SUMMARY OF APPLICATIONS FOR GENETICALLY MODIFIED PLANTSAND/OR DERIVED FOOD AND FEED

A. GENERAL INFORMATION

1. Details of application

a) Member State of application

The Netherlands

b) Application number

EFSA-GMO-NL-2009-

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

The product described in this application is an insect resistant and herbicide tolerant cotton, resulting from the conventional breeding cross between the events 281-24-236x3006-210-23 cotton and MON88913 cotton, referred to as : 281-24-236x3006-210-23xMON88913 cotton. The inserts inherited by 281-24-236x3006-210-23xMON88913 cotton, express the Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins, conferring resistance to certain lepidopteran insect pests and tolerance to glyphosate herbicide under field conditions.

d) Date of acknowledgement of valid application

2. Applicant

a) Name of applicant

This is an application submitted by Agrigenetics, Inc. d/b/a Mycogen Seeds.

b) Address of applicant

Dow AgroSciences Europe	Agrigenetics, Inc. *d/b/a* Mycogen Seeds
European Development Centre	c/o DowAgroSciences LLC
3 Milton Park, Abingdon	9330 Zionsville Road
Oxon OX14 4RN	Indianapolis, IN 46268-1054
United Kingdom	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))

Not applicable.

3. Scope of the application

☒GM plants for food use
☒ Food containing or consisting of GM plants
☒ Food produced from GM plants or containing ingredients produced from GM plants
☒ GM plants for feed use
☒ Feed containing or consisting of GM plants
☒ Feed produced from GM plants
☒ Import and processing (Part C of Directive 2001/18/EC)
☐ Seeds and plant propagating material for cultivation in Europe (Part C of Directive 2001/18/EC)

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

Yes No ☒

If *yes*, specify

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

Yes No ☒

If yes, refer to risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC

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

Yes No ☒

If *yes*, specify

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

Yes ☒ No

Yes, a notification concerning foods derived from 281-24-236x3006-210-23xMON88913 cotton was submitted to the US Food and Drug Administration (FDA) in Feb 8, 2006. A notification letter was sent to the Canadian Food Inspection Agency and to Health Canada on Dec 9, 2005 and to FSANZ on Feb 26, 2006.

In addition, applications have been submitted to Japan (MAFF Environment, MAFF Feed and Ministry of Health) and approved on June 18, 2006 and to Mexico (Ministry of Health, COFEPRIS) and approved on May 3, 2006.

8. General description of the product

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

Cotton is extensively cultivated and has a long history of safe use. Cottonseeds and derived products are not considered to have harmful characteristics, despite the plant producing low levels of gossypol and cyclopropenoids. Seeds derived from 281-24-236x3006-210-23xMON88913 cotton, have inherited the inserts to express Cry1F and Cry1Ac proteins, conferring resistance to certain lepidopteran insect pests under field conditions, and PAT and CP4-EPSPS protein, conferring tolerance to glufosinate-ammonium during the selection stages of the genetic modification and to glyphosate, respectively.

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

The product consists of food and feed from genetically modified 281-24-236x3006-210-23xMON88913 cotton and cotton products from progeny, containing 281-24-236x3006-210-23xMON88913 cotton genetic modification. The term “281-24-236x3006-210-23xMON88913 cotton” refers to seeds derived from 281-24-236x3006-210-23xMON88913 cotton.

c) Intended use of the product and types of users

Products from 281-24-236x3006-210-23xMON88913 cotton will be used in a manner consistent with current uses of cotton and derived products, including use of cotton in the EU for animal feed, storage, and processing into food and feed products.

