Application for authorisation of COT102 cotton import in the European Union under Regulation (EC) No 1829/2003

PART VII: SUMMARY

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PART VII

SUMMARY

APPLICATION FOR AUTHORISATION OF COT102 COTTON UNDER REGULATION (EC) 1829/2003

1. GENERAL INFORMATION

1.1. Details of application

(a) Member State of application

Germany

(b) Application Number

Not available at time of submission.

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

COT102 cotton (OECD code SYN-IR1Ø2-7).

(d) Date of acknowledgement of valid application

Not available at time of submission.

1.2. Applicant

(a) Name of applicant

Syngenta Crop Protection NV/SA on behalf of Syngenta Crop Protection AG.

(b) Address of applicant

Syngenta Crop Protection NV/SA
Avenue Louise 489
1050 Brussels
Belgium

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

Not applicable.

1.3. Scope of the application

(a) GM food

☒ Food containing or consisting of GM plants

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

(b) GM feed

☒ Feed containing or consisting of GM plants

☒ Feed produced from GM plants

(c) GM plants for food or feed use

☒ Products other than food and feed containing or consisting of GM 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 procedure within the Union?

No ☒

Yes ☐ (in that case, specify)

1.5. Has the GM 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)

Risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC is provided in the application.

1.6. Has the GM plant or derived products been previously notified for marketing in the Union 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, and provide a copy of the risk assessment conclusions, the date of the authorisation and the scope of the application)

Submissions covering COT102 cotton have been made in third countries around the world and are at different stages in the approval process. COT102 cotton is currently authorized for cultivation in the US; and is authorized for import in Australia, Canada, China, Colombia, Japan, South Korea, Mexico, Philippines, and Taiwan.

1.8. General description of the product

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

The recipient plant is *Gossypium hirsutum* (cotton). Event COT102 cotton

was produced by *Agrobacterium*-mediated transformation of cotton to confer resistance to some lepidopteran pest species. COT102 cotton contains a variant of the *vip3Aa* (namely, *vip3Aa19*) gene from *Bacillus thuringiensis* that expresses a vegetative insecticidal protein (Vip) that exhibits insecticidal activity against several lepidopteran pests of cotton. COT102 cotton also contains the *aph4* gene which encodes the selectable marker enzyme, hygromycin-B phosphotransferase (APH4), that was utilized in the production of transformed plants.

(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 (seeds, cut-flowers, vegetative parts, etc.) as a proposed condition of the authorisation applied for

This application, under Regulation (EC) No 1829/2003, covers the import, food and feed use, and processing of COT102 cotton. It does not cover cultivation. The scope of the application includes all food and feed products containing, consisting or produced from COT102 cotton including products from inbreds and hybrids obtained by conventional breeding of the cotton product. The application also covers the import and industrial processing of COT102 cotton for all potential uses as any other cotton.

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

It is intended that COT102 cotton will be used as any other conventional cotton for all food, feed and industrial purposes.

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

The characteristics of COT102 cotton and products derived from it are not different from those of its conventional counterpart, apart from the introduced traits. COT102 cotton has been shown to be as safe and as wholesome as existing varieties of cotton. Therefore, there are no specific instructions or recommendations for use, storage and handling of COT102 cotton.

(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

The COT102 cotton and derived products are suitable for use as any other cotton under the terms of the authorisation applied for.

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

This application under Regulation (EC) No 1829/2003 covers the import, food and feed use, and processing of COT102 cotton. It does not cover

cultivation.

(g) Any proposed packaging requirements

The characteristics of COT102 cotton and products derived from it are not different from those of its conventional counterpart. COT102 cotton has been shown to be as safe and as wholesome as existing varieties of cotton. Therefore, there are no specific instructions for packaging.

(h) Any proposed labelling requirements in addition to those required by other applicable EU legislation than regulation (EC) N° 1829/2003 and when necessary a proposal for specific labelling in accordance with Articles 13(2), and (3), Articles 25(2)(c), and (d) and Articles 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.

A proposal for labelling has been included in the application (refer to Part IV). This includes the labelling requirements outlined by Regulation (EC) No 1829/2003 and Annex IV of Directive 2001/18/EC. COT102 cotton will, therefore, be labelled as "genetically modified cotton" and products derived from it will be labelled as "containing (or produced from) genetically modified cotton". Since COT102 cotton and derived products are not different from those of its conventional counterpart, no additional labelling is required.

(i) Estimated potential demand

(i) In the EU

There are no anticipated changes to the intake/extent of use of cotton as a result of the introduction of COT102 cotton to the cotton supply. It is anticipated that the introduction of COT102 cotton will replace some of the cotton in existing food and feed products.

(ii) In EU export markets

There are no anticipated changes to the extent of cotton production in export markets for EU supplies as a result of the introduction of COT102 cotton products.

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

The unique identifier assigned to this product in accordance with Regulation (EC) No 65/2004 is SYN-IR1Ø2-7 (also referred to as COT102 cotton).

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

Cotton is incapable of sustained reproduction outside domestic cultivation and is non-invasive of natural habitats. The characteristics of COT102 cotton and products derived from it are not different from those of its conventional counterpart, apart from the intended traits.

The scope of this application does not include cultivation of COT102 cotton in the EU.

In the unlikely event that small amounts of seed from COT102 cotton accidentally found their way into the environment, this would represent extremely low levels of exposure and the survival of these seeds to produce flowering plants would be very unlikely. In addition, volunteers could be easily controlled using any of the current agronomic measures taken to control other commercially available cotton.

Exposure to the environment will be limited to unintended release of COT102 cotton, which could occur for example via substantial losses during loading/unloading of the viable commodity including COT102 cotton destined for processing into animal feed or human food products. In the event that small amounts of COT102 grain accidentally found their way into the environment, this would represent extremely low levels of exposure and the survival of this grain to produce flowering plants would be very unlikely. 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. In addition, volunteers could be easily controlled using any of the current agronomic measures taken to control other commercially available cotton.

The COT102 cotton and derived products have been shown to be as safe and as wholesome as existing varieties of cotton. Any unintended releases or misuse can be dealt with in the same way as any other conventional cotton.

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

2.1. Complete name

(a) Family name

Malvaceae

(b) Genus

Gossypium L.

