PART II

SUMMARY OF THE APPLICATION FOR REQUEST FOR AUTHORIZATION

GLUFOSINATE-AMMONIUM-TOLERANT COTTON GHB119 FOR FOOD AND FEED USES, AND IMPORT AND PROCESSING, IN ACCORDANCE WITH ARTICLES 5 AND 17 OF REGULATION 1829/2003 GM FOOD AND GM FEED, AND FOR INDUSTRIAL USES

A. GENERAL INFORMATION

1. Details of application

a) **Member State of application:** The Netherlands
b) **Application number:** Not available at the date of application.
c) **Name of the product (commercial and other names):** Cotton, Event GHB119 (OECD code BCS-GHØØ5-8) Seed of genetically modified cotton (*Gossypium* spp.) with resistance to some *Lepidoptera* and tolerance to herbicide products containing the active ingredient glufosinate-ammonium, derived by traditional breeding methods from crosses between GM cotton event GHB119 (OECD code BCS-GHØØ5-8) and non-GM cotton varieties.
d) **Date of acknowledgement of valid application:** Not available at the date of application

2. Applicant

a) **Name of applicant:** Bayer CropScience AG, represented by Bayer BioScience NV
b) **Address of applicant:** Bayer CropScience AG Alfred-Nobel-Strasse 50 D - 40789 Monheim am Rhein Bayer BioScience NV Technologiepark 38 B-9052 Gent **E-mail address:** info@bayercropscience.com
c) **Name and address of the person established in the Community who is responsible for the placing on the market, whether it be the manufacturer, the importer or the distributor, if different from the applicant (Commission Decision 2004/204/EC Art 3(a)(ii)):** GHB119 cotton will be imported and processed in the EU by the same groups who currently import, process and distribute commodity cottonseed.

3. Scope of the application

☒ GM plants for food use

☒ Food containing or consisting of GM plants

☒ Food produced from GM plants or containing ingredients produced from GM plants

☒ GM plants for feed use

☒ Feed containing or consisting of GM plants

☒ Feed produced from GM plants

☒ Import and processing (Part C of Directive 2001/18/EC)

☐ Seeds and plant propagating material for cultivation in Europe (Part C of Directive 2001/18/EC)

4. Is the product being simultaneously notified within the framework of another regulation (*e.g.* Seed legislation)?

Yes ☐	No ☒
If *yes*, specify	

5. Has the GM plant been notified under Part B of Directive 2001/18/EC and/or Directive 90/220/EEC?

Yes ☒	No ☐
If *no*, refer to risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC	

6. Has the GM plant or derived products been previously notified for marketing in the Community under Part C of Directive 2001/18/EC or Regulation (EC) 258/97?

Yes ☐	No ☒
If *yes*, specify:	

7. Has the product been notified in a third country either previously or simultaneously?

Yes ☒	No ☐
If *yes*, specify: FSANZ approval for import granted in 2011 for Australia/New Zealand. CTNBio approval for cultivation granted in 2011 for Brazil. Authorisation requested for cultivation and commercial use in USA and Argentina. Authorisations requested for food, feed and industrial uses in Canada, Colombia, Japan, Korea and Mexico.	

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, *Gossypium hirsutum*. The genetic modification confers resistance to some Lepidoptera and tolerance to the active ingredient glufosinate-ammonium through the genetic locus defined as GHB119. GHB119 cotton varieties are developed by traditional breeding methods from crosses between GHB119 and conventional cotton adapted for planting in the temperate cotton production regions of the Americas. Glufosinate-ammonium (N-phosphonomethyl-glycine) is a non-selective, foliar applied, broad-spectrum and post emergent herbicide.

The introduced insect resistance trait in GHB119 cotton is conferred by the insecticidal crystal protein, Cry2Ae, encoded by the *cry2Ae* gene, from the common soil bacterium, *Bacillus thuringiensis* subsp. *dakota* (*B.t. dakota*). The Cry2Ae protein is effective in controlling lepidopteran plant feeding larvae such as cotton bollworm larvae (CBW, *Helicoverpa zea*), tobacco budworm larvae (TBW, *Heliothis virescens*) and fall armyworm larvae (FAW, *Spodoptera frugiperda*), which are common pests of cotton.

The herbicide tolerance trait (OECD, 1999 [M-204493-01-1]) is based upon the *bar* gene, a bialaphos resistance gene, isolated from the soil microorganism, *Streptomyces hygroscopicus*. The *bar* gene, when expressed, enables the production of the enzyme, Phosphinothricin-Acetyl-Transferase (PAT) that acetylates L-glufosinate ammonium and thereby confers tolerance to herbicides based upon glufosinate ammonium.

Agricultural production of commercial cotton requires insect and weed control, and successful control depends upon a combination of management practices. For temperate cotton production, farmers use the planting of weed-free seed, crop rotations to break weed cycles, precision land levelling to aid irrigation, seed bed preparation, conservation tillage programs, the application of one or more herbicides and herbicide rotation.

b) Types of products planned to be placed on the market according to the authorisation applied for:

Two different types of product are planned to be placed on the market: 1) grain from GHB119 cotton containing varieties and 2) cottonseed products derived from events containing GHB119.

1) GHB119 grain will be imported, processed and distributed in the European Union similar to current cottonseed usage (food, feed and industrial uses) excluding cultivation.

2) Cottonseed products derived from event GHB119 (cottonseed oil, meal and linters) will be imported in the EU, similar to current usage of products derived from cottonseed (food, feed and industrial uses).

c) Intended use of the product and types of users:

In the EC, cotton grain and meal are used as high protein sources especially in the dairy industry. Cottonseed oil is an important vegetable oil source. GHB119 grain and cottonseed products derived from event GHB119 will be imported in the EU from the major cotton growing areas as a commodity and will be used for downstream purposes for food, feed and industrial products identical to current cottonseed and cottonseed products imports.

d) Specific instructions and/or recommendations for use, storage and handling, including mandatory restrictions proposed as a condition of the authorisation applied for:

No mandatory restrictions for use, storage and handling are proposed as a condition of the authorisation. All standard practices applicable to cotton today remain adequate for the handling of insect resistant and glufosinate-ammonium-tolerant, GHB119 cotton varieties.