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

The genetic modifications inherited by 281-24-236x3006-210-23xMON88913 cotton are not expected to impact the existing processing conditions used for cotton, which are well known and have a long history of use. The safety evaluation contained in this application for the placing on the market of 281-24-236x3006-210-23xMON88913 cotton provides further verification that no specific conditions of use and handling are required for 281-24-236x3006-210-23xMON88913 cotton. 281-24-236x3006-210-23xMON88913 cotton products will be used, stored and handled as any other commercial cotton products.

e) Any proposed packaging requirements

The packaging, handling, and storage systems that are currently used for cotton will apply. Cotton and processed products of 281-24-236x3006-210-23xMON88913 cotton will be packaged in the same manner as other cotton products.

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)

Product information to indicate that genetic modification has been used in the development of 281-24-236x3006-210-23xMON88913 cotton will be provided. A proposal for labelling of 281-24-236x3006-210-23xMON88913 cotton has been developed in accordance with Regulation (EC) N° 1829/2003, articles 13 and 25. This will enable seed and seed by-products derived from 281-24-236x3006-210-23xMON88913 cotton to be labelled in accordance with above regulations, when imported to the EU.

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)

In accordance with the OECD guidance for the designation of a unique identifier for transgenic plants (ENV/JM/MONO(2002)7), the unique identification code assigned to 281-24-236x3006-210-23xMON88913 cotton is: DAS-24236-5xDAS-21Ø23-5xMON-88913-8

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

Not applicable.

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

Misuse of 281-24-236x3006-210-23xMON88913 cotton is unlikely, as the proposed food and feed are substantially equivalent to other food and feed products derived from conventional cotton varieties. Therefore the measures of waste and disposal and treatment of 281-24-236x3006-210-23xMON88913 cotton food and feed derived products are the same as those for traditional cotton varieties.

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

1. Complete name

a) Family name: Malvaceae

b) Genus: Gossypium

c) Species: spp

d) Subspecies: None

e) Cultivar/breeding line: 281-24-236x3006-210-23xMON88913 cotton

f) Common name: Cotton

2 a. Information concerning reproduction

(i) Mode(s) of reproduction

Cotton is a perennial woody shrub, which is grown as an annual crop by planting seed. It reproduces sexually, is self-fertile, and generally self-pollinating. Cotton pollen is heavy and sticky and therefore not wind-borne under typical environmental conditions, thus, it is transferred by insects, such as bees, bumble- and honey- bees.

(ii) Specific factors affecting reproduction

Cotton plants will grow and be productive on a wide variety of soils. They are most productive on fertile soil under hot weather and irrigated conditions if rainfall is deficient. Generally is self-pollinating, but in the presence of suitable insect pollinators, allows for limited cross-pollination. Even if suitable pollinators are present, distribution of pollen decreases considerably with increasing distance.

(iii) Generation time

Cotton plants cultural cycle ranges from 120 to 200 growing days covering the period from emergence of the seedling to maturity.

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

Cotton will intra-pollinate and transfer genetic material between cotton of similar genotypes. The extent of pollination will depend upon insect pollinators and geographical location. In addition, no genera in the Gossypeae tribe occurs naturally in the EU preventing its gene transfer to wild relatives.

3. Survivability

a) Ability to form structures for survival or dormancy

Cottonseeds, the only survival structures of cotton plants, are not able to persist in the environment for long periods of time.

b) Specific factors affecting survivability

Cotton is not considered to be able to survive in the environment over long periods because they lack of: dormancy, are not able to germinate under diverse conditions, short life cycle and high seed dispersal. In most cotton growing areas in Europe, seeds which may remain in the soil may germinate in the autumn if conditions are right, otherwise, they are likely to rot and die. Cotton volunteers, can be easily controlled by current agronomic practices such as cultivation, and use of selective herbicides (atrazine, bromoxynil, paraquat and glyphosate).

4. Dissemination

a) Ways and extent of dissemination

Cotton dissemination occurs only by means of seeds.

b) Specific factors affecting dissemination

Mechanical harvesting, wind damage, which may cause some mature bolls to fall to the ground, and transport, are ways of disseminating cottonseeds. Regardless of these routes of dissemination, commercial cotton varieties cannot survive without human assistance.

