Part VII - Summary

Request for Authorization of genetically modified insect resistant and herbicide tolerant cotton

GHB614 x T304-40 x GHB119

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

EFSA-GMO-NL-2014-XXX

Version CC1

Submitted on
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PART VII – SUMMARY

EFSA-GMO-NL-2014-XXX (GHB614 x T304-40 x GHB119)

1. GENERAL INFORMATION

1.1. Details of application

(a) Member State of application

The Netherlands

(b) Application number

Not available at the time of submission (EFSA-GMO-NL-2014-XXX)

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

GHB614 x T304-40 x GHB119, also known as GLT or GlyTol x TwinLink

(d) Date of acknowledgement of valid application

Not available at the time of submission

1.2. Applicant

(a) Name of applicant

Bayer CropScience LP

(b) Address of applicant

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

Bayer CropScience N.V. is the contact for this submission and all correspondence should be directed to:

Bayer CropScience N.V.
Seeds – Regulatory Affairs
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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

GHB614 x T304-40 x GHB119 cotton has been authorized for import in Canada, Japan, Korea and Mexico. GHB614 x T304-40 x GHB119 cotton has been authorized for cultivation in Mexico (under permit) and Brazil.

In the USA since the parental events are authorized, GHB614 x T304-40 x GHB119 cotton can be cultivated.

1.8. General description of the product

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

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton. GHB614 x T304-40 x GHB119 cotton (OECD ID: BCS-GHØØ2-5 x BCS-GHØØ4-7 x BCS-GHØØ5-8) contains the stably integrated *2mepsps* gene which confers tolerance to the herbicide glyphosate, the *bar* gene which confers tolerance to the herbicide glufosinate ammonium, the *cry1Ab* and the *cry2Ae* genes which confer resistance to certain lepidopteran pests. The *2mepsps* gene was introduced in the GHB614 cotton genome, the *pat* and the *cry1Ab* genes were introduced in the T304-40 cotton genome and the *pat* and the *cry2Ae* genes were introduced in the GHB119 cotton genome.

(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.

GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 authorization, will be used as any other commercial cotton, with the exception of cultivation.

GHB614 x T304-40 x GHB119 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 cottonseeds – whole cottonseeds, oil and meal.

This application requests import and processing only and does not include cultivation of GHB614 x T304-40 x GHB119 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, meal and other products derived from GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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.

GHB614 x T304-40 x GHB119 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 then (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.

GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton in the cotton supply, the introduced traits have only an agronomical benefit. It is anticipated that the introduction of GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton. It is anticipated that the introduction of GHB614 x T304-40 x GHB119 cotton will replace some of the existing cotton derived products.

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

OECD code: BCS-GHØØ2-5 x BCS-GHØØ4-7 x BCS-GHØØ5-8

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.

GHB614 x T304-40 x GHB119 cotton is resistant to certain lepidopteran pests and tolerant to herbicide products having glyphosate and/or glufosinate as the active ingredients. GHB614 x T304-40 x GHB119 cotton remains susceptible to a wide variety of other herbicides and GHB614 x T304-40 x GHB119 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*

(c) Species: *hirsutum*

(d) Subspecies: Not applicable

(e) Cultivar/breeding line: GHB614, T304-40, GHB119

(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. Cotton production has increased over the last few years, going from 102.8 million bales in 2009/10 to 117.1 million bales in 2013/14.

In Europe, the cultivated cotton is mainly *G. hirsutum*. No wild relatives have been reported. Currently, cotton is produced only in three Members States in the EU. Greece is the main cotton grower, followed by Spain and limited production in Bulgaria

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.

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

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton.

Agrobacterium tumefaciens mediated transformation was used in the development of the parental lines GHB614, T304-40 and GHB119.

(b) Nature and source of the vector used

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton.

For GHB614, the plasmid vector used was pTEM2.

For T304-40, the plasmid vector used was pTDL008.

For GHB119, the plasmid vector used was pTEM12.

(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

GHB614 x T304-40 xGHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton. The DNA inserts in GHB614 x T304-40 x GHB119 cotton are inherited from GHB614, T304-40 and GHB119. Information on the genetic elements in GHB614, T304-40 and GHB119 are provided below.

