

**Application for renewal of the
authorization for continued marketing of
existing foods and food ingredients
produced from MON 1445 cotton, as well as
food additives, feed materials and feed
additives produced from MON 1445 cotton
that were notified according to Articles
8(1)(a), 8(1)(b) and 20(1)(b) of Regulation
(EC) No 1829/2003 on genetically modified
food and feed**

Part II
Summary

April 2007

Updated June 2011

Data protection.

This application contains scientific data and other information which are protected in accordance with Art. 31 of Regulation (EC) No 1829/2003.

Part II – Summary

1

Regulation (EC) No 1829/2003
MON 1445

Monsanto Company

A. GENERAL INFORMATION

1. Details of application

a) Member State of application Not applicable
b) Notification number EFSA-GMO-RX-MON1445
c) Name of the product (commercial and other names) The Monsanto development code for this genetically modified cotton is: MON 1445. In countries where MON 1445 is being cultivated, packages of this cotton are marketed under the name of the local variety, in association with the Roundup Ready® trademark indicating clearly to growers that the hybrid is tolerant to Roundup® herbicide, containing the active ingredient glyphosate.
d) Date of acknowledgement of notification 15 May 2007

2. Applicant

a) Name of applicant Monsanto Company, represented by Monsanto Europe S.A.		
b) Address of applicant <table><tr><td>Monsanto Europe S.A. Avenue de Tervuren 270-272 B-1150 Brussels BELGIUM</td><td>Monsanto Company 800 N. Lindbergh Boulevard St. Louis, Missouri 63167 U.S.A</td></tr></table>	Monsanto Europe S.A. Avenue de Tervuren 270-272 B-1150 Brussels BELGIUM	Monsanto Company 800 N. Lindbergh Boulevard St. Louis, Missouri 63167 U.S.A
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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)) Food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 will continue to be traded and used in the E.U. in the same manner as current commercial cotton and by the same operators currently involved in the trade and use of cotton.		

® Roundup Ready and Roundup are registered trademarks of Monsanto Technology LLC.

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 (<input type="checkbox"/>)	No (<input checked="" type="checkbox"/>)
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 (<input type="checkbox"/>)	No (<input checked="" type="checkbox"/>)
If no, refer to risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC See following sections	

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 (<input checked="" type="checkbox"/>)	No (<input type="checkbox"/>)
If yes, specify Cottonseed oil produced from MON 1445 has been notified under Regulation (EC) No 258/97 in July 2002, on the basis of an opinion of substantial equivalence delivered by the UK Advisory Committee on Novel Foods and Processes (ACNFP). Previously, in 1998, MON 1445 had also received a favourable opinion by the Scientific Committee on Plants (SCP).	

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

Yes (x)	No ()
<p>If yes, specify</p> <p>Cultivation of MON 1445 is lawful in six countries, including Argentina, Australia/New Zealand, Colombia, South Africa, and the U.S.A. Importation of MON 1445-derived foods and feeds is approved in the E.U., Canada, China, Japan, Korea, Mexico, the Philippines, and Singapore.</p>	

8. General description of the product

<p>a) Name of the recipient or parental plant and the intended function of the genetic modification</p> <p>MON 1445 was produced through genetic modification. MON 1445 expresses the CP4 EPSPS protein, which carries an herbicide-tolerance trait, as well as a trait for selection on kanamycin containing media. The CP4 EPSPS protein provides tolerance to glyphosate, the active ingredient in the Roundup family of agricultural herbicides.</p>
<p>b) Types of products planned to be placed on the market according to the authorisation applied for</p> <p>The scope of this renewal application includes food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445, which are lawfully placed on the market in the E.U., as listed in the Community Register of GM Food and Feed¹. The range of uses of MON 1445-derived products will be identical to the full range of equivalent uses of current commercial cotton derived products.</p>
<p>c) Intended use of the product and types of users</p> <p>MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives will continue to be traded and used in the E.U. in the same manner as equivalent products from current commercial cotton and by the same operators currently involved in the trade and use of cotton.</p>
<p>d) Specific instructions and/or recommendations for use, storage and handling, including mandatory restrictions proposed as a condition of the authorisation applied for</p> <p>MON 1445 is substantially equivalent to conventional cotton varieties except for its introduced trait, namely tolerance to glyphosate, which is a trait of agronomic interest. MON 1445 was shown to be as safe and as</p>

¹ http://ec.europa.eu/food/dyna/gm_register/index_en.cfm

nutritious as conventional cotton. Therefore, MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives will be stored, packaged, transported, handled, and used in the same manner as products derived from current commercial cotton. No specific conditions are warranted or required for the food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445.

e) Any proposed packaging requirements

MON 1445 is substantially equivalent to conventional cotton varieties (except for its tolerance to glyphosate). Therefore, MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives will continue to be used in the same manner as other equivalent cotton derived products and no specific packaging is foreseen. [For the labeling, *see* question 8.(f)].

f) A proposal for labeling in accordance with Articles 13 and 25 of Regulation (EC) 1829/2003. In the case of GMOs, food and/or feed containing, consisting of GMOs, a proposal for labeling 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.