When genetically modified cotton is placed on the EU market (including co-mingled with conventional cotton during use, storage and handling), the corresponding batch will be labelled and handled according to the relevant EU legislation, in particular Regulation (EC) 1830/2003.

e) **Any proposed packaging requirements:**

Cotton grain will be imported as a bulk and will not be packaged.

f) **A proposal for labelling in accordance with Articles 13 and Articles 25 of Regulation ((EC) 1829/2003. In the case of GMOs, food and/or feed containing or consisting of GMOs, a proposal for labelling has to be included complying with the requirements of Article 4, B(6) of Regulation (EC) 1830/2003 and Annex IV of Directive 2001/18/EC:**

GHB119 does not harbour characteristics that require specific labelling. Hence, no additional labelling is proposed other than the GM labelling requirements under regulations (EC) 1829/2003 and 1830/2003.

g) **Unique identifier for the GM plant (Regulation (EC) 65/2004; does not apply to applications concerning only food and feed produced from GM plants, or containing ingredients produced from GM plants):**

BCS-GHØØ5-8.

h) **If applicable, geographical areas within the EU to which the product is intended to be confined under the terms of the authorisation applied for. Any type of environment to which the product is unsuited:**

No restrictions are necessary as GHB119 is suitable for food, feed and industrial uses in all regions of the European Union.

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

The majority of imported cotton commodities will be processed products from different levels of downstream processing without the ability for natural reproduction. Viable cottonseed will be imported in small quantities only. The safety profile in terms of human and animal health and environmental impact of grains of GHB119 and conventional cottons are identical and do not constitute a hazard.

The case of accidental spillage of non-processed GHB119 grains, in transit or at the processing facility, has been assessed in the risk assessment and foreseen in the post market monitoring plan (see paragraph 11.4).

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

1. Complete name

a) Family name:	*Malvaceae*
b) Genus:	*Gossypium*
c) Species:	*hirsutum*
d) Subspecies:	Not applicable
e) Cultivar/breeding line or strain:	GHB119 cotton
f) Common name:	cotton

2 a. Information concerning reproduction

(i) Mode(s) of reproduction

Vegetative proliferation of cotton requires human intervention; therefore the mode of reproduction can be restricted to sexual reproduction only, through the production of seeds.

Cotton is mainly an autogamous species however some degree of insect mediated cross-pollination may take place.

Gene flow can occur into an adjacent cotton crop however, the rate is likely to be very low because there exists a combination of genetic, botanical, geographic and agricultural barriers to gene flow. Gene flow will not occur into compatible wild *Gossypium* species, as these are not present in Europe.

(ii) 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.

(iii) Generation time

Cotton when found in nature is a perennial shrub, which has been domesticated and converted to an annual crop. The generation time of cultivated cotton varies between 100 and 200 days.

2 b. Sexual compatibility with other cultivated or wild plant species

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* 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 an, 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.

3. Survivability

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.

4. Dissemination

a) Ways and extent of dissemination

The two differentiated reproductive structures suitable for dispersal of cotton genes in the environment are the seed and pollen.

- **Seed dispersal** could occur during transport, at sowing and essentially before and during harvest.
- **Pollen dispersal** 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.

5. Geographical distribution and cultivation of the plant, including the distribution in Europe of the compatible species

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.

Gossypium hirsutum in its wild form is distributed over the most arid areas of Central America and in the South and North of America, with wild populations that are rare and sporadic, while South America is considered to be the center of origin of the species *G. barbadense*. 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.

In Europe, the cultivated cotton is mainly *G. hirsutum*. No wild relatives have been reported.

6. In the case of plant species not normally grown in the Member State(s), description of the natural habitat of the plant, including information on natural predators, parasites, competitors and symbionts

Today, cotton is commercially grown in **Greece** and **Spain**, and very few hectares also in **Bulgaria** and **Portugal**.

7. Other potential interactions, relevant to the GM 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

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**. The crop has been cultivated in Spain and Greece for centuries and has a history of safe use.

The cotton crop was produced for fibre for thousands of years, and was first utilized for food and feed in the 20th century. Cotton is not considered harmful or pathogenic to animals or humans, however the plant does produce a small amount of natural anti nutritional factors such as **gossypol and cyclopropenoid fatty acids.**

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.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

The genetic modification was performed by *Agrobacterium*-mediated transformation.

2. Nature and source of the vector used

The vector pTEM12 is derived from pGSC1700, which was constructed in *Escherichia coli*, and thereafter transferred to a suitable *Agrobacterium tumefaciens* strain.

3. Source of donor DNA, size and intended function of each constituent fragment of the region intended for insertion

The genetic elements to be transferred into the plant are described below:

Table 1. Size, source and intended function of each constituent fragment of the region intended for insertion

Definition Source	Size (bp)	Reference	Function
Left border repeat from *Agrobacterium tumefaciens*	24	Zambryski, 1988	*Cis*-acting element for T-DNA transfer
Terminating signal (3'nos) of *bar* gene from *Agrobacterium tumefaciens*	309	Depicker *et al.*, 1982	Stop signal
Glufosinate ammonium-tolerance *bar* gene from *Streptomyces hygroscopicus*	551	Thompson *et al.* 1987	Herbicide tolerance and selectable marker
Promoter (PcsvmvXYZ) from cassava vein mosaic virus	535	Verdaguer *et al.*, 1996	High level constitutive expression
Promoter (P35S2) from cauliflower mosaic virus	476	Odell *et al.*, 1985	High level constitutive expression, especially in cotton green tissue
Leader sequence (5'cab22L) from *Petunia hybrida*	69	Harpster *et al.*, 1988	
Transit peptide (TPssuAt) from *Arabidopsis thaliana*	164	De Almeida *et al.* 1989	Targeting of the protein to the plastids
Insect resistance *cry2Ae* gene*Bacillus thuringiensis*	1895	Arnaut *et al.*, 2005	Insect resistance
Terminating signal (3'35S) of *cry2Ae* gene cauliflower mosaic virus	268	Sanfaçon *et al.*, 1991	Stop signal
Right border repeat from *Agrobacterium tumefaciens*	24	Zambryski, 1988	*Cis*-acting element for T-DNA transfer