(c) Species

Gossypium hirsutum L.

(d) Subspecies

Not applicable.

(e) Cultivar/breeding line

Coker 312

(f) Common name

Cotton

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

Four species of the genus *Gossypium* L. are known as cultivated cotton: *Gossypium hirsutum*, *Gossypium barbadense*, *Gossypium arboreum* and *Gossypium herbaceum*. The most commonly cultivated species is *Gossypium hirsutum*, widely known as upland cotton, also known as American, Mexican or Acala cotton. *G. hirsutum* accounts for over 90 % of the world's cotton production. Some 5 % of the cotton production is attributable to *G. barbadense*, the extra-long staple cotton, also known as Pima or Egyptian cotton.

Cotton originated in the tropics and subtropics, but is now typically cultivated in subtropical and warm-temperate zones. The world's five largest cotton-producing countries are China, India, USA, Pakistan and Brazil which together account for three-quarters of world production. [1]

In the European Union, the main cultivated cotton species is *Gossypium hirsutum*. The potential growing area of cotton is restricted to southern Europe. Currently, cotton is grown on approx. 300,000 hectares in only three Member States. Greece is the main cotton grower (approx. 80 % of European cotton area), followed by Spain (approx. 20 % of European cotton area) and limited production in Bulgaria (less than 1,000 ha). Italy and Portugal have ceased cotton production in 1991 and 1996, respectively. In 2013, the EU cotton production account for only 1 % of the world cotton production. [2]

[1] http://faostat3.fao.org/home/E; FAOSTAT (cottonseed 2014 and cotton lint 2013); accessed June 2016
[2] http://ec.europa.eu/agriculture/cotton/index_en.htm; accessed June 2016

2.3. Information concerning reproduction (for environmental safety aspects)

(a) Mode(s) of reproduction

Cotton is a perennial plant which is grown as an annual crop and is propagated by seed. Cotton is normally considered to be a self-pollinating crop, but cross-pollination is possible when pollinators are present.

(b) Specific factors affecting reproduction

Although cross-pollination can occur, cotton is normally considered to be a self-pollinating crop. Cotton pollen is very large (120 – 200 µm), sticky and heavy, and not easily dispersed by wind under typical environmental conditions. Pollen can be transferred instead by insect pollinators such as bumble bees (*Bombus* spp.) and honeybees (*Apis mellifera*).

Rainfall, temperature, sunshine and spring warming all impact optimal growth. Successful cultivation of cotton requires a long frost-free period (180 - 200 days), plenty of sunshine, and a moderate rainfall. The optimum daytime temperature range for *G. hirsutum* is 30 – 35 ºC, with a loss of fruit above 35 ºC, and with a 50 % yield reduction at 25 °C. Soils usually need to be fairly heavy, with good drainage, filled with organic matter and with a high moisture-retention capacity, although the level of nutrients does not need to be exceptional.

(c) Generation time

The cultural cycle for cotton ranges from 120 to 200 growing days from seedling emergence to maturity. Rainfall, temperature, sunshine and spring warming all impact optimal growth.

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

Pollen that is transferred between cotton of similar genotypes has the potential to produce hybrid seed. Therefore, the allotetraploid species *G. hirsutum* (and *G. barbadense*) will only hybridise with other tetraploid members of the *Gossypium* genus, which species are not known to have a natural habitat in the EU.

No closely related feral or wild relatives of cotton exist in the EU.

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

Since the scope of the current application excludes cultivation of COT102 varieties in the EU, out-crossing with cultivated *Gossypium* varieties is not expected.

2.5. Survivability (for environmental safety aspects)

(a) Ability to form structures for survival or dormancy

Cotton is a perennial plant which is grown as an annual crop. Cottonseeds are the only surviving structures of cotton plants. Cultivated cotton does not produce seeds that are able to persist in the environment for long periods of time.

(b) Specific factors affecting survivability

Cotton cannot survive without human assistance. It is not capable of surviving as a weed. Cultivated cottonseeds lack the ability to develop dormancy and are not able to persist in the environment for long periods of time. Temperature and humidity factors can play a role in affecting the survivability of cotton. Following harvest of cultivated cotton in the EU, some seeds remaining in the field may germinate in the autumn if conditions are favourable, otherwise they are likely to rot and die. In the unlikely event that cottonseeds would over-winter and germinate the following spring in the EU cotton growing regions, cotton volunteers can be easily controlled by current agronomic practices such as cultivation and the use selective herbicides, such as glyphosate and paraquat.

The current application excludes cultivation of COT102 cotton in the EU.

2.6. Dissemination (for environmental safety aspects)

(a) Ways and extent of dissemination

Dissemination of cotton may occur by pollen and cottonseed dispersal. Cotton pollen is very large (120 – 200 µm), sticky and heavy, and not easily dispersed by wind under typical environmental conditions. A number of studies showed that the frequency of cross-pollination decreases rapidly with increasing distance from the pollen source; typically, pollen-mediated gene flow is less than 1 % beyond 10 m from the source. Cottonseed dispersal can occur during planting, harvest, and transport.

The current application excludes cultivation of COT102 cotton in the EU.

(b) Specific factors affecting dissemination

Pollen dispersal is influenced by the presence in numbers of insect pollinators which in turn are affected by a number of factors including climate, surrounding vegetation and insect management. Cottonseed dispersal is influenced by human intervention including mechanical harvesting and transport; wind damage, in which the cotton bolls fall to the ground, can also influence cottonseed dispersal.

The current application excludes cultivation of COT102 cotton in the EU.

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

Cotton is currently cultivated in Greece, Spain and Bulgaria. No closely related feral or wild relatives of cotton exist in the EU.

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)

Cotton is currently cultivated in Greece, Spain and Bulgaria.

2.9. 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 (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, birds, mammals, surrounding weed species, and humans. Cotton is widely cultivated and has a history of safe use. The crop has been cultivated in Greece and Spain for centuries. However, cotton plants do contain several compounds which can have adverse effects on human and animal health. Most important with respect to human health are gossypol and cyclopropenoid fatty acids which are toxicants.

3. MOLECULAR CHARACTERISATION

3.1. Information relating to the genetic modification

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

COT102 cotton is a GM cotton that is produced by *Agrobacterium*-mediated transformation.