In accordance with Regulations (EC) N° 1829/2003 and 1830/2003, a labelling threshold of 0.9 % is applied for the placing on the market of MON 1445 seed and derived products.

According to Regulation (EC) No 1829/2003, Articles 13 and 25, the operators placing on the market food and feed products produced from MON 1445 shall ensure that those products are labeled with the words “*produced from genetically modified cotton*”. In the case of products for which no list of ingredients exists, operators shall ensure that an indication that the food or feed product is produced from this GM plant is transmitted in writing to the operator receiving the product.

Operators handling or using foods and feeds produced from MON 1445 in the E.U. are required to be aware of the legal obligations regarding traceability and labeling of these products.

Given that explicit requirements for the traceability and labeling of GMOs and derived foods and feeds are described in Regulations (EC) No 1829/2003 and 1830/2003, and that authorized foods and feeds shall be entered in the Community Register, operators in the food and feed chain will be fully aware of the traceability and labeling requirements for foods and feeds produced from MON 1445. Therefore, no further specific measures are to be taken by the applicant.

<p>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)</p> <p>Not applicable</p>
<p>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</p> <p>MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives are suitable for use throughout the E.U.</p>

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

<p>Misuse of food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as misuse of food additives, feed materials and feed additives produced from MON 1445 is unlikely, as the proposed uses for this cotton are included in the current food and feed uses of conventional cotton. MON 1445 is substantially equivalent to other cotton except for the introduced trait, which is a trait of agronomic interest. MON 1445 has been shown to be as safe and as nutritious as conventional cotton. Therefore, any measures for waste disposal and treatment of MON 1445-derived products are the same as those for conventional cotton. No specific conditions are warranted or required for the placing on the market of MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives.</p>
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B. INFORMATION RELATING TO (A) THE RECIPIENT OR (B) (WHERE APPROPRIATE) PARENTAL PLANTS

1. Complete name

a) Family name Malvaceae
b) Genus <i>Gossypium</i>
c) Species <i>hirsutum</i>
d) Subspecies N/A
e) Cultivar/breeding line Coker 312
f) Common name Cotton

2. a) Information concerning reproduction

(i) Mode(s) of reproduction Cotton production is generally carried out with seeds. Cotton is a perennial plant that is harvested and planted annually. Cross-pollination can occur, but cotton is normally considered to be a self-pollinating crop.
(ii) Specific factors affecting reproduction Although natural crossing can occur, cotton is normally considered to be a self-pollinating crop. The pollen is heavy and sticky and transfer by wind is unlikely. Regardless, there are no morphological barriers to cross-pollination based on flower structure. Pollen is transferred by insects, in particular by various wild bees, bumble bees (<i>Bombus</i> sp.), and honeybees (<i>Apis mellifera</i>).
(iii) 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 b) Sexual compatibility with other cultivated or wild plant species

The scope of the current application does not include the environmental release of MON 1445.

Gene transfer to cultivated genotypes

In as much as similar cotton genotypes are fully sexually compatible; any pollen that is transferred has the potential to produce a hybrid seed. The degree of out-crossing in a production field is strongly dependent upon the geographic location of the field, which depends upon the crop ecology. Cross-pollination decreased from five to less than one percent from one to seven meters, respectively, away from the source plot. Regardless, outcrossing with cultivated *Gossypium* varieties is not expected in the context of this renewal application.

Gene transfer to wild plant species

The criterion of sexual compatibility greatly limits the potential of gene flow from cultivated *Gossypium* in the geopolitical boundaries of Spain, Greece or other countries of the E.U. No genera in the *Gossypieae* tribe occur naturally in these countries.

3. Survivability

a) Ability to form structures for survival or dormancy

Cotton is a perennial plant that is harvested and planted annually and is not considered to have weedy characteristics.

b) Specific factors affecting survivability

Cultivated cotton does not possess any of the attributes associated with long term survivability such as seed dormancy, long soil persistence, germination under diverse environmental conditions, rapid vegetative growth, a short life cycle, high seed output, high seed dispersal, or long distance dispersal of seeds. In most cotton growing areas of the E.U. some of the seed remaining in the field following harvest and cultivation may germinate in the autumn if conditions are favorable. The seeds not germinating are likely to rot and die. In cotton growing regions with mild and dry winters, such as Spain and Greece, cottonseed may over-winter and germinate the following spring. These cotton volunteers can be easily controlled by current agronomic practices including cultivation and the use of appropriate herbicides. However, it should be noted that cultivation and import of whole seed of MON 1445 is not in the scope of this application.

