Application for authorization of NK603 × MON 810 maize for cultivation in the European Union under Regulation (EC) No 1829/2003 on genetically modified food and feed

Part II

Summary

October 2005

A. GENERAL INFORMATION

1. Details of application

a) Member State of application

The Netherlands

b) Notification number

Not known at the time of application

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

The Monsanto development code for this genetically modified maize is: NK603 × MON 810. NK603 × MON 810 varieties are marketed under the name of the hybrid variety, in association with the trademarks YieldGard® Corn Borer with Roundup Ready® Corn 2, indicating clearly to growers that the hybrid is protected from specific lepidopteran insect pests and that it is tolerant to Roundup® herbicide.

d) Date of acknowledgement of notification

Not known at the time of application

2. Applicant

a) Name of applicant

Monsanto Company, represented by Monsanto Europe S.A./N.V.

b) Address of applicant

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Avenue de Tervuren 270-272
B-1150 Brussels
BELGIUM

Monsanto Company
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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))

NK603 × MON 810 maize[1] will be cultivated, traded and used in the European Union in the same manner as current commercial maize and by the same growers and operators currently involved in the planting, trade and use of traditional maize.

® Roundup, Roundup Ready and YieldGard are registered trademarks of Monsanto Technology LLC.
[1] Hereafter referred to as NK603 × MON 810

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)
(x) 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 (x)**
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 (x)	**No ( )**
If *no*, refer to risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC NK603 × MON 810 has been notified for field-testing in the E.U. since 2000 (B/FR/00/02/06; B/ES/04/18; B/ES/04/20; B/DE/04/163; B/FR/04/02/01).	

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 (x)	**No ( )**
If *yes*, specify A notification pursuant to Directive 2001/18/EC (C/GB/02/M3/3) for import of NK603 × MON 810 in the E.U. and use thereof as any other maize, excluding the cultivation of varieties but including the use for animal feed, was submitted in April 2002. The notification has received a favourable opinion from the UK Lead Member State in March 2004, progressed through the Member States consultation period and is currently under evaluation by EFSA. A second notification pursuant to Directive 2001/18/EC (C/ES/04/01) for import of NK603 × MON 810 in the E.U. and use thereof as any other maize, including the cultivation of varieties, is pending since January 2004.	

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

Yes (x)	No ( )

If *yes*, specify

In the U.S.A. and Canada, NK603 maize[2], MON 810 maize[2] and the combined-trait product NK603 × MON 810 can be lawfully used for the full range of uses of traditional maize.

The scope of the approvals already granted for these genetically modified organisms and the status of pending regulatory reviews, in progress in numerous countries around the world, typically depend on the country and its local regulatory framework.

8. General description of the product

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

NK603 × MON 810 consists of maize produced from NK603 and MON 810 using traditional breeding methods. Although genetic modification was used in the development of NK603 and MON 810, no additional genetic modifications were involved for the production of NK603 × MON 810.

Like the single-trait product NK603, NK603 × MON 810 expresses CP4 EPSPS proteins derived from *Agrobacterium* sp. strain CP4, which confer tolerance to Roundup® agricultural herbicide (containing glyphosate). Like the second parental single-trait product MON 810, NK603 × MON 810 also expresses the Cry1Ab protein, derived from *Bacillus thuringiensis* subsp. *kurstaki*, which confers protection from predation by certain lepidopteran insect pests, including the European Corn Borer (*Ostrinia nubilalis*) and pink borers (*Sesamia* spp).

The use of NK603 × MON 810 plants enables the farmer to use Roundup herbicide for effective control of weeds during the growing season and to take advantage of the favourable environmental and safety characteristics of Roundup herbicide. The use of NK603 × MON 810 also enables farmers to effectively control certain lepidopteran insect pests in maize, ensuring maximum realization of yield potential, while removing the environmental burden of the production, packaging and transport of insecticides, previously used to control *Ostrinia nubilalis* and *Sesamia* spp.

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

NK603 × MON 810 and its progeny are intended to be used as any other maize, including for use as or in foods and feeds.

The scope of this new application is for cultivation of NK603 × MON 810 in the E.U. and complements the scope of Monsanto's pending application EFSA-GMO-UK-2004-01, which covers the uses of NK603 × MON 810 and its progeny for food, feed, import and processing as any other maize in the E.U.

[2] Hereafter referred to as NK603 and MON 810, respectively

c) Intended use of the product and types of users

NK603 × MON 810 will be planted, traded and used in the European Union in the same manner as current commercial maize and by the same growers and operators currently involved in the planting, trade and use of traditional maize.

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

NK603 × MON 810 is substantially equivalent to traditional maize except for its introduced (*i.e.* inherited) traits: tolerance to glyphosate and protection from certain lepidopteran insect pests, which are traits of agronomic interest. This maize was shown to be as safe and as nutritious as traditional maize. Therefore, NK603 × MON 810 and derived products will be stored, packaged, transported, handled and used in the same manner as traditional maize products. No specific conditions are warranted or required for the food and feed use of NK603 × MON 810.

e) Any proposed packaging requirements

NK603 × MON 810 is substantially equivalent to traditional maize (except for the introduced glyphosate-tolerance and protection from targeted lepidopteran insect pests). Therefore, NK603 × MON 810 and derived products will be used in the same manner as other maize and no specific packaging is required. (For the labelling, *see* question 8.(f)).

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

In accordance with Regulations (EC) N° 1829/2003 and 1830/2003, a labelling threshold of 0.9 % is applied for the placing on the market of NK603 × MON 810 grain and derived products.

The applicant and his licencees will sell certified NK603 × MON 810 seed for planting in the E.U. Seed vendors shall be required to label seed bags containing NK603 varieties with the words "genetically modified maize" or "contains genetically modified maize" as well as the product's unique identifier MON-ØØ6Ø3-6 × MON-ØØ81Ø-6.