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

Plants of the Gossypium genus originated in different areas of the world, with centres of diversity in Australia Southern Asia, Africa and the New World. Except as a cultivated crop, they are essentially excluded from temperate climates.

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

Not applicable as 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 insects, birds, and mammals. It is susceptible to a range of fungal diseases and insect pests, as well as competition from surrounding weeds. Cotton is extensively cultivated and has a history of safe use; however, the plant produces gossypol and cyclopropenoid fatty acids which are toxicants.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

The 281-24-236x3006-210-23xMON88913 cotton is the result of a conventional breeding cross between two genetically modified cotton lines - a Cry1F and Cry1Ac insect resistant line : 281-24-236x3006-210-23 cotton and a CP4 EPSPS glyphosate tolerant line : MON88913 cotton.

2. Nature and source of the vector used

The 281-24-236x3006-210-23xMON88913 cotton inherited the inserts of the below genetically modified lines:

3006-210-23 cotton was genetically modified with the TDNA from the binary vector pMYC3006 in which the *cry*1Ac gene is driven by the maize UbiZm1 promoter and *pat* gene is driven by the 4ocsΔMas2' promoter.

281-24-236 cotton was genetically modified with the T-DNA of pAGM281 that contains the full-length *cry*1F gene driven by the promoter 4ocsΔMas2' and the *pat* gene driven by UbiZm1 promoter from maize.

MON88913 cotton the double-border, binary vector PV-GHGT35 was used for the transformation of cotton hypocotyl tissue to produce MON88913. 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 (name) of donor organism(s) size and intended function of each constituent fragment of the region intended for insertion

The 281-24-236x3006-210-23xMON88913 cotton inherited the inserts from the following genetically modified lines: 281-24-236x3006-210-23 cotton and MON88913 cotton. Individual components and the function of these inherited DNA sequences are given in Tables 1, 2 and 3.

TABLE 1: Table of components of transformation vector pMYC3006 used in the production of the event 3006-210-23 cotton

Genetic element	Location on plasmid (from bp to bp)	Size (kbp)	Details
UbiZm1 (intron)	6080-8072	1.993	*Zea mays* promoter plus *Zea mays* exon1 (untranslated enhancer) and intron1 (Christiansen, A.H. *et al.*, 1992) Plant Mol Biol 18: 675-689) (US Patent 5614399, GenBank Accession I38571)
*cry*1Ac(synpro)	2587-6057	3.471	Synthetic, plant-optimised, full length version of Cry1Ac1 from *B.t*. var. *kurstaki*.
orf25 polyA	1835-2561	0.727	Bidirectional terminator from *Agrobacterium tumefasciens* pTi15955 (Barker *et al.*, 1983) Plant Mol. Biol. 2, 335-350, GenBank Locus ATACH5, Accession x00493)
(4OCS)Δmas 2'	643-1251	0.609	Mannopine synthase promoter from pTi15955 (Barker *et al.*, 1983) Plant Mol. Biol. 2, 335-350, GenBank Locus ATACH5, Accession x00493), including 4 copies of the octopine synthase (OCS) enhancer from pTiAch5 (Ellis *et al.*, 1987) EMBO Journal 6:3202-3208, GenBank Accession Numbers I05704 to I05712).
Pat	1276-1827	0.552	The synthetic plant optimised glufosinate resistance gene, based on a phosphinothricin acetyltransferase gene sequence from *Streptomyces viridochromogenes* (Eckes P. *et al.*, 1989) J. Cell. Biochem. 13D, 334.