4. Dissemination

a) Ways and extent of dissemination

Cotton is a perennial plant that is harvested and planted annually. Dissemination occurs only by means of seeds. Genetic material can be disseminated by pollen movement. However, the current renewal application does not include the cultivation of MON 1445 varieties in the E.U. but only the continued use of existing food and feed products derived from MON 1445.

b) Specific factors affecting dissemination

Seed dissemination is impacted by mechanical harvesting and transport as well as wind damage, which may cause some mature bolls to fall to the ground. Pollen dispersal is influenced by insect vectors, particularly, bumble bees (*Bombus* spp.) and honey bees (*Apis mellifera*), with the former being the most efficient pollinator.

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

The major type of cotton being grown commercially around the world is the upland cotton *G. hirsutum*. There are, however, other two minor categories of cotton grown globally: the long staple cotton, *G. barbadense* (commonly known as Pima or Egyptian cotton) and the Asiatic cotton, including *G. arboreum* and *G. herbaceum*.

Cotton is grown worldwide between latitudes of 45° north and 30° south, in areas that have at least 160 frost-free days. Cotton is a 'heat loving' plant, however more than 50% of the world crop is grown in temperate zones above 30° N latitude. Additionally, cotton is grown under similar climatic and soil constraints. The majority of cotton is grown in areas that receive between 50 and 150 cm of rainfall per year.

The major cotton producing countries in the world include the United States, Peoples Republic of China, India, Pakistan, and the Republic of Uzbekistan. Brazil, Australia, Egypt, Argentina, Turkey, Greece, Syria, and others produce significant, but lesser amounts.

There are no close wild relatives of cotton in the E.U.

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

In the E.U., cotton is commercially grown in Spain and Greece.

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 environment including a range of beneficial and pestiferous arthropods, fungal diseases and surrounding weed species. Cotton is cultivated in Spain and Greece and has a history of safe use in those countries. Cotton is not considered harmful, nor pathogenic to humans, however, the plant does produce gossypol and cyclopropenoid fatty acids, which are natural toxicants. Both gossypol and cyclopropenoid fatty acids contents are reduced via processing of the cottonseed into oil or meal.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

The *cp4 epsps*, *nptII*, and *aad* coding sequences were stably transferred into the genome of cotton cells using *Agrobacterium tumefaciens* mediated transformation.

2. Nature and source of the vector used

The plasmid vector, PV-GHGT07, is a 12 kb single-border, binary transformation vector. It contains well-characterized DNA segments required for selection and replication of the plasmid in bacteria as well as a right border for initiating the transfer of this DNA into the plant genomic DNA.

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

The individual components and the size, source and function of these inherited DNA sequences are given in Table 1. A schematic representation of the insert is shown in Figure 1.

Table 1. Summary of genetic elements of the T-DNA insert in MON 1445.

Genetic element	Approximate size (kb)	Description/source (Reference)
B- Right Border	0.02	DNA sequences derived from <i>Agrobacterium</i> containing the right border sequence essential for transfer of the T-DNA.
<i>cp4 epsps cassette</i>		
E9 3'	0.64	3' non-translated region of the pea ribulose-1,5-bisphosphate carboxylase small subunit (<i>rbcS</i>) E9 gene, which functions to terminate transcription and directs polyadenylation of the mRNA.
<i>cp4 epsps</i>	1.37	Coding region for the synthetic CP4 EPSPS protein (5-enolpyruvylshikimate-3-phosphate synthase) from <i>Agrobacterium</i> sp. strain CP4 (<i>aroA</i> gene).
<i>ctp2</i>	0.29	DNA coding sequence for the N-terminal chloroplast transit peptide from <i>Arabidopsis thaliana epsps</i> gene.
FMV	0.56	Modified figwort mosaic virus promoter.
<i>aad coding sequence</i>		
<i>aad</i>	0.83	Coding region for an aminoglycoside-modifying enzyme, 3'(9)-O-nucleotidyltransferase from the transposon Tn7.
<i>nptII cassette</i>		
NOS 3'	0.25	3' non-translated region of the nopaline synthase (NOS) gene from <i>Agrobacterium tumefaciens</i> , which terminates transcription and directs polyadenylation.
<i>nptII</i>	0.79	DNA region isolated from bacterial transposon Tn5 coding for neomycin phosphotransferase type II. Expression of this sequence in plant cells confers resistance to kanamycin and serves as a selectable marker for transformation.
35S	0.32	Cauliflower mosaic virus (CaMV) promoter.
<i>ori-V origin of replication</i>		
<i>ori-V</i>	0.22	Origin of replication for <i>Agrobacterium</i> derived from the broad host range plasmid RK2.

