Part VII - Summary

Request for Authorization of genetically modified herbicide tolerant cotton

GHB811

for food and feed uses, and import and processing, in accordance with articles 5 and 17 of Regulation (EC) N° 1829/2003

EFSA-GMO-ES-2018-154

Version CC2

Submitted on
13 Dec 2018

PART VII – SUMMARY

EFSA-GMO-ES-2018-154 (GHB811)

1. GENERAL INFORMATION

1.1. Details of application

(a) Member State of application

Spain

(b) Application number

EFSA-GMO-ES-2018-154

(c) Name of the product (commercial and any other names)

GHB811 (OECD ID: BCS-GH811-4)

(d) Date of acknowledgement of valid application

Not available at the time of submission

1.2. Applicant

(a) Name of applicant

BASF Agricultural Solutions Seed US LLC

(b) Address of applicant

BASF Agricultural Solutions Seed US LLC
100 Park Avenue
07932
Florham Park, New Jersey
USA

(c) Name and address of the representative of the applicant established in the Union (if the applicant is not established in the Union)

Representative of the applicant established in the Union:
BASF SE
Carl-Bosh-Str. 38
D-67063 Ludwigshafen
Germany

BASF Agricultural Solutions Belgium NV is the contact for this submission and all correspondence should be directed to:

BASF Agricultural Solutions Belgium NV

Rue Marie de Bourgogne 58
B - 1000
Brussels
Belgium

1.3. Scope of the application

(a) Genetically modified food

☑ Food containing or consisting of genetically modified plants

☑ Food produced from genetically modified plants or containing ingredients produced from genetically modified plants

(b) Genetically modified feed

☑ Feed containing or consisting of genetically modified plants

☑ Feed produced from genetically modified plants

(c) Genetically modified plants for food or feed uses

☑ Products other than food and feed containing or consisting of genetically modified plants with the exception of cultivation

☐ Seeds and plant propagating material for cultivation in the Union

1.4. Is the product or the uses of the associated plant protection product(s) already authorised or subject to another authorisation within the Union?

No ☑

Yes ☐ (in that case, specify)

1.5. Has the genetically modified plant been notified under Part B of Directive 2001/18/EC?

Yes ☐

No ☑ (in that case, provide risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC)

This application requests authorization for food and feed uses, and for import and processing and does not include cultivation in the EU.

1.6. Has the genetically modified plant or derived products been previously notified for marketing in the Community under Part C of Directive 2001/18/EC?

No ☑

Yes ☐ (in that case, specify)

1.7. Has the product been subject to an application and/or authorised in a third country either previously or simultaneously to this application?

No ☐

Yes ☑ in that case, specify the third country, the date of application and, where available, a copy of the risk assessment conclusions, the date of the authorisation and the scope of the application

Submissions have been made in third countries around the world and are at different stages in the approval process. GHB811 cotton applications have been submitted in USA, Korea, Japan, Canada, Australia, New Zealand and Argentina.

GHB811 cotton is authorized for food and feed uses in Australia and New Zealand, and for food use in Japan and Argentina. GHB811 has been approved for cultivation in the USA.

1.8. General description of the product

(a) Name of the recipient or parental plant and the intended function of the genetic modification.

The recipient plant is cotton, which is extensively cultivated and has a long history of safe use.

GHB811 cotton was developed by means of *Agrobacterium*-mediated transformation using the vector pTSIH09 containing the *2mepsps* and *hppdPfW336-1Pa* expression cassettes. The *2mepsps* coding sequence was developed by introducing two-point mutations to the wild-type *epsps* gene cloned from maize (*Zea mays*). The double mutant 5-enol pyruvylshikimate-3-phosphate synthase (*2mepsps*) gene that encodes for the 2mEPSPS protein Expression of the 2mEPSPS protein confers tolerance to glyphosate herbicides. The *hppdPfW336-1Pa* coding sequence was developed by introducing a single point mutation to the wild type *hppd* gene derived from *Pseudomonas fluorescens* gene. The *hppdPfW336-1Pa* gene encodes for the HPPD W336 protein. Expression of the HPPD W336 protein confers tolerance to HPPD inhibitors, such as isoxaflutole (IFT).

(b) Types of products planned to be placed on the market according to the authorisation applied for and any specific form in which the product must not be placed on the market (such as seeds, cut-flowers, vegetative parts) as a proposed condition of the authorisation applied for.

GHB811 cotton will enter the European Union (EU) by import as commodity cottonseed and derived products. Crushing, processing and consumer packaging will be accomplished in the EU. The same production processes applied to conventional cottonseeds will be used for GHB811 cotton.

The scope of the application does not include cultivation in the EU.

(c) Intended use of the product and types of users.

The products, covered by this application, will be used as any other commercial cotton, with the exception of cultivation.

GHB811 cotton will enter the EU by import as commodity cottonseed and derived products and will be used for the same downstream purposes as conventional cotton. There are three major food/feed products derived from cotton seeds: whole cottonseeds, oil and meal.

This application request import and processing only and does not include cultivation of GHB811 cotton in the EU. The milling, processing and consumer packaging however will be accomplished in the EU.

Therefore, the intended categories of users belong to the cotton crushing and packaging industry and their customers, the consumers of cottonseed and cottonseed products.

(d) Any specific instructions and recommendations for use, storage and handling, including mandatory restrictions proposed as a condition of the authorisation applied for.

Cottonseed, oil, mal and other products derived from GHB811 cotton will be imported from outside the EU and will be handled in the same way as other imported cotton and derived products produced within the EU. Therefore, no specific conditions for use or handling are foreseen for GHB811 cotton besides the labelling and traceability requirements according to Regulation (EC) N° 1829/2003 and Regulation (EC) N° 1830/2003.

(e) If applicable, geographical areas within the EU to which the product is intended to be confined under the terms of the authorisation applied for.

No restrictions are necessary as GHB811 cotton is suitable for all food, feed and industrial uses in all regions of the European Union, the same as conventional cotton. This application requests import and processing only and is not covering cultivation in the EU.

(f) Any type of environment to which the product is unsuited.

No restrictions are necessary as GHB811 cotton is suitable for all food, feed and industrial uses in all regions of the European Union, the same as conventional cotton. This application requests import and processing only and is not covering cultivation in the EU.

(g) Any proposed packaging requirements.

GHB811 cotton will be handled in the same way as other imported cotton and derived products. No specific packaging is required.

(h) Any proposed labelling requirements in addition to those required by other applicable EU legislation than (EC) No 1829/2003 and when necessary a proposal for specific labelling in accordance with Article 13(2) and (3), Article 25(2)(c) and (d) and Article 25(3) of Regulation (EC) No 1829/2003.