Size, source and intended function of each constituent component of the inserted DNA fragment inherited from GHB614

Genetic Element	Description	Source	Size (bp)	Intended function
LB	T-DNA left border sequence	*Agrobacterium tumefaciens*	4	T-DNA integration
Ph4a748At	Promoter region of the histone H4 gene	*Arabidopsis thaliana*	1010	High level constitutive expression, especially in the rapidly growing plant tissues
intron1 h3At	Sequence of the first intron of the histone H3.III	*Arabidopsis thaliana*	516	
TPotpC	Transit peptide	*Zea mays* and *Helianthus annuus*	372	Targeting of the protein to the plastids
2mepsps	Coding sequence of the modified 5-enol-pyruvylshikimate-3-phosphate synthase gene	*Zea mays*	1337	Glyphosate herbicide tolerance and selectable marker
3'histon At	3´ untranslated region of the histone H4 gene	*Arabidopsis thaliana*	742	Transcription termination signal

RB	T-DNA right border sequence	*Agrobacterium tumefaciens*	4	T-DNA integration

Size, source and intended function of each constituent component of the inserted DNA fragment inherited from T304-40

Symbol	**Definition**	**Source**	**Size (bp)**	**Function**
LB	Left border repeat	*Agrobacterium tumefaciens*	24	*Cis*-acting element for T-DNA transfer
3'me1	Terminating signal of *cry1Ab* gene	*Flaveria bidentis*	936	Stop signal
cry1Ab	Insect resistance *cry1Ab* gene	*Bacillus thuringiensis*	1853	Insect resistance
5'e1	Leader sequence	*Oryza sativa*	60	High level constitutive expression, especially in cotton leaves and squares
Ps7s7	Duplicated promoter	subterranean clover stunt virus	1041	
P35S3	Promoter	cauliflower mosaic virus	857	High level constitutive expression
bar	Glufosinate ammonium-tolerance *bar* gene	*Streptomyces hygroscopicus*	551	Herbicide tolerance and selectable marker
3'nos	Terminating signal of *bar* gene	*Agrobacterium tumefaciens*	309	Stop signal
RB	Right border repeat	*Agrobacterium tumefaciens*	24	*Cis*-acting element for T-DNA transfer

Size, source and intended function of each constituent component of the inserted DNA fragment inherited from GHB119

Definition / Source	**Size (bp)**	**Function**
Left border repeat from *Agrobacterium tumefaciens*	24	*Cis*-acting element for T-DNA transfer
Terminating signal (3'nos) of *bar* gene from *Agrobacterium tumefaciens*	309	Stop signal
Glufosinate ammonium-tolerance *bar* gene from *Streptomyces hygroscopicus*	551	Herbicide tolerance and selectable marker
Promoter (PcsvmvXYZ) from cassava vein mosaic virus	535	High level constitutive expression
Promoter (P35S2) from cauliflower mosaic virus	476	High level constitutive expression, especially in cotton green tissue
Leader sequence (5'cab22L) from *Petunia hybrida*	69	
Transit peptide (TPssuAt) from *Arabidopsis thaliana*	164	Targeting of the protein to the plastids
Insect resistance *cry2Ae* gene*Bacillus thuringiensis*	1895	Insect resistance
Terminating signal (3'35S) of *cry2Ae* gene cauliflower mosaic virus	268	Stop signal
Right border repeat from *Agrobacterium tumefaciens*	24	*Cis*-acting element for T-DNA transfer

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

GHB614 x T304-40 xGHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton.

The following traits have been inherited from the respective parental lines in GHB614 x T304-40 x GHB119 cotton:

Resistance to certain lepidopteran pests

The resistance to certain lepidopteran pest trait in GHB614 x T304-40 x GHB119 cotton is inherited from the parental lines T304-40 and GHB119.

T304-4 produces the *Bacillus thuringiensis* subsp. Berliner Cry1Ab protein (encoded by the *cry1Ab* gene) that is effective in controlling lepidopteran larvae such as cotton bollworm (CBW) and tobacco budworm (TBW), which are common pest of cotton.