TABLE 2: Table of components of transformation vector pAGM281 used in the production of the event 281-24-236 cotton

Genetic element	**Location on plasmid (from bp to bp)**	**Size (kbp)**	**Details**
(4OCS)Δmas 2'	7028-7636	0.609	Mannopine synthase promoter from pTi15955 (Barker *et al.*, 1983) Plant Mol. Biol. 2, 335-350, GenBank Locus ATACH5, Accession x00493), including 4 copies of the octopine synthase (OCS) enhancer from pTiAch5 (Ellis *et al.*, 1987) EMBO Journal 6:3202-3208, GenBank Accession Numbers I05704 to I05712).
*cry*1F(synpro)	3571-7017	3.447	Synthetic, plant-optimised, full length version of Cry1F from *B.t.* var. *aizawai*.
orf25 polyA	2818-3544	0.727	Bidirectional terminator from *Agrobacterium tumefasciens* pTi15955 (Barker *et al.*, 1983) Plant Mol. Biol. 2, 335-350, GenBank Locus ATACH5, Accession x00493)
pat	2259-2810	0.552	The synthetic plant optimised glufosinate resistance gene, based on a phosphinothricin acetyltransferase gene sequence from *Streptomyces viridochromogenes* (Eckes P. *et al.*, 1989) J. Cell. Biochem. 13D, 334.
UbiZm1 (intron)	260-2252	1.993	*Zea mays* promoter plus *Zea mays* exon1 (untranslated enhancer) and intron1 (Christiansen, A.H. *et al.*, 1992). Plant Mol Biol 18: 675-689) (US Patent 5614399, GenBank Accession I38571).

TABLE 3: Table of components of transformation vector pV-GHGT35used in the production of the event MON88913 cotton

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

D. INFORMATION RELATING TO THE GM PLANT

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

281-24-236x3006-210-23xMON88913 cotton has four new genetic traits which are the result of the expression of the following proteins: Cry1F, Cry1Ac, PAT and CP4-EPSPS.

The Cry1F and Cry1Ac proteins provide control against lepitopteran insect pest damage to the above-ground parts of the cotton plant including those parts which are beyond the reach of chemical insecticides. Specifically, the Cry1F and Cry1Ac proteins confer season-long resistance against the Tobacco Budworm (*Heliothis virescens*) and Pink Bollworm (*Pectinophora gossypell*a Sanders).

The PAT protein confers tolerance to application of glufosinate-ammonium herbicide used during the selection stages of the genetic modification.

The CP4-EPSPS protein confers tolerance to glyphosate herbicide.

No other new traits have been inherited by 281-24-236x3006-210-23xMON88913 cotton; as confirmed by the molecular characterisation and protein expression data included in this application.

2. Information on the sequences actually inserted or deleted

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

Southern blot analysis using genomic DNA confirmed that 281-24-236x3006-210-23xMON88913 cotton contains identical Southern blot patterns as previously determined for the parental transgenic lines: 281-24-236x3006-210-23 cotton and MON88913 cotton.

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 inserts are integrated into the plant genome as confirmed by the molecular characterisation of 281-24-236x3006-210-23xMON88913 cotton, based on detailed Southern blot analysis.

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

The results show that 281-24-236x3006-210-23xMON88913 cotton contains a single DNA insert of both parental lines: 281-24-236x3006-210-23 cotton and MON88913 cotton.

Insert Structure of 281-24-236 cotton contains: a PAT and Cry1F cassette, starting with UbiZm1 promoter, plus the full length *pat* gene and the orf25 poly A followed by the *cry*1F gene driven by the (4OCS)DeltaMAs 2' promoter.

Insert structure of 3006-210-23 cotton contains: a PAT and Cry1Ac cassette, starting with a partial orf25 poly A, (4OCS)DeltaMas promoter, plus the full length *pat* gene and the bidirectional orf25 poly A, followed by the *cry*1Ac gene driven by the UbiZm1 promoter.

Insert structure of MON88913 cotton contains: 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.