In the case of products other than food and feed containing or consisting of genetically modified plants, a proposal for labelling which complies with the requirements of point A(8) of Annex IV to Directive 2001/18/EC must be included.

GHB811 cotton does not have characteristics that require specific labelling. Therefore, no additional labelling is proposed in addition to the GM labelling requirements foreseen in regulations (EC) 1829/2003 and 1830/2003.

(i) Estimated potential demand

(i) In the EU

There are no anticipated changes to the demand as a result of the introduction of GHB811 cotton in the cotton supply, the introduced traits have only an agronomical benefit. It is anticipated that the introduction of GHB811 cotton will replace some other cotton in existing food and feed products

(ii) In EU export markets

There are no anticipated changes in the cotton production in export markets as a result of the introduction of GHB811 cotton. It is anticipated that the introduction of GHB811 cotton will replace some of the existing cotton derived products.

(j) Unique identifier in accordance with Regulation (EC) No 65/2004

OECD code: BCS-GH811-4

1.9. Measures suggested by the applicant to take in case of unintended release or misuse as well as measures for its disposal and treatment

Any unintended release or misuse will not have detrimental effects on the environment or on human and animal health as has been determined by the risk analysis. Therefore, no special measures are foreseen.

GHB811 cotton is tolerant to herbicide products having glyphosate and/or HPPD inhibitors such as isoxaflutole (IFT) as the active ingredients. GHB811 cotton remains susceptible to a wide variety of other herbicides and GHB811 cotton plants can thus be easily eliminated. Besides chemical means, mechanical removal is also an option.

No additional specific measures are suggested in case of waste disposal and treatment.

2. INFORMATION RELATING TO THE RECIPIENT OR (WHERE APPROPRIATE) PARENTAL PLANTS

2.1. Complete name

(a) Family name

Malvaceae

(b) Genus

Gossypium L.

(c) Species

Gossypium hirsutum L.

(d) Subspecies

Not applicable

(e) Cultivar/breeding line

GHB811

(f) Common name

cotton

2.2. Geographical distribution and cultivation of the plant, including the distribution within the Union

Plants of the tribe *Gossypiae* originated in the tropics and subtropics. Wild species of the tribe are extremely sensitive to photoperiod conditions and do not flower in long day-light regime, therefore they are essentially excluded from temperate climates. In spite of their origin, more than 50 % of cultivated cottons are produced in temperate zone above 30° Latitude N, but they also tend to be plants of the southern hemisphere.

Cultivated *G. hirsutum* (Upland or Mexican cotton) represents over 90 % of world-wide production besides one only "New World" tetraploid species, *G. barbadense* (Pima, South American cotton or Egyptian cotton) and two "Old World" diploid species: *G. arboreum* and *G. herbaceum*. Main cotton producers are China, USA, India, Pakistan, Uzbekistan, Brazil and Turkey. China, India and the United States are the largest producers of cotton globally[1].

In the European Union, currently, cotton is produced only in three Member States on around 300.000 ha. Greece is the main cotton grower, with 80% of European cotton area, followed by Spain (mainly the region of Andalucía) with a share of 20%. Bulgaria produces cotton on less than 1 000 ha. In 2013, the EU cotton production is estimated less than 300 000 t, which represents only 1% of world cotton production. With 230 000 t, Greece accounts for 85% of EU production, whereas Spain produces the remaining 15% (40 000 t)[2].

2.3. Information concerning reproduction (for environmental safety aspects)

(a) Mode(s) of reproduction

Cultivated cotton is propagated by seeds. In the absence of insect pollinators, cotton is a self-pollinator, but cross-pollination may take place when pollinators are present.

(b) Specific factors affecting reproduction

The main abiotic environmental factors affecting cotton reproduction which also determine the areas of cotton production are high light intensity and optimal temperature profiles, such as a) active vegetative growth range: 15 - 38 °C, b) accumulated heat GD 15.5°C need: 1,200 units, c) number of frost free days: 200, d) rapid and consistent spring warming pattern.

Although cotton is mainly autogamous, the frequency of cross-pollination varies with the insect pollinator population, in particular with various wild bees, bumble bees (*Bombus ssp*.) and honey bees (*Apis mellifera*). All the factors reducing the density of pollinators such as the use of insecticides, or increased air humidity as the result of irrigation will essentially limit the extent of cross-pollination.

(c) Generation time

The cultural cycle for cotton ranges from less than 100 days, to 200 growing days from seedling emergence to maturity depending on the variety. Rainfall, temperature, sunshine and spring warming, all have an impact on optimal growth.

2.4. Sexual compatibility with other cultivated or wild plant species (for environmental safety aspects)

There are no identified non-cotton plants that are sexually compatible with cultivated cotton varieties presently found in the EU.

Pre-zygotic, and post-zygotic barriers greatly limit the sexual compatibility of *G. hirsutum* and *G. barbadense* with other plant species in the *Gossypiae* tribe. In addition plants of the *Gossypium* genus are not native to Europe. Several members of the *Malvaceae* family are cultivated as ornamental plants (e.g. *Hibiscus rosa-sinensis*) or vegetables (e.g. *Abelmoschus esculentus–okra*), but hybridisation experiments of these species with *Gossypium* spp. failed or resulted in sterile seeds.

[1] http://faostat3.fao.org/ FAOStat accessed July 2018
[2] http://ec.europa.eu/agriculture/cotton_en; accessed July 2018

G. hirsutum and *G. barbadense*, allotetraploid species that combine the AADD genomes, will hybridise only with other tetraploid members of the Gossypium genus including G. tomentosum, *G. darwinii*, *G. mustelinum*, *G. hirsutum*, *G. barbadense* and *G. lanceolatum*, which species are not known to have a habitat in Europe

2.5. Survivability (for environmental safety aspects)

(a) Ability to form structures for survival or dormancy

Cotton is cultivated annually and cannot survive without human assistance. Seeds are the only vegetative structure for survival. Some wild forms may produce "hard seeds" that, upon drying, become impermeable to water and suffer delayed germination. However this trait is undesirable agronomically and has been largely eliminated from modern cultivars through breeding and selection.

Cultivated cotton does not produce seeds which can persist in the environment for long periods of time, furthermore cotton seed lacks the ability to develop dormancy.

(b) Specific factors affecting survivability

The main factors affecting survivability of cotton are related to soil microclimate such as temperature and humidity. If planted in moist soil before the soil temperature reaches 15 °C, the cotton seed is likely to rot and die.