GHB119 produces the *Bacillus thuringiensis* subsp. Dakota Cry2Ae protein (encoded by the *cry2Ae* gene) that is effective in controlling lepidopteran plant feeding larvae such as cotton bollworm (CBW), tobacco dubworm (TBW) and fall army worm (FAW), which are common pest of in cotton crop.

Tolerance to glyphosate herbicide

The glyphosate herbicide tolerance trait in GHB614 x T304-40 x GHB119 cotton is inherited from the parental line GHB614.

GHB614 cotton contains the *2mepsps* gene, which encodes a modified 5-enolpyruvylshikimate 3-phosphate synthase (2mEPSPS). The 2mEPSPS protein confers tolerance to the herbicide glyphosate.

Tolerance to glufosinate ammonium herbicide

The glufosinate ammonium herbicide tolerance trait in GHB614 x T304-40 x GHB119 cotton is inherited from the parental lines T304-40 and GHB119.

T304-40 and GHB119 contain the *bar* gene. The *bar* gene has been isolated from *Streptomyces hygroscopicus*, a microorganism that produces bialaphos. Bialaphos or its synthetically produced component glufosinate ammonium has phosphinothricin as the active ingredient. Phosphinothricin acts by the inhibition of a specific amino acid biosynthesis pathway in plants. Phosphinothricin based herbicides (glufosinate ammonium) are highly effective against plants. The *bar* gene, when expressed, enables the production of the enzyme, Phosphinothricin-Acetyl-Transferase (PAT/*bar*) that acetylates L-glufosinate ammonium and thereby confers tolerance to glufosinate ammonium herbicides.

The combination of the insecticidal crystal proteins Cry1Ab (from T304-40) and Cry2Ae (from GHB119) provide enhanced insect control and offer an additional insect-resistance management tool for growers. The dual herbicide tolerance to glyphosate herbicides (from GHB614) and glufosinate-ammonium herbicides (from T304-40 and GHB119) also offers growers additional weed control options.

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

Southern blot analysis of GHB614 x T304-40 x GHB119 cotton confirmed the presence of GHB614, T304-40 and GHB119 DNA inserts in GHB614 x T304-40 x GHB119 cotton.

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

Not applicable. GHB614 x T304-40 xGHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods

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

As supported by the Southern blot analysis of GHB614 x T304-40 x GHB119 cotton, the inserted DNA fragments from the parental lines, GHB614, T304-40 and GHB119 are inherited in GHB614 x T304-40 x GHB119 cotton.

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

Since the inserts in the single events GHB614, T304-40 and GHB119 were retained in GHB614 x T304-40 x GHB119 cotton, the characteristics of the insertions and the 5' and 3' flanking sequences should be conserved in GHB614 x T304-40 x GHB119 cotton.

(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

Expression levels of 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2Ae proteins were analysed in various plant tissues (root, leaf, squares, pollen, bolls, whole plants and seeds) at different growth stages of GHB614 x T304-40 x GHB119 cotton. As expected, the 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2Ae proteins were detected in the analysed GHB614 x T304-40 x GHB119 cotton tissues. In this application, the expression in seeds is considered, since is the part of the cotton plant relevant to the scope of this application.

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

The 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2Ae proteins content was determined in root, leaf, squares, pollen, bolls, whole plants and seeds. In this application, the expression in seeds is considered, since is the part of the cotton plant relevant to the scope of this application. The expression level of 2mEPSPS, PAT/bar, Cry1Ab and Cry2Ae proteins was determined in GHB614 x T304-40 x GHB119 cotton seed harvested from field grown plants in the USA.

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

The results of the Southern blot analysis of GHB614 x T304-40 x GHB119 cotton demonstrated the stability of the inserted sequences of GHB614, T304-40 and GHB119 in GHB614 x T304-40 x GHB119 cotton, and confirmed that no detectable rearrangements of these inserts occurred.

The results of the analysis of 2mEPSPS, Cry1Ab and Cry2Ae proteins in GHB614 x T304-40 x GHB119 cotton showing comparable levels to the expression in the single parental lines GHB614, T304-40 and GHB119 and higher levels for PAT/*bar* protein, which was due to the presence of two copies of the *bar* gen (one from T304-40 and one from GHB119), confirmed the phenotypic stability of GHB614 x T304-40 x GHB119 cotton.

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 and lepidopeteran pest resistance traits have no effect on the mode and rate of reproduction.

