in the usual practices in unloading, and loading, hauling, transport and storage, and processing. As such, the regulated article is as safe as its conventional counterpart and is not expected to pose any significant risk to human and animal health and environment while in transit, storage and processing.
2. Scientific pieces of evidences from provided references i.e. literatures show that regulated article applied for direct use for FFP is as safe as its conventional counterpart and shall not pose any significant risk to human and animal health and on the environment.
3. It is suggested that the BPI ensure the following:
  - a. Strict monitoring of the regulated article from the port of entry to the traders/importers storage/warehouse as stated in Section 32 of the JDC No. 1 series 2016.
  - b. The BPI to include in the issuance of permit for the release of this product the following conditions:
    - b.1 any spillage (during unloading and loading/hauling and transport unloading and storage) shall be collected and cleaned up immediately
    - b.2 transportation of the consignment from the port of entry to any destination within the country shall be in closed containers.

b.3 there shall be a clear labeling of the product from the importation down to all levels of marketing stating that it is only for the purpose of direct use for FFP and is not to be used as planting materials

4. Based on the above consideration and with the submitted sworn statement and accountability of the proponent, this recommendation is being submitted to BPI related to the processing and issuance of a biosafety permit for direct use as FFP of soybean FG72 x A5547-127

#### **SEC ASSESSMENT AND RECOMMENDATIONS**

The SEC expert states that approval of this event will not drastically affect the current patterns of production, consumption/utilization and trade. Current production pattern will not be affected since Bayer CropScience Event FG72 x A5547 – 127 will not be grown and propagated locally. On the other hand, the approval of Bayer CropScience Event FG72 x A5547 – 127 for utilization for the food and feed industries may stabilize prices thus, current consumption of soybean will not be affected drastically. In addition, being only one of the ingredients in feed formulation for livestock, poultry and aquaculture sub-sector, Bayer CropScience Event FG72 x A5547 – 127 is expected not to influence the consumption pattern of the consumers.