Operators shall be required to label products containing or consisting of NK603 × MON 810 with the words "genetically modified maize" or "contains genetically modified maize", and shall be required to declare the unique identifier MON-ØØ6Ø3-6 × MON-ØØ81Ø-6 in the list of GMOs that have been used to constitute the mixture that contains or consists of this GMO.

Operators shall be required to label foods and feeds derived from NK603 × MON 810 with the words "produced from genetically modified maize". 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 NK603 × MON 810 and derived foods and feeds in the EU 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 labeling requirements for NK603 × MON 810. 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)

MON-ØØ6Ø3-6 × MON-ØØ81Ø-6

NK603 × MON 810 is uniquely identified using this combination of the unique identifiers for the event NK603 (MON-ØØ6Ø3-6), and event MON 810 (MON-ØØ81Ø-6).

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

NK603 × MON 810 is suitable for use 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

Misuse of NK603 × MON 810 is unlikely, as Monsanto's applications for authorization of this maize cover all uses, as for traditional maize.

NK603 × MON 810 is substantially equivalent to traditional maize except for the introduced (*i.e.* inherited) traits: tolerance to glyphosate herbicide and protection from certain lepidopteran insect pests, which are traits of agronomic interest. This maize is shown to be as safe and as nutritious as traditional maize. Therefore, any measures for waste disposal and treatment of NK603 × MON 810 products are the same as those for traditional maize.

No specific conditions are warranted or required for the placing on the market of NK603 × MON 810.

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

1. Complete name

a) Family name

Poaceae (formerly Gramineae)

b) Genus

Zea

c) Species

mays (2n=20)

d) Subspecies

Not applicable

e) Cultivar/breeding line

NK603 × MON 810 (synonym: MON 810 × NK603)

f) Common name

Maize; Corn

2. a) Information concerning reproduction

(i) Mode(s) of reproduction

Maize (*Zea mays* L.) is an annual, wind-pollinated, monoecious species with separate staminate (tassels) and pistillate (silk) flowers. Self- and cross-pollination are generally possible, with frequencies of each normally determined by proximity and other physical influences on pollen transfer.

(ii) Specific factors affecting reproduction

Tasselling, silking, and pollination are the most critical stages of maize development and, consequently, grain yield may ultimately be greatly impacted by moisture and fertility stress.

(iii) Generation time

Maize is an annual crop with a cultural cycle ranging from as short as 60 to 70 days to as long as 43 to 48 weeks from seedling emergence to maturity.

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

Out-crossing with cultivated *Zea* varieties

In Europe, the potential for genetic transfer and exchange with other organisms is limited to other maize plants. Maize is wind pollinated, and the distance that viable pollen can travel depends on prevailing wind patterns, humidity, and temperature. All maize will inter-pollinate, except for certain popcorn varieties and hybrids that have one of the gametophyte factors (Ga^S, Ga, and ga allelic series on chromosome 4). Maize pollen, therefore, moves freely within an area, lands on silks of the same variety or different varieties, germinates almost immediately after pollination, and within 24 hours completes

fertilisation.

Out-crossing with wild *Zea* species

Wild relatives of maize do not exist in Europe.

3. Survivability

a) Ability to form structures for survival or dormancy

Maize is an annual crop and seeds are the only survival structures. Natural regeneration from vegetative tissue is not known to occur.

b) Specific factors affecting survivability

Maize cannot survive without human assistance and is not capable of surviving as a weed due to past selection in its evolution. Volunteer maize is not found growing in fencerows, ditches or roadsides as a weed. Although maize seed from the previous crop year can over-winter in mild winter conditions and germinate the following year, it cannot persist as a weed. The appearance of "volunteer" maize in fields following a maize crop from the previous year is rare under European conditions. Maize volunteers are killed by frost or, in the unlikely event of their occurrence, are easily controlled by current agronomic practices including cultivation and the use of selective herbicides.

Maize grain survival is dependent upon temperature, moisture of seed, genotype, husk protection and stage of development. Freezing temperatures have an adverse effect on maize seed germination and have been identified as being a major risk in seed maize production. Temperatures above 45 °C have also been reported as injurious to maize seed viability.

4. Dissemination

a) Ways and extent of dissemination

Dissemination of maize may occur by means of seed dispersal and pollen dispersal. Dispersal of the maize grain is highly restricted in domesticated maize due to the ear structure including husk enclosure. For maize pollen, the vast majority is deposited in the same field due to its large size (90 to 100 µm) with smaller amounts of pollen deposited usually in a downwind direction.

b) Specific factors affecting dissemination

Dispersal of maize seeds does not occur naturally because of the structure of the ears of maize. Dissemination of isolated seeds may result from mechanical harvesting and transport as well as insect or wind damage, but this form of dissemination is highly infrequent. Genetic material can be disseminated by pollen dispersal, which is influenced by wind and weather conditions. Maize pollen is the largest of any pollen normally disseminated by wind from a comparably low level of elevation. Dispersal of maize pollen is limited by its large size and rapid settling rate.

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

Because of its many divergent types, maize is grown over a wide range of climatic conditions. The bulk of the maize is produced between latitudes 30° and 55°, with relatively little grown at latitudes higher than 47° latitude anywhere in the world. The greatest maize production occurs where the warmest month isotherms range between 21° and 27° C and the freeze-free season lasts 120 to 180 days. A summer rainfall of 15 cm is approximately the lower limit for maize production without irrigation with no upper limit of rainfall for growing maize, although excess rainfall will decrease yields.

There are no wild relatives of maize in Europe.

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

Maize is widely grown in the European Union. The most important areas of maize production in Europe include the Danube Basin, from southwest Germany to the Black Sea, along with southern France through the Po Valley of northern Italy.

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

Maize 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 nematode, insect and mite pests. Maize has a history of safe use for human food and animal feed.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

No novel method of genetic modification is utilized in the production of NK603 × MON 810. Instead, NK603 × MON 810 is produced from NK603 and MON 810, using traditional maize breeding methods. While NK603 × MON 810 results from traditional breeding, genetic modification was used in the development of the single-trait, parental NK603 and MON 810 lines. NK603 and MON 810 were produced using the particle acceleration transformation method.