(b) Dissemination

The tolerance to the herbicides glyphosate, glufosinate and resistance to certain lepidopteran pest has not affected dissemination characteristics. GHB614 x T304-40 x GHB119 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

GHB614 x T304-40 x GHB119 cotton plants are tolerant to glyphosate and glufosinate and resistant to certain lepidopteran pest.

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

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. Therefore the inserted DNA fragments from the parental lines are inherited in GHB614 x T304-40 x GHB119 cotton. The inserted sequences in the single events 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 stacking of the single events using conventional breeding techniques has not resulted in any alteration on the inserts in GHB614 x T304-40 x GHB119 cotton. Therefore, the likelihood that plant to bacteria gene transfer 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 GHB614 x T304-40 x GHB119 cotton for food and feed uses and import and processing and does not include cultivation of GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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

Description of the experimental design (Number of locations, growing seasons, geographical spread, replicates and number of commercial varieties in each location) and of the statistical analysis:

The production of material for the comparative assessment of GHB614 x T304-40 x GHB119 cotton took place in eight field trials planted in 2012 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 GHB614 x T304-40 x GHB119 cotton, the experimental design included GHB614 x T304-40 x GHB119 cotton treated with the intended herbicides, GHB614 x T304-40 x GHB119 cotton with conventional herbicide management and the conventional counterpart with conventional herbicide management. In addition, 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. Fuzzy cottonseeds were analysed for proximates, fibre fractions, minerals, tocopherols, anti-nutrients, total amino acids, and total fatty acids.

The comparative assessment of compositional parameters identified no biological relevant differences and/or lack of equivalence between GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton and its conventional counterpart was performed, based on data collected at the eight field trials in the USA in 2012 (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 GHB614 x T304-40 x GHB119 cotton and its comparator, taking into account natural variation.

4.5. Effect of processing

The effects of processing on GHB614 x T304-40 x GHB119 cotton are not expected to be different from the effects on conventional cotton.

GHB614 x T304-40 x GHB119 cotton is not different from conventional cotton, except for the expressed 2mEPSP, PAT/*bar*, Cry1Ab and Cry2Ae 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, PAT/*bar*, Cry1Ab and Cry2Ab proteins. Thus, dietary exposure to functionally active proteins in processed food products can be negligible. Therefore, GHB614 x T304-40 x GHB119 cotton and its derived food and feed products are highly unlikely to be different from the equivalent foods and feeds from conventional cotton and as a consequence, toxicological tests with GHB614 x T304-40 x GHB119 cotton processed products are not scientifically justified.

5. TOXICOLOGY

(a) Toxicological testing of the newly expressed proteins

GHB614 x T3.04-40 x GHB119 cotton expresses the proteins 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2A. These 4 proteins have very specific activities, with different pathways in GHB614 x T304-40 x GHB119 cotton.

The available information for the assessment of the newly expressed proteins present in GHB614 x T304-40 x GHB119 cotton, indicates that no adverse effects on human or animal health are expected. Furthermore, in absence of indications of potential interactions between the 4 proteins as well as between the GHB614, T304-40 and GHB119 events, as suggested in the molecular analysis and comparative assessment, the conclusions of the safety assessment for the individual 2mEPSPS, PAT/bar, Cry1Ab and Cry2A proteins are not changed when their expression in GHB614 x T304-40 x GHB119 cotton is considered.

(b) Testing of new constituents other than proteins

No new constituents other than the 2mEPSPS, PAT/bar, Cry1Ab and Cry2A proteins are expressed in GHB614 x T304-40 x GHB119 cotton. The comparative assessment of GHB614 x T304-40 x GHB119 cotton showed no biologically relevant differences between GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton were identified, therefore the levels of food and feed constituents in GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton demonstrated the integrity of the inserts in GHB614 x T304-40 x GHB119 cotton when compared to the single parental lines. The comparative assessment of GHB614 x T304-40 x GHB119 cotton showed no biologically relevant differences between GHB614 x T304-40 x GHB119 cotton and its conventional counterpart and/or lack of equivalence, taking into account natural variation. Therefore, there are not indications of possible interactions between GHB614, T304-40 and GHB119 events in GHB614 x T304-40 x GHB119 cotton and whole food and/or feed testing with GHB614 x T304-40 x GHB119 cotton is not deemed necessary.