3. Information on the expression of the insert

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

Levels of expression of the Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins were evaluated in several tissue samples of 281-24-236x3006-210-23xMON88913 cotton and corresponding parental lines 281-24-236x3006-210-23 cotton and MON88913 cotton, collected from several field locations in the US during 2005. Tissue samples of cottonseed, pollen, nectar, and cottonseed-processed samples: meal and oil were analysed using ELISA methods at a limit of detection ranging from 0.001 – 0.4 ng protein/mg sample weight.

b) Parts of the plant where the insert is expressed

The Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins are expressed across several tissues of 281-24-236x3006-210-23xMON88913 cotton. Nevertheless, since the scope of this application is to place on the market 281-24-236x3006-210-23xMON88913 cotton for use as any other cotton including processing and use as food and feed, but not for cultivation, the results of expression of Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins were focused on cottonseeds only.

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

a) Reproduction

Comparisons between 281-24-236x3006-210-23xMON88913 cotton and non-transgenic recurrent parent were made on: growth habit, field emergence, vegetative- and flowering-vigour and reproductive potential. Data collected from field trials conducted during 2005 demonstrated no significant morphological, growth or developmental differences between 281-24-236x3006-210-23xMON88913 cotton and conventional cotton.

b) Dissemination

The 281-24-236x3006-210-23xMON88913 cotton plants show no difference in dissemination compared to non-GM cotton. Commercial cotton has been domesticated to the extent that it cannot be disseminated without human intervention.

c) Survivability

Cultivated cotton varieties have been domesticated to the extent that they can not survive outside managed agricultural environments. Lack of weediness traits prevents cottonseeds to readily survive from one growing season to the next. The genetic modifications inherited by 281-24-236x3006-210-23xMON88913 cotton result in expression of Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins conferring resistance to certain lepidopteran insect pests and tolerance to glyphosate under field conditions. The survival characteristics of 281-24-236x3006-210-23xMON88913 cotton in the environment remain comparable to those of non-GM cotton.

d) Other differences

Cotton does not exhibit any weedy tendencies and is non-invasive in natural ecosystems. Based on the agronomic data, there is no evidence for altered survival, multiplication, or dissemination of 281-24-236x3006-210-23xMON88913 cotton in the environment when compared to conventional cotton. In addition, the inserted traits do not alter the phenotype of cotton in a way that would confer a fitness advantage for cotton outside managed agricultural environments.

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

The 281-24-236x3006-210-23xMON88913 cotton is the result of a conventional cross between two genetically modified cotton lines - a Cry1F and Cry1Ac insect resistant line: 281-24-236x3006-210-23 cotton and a CP4 EPSPS glyphosate tolerant line: MON88913 cotton.

The inserts from the corresponding parental lines were inherited in a Mendelian fashion, as confirmed by Southern data.

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 inherited by 281-24-236x3006-210-23xMON88913 cotton has a genetic transfer function; therefore, no changes are expected in their ability transfer DNA to bacteria - a negligible concern.

b) Plant to plant gene transfer

The potential for gene transfer to sexually compatible plant species will be negligible because this application is for the import of 281-24-236x3006-210-23xMON88913 cotton and not for cultivation.

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

The comparator chosen for the safety evaluation of 281-24-236x3006-210-23xMON88913 cotton consisted of non-genetically modified cotton of comparable genetic background.

7.2 Production of material for comparative assessment

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

Composition studies were performed in several locations, including replicates at each site, throughout the US, where cotton is commercially grown, during 2005 growing season.

b) the baseline used for consideration of natural variations

Publicly available data on commercial cotton have been compiled from the literature and used as the baseline in the comparisons with 281-24-236x3006-210-23xMON88913 cotton, in addition to the comparative assessment with non-GM cotton of near genetic background.

7.3 Selection of compounds for analysis

The major identified constituents of cotton, included in composition analyses were: *proximates, minerals, amino acids,* and *fatty acids.* Conversely, key anti-nutrients

identified in cotton, included in the composition studies were: *gossypol, cyclopropenoid fatty acids*.

7.4 Agronomic traits

This application under Reg. (EC) N° 1829/2003 does not include cultivation of 281-24-236x3006-210-23xMON88913 cotton in the EU. Nevertheless, the behaviour of 281-24-236x3006-210-23xMON88913 cotton has been evaluated in field trials carried out across the US. These studies have shown 281-24-236x3006-210-23xMON88913 cotton to be significantly comparable to any other cotton, apart from the protection to some lepidopteran pests and tolerance to certain herbicides.