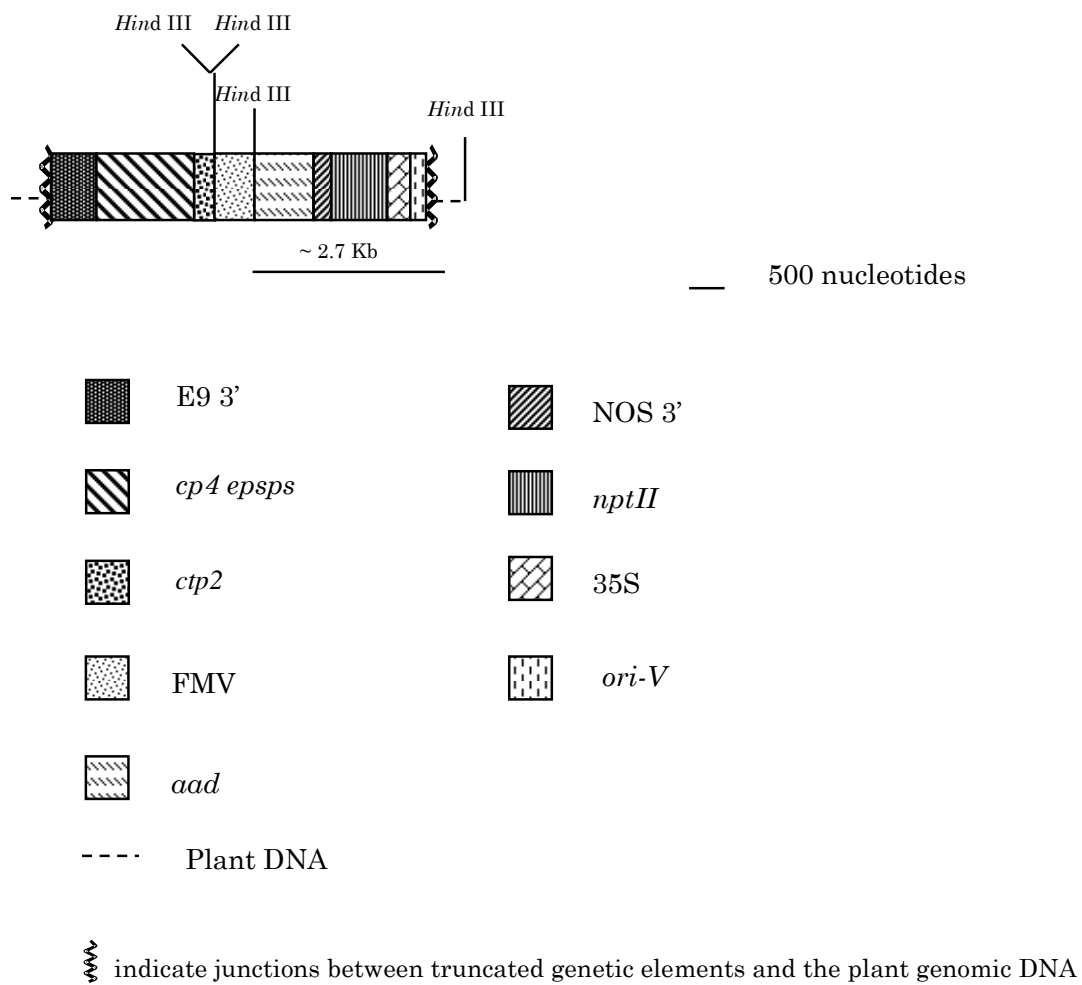


Figure 1. Schematic representation of MON 1445 insert

D. INFORMATION RELATING TO THE GM PLANT

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

MON 1445 was produced by genetic modification. MON 1445 expresses the CP4 EPSPS protein, which confers tolerance to glyphosate, as well as a trait for selection on kanamycin containing media. The glyphosate-tolerance trait provides a novel, highly efficacious weed control option for farmers, and allows the farmer to take advantage of the favorable environmental properties exhibited by Roundup. The trait and characteristics introduced in MON 1445 have been described previously in a notification pursuant to Regulation (EC) No 258/97.

2. Information on the sequences actually inserted or deleted

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

Data from Southern blots showed that MON 1445 contains a single insert of T-DNA derived from PV-GHGT07. This inserted DNA contains the CMoVb promoter, *Arabidopsis* EPSPS CTP2 targeting sequence, *cp4 epsps* coding sequence, T-E9 transcription termination sequence, *aad* coding sequence, *nptII* cassette, and a portion of the *ori-V* genetic element. The remainder of PV-GHGT07, including the *ori-PBR322* sequence and the *gox* coding sequence, was not integrated into the plant genome. Table 1 summarizes the genetic elements in MON 1445. A schematic representation of the T-DNA insert in MON 1445 is shown in Figure 1.

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

At the insertion site of the MON 1445 T-DNA, a 67 bp genomic DNA region was deleted. However, the compositional and agronomic studies indicate that this fragment may not be essential for any plant function.

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

Stable integration and maintenance of a single-copy insert in MON 1445 is evident from the Southern blot data (R₀ generation), segregation ratios from selfed progeny (R₁ generation) and Southern blot analysis of subsequent, backcrossed generations, R₃ and R₅.

