This is to inform the public that the National Biosafety Board (NBB) is currently assessing an application for approval submitted by *Instituto De Agrobiotecnologia Rosario* to release genetically modified Soybean event IND-ØØ41Ø-5 (HB4 soybean) for the purpose of supply or offer to supply for sale/placing in the market with the Reference Number of NBB: **JBK(S) 600-2/1/20**.

NBB welcomes written submissions of opinions/comments from the public regarding the application. More information on the application can be obtained from **www.biosafety.gov.my** under Public Consultation. Please quote NBB Reference number for correspondence.

Submissions must be addressed to:

***The Director General,***
***Department of Biosafety,***
***Level 4, Block F11, Complex F,***
***Lebuh Perdana Timur, Precinct 1,***
***62000 Putrajaya, MALAYSIA.***
***Email: dob@biosafety.gov.my***

The closing date for submissions is *18 November 2021*

**FACT SHEET**

**APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF HB4 SOYBEAN FOR SUPPLY OR OFFER TO SUPPLY FOR SALE OR PLACING IN THE MARKET**

**NBB REF NO: JBK(S) 600-2/1/20**

The objective of the Biosafety Act 2007 is to protect human, plant and animal health, the environment and biological diversity. Under the Biosafety Act 2007, the National Biosafety Board (NBB) is currently assessing an application for approval submitted by Instituto de Agrobiotecnologia Rosario (INDEAR).

## 1. What is the application for?

This application is for the approval to import and release genetically modified HB4 soybean and its products.

## 2. What is the purpose of the import and release?

The purpose of the import and release is to supply or offer for sale or placing in the market genetically modified HB4 soybean and its products for direct use as food, feed and for processing.

HB4 soybean is not intended for cultivation in Malaysia.

## 3. How has HB4 soybean been modified?

Genetically modified drought and glufosinate tolerant HB4 soybean was developed via *Agrobacterium tumefaciens*-mediated transformation of conventional soybean with the introduction of two genes, the *HaHB4* gene, conferring tolerance to water deficit, and the *bar* gene providing the crop with tolerance to glufosinate herbicides.

The *HaHB4* gene expresses the HAHB4 protein, a plant transcription factor that regulates the plant response to environmental stress. The presence of HAHB4 protein allows HB4 soybean to keep active the productive processes under water deficit conditions rendering higher yield.

The *bar* gene codes for phosphinothricin-N-acetyltransferase (PAT) enzyme, which inactivates the active principle in glufosinate-based herbicides, conferring tolerance to the herbicide glufosinate.

## 4. Characteristics of HB4 soybean

### (a) Details of the parent organism

Soybean, *Glycine max* L. Merr, was grown in North and Central regions of China as early as 5,000 years ago.

Soybean is considered a self-pollinated species, propagated commercially by seed. It is a non-invasive crop, unable to survive in the wild due to its long domestication process. Its potential to survive from one growing season to the next is very low.

HB4 soybean does not differ from the parent organism in any of its agronomic features except those intentionally added by the genetic modification.

**(b) Details of the donor organism**

*Helianthus annuus* (sunflower): donor of the *HaHB4* gene

Sunflower is grown as a crop for its edible oil and edible fruits and also used as wild bird food, as livestock forage, in some industrial applications and as an ornamental in domestic gardens. It does not have any toxic or pathogenic history and it not recognized as a main allergen source.

*Streptomyces hygroscopicus*: donor of the *bar* gene

*Streptomyces hygroscopicus* is a common soil bacterium that is not considered pathogenic to humans or animals. The *bar* gene from *Streptomyces hygroscopicus* encoding the phosphinothricin acetyl transferase (PAT) protein confers tolerance to glufosinate based herbicides.

**(c) Description of the trait(s) and characteristics which have been introduced or modified**

HB4 soybean was developed to provide two traits: 1) tolerance to stress caused by water deficit, thereby giving the crop opportunity of increased yield, and 2) herbicide tolerance.

**(d) Safety of the Expressed Proteins**

Several relevant features support the safety of the HAHB4 protein in soybean event HB4: a) the source of this protein (sunflower) has been in the food chain for a long time and therefore has a history of safe food use; b) HAHB4 is a transcriptional regulator of normal endogenous pathways, and therefore, no new proteins or metabolites other than those of the natural plant are expressed in the transgenic event; c) HAHB4 is expressed at extremely low levels which, added to the safety of the source, makes its presence in foods of no safety concern.

Expression levels of the new proteins are very low. The content of HAHB4 is below 0.000002% of the total content of soybean grain proteins, and PAT expression levels correspond to up to 0.02% of the total soybean proteins.

**(e) Utilization of soybean**

Whole soybeans are utilized to produce edible oil, full fat and defatted soy flour, soy sprouts, baked soybeans, roasted soybeans, and the traditional soy foods (miso, soy milk,

soy sauce, tempeh and tofu). In addition to its wide edible use, refined soybean oil has many other technical and industrial applications, e.g., the production of biodiesel. Secondary products from soybean industrial processing are lecithin, fatty acids, and tallow.

## 5. Assessment of Risks to Human Health

### a. Nutritional data

Compositional assessments of HB4 soybean were evaluated in comparison to concurrently grown non-modified soybean (referred to as control soybean) to identify statistical differences and subsequently were evaluated in the context of normal ranges of variation of commercial soybean. Nutrient composition analysis of HB4 soybean included proximates, fiber, minerals, fatty acids, amino acids, vitamins and anti-nutrients.

