

**Application for authorization of MON 88913 cotton in
the European Union, according to Regulation (EC)
No 1829/2003 on genetically modified food and feed**

Part II
Summary

Data protection.

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

A. GENERAL INFORMATION

1. Details of application

a) Member State of application UK
b) Notification number Not available at the time of application.
c) Name of the product (commercial and other names) The Monsanto development code for this genetically modified cotton is: MON 88913. In countries where MON 88913 is being cultivated, packages of this cotton are marketed under the name of the variety, in association with the trademark Roundup Ready ^{®1} Flex.
d) Date of acknowledgement of notification Not available at the time of application.

2. Applicant

a) Name of applicant Monsanto Company, represented by Monsanto Europe S.A.
b) Address of applicant 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
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)) MON 88913 will be traded and used in the European Union (E.U.) in the same manner as the equivalent products from current commercial cotton varieties and by the same operators currently involved in the trade and use of conventional cotton.

¹ Roundup Ready is a registered trademark of Monsanto Technology LLC.

3. Scope of the application

<p><input type="checkbox"/> GM plants for food use</p> <p><input type="checkbox"/> Food containing or consisting of GM plants</p> <p><input checked="" type="checkbox"/> Food produced from GM plants or containing ingredients produced from GM plants</p> <p><input type="checkbox"/> GM plants for feed use</p> <p><input type="checkbox"/> Feed containing or consisting of GM plants</p> <p><input checked="" type="checkbox"/> Feed produced from GM plants or containing ingredients produced from GM plants</p> <p><input checked="" type="checkbox"/> Import and processing (Part C of Directive 2001/18/EC)</p> <p><input type="checkbox"/> Seeds and plant propagating material for cultivation in Europe (Part C of Directive 2001/18/EC)</p>

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 <i>yes</i> , 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 <i>no</i> , 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 type="checkbox"/>)	No (<input checked="" type="checkbox"/>)
If <i>yes</i> , specify	

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

Yes (<input checked="" type="checkbox"/>)	No (<input type="checkbox"/>)
<p>If yes, specify</p> <p>MON 88913 has been authorized in the U.S.A., Australia and South Africa for the full range of uses. The scope of other approvals already granted for this genetically modified cotton product and the status of pending regulatory reviews, which are currently in progress in numerous countries around the world, depend on the country and its local regulatory framework. Final approvals are posted by these regulatory agencies on their official websites.</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 88913 has been developed to produce the CP4 EPSPS protein that confers tolerance to glyphosate². MON 88913 was produced by <i>Agrobacterium</i>-mediated transformation of cotton cells with plasmid vector PV-GHGT35.</p>
<p>b) Types of products planned to be placed on the market according to the authorization applied for</p> <p>The scope of the current application covers the import of MON 88913 for processing and the use of food and feed produced from MON 88913 in the E.U. Neither the use of the whole cottonseed as such nor the cultivation of MON 88913 varieties in the E.U. are included in this application.</p>
<p>c) Intended use of the product and types of users</p> <p>MON 88913 will be traded and used in the E.U. in the same manner as the equivalent products from current commercial cotton varieties and by the same operators currently involved in the trade and use of conventional cotton.</p>

² N-phosphonomethyl-glycine, the active ingredient in the non-selective, foliar-applied, broad-spectrum, post-emergent Roundup[®] herbicides. Roundup is a registered trademark of Monsanto Technology LLC.

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

No specific conditions are considered necessary for the placing on the market of MON 88913 for processing and use of foods and feeds produced from MON 88913. MON 88913 is substantially equivalent to conventional cotton except for its tolerance to glyphosate, which is a trait of agronomic interest. This cotton is as safe and nutritious as conventional cotton. Therefore, MON 88913 and the food and feed products produced from MON 88913 will be stored, packaged, transported, used and handled in the same manner as current commercial cotton, and the measures for waste disposal and treatment of MON 88913 products are the same as those of conventional cotton.

e) Any proposed packaging requirements

MON 88913 is substantially equivalent to conventional cotton varieties (except for its tolerance to glyphosate). Therefore, MON 88913 and the food and feed products produced from MON 88913 will be used in the same manner as other cotton and no specific packaging is foreseen (for the labelling, *see* question A.8.(f)).

f) Any proposed labelling requirements in addition to those required by Community law (Annex IV of Directive 2001/18/EC; Regulation 1829/2003 art. 13 and 25)

In accordance with Regulations (EC) No 1829/2003 and 1830/2003, a labelling threshold of 0.9 % is applied for the placing on the market of MON 88913 and derived products.

Operators shall be required to label foods and feeds derived from MON 88913 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 GMOs is transmitted in writing to the operator receiving the product.