Author(s), year, title, source, edition, pages
Arnaut, G., Boets A., Vannest S., Van Rie J., and Van Houdt S. 2002. Novel *Bacillus thuringiensis* insecticidal proteins *Patent Application: WO 02/057664 A2 2005* 68 pages.
De Almeida R.P.E., Gossele V., Muller C.G., Dockx J., Reynaerts A., Botterman J., Krebbers E. and Timko M.P. 1989. Transgenic expression of two marker genes under the control of an Arabidopsis rbcS promoter: Sequences encoding the Rubisco transit peptide increase expression levels. *Mol Gen Genet* (1989) 218:78-86 .
Depicker A., Stachel S., Dhaese P., Zambryski P and Goodman H.M. 1982. Nopaline Synthase: Transcript Mapping and DNA Sequence *Journal of Molecular and Applied Genetics* Vol. 1, No. 6561-573.
Harpster H.M., Townsend A.J., Jones J.G.G., Bedbrook J and Dunsmuir P. 1988. Relative strengths of the 35S califlower mosaic virus, 1', 2', and nopaline synthase promoters in transformed tobacco sugarbeet and oilseed rape callus tissue. *Mol Gen Genet* (1988) 212:182-190.
Odell J.T., Nagy F. and Chua N.H. 1985. Identification of DNA sequences required for activity of the cauliflower mosaic virus 35S promoter *Nature* Vol. 313 28 February 1985.
Sanfaçon H., Brodman P. and Hohn T. 1991. A dissection of the cauliflower mosaic virus polyadenylation signal *Genes & Development* 5:141-149.
Thompson C.J. *et al.* 1987. Characterization of the herbicide-resistance gene bar from *Streptomyces hygroscopicus The EMBO Journal* vol.6 no.9 pp.2519-2523, 1987.
Verdaguer B., Kochko A., Beachy N.R. and Fauquet C. 1996. Isolation and expression in transgenic tobacco and rice plants, of the cassava vein mosaic virus (CVMV) promoter. *Plant Molecular Biology* 31: 1129-1139.
Zambryski P. 1988. Basic processes underlying *Agrobacterium*-mediated DNA transfer to plant cells. *Ann. Rev. Genet. 22: 1-30.* 30 pages.

D. INFORMATION RELATING TO THE GM PLANT

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

GHB119 cotton varieties belong to the species, *Gossypium hirsutum* L. and are distinguished from other cotton by the traits of insect resistance and tolerance to the herbicide, glufosinate.

The introduced insect resistance trait in GHB119 cotton is conferred by the insecticidal crystal protein, Cry2Ae, encoded by the *cry2Ae* gene, from the common soil bacterium, *Bacillus thuringiensis* subsp. *dakota* (*B.t. dakota*). The Cry2Ae protein is effective in controlling lepidopteran plant feeding larvae such as cotton bollworm larvae (CBW, *Helicoverpa zea*), tobacco budworm larvae (TBW, *Heliothis virescens*) and fall armyworm larvae (FAW, *Spodoptera frugiperda*), which are common pests of cotton. Cry2Ae is insecticidal only when eaten by the larvae of specific lepidopteran insects. The specificity of action is most likely directly attributable to the presence of specific binding sites in the target insects, as described for other Cry proteins. Not only must the insect have the correct physiology and be at a susceptible stage of development, but sufficient quantities of the crystal proteins must be ingested.

The herbicide tolerance trait is based upon the *bar* gene, a bialaphos resistance gene, isolated from the soil microorganism, *Streptomyces hygroscopicus*. The *bar* gene, when expressed, enables the production of the enzyme, Phosphinothricin-Acetyl-Transferase (PAT) that acetylates L-glufosinate ammonium and thereby confers tolerance to herbicides based upon glufosinate ammonium. Numerous regulatory agencies have authorized PAT expressing plants for human and animal consumption in many countries.

2. Information on the sequences actually inserted or deleted

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

Southern blot, PCR and sequence analysis demonstrated that the glufosinate-ammonium-tolerant cotton event GHB119 contains one copy of the *Cry2Ae-bar* gene cassette.

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

Not relevant. No deletion occurred.

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

Based upon Southern blot and Mendelian segregation analysis, it was demonstrated that the DNA is integrated in a single genetic locus in the cotton nuclear genome (chromosome).

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

The characterization of the inserted sequences in event GHB119 confirmed the presence of one intact copy of the *Cry2Ae-bar* gene cassette, and the absence of the vector backbone. There are no antibiotic resistance markers present in GHB119.

3. Information on the expression of the insert

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

The *cry2Ae* regulatory elements direct high level constitutive expression, especially in the green tissues of GHB119 cotton. The constitutive cassava vein mosaic virus promoter and nos terminator sequences control expression of the *bar* gene, resulting in a high level constitutive expression throughout the GHB119 cotton plant.

The amount of cry2Ae and PAT proteins in the leaves of GHB119 during the vegetative life cycle of the plant has an upper limit of approximately 9.33 µg/g and 28.4 µg/g fresh weight, respectively. The mean amount of cry2Ae protein in fuzzy seed is 0.9 µg/g fresh weight. The mean amount of PAT protein in fuzzy seed is 2.37 µg/g fresh weight.

b) Parts of the plant where the insert is expressed

The PAT protein was detected in all plant tissues analysed. The Cry2Ae protein was detected in all plant tissues except for nectar, where it was below the limit of detection. Expression level was measured by cry2Ae and PAT protein specific ELISA. Tissue samples were harvested from greenhouse grown cotton, under conditions representative of cotton cultivation, at the various developmental stages.

The following order of PAT expression was demonstrated: leaf, apex >> stem, whole plant >> square, root >> flowers >> boll >> grain and the following Cry2Ae expression was shown: whole plant >> leaf >> >> root, apex, stem >> squares >> flowers >> grain, boll

4. Information on how the GM plant differs from the recipient plant in

a) Reproduction

The traits of insect resistance and herbicide tolerance had no effect on the mode and rate of seed reproduction which was found to be the same as for conventional cotton, as observed during three seasons of field trials.

b) Dissemination

Two developmental stages in cotton are susceptible to dispersal: pollen and seed. No differences in dissemination capacity have been observed between GHB119 and conventional cotton. Studies show that the genetic modification did not change any characteristics of the cotton that could impact dissemination:

- no difference in pollen characteristics including viability, fertility in crosses as either a male or female parent;
- no difference in pollen dispersal to cultivated cotton;
- no difference in seed morphology or fecundity measured as number of seed per boll and 100 seed weight;
- no difference in germination/stand count, seedling vigour over-wintering or dormancy as measured by standard laboratory cotton seed physiology tests.

c) Survivability

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

d) Other differences

The only biologically significant difference observed in field evaluations is that cotton varieties based upon transformation event GHB119 are resistant to certain Lepidopterae and are tolerant to herbicide products containing glufosinate-ammonium.