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

The organization of the elements within the T-DNA insert in MON 1445 was confirmed by PCR amplification of MON 1445 genomic DNA. Furthermore, sequencing of these PCR products confirmed that MON 1445 contains the T-DNA that was intended to be inserted by transformation. The consensus sequence representing the T-DNA insert in MON 1445 was generated by compiling data from numerous sequencing reactions performed with three overlapping PCR products. The sequence data demonstrate that the T-DNA insert in MON 1445 is 5734 bp. Additionally, PCR and sequencing analysis were done to verify the DNA sequences flanking the 5' and 3' ends of the T-DNA insert in MON 1445. Based on this analysis, it can be concluded that the DNA sequences flanking the 5' and 3' ends of the T-DNA insert in MON 1445 were native to the cotton genome. Further, the analysis of this sequence revealed no homology with any cotton coding sequence (nuclear, chloroplastic, or mitochondrial).

Southern blot data indicated that a single T-DNA insert of no more than 6.1 kb, containing the CMoVb promoter, *Arabidopsis CTP2* targeting sequence, *cp4 epsps* coding sequence, *T-E9* transcription termination sequence, *aad* coding sequence, *nptII* cassette, and a portion of the *ori-V* genetic element, was transferred from PV-GHGT07 into MON 1445. Additionally, the organization and intactness of the elements within the T-DNA insert was confirmed by PCR analyses that amplified three overlapping regions of DNA, which span the entire length of the T-DNA insert.

3. Information on the expression of the insert

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

Studies were conducted to measure the amount of CP4 EPSPS and NPTII proteins in leaf and/or seed tissues collected from 1993 and 1994 U.S. field trials. The field trial sites provided a variety of environmental conditions representative of regions where cotton is grown for commercial use.

Enzyme-Linked Immunosorbent Assay (ELISA) methods were developed and validated to quantify, CP4 EPSPS and NPTII protein levels in leaf and/or seed. Mean levels of the CP4 EPSPS and NPTII proteins in cottonseed samples across six field sites in 1993 and 1994 are summarized below.

The CP4 EPSPS and NPTII proteins were produced at extremely low and relatively consistent levels across all field sites and both years evaluated. In 1993, MON 1445 contained 0.082 µg/mg tissue fresh weight of CP4 EPSPS and 0.0067 µg/mg fresh weight of NPTII in seed

tissues. In 1994, MON 1445 contained 0.060 µg/mg tissue fresh weight of CP4 EPSPS and 0.007 µg/mg fresh weight of NPTII in seed tissues

b) Parts of the plant where the insert is expressed

The levels of CP4 EPSPS and NPTII proteins were assessed in leaf and seed, using validated enzyme-linked immunosorbent assays (ELISA). Results for seed tissue are the most relevant for the evaluation of the food and feed safety of MON 531 x MON 1445 and are, therefore, presented in this summary.

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

a) Reproduction

Comparative assessments of the phenotypic and agronomic characteristics of MON 1445 and conventional cotton have been conducted at multiple sites in the U.S.A. since development of these products began. The extensive experience from commercial release of this product has demonstrated that, except for the glyphosate tolerance trait, there are no biologically significant differences in the reproductive capability, dissemination or survivability of MON 1445 compared to conventional cotton.

Field studies support the conclusion that MON 1445 behaves similarly agronomically to conventional cotton, with the exception of tolerance to glyphosate.

Regardless, it should be noted that the scope of the current renewal application does not include the cultivation of MON 1445 varieties in the E.U. but only the renewal of the authorisation for the continued marketing of existing MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives, entered in the Community Register of GM Food and Feed, in the E.U.

b) Dissemination

The introduced trait has no influence on cotton reproductive morphology and hence no changes in seed dissemination are to be expected.

c) Survivability

Cotton is known to be a weak competitor in the wild, which cannot survive outside cultivation without human intervention. Field observations have demonstrated that MON 1445 has not been altered in its survivability when compared to conventional cotton.

d) Other differences

Comparative assessments in the field did not reveal any biologically significant differences between MON 1445 and conventional cotton, except for the introduced trait that is of agronomic interest.

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

Molecular stability of the insert

The data from the molecular analysis of MON 1445 demonstrated that a single T-DNA containing one copy of the insert was present in MON 1445. Additionally, the observed R₁ segregation ratios support the conclusion that the inserted sequence of MON 1445 segregates as a single Mendelian locus. Further, Southern blot data also indicated that the T-DNA in MON 1445 is stably maintained in R₃ and R₅ generations of MON 1445.

No increased hazard is to be expected from potential recombination

Recombination is unlikely to occur. This fact is supported by the stability of the genetic elements over generations. Due to the safety properties associated with the introduced proteins, the hazard arising from a hypothetical recombination event is negligible.

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

a) Plant to bacteria gene transfer

None of the genetic elements introduced MON 1445 carries a genetic transfer function. Therefore, no changes are expected in the ability of MON 1445 to transfer genetic material to bacteria.

b) Plant to plant gene transfer

The scope of the current renewal application does not include the cultivation of MON 1445 varieties in the E.U. but only the renewal of the authorisation for continued marketing of existing MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives, entered in the Community Register of GM Food and Feed, in the E.U. Therefore, plant to plant gene transfers would have no opportunity to occur. However, based on the fact that pollen production and pollen viability as measured by yield are unchanged by the genetic modification, the outcrossing frequency to other cotton varieties or to wild relatives (which are not present in the E.U.) is unlikely to be different for MON 1445 when compared to other cotton.