2.6. Dissemination (for environmental safety aspects)

(a) Ways and extent of dissemination

Two differentiated reproductive structures are suitable for the dispersal of cotton genes in the environment:

- Seed dispersal. It could occur during transport, at planting and essentially before and during harvest.
- Pollen dispersal. A number of studies conclude that when out-crossing occurs it is principally located around the pollen source and decreases significantly with distance.

(b) Specific factors affecting dissemination

Seed dispersal: Cotton seed has no structural modifications to facilitate transfer by animals. Dissemination is mainly the result of human activity.

Pollen dispersal in cotton shows a correlation with insect prevalence. Proximity of more attractive vegetation, climate and insect management will essentially limit the extent of cross-pollination.

2.7. Geographical distribution within the Union of the sexually compatible species (for environmental safety aspects)

In the EU, the only sexually compatible species is the cultivated cotton, this would only include *G. hirsutum* and *G. barbadense*. Cotton is currently cultivated in Greece, Spain and Bulgaria.

2.8. In the case of plant species not normally grown in the Union, description of the natural habitat of the plant, including information on natural predators, parasites, competitors and symbionts (for environmental safety aspects)

Not applicable, since cotton is grown in the EU.

2.9. Other potential interactions, relevant to the genetically modified plant, of the plant with organisms in the ecosystem where it is usually grown, or used elsewhere, including information on toxic effects on humans, animals and other organisms (for environmental safety aspects)

Cotton is known to interact with other organisms in the ecosystem including a range of beneficial and pestiferous arthropods, bacteria, fungi, nematodes, surrounding weed species, animals and humans.

Cotton is widely cultivated and has a history of safe use. Cotton is not considered harmful or pathogenic to humans; however the plant does produce gossypol and cyclopropenoid fatty acids (CPFA), which are anti-nutrients.

All of the anti-nutritional factors are subject to neutralisation during processing. Free gossypol binds to lysine and other products, and then becomes unavailable to animals. Cyclopropenoid fatty acids are deactivated or removed from the oil by hydrogenation or during deodorization at 230-235°C.

3. MOLECULAR CHARACTERISATION

3.1. Information relating to the genetic modification

(a) Description of the methods used for the genetic modification

GHB811 was developed by means of *Agrobacterium*-mediated transformation using the vector pTSIH09 containing the *2mepsps* and *hppdPfW336-1Pa* expression cassettes.

(b) Nature and source of the vector used

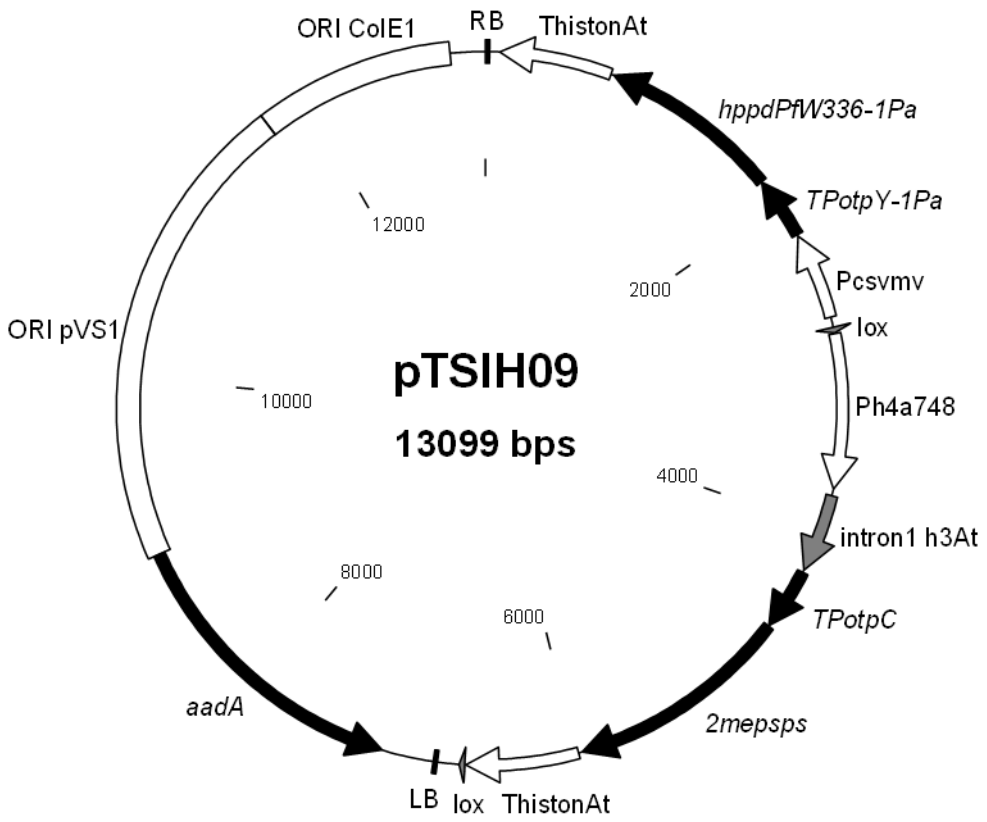

Figure 1: Map of vector pTSIH09.

(c) Source of donor nucleic acid(s) used for the transformation, size and intended function of each constituent fragment of the region intended for insertion

Table 1: Description of the genetic elements of pTSIH09

Nt Positions	Orientation	Origin
1 - 25		**RB:** right border repeat from the T-DNA of *Agrobacterium tumefaciens* (Zambryski, 1988)
26 - 82		Synthetic polylinker derived sequences
83 - 749	Counter clockwise	ThistonAt: sequence including the 3´ untranslated region of the histone H4 gene of *Arabidopsis thaliana* (Chabouté *et al.*, 1987)
750 - 765		Synthetic polylinker derived sequences
766 - 1842	Counter clockwise	*hppdPfW336-1Pa*: coding sequence of the 4-hydroxyphenylpyruvate dioxygenase gene of *Pseudomonas fluorescens* strain A32 modified by the replacement of the amino acid Glycine 336 with a Tryptophane (Boudec *et al.*, 2001), adapted to cotton codon usage
1843 - 2214	Counter closkwise	*TPotpY-1Pa:* coding sequence of an optimized transit peptide derivative (position 55 changed into Tyr), containing sequence of the RuBisCO small subunit genes of *Zea mays* and *Helianthus annuus* (Lebrun *et al.*, 1996), adapted for cotton codon usage
2215 - 2222		Synthetic polylinker derived sequences
2223 -	Counter	Pcsvmv: sequence including the promoter region of the Cassava Vein