5. Genetic stability of the insert and phenotypic stability of the GM plant

The trait is inherited as a single dominant gene. To demonstrate the stability of the inserted DNA, Southern blot analysis was completed for plants of different generations, different environmental growth conditions and from crosses into different genetic backgrounds.

The isolated DNA was digested with the restriction enzyme *EcoRV*, which has two recognition sites in the transforming DNA. Hybridization of these samples with the T-DNA probe revealed the expected profile in all tested samples.

The resulting Southern blots demonstrate the molecular stability of the cotton GHB119 at the genetic level over multiple generations, different locations, and in 2 distinctive genetic backgrounds.

Phenotypic stability was demonstrated by Mendelian inheritance.

6. Any change to the ability of the GM plant to transfer genetic material to other organisms

a) Plant to bacteria gene transfer

No aspect of the nature of the genetic elements used gives any indication that a transfer from GHB119 to bacteria could occur.

b) Plant to plant gene transfer

Genetic transfer possible only to cotton. 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.

7. Information on any toxic, allergenic or other harmful effects on human or animal health arising from the GM food/feed

7.1 Comparative assessment

Choice of the comparator

GHB119 was compared to its parent variety, Coker 312.

7.2 Production of material for comparative assessment

a) Number of locations, growing seasons, geographical spread and replicates

The geographic range included in South of European Union, cotton growing country Spain (2007 and 2008) and the Southern United States (US) cotton growing regions of Arkansas, Georgia, Mississippi and Texas (2006). Seed samples were collected from US one growing season (2006; six locations), and from Spain (2007 and 2008; 8 locations), three treatments from every location, and a 3-fold replication per treatment.

The three treatments consisted of: a) conventional cotton grown using conventional herbicide weed control, b) GHB119 cotton grown using conventional herbicide weed control, and c) GHB119 cotton grown with glufosinate-ammonium herbicide weed control.

b) The baseline used for consideration of natural variations

A range of values to be expected for each nutritional component was established from published literature, as well as from the values for the reference counterpart variety, Coker 312 and commercial varieties.

7.3 Selection of material and compounds for analysis

Bayer CropScience undertook a systematic review of the composition of the seed derived from GHB119. The scope of the evaluation included the seed and selected processed seed products. The components selected for compositional and nutritional analyses comprise the important nutrients of cotton, as defined by the OECD. These are proximates, amino acids and fatty acids, micronutrients such as vitamins and minerals, and anti-nutrients such as gossypol and cyclopropenoid fatty acids. The data demonstrate that grain from GHB119 has the same nutritional composition as its conventional counterpart, and values for nutritional components fall within the range of values reported for commodities in commerce.

Cottonseed oil is a high-quality cooking oil, due to its balance in unsaturated fatty acids, and high tocopherol (vitamin E) content. The lipid profile is preserved in GHB119: the fatty acid levels in the cottonseed oil samples are similar to those of the conventional counterpart and within the range reported by the literature, and the tocopherol determinations show an excellent correspondence for crude and refined-deodorised cottonseed oil samples.

7.4 Agronomic traits

Throughout the field testing history of GHB119 there were no differences observed that could be attributed to pleiotropic effects of the *cry2Ae-bar* gene insertion. Neither did GHB119 differ from the parent variety in agronomic or reproductive characters. The agronomic evaluations included a detailed phenotypic analysis based upon plant variety description, agronomic performance evaluations common to yield trials, pest resistance evaluations and agronomic practice evaluations. The comparisons between GHB119 and its parent cotton variety, Coker 312 shows no differences in agronomic traits.

There is no indication in the data of agronomic performance that GHB119 is unlike cotton that is currently grown and consumed.

7.5 Product specification

The derived food is cottonseed oil and cottonseed linters, and the derived feed the by-products of cottonseed processing (e.g. cottonseed meal).

Glufosinate-ammonium-tolerant cotton event GHB119 has been conventionally bred with other biotech events and an array of varieties with adaptation to the various zones of cotton cultivation. GHB119 cotton containing varieties belong to the species, *Gossypium hirsutum* L. and are distinguished from other cotton only by resistance to some Lepidopterae and tolerance to herbicide products containing glufosinate-ammonium, the genetic locus defined as GHB119 and the presence of the cry2Ae and PAT proteins.

7.6 Effect of processing

The GHB119 cotton containing varieties are grown using the agronomic practices of the region of production, and the seed is harvested, transported, stored and processed using the same processes as cotton currently in commerce. The genetic modification was not aimed at changing the processing method.

Upon chemical analysis, the nutritional composition of whole seed were found to be equivalent to any other conventional cotton variety.

The same production process applied to cotton will be used for the seed derived from GHB119 varieties.

7.7 Anticipated intake/extent of use

The intake of cottonseed oil and linters in the diet of the European Union is not anticipated to change with the introduction of GHB119 varieties. Cottonseed and cottonseed products derived from GHB119 varieties are not different in quality or nutritional composition from the cottonseed products now consumed. No change in the use patterns for cotton is anticipated. No potential dietary and nutritional impacts have been identified for cottonseed and cottonseed products derived from GHB119 varieties.

The *per capita* consumption of cottonseed oil for the European diet is 0.04 kg/year. The extremes of cottonseed oil consumption in the Member States include 0.50 kg/person/year in Spain and 0.58 kg/person/year in Greece. Austria, Luxembourg, Germany and Italy do not consume any. The *per capita* consumption in Turkey is 2.71 kg/year.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

The Cry2Ae and PAT proteins are not toxic to mammals and do not possess any of the characteristics associated with food allergens. Findings to support this conclusion include:

- The *cry2Ae* gene which encodes the Cry2Ae protein is derived from *Bacillus thurigiensis* (*Bt*). The *Bt* crystal proteins are ubiquitous in nature and almost a century of studies of insecticidal proteins has brought a detailed understanding of their structure and function. The *bar* gene, which encodes the PAT protein, is derived from *Streptomyces hygroscopicus* which is a common soil saprophytic bacterium not known to be pathogenic to humans and animals.
- the Cry2Ae and PAT proteins are quickly degraded in simulated gastric and intestinal fluids of domestic animals and humans and by heat;
- No potential N-glycosylation site was identified for the PAT amino acid sequence and eleven potential N-glycosylation sites were identified for the Cry2Ae protein and proven to be inactive.
- the PAT enzyme is highly substrate-specific. It acetylates its target, glufosinate-ammonium, but not glutamate, the closest structural analogue of L-glufosinate ammonium or other L-amino acids;
- exposure to Cry2Ae protein via an oral route was assessed in mice at a high dose of 2000 mg/kg body weight. In addition exposure to PAT protein via parenteral route was assessed in mice at a high dose of 10 mg/kg body weight. These tests confirmed that the Cry2Ae and the PAT proteins are not acutely toxic.
- a repeated dose oral toxicity study in rats with the cry2Ae and PAT protein, further confirmed absence of toxicity for the cry2Ae and PAT protein.
- A 90 day rat feeding study confirmed the absence of any harmful effect due to the inclusion in the diet of GHB119 cotton.