(b) Nature and source of the vector used

The COT102 cotton was produced through *A. tumefaciens*-mediated transformation with the binary plasmid vector, pCOT1. The pCOT1 plasmid contains the insecticidal Vip3A gene (*vip3Aa19*) and the selectable marker hygromycin-B phosphotransferase gene, *aph4*. The pCOT1 plasmid backbone is derived from plasmid pHiNK078, the selectable marker gene cassette from plasmid pNOV101, and the insecticidal gene cassette from plasmid pNOV1417.

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

The genetic elements within the right and left borders of the T-DNA of the

transformation plasmid pCOT1 constitute the region intended for integration into the genome of the cotton plant cell. The T-DNA contains two gene cassettes – *vip3Aa19* and *aph4* gene cassettes.

The *vip3Aa19* gene cassette contains the vip3Aa19 coding sequence under the regulation of the Act2 promoter and first intron, and the NOS terminator. The *aph4* gene cassette contains the aph4 coding sequence under the regulation of the Ubq3 promoter and first intron, and the NOS terminator.

The source of each genetic element contained in the *vip3Aa19* gene cassette is as follows: Act2 promoter and intron from the *actin 2* gene of *Arabidopsis thaliana*; *vip3Aa19* coding sequence modified from the native gene, *vip3Aa1*, of *Bacillus thuringiensis* strain AB88; the NOS terminator sequence from the nopaline synthase gene of *Agrobacterium tumefaciens*.

The source of each genetic element contained in the *aph4* gene cassette is as follows: Ubq3 promoter and first intron from the ubiquitin 3 gene, *ubq3*, of *Arabidopsis thaliana*; *aph4* coding sequence from the hygromycin-B phosphotransferase gene of *Escherichia coli* strain K-12; the NOS terminator sequence from the nopaline synthase gene of *Agrobacterium tumefaciens*.

Plasmid pCOT1 contains right and left border sequences that are necessary for the transfer of T-DNA into the plant cell. These border sequences, each 25 bp long, flank the T-DNA allowing for the transfer and integration of the T-DNA into the plant genome during transformation. The right and left border regions in pCOT1 was originally derived from the Ti plasmid of an *Agrobacterium tumefaciens* nopaline strain.

The individual genetic elements intended for insertion into COT102 are provided in Table 1.

Table 1. Genetic elements of the T-DNA region intended for insertion in COT102.

Genetic element	Size (bp)	Description
Left border	25	Left border (LB) region of T-DNA. It is required for the transfer of the T-DNA into the plant cell.
NOS terminator	253	Terminator sequence from the nopaline synthase gene. Its function is to provide a polyadenylation site.
aph4	1026	Sequence encoding the hygromycin-B phosphotransferase. The enzyme enables selection of transformed cells in the presence of hygromycin.
Ubq3 promoter and intron	1721	Promoter region plus first intron from the ubiquitin 3 gene. They are required for the constitutive expression of *aph4*.

Act2 promoter and intron	1408	Promoter region plus first intron from the actin-2 gene. They are required for the constitutive expression of *vip3Aa19*.
vip3Aa19	2370	Sequence encoding the Vip3Aa19 protein. It confers resistance to several lepidopteran insects.
NOS terminator	253	Terminator sequence from the nopaline synthase gene. Its function is to provide a polyadenylation site.
Right border	25	Right border (RB) region of T-DNA. It is required for the transfer of the T-DNA into the plant cell.

3.2. Information relating to the GM plant

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

COT102 cotton is a genetically modified cotton which produces two traits, namely, the Vip3Aa19 protein that confers resistance to some lepidopteran insects, and the APH4 protein that was utilized as a selectable marker in the production of transformed plants.

3.2.2. Information on the sequences actually inserted or deleted

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

Molecular characterisation of COT102 cotton by Southern blot analyses confirmed that COT102 cotton carries a single, intact copy of the pCOT1 T-DNA. There are no extraneous T-DNA fragments of plasmid pCOT1 inserted elsewhere in the cotton genome and there is no backbone sequence from transformation plasmid pCOT1 in COT102 cotton.

The COT102 cotton contains a single copy of each of the functional elements (Act2 promoter and intron, *vip3Aa19*, NOS terminator, Ubq3 promoter and intron, *aph4*, and NOS terminator).

In addition, sequencing data demonstrated that the insert is intact and that the contiguousness of the functional elements within the insert as intended in pCOT1 has been maintained.

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

Comparison of the COT102 insert sequence with the transformation plasmid pCOT1 showed that the COT102 insert was intact, with no rearrangements or base-pair changes. Sequence analysis revealed that some truncation occurred at the RB and LB ends of the T-DNA during the transformation process. Twenty-four base pairs of the RB and nineteen base pairs of the LB were truncated. These deletions have no effect on the functionality of the insert as this phenomenon has been previously observed in transformations with *A. tumefaciens*.

Alignment of genomic sequence flanking the COT102 cotton insert with genomic sequence obtained from the transformation recipient line Coker 312 cotton showed that an 86-bp deletion occurred in the cotton genome during integration of the COT102 T-DNA.

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

Chi square analysis of the segregation data indicated that the COT102 cotton insert segregated according to Mendelian principles and was consistent with a single site of insertion into the cotton nuclear genome. Southern blot analyses demonstrated that COT102 cotton has maintained the integrity number, structure and organization of the COT102 cotton insert.

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

Southern blot data have demonstrated that COT102 cotton contains a single insert that is intact with no rearrangements or base pair changes.

Sequencing data demonstrated that the insert is intact and that the contiguousness of the functional elements within the insert as intended in pCOT1 has been maintained. The sequences of *vip3Aa19*, *aph4*, the Ubq3 and Act2 promoters, and the NOS terminators in COT102 cotton were identical to those in the transformation plasmid pCOT1. Sequence analysis revealed that some truncation occurred at the RB and LB ends of the T-DNA during the transformation process. Twenty-four base pairs of the RB and nineteen base pairs of the LB were truncated. These deletions have no effect on the functionality of the insert as this phenomenon has been previously observed in transformations with *A. tumefaciens*.