7.5 Product specification

Food and feed products containing and derived from 281-24-236x3006-210-23xMON88913 cotton (produced by conventional crosses between genetically modified 281-24-236x3006-210-23xMON88913 cotton and other traditionally bred cotton) will be imported and used in the EU, likely by the same operators involved in the processing and commerce of cotton.

7.6 Effect of the production and processing

281-24-236x3006-210-23xMON88913 cotton will undergo existing production processes used for conventional cotton. No novel production process is envisaged.

7.7 Anticipated intake/extent of use

281-24-236x3006-210-23xMON88913 cotton nutritional value and compositional characteristics are comparable to those from conventional, non-GM, cotton varieties; therefore, the anticipated uses of 281-24-236x3006-210-23xMON88913 cotton food products will be no different from those corresponding to conventional cotton varieties.

7.8 Toxicology

7.8.1 Safety evaluation of newly expressed proteins

The genetic modifications inherited by 281-24-236x3006-210-23xMON88913 cotton, result in the expression of Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins. The Cry1F and Cry1Ac proteins have specific toxicity against certain lepidopteran insect pests (target organisms). An acute toxicity study with an approximately 50:50 mixture of Cry1F and Cry1Ac proteins in mice has confirmed the safety of the Cry1F and Cry1Ac proteins to human and animal health.

No mortality, toxicity or adverse clinical signs were observed at the highest dose tested of 375 mg and 350 mg of Cry1F and Cry1Ac pure proteins/kg of body weight. In

addition, there is no evidence for Cry proteins originating from *Bacillus thuringiensis* to have harmful effects on the health of humans and animals.

The safety in terms of toxicity for the PAT protein has already been analysed. The *pat* gene was originally obtained from *Streptomyces viridochromogenes* strain Tü494 which has no known toxic or pathogenic potential. In 1997, EPA issued a final rule exempting PAT from the requirement of a tolerance in all raw agricultural commodities when used as "plant incorporated protectants" (PIP) (FR April the 11, 1997, vol. 62, N°70). In exempting PAT, EPA evaluated data submitted regarding its behaviour in simulated digestive fluid and the acute oral toxicity of the protein. PAT protein didn't show mortality in the high-dose 2500 mg/kg subgroup test of animals and *in vitro* digestibility data indicated that PAT is degraded rapidly.

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 MON88913, is rapidly digested in simulated gastric fluids and is present at very low level in MON88913.

7.8.2 Testing of new constituents other than proteins

Not applicable.

7.8.3 Information on natural food and feed constituents

Detailed compositional analyses of 281-24-236x3006-210-23xMON88913 cotton demonstrated that composition of 281-24-236x3006-210-23xMON88913 cotton is substantial equivalent to that of conventional cotton.

7.8.4 Testing of the whole GM food/feed

281-24-236x3006-210-23xMON88913 cotton is compositionally and nutritionally equivalent to conventional non-genetically modified cotton varieties.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

The most important factor to consider in assessing allergenic potential is whether the source of the gene being introduced into plants, is known to be allergenic. Neither *Bacillus thuringiensis* (the source of the *cry*1F and *cry*1Ac genes), *Streptomyces viridochromogenes* (the source of the *pat* gene) nor *Agrobacterium tumefasciens* (the source of cp4-*epsps* gene) have a history of causing allergy. Also, all donor organisms are common soil bacteria.

The assessment of the allergenic potential of the Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins has been made following the Commission/EFSA recommendations and the application of the decision-tree from FAO/WHO. The results indicate that the proteins <u>are not</u> from an allergenic source, lack of amino acid sequence homology with known allergens, are rapidly degraded in simulated gastric fluids and/or high temperatures, have a relatively low level of expression and lack of glycosylation. The results confirm that the Cry1F, Cry1Ac, EPSPS and PAT proteins do not pose any significant risk of being a potential allergen.