Supplemental information was also provided by a poultry feeding study showing no adverse effects on chickens.

7.8.2 Testing of new constituents other than proteins

No other constituent than the cry2Ae and PAT proteins are novel and no changes in composition of cotton were discovered by chemical analysis.

7.8.3 Information on natural food and feed constituents

Plants are known to naturally produce toxins and allergens that often serve the plant as natural defence

compounds against pests and pathogens. The inclusion of cottonseed products in human food or animal feed is limited due to the presence of some anti-nutrients in cottonseed that could act as toxic compounds. These anti-nutritional and toxic factors are gossypol and cyclopropenoid fatty acids (CPFA). Gossypol is present in the meal and the seed. Thus, the cottonseed is processed to reduce the content of gossypol and CPFA to acceptable levels as well as to minimise the toxicological properties of these two compounds.

Cottonseed oil intended for human consumption is highly purified: the purification process substantially reduces the content of CPFA and gossypol. Therefore, cottonseed oil and meal are currently considered not to contain common food toxins or anti-nutritional compounds of concern for human and animal health, because either the product only has minor amounts of these active compounds or their levels decrease (or they even disappear) during processing.

Natural constituents of cotton have not been changed in GHB119. Extensive compositional analysis was undertaken, taking into consideration the OECD consensus document on "compositional considerations for new varieties of cotton: key food and feed nutrients and anti-nutrients". Equivalence in the fuzzy seed was demonstrated for all proximates, fiber compounds, and the total amino acids. Good agreement between the findings for GHB119, the comparator and the baseline support the conclusion of compositional equivalence to cotton currently in commerce.

7.8.4 Testing of the whole GM food/feed

Although not scientifically requested, a zootechnical study was conducted to supplement the safety evaluation: this study was performed with male broiler chickens. Poultry were selected to evaluate the effects of a feed component over an entire life span and under conditions of rapid growth, thus the assay is highly sensitive for nutritional deficiencies or toxic effects.

The broiler chicken is an economically significant and widely distributed food animal. The species used is based upon commercial practice and is very sensitive for the detection of differences in nutrient quality because of its rapid growth (45-fold increase in body weight over 40 days). This study showed no indications that neither the event GHB119 nor the transformation process itself, has adverse effects on feeding, growth or general health. Moreover, no negative impacts of the nutritional quality of the event GHB119 were observed on poultry.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

The cry2Ae and PAT proteins do not possess any of the characteristics associated with food allergens.

The cry2Ae and PAT proteins have no homology with any known allergens, toxins or anti-nutrients.

The cry2Ae has eleven potential glycosylation sites proven experimentally to be inactive; the PAT protein has no glycosylation sites present on certain food allergens.

The cry2Ae and PAT proteins form only an extremely minor part of the crude protein fraction in GHB119, making it unlikely to become a food allergen, as food allergens tend to be major proteins.

7.9.2 Assessment of allergenicity of the whole GM plant or crop

Cotton (*Gossypium hirsutum*) is not considered an allergenic food crop.

A consideration of specific food safety issues did not identify food allergenic potential as one outcome that would cause concern for human consumption. Edible oils that are refined, bleached and deodorised do not appear to pose a risk to allergic individuals, as they contain virtually no proteins. Literature to date on cottonseed oil validates this theory: the absence of water-soluble allergens in cottonseed oil is correlated with no clinical allergy observations after consumption of cottonseed oil. Therefore, no allergic reaction is expected from its current use pattern.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

The introduced trait in GHB119 is intended for agronomic benefits. Extensive compositional analysis was undertaken, taking into consideration the OECD consensus document on "compositional considerations for new varieties of cotton: key food and feed nutrients and anti-nutrients". No change in the nutritional composition was intended and upon extensive analysis, none was found.

The primary use of cotton is for the textile industry. However the by-products of cotton ginning find many uses in human and animal diets. Compositional equivalence was demonstrated for the food proprieties of the cottonseed oil. The key nutrients, fatty acids and vitamin E (tocopherol), which are the principal components of cottonseed oil, were investigated. The lipid profile is preserved in GHB119, and the fatty acid levels in the cottonseed samples are similar to those of the conventional cottonseed samples and within the range reported in the literature and of the commercial varieties analysed.

Cottonseed oil from GHB119 has the same nutritional composition as its conventional counterpart, and values for nutritional components fall within the range of values reported for cotton commodities in commerce.

7.10.2 Nutritional assessment of GM feed

Extensive compositional analysis was undertaken, taking into consideration the OECD consensus document on "compositional considerations for new varieties of cotton: key food and feed nutrients and anti-nutrients". The by-products of cottonseed processing (cottonseed meal and cottonseed hulls) can be used in animal feed. Cotton contains some anti-nutritional factors, most of which are concentrated in the meal fraction. The anti-nutritional compounds include gossypol and cyclopropenoid fatty acids, which are subject to heat denaturation. Cottonseed meal is typically subjected to a moist heat treatment to facilitate oil removal. This treatment denatures proteins and detoxifies the gossypol that otherwise would cause the cottonseed meal to be unsuitable as an animal feed.

In addition, the wholesomeness of GHB119 has been demonstrated in a zootechnical study with chicken.

7.11 Post-market monitoring of GM food/feed

No post-market monitoring plan is required for GM food/feed produced from GHB119. A traditional comparator, the cotton variety Coker 312, was used in the comparative analysis (D.7.1-3). The intent of the genetic modification was for agronomic benefits (D.7.4), no change in the nutritional composition or value was intended and no change was identified (D.7.6, D.10). No health claims are intended and GHB119 will not be marketed as an alternative to or replacement for traditional cotton (D7.5). GHB119 has no specific properties that might increase the dietary intake compared to traditional cotton (D.7.7). There is no evidence that the long term nutritional and health status of the European population could be impacted by the marketing of GHB119 (D.7.8-10).