Operators handling or using MON 88913 cottonseed and derived foods and feeds in the E.U. are required to be aware of the legal obligations regarding traceability and labelling of these products. Given that explicit requirements for the traceability and labelling of GMOs and derived foods and feeds are laid down 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/feed chain will be fully aware of the traceability and labelling requirements for MON 88913. Therefore, no further specific measures are to be taken by the applicant.

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)

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

The use in foods and feeds produced from MON 88913 is suitable throughout the E.U.

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

Because this application is for consent to import MON 88913 for processing and to use food and feed produced from MON 88913 as any other cotton product, not including the cultivation of varieties of MON 88913 in the E.U., environmental release would more likely occur through incidental release during import, handling, storage and processing. However, modern methods of transporting and handling minimize such losses of cottonseed, so there is little chance of germination, growth and reproduction of cotton destined for processing in the E.U. In practice, the cottonseed will mostly be confined to fixed locations (seaports, seed elevators and processing facilities) and enclosed to minimize or prevent spillage (transport vehicles including trucks and railroad cars). Such conditions significantly limit entry into the environment. Moreover, in the event of incidental spillage, the establishment of volunteer plants would be unlikely, since cotton cannot survive without human assistance and is not capable of surviving as a weed. Although cottonseed could over-winter in mild conditions and germinate the following year, cotton does not persist as a weed. The appearance of cotton volunteers in rotational fields is highly unlikely under European conditions and, if they occur, they can be easily controlled by current agronomic practices, including cultivation or the use of appropriate herbicides such as glufosinate and paraquat.

In addition, the information presented in this application established that MON 88913 is unlikely to be different from other cotton, and therefore, is unlikely to pose any threat to the environment or to require special measures for its containment.

No specific conditions are warranted or required for the import of MON 88913 for processing and for the use of foods and feeds produced from MON 88913.

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 spp.
d) Subspecies N/A
e) Cultivar/breeding line MON 88913
f) Common name Cotton

2. a) Information concerning reproduction

<p>(i) Mode(s) of reproduction</p> <p>Cotton (<i>Gossypium</i> spp.) reproduction 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.</p>
<p>(ii) Specific factors affecting reproduction</p> <p>Cotton is normally considered to be a self-pollinating crop. However, since there are no morphological barriers to cross-pollination based on flower structure, cross-pollination can also occur. In practice, though, cotton pollen is heavy and sticky and transfer by wind is unlikely. Pollen is transferred instead by insects, in particular by various wild bees, bumble bees (<i>Bombus</i> sp.) and honeybees (<i>Apis mellifera</i>).</p>
<p>(iii) Generation time</p> <p>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.</p>

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

Out-crossing with cultivated *Gossypium* varieties

In as much as similar cotton genotypes are fully compatible, any pollen that is transferred has the potential to produce a hybrid seed. The degree of outcrossing in a production field is strongly dependent upon the geographic location of the field, which means upon the crop ecology. Regardless, since the scope of the current application does not include cultivation of MON 88913 varieties in the E.U., outcrossing with cultivated *Gossypium* varieties is not expected.

Out-crossing with wild *Gossypium* species

Closely related feral or wild relatives of cotton do not exist in Spain, Greece or other countries of the E.U.

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. Seeds are the only survival structures. Cotton is not considered to have seed that can persist in the environment for long periods of time. Natural regeneration from vegetative tissue is not known to occur.

b) Specific factors affecting survivability

Cotton cannot survive without human assistance and is not capable of surviving as a weed. 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, 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. Even in cotton growing regions with mild and dry winters, such as in Spain and Greece, it is highly unlikely that cottonseed would over-winter and germinate the following spring. Nevertheless, in the case it would, cotton volunteers can be easily controlled by current agronomic practices including cultivation and the use of appropriate herbicides such as glufosinate and paraquat. Volunteer cotton is not found growing in fencerows, ditches or roadsides as a weed. Regardless, it should be noted that cultivation of MON 88913 is not in the scope of this application.

4. Dissemination

a) Ways and extent of dissemination

As cotton does not generally reproduce vegetatively, dissemination of cotton may occur by means of seed dispersal and pollen dispersal. However, the current application does not include the environmental release of MON 88913 in the E.U.

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. However, most recent cotton pollen dispersal studies consistently demonstrate that the frequency of cross-pollination decreases significantly (from five to less than one per cent from one to seven meters, respectively) with distance from the pollen source.

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 Peoples Republic of China, U.S.A., India, Pakistan and the Republic of Uzbekistan. Turkey, Brazil 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 neither 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 cottonseed oil or cottonseed meal.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

MON 88913 was produced by *Agrobacterium*-mediated transformation of cotton hypocotyl tissues.