2. Nature and source of the vector used

While NK603 × MON 810 results from traditional breeding, genetic modification was used in the development of the single-trait parental maize lines. NK603 was produced by a particle acceleration transformation method using a gel-isolated *Mlu*I fragment of plasmid vector PV-ZMGT32, containing a 5 enolpyruvylshikimate-3-phosphate synthase (*epsps*) gene that was

derived from the common soil bacterium *Agrobacterium* sp. strain CP4 (*cp4 epsps*). MON 810 was generated by the integration of sequences from the plasmid vector PV-ZMBK07, containing the *cry1Ab* coding sequence of interest, which was derived from *Bacillus thuringiensis* subsp. *kurstaki*. MON 810 was produced using the particle acceleration method.

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

NK603 × MON 810 is produced from NK603 and MON 810 by traditional breeding. Typically, NK603 × MON 810 hybrids are produced by a single cross from NK603 and MON 810 inbred lines (homozygous for the respective insert). Less frequently, NK603 × MON 810 varieties can also be produced from a single cross of a traditionally-bred NK603 × MON 810 inbred line with a traditional maize inbred. NK603 × MON 810 hybrid seed (F1) thereby inherits the NK603 and MON 810 inserts from its parental lines. The individual components of the inserts and the function of these inherited DNA sequences are given in Tables 1 and 2.

Table 1. Components of the NK603 insert

Genetic Element	Source	Size (kb)	Function
First *cp4 epsps* gene cassette			
P-ract1/ ract1 intron	*Oryza sativa*	1.4	Contains promoter, transcription start site and first intron.
ctp 2	*Arabidopsis thaliana*	0.2	Encodes chloroplast transit peptide, which directs the CP4 EPSPS protein to the chloroplast
cp4 epsps	*Agrobacterium* sp. strain CP4	1.4	Encodes glyphosate-tolerant CP4 EPSPS protein
NOS 3'	*Agrobacterium tumefaciens*	0.3	Ends transcription and directs polyadenylation of the mRNA.
Second *cp4 epsps* gene cassette			
e35S	Cauliflower mosaic virus	0.6	Promoter
Zmhsp70	*Zea mays L.*	0.8	Stabilizes the level of gene transcription.
ctp 2	*Arabidopsis thaliana*	0.2	Encodes chloroplast transit peptide, which directs the CP4 EPSPS protein to the chloroplast
cp4 epsps l214p	*Agrobacterium* sp. strain CP4	1.4	Encodes glyphosate-tolerant CP4 EPSPS L214P protein[3]
NOS 3'	*Agrobacterium tumefaciens*	0.3	Ends transcription and directs polyadenylation of the mRNA.

Table 2. Components of the MON 810 insert

Genetic Element	Source	Size (kb)	Function
e35S	Cauliflower mosaic virus	0.32	Promoter

Zmhsp70	*Zea mays* L.	0.8	Stabilizes level of gene transcription.
cry1Ab	*Bacillus thuringiensis*	3.5	Encodes Cry1Ab protein, which targets specific lepidopteran insect pests

D. INFORMATION RELATING TO THE GM PLANT

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

NK603 × MON 810 is produced by traditional methods of maize breeding, starting from NK603 and MON 810 single-trait lines. NK603 × MON 810 therefore expresses the CP4 EPSPS protein, which provides tolerance to Roundup herbicide (containing glyphosate) and the Cry1Ab protein, which confers protection from certain lepidopteran insect pests.

- As NK603, NK603 × MON 810 expresses the CP4 EPSPS protein, which imparts tolerance to glyphosate (N-phosphonomethyl-glycine), the active ingredient in the non-selective, foliar-applied, broad-spectrum, post-emergent herbicide Roundup. Roundup has excellent weed control capabilities and well-known, favourable environmental and safety characteristics. However, the sensitivity of crop plants to Roundup herbicide has hampered the in-season use of this herbicide in the crop. The extension of the use of Roundup agricultural herbicide to allow in-season application in major crops such as maize provides a novel weed control option for farmers. The use of Roundup in maize is significant as it enables the farmer to take advantage of the herbicide's favourable environmental properties.

- As its second parental line containing the MON 810 insert, NK603 × MON 810 expresses the Cry1Ab protein derived from *Bacillus thuringiensis* subsp. *kurstaki*, which provides protection from certain lepidopteran insect pests, including European corn borer (*Ostrinia nubilalis*) and pink borers (*Sesamia* spp).

2. Information on the sequences actually inserted or deleted

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

As described in the respective applications for the single-trait parental maize lines, NK603 and MON 810 each contain a single DNA insert containing a single copy of the introduced DNA fragment, and this at different loci in the maize genome.

In the progeny of NK603 and MON 810, each fragment is inherited as a single gene in a Mendelian fashion.

As the parental maize lines, used to produce NK603 × MON 810 through traditional breeding, are inbred lines that are homozygous for the NK603 or MON 810 inserts, respectively, both of the inserted fragments are inherited in NK603 × MON 810 hybrid seed, *i.e.* one fragment conferring the glyphosate-tolerance and one for the insect-protection trait. The presence of both inserts in NK603 × MON 810 was confirmed through Southern blot analysis, showing that the integrity of the inserts has been conserved in the combined-trait product.

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

NK603 × MON 810 contains both of the parental inserts on separate chromosomes in the nuclear genome. The presence of these inserts in the combined-trait product was confirmed through Southern blot analysis.

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

As NK603 × MON 810 is the product of traditional breeding of NK603 and MON 810 and no additional genetic modification methods have been applied, and as the inherited DNA fragments have negligible potential to interact with one another, it is highly likely that NK603 × MON 810 contains each of the inserts as they were present in the parental NK603 and MON 810 lines. Therefore, the molecular characteristics of the introduced DNA sequences, known for the single-trait NK603 and MON 810 products, also apply to NK603 × MON 810, including the structural organization and integrity of the inserts, as well as the characteristics of the sites of insertion and the flanking sequences, immediately adjacent to the introduced sequences.