8. Mechanism of interaction between the GM plant and target organisms (if applicable)

Cotton containing the GHB119 event expresses the cry2Ae and PAT proteins that confer reistance to some Lepidopterae insects and tolerance to herbicide products containing glufosinate-ammonium. These lepidopteran insects may be considered as target organisms which interact with the GHB119 cotton plants. However, the scope of the GHB119 cotton application is food and feed, import and processing and does not include cultivation in the EU. Therefore, no interactions between GHB119 cotton plants and lepidopteran insects are expected.

9. Potential changes in the interactions of the GM plant with the biotic environment resulting from the genetic modification

9.1 Persistence and invasiveness

A review of the reproductive and vegetative fitness finds that GHB119 compares to its parent variety Coker 312 in all aspects except for the resistance to some Lepidopterae insects and tolerance to herbicide products containing glufosinate-ammonium. Subsequent season monitoring for volunteers has found no indication of increased persistence or invasiveness of GHB119 cotton.

9.2 Selective advantage or disadvantage

None. Agronomic performance shows no disadvantage. The only circumstance in which a selective advantage could occur would be if some plants from escaped seed would be sprayed with herbicide products containing glufosinate-ammonium. The likelihood that some escaped seed would germinate is very low because most of the imported seed is non-viable. In any case it could be controlled with any other herbicide active on cotton.

9.3 Potential for gene transfer

Plant to bacteria gene flow. In order for any horizontal gene transfer to lead to a new type of micro-organism and therefore to introduce a significant impact, some of the following conditions will have to be fulfilled:
- the uptake should result in the incorporation of complete undegraded DNA
- the plant targeted genes should result in significant expression in a prokaryotic background
- the expression should represent a significant increase over the background level
- the traits should convey a competitive advantage to the strain in which they are incorporated.

Sequence analysis of cotton event GHB119 confirmed the insertion of one copy of the *cry2Ae-bar* gene cassette only and also the absence of vector backbone sequences. GHB119 does not contain either an origin of replication from plasmid pTEM12, or any sequences responsible for an enhanced frequency of recombination. Furthermore the introduced *cry2Ae-bar* gene cassette is under the control of a eukaryotic promoter, which is not functional in bacteria. Considered altogether, these facts make the possibility of gene transfer from plants of GHB119 to bacteria to be unlikely.

Plant to plant gene flow. GHB119 cotton is not intended for cultivation in EU at the moment. Gene flow to other cotton crop is possible in cotton producing areas of Europe only in the very unlikely event of spillage of viable seed and if growing and flowering plants establish within 12 meters of cultivated cotton. However seeds of cotton typically require some form of treatment to ensure adequate germination: heat treatment and a sulfuric acid delinting treatment to remove fuzz or linters from the seed coat (the delinted seed is also known as 'black' seed). Cotton seed and fuzzy seed germinate poorly, probably because the lint and linters attached to the seed coat limit contact with soil thereby inhibiting imbibing soil moisture.

Likelihood of gene flow. Provided the GHB119 cotton is not intended for cultivation in EU the likelihood of gene flow is extremely low. This statement is also supported by the fact that there is a combination of genetic, botanical, geographic and agricultural barriers to gene flow. Compatible wild *Gossypium* species are not present in Europe.

The only foreseeable chance for GHB119 to outcross to cotton in Europe would be the unlikely case of imported seed spilled in transit, if plants established within 12 meters of cultivated cotton.

Consequence of gene flow. In the unlikely event of the transfer of the *cry2Ae* and *PAT* genes into cultivated cotton, it is not expected to exacerbate problems of weed control or adversely impact agriculture.

The scope of the present application is limited to “import and processing” in the EU of GHB119 and does not include cultivation.

9.4 Interactions between the GM plant and target organisms

The insect protection trait of GHB119 cotton provides control against certain key cotton pests of the

lepidopteran family. In case GHB119 enters the environment the target organisms may develop resistance to the insecticidal Cry2Ae protein.

However, the scope of this application is for authorization of GHB119 cotton for food and feed uses, as well as import and processing and does not include authorization for cultivation of GHB119 cotton seeds in the EU. As a consequence, exposure to the environment will be limited to unintended release of the GHB119 cottonseed, which could occur via incidental spillage during transportation and processing. Taking into consideration the poor survival characteristics of conventional cotton under most European non-agricultural conditions and the fact that GHB119 cotton will be imported as mostly non-viable seed, the likelihood that GHB119 cotton will establish a feral population and interact with potential target organisms affecting their insecticidal properties can be considered as negligible.

9.5 Interactions of the GM plant with non-target organisms

Taking into account that GHB119 is not intended for cultivation and it will only be commercialised in conventionally-bred stacked event products, interactions with other organisms is very unlikely. Cotton is not known to establish feral populations and it is very unlikely that this might happen. The genetic modification, tolerance to the herbicide glufosinate, did not change the interaction of GM cotton varieties with other organisms in the absence of herbicide application. Under agricultural conditions when the herbicide is used: some advantage may be gained in plant population dynamics (the intended effect is weed control); in habitats outside agriculture the interaction with other plant communities is like any other cotton;

9.6 Effects on human health

No effects on human health are indicated for people working with, coming into contact with or in the vicinity of an environmental release of GHB119. Cotton grain of GHB119 has the same nutritional quality as cotton in commerce. The plants of GHB119 have the same qualities as other cotton. No toxic or allergic effect from handling GHB119 has been observed on workers in the field since 2002, year of its first field release.

9.7 Effects on animal health

The primary use of cotton is for its lint; however cotton seed and the by-products of cotton processing are often included in animal diets. The nutritional composition of the seed was demonstrated to be equivalent to other cotton by chemical analysis.

To support the finding of nutritional equivalence and to demonstrate bioavailability, poultry were fed diets containing cotton under study conditions designed to evaluate growth and health parameters. Poultry were selected to evaluate the effects of a feed component over an entire life span and under conditions of very rapid growth, thus the assay is highly sensitive for nutritional deficiencies or toxic effects. No differences were identified for nutritive value of the seed and no indications of toxic or adverse effects were associated with any of the sources of cotton in the tested animal species. Cottonseed of GHB119 is not anti-nutritional or toxic for animals and no effects on animal health are expected.

9.8 Effects on biogeochemical processes

Potential effects on biogeochemistry were assessed indirectly in agronomic studies designed to identify best agronomic practices for growing glufosinate-ammonium-tolerant cotton. For example, studies to evaluate the fitness of the event found cotton varieties containing the transformation event, GHB119 are not different in seed yield in response to soil composition than comparable cotton varieties.