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

MON 1445 was compared with a conventional cotton control and other commercially available cotton.

7.2 Production of material for comparative assessment

a) number of locations, growing seasons, geographical spreading and replicates

Materials for the compositional analysis were produced in 1993 U.S. field trials at six sites with replicated plots. The six trials, located in the states of TX; MS; LA; AZ; AL; and GA, provided a variety of environmental conditions representative of regions in the U.S.A. where cotton is grown commercially. Materials for the second year of compositional analysis were produced in 1994 U.S. field trials at six sites with replicated plots. The six replicated trials, located at AR; CA; LA; MS; TX; and TX, provided a variety of environmental conditions representative of regions in the U.S.A. where cotton is grown commercially. At each site, MON 1445 and the Coker 312 control were planted.

b) the baseline used for consideration of natural variations

For the compositional studies, statistical comparisons were made between the test, MON 1445, and the control, Coker 312, cotton. For statistically significant differences ($p < 0.05$) observed for the combined site analyses, the range of the values were compared to established ranges cited in the peer-reviewed literature. When differences fell within the literature ranges, they were not considered to be biologically relevant.

7.3 Selection of material and compounds for analysis

The compounds that were selected for analysis in the compositional studies were chosen on the basis of internationally accepted guidance, and animal feed manufacturers.

The results of the compositional analyses conducted for MON 1445 in comparison to control cotton demonstrate equivalence and do not indicate a need for further analysis of selected compounds in these cotton products.

7.4 Agronomic traits

The scope of this application is limited to the renewal of the authorisation for continued marketing of existing MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives in the E.U., but does not include the cultivation of MON 1445 varieties in the E.U. The observations from previous environmental releases provide additional evidence to confirm the absence of any significant unintended or unanticipated effects of the genetic modifications present in this cotton. MON 1445 varieties have been commercially grown in the U.S.A. since 1997, where variety development was based on agronomic field data.

7.5 Product specification

MON 1445-derived food food and food ingredients (cottonseed oil), additives, feed materials and feed additives are currently imported into the EU in mixed shipments of cotton products, produced in other world areas. These products are handled by operators that have traditionally been involved in the commerce, processing and use of cotton and cotton derived products in the European Union.

MON 1445 comprises all traditionally bred cotton produced by the combination of MON 1445 and conventional cotton. The presence of the glyphosate-tolerance trait in MON 1445-derived products can be detectable using the insert-specific PCR method for detecting the introduced DNA present in MON 1445. The event specific method of detection of MON 1445 will be published on the Community Reference Laboratory (CRL) website⁶ once they complete the process of validation.

7.6 Effect of processing

The compositional analyses of MON 1445 have demonstrated that MON 1445 is substantially equivalent to conventional cotton, except for the inherited MON 1445 trait and the resulting expression of CP4 EPSPS, which was shown to be safe for human and animal health.

As MON 1445 is substantially equivalent and as safe and nutritious as conventional cotton, the use of MON 1445 seed for the production of foods and feeds is no different from that of conventional cotton. Consequently, the effects of the processing of MON 1445 are not expected to be any different from the processing of the equivalent foods and feeds, originating from conventional cottonseed.

7.7 Anticipated intake/extent of use

Food additives, feed materials and feed additives produced from MON 1445 were first placed on the E.U. market in 1997. In 2004, these products were notified to the European Commission, following Articles 8(1)(b) and 20(1)(b) of Regulation (EC) No 1829/2003, in order to allow for their continued marketing in the E.U. given that they had been

⁶ <http://gmo-crl.jrc.it/statusofdoss.htm>

lawfully placed on the market before Regulation (EC) No 1829/2003 came into force, on 18 April 2004. Oil and its constituents produced from MON 1445 were first placed on the EU market in 2002 following notification under Article 5 of Regulation (EC) No 258/97.

MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives replace a portion of current commercial cotton products, such that the dietary intake and/or extent of use of of current commercial cotton products is not expected to be altered upon renewal of the authorisation of existing MON 1445-derived products.

7.8 Toxicology

7.8.1 Safety evaluation of newly expressed proteins

The scope of the current application covers food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445.

The introduced proteins in MON 1445 have shown no evidence of adverse effects on human or animal safety. The human and animal safety assessment of the CP4 EPSPS protein was demonstrated on the basis of a) an extensive characterization of each protein, b) comparison of these proteins to known protein toxins and allergens, c) their digestion in simulated gastric and intestinal fluids, and d) the assessment of each protein for evidence of any acute toxicity in oral gavage studies in rodents. All these studies confirmed the absence of any toxic effects associated with the introduced proteins and confirmed the absence of any unanticipated or pleiotropic effects of the genetic modification.