(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

COT102 cotton produces two newly expressed proteins: (1) Vip3Aa19 protein, which exhibits insecticidal activity against several lepidopteran pests of cotton, and (2) APH4 protein, which is a selectable marker enzyme, hygromycin-B phosphotransferase.

The concentrations of Vip3Aa19 and APH4 proteins were measured in various tissue types and developmental stages of COT102 cotton plants obtained from four replicate plots planted in a randomized complete block design grown at six locations in the cotton-producing regions of the USA in 2012.

The enzyme-linked immunosorbent assay (ELISA) was used to quantify the

newly expressed proteins, Vip3Aa19 and APH4, in each cotton tissue sample, except for APH4 protein in pollen tissue due to matrix effects present in the ELISA analysis. Expression of APH4 protein in cotton pollen tissue was measured by Western blotting analysis.

The overall arithmetic mean expression values for Vip3Aa19 protein ranged from 2.15 µg/g dry weight in pollen at the early bloom stage to 460.78 µg/g dry weight in leaf at the 4-leaf stage. The arithmetic mean expression value for Vip3Aa19 protein in cottonseed at the maturity stage is 10.65 µg/g dry weight.

The APH4 protein was either non-detectable or the concentrations were at the limit of detection when all tissues (except pollen) of COT102 cotton were analysed by ELISA; expression in pollen was detectable by Western blot analysis. The APH4 protein was either not detected or at the limit of detection for leaf from three different growth stages (*i.e.* 4-leaf, 1st white bloom and 1st open boll), bolls, flower, root, cottonseed, squares, and whole plants in COT102 cotton.

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

Samples from a broad range of tissues including cottonseed (*i.e.* leaves, squares, flowers, bolls, pollen, roots, and whole plants) were collected and analysed from plants at various stages of development. Quantifiable amounts of Vip3Aa19 protein are expressed in most tissues analysed, whereas expression of APH4 protein was either not detectable or at the limit of detection in all tissues analysed by ELISA. For pollen tissue, APH4 protein expression was detectable at low levels by Western blotting analysis.

Taking the scope of this application into consideration, the main route of exposure to the newly expressed proteins is via COT102 cottonseed which is used to produce cottonseed oil for human consumption or meal (oilseed cake) for animal feed.

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

Southern blot and Chi square analyses showed that the insert is stably inherited as a single locus in the cotton nuclear genome across multiple generations. The protein expression levels of Vip3Aa19 and APH4 proteins were similar across multiple generations.

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

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

No changes in the reproduction compared to the conventional counterpart have been observed in agronomic assessments conducted with COT102 cotton.

(b) Dissemination

No changes in the dissemination compared to the conventional

counterpart have been observed in agronomic assessments conducted with COT102 cotton.

(c) Survivability

No changes in the survivability compared to the conventional counterpart have been observed in agronomic assessments conducted with COT102 cotton.

(d) Other differences

No changes in the reproduction, dissemination or survivability compared to the conventional counterpart have been observed in agronomic assessments conducted with COT102 cotton.

In summary, the results of these studies indicate that the genetic modification to produce COT102 cotton does not result in any biologically relevant agronomic or phenotypic differences related to reproduction, dissemination or survivability of COT102 cotton.

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

(a) Plant to bacteria gene transfer

The probability of horizontal gene transfer (HGT) between the COT102 cotton insert and microorganisms was investigated *in silico*, and no sequences were identified as being able to promote homologous recombination.

The horizontal gene transfer from GM plants to bacteria with subsequent expression of the transgene is regarded as a highly unlikely event under natural conditions, especially in the absence of selective pressure. No changes in the ability of the COT102 cotton to transfer genetic material to other organism are expected compared to conventional cotton since no sequences have been introduced to allow this to occur.

(b) Plant to plant gene transfer

The genetic modification in COT102 cotton is not intended to change any of the typical crop characteristics of cotton (except for resistance to several lepidopteran insects). Observations from field trials have confirmed that the agronomic and phenotypic characteristics of COT102 cotton have not changed in comparison with the conventional counterpart, and, therefore, there is no increase or decrease in the potential for plant-to-plant gene transfer of COT102 cotton compared to traditional cotton. Gene transfer from COT102 cotton to other sexually compatible plant species is not possible since cotton has no wild relatives in the EU. In addition, since the scope of this application does not include authorisation for the cultivation, the likelihood of dissemination of pollen to other plants (including cultivated cotton plants) is considered to be negligible.

4. COMPARATIVE ANALYSIS

4.1. Choice of the conventional counterpart and additional comparators

COT102 cotton was compared with the conventional counterpart with a genetic background similar to COT102, as well as with commercially available cotton varieties.

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

COT102 cotton and the conventional counterpart were grown at 11 locations in the USA over two growing seasons (2012 and 2013). Several non-transgenic commercial varieties were used as reference varieties which were of similar maturity to COT102 and the conventional counterpart, and appropriate for the receiving environment. At each location, test, the conventional counterpart and reference plants were grown in a randomized complete block design with four replicate plots per entry. The locations of the trial sites were selected to be representative of the agricultural regions suitable for the cultivation of the selected cotton plants. Appropriate agronomic practices (*i.e.,* insect, weed, and disease control) were implemented at each field testing site to produce a commercially acceptable crop. The experimental design for comparative analysis was in accordance with EFSA guidance. The statistical analysis of data for comparative analysis including the difference and equivalence tests following EFSA's scientific opinion on statistical considerations for the safety evaluation of GMOs were performed.

4.3. Selection of materials and compounds for analysis

The genetic modification in COT102 cotton are not intended to modify the nutritional status of individuals or populations or to be processed into products with enhanced functionality. The use of the food and feed derived from COT102 cotton will be the same as food and feed from non-GM cotton. Therefore, the selected material for analysis is cottonseed (raw material). Samples of cottonseed were analysed for nutrient and anti-nutrient content. The analytes examined were chosen on the basis of the OECD guidance document on compositional considerations for cotton.

The vast majority of nutritional components in COT102 cotton are equivalent to those in the reference lines, and are not significantly different from those in the conventional counterpart cotton.

These data support the conclusion that COT102 cotton is compositionally equivalent to conventional cotton.