3. Information on the expression of the insert

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

Production levels of the introduced proteins were measured in tissues collected from NK603 × MON 810 grown in the field. The levels of CP4 EPSPS and Cry1Ab proteins measured in forage and grain samples of NK603 × MON 810 are summarized below.

The mean levels of CP4 EPSPS across all sites was 36.3 µg/g fw in forage samples of NK603 × MON 810 and 12.7 µg/g fw in the grain. The mean level of the Cry1Ab protein across all sites was 6.06 µg/g fw in the forage and 0.73 µg/g fw in grain samples.

The values given for CP4 EPSPS represent the sum of both CP4 EPSPS and CP4 EPSPS L214P, as the ELISA analytical method recognizes both these proteins expressed in NK603 × MON 810 and NK603.

b) Parts of the plant where the insert is expressed

The production of the CP4 EPSPS and Cry1Ab proteins occurs throughout the plant since the rice actin and CaMV *e35S* promoters have been shown to drive constitutive expression in genetically modified maize.

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

a) Reproduction

Comparative assessments of the characteristics of the single-trait products versus traditional maize have been conducted at multiple sites in the field. The experience gathered from these trials and from extensive commercial planting of NK603 and MON 810 varieties demonstrates that, except for the introduced tolerance to Roundup herbicide (glyphosate) or the protection against certain lepidopteran insect pests, respectively, there are no biologically relevant differences in the reproductive capability, dissemination or survivability of NK603 and MON 810 when compared to traditional maize.

Confirmatory observational data from comparative assessments in the field using NK603 × MON 810 and experience from commercial plantings in the U.S.A. confirm that no biologically relevant differences exist in maize that contains the NK603 and MON 810 inserts in combination. Compared to traditional maize, NK603 × MON 810 has not been significantly changed with respect to its dispersal or survival characteristics as assessed by a number of phenotypic (developmental, morphological, and agronomic) characteristics. NK603 × MON 810 is also not different from traditional maize in terms of potential invasiveness into natural environments and persistence in the environment. No significant differences in incidence of stressor symptoms were observed, other than the introduced protection of NK603 × MON 810 against certain target lepidopteran insect pests. Importantly, there is no information to indicate that there is a potential for NK603 × MON 810 to establish, persist and disperse to a greater extent than traditional maize.

b) Dissemination

The introduced herbicide-tolerance and insect-protection have no influence on maize reproductive morphology and hence no changes in seed dissemination are to be expected.

c) Survivability

Maize is known to be a weak competitor in the wild, which cannot survive in Europe outside cultivation without the aid of human intervention. Field observations have demonstrated that NK603 × MON 810 has not been altered in its survivability when compared to traditional maize.

d) Other differences

Comparative assessments of the phenotypic and agronomic characteristics did not reveal biologically significant differences between NK603 × MON 810 and traditional maize, except for the two introduced traits.

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

NK603 × MON 810 hybrid seed (F1) is produced by traditional breeding, starting from NK603 and MON 810 inbred lines (made homozygous for either the NK603 or the MON 810 insert, respectively). Thereby, each parental line passes on its inserted DNA sequence to the resulting NK603 × MON 810 plant.

The single-trait products, NK603 and MON 810, each contain one insert with a single copy of the respective transformed DNA, which is stably integrated into the nuclear maize genome. In the progeny of NK603 and MON 810, each introduced trait is inherited as a single dominant gene in a Mendelian fashion. This has been confirmed by Southern blot analyses and by studies of the inheritance pattern of these traits in maize.

Southern blot analysis of NK603 × MON 810 confirmed that the inserts from NK603 and MON 810 are stably inherited in the 'combined-trait progeny', which could be expected on the basis of the characterization of the single-trait products.

It is noted that the F_2 grain that is harvested from the F_1 crop contains a complex mixture of progeny. As the F_2 kernels originate from pollination of F_1 plants that are heterozygous for the parental inserts, the introduced traits are repartitioned in the F_2 grain following the independent Mendelian segregation patterns that were shown to apply to each of the parental traits.

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

a) Plant to bacteria gene transfer

In comparison with the possible transfer of genetic material between bacteria and traditional maize, and based on the nature of the DNA elements used in the inserts that have been inherited by NK603 × MON 810, no changes are to be expected in the ability of the GM plant to exchange genetic material with bacteria.

b) Plant to plant gene transfer

Since reproductive morphology in the single-trait products and the NK603 × MON 810 combined-trait product are unchanged compared to traditional maize, pollen production and pollen viability are not expected to be affected by the genetic modifications. Therefore, the outcrossing frequency to other maize or to wild relatives (which are not present in the E.U.) is unlikely to be different for NK603 × MON 810 when compared to traditional maize.

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

NK603 and MON 810 were previously shown to be substantially equivalent to traditional maize. Confirmatory compositional analyses

were performed on forage and grain samples from the combined-trait product, NK603 × MON 810, grown under representative field conditions in the E.U. in 2000. The study also included compositional analyses of forage and grain collected from a near-isogenic, non-transgenic control hybrid with similar background genetics as the test product. The analytical results have shown that NK603 × MON 810 is substantially equivalent to the near-isogenic comparator used in the study. Some statistically significant differences between the test and control product were observed for some of the components, but further investigation showed that they likely occurred by chance and none of them were considered to be of biological significance. The observed differences were generally small and were not consistent across trial sites. Moreover, the component concentrations in NK603 × MON 810 were consistent with baseline concentrations from commercial reference hybrids, and they fell within the wide compositional variability of component concentrations known for traditional maize.

In conclusion, as expected based on the substantial equivalence of NK603 and MON 810 to traditional maize, the field trials confirmed that NK603 × MON 810 is substantially equivalent to traditional maize, with the exception of the introduced (*i.e.* inherited) glyphosate-tolerance and insect protection traits.