6. ALLERGENICITY

(a) Assessment of allergenicity of the newly expressed protein

The data provided lead to the conclusion that the 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2Ae proteins are unlikely to be allergenic. In addition, there is no evidence that there could be interactions between these 4 proteins that would lead to additive, synergistic or antagonistic activities. Therefore, Bayer CropScience considers it to be unlikely that potential interactions could occur that would change the allergenicity of these proteins in GHB614 x T304-40 x GHB119 cotton.

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

Equivalence of GHB614 x T304-40 x GHB119 cotton (with the exception of the introduced traits) to the conventional counterpart has been demonstrated on the basis of the compositional analysis. The 2mEPSP, PAT/*bar*, Cry1Ab and Cry2Ae proteins expressed in GHB614 x T304-40 x GHB119 cotton are unlikely to be allergenic. Therefore no increased allergenicity is anticipated for GHB614 x T304-40 x GHB119 cotton.

7. NUTRITIONAL ASSESSMENT

(a) Nutritional assessment of the genetically modified food

The genetic modifications in GHB614 x T304-40 x GHB119 cotton are not intended to change nutritional characteristics of GHB614 x T304-40 x GHB119 cotton compared to conventional cotton. Therefore GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

Compositional analysis demonstrated that GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

(b) Nutritional assessment of the genetically modified feed

The genetic modifications in GHB614 x T304-40 x GHB119 cotton are not intended to change nutritional characteristics of GHB614 x T304-40 x GHB119 cotton compared to conventional cotton. Therefore GHB614 x T304-40 x GHB119 cotton is not expected to be more or less attractive for use as feed.

Compositional analysis demonstrated that GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

8. EXPOSURE ASSESSMENT – ANTICIPATED INTAKE/EXTENT OF USE

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single cotton parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. The intended traits are insect resistance and herbicide tolerance, therefore not intended to modify the nutritional parameters of GHB614 x T304-40 x GHB119 cotton. GHB614 x T304-40 x GHB119 cotton is not intended to be processed into products with enhanced functionality. The dietary role of GHB614 x T304-40 x GHB119 cotton will be the same as non-GM cotton. The use of the food

and feed derived from GHB614 x T304-40 x GHB119 cotton will be the same as food and feed from non-GM cotton. It is expected that the introduction of GHB614 x T304-40 x GHB119 cotton will replace some of the existing commercial cotton-derived products. Therefore, no change is expected in the consumption of cotton and cotton-derived products.

The exposure assessment in humans and animals indicates that there is minimal dietary exposure to 2mEPSPS, PAT/*bar*, Cry1Ab and Cry2Ae from consumption of foods and feed derived from GHB614 x T304-40 x GHB119 cotton.

9. RISK CHARACTERISATION

GHB614 x T304-40 x GHB119 cotton was developed by crossing the single parental lines GHB614, T304-40 and GHB119 using traditional breeding methods. No new genetic modification was introduced in GHB614 x T304-40 x GHB119 cotton. GHB614, T304-40 and GHB119 have been previously assessed in applications EFSA-GMO-NL-2008-51, EFSA-GMO-NL-2011-97 and EFSA-GMO-NL-2011-96 respectively.

A comprehensive risk characterization of GHB614 x T304-40 x GHB119 cotton has been carried out by considering all available evidence from the analyses discussed through this application. The following conclusions from molecular characterization, phenotypic and agronomic analyses, compositional analyses, toxicology assessment, allergenicity assessment and exposure assessment have been considered:

•Southern analyses demonstrated that the structures of the inserts in the single events GHB614, T304-40 and GHB119 were retained in GHB614 x T304-40 x GHB119 cotton.

Expression studies show that the mean 2mEPSPS, Cry1Ab and Cry2Ae protein levels in GHB614 x T304-40 x GHB119 cotton seeds are comparable to the protein levels in each single event GHB614, T304-40 and GHB119 respectively. The PAT/bar protein content is higher than in either parental event (T304-40 or GHB119) which is due to the presence of two copies of the bar gene expressing in GHB614 x T304-40 x GHB119 (one copy in event T304-40 and one copy in event GHB119). Consequently the stacking of the three single parental events does not alter the expression of the inserted genes and therefore there is no evidence of interactions between the inserts.