4.4. Comparative analysis of agronomic and phenotypic characteristics

An assessment of the agronomic and phenotypic characteristics of COT102 cotton compared to conventional cotton has been performed. Data were collected for multiple agronomic characteristics: early stand count; seedling vigour, flower initiation, nodes above first white flower, plant height, percent open bolls, yield, disease incidence and insect damage. The results of these trials showed that COT102 cotton is agronomically and phenotypically equivalent to conventional cotton, apart from the introduced traits.

4.5. Effect of processing

COT102 cotton will be produced and processed in the same way as any conventional counterpart cotton and there is no evidence to suggest that the expression of the proteins, Vip3Aa19 and APH4, produced by COT102 cotton will influence this processing in any way.

5. TOXICOLOGY

(a) Toxicological testing of newly expressed proteins

Newly expressed proteins are expressed from the *vip3Aa19* and *aph4* genes in COT102 cotton. The *vip3Aa19* gene encodes a Vip3Aa19 insecticidal protein with activity against several lepidopteran pests. The *aph4* gene encodes the selectable marker enzyme hygromycin-B phosphotransferase (APH4), which was utilized during transformation.

To demonstrate the safety of each newly expressed protein, a series of studies have been conducted. For the Tier 1 assessment, no hazard was identified for Vip3Aa19 protein. The weight of evidence strongly supports the conclusion that Vip3Aa19 protein from COT102 are not toxic to humans or vertebrate animals. Humans have a history of safe exposure to Vip3A proteins. The mechanisms of action of Vip3Aa19 is well-characterized, target-specific, and not of toxicological concern to mammals. Vip3Aa19 does not share amino acid sequence similarity to known or putative mammalian toxins. Importantly, the exposure of humans and vertebrate animals to VIP3Aa19 by the consumption of food or feed products containing COT102 is negligible and any residual intact or active protein present after processing would be denatured by mammalian digestive enzymes within minutes. These results support the conclusion that the VIP3Aa19 protein does not present a toxicological hazard and that COT102 is safe for food and feed uses. The acute oral toxicity study conducted as a Tier 2 assessment confirms the conclusion from the weight of evidence from the Tier 1 toxicity assessment, and combined with the negligible dietary exposure potential of Vip3Aa19 protein to humans and animals (due to low levels of expression in COT102 cottonseed, the denaturing effects of crop processing on proteins, and the rapid digestion by pepsin), provides clear and convincing evidence of safety.

Taken together, the lack of an identifiable hazard associated with Vip3Aa19 and the negligible exposure potential of COT102 trait proteins to humans and animals, suggests that repeated-dose toxicity testing of

Vip3Aa19 would needlessly expend animals without providing useful new information regarding the safe use of COT102 food and feed products. Therefore, Syngenta believes that the above data, without the need to perform a repeated-dose 28-day oral toxicity study, supports both the conclusion that no concerns regarding potential toxicity of Vip3Aa19 protein have been identified and the safe use of COT102 food and feed products.

For the Tier 1 assessment, no hazard was identified for APH4 protein. The weight of evidence strongly supports the conclusion that APH4 protein from COT102 is not toxic to humans or animals. It is highly probable that humans have a history of safe exposure to APH4 protein. The mechanisms of action of APH4 is well-characterized, target-specific, and not of toxicological concern to mammals. APH4 does not share amino acid sequence similarity to known or putative mammalian toxins. Importantly, the exposure of humans and vertebrate animals to APH4 by the consumption of food or feed products containing COT102 cotton is negligible and any residual intact or active protein present after processing would be denatured by mammalian digestive enzymes within minutes. These results support the conclusion that the APH4 protein does not present a toxicological hazard and that COT102 cotton is safe for food and feed uses. The acute oral toxicity study conducted as a Tier 2 assessment confirms the conclusion from the weight of evidence from the Tier 1 toxicity assessment, and combined with the negligible dietary exposure potential of APH4 protein to humans and animals (due to low levels of expression in COT102 cottonseed and the rapid digestion by pepsin), provides clear and convincing evidence of safety.

Taken together, the lack of an identifiable hazard associated with APH4 and the negligible exposure potential of COT102 trait proteins to humans and animals, suggests that repeated-dose toxicity testing of APH4 would needlessly expend animals without providing useful new information regarding the safe use of COT102 food and feed products. Therefore, Syngenta believes that the above data, without the need to perform a repeated-dose 28-day oral toxicity study, supports both the conclusion that no concerns regarding potential toxicity of APH4 protein have been identified and the safe use of COT102 food and feed products.

(b) Testing of new constituents other than proteins

Cotton is a common source of food and feed and has a long history of safe use. COT102 cotton has been modified to produce the Vip3Aa19 and APH4 proteins. No other new constituents apart from these proteins are expected to be produced in COT102 cotton and compositional analyses have confirmed the compositional equivalence of COT102 cotton to conventional cotton. Therefore, no testing of any other constituent is considered necessary.

(c) Information on natural food and feed constituents

Cotton is a common source of food and feed and has a long history of

safe use. All cotton contains gossypol and several cyclopropenoid fatty acids (CPFAs) which are considered to be anti-nutritional. COT102 cotton has been found to be compositionally equivalent to conventional cotton varieties. These analyses showed that the levels of the components measured had not changed beyond the natural variation in cotton. No significant differences emerged to suggest that biologically relevant changes in composition or nutritive value of the cotton had occurred as an unintended result of the expression of the novel proteins in COT102 cotton.

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

Although COT102 cotton have been found to be compositionally equivalent to conventional cotton varieties except for the presence of the intended traits, a 90-day feeding study with COT102 cottonseed meal in rodents was performed since it is a requirement under Article 12 of the Regulation (EU) No 503/2013.

The 90-day whole food safety study was conducted in line with OECD TG 408 guidelines on 10 animals/sex/treatment fed diets incorporating COT102 toasted cottonseed meal (CSM) or non-transgenic near-isogenic control toasted CSM at two dose levels (3 or 10%). The low dose (dietary inclusion levels of 3% CSM) exceed anticipated levels of human and animal dietary intake. The incorporation of COT102 toasted CSM in diets fed to rats for at least 91 consecutive days produced no toxicological effects on body weight, food consumption, clinical condition (including neurotoxicity assessments), ophthalmoscopy, haematology, coagulation, chemical chemistry, organ weights, macroscopic or microscopic pathology at inclusion levels up to and including 10%.