7.2 Production of material for comparative assessment

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

A comparative assessment of the composition of NK603 × MON 810 and traditional maize was conducted in France in 2000 (B/FR/00.02.06). The NK603 × MON 810 test hybrid, the near-isogenic control and five commercial reference products were grown at three sites located within important maize producing regions, representing a diversity of environmental conditions representative for regions in Europe where maize is grown commercially. The plants were grown under agricultural practices that are typical of maize production. At each location, the test product, the non-transgenic control, and the five commercial reference hybrids were planted in single plots randomly assigned within each of four replication blocks. Within each replicate, products were blocked according to their glyphosate-tolerance.

b) the baseline used for consideration of natural variations

Compositional analyses were made for forage and grain samples from NK603 × MON 810. The study also included analyses of forage and grain collected from a non-transgenic control hybrid and five different non-transgenic commercial maize hybrids, grown in replicated plots at the same field sites as NK603 × MON 810. Additional data from six commercial reference hybrids grown in the E.U. during the 1999 growing season were included for the construction of a statistically valid 99% tolerance interval for component concentrations in the population of commercial hybrids. Finally, also comparisons with baseline data from numerous other field trials and from the peer-reviewed literature were made. The literature on the composition of maize reveals a wide compositional

variability across maize hybrids.

7.3 Selection of material and compounds for analysis

As described in Section D.7.1, compositional analyses were conducted on grain and forage from NK603 × MON 810 and non-transgenic counterpart.

Grain samples were analysed for proximates (protein, fat, ash, moisture), acid detergent fiber (ADF), neutral detergent fiber (NDF), amino acids, fatty acids, vitamins (B1, B2, E), minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc), folic acid, phytic acid and trypsin inhibitor content. The amounts of the secondary metabolites, raffinose, inositol, 2-furaldehyde (furfural), ferulic acid and p-coumaric acid, were also determined in grain. In forage, the proximate, ADF and NDF contents were determined. Carbohydrate values in forage and grain were estimated by calculation. The selected compounds in the compositional study were chosen on the basis of internationally accepted guidance provided by the OECD.

Based on the long history of safe use of the host plant, maize, as well as the positive results of the compositional analyses conducted for NK603 × MON 810 and its parental single-trait lines, NK603 and MON 810, there is no indication of a need to further analyse other selected compounds in this maize.

7.4 Agronomic traits

The phenotypic and agronomic characteristics of NK603 and MON 810 and the efficacy of the newly introduced agronomic traits have already been studied in the context of the single-trait products. Supplementary field trials in Iowa (IA), Missouri (MO), Nebraska (NE) and Ohio (OH) in the U.S.A. showed no biologically significant differences between NK603 × MON 810 and traditional maize in agronomic and phenotypic characteristics (such as growth and developmental parameters, plant morphology, vigour, and yield characteristics), except for the tolerance of NK603 × MON 810 plants to glyphosate and their protection from certain lepidopteran insect pests. No statistically significant differences were detected for NK603 × MON 810 compared to the near-isogenic control for any of the measured phenotypic characteristics pooled across sites. In addition, no ecological observational differences between the test and control substances for insect, disease, or abiotic stressor incidences supports a conclusion of no increased weed potential of NK603 × MON 810 and no unintentionally altered plant interactions with non-target organisms. These results also infer that NK603 × MON 810 has equivalent reproductive, dissemination and survival characteristics to traditional maize, resulting in a similar lack of persistence and invasiveness as known for traditional maize.

The lack of differences in phenotypic and agronomic characteristics is consistent with the results of the compositional analyses (Section D.7.1.) Taken together, the agronomic, phenotypic and compositional analyses support the conclusion that NK603 × MON 810 is substantially equivalent to traditional maize except for the introduced traits of glyphosate-tolerance and insect pest protection.

7.5 Product specification

NK603 × MON 810 comprises all maize, produced by traditional breeding, starting from NK603 and MON 810 lines.

7.6 Effect of processing

Using both wet and dry milling processes, maize is converted into a diverse range of food and feed products and derivatives used as food and feed ingredients or additives. As NK603 × MON 810 is substantially equivalent and as safe and as nutritious as traditional maize, the use of NK603 × MON 810 for the production of foods and feeds is not different from that of traditional maize. Consequently, any effects of the production and processing of NK603 × MON 180 foods and feeds are not expected to be any different from the production and processing of the equivalent foods and feeds, originating from traditional maize.

7.7 Anticipated intake/extent of use

There are no anticipated changes in the intake and/or extent of use of maize or derived products as a result of the addition of NK603 × MON 810 to the maize supply. NK603 × MON 810 is expected to replace a portion of current maize products such that the intake and use of NK603 × MON 810 will represent some fraction of the total products derived from maize.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

NK603 × MON 810 results from traditional breeding, starting from two genetically modified parental lines, *i.e.* one containing the NK603 insert and one containing the MON 810 insert. Both of the introduced traits are inherited by the NK603 × MON 810 combined-trait progeny. This results in the combined expression of the CP4 EPSPS proteins and the Cry1Ab protein in the same plant. These introduced proteins are present at low levels in the plant and have previously been demonstrated as safe for animal and human health, as part of the safety evaluation of the single-trait products, NK603 and MON 810.

The CP4 EPSPS and Cry1Ab proteins have negligible potential to cause adverse effects to animal or human health. The CP4 EPSPS proteins belong to the safe class of EPSPS enzymes, that are commonly found in a wide variety of food sources and which have a long history of safe use. In addition, there is a history of safe use of CP4 EPSPS-expressing crops, such as Roundup Ready soybean, Roundup Ready canola and Roundup Ready Corn 2 (NK603). Cry1Ab has a highly specific, insecticidal mode of action in the gut of target insects that is based on binding to specific receptors for *Bt* proteins. The long history of safe use of this protein in microbial *Bt* products and its history of safe use in previously approved GM products, such as products derived from MON 810, further support its safety to humans and animals.