Chemical analysis of the components seed and lint found no differences in the mineral composition and thus no reason to consider mineral utilisation from the soil to be different than for conventional cotton.

Moreover the scope of the present application does not include cultivation in Europe.

9.9 Impacts of the specific cultivation, management and harvesting techniques

The scope of this application does not include cultivation in the EU and therefore no impact on the cultivation, management and harvesting techniques is expected.

10. Potential interactions with the abiotic environment

The traits introduced in GHB119 cotton are not intended to modify the interactions of the plant with the abiotic environment. The intended commercial effect of GHB119 is to protect cotton from certain Lepidoptera and expand weed management options for the crop.

Moreover the scope of the present application does not include cultivation in Europe.

11. Environmental monitoring plan (not if application concerns only food and feed produced from GM plants, or containing ingredients produced from GM plants and if the applicant has clearly shown that environmental exposure is absent or will be at levels or in a form that does not present a risk to other living organisms or the abiotic environment)

11.1 General (risk assessment, background information)

As required by Article 5(5)(b) and 17(5)(b) of Regulation (EC) No. 1829/2003 the proposed monitoring plan for 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 the Annex VII.

11.2 Interplay between environmental risk assessment and monitoring

The scope of this application is the authorisation of GHB119 cotton varieties 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 GHB119 cotton seed products in the EU.

An environmental risk assessment (e.r.a.) was carried out for GHB119 cotton according to the principles laid down in Annex II to Directive 2001/18/EC and Decision 2002/623/EC. The scientific evaluation of the characteristics of 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 GHB119 cotton.

11.3 Case-specific GM plant monitoring (approach, strategy, method and analysis)

The scientific evaluation of the characteristics of 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 GHB119 cotton. It is therefore considered that there is no need for case-specific monitoring.

11.4 General surveillance of the impact of the GM plant (approach, strategy, method and analysis)

11.4.1 Approach

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 GHB119 cotton for import, processing, food and feed uses. The scope of the application does not include authorisation for the cultivation of GHB119 cotton.

Therefore, exposure to the environment will be limited to unintended release of GHB119cotton, which could occur for example via substantial losses during loading/unloading of the viable commodity including GHB119 cottonseed 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 glufosinate ammonium herbicide).

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 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 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 GHB119 cotton seed. The operators will be provided with guidance to facilitate reporting of any unanticipated adverse effect from handling and use of viable GHB119 cotton seed.

11.4.2 Baselines

Since the intended use of GHB119 cotton is the same as that of any other commercial cotton, the procedures for the import, handling and processing of cotton seed will be the same and have been considered in the development of the monitoring plan. The baseline and controls for general surveillance will rely on the historical knowledge and experience with non-GM cotton as comparable reference where necessary.

11.4.3 Time-period

General surveillance of GHB119 cotton will be undertaken for the duration of the authorisation period for GHB119 cotton for import and processing.

11.4.4 Assigning responsibilities

The authorisation holder is responsible for ensuring that the monitoring plan is put in place and properly implemented in accordance with the conditions of the authorisation.

The authorization holder shall be in the position to give evidence to the Commission and the competent authorities of the Member States:

- That the monitoring networks as specified in the monitoring plan collect the information relevant for the monitoring of GHB119 cotton.
- That the members of these networks have agreed to make available that information to the authorisation holder before the date of the submission of the monitoring report.

The third parties involved in the general surveillance will report any potential unanticipated adverse effects to the authorisation holder, who will immediately investigate and inform the European Commission in accordance with Regulation (EC) No 1829/2003, as described in Section 5.

11.4.5 Existing systems

Primary sources of information
The authorisation holder is not involved in commodity trade with GHB119 cotton. The monitoring methodology hence needs to be predominantly based on collaboration with third parties, such as operators involved in the import, handling and processing of viable GHB119 cotton seed. They are exposed to the imported viable GHB119 cotton and therefore are the best placed to observe and report any unanticipated adverse effects in the framework of their routine surveillance of the commodities they handle and use.

Since traders may commingle GHB119 cotton with other commercial cotton, including authorised GM cotton, the authorisation holder is working together with other members of the plant biotechnology industry within the European Association of Bioindustries (EuropaBio) and trade associations representing the relevant operators in order to implement a harmonised monitoring methodology. The following networks are currently involved:

⇒ *Importers / Traders*
COCERAL is the European association representing the cereals, rice, feedstuffs, oilseeds, oils and fats and agro-supply trade in the European Union. Its members are the national trade organisations that represent collectors, distributors, exporters, importers and agribulk storers of the above mentioned commodities in the majority of Member States. The main importers of cereals and feedstuffs into the EU are members of COCERAL.
Also see: http://www.coceral.com/cms/beitrag/10010169/227870.

⇒ *Silo Operators*
UNISTOCK is the European association representing professional storekeepers for agribulk commodities within the EU. It regroups representatives from 11 Member States and is itself a member of COCERAL. Commodity imports enter the EU by sea and transit through sea-port silos. The main storekeepers managing these silos are members of UNISTOCK.
Also see: http://www.coceral.com/cms/beitrag/10010260/232602

⇒ *Processors*
FEDIOL, the federation of the EU Oil and Protein Meal Industry, represents the interests of the European crushers of oilseeds meals producers and vegetable oils producers/processors. Its members represent 80% of the EU industry and hold 147 oilseeds processing and vegetable oils and fats production facilities across Europe.
Also see: http://www.fediol.be/1/main1.php.

These associations represent the majority of European operators importing, handling and processing viable cotton commodity. They work closely together with a continuous and efficient flow of communication between them, particularly, through the documentation that needs to accompany any shipment containing GMOs in accordance with the labelling and traceability requirements of Regulation (EC) No 1830/2003, and are therefore best placed to observe and report any unanticipated adverse effects.

Other networks consisting of operators further down the food and feed chain have not been selected for the general surveillance of viable T304-40, because they focus on processed, non-viable material.

Additional sources of information
In addition to the aforementioned existing monitoring systems, extensive independent research by scientists with a wide range of expertise is another valuable source of information on potential adverse effects arising from the use of GMOs. The authorisation holder will actively screen relevant reports and peer-reviewed publications on the use of GHB119 cotton, in order to identify potential unforeseen adverse effects linked to GHB119cotton.