It was concluded that cottonseed meal from COT102 cotton is safe for food and feed consumption and no differences in wholesomeness are expected with comparable conventional counterpart cotton varieties.

6. ALLERGENICITY

(a) Assessment of allergenicity of the newly expressed protein

The weight-of-evidence indicates that the newly expressed proteins produced by COT102 cotton are not likely to be food allergens because:

1. the Vip3Aa19 and APH4 proteins are not derived from allergenic sources,
2. Vip3Aa19 and APH4 do not have biologically relevant amino acid sequence similarity to known or putative allergenic proteins,
3. Vip3Aa19 and APH4 are readily degraded in *in vitro* digestibility assays.

From these data, it can be concluded that Vip3Aa19 and APH4 produced by COT102 cotton are highly unlikely to be allergenic.

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

Cotton is widely cultivated and has a history of safe use; it is not

considered an allergenic food crop. There is no expectation that COT102 cotton plants have increased allergenic potential compared to their non-GM counterparts since equivalence of COT102 cotton (with the exception of the introduced traits) to the conventional comparator was demonstrated on the basis of compositional analysis.

7. NUTRITIONAL ASSESSMENT

(a) Nutritional assessment of the genetically modified food

COT102 cotton is not intended to change the nutritional status of individuals or populations or to be processed in products with enhanced functionality. Compositional analysis and whole food safety tests have demonstrated that no unexpected alterations in nutrients and other food components have occurred and that no nutritional imbalances were introduced in COT102 cotton, and derived food products.

(b) Nutritional assessment of the genetically modified feed

COT102 cotton is not intended to change the nutritional status of livestock animals or to be processed in products with enhanced functionality. Compositional analysis has demonstrated that no unexpected alterations in nutrients and other food or feed components have occurred and that no nutritional imbalances were introduced in COT102 cotton, and derived feed products.

8. EXPOSURE ASSESSMENT – ANTICIPATED INTAKE/EXTENT OF USE

The primary food uses of cotton are limited to refined cottonseed oil and cottonseed linters. Since total protein is essentially removed from cottonseed oil during processing and is not present in linters, the potential for human dietary exposure to APH4 and Vip3Aa19 proteins from COT102 cotton plants is negligible. Given the lack of (1) measurable trait protein concentrations in COT102 cotton food products and (2) consumption data of protein containing cotton food products, dietary exposure assessments were not performed to estimate consumption of APH4 and Vip3Aa19 proteins via COT102 cotton-based products by human consumers in the EU. Given the lack of high dose acute oral toxicity of APH4 or Vip3Aa19 and the negligible potential for human dietary exposure to COT102 trait proteins, safety margins of exposure would provide a reasonable certainty of no harm to consumers of any transgenic protein residues that might be present in COT102 food products.

A dietary exposure assessment was performed to estimate consumption of the Vip3Aa19 protein from COT102 cottonseed and cottonseed by-products by livestock. A similar assessment was not made for the APH4 protein because it was not quantifiable (levels below the limit of detection). The dietary exposure assessment used OECD feed intake datasets to conservatively calculate concentrations of Vip3Aa19 that could be consumed by livestock fed COT102 cottonseed or cottonseed by-products, applying a “reasonable worst case feed” (RWCF) model. The worst case exposure to the Vip3Aa19 protein is low, and based on the fact that APH4 levels were below the LOD, the worst case exposure to the APH4 protein is extremely low. The exposure to Vip3Aa19 has been

calculated using conservative assumptions that do not account for potentially lower exposures due to loss during processing or digestion. The estimated exposure to the Vip3Aa19 protein is less than 1 part per million in all livestock investigated. Toxicological assessments of both proteins indicate no adverse effects on animal health due to the consumption of COT102 cotton. Considering the lack of hazard associated with either Vip3Aa19 or APH4 proteins, the fact that the concentration of the APH4 protein could not be accurately measured because its amount in COT102 cotton was below the assay LOD, and the small amount of Vip3Aa19 protein that has been estimated as likely to be consumed by livestock under a reasonable worst case feeding model, the risk to livestock consuming COT102 cottonseed or cottonseed by-products is very low, and there is a reasonable certainty that no harm will come to livestock consumers of COT102 cotton.

9. RISK CHARACTERISATION

The information presented in the application confirms that COT102 cotton and derived food and feed products are not different from those of its conventional counterpart. The molecular characterization of COT102 cotton did not raise any safety concerns nor identified any unintended changes as a result of the genetic modification. Compositional analysis concluded that the levels of the vast majority of nutritional components in COT102 cotton are equivalent to those in the non-transgenic reference lines, and are not significantly different from those in the non-transgenic, conventional counterpart cotton. The agronomic and phenotypic characteristics of COT102 cotton plants, except for the introduced traits, are not different to those of its conventional counterpart comparator, taking into account natural variation. Characterisation of Vip3Aa19 and APH4 proteins, and evidence of history of safe use, continue to confirm that these proteins are safe for human and animal consumption, and that no adverse effects on human and animal health can be expected. The genetic modification in COT102 cotton is not intended to improve the nutritional status of individuals or populations or to be processed in products with enhanced functionality. The exposure assessment in humans and animals did not indicate any safety concerns, and dietary role of COT102 is intended to be the same as the dietary role of conventional cotton.

10. POST-MARKET MONITORING ON THE GENETICALLY MODIFIED FOOD OR FEED

As described in Sections 4 to 9 above, the presence of COT102 cotton or its derived products in food and feed will not result in any nutritional changes. Therefore, post-market monitoring of COT102 cotton food/feed is not considered necessary.

11. ENVIRONMENTAL ASSESSMENT

11.1. Mechanism of interaction between the GM plant and target organisms

COT102 cotton has been developed to confer resistance to some lepidopteran insects. These lepidopteran insects may be considered as target organisms which interact with the COT102 cotton plants. However, the scope of this

application covers the food and feed, import and processing in the EU. COT102 cultivation in the EU is not included in the scope. Therefore, exposure of target organisms to COT102 cotton plants will be highly unlikely.