Nt Positions	Orientation	Origin
2735	clockwise	Mosaic Virus (Verdaguer *et al.*, 1996)
2736 - 2795		Synthetic polylinker derived sequences
2796 - 2829	Clockwise	**lox:** sequence including the 34bp recognition sequence for the Cre recombinase of bacteriophage P1 (Hoess and Abremski, 1985)
2830 - 2833		Synthetic polylinker derived sequences
2834 - 3750		Ph4a748: sequence including the promoter region of the histone H4 gene of *Arabidopsis thaliana* (Chabouté *et al*., 1987)
3751 - 3789		Synthetic polylinker derived sequences
3790 - 4255	Clockwise	**intron1 h3At:** first intron of gene II of the histone H3.III variant of *Arabidopsis thaliana* (Chaubet *et al.*, 1992)
4256 - 4268		Synthetic polylinker derived sequences
4269 - 4640	Clockwise	*TPotpC:* coding sequence of the optimized transit peptide, containing sequence of the RuBisCO small subunit genes of *Zea mays* and *Helianthus annuus* (Lebrun *et al*., 1996)
4641 - 5978	Clockwise	*2mepsps:* coding sequence of the double-mutant 5-enol-pyruvylshikimate-3-phosphate synthase gene of *Zea mays* (Lebrun, M. et al., 1997)
5979 - 5998		Synthetic polylinker derived sequences
5999 - 6665	Clockwise	ThistonAt: sequence including the 3´ untranslated region of the histone H4 gene of *Arabidopsis thaliana* (Chabouté *et al*., 1987)
6666 - 6669		Synthetic polylinker derived sequences
6670 - 6703	Clockwise	**lox:** sequence including the 34bp recognition sequence for the Cre recombinase of bacteriophage P1 (Hoess and Abremski, 1985)
6704 - 6831		Synthetic polylinker derived sequences
6832 - 6856		**LB:** left border repeat from the T-DNA of *Agrobacterium tumefaciens* (Zambryski, 1988)

3.2. Information relating to the genetically modified plant

3.2.1. Description of the trait(s) and characteristics which have been introduced or modified

GHB811 cotton was developed through *Agrobacterium*-mediated transformation using the vector pTSIH09 containing *2mepsps* and *hppdPfW336-1Pa* expression cassettes. Expression of the 2mEPSPS protein confers tolerance to glyphosate herbicides. Expression of the HPPD W336 protein confers tolerance to HPPD inhibitors, such as isoxaflutole herbicides.

3.2.2. Information on the nucleic acid(s) sequences actually inserted or deleted

(a) The copy number of all detectable inserts, both complete and partial

GHB811 contains a single copy of the complete T-DNA, which consists of one copy of the *hppdPfW336-1Pa* gene cassette and one copy of the *2mepsps* gene cassette, at a single locus. No plasmid backbone sequences are present in GHB811 cotton.

(b) In case of deletion(s), size and function of the deleted region(s)

In the GHB811 insertion locus sequence, 13 bp were observed which are not present in the GHB811 transgenic locus. These base pairs were deleted during the transformation process.

(c) Subcellular location(s) of insert(s) (nucleus, chloroplasts, mitochondria, or maintained in a non-integrated form), and methods for its determination

The Southern blot results demonstrated that a single copy of the complete T-DNA was inserted at a single locus of the cotton GHB811 genome. The GHB811 cotton insert is integrated at the chromosome level as demonstrated by flanking sequence analysis and the Mendelian inheritance of a single gene locus.

(d) The organisation of the inserted genetic material at the insertion site

The GHB811 cotton insert as well as the 5' and 3' flanking regions have been sequenced and characterized in detail. The analyses demonstrated that the cotton GHB811 flanking sequences are of cotton origin within its original genomic organization. Annotation of the inserted sequences in the GHB811 transgenic locus sequence demonstrated that it corresponds to the complete T-DNA region of pTSIH09 and did not indicate any T-DNA rearrangements.

(e) In case of modifications other than insertion or deletion, describe function of the modified genetic material before and after the modification, as well as direct changes in expression of genes as a result of the modification

Not applicable

3.2.3. Information on the expression of the insert

(a) Information on developmental expression of the insert during the life cycle of the plant

The expression levels of 2mEPSPS and HPPD W336 proteins in different tissues of GHB811 cotton collected at different developmental stages were measured. The expression levels of 2mEPSPS and HPPD W336 proteins were similar between GHB811 cotton treated and not treated with the intended herbicides.

(b) Parts of the plant where the insert is expressed

Results of the analyses confirm expression of 2mEPSPS and HPPD W336 proteins throughout key development stages of GHB811 cotton. Fuzzy cottonseed is the raw agricultural commodity and represents the main point of entry of the material into the food and feed production and processing chain. Therefore, expression levels in fuzzy seeds is the most relevant for food and feed safety evaluation.

3.2.4. Genetic stability of the insert and phenotypic stability of the genetically modified plant

The genetic stability of the GHB811 transgenic locus was demonstrated by assessing individual GHB811 cotton plants from five generations by means of Southern blot analysis.

3.2.5. Information (for environmental safety aspects) on how the genetically modified plant differs from the recipient plant in

(a) Mode(s) and /or rate of reproduction

The herbicide tolerance traits have no effect on the mode and rate of reproduction.

(b) Dissemination

The tolerance to the herbicides glyphosate and HPPD inhibitors, such as isoxaflutole (IFT) has not affected dissemination characteristics of GHB811 cotton. GHB811 cotton retains the same

growth rate and growth habit as conventional cotton, continue to be self-pollinating plants and disperse their seed in the same way as conventional cotton.

(c) Survivability

For cultivated cotton, survival is mostly determined by seed characteristics. There is no indication of changes in the seed characteristics as a result of the genetic modification.

(d) Other differences

GHB811 cotton plants are tolerant to glyphosate and HPPD inhibitors, such as isoxaflutole (IFT).

3.2.6. Any change to the ability of the genetically modified plant to transfer genetic material to other organisms (for environmental safety aspects)

(a) Plant to bacteria gene transfer

The inserted sequences in GHB811 cotton are not providing different abilities to transfer genetic material compared to conventional cotton and no other elements in the inserts suggest that there could be an increase of the probability of homologous recombination. The likelihood that plant to bacteria gene transfers occurs is highly unlikely

(b) Plant to plant gene transfer

There is no evidence of genetic transfer and exchange under natural conditions with organisms other than those with which cotton is able to produce fertile crosses through sexual reproduction. There are no indications that the potential for successful exchange of genetic material has changed due to the genetic modification.