11.4.6 Monitoring Methodology

The authorisation holder, together with other members of the plant biotechnology industry and EuropaBio, will implement general surveillance of viable GM cotton, including GHB119, with the help of the selected networks described in Section 4.5.

The different parties agreed on a general framework for monitoring of GMOs, including GHB119, as follows:

⇒ The authorisation holder represented by EuropaBio will:

- Agree with the operators before adding or amending activities that fall under their responsibility in accordance with the proposed monitoring plan.
- Inform operators concerning the authorisation, safety and general characteristics of GHB119cotton and of the conditions as to general surveillance
- Set up and maintain a website dedicated to operators including detailed information on GHB119cotton. The website, hosted on the EuropaBio website under www.europabio.org/InfoOperators, contains the following information:

  - An introduction to the purpose of the website
  - A table giving an overview of all currently approved GM plant products subject to general surveillance
  - A profile for every approved GM plant product providing documentation on characteristics and safety, positive EFSA opinion(s) and Commission Decision(s) authorising the GM plant product in the EU
  - A contact point at EuropaBio for information exchange on any of the GM plant products

  The website will be regularly updated in order to further facilitate and ensure a transparent process for general surveillance and easy access to relevant information for operators.

- Contact the selected networks of operators annually reminding them of their agreement to report on any unanticipated adverse effects (or absence thereof).

⇒ The selected networks of operators (European trade associations) will:

- Inform and remind their member organisations and companies on an annual basis:

  - to monitor for potential unanticipated adverse effects
  - that, in the framework of their management or safety standards (ISO, HACCP, …), procedures must be in place and implemented to limit losses and spillage of viable CROP and to routinely eradicate adventitious populations on their premises – any such adventitious populations, resisting routine eradication procedures, shall be treated as potential adverse effects
  - to inform and remind their own member companies of this requirement
  - to report back any adverse effect reported to them to the European trade associations

- Report to the authorisation holders directly or via EuropaBio
  - at least annually, regardless whether an adverse effect was observed or not
  - immediately any adverse effects reported to them.

Consequently, the European trade associations COCERAL, UNISTOCK and FEDIOL will notify EuropaBio of the results of the general surveillance on an annual basis. EuropaBio will forward this report to the respective authorisation holders for inclusion in their annual report to the European Commission, as described in Section 5.

The general surveillance information reported to and collected by the authorisation holder from the European trade associations or other sources will be analysed for its relevance. Where information indicates the possibility of an unanticipated adverse effect, the authorisation holder will immediately investigate to determine and confirm whether a significant correlation between the effect and GHB119cotton can be established. If the investigation establishes that GHB119 cotton was present when the adverse effect was identified, and confirms that GHB119 cotton is the cause of the adverse effect, the authorisation holder will immediately inform the European Commission, as described in Section 5.

11.5 Reporting the results of monitoring

If information that confirms an adverse effect of GHB119 cotton and that alters the existing risk assessment becomes available, Bayer CropScience will immediately investigate and inform the European Commission. Bayer CropScience, 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.

Bayer CropScience 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 GHB119 cotton.

The report will include a scientific evaluation of the confirmed adverse effect, a conclusion of the safety of GHB119 cotton and, as appropriate, the measures that were taken to ensure the safety of human and animal health or the environment.

12. Detection and event-specific identification techniques for the GM plant

The detection method for GHB119 cotton has been sent to the Community Reference Laboratory (CRL) (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm) 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 JRC-CRL

E. INFORMATION RELATING TO PREVIOUS RELEASES OF THE GM PLANT AND/OR DERIVED PRODUCTS

1. History of previous releases of the GM 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 GHB119 have been notified under Part B of the Directive 2001/18/EC in Spain in 2007 (B/ES/07/43), 2008 (B/ES/08/36, B/ES/08/39), 2009 (B/ES/09/32) and 2010 (B/ES/10/24).

b) Conclusions of post-release monitoring

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

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

No human health or environmental risks were observed.

2. History of previous releases of the GM plant carried out outside the Community by the same notifier

a) Release country :

GHB119 has been field tested in the USA since 2005 under USDA notification numbers 05-035-10n, 05-257-05n, 06-047-03n, 06-072-04n, 07-044-103n, 07-065-119n, 08-254-117n, 08-254-118n, 08-036-127n, 08-022-101n, 09-033-102n, 09-033-103n,09-096-103n, 09-253-102n, 09-107n, 10-044-101n, 10-106-108n, 10-216-101n.

GHB119 has been also field tested in Argentina in 2007 under permit number N° 281.585/06.

b) Authority overseeing the release

USA: United States Department of Agriculture (USDA)

Argentina: National Advisory Committee on Agricultural Biosafety (CONABIA).

c) Release site

USA: Information on the releases at www.aphis.usda.gov/

Argentina: information on the releases at http://www.sagpya.mecon.gov.ar/new/0-0/programas/conabia/bioseguridad_agropecuaria2.php

d) Aim of the release

See E.2.a., field releases for breeding and variety development, technical developments for best agronomic practices and cotton integrated pest management systems have been conducted.

e) Duration of the release

The generation time for cotton from planting to harvest is 100 to 200 days.

f) Aim of post-releases monitoring

Volunteer GHB119 plants in subsequent season.

g) Duration of post-releases monitoring

One or two seasons, until no volunteers observed.
h) Conclusions of post-release monitoring Occurrence of volunteers is very infrequent and dependent upon mild conditions in the winter season.
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.

3. Links (some of these links may be accessible only to the competent authorities of the Member States, to the Commission and to EFSA):

a) Status/process of approval The JRC websites http://gmoinfo.jrc.ec.europa.eu/gmp_browse.aspx and http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm provide publicly accessible links to up-to-date databases on the regulatory progress of notifications under Directive 2001/18/EC and Regulation (EC) No 1829/2003.
b) Assessment Report of the Competent Authority (Directive 2001/18/EC) A notification for GHB119 cotton according to Directive 2001/18/EC has not been submitted by Bayer CropScience.
c) EFSA opinion Not available at the time of submission of this application.
d) Commission Register (Commission Decision 2004/204/EC) Not yet available.
e) Molecular Register of the Community Reference Laboratory/Joint Research Centre Information on detection protocols will likely be posted at http://gmo-crl.jrc.it/statusofdoss.htm
f) Biosafety Clearing-House (Council Decision 2002/628/EC http://bch.biodiv.org/
g) Summary Notification Information Format (SNIF) (Council Decision 2002/812/EC) http://gmoinfo.jrc.it/