2. Nature and source of the vector used

The double-border, binary vector PV-GHGT35 was used for the transformation of cotton hypocotyl tissue to produce MON 88913. This vector contains left and right border T-DNA sequences. This T-DNA region of approximately 8.1 kb contains two tandem *cp4 epsps* expression cassettes that were transferred into the cotton genome by *Agrobacterium tumefaciens* during the *in vitro* transformation process.

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

Starting from the right border region (B-Right Border), the region intended for insertion contains: 1) the first *cp4 epsps* coding sequence (CS-*cp4 epsps*) under the regulation of a chimeric transcriptional promoter (P-*FMV/Tsf1*), *Tsf1* leader and intron sequences (L-*Tsf1* and I-*Tsf1*, respectively), a chloroplast transit peptide sequence (TS-*ctp2*) and a *E9* transcript termination and polyadenylation sequence (T-*E9*) and 2) the second *cp4 epsps* coding sequence regulated by a chimeric transcriptional promoter (P-*35S/act8*), *act8* leader and intron sequences (L-*act8*, and I-*act8*, respectively) and the same chloroplast targeting and transcript termination sequences as utilized in the first *cp4 epsps* gene expression cassette

Detailed description of all elements is presented in Table 1.

Table 1. Size and intended function of each constituent fragment of the region intended for insertion in MON 88913

Sequence	Size (kb)	Source	Function
B-Right Border	0.02	<i>Agrobacterium</i>	Border
First <i>cp4 epsps</i> gene cassette			
P-FMV/<i>Tsf1</i>	1.04	Figwort mosaic virus/ <i>Arabidopsis thaliana</i>	Promoter
L-<i>Tsf1</i>	0.05	<i>Arabidopsis thaliana</i>	Leader
I-<i>Tsf1</i>	0.62	<i>Arabidopsis thaliana</i>	Intron
TS-<i>ctp2</i>	0.23	<i>Arabidopsis thaliana</i>	Targeting sequence
CS-<i>cp4 epsps</i>	1.37	<i>A. tumefaciens</i>	Coding sequence
T-<i>E9</i>	0.64	<i>Pisum sativum</i>	Transcript termination sequence
Second <i>cp4 epsps</i> gene cassette			
P-35S/<i>act8</i>	1.17	<i>Cauliflower mosaic virus</i> <i>/Arabidopsis thaliana</i>	Promoter
L-<i>act8</i>	0.14	<i>Arabidopsis thaliana</i>	Leader
I-<i>act8</i>	0.47	<i>Arabidopsis thaliana</i>	Intron
TS-<i>ctp2</i>	0.23	<i>Arabidopsis thaliana</i>	Targeting sequence
CS-<i>cp4 epsps</i>	1.37	<i>A. tumefaciens</i>	Coding sequence
T-<i>E9</i>	0.64	<i>Pisum sativum</i>	Transcript termination sequence
B-Left Border	0.28	<i>Agrobacterium</i>	Border

D. INFORMATION RELATING TO THE GM PLANT

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

MON 88913 produces the CP4 EPSPS protein, which provides tolerance to glyphosate. The EPSPS enzyme catalyses the penultimate step of the shikimic acid pathway for the biosynthesis of aromatic amino acids, which is present in all green plants. Inhibition of this enzyme by glyphosate leads to a reduction of aromatic amino acids, interfering with plant growth, and ultimately leading to plant death. With the expression of the glyphosate-tolerant CP4 EPSPS enzyme in MON 88913, the continued function of the aromatic amino acid pathway is ensured in the crop, even in the presence of the herbicide.

Since the commercial introduction in the U.S.A. in 1997, growers have rapidly adopted the use of the first generation glyphosate-tolerant cotton product, MON 1445, which now accounts for at least 60% of the U.S.A. cotton acreage. The introduction of MON 88913 is expected to continue to enable the grower to take advantage of the herbicide's well-known, favorable environmental and safety characteristics and to provide superior weed control benefits to those provided by MON 1445.

2. Information on the sequences actually inserted or deleted

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

MON 88913 contains one DNA insert containing a single copy of the introduced DNA fragment, and this at a single locus in the cotton genome.

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

Not applicable.

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

The Chi square analysis of the segregation pattern, according to Mendelian genetics, was consistent with a single site of insertion into the cotton nuclear DNA.