When the results obtained from HB4 soybean samples coming from several field trials were analyzed together and compared to those of the non-transgenic control line, seven components showed significant differences. However, the levels measured in HB4 soybean were found to either fall within the reference ranges provided by the commercial varieties or the literature values.

These results, support the compositional equivalence of soybean HB4 with the non-modified counterpart and with current commercial varieties and within the natural variability of conventional commercial reference varieties.

### b. Toxicology

The absence of putative toxic effect derived from the food/feed use of HB4 soybean is based on the following:

1) From the food safety perspective, the use of the newly expressed HAHB4 and PAT proteins in HB4 soybean does not raise any safety concern. Both have a history of safe use with no evidence of toxic effects (Herouet et al., 2005; ILSI, 2016; Khurana and Singh, 2021).

2) Comprehensive risk/safety assessment of HB4 soybean including molecular, compositional, agronomic and phenotypic analyses, shows no significant modifications in the composition, no indication of possible unintended effects and no indication of interactions relevant for food/feed safety.

3) Both, HAHB4 and PAT proteins, has been subjected to many safety studies including acute rodent toxicology tests, with no indication of adverse health effects (Herouet et al., 2005; MOA, 2017).

4) Bioinformatic assessment did not find significant similarities of the new expressed proteins with known protein toxins.

5) A sub-chronic animal feeding study performed with whole HB4 soybean seeds confirmed its lack of toxicity (Bultman, 2019).

**c. Allergenicity**

The two new proteins expressed in HB4 soybean, HAHB4 and PAT, showed not to have allergenic properties (Herouet et al., 2005; Revale et al., 2020). Bioinformatic assessment did not find significant similarities with allergens and digestion assays have demonstrated rapid degradation of these proteins under simulated digestive conditions (Herouet et al., 2005; Fazio et al., 2020; Revale et al., 2020).

Soybean is one of the most important sources of edible oil and proteins, making a relevant nutritional contribution to humans and animals. However, soybean contains some natural endogenous allergens that may have a negative effect on susceptible individuals. The levels of these compounds in HB4 soybean do not differ from those in the non-modified soybean.

**6. Assessment of Risks to the Environment**

Soybean is not cultivated in Malaysia (GAIN, 2020). Results of a study showed that when grown in a more favourable environment, soybean varieties showed better performances (Nor Hafizah et al., 2017), however further studies are required for successful soybean cultivation in Malaysia.

Since this application does not cover an environmental release or cultivation but is intended only for approval to import HB4 soybean and its products and that it may enter Malaysia as grain, food ingredients for processing or packaging or as finished products ready for distribution, or as feed meal for animals, thus the potential exposure to the environment is limited to unintended release via spillage during transportation of the grain which is most likely to occur near ports or along roads from ports to manufacturing sites (Roberts et al., 2014). These spilled seeds are unlikely to survive long and circumstances for seed germination would not be adequate. Soybean plants rarely grow outside agricultural managed environments and most operations associated to import are carried out outside agricultural settings.

A wild perennial species related to soybean, *Glycine javanica*, has been reported to occur in Malaysia (Singh, 2017). However, the risk of gene flow from soybean to its wild relative is very low since *G. javanica* plants are self-seeding (Duke, 1981) and soybeans do not hybridize with any species outside of the genus *Glycine* (Hymowitz and Singh, 1987). Soybean, including HB4 soybean, is not a weedy species, is not native to Malaysia and is unlikely to persist in the environment outside of cultivation.

**7. What is the Emergency Response Plan?**

As the scope of this application does not include authorization for the cultivation of HB4 soybean, any exposure to the environment from the import of HB4 soybean is limited and may be due to unintended release via spillage during transportation of the grain.

Any unintended release can be controlled with current agronomic measures taken to control other commercially available soybean, such as selective use of herbicides (with the exception of glufosinate-ammonium), and manual or mechanical removal of plants.

**a. First Aid Measures**

Exposure to HB4 soybean or derived products does not call for specific first aids measures.

**b. Accidental Release Measure**

Accidental release of HB4 materials, e.g., seeds or grain spilled during transportation, should be collected (sweeping, vacuum cleaning) and disposed with the same precautions as any similar soybean material. No specific measures are needed.

**c. Handling and Storage**

Handling and storage of soybean HB4 and materials derived therefrom should be done as with conventional soybean seed or derived materials.

**d. Disposal Consideration**

There are not special considerations regarding disposal of HB4 soybean or products derived therefrom. The same measures for waste disposal and treatment for conventional soybean are valid for HB4 soybean.

**8. How can I comment on this application?**

Any member of the public may submit their comments or queries on publicly notified information about the application. Before submission of comments or queries, the person should review the information provided. Your comments or queries on any possible impacts/risks to the health and safety of the people and the environment that may be posed by the proposed release are appreciated. The submission of the comments or queries should be prepared carefully as it will be given the same scrutiny as the application by the NBB. The submission of comments and clarifications of queries should contribute to the NBB's assessment. Even if the submission is not science-based, and focuses on cultural or other values, it should still be developed in the form of a well-founded argument.

Please note that the consultation period closes on **18 November 2021** and written submissions are required **before/on** that date. Submissions must be addressed to:

**The Director General**
**Department of Biosafety**
**Ministry of Environment and Water**
**Level 4, Block F11, Complex F,**
**Lebuh Perdana Timur, Precinct 1,**
**62000, Putrajaya**
**MALAYSIA**
**E-mail: dob@biosafety.gov.my**

**Please include your full name, address and contact details in your submission.**

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