In addition to their long history of safe use, the acute toxicity of each protein was directly assessed in an acute oral gavage study. There were no indications of acute toxicity for either of these proteins when administered by gavage to laboratory mice at doses which are orders of

magnitude higher than expected consumption levels from food or feed products containing or consisting of NK603 × MON 810. This lack of toxicity was expected based on the absence of a toxic mechanism in animals, the history of exposure, and the rapid degradation of each protein in simulated human gastric fluids. In addition, CP4 EPSPS and Cry1Ab are not homologous to any known allergens or protein toxins (except for the expected homology of Cry1Ab to other *Bt* proteins). Compared to other proteins, CP4 EPSPS and Cry1Ab are present at very low levels in NK603 × MON 810, and their expression levels are consistent with those observed for the respective single-trait products. As the potential for CP4 EPSPS and Cry1Ab proteins to interact is negligible, the conclusions of the safety assessments for the individual proteins are unaffected when the proteins are expressed in combination in NK603 × MON 810.

7.8.2 Testing of new constituents other than proteins

Since maize is known as a common source of food and feed with a centuries-long history of safe use and consumption around the world, and as NK603 × MON 810 was shown to be substantially equivalent to traditional maize, testing of any constituents other than the introduced proteins is not indicated.

7.8.3 Information on natural food and feed constituents

Maize is known as a common source of food and feed with a centuries-long history of safe use and consumption around the world. No particular natural constituents of maize 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 grain and forage from NK603 × MON 810 and traditional maize have been established by compositional analysis. In addition, the wholesomeness and safety of NK603 × MON 810 has been confirmed in a 42-day feeding study using broiler chickens.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

Absence of any allergenic potential associated with the introduced CP4 EPSPS and Cry1Ab proteins expressed in NK603 × MON 810 has previously been demonstrated for the single-trait products. CP4 EPSPS and Cry1Ab are present at very low levels in maize grain. These proteins were assessed for their potential allergenicity by a variety of tests, including a) whether the genes came from allergenic or non-allergenic sources, b) sequence similarity to known allergens, and c) pepsin stability of the protein in an *in vitro* digestion assay. In all cases, the proteins did not exhibit properties characteristic of allergens.

7.9.2 Assessment of allergenicity of the whole GM plant or crop

As the introduced proteins do not have any allergenic potential, it was concluded that the use of NK603 × MON 810 for food or feed does not lead to an increased risk for allergenic reactions compared to the

equivalent range of food and feed uses of traditional maize.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

NK603 × MON 810 is produced from NK603 and MON 810 using traditional breeding methods, and thereby inherits both inserts from the single-trait parental lines. The introduced traits of glyphosate-tolerance and insect-resistance are of agronomic interest, and do not change the nutritional aspects of this maize. Hence this maize is not expected to be more or less attractive for use as food or feed, for processing, or as a food or feed ingredient. Therefore, anticipated dietary intake of maize-derived foods and feeds is not expected to be altered upon authorisation of NK603 × MON 810, and no nutritional imbalances are expected as a result of the use of NK603 × MON 810.

7.10.2 Nutritional assessment of GM feed

A confirmatory feeding study in broiler chickens was conducted to compare the nutritional value of NK603 × MON 810 and non-transgenic control grain, as well as commercial reference hybrids, and to provide additional confirmation of the safety of this maize. The results of this study show that there were no biologically relevant differences in the parameters tested between broilers fed the NK603 × MON 810-containing diet and the non-transgenic control diet. In addition, when individual treatment comparisons were made, broilers in general performed and had similar carcass yields and meat composition when fed diets containing NK603 × MON 810, the non-transgenic hybrid, and commercially available reference maize hybrids. The NK603 × MON 810-diet was as wholesome as its corresponding non-transgenic control diet and commercially available reference diets regarding its ability to support the rapid growth of broiler chickens. This conclusion was consistent with the evaluation of the composition of NK603 × MON 810, which showed that there were no biologically relevant differences in nutritional and compositional properties relative to control and reference maize hybrids. These data confirm the conclusion that NK603 × MON 810 is as safe and nutritious as traditional maize.

7.11 Post-market monitoring of GM food/feed

There are no intrinsic hazards related to NK603 × MON 810 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 characterisation for food and feed use of NK603 × MON 810 demonstrates that the risks of consumption of NK603 × MON 810 or its derived products are consistently negligible and not different from the risks associated with the consumption of traditional maize and maize-derived products. As a consequence, no specific risk management measures are indicated, and post-market monitoring of the use of this maize for food or feed is not appropriate.

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

The parental maize line NK603 is herbicide-tolerant and does not have any target organisms. The spectrum of target organisms of NK603 × MON 810 is therefore identical to the target organisms of the second parental line, MON 810, which expresses the Cry1Ab protein. MON 810 has already been approved for cultivation and use under Directive 90/220/EEC since 1998.

In order to exert its toxic activity in a target organism, the following steps need to occur to the Cry1Ab protein: ingestion of the Cry1Ab protein crystals by the insect, solubilization of the crystals in the insect midgut, proteolytic processing of the released protein by digestive enzymes to activate the toxin, binding of the toxin to receptors on the surface of midgut epithelial cells of target organisms, formation of membrane ion channels or pores, and consequent disruption of cellular homeostasis. Electrolyte imbalance and pH changes render the gut paralyzed, which causes the insect to stop eating and die.

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

9.1 Persistence and invasiveness

As for traditional maize, the likelihood of NK603 × MON 810 spreading in the environment is negligible, as maize is neither persistent nor invasive and these parameters are unaltered in NK603 × MON 810 when compared to traditional maize. Hence the risk of establishment and spreading of NK603 × MON 810 in the environment is negligible.

9.2 Selective advantage or disadvantage

Compared with traditional maize, the presence of the introduced traits in a NK603 × MON 810 volunteer would only confer a meaningful advantage where target lepidopteran pest species would be present in high numbers or where plants would be treated with glyphosate herbicide, and if no other, more important factors limiting its establishment in the environment would be present. The risk of the protective trait against target lepidopteran pests or the introduced glyphosate-tolerance in NK603 × MON 810 to be the cause of any competitive advantage or disadvantage adversely impacting the environment is negligible, as maize is unlikely to establish outside cultivation under European conditions (*see* Section D.9.1).