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

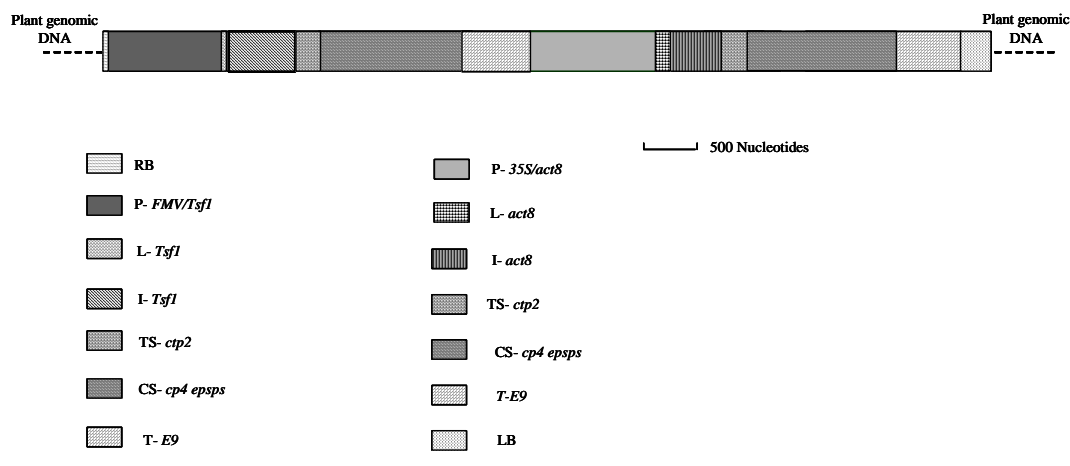
MON 88913 was developed through *Agrobacterium*-mediated transformation of cotton hypocotyl tissue to produce the CP4 EPSPS protein, using the double-border, binary vector PV-GHGT35. This vector contains a T-DNA region with two tandem *cp4 epsps* expression cassettes, which were transferred into the cotton genome by *Agrobacterium tumefaciens*.

Genomic DNA from MON 88913 was analyzed by Southern blotting to confirm the presence and intactness of the elements comprising both *cp4 epsps* expression cassettes and to confirm the absence of plasmid backbone sequences. The organisation of the elements within the insert in MON 88913 was further confirmed using PCR analysis and sequencing of the insert.

It has been demonstrated that MON 88913 contains one DNA insert containing a single copy of the introduced DNA that resides at a single locus of integration. No additional elements from the transformation vector PV-GHGT35 were detected in the genome of MON 88913. Additionally, MON 88913 does not contain any detectable plasmid backbone sequence.

A schematic representation of the MON 88913 insert is given in Figure 1.

Figure 1. Schematic representation of the MON 88913 insert



3. Information on the expression of the insert

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

The levels of CP4 EPSPS protein in various tissues of MON 88913 were estimated using enzyme-linked immunosorbent assay (ELISA). To produce the tissues for analysis, MON 88913 and its control were planted in four locations during the 2002 growing season in the U.S.A.

and in four locations during the 2003-2004 growing season in Australia. The field sites provided a range of environmental and agronomic conditions representative of locations where MON 88913 is expected to be produced commercially. A randomized complete block design with four replications was used at all sites.

2002 U.S.A. growing season

Tissues were collected for young leaf, overseason leaf (OSL 1-3), root, seed and pollen. Mean CP4 EPSPS protein level across all sites for seed tissues of the test plant was 340 µg/g dw.

2003-2004 Australia growing season

Tissues were collected for overseason leaf (OSL 1-4) and seed. Mean CP4 EPSPS protein level across all four sites for seed tissues of the test plant was 310 µg/g dw.

b) Parts of the plant where the insert is expressed

Young leaf, overseason leaf, root, pollen and seed were collected at appropriate times of plant development. Since food and feed are produced from cottonseed, the measurement of protein expression in seed should be considered the most relevant in terms of food and feed safety.

The results of the protein expression analysis is reported in Section D.3.a) of this document.

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

a) Reproduction

Agronomic data collected from trials performed with MON 88913 have demonstrated that MON 88913 has not been altered in survival, multiplication or dissemination characteristics when compared to the control and commercial conventional cotton varieties. The introduced glyphosate-tolerance trait has no influence on cotton reproductive morphology and hence no changes in seed dissemination would be expected.

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 88913 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 88913 and conventional cotton varieties, except for the introduced glyphosate-tolerance trait that is of agronomic interest.

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

MON 88913 contains one insert with a single copy of the transformed DNA, which is stably integrated into the nuclear cotton genome. The insert is inherited in a Mendelian fashion. This has been confirmed by Southern blot analyses.

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 inserted in MON 88913 has a genetic transfer function. Therefore, no changes are expected in the ability of these cotton lines to transfer genetic material to bacteria.

b) Plant to plant gene transfer

Not applicable. The scope of the current application does not include the cultivation of MON 88913 varieties in the E.U.

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 88913 was compared to a near-isogenic control, with background genetics representative of MON 88913 but without the T-DNA insert. MON 88913 was also compared to other commercial conventional cotton varieties.