7.9.2 Assessment of allergenicity of the whole GM plant or crop

Cotton is extensively cultivated and has a history of safe use; cotton or derived products of cotton are not considered to have allergenic characteristics.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

Results from the compositional analyses demonstrate equivalence between the control and transgenic cotton lines, therefore, food products derived from 281-24-236x3006-210-23xMON88913 cotton are nutritionally equivalent to food products derived from conventional cotton.

7.10.2 Nutritional assessment of GM feed

Results from the compositional analyses demonstrate equivalence between the control and transgenic cotton, therefore, feed products derived from 281-24-236x3006-210-23xMON88913 cotton are nutritionally equivalent to feed products derived from conventional commercial cotton varieties.

7.11 Post-market monitoring of GM food/feed

Based on the safety evaluation discussed throughout Point 7, no specific risks to human and animal health and the environment have been identified from the use of 281-24-236x3006-210-23xMON88913 cotton in food, feed and industrial products when

compared to non GM cotton. In addition, the use of food and feed products derived from 281-24-236x3006-210-23xMON88913 cotton will not be different to those derived from conventional cotton varieties. Consequently, post market monitoring of GM food/feed products, derived from 281-24-236x3006-210-23xMON88913 cotton, is not necessary.

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

Not applicable, this application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation.

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

9.1 Persistence and invasiveness

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds.

9.2 Selective advantage or disadvantage

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds.

9.3 Potential for gene transfer

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds; therefore the potential for gene transfer from 281-24-236x3006-210-23xMON88913 cotton will be negligible.

9.4 Interactions between the GM plant and target organisms

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during

transportation of the cottonseeds, therefore the interactions between 281-24-236x3006-210-23xMON88913 cotton and the target organisms will be negligible.

9.5 Interactions of the GM plant with non-target organisms

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds, therefore the interactions between 281-24-236x3006-210-23xMON88913 cotton and the non-target organisms will be negligible.

9.6 Effects on human health

Cotton is not considered to have harmful effects on human health. As summarised in point 7, a very detailed evaluation for the potential toxicity to humans of the Cry1F, Cry1Ac, CP4-EPSPS and PAT proteins, expressed in 281-24-236x3006-210-23xMON88913 cotton, revealed its lack of toxicity and allergenicity.

9.7 Effects on animal health

The genetic modifications in 281-24-236x3006-210-23xMON88913 cotton did not introduce any new compounds known to cause, or expected to cause, any possible immediate and/or delayed effects on animal health, and therefore consumption of 281-24-236x3006-210-23xMON88913 cotton animal feed products will not have adverse consequences for the food/feed chain.

9.8 Effects on biogeochemical processes

This application is to market in the EU, 281-24-236x3006-210-23xMON88913 cotton and derived products, excluding cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds, therefore the impact of 281-24-236x3006-210-23xMON88913 cotton on the biogeochemical processes will be negligible.

9.9 Impacts of the specific cultivation, management and harvesting techniques

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of cottonseeds, therefore the impact on the specific cultivation, management and harvesting techniques will be negligible.

10. Potential interactions with the abiotic environment

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products and not for cultivation. Exposure to the environment from the import of 281-24-236x3006-210-23xMON88913 cotton will be limited to unintended release of 281-24-236x3006-210-23xMON88913 cotton e.g. via spillage during transportation of the cottonseeds.

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

This application is to market in the EU of 281-24-236x3006-210-23xMON88913 cotton and derived products, excluding cultivation.

11.1 General (risk assessment, background information)

No specific measures, differing from those for any other commercial cottonseed, need to be taken in case of unintended release or misuse or for disposal and treatment. Any unintentional release or misuse of 281-24-236x3006-210-23xMON88913 cotton would be limited and highly unlikely to have any adverse effect. Furthermore, and if necessary, such limited release can be controlled by current agronomic practices such as selective use of herbicides (with the exception of glufosinate-ammonium and glyphosate).