The scope of this application is for authorization of GHB811 cotton for food and feed uses and import and processing and does not include cultivation of GHB811 cotton in the EU. As a consequence, exposure to the environment will be very limited.

4. COMPARATIVE ANALYSIS

4.1. Choice of the conventional counterpart and additional comparators

In each field site GHB811 cotton was compared to its conventional counterpart as well as to other non-GM reference varieties.

4.2. Experimental design and statistical analysis of data from field trials for comparative analysis

The production of material for the comparative assessment of GHB811 cotton took place in fifteen field trials planted in 2014 and 2015 in the USA. The field locations were representative of the regions for cotton production in the USA and the field trials were conducted following typical agricultural practices.

For the comparative assessment of GHB811 cotton, the experimental design included GHB811 cotton treated with the intended herbicides, GHB811 cotton with conventional herbicide management and the conventional counterpart with conventional herbicide management. In addition, at least six non-GM reference varieties (conventional herbicide management) were included over the entire set of trials.

Each field location consisted of six cotton entries replicated four times resulting in 24 plots per trial planted in a randomized complete block design. In each field location 3 non-GM reference varieties were grown.

4.3. Selection of material and compounds for analysis

Fuzzy cottonseed is the raw agricultural commodity and represents the main point of entry of the material into the food and feed production and processing chain. The key constituents included in the compositional analysis were selected according to OECD recommendations.

The comparative assessment of compositional parameters identified no biological relevant differences and/or lack of equivalence between GHB811 cotton and its comparator, taking into account natural variation.

4.4. Comparative analysis of agronomic and phenotypic characteristics

A comparative assessment of the phenotypic and agronomic characteristics of GHB811 cotton and its conventional counterpart was performed, based on data collected at the fifteen field trials in the USA in 2014 and 2015 (the same field study used to collect samples for compositional analysis).

The comparative assessment of phenotypic and agronomic characteristics identified no biological relevant differences and/or lack of equivalence between GHB811 cotton and its comparator, taking into account natural variation.

4.5. Effect of processing

GHB811 cotton will be processed in the same way as any conventional commercial cotton. The effects of processing on GHB811 cotton are not expected to be different from the effects on conventional cotton.

GHB811cotton is not different from conventional cotton, except for the expressed 2mEPSPS and HPPD W336 proteins. During processing, proteins are subjected to harsh conditions that drastically change the physical forces leading to denaturation and loss of protein function. Processing using heat, for example cooking, high pressure steam, plus solvents and alkali treatments, will degrade the 2mEPSPS and HPPD W336 proteins. Thus, dietary exposure to functionally active proteins in processed food products can be negligible. Therefore, GHB811 cotton and its derived food and feed products are highly unlikely to be different from the equivalent foods and feeds from conventional cotton.

5. TOXICOLOGY

(a) Toxicological testing of the newly expressed proteins

GHB811 cotton expresses the proteins 2mEPSPS and HPPD W336. These 2 proteins have very specific activities, with different pathways in GHB811 cotton.

The available information for the assessment of the newly expressed proteins present in GHB811 cotton, indicates that no adverse effects on human or animal health are expected.

The EFSA GMO Panel has previously evaluated the safety of the HPPD W336 and 2mEPSPS proteins in the context of several applications for the placing on the EU market of GM crops expressing these proteins, and no safety concerns were identified.

(b) Testing of new constituents other than proteins

No new constituents other than the 2mEPSPS and HPPD W336 proteins are expressed in GHB811 cotton. The comparative assessment of GHB811 cotton showed no biologically relevant differences between GHB811 cotton and its conventional counterpart and/or lack of equivalence, taking into account natural variation. Therefore, there is no need for further assessment.

(c) Information on natural food and feed constituents

No relevant changes in the composition of GHB811 cotton were identified, therefore the levels of food and feed constituents in GHB811 cotton have not been altered and there is no need for further assessment

(d) Testing of the whole genetically modified food and feed

The molecular characterization of GHB811 demonstrated that the sequence of the insert is as intended, the insert does not disrupt any known endogenous genes and no proteins other than the intended proteins are likely to be produced, the event does not contain backbone sequences from the vector used for the transformation, the insert is stable over several generations and the segregation pattern follows the expected Mendelian inheritance rations and the expression of the insert is as intended. The comparative assessment of GHB811 cotton showed no biologically relevant differences between GHB811 cotton and its conventional counterpart and/or lack of equivalence, taking into account natural variation. The toxicological evaluation of the newly expressed proteins 2mEPSPS and HPPD W336 in GHB811 cotton did not identify potential adverse effects. Therefore, whole food and/or feed testing with GHB811 cotton is not deemed to be necessary. However, the submission of the 90-day study is a mandatory requirement, according to Commission Implementing Regulation (EU) No 503/2013 which is not triggered by any uncertainties identified in the course of the safety assessment. A 90-day feeding study in rodents was provided. Based on the results of this study, dietary administration of GHB811 cottonseed meal incorporated in the diet for 90 consecutive days had no adverse effects on the growth or health of Sprague Dawley rats.

6. ALLERGENICITY

(a) Assessment of allergenicity of the newly expressed proteins

The data provided lead to the conclusion that the 2mEPSPS and HPPD W336 proteins are unlikely to be allergenic.

The EFSA GMO Panel has previously evaluated the safety of the 2mEPSPS and HPPD W336 proteins in the context of other applications for the placing on the EU market of GM crops expressing these proteins, and no safety concerns were identified with respect to the 2mEPSPS and HPPD W336 proteins.

(b) Assessment of allergenicity of the whole genetically modified plant

Equivalence of GHB811 cotton (with the exception of the introduced traits) to the conventional counterpart has been demonstrated on the basis of the compositional analysis. The 2mEPSPS and HPPD W336 proteins expressed in GHB811 cotton are unlikely to be allergenic. Therefore, no increased allergenicity is anticipated for GHB811 cotton.

7. NUTRITIONAL ASSESSMENT

(a) Nutritional assessment of the genetically modified food

The genetic modifications in GHB811 cotton is not intended to change nutritional characteristics of GHB811 cotton compared to conventional cotton. Therefore, GHB811 cotton is not expected to be more or less attractive for use as food, so anticipated dietary intake of cottonseed-derived foods is not expected to be changed upon commercialization of GHB811 cotton.

Compositional analysis demonstrated that GHB811 cotton is not different from its conventional counterpart (identified differences were found not biologically relevant), expect for the introduced traits taking into account natural variation. Therefore, there is no need to carry out further nutritional studies with food derived from GHB811 cotton.