9.3 Potential for gene transfer

There is no potential for gene transfer from NK603 × MON 810 to wild plant species in the E.U. and low to negligible likelihood for gene transfer to other maize crops depending on wind patterns, flowering synchrony and distance between the crops. In the event that an introduced gene would outcross to other maize varieties, its transfer would, in any event, have negligible consequences for the environment, as is the case for the source crop. Therefore the environmental risk of potential gene transfer is negligible.

9.4 Interactions between the GM plant and target organisms

The insecticidal trait in NK603 × MON 810 is identical to that in

MON 810, which was previously authorised for cultivation in the E.U. Extensive testing of MON 810 in the laboratory and in the field did not indicate any direct or indirect adverse environmental effects on non-target organisms. Therefore, the plants of this maize would have no potential to cause harm on non-target organisms through their interaction with target organisms. Important environmental benefits of the planting of this insect-protected maize include: 1) a reliable means to control specific lepidopteran maize pests while maintaining beneficial species; 2) potential for reduced use of hazardous chemical insecticides; 3) excellent fit with integrated pest management (IPM) and sustainable agricultural systems; 4) potentially reduced levels of fungal mycotoxins such as fumonisins in maize kernels.

9.5 Interactions of the GM plant with non-target organisms

The introduced Cry1Ab and CP4 EPSPS proteins present a negligible hazard to non-target organisms. Numerous studies have established that Cry1Ab exhibits toxicity to specific Lepidoptera, but not to other insect orders or other non-target organisms. Based on the ubiquity of natural EPSPSs in the environment and the history of safe use of CP4 EPSPS-expressing crops such as Roundup Ready soybean, it is highly unlikely that the introduced CP4 EPSPS enzymes in NK603 × MON 810 would possess biological activity towards any non-target organisms. As a consequence, there is negligible risk for harmful effects of NK603 × MON 810 on non-target organisms, either through direct or indirect interactions with this maize or through contact with the newly expressed proteins.

Furthermore, no evidence of any adverse effects was found since the commercial introduction of MON 810, NK603 and NK603 × MON 810 in North America. No evidence has been brought forward by the many farmers and operators handling these products of any harmful or undesirable effects associated with this maize or with the introduced proteins.

9.6 Effects on human health

The data demonstrating the safety of NK603 × MON 810 for human health were summarized in Sections D.7.1 to D.7.11. Based on the extensive characterization of the inserted traits, and the safety demonstrated for the expressed proteins, for the single-trait products and for the combined-trait product, no adverse effects on human occupational health are to be expected.

9.7 Effects on animal health

Based on the safety data presented in Sections D.7.1 to D.7.11, no adverse effects on animal health nor effects on the food/feed chain are to be expected.

9.8 Effects on biogeochemical processes

The risk for direct or indirect, immediate or delayed adverse effects on biogeochemical processes can be considered as negligible. There is no evidence that NK603 × MON 810 plants would be any different from traditional maize regarding their direct influence on biogeochemical processes or nutrient levels in the soil, as NK603 × MON 810 is

compositionally equivalent and has equivalent growth and development, morphology, yield, plant health and survival characteristics to non-transgenic maize (*see* Sections D.4, D.7.1 and D.7.4). Furthermore, any indirect interactions of the GMO and target or non-target organisms in the vicinity of an incidental release of the grain are not likely to cause hazardous effects on the biogeochemical processes in the soil. The Cry1Ab protein is subject to rapid degradation in soil. The CP4 EPSPS proteins belong to the safe class of EPSP synthases that are ubiquitous in the environment.

9.9 Impacts of the specific cultivation, management and harvesting techniques

No specific cultivation techniques are required to grow NK603 × MON 810. Traditional crop rotational practices, planting regimes for maize, techniques for soil preparation (tillage), maize drilling techniques and all technical equipment remain applicable.

Similarly, no new or specific crop management techniques are necessary for NK603 × MON 810. All the conventional management techniques to cultivate maize remain at the farmer's disposition, *e.g.* application of fertiliser, irrigation techniques, mechanical operations or the use of approved plant protection products for disease, insect pest and weed control. The introduced glyphosate-tolerance trait merely provides the farmer with an additional option to remove competing weeds from his crop, *i.e.* by employing a glyphosate-containing herbicide approved for that purpose. The insect-protection trait allows the farmer to effectively control certain insect pests, while avoiding potentially harmful operator exposure to the insecticides traditionally used to control these pests and reducing costly field operations.

Finally, no changes in harvesting techniques are required. Traditional harvesting equipment as well as post-harvest storage techniques and conditions remain applicable..

10. Potential interactions with the abiotic environment

NK603 × MON 810 is substantially equivalent to traditional maize, with the exception of the two introduced (*i.e.* inheritied) traits of agronomic interest, which are imparted by the expression of the CP4 EPSPS and Cry1Ab proteins. CP4 EPSPS and Cry1Ab have a safe history of use and have no known negative interactions with the abiotic environment.

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

11.1 General (risk assessment, background information)

As the scope of this application under Regulation (EC) No 1829/2003 is to extend the use of NK603 × MON 810 to the cultivation of varieties in the E.U., a general surveillance plan in accordance to Annex VII of Directive 2001/18/EC was included, as required by Articles 5(5) and

17(5) of the said Regulation.

11.2 Interplay between environmental risk assesment and monitoring

An environmental risk assessment (e.r.a.) for NK603 × MON 810 was conducted as required by Articles 5(5) and 17(5) of Regulation (EC) No 1829/2003. Analysis of the characteristics of NK603 × MON 810 has shown that the risk for potential adverse effects on human health and the receiving environment, resulting from the proposed use of NK603 × MON 810 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 the 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 NK603 × MON 810 on human health and the environment, which were not anticipated in the environmental risk assesment, are addressed by the general surveillance plan in accordance with the principles of Directive 2001/18/EC, Annex VII. 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 notifier will ensure that appropriate technical information on NK603 × MON 810 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.