Updated bioinformatics analyses have been performed on CP4 EPSPS and NPTII proteins expressed in MON 1445. The results of these bioinformatics analyses confirm the initial conclusions: neither of these proteins shares significant sequence similarity with protein toxins relevant to animal or human health.

7.8.2 Testing of new constituents other than proteins

The introduced coding sequences are not intended to produce new constituents other than the two proteins, CP4 EPSPS and NPTII. Since cotton is known as a common source of food and feed products, with a long history of safe use and consumption globally, and as MON 1445 was shown to be substantially equivalent to conventional cotton, toxicological testing of any constituents, other than the introduced proteins, is not indicated.

7.8.3 Information on natural food and feed constituents

Cotton is known as a common source of human food and feed products, with a long history of safe use and consumption around the world. All cotton contains cyclopropenoid fatty acids (CPFA) and gossypol, natural compounds that are considered to be undesirable and anti-nutritional. The steps taken during cottonseed processing, in order to produce cottonseed oil, detoxify gossypol and greatly reduce the CPFA content. No other particular natural constituents of cotton are considered to be of significant concern to require additional information or further risk assessment.

7.8.4 Testing of the whole GM food/feed

The notification for MON 1445 under Regulation (EC) No 258/97 included a detailed safety assessment for MON 1445 and its CP4 EPSPS and NPTII proteins, which were reproduced in this renewal application. Compositional analyses and comparative phenotypic assessments have demonstrated that MON 1445 is substantially equivalent to conventional cotton, with the exception of the glyphosate-tolerance trait.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

The scope of the current application covers food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445. In support of our notification for MON 1445 under Regulation (EC) No 258/97, it has been demonstrated that there is no detectable level of protein in refined cottonseed oil produced from genetically modified or conventional cottonseeds. Similarly, highly processed products such as food additives produced from cotton are unlikely to contain proteins at detectable levels. Therefore, the information related to the assessment of allergenicity of the newly expressed proteins can be considered as mainly informative.

Absence of any allergenic potential associated with the introduced CP4 EPSPS and NPTII protein expressed in MON 1445 has been previously demonstrated.

These proteins were assessed for their potential allergenicity by a variety of tests, including a) whether the genes came from allergenic or non-allergenic sources, b) sequence similarity to known allergens, and c) pepsin stability of the protein in an *in vitro* digestion assay. In all cases, the proteins did not exhibit properties characteristic of allergens.

7.9.2 Assessment of allergenicity of the whole GM plant or crop

MON 1445 is substantially equivalent to conventional cotton except for the introduced trait. As the introduced proteins do not have any allergenic potential, it was concluded that MON 1445-derived food and food ingredients (cottonseed oil), food additives, feed materials and feed additives do not pose an increased risk for allergenic reactions compared to the equivalent range of food and feed products derived from conventional cottonseed.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

MON 1445 expresses the introduced trait of glyphosate tolerance, which is an agronomic trait, and is not intended to change any nutritional aspects of MON 1445. Hence, MON 1445 is not expected to be more or less attractive for use as a food additive. Therefore, the dietary intake of cotton-derived foods is not expected to be altered upon continued placing on the market of MON 1445, and no nutritional imbalances are expected as a result of the use of MON 1445.

7.10.2 Nutritional assessment of GM feed

Once compositional equivalence has been established in GM feed modified with an agronomic input trait, nutritional equivalence can be assumed. The results of the compositional analyses have established the compositional equivalence of MON 1445 cottonseed and conventional cottonseed, and as a consequence, no further nutritional assessments of MON 1445 seed for use as feed are considered necessary.

Considering the compositional equivalence of MON 1445 it can be concluded that feed materials and feed additives produced from MON 1445 are equivalent to the counterpart products produced from conventional cottonseed and have equivalent nutritional properties.

7.11 Post-market monitoring of GM food/feed

The assessment of the human and animal safety of MON 1445 was conducted on the basis of these products' substantial equivalence to conventional cotton (except for the introduced trait) and by extensive characterisation of the introduced trait, which is of agronomic interest, resulting in the expression of CP4 EPSPS.

Based on compositional comparisons of cottonseeds, it can be concluded that food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 are not different from the counterpart products produced from conventional cottonseed.

There are no intrinsic hazards related to MON 1445 as no signs of adverse or unanticipated effects have been observed in a number of safety studies. The pre-market risk assessments of MON 1445 have demonstrated that the risks of consumption of food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 are negligible and no different from the risks associated with the consumption of conventional cotton-derived products. Therefore, as previously stipulated in the Community Register of GM food and feed, no specific risk management measures are indicated for MON 1445, and post-market monitoring of the use of MON 1445 for food and feed products is not considered appropriate.

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

Not applicable as the scope of this renewal application under Regulation (EC) No 1829/2003 does not cover the deliberate release of cottonseeds into the environment, but only the food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 cottonseed.

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

Not applicable as neither the GMO, nor the food and feed containing or consisting of the GMO, are within the scope of this renewal application under Regulation (EC) No 1829/2003. This renewal application includes only food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 cottonseed.