(b) Nutritional assessment of the genetically modified feed

The genetic modification in GHB811 cotton is not intended to change nutritional characteristics of GHB811 cotton compared to conventional cotton. Therefore, GHB811 cotton is not expected to be more or less attractive for use as feed.

Compositional analysis demonstrated that GHB811 cotton is not different from its conventional counterpart (identified differences were found not biologically relevant), except for the introduced traits taking into account natural variation. Therefore, there is no need to carry out further nutritional studies with feed derived from GHB811 cotton.

8. EXPOSURE ASSESSMENT – ANTICIPATED INTAKE/EXTENT OF USE

The intended traits in GHB811 cotton are herbicide tolerance, thus there was no intention to modify the nutritional parameters of GHB811 cotton. GHB811 cotton is not intended to be processed into products with enhanced functionality. The dietary role of GHB811 cotton will be the same as non-GM cotton. The use of food and feed derived from GHB811 cotton will be the same as food and feed from non-GM cotton. It is expected that the introduction of GHB811 cotton will replace some of the existing commercial cottonseed-derived products. Therefore, no change is expected in the consumption of cottonseed and cottonseed-derived products.

The dietary exposure of the European consumers to the GHB811 cotton and its newly expressed protein was considered to be negligible. The exposure assessment in animals indicates that there is minimal dietary exposure to 2mEPSPS and HPPD W336 proteins from consumption of feed derived from GHB811 cotton.

9. RISK CHARACTERISATION

A comprehensive risk characterization of GHB811 cotton has been carried out by considering all available evidence from the analyses discussed through the application. The following conclusions from molecular characterization, phenotypic and agronomic analyses, compositional analyses, toxicology assessment, allergenicity assessment, nutritional assessment and exposure assessment have been considered:

The molecular characterization of GHB811 cotton did not raise any safety concerns nor identified any unintended changes as a result of the genetic modification.

The comparative assessment for compositional endpoints established the comparability of GHB811 cotton to its conventional counterpart and equivalence of GHB811 cotton to the reference varieties. The results of the comparative assessment for agronomics and phenotypic

characteristics identified no biological relevant differences and/or lack of equivalence between GHB811 cotton and its comparator, taking into account natural variation. The comparative assessment of GHB811 cotton showed no differences for the agronomic and phenotypic characteristics and for the cottonseed composition parameters that would require further assessment with respect to their possible impact on food and feed safety and nutritional properties. Based on the results of the comparative assessment, it can be concluded that there are no unexpected or unintended effects and no impact on either the agronomic performance of the GHB811 cotton plants or the nutritional value of the cottonseed from GHB811 cotton as a result of the genetic modification of GHB811 cotton.

The assessment of the newly expressed proteins 2mEPSPS and HPPD W336 expressed in GHB811 cotton indicates that no adverse effects on human or animal health are expected. The results of the toxicological assessment indicate that consumption of GHB811 cotton food and feed products will be as safe as consumption of equivalent products from conventional cotton, regardless of the anticipated intake level.

The assessment of the newly expressed proteins 2mEPSPS and HPPD W336 proteins expressed in GHB811 cotton indicates that they are unlikely to be allergenic. There is no evidence to suggest that GHB811 cotton has greater allergenic potential compared to conventional commercial cotton varieties.

The comparative assessment of GHB811 cotton no indications of unintended changes in nutritional value due to the genetic modification have been observed. Therefore, the food and feed derived from GHB811 cotton is assumed to be nutritionally equivalent to food and feed derived from conventional cotton varieties.

The exposure assessment did not indicate any safety concerns.

The evidences presented throughout this application demonstrate that:

- The consumption of food and feed derived from GHB811 cotton is as safe as the respective comparators;
- The food derived from GHB811 cotton is not nutritionally disadvantageous for the consumer compared to the food which is intended to replace;
- The feed derived from GHB811 cotton is not nutritionally disadvantageous for animals compared to the feed which is intended to replace;
- The feed derived from GHB811 cotton does not harm or mislead the consumer by impairing distinctive features of the animal products compared to conventionally produced feed.

10. POST-MARKET MONITORING ON GENETICALLY MODIFIED FOOD/FEED

The risk characterization of GHB811 cotton has shown that the risk for potential adverse effects on human and animal health is negligible in the context of the intended uses of GHB811 cotton. It is therefore considered that there is no need for post marketing monitoring of food and feed derived from GHB811 cotton.

11. ENVIRONMENTAL ASSESSMENT

11.1. Mechanism of interaction between the genetically modified plant and target organisms

In this area of assessment, the main environmental concern, according to the EFSA ERA Guidance, is that target organisms develop resistance to the insect or pathogen tolerance traits expressed by the GM plant.

The scope of this application covers the import, processing and food and feed use of GHB811 cotton in the EU. According to the EFSA ERA Guidance:

"resistance development is only relevant for applications with scope cultivation of GM plants and not for applications restricted to import and processing of GM plants and their products"

Therefore, an assessment of the potential resistance development in target organisms resulting from the import, processing and food and feed use GHB811 cotton is not relevant for this application.

In addition, GHB811 cotton has been developed to confer tolerance to herbicides, no target organisms are associated with this product, and therefore an assessment of the potential resistance development in target organisms resulting from the import, processing and food and feed use GHB811 cotton is not relevant for this application.

11.2. Potential changes in the interactions of the genetically modified plant with the biotic environment resulting from the genetic modification

The scope of the application is for food and feed uses, import and processing and excludes cultivation. The environmental exposure is limited to accidental release of GHB811 cotton during transportation and processing for food and feed.

(a) Persistence and invasiveness

The traits introduced in GHB811 cotton do not alter the persistence and invasiveness characteristics. Since the agronomic and phenotypic studies presented in this application also show that GHB811 cotton does not differ in characteristics indicative of persistence and invasiveness from the conventional crop, it can be concluded that the genetic modification n GHB811 cotton does not result in potentially harmful changes in persistence and invasiveness characteristics with respect to the conventional crop.

(b) Selective advantage or disadvantage

The provided information demonstrates that the main factors limiting the survival and spread of the conventional crop are human dependence and frost tolerance. An assessment of the potential that the introduced traits confer selective advantage or disadvantage to the cotton has also been conducted. The 2mEPSPS and HPPD W336 proteins in GHB811 cotton confers herbicide tolerance to glyphosate and HPPD inhibitors such as isoxaflutole. Since these are not the main limiting factors for the survival of the crop outside agro-ecosystems, it is highly unlikely that the traits introduced will provide a selective advantage or disadvantage.