7.2 Production of material for comparative assessment

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

2002 U.S.A. growing season

MON 88913, the control and four commercially available cotton varieties were grown at four field sites in major cotton-growing areas of the U.S.A. (California, Georgia, Alabama and Texas) during the 2002 field season.

2004 U.S.A. growing season

MON 88913, the control and four commercially available cotton varieties were grown at four sites, representing the major cotton-growing areas of the U.S.A. (Georgia, Mississippi, New Mexico and

Texas) during 2004 growing season

b) the baseline used for consideration of natural variations

Both studies compared the test with a near-isogenic control. Reference varieties were grown in the same field locations and under the same conditions as the test and control. Where statistical differences occurred, the measured analyte was compared to a confidence interval developed from the reference varieties. Differences were also compared to historical ranges and ranges reported in literature.

The results of the compositional analyses for MON 88913 in comparison with control cotton, demonstrate equivalence and do not indicate a need for further analysis of selected compounds.

7.3 Selection of material and compounds for analysis

The numerous compounds that were selected for analysis in the compositional study were chosen on the basis of internationally accepted guidance provided by the OECD.

Based on the results of these extensive compositional analyses, there is no indication to further analyze other selected compounds in this cotton.

7.4 Agronomic traits

Field trials with MON 88913 were performed and the set of agronomic observations supports a conclusion that from an agronomic and phenotypic (morphological) point of view, MON 88913 is equivalent to conventional cotton, except for the introduced glyphosate-tolerance trait.

7.5 Product specification

Upon approval of the import of MON 88913 for processing and of the use of MON 88913 derived products in food and feed, these products will be imported and used, likely by operators traditionally involved in the processing and commerce of cottonseed in the E.U.

7.6 Effect of processing

As MON 88913 is substantially equivalent and as safe and nutritious as conventional cotton, the use of MON 88913 cottonseed for the production of foods and feeds is not different from that of conventional cotton. Consequently, any effects of the processing of MON 88913 are not expected to be different from the processing of the equivalent foods and feeds, originating from conventional cottonseed.

7.7 *Anticipated intake/extent of use*

MON 88913 is not expected to alter current usage patterns or volumes of cottonseed. Therefore, anticipated dietary intake of cottonseed-derived foods and feeds is not expected to be altered upon E.U. authorization of MON 88913 derived products for food and feed use. MON 88913 is expected to replace a portion of the current cotton in the market such that its intake or use will represent some fraction of the total cotton-derived products.

7.8 *Toxicology*

7.8.1 *Safety evaluation of newly expressed proteins*

The CP4 EPSPS protein has been assessed for its potential toxicity according to the recommendations of Codex. The protein is functionally similar to endogenous plant EPSPS enzymes, with a demonstrated history of safe use, lacks structural similarity to known toxins or biologically active proteins known to have adverse effects on mammals, does not show acute oral toxicity in mice, using doses that are orders of magnitude higher than expected consumption levels from feed products derived from MON 88913, is rapidly digested in simulated gastric fluids and is present at very low level in MON 88913.

Taken together, these data lead to the conclusion that CP4 EPSPS is unlikely to have any toxic effect on humans or animals.

7.8.2 *Testing of new constituents other than proteins*

Since cotton is known as a common source of food and feed products with a long history of safe use and consumption around the world and as MON 88913 was shown to be substantially equivalent to conventional cotton except for the introduced glyphosate-tolerance trait, no testing of any constituent other than the introduced protein is 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 compositional and nutritional equivalence of MON 88913 and conventional cotton have been established by compositional analysis. Additionally, the wholesomeness of MON 88913 has been confirmed by feeding studies in rat and catfish, using MON 88913 cottonseed and cottonseed meal-containing diets, which demonstrate the absence of any toxic or pleiotropic effects linked to the genetic modification.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

CP4 EPSPS protein was assessed for its 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, c) pepsin stability of the protein in an *in vitro* digestion assay and d) proportion of CP4 EPSPS of the total protein. 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

As the introduced protein does not have any allergenic potential, it was concluded that the use of food or feed derived from MON 88913 does not lead to an increased risk for allergic reactions compared to the equivalent range of food and feed uses derived from conventional cotton.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

The introduced trait in MON 88913 is of agronomic interest, and is not intended to change any nutritional aspects of this cotton. In addition to the extensive compositional analyses which demonstrated the substantial equivalence of MON 88913 to conventional cotton (except for the introduced trait), a confirmatory feed performance study was conducted in channel catfish, confirming the nutritional equivalence of food and feed products produced from MON 88913 cottonseed, and demonstrating the absence of any pleiotropic or unanticipated effects from the introduced trait.

In conclusion, MON 88913 is nutritionally equivalent to its control, as well as to conventional cotton varieties in commerce.