Bioinformatics analysis of GHB614, T304-40 and GHB119 5’ and 3’ flanking regions did not provide any evidence that functional endogenous genes or ORFs were interrupted upon transformation in GHB614, T340-40 and GHB119. In GHB614, T340-40 and GHB119 inserted sequences there are neither allergenic nor toxicological *in silico* findings associated with the presence of the putative ORF polypeptides or putative products of predicted genes.

No unintended changes and no indications of potential interactions between the single events or between the newly expressed proteins were identified. Therefore it can be concluded that the molecular characterization of GHB614 x T304-40 x GHB119 cotton did not indicate safety concerns or potential interactions and there is no evidence of unintended changes in GHB614 x T304-40 x GHB119 cotton.

•The comparative assessment of GHB614 x T304-40 x GHB119 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.

The comparative analysis showed that most composition parameters determined for the GHB614 x T304-40 x GHB119 cottonseeds that were found to be different from the conventional counterpart were equivalent or “more” likely equivalent to the reference varieties. Three composition parameters were found to be different between GHB614 x T304-40 x

GHB119 cotton and its conventional counterpart and "less likely" or not equivalent to the reference varieties. However, the mean values of these composition parameters were within the minimum to maximum range of the six non-GM commercial reference varieties and within the ranges reported from literature. The absolute differences between the mean values of the conventional counterpart and of the GHB614 x T304-40 x GHB119 cotton were lower than the variation within the conventional counterpart entry. Hence, the differences found were considered to be not biologically relevant. Therefore, no further assessment is needed as the kind and magnitude of the observed differences have no relevance from a health and nutrition point of view.

Based on the comparative analysis of the agronomic and phenotypic characteristics as well as of composition parameters, it can be concluded that there are no unexpected and unintended effects and no impact on the agronomic performance of the cotton plants and the nutritional value of the cottonseed from GHB614 x T304-40 x GHB119 cotton as a result of the genetic modification of the parental events GHB614, T304-40 and GHB119 and their stacking by conventional plant breeding techniques. No indications of interactions between the events GHB614, T304-40 and GHB119 stacked in GHB614 x T304-40 x GHB119 cotton were identified.

•The available information for the assessment of the newly expressed proteins present in GHB614 x T304-40 x GHB119 cotton indicates that no adverse effects on human or animal health are expected. Furthermore, in absence of interactions between the 4 proteins as well as between the GHB614, T304-40 and GHB119 events, as suggested in the molecular analysis and comparative assessment, the conclusions of the safety assessment for the individual 2mEPSPS, PAT/bar, Cry1Ab and Cry1Ae proteins are not changed when their expression in GHB614 x T304-40 x GHB119 cotton is considered.

The results of the toxicological assessment indicate that consumption of GHB614 x T304-40 x GHB119 cotton food and feed products will be as safe as consumption of equivalent products from conventional cotton, regardless of the anticipated intake level.

•The 2mEPSPS, PAT/bar, Cry1Ab and Cry2Ae proteins expressed in GHB614 x T304-40 X GHB119 cotton have been evaluated previously and it was found unlikely that they are allergenic.

The bioinformatics results demonstrated there were no biologically relevant sequence similarities to allergens when 2mEPSPS, PAT/bar, Cry1Ab and Cry2Ae protein sequences were used as query sequences for a FASTA search against the allergen database.

There is no evidence to suggest that GHB614 x T304-40 x GHB119 cotton has greater allergenic potential compared to conventional commercial cotton varieties.

•In the comparative assessment of GHB614 x T304-40 x GHB119 cotton no indications of unintended changes in nutritional value due to the combination of the single parental lines have been observed. Therefore the food and feed derived from GHB614 x T304-40 x GHB119 cotton is assumed to be nutritionally equivalent to food and feed derived from conventional cotton varieties. The genetic modifications in GHB614 x T304-40 x GHB119 cotton are not intended to change nutritional characteristics of GHB614 x T304-40 x GHB119 cotton compared to conventional cotton. Therefore, GHB614 x T304-40 x GHB119 cotton is not expected to be more or less attractive for use as food and/or feed, so anticipated dietary intake of cottonseed-derived foods and feeds is not expected to be changed upon commercialization of GHb614 x T304-40 x GHB119 cotton. The dietary role of GHB614 x T304-40 x GHB119 cotton will be the same as of non-GM cotton.