10. Potential interactions with the abiotic environment

Not applicable as neither the GMO, nor the food and feed containing or consisting of the GMO, are within the scope of this renewal application under Regulation (EC) No 1829/2003. This renewal application includes only food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 cottonseed.

11. Environmental monitoring plan (not if application concerns only food and feed produced from GM plants, or containing ingredients produced from GM plants)

Not applicable as neither the GMO, nor the food and feed containing or consisting of the GMO, are within the scope this renewal application under Regulation (EC) No 1829/2003. This renewal application includes only food and food ingredients produced from MON 1445 cotton (cottonseed oil), as well as food additives, feed materials and feed additives produced from MON 1445 cottonseed.

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

MON 1445 is detectable using an event-specific PCR method for detecting the introduced DNA present in MON 1445. A MON 1445-specific PCR assay allowing the identification and the quantification of MON 1445 has been provided to the Joint Research Center (JRC) acting as the European Union Reference Laboratory (EURL). The MON 1445 method validation report was published on 10 June 2008⁷.

⁷ http://gmo-crl.jrc.ec.europa.eu/summaries/MON1445_val_report.pdf - Accessed 16 June 2011.

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
Not applicable as environmental release of MON 1445 is not in scope of this renewal application.
b) Conclusions of post-release monitoring
Not applicable as environmental release of MON 1445 is not in scope of this renewal application.
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)
Not applicable as environmental release of MON 1445 is not in scope of this renewal application.

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

a) Release country
MON 1445 has been commercially introduced in the U.S.A. (1997), Argentina, Australia, Colombia, Mexico and South Africa. Globally, the production of MON 1445 has grown rapidly since its introduction in the various production markets. In the past four years, MON 1445 was grown on more than 5 million hectares, globally.
b) Authority overseeing the release
United States: Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and the United States Department of Agriculture (USDA).
Argentina: National Service for Agri-Food Safety and Quality (SENASA), National Advisory Committee on Agricultural Biosafety (CONABIA), Market Risk Assessment Department (DNMA), and Secretary of Agriculture.
Australia: Office of the Gene Technology Regulator (OGTR) and Food Standards Australia and New Zealand (FSANZ).
Columbia: The National Institute for the Surveillance of Drugs and Food (INVIMA), Colombian Institute of Agriculture (ICA), and Ministry of Health (MOH).

	<p>Mexico: Ministry of Health (MOH) and Ministry of Agriculture (MOA). South Africa: National Department of Agriculture.</p>
c)	<p>Release site</p> <p>Commercial production sites of MON 1445 cotton, as for any other cotton.</p>
d)	<p>Aim of the release</p> <p>Commercial release in the U.S, Argentina, Australia, Colombia, Mexico and South Africa, including all uses as for conventional cotton.</p>
e)	<p>Duration of the release</p> <p>Please see question E.2.(a)</p>
f)	<p>Aim of post-releases monitoring</p> <p>Extensive pre-market risk assessment did not provide evidence of adverse effects potentially associated with the cultivation, handling or use of MON 1445, indicating that post-release monitoring would not be necessary.</p> <p>In addition, the commercialisation of MON 1445 is accompanied by stewardship programmes to ensure correct handling of this cotton by downstream stakeholders (implementation of good agricultural practice for cultivation; ensure a channel of communication in the unlikely event that unanticipated adverse effects might occur).</p> <p>No unanticipated effects have been observed during field testing or since commercialization of MON 1445.</p>
g)	<p>Duration of post-releases monitoring</p> <p>Please see question E.2.(f).</p>
h)	<p>Conclusions of post-release monitoring</p> <p>Please see question E.2.(f).</p>
i)	<p>Results of the release in respect to any risk to human health and the environment</p> <p>Field-testing and post-marketing experience provided no significant evidence that cottonseed or derived products from MON 1445 are likely to cause adverse effects to human health, animal health or the environment.</p>

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 EFSA website http://www.efsa.europa.eu/en/science/gmo/gm_ff_applications.html provides information related to the applications submitted under Regulation (EC) No 1829/2003 on genetically modified food and feed.
b) Assessment Report of the Competent Authority (Directive 2001/18/EC)
Not applicable
c) EFSA opinion
No EFSA opinion is available at the time of this application.
d) Commission Register (Commission Decision 2004/204/EC)
http://ec.europa.eu/food/dyna/gm_register/index_en.cfm
e) Molecular Register of the Community Reference Laboratory/Joint Research Centre
Information on detection protocols is posted at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm .
f) Biosafety Clearing-House (Council Decision 2002/628/EC)
The publicly accessible portal site of the Biosafety Clearing-House (BCH) can be found at http://bch.biodiv.org/
g) Summary Notification Information Format (SNIF) (Council Decision 2002/812/EC)
This public summary for the renewal application of MON 1445 under Regulation (EC) No 1829/2003 will be posted at http://www.efsa.europa.eu/en/science/gmo/gm_ff_applications.html