(c) Potential for gene transfer

The background data collected on horizontal gene transfer, the bioinformatics analysis, the molecular characterisation data gathered on GHB811 cotton and the results of the comparative safety assessment, allow a full risk characterisation. The conclusion is that the *2mepsps* and *hppdPfW336-1Pa* genes expressed in GHB811 cotton are unlikely to be transferred to microorganisms and, even if they were, this would not lead to human, animal or environmental

harm. Thus, the likelihood that the import, processing or food and feed use of GHB811 cotton will result in harm to humans or animals or the environment is "highly unlikely". Considering the function of the genes, the consequences of HGT can be considered "marginal". Therefore the risk will be negligible.

(d) Interactions between the genetically modified plant and target organisms

In this area of assessment, the main environmental concern, according to the EFSA ERA Guidance, is that target organisms develop resistance to the insect or pathogen tolerance traits expressed by the GM plant.

The scope of this application covers the import, processing and food and feed use of GHB811 cotton in the EU. According to the EFSA ERA Guidance:

"resistance development is only relevant for applications with scope cultivation of GM plants and not for applications restricted to import and processing of GM plants and their products"

Therefore an assessment of the potential resistance development in target organisms resulting from the import, processing and food and feed use GHB811 cotton is not relevant for this application.

In addition, GHB811 cotton has been developed to confer tolerance to herbicides, no target organisms are associated with this product, and therefore an assessment of the potential resistance development in target organisms resulting from the import, processing and food and feed use GHB811 cotton is not relevant for this application.

(e) Interactions of the genetically modified plant with non-target organisms

The scope of this application covers the import, processing and food and feed use of GHB811 cotton in the EU, no deliberate release of viable plant material in the EU environment is expected. Given the reproductive biology of cotton, it is highly unlikely that accidental spillage of viable plant material would result in feral populations in the EU. Therefore, an assessment of potential direct effects of GHB811 cotton on NTO populations is not relevant for this application. However, the assessment considers potential indirect adverse effects on NTO populations due to exposure through faeces of animals fed with GHB811 cotton.

Exposure to faeces of animals fed with GHB811 cotton would lead to very low levels. The newly expressed proteins are expressed at low levels in seed and they are readily degraded by enzymatic activity in the gastro-intestinal tract of animals. Only minimal amounts of these proteins will be present in animal faeces. There would subsequently be further degradation of these proteins due to microbial processes. Exposure of soil and water environments to these proteins from disposal of animal wastes is likely to be very low and localized. Thus exposure of potentially sensitive NTOs to the GHB811 cotton is likely to be very low and of no ecological relevance.

(f) Effects on human health

See point 9

(g) Effects on animal health

See point 9

(h) Effects on biogeochemical processes

The scope of this application covers the import, processing and food and feed use of GHB811 cotton in the EU. Cultivation of GHB811 cotton in the EU is not included in the scope. Although environmental exposure could occur through the accidental spillage of GHB811

cotton, or through manure or faeces of animals fed on GHB811 cotton, or through organic matter or by-products from GHB811 cotton, these routes of exposure would represent very low levels of exposure that would be limited spatially and temporally. It is highly unlikely that adverse effects on biogeochemical processes could occur. Therefore, an assessment of the impacts of GHB811 cotton on biogeochemical processes resulting from specific cultivation, management and harvesting techniques is not relevant given the scope of this application.

(i) Impacts of the specific cultivation, management and harvesting techniques

The scope of this application covers the import, processing and food and feed use of GHB811 cotton in the EU. Cultivation of GHB811 cotton in the EU is not included in the scope. Therefore, an assessment of the impacts of specific cultivation, management and harvesting techniques it is not relevant given the scope of this application.

11.3. Potential interactions with the abiotic environment

The scope of this application is the authorization of the GHB811 cotton for food and feed uses, and for import and processing in accordance with articles 5 and 17 of Regulation (EC) No 1829/2003. The scope of this application does not include cultivation of GHB811 cotton in the EU.

11.4. Risk characterisation

The ERA has been conducted following the requirements and methodology described in the EFSA Guidance documents. The baseline considered for this risk assessment is the use of conventional cotton in the EU, applying the concept of “familiarity”, where the fact that cotton is a common crop in the EU, previously used as food and feed for centuries and considered safe for human and animal health and the environment.

A comparative safety assessment has been conducted using a weight-of-evidence approach, considering molecular characterization data as well as expression, compositional and agronomic comparisons between the product and its conventional counterpart. This assessment has been used to establish whether unintended changes in the GM plant have occurred as a result of the genetic modification. The results of this comparative safety assessment demonstrated that the only differences of biological relevance identified between GHB811 cotton and the conventional counterpart are the intended traits. Despite the large number of parameters compared, no unintended differences of biological relevance were found. Therefore, the main focus of the ERA is potential harmful effects due to the intended traits.

An assessment whether GHB811 cotton will be more persistent than the conventional crop in agricultural habitats or more invasive in natural habitats has been conducted. The results of this assessment allowed the conclusion that the risk that the import, processing or food and feed use of GHB811 cotton in the EU will result in harm to sustainable agricultural production or biodiversity because of changes in persistence or invasiveness compared with the conventional crop is negligible.

An assessment whether the new genes present in GHB811 cotton could be transferred into micro-organisms and become integrated into their genome leading to adverse effects in human and animal health or the environment has been performed. The conclusion from this assessment was that it is very unlikely that these genes would become established in the genome of micro-organisms in the environment or human and animal digestive tract. In the very unlikely event that such a horizontal gene transfer would take place, no adverse effects on human and animal health or the environment are expected.

Potential interactions with target and non-target organisms that could lead to harmful environmental effects have also been assessed. The conclusion from these assessments is that adverse effects on sustainable agricultural production or biodiversity due to adverse effects on populations of NTOs as resulting from the import, processing or food and feed use GHB811 cotton will be negligible.

No assessment of adverse environmental effects due to changes in management practices or effects on biogeochemical processes has been performed since cultivation of GHB811 cotton is not within the scope of this application.

Finally, risks associated with the import, processing and food and feed use of GHB811 cotton in the EU on human and animal health, have been assessed. The conclusion from this assessment was that food and feed derived from GHB811 cotton is as safe for humans and animal consumption as food and feed derived from the conventional crop.

In summary the import, processing and food and feed use of GHB811 cotton in the EU will pose negligible risk to human and animal health or the environment. The uncertainties associated with this risk characterisation are very low and no long-term adverse environmental effects are expected.