•The exposure assessment in humans and animals indicates that there is minimal dietary exposure to 2mEPSPS, PAT/bar, Cry1Ab and Cry2Ae from consumption of foods and feed derived from GHB614 x T304-40 x GHB119 cotton.

The evidences presented throughout this application and summarized above demonstrate that:

- The consumption of food and feed derived from GHB614 x T304-40 x GHB119 cotton is as safe as the respective comparators
- The food derived from GHB614 x T304-40 x GHB119 cotton is not nutritionally disadvantageous for the consumer compared to the food which is intended to replace
- The feed derived from GHB614 x T304-40 x GHB119 cotton is not nutritionally disadvantageous for animals compared to the feed which is intended to replace
- The feed derived from GHB614 x T304-40 x GHB119 cotton does not harm or mislead the consumer by impairing distinctive features of the animal products compared to conventionally produced feed.

The assumptions made during the risk assessment are very conservative and include the following: all cottonseeds consumed in the EU would be from GHB614 x T304-40 x GHB119 cotton plants, and no loss or degradation of protein would occur during processing and food preparation of cottonseed products.

The labelling requirements specified in Articles 5(3)(f) and 17(3)(f) of Regulation (EC) No 1829/2003 are not applicable because the characteristics of the food and feed products from GHB614 x T304-40 x GHB119 cotton are not different from the characteristics of its conventional counterpart taking into account natural variation.

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

The risk characterization of GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton. It is therefore considered that there is no need for post marketing monitoring of food and feed derived from GHB614 x T304-40 x GHB119 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..

GHB614 x T304-40 x GHB119 cotton has been developed to confer resistance to certain lepidopteran pest and tolerance to herbicides. The scope of this application covers the import, processing and food and feed use of GHB614 x T304-40 x GHB119 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 of GHB614 x T304-40 x GHB119 cotton is not relevant for this application. Even considering a scenario where accidental spillage of viable material of GHB614 x T304-40 x GHB119 cotton occurred and some plants grew in the EU, the levels of exposure would be low and limited temporally and spatially. The likelihood of target organisms developing resistance under this scenario would be “highly unlikely” and any consequences on target organism populations would be “marginal”, therefore the risk would be “negligible”.

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 GHB614 x T304-40 x GHB119 cotton during transportation and processing for food and feed.

(a) Persistence and invasiveness

The persistence and invasiveness of each of the single events present in GHB614 x T304-40 x GHB119 cotton have been previously assessed. The conclusion was that the genetic modification introduced in each of these events does not alter the persistence and invasiveness characteristics of these single events in the EU. Since the agronomic and phenotypic studies presented in this application also show that GHB614 x T304-40 x GHB119 cotton does not differ in characteristics indicative of persistence and invasiveness from the conventional crop, it can be concluded that the stacking of GHB614, T304-40 and GHB119 using conventional breeding techniques does not result in a stacked trait product with 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, PAT/*bar*, Cry1Ab and Cry2Ae proteins in GHB614 x T304-40 x GHB119 cotton confers resistance to specific lepidopteran pests and herbicide tolerance to glyphosate and glufosinate ammonium herbicides. 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 GHB614 x T304-40 x GHB119 cotton and the results of the comparative safety assessment, allow a full risk characterisation. The conclusion is that the *2mepsps*, *bar*, *cry1Ab* and *cry2Ae* genes expressed in GHB614 x T304-40 x GHB119 cotton are unlikely to be transferred to micro-organisms 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 GHB614 x T304-40 x GHB119 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..

GHB614 x T304-40 x GHB119 cotton has been developed to confer resistance to certain lepidopteran pest and tolerance to herbicides. The scope of this application covers the import, processing and food and feed use of GHB614 x T304-40 x GHB119 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 of GHB614 x T304-40 x GHB119 cotton is not relevant for this application. Even considering a scenario where accidental spillage of viable material of GHB614 x T304-40 x GHB119 cotton occurred and some plants grew in the EU, the levels of exposure would be low

and limited temporally and spatially. The likelihood of target organisms developing resistance under this scenario would be "highly unlikely" and any consequences on target organism populations would be "marginal", therefore the risk would be "negligible".