7.10.2 Nutritional assessment of GM feed

The introduced trait in MON 88913 is of agronomic interest, and is not intended to change any nutritional aspects of this cotton. In addition to the extensive compositional analyses which demonstrated the substantial equivalence of MON 88913 to conventional cotton (except for the introduced trait), a

confirmatory feed performance study was conducted in channel catfish. Catfish were fed diets containing cottonseed meal from MON 88913, and their performance was compared to control groups fed diets containing a non-transgenic control variety or commercially available reference varieties. This study confirms the nutritional equivalence of food and feed products produced from MON 88913 cottonseed, and demonstrates the absence of any pleiotropic or unanticipated effects from the introduced trait.

In conclusion, MON 88913 is nutritionally equivalent to its control, as well as to conventional cotton varieties in commerce.

7.11 Post-market monitoring of GM food/feed

The assessment of the human and animal safety of MON 88913 was conducted on the basis of its substantial equivalence to conventional cotton, (except for the introduced trait) and by extensive characterization of the newly expressed protein, which is of agronomic interest.

There are no intrinsic hazards related to MON 88913 as no signs of adverse or unanticipated effects have been observed in a number of safety studies, including animal feeding studies using doses of administration that are orders of magnitude above expected consumption levels. The pre-market risk characterization for food and feed use of MON 88913 demonstrates that the risks of consumption of food and feed products produced from MON 88913 are consistently negligible and no different from the risks associated with the consumption of their counterparts derived from conventional cotton.

As a consequence, specific risk management measures are not indicated, and post-market monitoring of the use of this cotton for food or feed is neither warranted, nor appropriate.

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

Not applicable. MON 88913 is glyphosate-tolerant and does not have any target organisms.

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

This application is limited to the import of MON 88913 for processing and use of food and feed produced from MON 88913, but it does not cover the cultivation of MON 88913 varieties in the E.U. As such, exposure to the environment will be rare, occurring only through incidental release during shipment and handling. The conditions where incidental release could occur are not conducive to establishment of cotton.

9.1 Persistence and invasiveness

Like for conventional cotton, the likelihood of MON 88913 spreading in the environment is negligible, as cotton is neither persistent nor

invasive and these parameters are unaltered in MON 88913 when compared to conventional cotton. In the event MON 88913 cottonseed is spilt in the environment, its introduced trait would have negligible consequences for the environment. Hence the risk of establishment and spreading of MON 88913 in the environment is negligible.

9.2 Selective advantage or disadvantage

Compared with conventional cotton, the presence of the glyphosate-tolerance trait confers a selective advantage only under specific conditions (*i.e.* following treatment with glyphosate), which are short in duration. The advantage is of purely agronomic interest and presents negligible risk to the non-agricultural environments because of the poor survival characteristics of cotton under most European conditions. The potential for the glyphosate-tolerance trait in MON 88913 to cause a selective advantage of cotton outside an agro-ecosystem is exceedingly low. Therefore, the risk of adversely impacting the receiving environment is negligible under the intended use for processing.

9.3 Potential for gene transfer

MON 88913 is unchanged in its potential for gene transfer compared to conventional cotton. There is no potential for gene transfer from MON 88913 to wild plant species and negligible likelihood for gene transfer to other cotton crops, as this application is not for consent to cultivate MON 88913 varieties in the E.U.

In the highly unlikely event that the introduced gene outcrosses to another cotton plant, its transfer would, in any event, have negligible consequences for the environment. The environmental risk posed by this transfer, and hence by the intended import of MON 88913 for processing is negligible.

9.4 Interactions between the GM plant and target organisms

The CP4 EPSPS protein, present in MON 88913, provides tolerance to glyphosate and has no known target organisms. Therefore, there is no characteristic that may cause an adverse effect.

9.5 Interactions of the GM plant with non-target organisms

Given the scope of the current application, which does not include the cultivation of MON 88913 varieties in the E.U., the likelihood for direct or indirect interactions of this cotton with non-target organisms is considered to be negligible. In addition, the newly expressed protein presents a negligible hazard to non-target organisms, even if incidental spillage of MON 88913 cottonseed during import, storage, transport or processing leads to the short survival of MON 88913 plants in the environment. As a consequence, there is negligible risk for harmful effects of MON 88913 on non-target organisms, either through direct or indirect interactions with this cotton or through contact with the newly expressed protein. Furthermore, no adverse effects were brought forward by the people handling these products during the extensive field trials conducted in the U.S.A.

9.6 *Effects on human health*

The likelihood for any adverse effects occurring in humans as a result of their contact with this cotton is no different from conventional cotton, as MON 88913 contains the CP4 EPSPS protein, which has negligible potential to cause any toxic or allergenic effects in humans. Therefore, the risk of changes in the occupational health aspects of this cotton is negligible.