12. ENVIRONMENTAL MONITORING PLAN

(a) General (risk assessment, background information)

As required by Article 5(5)(b) and 17(5)(b) of Regulation (EC) No 1829/2003 the proposed Post-Market Environmental Monitoring (PMEM) plan for GHB811 cotton has been developed according to the principles and objectives outlined in Annex VII of Directive 2001/18/EC and Decision 2002/811/EC establishing guidance notes supplementing Annex VII to Directive 2001/18/EC. The PMEM plan also takes into account the EFSA Scientific Opinion on guidance on the Post-Market Environmental Monitoring of genetically modified plants.

(b) Interplay between environmental risk assessment and monitoring

The scope of this application is the authorisation of GHB811 cotton for import, processing, food and feed use in the European Union (EU) under Regulation (EC) No 1829/2003. The scope of the application does not include authorisation for the cultivation of GHB811 cotton seed products in the EU.

An environmental risk assessment (ERA) was carried out for GHB811 cotton according to the principles laid down in Annex II to Directive 2001/18/EC and Decision 2002/623/EC establishing guidance notes supplementing Annex II to Directive 2001/18/EC and the EFSA guidance on the environmental risk assessment of genetically modified plants. The scientific evaluation of the characteristics of GHB811 cotton in the E.R.A. has shown that the risk for potential adverse effects on human and animal health or the environment is negligible in the context of the intended uses of GHB811 cotton.

(c) Case-specific genetically modified plant monitoring (approach, strategy, method and analysis)

The scientific evaluation of the characteristics of GHB811 cotton in the ERA has shown that the risk for potential adverse effects on human and animal health or the environment is negligible in the context of the intended uses of GHB811cotton. It is therefore considered that there is no need for case-specific monitoring.

(d) General surveillance of the impact of the genetically modified plant (approach, strategy, method and analysis)

General surveillance is not based on a particular hypothesis and it should be used to identify the occurrence of unanticipated adverse effects of the viable GMO or its use for human and animal health or the environment that were not predicted in the ERA.

The scope of this application is the authorisation of GHB811 cotton for import, processing, food and feed uses. The scope of the application does not include authorisation for the cultivation of GHB811 cotton seed products.

Therefore, exposure to the environment will be limited to unintended release of GHB811 cotton, which could occur for example via substantial losses during loading/unloading of the viable commodity including GHB811 cotton destined for processing into animal feed or human food products. Exposure can be controlled by clean up measures and the application of current practices used for the control of any adventitious cotton plants, such as manual or mechanical removal and the application of herbicides (with the exception of glyphosate and HPPD inhibitors, such as isoxaflutole (IFT)).

However and in order to safeguard against any adverse effects on human and animal health or the environment that were not anticipated in the ERA, general surveillance on GHB811 cotton will be undertaken for the duration of the authorisation. The general surveillance will take into consideration, and be proportionate to, the extent of imports of GHB811 cotton and use thereof in the Member States.

In order to increase the possibility of detecting any unanticipated adverse effects, a monitoring system will be used, which involves the authorisation holder and operators handling and using viable GHB811 cotton. The operators will be provided with guidance to facilitate reporting of any unanticipated adverse effect from handling and use of viable GHB811 cotton.

(e) Reporting the results of monitoring

In accordance with Regulation (EC) No 1829/2003, the authorisation holder is responsible to inform the European Commission of the results of the general surveillance.

If information that confirms an adverse effect of GHB811 cotton and that alters the existing risk assessment becomes available, the authorisation holder will immediately investigate and inform the European Commission. The authorisation holder, in collaboration with the European Commission and based on a scientific evaluation of the potential consequences of the observed adverse effect, will define and implement management measures to protect human and animal health or the environment, as necessary. It is important that the remedial action is proportionate to the significance of the observed effect.

The authorisation holder will submit an annual monitoring report including results of the general surveillance in accordance with the conditions of the authorisation. The report will contain information on any unanticipated adverse effects that have arisen from handling and use of viable GHB811 cotton.

The report will include a scientific evaluation of the confirmed adverse effect, a conclusion of the safety of GHB811 cotton and, as appropriate, and the measures that were taken to ensure the safety of human and animal health or the environment.

The report will also clearly state which parts of the provided information are considered to be confidential, together with a verifiable justification for confidentiality in accordance with Article 30 of Regulation (EC) No 1829/2003. Confidential parts of such report shall be submitted in separate documents.

13. DETECTION AND IDENTIFICATION TECHNIQUES FOR THE GENETICALLY MODIFIED PLANT

The method for detection, sampling and identification of GHB811 cotton has been submitted to the European Union Reference Laboratory for GM Food and Feed (EURL GMFF) of the Joint Research Centre of the European Commission (EC-JRC) for the purpose of experimental testing and validation.

Appropriate control samples have also been made available to the EURL.

14. INFORMATION RELATING TO PREVIOUS RELEASES OF THE GENETICALLY MODIFIED PLANT (FOR ENVIRONMENTAL SAFETY ASPECTS)

14.1. History of previous releases of the genetically modified plant notified under Part B of the Directive 2001/18/EC and under Part B of Directive 90/220/EEC by the same notifier

Field trials with GHB811 cotton have not been carried out in the EU.

(a) Notification number

(b) Conclusions of post-release monitoring

(c) Results of the release in respect to any risk to human health and the environment, submitted to the Competent Authority in accordance with Article 10 of Directive 2001/18/EC)

14.2. History of previous releases of the genetically modified plant carried out outside the Union by the same notifier

(a) Release country

Argentina, Chile, USA.

(b) Authority overseeing the release

Argentina: National Advisory Committee on Agricultural Biosafety (CONABIA) and the Secretary of Agriculture, Fisheries and Livestock

Chile: SAG

USA: United States Department of Agriculture (USDA)

(c) Release site

Information on the releases at:

Argentina: http://64.76.123.202/site/agregado_de_valor/biotecnologia/50-EVALUACIONES/index.php

Chile: http://www.sag.cl/ambitos-de-accion/organismos-geneticamente-modificados-ogm

USA: www.aphis.usda.gov/

(d) Aim of the release

Aim of the field releases: Regulatory trials, Trait development, and/or Seed increase

(e) Duration of the release

The generation time for cotton from planting to harvest, is 5 to 7 months in the primary growing areas.

(f) Aim of post-releases monitoring

Volunteer monitoring

(g) Duration of post-releases monitoring

From 6 months to 3 seasons, depending of the country

(h) Conclusions of post-release monitoring

Occurrence of volunteers is very infrequent and no different from cotton derived through conventional breeding practices.

(i) Results of the release in respect to any risk to human health and the environment

No risk to human health or the environment has been indicated by the field release experience