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

(a) Persistence and invasiveness

Taking into account the results obtained in agronomic comparisons and the fact that the scope of this application does not include cultivation of COT102 cotton, the growth of any cotton plants outside cultivated areas is very unlikely, which means that environmental exposure in the EU would be very low and localised. It can be concluded that: The genetic modification introduced in COT102 cotton has not altered agronomic and phenotypic characteristics of COT102 cotton associated with persistence or invasiveness potential compared to conventional cotton. In addition, the genes introduced in COT102 cotton will not confer any selective advantage or disadvantage to COT102 cotton compared to conventional cotton, apart from the intended modifications. Therefore COT102 cotton will not differ in persistence and invasiveness from conventional cotton.

In summary, the likelihood that COT102 cotton will become more persistent than the recipient or parental plants in agricultural habitats or more invasive in natural habitats as a result of import, processing or food and feed use, in the EU can be considered negligible.

(b) Selective advantage or disadvantage

An assessment of whether the transfer of the newly introduced genes in COT102 cotton (*vip3Aa19* and *aph4*) could confer any selective advantage or disadvantage to other cotton plants or to sexually compatible wild relatives and the potential consequences of this transfer has been conducted. Taking into account the results obtained from the Environmental Risk Assessment (ERA), the results of the comparative safety assessment and the fact that the scope of this application does not include cultivation of COT102 cotton in the EU, the conclusion from the assessment is that the expression of *vip3Aa19* and *aph4* will not confer any selective advantage or disadvantage to COT102 cotton.

(c) Potential for gene transfer

The scope of this application covers the import, processing, and food and feed use of COT102 cotton and derived products in the EU. Cultivation of COT102 cotton in the EU is not included in the scope. Therefore, it is highly unlikely that COT102 cotton plants will grow in the EU.

There is also no change in the ability of COT102 cotton to transfer genetic material to other organisms when compared to conventional cotton. The horizontal gene transfer from GM plants to bacteria with subsequent expression of the transgenes is regarded as highly unlikely under natural conditions, especially in the absence of selective pressure.

Gene transfer from COT102 cotton to other sexually compatible plant species is not possible since there are no wild relatives of cotton in the EU and vertical gene transfer would be limited to other cotton plants. Therefore, it is highly unlikely that the import, processing, and food and feed use of COT102 cotton and derived products in the EU would lead to any adverse environmental effects due to plant-to-plant gene transfer.

Given the low levels of exposure to micro-organisms that could arise from the import, processing, and food and feed use of COT102 cotton in the EU and the characteristics of the transgenes, *vip3Aa19* and *aph4*, it is highly unlikely that horizontal gene transfer will occur. If gene transfer did occur, it is unlikely that the transgenes would become established in the genome of microorganisms in the environment or human and animal digestive tract.

In the very unlikely event that any of the genes were established in the genome of microorganisms, no adverse effects on human and animal health or the environment are expected.

(d) Interactions between the GM plant and target organisms

The scope of this application covers the import, processing, and food and feed use of COT102 cotton in the EU, no deliberate release of viable plant material in the EU environment is expected. Therefore an assessment of the potential resistance development in target organisms resulting from the import, processing and food and feed use COT102 cotton is not relevant for this application.

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

The scope of this application does not include cultivation of COT102 cotton in the EU. Therefore, potential immediate or delayed effects in the environment due to direct or indirect interactions between COT102 cotton plants and non-target organisms as a result of the import, processing or products for food and feed use of COT102 cotton in the EU can be considered highly unlikely.

(f) Effects on human health

Compositional analysis with COT102 cotton has confirmed that COT102 cotton is equivalent in composition to conventional cotton and is as safe and nutritious as conventional cotton.

There is no reason to anticipate that COT102 cotton would result in a product that differs in toxicity or allergenic potential to humans. None of the proteins (Vip3Aa19 and APH4) produced by COT102 cotton are known to be toxic or allergenic to humans and there are no known precedents where interactions between non-toxic proteins lead to toxic effects. The results of the toxicological and allergenicity assessment indicate that consumption of COT102 cotton food products will be as safe as consuming equivalent products from conventional cotton, regardless of the anticipated intake level.

In summary, no adverse effects on human health or adverse consequences for the food chain are expected following consumption of food consisting, containing or derived from COT102 cotton.

(g) Effects on animal health

The potential adverse effects of importing COT102 cotton or derived products into the EU on animal health have been assessed. Studies conducted with Vip3Aa19 and APH4 show that these proteins are unlikely to be toxic to humans or animals. None of these proteins shows significant sequence identity to known protein toxins. In addition, Vip3Aa19 and APH4 are unlikely to be allergenic.

The results obtained from the comparative analysis of composition of COT102 cotton with conventional cotton have shown that the levels of natural food and feed constituents have not changed beyond the natural variation in cotton and no evidence of unintended effects has been observed. The conclusion of this assessment is that feed derived from COT102 cotton is as safe for animal consumption as feed derived from conventional cotton.

In summary, no adverse effects on animal health or adverse consequences for the feed chain are expected following consumption of feed consisting, containing or derived from COT102 cotton.

(h) Effects on biogeochemical processes

The scope of this application does not include cultivation of COT102 cotton in the EU. Interactions with target or non-target organisms that could lead to effects on biogeochemical processes are therefore highly unlikely.

In the unlikely event that small amounts of COT102 cotton accidentally found their way into the EU environment, their survival would be very unlikely, as cotton is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. Moreover, these plants could be easily controlled using any of the current agronomic measures taken to control other commercially available cotton. In the unlikely event that some plants of COT102 cotton survived, the potential effects on biogeochemical processes as a result of interactions with target and non-target organisms are likely to be the same as those effects resulting from cultivation of non-modified cotton.

In summary, the risk of adverse effects on biogeochemical processes resulting from changes in management practises or interactions of COT102 cotton and target or non-target organisms can be considered negligible under the scope of this application.

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

Not applicable since the scope of this application does not include cultivation of COT102 cotton in the EU.

11.3. Potential interactions with the abiotic environment

The scope of this application does not include cultivation of COT102 cotton in the EU. Therefore, interactions of COT102 cotton with the abiotic environment are highly unlikely. In the unlikely event that small amounts of COT102 cotton accidentally found their way into the EU environment, their survival would be very unlikely, as cotton is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. Moreover, these plants could be easily controlled using any of the current agronomic measures taken to control other commercially available cotton. In the unlikely event that some plants of COT102 cotton survive, the potential effects on the abiotic environment will be negligible.