9.7 *Effects on animal health*

The likelihood of potential adverse effects in animals fed on MON 88913 and in humans, consuming those animals, is negligible (*see* Sections D.7.8, D.7.9 and D.7.10 of this document). Therefore, the risk of MON 88913 for the feed/food chain is also negligible.

9.8 *Effects on biogeochemical processes*

In the event of an incidental release of MON 88913 in the environment, the risk for direct or indirect, immediate or delayed adverse effects on biogeochemical processes can be considered as negligible. There is no evidence that MON 88913 plants would be any different from conventional cotton regarding their direct influence on biogeochemical processes or nutrient levels in the soil, as MON 88913 is compositionally equivalent to conventional cotton and presents no biologically meaningful differences in its growth and development, morphology, yield, plant health and survival characteristics (*see* Sections D.4, D.7.1 and D.7.4 of this document). Furthermore, any indirect interactions of the GMHP and non-target organisms in the vicinity of an incidental release of the cottonseed are not likely to cause hazardous effects on the biogeochemical processes in the soil.

9.9 *Impacts of the specific cultivation, management and harvesting techniques*

Not applicable. This application is for consent to import MON 88913 in the E.U. for processing and for the use of food and feed produced from this cotton as any other cotton, excluding the use for cultivation of varieties in the E.U. The above data requirement is meant to evaluate the cultivation of a GMHP in the E.U.

10. Potential interactions with the abiotic environment

As MON 88913 was shown to be substantially equivalent to conventional cotton, except for the introduced glyphosate-tolerance trait, imparted by the expression of the CP4 EPSPS protein, there is no evidence that this cotton would be any different from conventional cotton with regard to its baseline interactions with the abiotic environment. No adverse impact on the abiotic environment is expected to result from the import of MON 88913 for processing and for use of food and feed products derived MON 88913 in the E.U.

Although CP4 EPSPS is an introduced protein in cotton, it has a safe history

of use and has no known negative effects on biochemical processes (see Sections D.7.8.1 and D.9.8 of this document). Therefore, no adverse impact on the abiotic environment is expected to result from the import of MON 88913 for processing and from the use of food and feed products derived from MON 88913 in the E.U.

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

11.1 General (risk assessment, background information)

As required by Article 5(5)(b) and 17(5)(b) of Regulation (EC) No 1829/2003, an environmental monitoring plan in accordance to Annex VII of Directive 2001/18/EC is included.

11.2 Interplay between environmental risk assessment and monitoring

An environmental risk assessment (ERA) of MON 88913 was undertaken in the context of the scope of the application, that is, for MON 88913 import and processing, and food and feed use of MON 88913 derived products in the E.U., but excluding the cultivation of MON 88913 varieties in the E.U.

Analysis of the characteristics of MON 88913 has shown that the risk for potential adverse effects on human health and the receiving environment, resulting from the import of MON 88913 and food and feed use of MON 88913 derived products in the E.U. is consistently negligible. Therefore, the overall environmental risk posed by this genetically modified higher plant is negligible, and no specific strategies for risk management and no case-specific post-marketing monitoring actions are considered required.

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

As the overall environmental risk posed by this genetically modified higher plant is negligible, and as the conclusions of this environmental risk assessment are derived from the results of scientific studies, rather than major assumptions, no case-specific post-market monitoring actions, typically aimed at testing assumptions made in this assessment, would be warranted or required.

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

Any potential adverse effects of MON 88913 on human health and the environment, which were not anticipated in the ERA, can be addressed under general surveillance in accordance with Directive 2001/18/EC. General surveillance is largely based on routine observation and implies the collection, scientific evaluation and reporting of reliable scientific evidence, in order to be able to identify whether unanticipated, direct or indirect, immediate or delayed adverse effects have been caused by the placing on the market of a genetically modified (GM) crop in its receiving

environment.

In order to allow detection of the broadest possible scope of unanticipated adverse effects, general surveillance is performed by either selected, existing networks, or by specific company stewardship programmes, or by a combination of both. The applicant will ensure that appropriate technical information on MON 88913 and relevant legislation will be available for the relevant networks, in addition to further relevant information from a number of sources, including industry and government websites, official registers and government publications.

Where there is scientifically valid evidence of a potential adverse effect (whether direct or indirect), linked to the genetic modification, then further evaluation of the consequence of that effect should be science-based and compared with available baseline information. Relevant baseline information will reflect prevalent use practices and the associated impact of these practices on the environment. Where scientific evaluation of the observation confirms the possibility of an unanticipated adverse effect, this would be investigated further to establish a correlation, if present, between the use of MON 88913 and the observed effect. The evaluation should consider the consequence of the observed effect and remedial action, if necessary, should be proportionate to the significance of the observed effect.