The environmental risk assessment (e.r.a.) for the placing on the market of 281-24-236x3006-210-23xMON88913 cotton was carried out in accordance to Annex II of Directive 2001/18/EC.

The proposal for an environmental monitoring plan for the placing on the market of 281-24-236x3006-210-23xMON88913 cotton, has been developed according to the principles and objectives outlined in Annex VII of Directive 2001/18/EC and Council decision 2002/811/EC establishing guidance notes supplementing Annex VII to Directive 2001/18/EC.

11.2 interplay between the environmental risk assessment and the monitoring

The design of the environmental monitoring plan is based on the conclusions of the environmental risk assessment (e.r.a.) for import of 281-24-236x3006-210-23xMON88913 cotton for food and feed use.

The conclusions obtained from the e.r.a. confirm that there are no identified adverse effects to human and animal health or the environment arising from import of genetically modified 281-24-236x3006-210-23xMON88913 cotton, for food and feed use, and therefore the risk to human and animal health or the environment is as negligible as for any commercial cotton.

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

The e.r.a. concluded that the risk to human and animal health or the environment from 281-24-236x3006-210-23xMON88913 cotton and any derived products is as negligible as for any commercial cotton and any derived products. As a result, case-specific monitoring is not applicable for the use of 281-24-236x3006-210-23xMON88913 cotton for all food and feed purposes and the import and processing of 281-24-236x3006-210-23xMON88913 cotton.

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

Any potential adverse effects of 281-24-236x3006-210-23xMON88913 cotton on human health and the environment, which were not anticipated in the e.r.a. 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, by specific company stewardship programmes, or by a combination of both. The applicant will ensure that appropriate technical information on 281-24-236x3006-210-23xMON88913 cotton 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 281-24-236x3006-210-23xMON88913 cotton 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.

11.6 Reporting the results of monitoring

The applicants will inform the European Commission, without delay, of any adverse effects arising from the handling and use of imported 281-24-236x3006-210-23xMON88913 cotton reported to them. Furthermore, the applicants will investigate such reports and inform the outcome to the European Commission.

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) Application number

Not applicable.

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)

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

a) Release country

USA.

b) Authority overseeing the release

USDA and EPA.

c) Release site

Multiple sites.

d) Aim of the release

Perform composition, expression and agronomic trials.

e) Duration of the release

One season.

f) Aim of post-releases monitoring

Control of potential volunteers.

g) Duration of post-releases monitoring

One season.

h) Conclusions of post-release monitoring

281-24-236x3006-210-23xMON88913 cotton plants performed as expected, with no evidence of any unintentional morphological or phenotypical characteristics. In particular, there was no evidence of enhanced weediness of 281-24-236x3006-210-23xMON88913 cotton.

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

No adverse effects on human health and environment were found.

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.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.

b) Assessment Report of the Competent Authority (Directive 2001/18/EC)

Information about the assessment report of application C/Nl/04/01 can be found on: http://gmoinfo.jrc.it/csnifs/C-NL-04-01_AssessmentReport.pdf

c) EFSA opinion

An EFSA opinion for 281-24-236x3006-210-23xMON88913 cotton was not available at the time of the submission

d) Commission Register (Commission Decision 2004/204/EC14)

http://europa.eu.int/comm/food/food/biotechnology/authorisation/commun_register_en.htm

e) Molecular Register of the Community Reference Laboratory/Joint Research Centre

Information on detection protocols will likely be posted at http://gmo-crl.jrc.it/

f) Biosafety Clearing-House (Council Decision 2002/628/EC15)

The publicly accessible portal site of the Biosafety Clearing-House (BCH) can be found at http://bch.biodiv.org/

g) Summary Application Information Format (SNIF) (Council Decision 2002/812/EC)

The SNIF of this application can be found on: http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_GMOApplications.htm