(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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

Exposure to faeces of animals fed with GHB614 x T304-40 x GHB119 cotton would lead to very low levels of environmental exposure. 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 (e.g. coprophagous Coleoptera species) to the GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton in the EU. Cultivation of GHB614 x T304-40 x GHB119 cotton in the EU is not included in the scope. Although environmental exposure could occur through the accidental spillage of GHB614 x T304-40 x GHB119 cotton, or through manure or faeces of animals fed on GHB614 x T304-40 x GHB119 cotton, or through organic matter or by-products from GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton in the EU. Cultivation of GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 combination of the single events or interactions between the gene products. The results of this comparative safety assessment demonstrated that the only differences of biological relevance identified between GHB614 x T304-40 x GHB119 cotton and the conventional counterpart are the intended traits. Despite the large number of parameters compared, no unintended differences of biological relevance were found. Thus the exposure and hazard assessment conducted for the single events have been used to support the ERA of GHB614 x T304-40 x GHB119 cotton.

An assessment whether GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton in the EU will result in harm to sustainable agricultural production or biodiversity as a result of changes in persistence or invasiveness compared with the conventional crop is negligible.

An assessment whether the new genes present in GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton is not within the scope of this application.

Finally, risks associated with the import, processing and food and feed use of GHB614 x T304-40 x GHB119 cotton in the EU on human and animal health, have been assessed. The conclusion from this assessment was that food and feed derived from GHB614 x T304-40 x

GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton seed products in the EU.

An environmental risk assessment (e.r.a.) was carried out for GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

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

The scientific evaluation of the characteristics of GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton. 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 e.r.a.

The scope of this application is the authorisation of GHB614 x T304-40 x GHB119 cotton for import, processing, food and feed uses. The scope of the application does not include authorisation for the cultivation of GHB614 x T304-40 x GHB119 cotton seed products.

Therefore, exposure to the environment will be limited to unintended release of GHB614 x T304-40 x GHB119 cotton, which could occur for example via substantial losses during

loading/unloading of the viable commodity including GHB614 x T304-40 x GHB119 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 glufosinate).

However and in order to safeguard against any adverse effects on human and animal health or the environment that were not anticipated in the e.r.a., general surveillance on GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton. The operators will be provided with guidance to facilitate reporting of any unanticipated adverse effect from handling and use of viable GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 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 GHB614 x T304-40 x GHB119 cotton.

The report will include a scientific evaluation of the confirmed adverse effect, a conclusion of the safety of GHB614 x T304-40 x GHB119 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 detection method for GHB614 x T304-40 x GHB119 cotton is based on the validated detection methods that are available for GHB614, T304-40 and GHB119 (http://gmo-crl.jrc.ec.europa.eu/gmomethods/).

The method for detection, sampling and identification of GHB614 x T304-40 x GHB119 cotton has been submitted to the European Union Reference Laboratory (EURL) 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.

13.1. 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

(a) Notification number

Releases of GHB614 x T304-40 x GHB119 cotton have been notified under Part B of the Directive 2001/18/EC in Spain: B/ES/12/21; B/ES/11/14; B/ES/10/26; B/ES/09/33; B/ES/08/42

(b) Conclusions of post-release monitoring

No persistent volunteers that could not be managed by current agricultural practices were observed

(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)

No negative effects on human health and the environment have been observed.

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

(a) Release country

Argentina, Brazil, Mexico, USA

(b) Authority overseeing the release

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

Brazil: CTNBio - Comissão Técnica Nacional de Biossegurança

Mexico: National Service for Agri-Food Health, Safety and Quality (SENASICA).SENASICA is part of the Ministry of Agriculture, Livestock, Rural Development, Fisheries and Food (SAGARPA)

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

Brazil: www.cntbio.gov.br

Mexico: http://www.senasica.gob.mx/default.asp?doc=25576

USA: www.aphis.usda.gov/

(d) Aim of the release

Aim of the field releases: Regulatory trials, Trait development, 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