11.4. Risk characterisation for the environmental risk assessment

Cultivation of cotton has a long history of environmental safety. Results from the environmental risk assessment support the conclusion that the import, processing, and food and feed uses of COT102 cotton in the EU represents negligible risk to human and animal health and the environment, and poses no greater risk than the import, processing, and food and feed uses of conventional cotton.

12. ENVIRONMENTAL MONITORING PLAN

(a) General (risk assessment, background information)

The scope of this application does not include cultivation of COT102 cotton. Environmental exposure to COT102 cotton could only occur in the unlikely event that small amounts of COT102 cotton accidentally found their way into the environment in the EU. However, the survival of this cotton would be very unlikely as cotton is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. If germinated, COT102 cotton could easily be controlled using any of the current agronomic measures taken to control other commercially available cotton.

An ERA has been conducted for COT102 cotton as recommended in the EFSA Guidance for risk assessment of food and feed from genetically modified plants and the EFSA Guidance on the ERA of GM plants, and taking into account the scope of this application. Risk assessment concepts described in recent scientific publications have also been used.

The overall conclusion of the ERA confirms that the import and food and feed use of COT102 cotton will not result in harmful effects on human or animal health or to the environment in the EU.

(b) Interplay between environmental risk assessment and monitoring

An ERA has been conducted for COT102 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.

The scientific evaluation of the characteristics of COT102 cotton in the ERA

has shown that the risk for potential adverse effects on human and animal health or the environment is negligible in the context of the intended uses of this GM cotton relative to:

- Persistence and invasiveness
- Selective advantage or disadvantage
- Potential for gene transfer
- Interactions between the GM plant and target organisms
- Interactions of the GM plant with non-target organisms
- Effects on human health
- Effects on animal health
- Effects on biogeochemical processes
- Impacts of the specific cultivation, management and harvesting techniques
- Potential interactions with the abiotic environment.

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

An ERA has been conducted in accordance with Annex II of Directive 2001/18/EC to evaluate potential adverse effects of COT102 cotton on human and animal health and the environment. The conclusions of this ERA confirm that the potential risks to human and animal health or the environment arising from the placing on the market of COT102 cotton can be considered negligible, under the scope of this application. Therefore, a case-specific monitoring plan is not considered necessary.

(d) General surveillance of the impact of the GM 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 GM plant or its use for human and animal health or the environment that were not predicted in the ERA.

The scope of this application does not include authorisation for the cultivation of COT102 cotton. Therefore, exposure to the environment will be limited to unintended release of COT102 cotton, which could occur for example via substantial losses during loading/unloading of the viable commodity 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.

However, and in order to safeguard against any adverse effects on human and animal health or the environment that were not anticipated in the ERA, general surveillance on COT102 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 COT102 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 COT102 cotton. The operators will be provided with guidance to facilitate reporting of any unanticipated adverse effect from handling and use of viable COT102 cotton.

(e) Reporting the results of monitoring

The applicant/consent holder is responsible, under Regulation (EC) No 1829/2003, to inform the Commission of the results of the surveillance. Consistent with the EFSA guidance, the applicant will submit a General Surveillance Report containing information related to the monitoring on an annual basis.

13. DETECTION AND EVENT-SPECIFIC IDENTIFICACION TECHNIQUES FOR THE GM PLANT

For specific detection of COT102 cotton genomic DNA, a real-time quantitative TaqMan® PCR method has been developed by Syngenta. This detection method has been submitted for validation to the European Union Reference Laboratory for GM Food and Feed (EURL GMFF) of the Joint Research Centre of the European Commission as part of this application.

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

14.1. 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

No trials of COT102 cotton have been carried out in the EU.

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

(a) Release country

United States: 2000-2005, 2007, 2012, 2015
Argentina: 2001, 2014, 2016
Brazil: 2001
South Africa: 2004-2006
Burkina Faso: 2003-2007
Zimbabwe: 2003-2005
Australia: 2001-2002
India: 2002
Vietnam: 2002
China: 2001

Japan: 2007

(b) Authority overseeing the release

United States: United States Department of Agriculture

Argentina: Comisión Nacional Asesora de Biotecnología Agropecuaria

Brazil: CTNBio and Ministry of Agriculture

South Africa: Department of Agriculture

Burkina Faso: Minister de L'environnement ETDU Cadre de Vie

Zimbabwe: Biosafety Board Research Council of Zimbabwe

Australia: Office of the Gene Technology Regulator

India: Review Committee on Genetic Manipulation

Vietnam: Ministry of Agriculture and Rural Development

China: Ministry of Agriculture

Japan: Ministry of Agriculture, Forestry, and Fisheries

(c) Release site

United States: Alabama; Arizona; Arkansas; California; Florida; Georgia; Hawaii; Louisiana; Missouri; Mississippi; North Carolina; Puerto Rico; South Carolina; Tennessee; Texas

Argentina: Santa Fe; Chaco

Brazil: Minas Gerais

South Africa: Groblersdal; Hartswater

Burkina Faso: Ouagadougou

Zimbabwe: Kadoma

Australia: New South Wales

India: Aurangabad

Vietnam: Ninh Thuan

China: Sichuan

Japan: Kanza, Shizuoka prefecture

(d) Aim of the release

COT102 was released for the purpose of regulatory trials, efficacy testing, yield testing, product development, and/or demonstration.

(e) Duration of the release

The duration of each release was one growing season.

(f) Aim of post-releases monitoring

Post-release monitoring was conducted to assess volunteers.

(g) Duration of post-releases monitoring

United States: 12 months

Argentina:	36 months
Brazil:	6 months
South Africa:	12 months
Burkina Faso:	12 months minimum
Zimbabwe:	12 months
Australia:	12 months
India:	6 months minimum
Vietnam:	6 months minimum
China:	36 months
Japan:	6 months

(h) Conclusions of post-release monitoring

No volunteers typically observed. If volunteers occur, practice is to eliminate them manually or chemically to prevent occurrence in subsequent crops.

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

Field-testing provided no evidence that COT102 would be the cause of any adverse effects to human health or to the environment.