Following the approval of this maize for cultivation in the E.U., Monsanto will approach key stakeholders and key networks of stakeholders of the product (including European farmers and their organisations, international grain traders, maize processors and users of maize grain for animal feed) and inform them that the product has been authorised and may be present in European maize production. Monsanto will request key stakeholders and networks for their participation in the general surveillance of the placing on the market of

this maize, in accordance with the provisions of Directive 2001/18/EC. Key stakeholders and networks will be requested to be aware of their use of this maize and to inform Monsanto in case of potential occurrence of any unanticipated adverse effects to health or the environment, which they might attribute to the use of this product. Appropriate technical and safety information on NK603 × MON 810 will be provided to them. As growers are constantly present in the environments where the GM crop will be released, they are well placed to ensure good stewardship in the cultivation of the GM crop, as well as being a valuable source of surveillance information. Therefore, in addition to already existing stewardship programmes, a number of farmers who have experience with the cultivation of NK603 will be contacted and requested to participate in regular environmental surveys. Monsanto will examine the information revealed by these farmer questionnaires (including where possible by applying tools for statistical data analysis) and include this information in the annual general surveillance reports. In addition to the above-mentioned general surveillance actions directed to NK603 × MON 810 growers, international traders, grain processors, users of maize grain, and other stakeholders, Monsanto experts will actively monitor existing information sources such as official websites and expert reports on GMOs in order to identify, collate and follow-up on potentially adverse observations made for this maize or any other relevant information, in particular with respect to occupational health, animal feed safety or putative ecological effects of the release of this maize.

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 NK603 × MON 810 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 an annual 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

As NK603 × MON 810 results from traditional breeding of NK603 and MON 810, both inserts are present in combination. Therefore, NK603 × MON 810 is detectable using either the insert-specific PCR method for detecting the introduced DNA present in NK603 or the equivalent method for MON 810. However, as for all plants in which inserts are combined by traditional breeding, the unambiguous detection of NK603 × MON 810 in mixed consignments of grain will require single kernels to be subjected to the detection methods for both NK603 and MON 810, and to test positive for both.

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

B/FR/00/02/06; B/ES/04/18; B/ES/04/20; B/DE/04/163; B/FR/04/02/01

b) Conclusions of post-release monitoring

The E.U. field trials with NK603 × MON 810 which were conducted to date, relate to the assessment of agronomic performance, phenotypic and morphological characteristics, yield, residues determination, protein expression and compositional analysis. Trials were conducted in France, Germany and Spain which represent principal growing areas in the European Union. Post-release surveillance provided no significant evidence that this maize would likely cause any adverse effects to human or animal health or to the environment.

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)

Post-release surveillance from environments inside and outside the E.U. provided no significant evidence that NK603 × MON 810 would pose any risk of adverse effects to human or animal health or to the environment.

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

a) Release country

First commercialisation of NK603 × MON 810 varieties took place in the U.S.A. in 2002. Prior to commercialisation of NK603 × MON 810 varieties in North America, this maize as well as the single-trait products, NK603 and MON 810, have been extensively tested at multiple locations in the field.

b) Authority overseeing the release

U.S.A.: United States Department of Agriculture (USDA) and Environmental Protection Agency (EPA)

c) Release site

All major maize growing regions in the U.S.A. - *see* Section E.2.(a).

d) Aim of the release

Commercial release for all uses as traditional maize.

e) Duration of the release

Please see Section E.2.(a)

f) Aim of post-releases monitoring

Extensive pre-market risk assessment did not provide evidence of adverse effects potentially associated with the cultivation, handling or use of NK603 × MON 810, indicating that a requirement for post-release monitoring would not be appropriate.

In addition, NK603 × MON 810 is commercialized alongside stewardship programmes such as insect resistance management programmes, involving downstream stakeholders in the use of this maize, 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.

However, no such unanticipated effects have been observed since the large-scale commercialization of NK603 × MON 810 in North America, nor during the field-testing programmes inside and outside the E.U.

g) Duration of post-releases monitoring

Please see Section E.2.(f)

h) Conclusions of post-release monitoring

Please see Section E.2.(f)

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

Field-testing and post-marketing experience provided no significant evidence that grain or derived products from NK603 × MON 810 are likely to cause any adverse effects to human or animal health, or to the environment.

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

a) Status/process of approval

The JRC websites http://gmoinfo.jrc.it/gmc_browse.asp and http://gmo-crl.jrc.it/statusofdoss.htm and the EFSA website http://www.efsa.eu.int/

science/gmo/gm_ff_applications/catindex_en.html provide publicly accessible links to up-to-date databases on the regulatory progress of notifications under Directive 2001/18/EC and applications under Regulation (EC) No 1829/2003, including the Monsanto dossiers for NK603 × MON 810.

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

The JRC website http://gmoinfo.jrc.it/gmc_browse.asp provides a link to the publicly accessible Initial Assessment Report from the UK Lead Member State for Monsanto notification C/GB/02/M3/3 on NK603 × MON 810.

c) EFSA opinion

An EFSA opinion for NK603 × MON 810 was not available at the time of submission of this application. However, the favourable safety opinions by EFSA for NK603 are posted at http://www.efsa.eu.int/science/gmo/gmo_opinions/catindex_en.html. The favourable safety opinion for MON 810 by the Scientific Committee on Plants can be found at http://europa.eu.int/comm/food/ fs/sc/scp/out02_en.html.

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

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 is posted at http://gmo-crl.jrc.it/

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

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

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

The JRC website http://gmoinfo.jrc.it/gmc_browse.asp provides a link to the publicly accessible SNIF summary of notifications under Directive 2001/18/EC, including Monsanto's pending notifications for NK603 × MON 810.

Further, EFSA provides a link to the publicly accessible summary of this application and that of application EFSA-GMO-UK-2004-01 under Regulation (EC) No 1829/2003 at http://www.efsa.eu.int/science/gmo/gm_ff_applications/catindex_en.html.