11.5 Reporting the results of monitoring

Monsanto will submit a General Surveillance Report containing information obtained from participating networks, and/or in case of an effect that was confirmed. If information that confirms an adverse effect which alters the existing risk assessment becomes available, Monsanto will submit a Report, consisting of a scientific evaluation of the potential adverse effect and a conclusion on the safety of the product. The report will also include, where appropriate, the measures that were taken to ensure the safety of human or livestock health and/or the environment.

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

MON 88913 will be detectable using the insert-specific PCR method for detecting the introduced DNA present in MON 88913. The protein present in MON 88913 may also be detected by an appropriate ELISA method.

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

There is no history of release of MON 88913 in the E.U.

b) Conclusions of post-release monitoring

Not applicable

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

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

a) Release country

MON 88913 has been grown commercially on approximately one million hectares in 2006 in the U.S.A.

Prior to its commercialization, MON 88913 has been field tested extensively in the U.S.A., Australia and South Africa since 2002.

b) Authority overseeing the release

U.S.A.: United States Department of Agriculture and Food and Drug Administration. Environmental Protection Agency (herbicide uses over the top).

Australia: Food Standards Australia New Zealand and Office of the Gene Technology Regulator. Australian Pesticide and Veterinary Medicines Authority (herbicide uses over the top).

South Africa: Regulated in terms of the GMO Act (No. 15 of 1997) which has the oversight of six Government Ministries in the decision making process.

c) Release site

U.S.A.: Releases across major cotton growing regions (Alabama, California, Georgia, Mississippi, New Mexico, Texas, Arizona, Arkansas, Oklahoma, Kansas, Missouri, Kentucky, Tennessee, Virginia, North Carolina, South Carolina, Louisiana, and Florida).

Australia: Queensland and New South Wales.

South Africa: Releases sites centered in the major cotton production province, Mpumalanga.

d) Aim of the release

Commercial release in U.S.A./Australia: All uses as conventional cotton

Field release in U.S.A. and Australia: Agronomic performance, efficacy, yield, breeding, residue; in South Africa: efficacy, phytotoxicity and residue.

<p>e) Duration of the release</p> <p>Commercial release in U.S.A.: 2006 growing season.</p> <p>Field release in U.S.A., Australia and South Africa: one or two field seasons.</p>
<p>f) 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 88913, indicating that a requirement for post-release monitoring would not be appropriate.</p> <p>In addition, MON 88913 is commercialized alongside stewardship programmes, involving downstream stakeholders in the use of this cotton, in order to ensure the implementation of good agricultural practice in its cultivation and to ensure a channel of communication in the unlikely event that unanticipated adverse effects might occur.</p> <p>However, no such unanticipated effects have been observed since the commercialization of MON 88913 in the U.S.A., nor during the extensive field-testing programmes.</p>
<p>g) Duration of post-releases monitoring</p> <p>Please see Section E.2.(f).</p>
<p>h) Conclusions of post-release monitoring</p> <p>Please see Section E.2.(f).</p>
<p>i) Results of the release in respect to any risk to human health and the environment</p> <p>Field testing or commercial release provide no evidence that MON 88913 is likely to cause any adverse effects to human or animal health and 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):

<p>a) Status/process of approval</p> <p>The EFSA website (http://www.efsa.eu.int/science/gmo/gm_ff_applications/catindex_en.html) provides information related to the applications submitted under Regulation (EC) No 1829/2003 on genetically modified food and feed.</p>
<p>b) Assessment Report of the Competent Authority (Directive 2001/18/EC)</p> <p>A notification for MON 88913 according to Directive 2001/18/EC has not been submitted by Monsanto.</p>
<p>c) EFSA opinion</p> <p>An EFSA opinion, specifically for MON 88913, was not available at the time of submission of this application.</p>
<p>d) Commission Register (Commission Decision 2004/204/EC)</p> <p>http://europa.eu.int/comm/food/dyna/gm_register/index_en.cfm</p>
<p>e) Molecular Register of the Community Reference Laboratory/Joint Research Centre</p> <p>Information on detection protocols can be found on the JRC website (http://gmo-crl.jrc.it/statusofdoss.htm).</p>
<p>f) Biosafety Clearing-House (Council Decision 2002/628/EC)</p> <p>The publicly accessible portal site of the Biosafety Clearing-House (BCH) can be found at http://bch.biodiv.org/</p>
<p>g) Summary Notification Information Format (SNIF) (Council Decision 2002/812/EC)</p> <p>A notification and SNIF according to Directives 2001/18/EC and 2002/812/EC, respectively, have not been submitted for MON 88913. EFSA provides a link to the summary of this application at http://www.efsa.eu.int/science/gmo/gm_ff_applications/catindex_en.html</p>