Application for authorization to use NK603 maize in the European Union, according to Regulation (EC) No 1829/2003 on genetically modified food and feed, including the use for cultivation of varieties

Part II

Summary

August 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. NK603 varieties are marketed under the name of the hybrid variety, in association with the trademark Roundup Ready® Corn 2, indicating clearly to growers that the hybrid is tolerant to Roundup® agricultural herbicide (based on the active ingredient glyphosate).

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

Monsanto Europe S.A./N.V.
Avenue de Tervuren 270-272
B-1150 Brussels
BELGIUM

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
U.S.A

c) Name and address of the person established in the Community who is responsible for the placing on the market, whether it be the manufacturer, the importer or the distributor, if different from the applicant (Commission Decision 2004/204/EC Art 3(a)(ii))

NK603 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 and Roundup Ready are registered trademarks of Monsanto Technology LLC.
[1] Hereafter referred to as NK603

3. Scope of the application

(x) GM plants for food use
(x) Food containing or consisting of GM plants
(x) Food produced from GM plants or containing ingredients produced from GM plants
(x) GM plants for feed use
(x) Feed containing or consisting of GM plants
(x) 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 has been notified for field-testing in the E.U. since 1999 (*see* Monsanto Part B notification numbers B/FR/99/04/06; B/IT/99/17; B/BE/00/WSP13; B/FR/00/03/05; B/DE/00/115; B/ES/00/06; B/FR/01/01/01; B/ES/01/05; B/IT/02/01; B/ES/02/03; B/DE/03/148; B/FR/04/02/02; B/ES/04/17; B/ES/04/19).	

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 for import of NK603 in the E.U. and use thereof as any other maize, not including the cultivation of varieties, was submitted in December 2000 (C/ES/00/01). In 2003, the notification received favourable scientific opinions from the Spanish Lead Member State and EFSA (www.efsa.eu.int). NK603 was approved for import, processing and feed use on 19 July 2004 (see Commission Decision 2004/643/EC). NK603 has also been approved for food use in the E.U. under Regulation (EC) No 258/97 (see Commission Decision 2005/448/EC). A second notification pursuant to Directive 2001/18/EC (C/ES/03/01), including the use of NK603 for the cultivation of varieties, is pending since January 2003.	

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., Canada, Argentina, and several other countries around the world, NK603 is lawfully placed on the market for the full range of uses as traditional maize, including the cultivation of varieties. In addition, NK603 has been approved for import, processing and consumption in many countries around the world, including the 25 countries of the E.U.

The scope of the approvals already granted for NK603 and the status of still 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 is genetically modified maize, produced by means of the particle acceleration method. NK603 expresses the protein CP4 EPSPS, derived from *Agrobacterium* sp. strain CP4, which confers tolerance to Roundup® agricultural herbicide (containing glyphosate).

The use of NK603 plants enables the farmer to use Roundup agricultural herbicide for effective control of weeds during the growing season and to take advantage of the favourable environmental and safety characteristics of its active ingredient glyphosate.

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

The scope of this dossier is for all uses of this maize for food and feed as well as the use of NK603 for the cultivation of varieties in the E.U. The scope also includes an application for renewal of the authorization of the existing feed materials and food and feed additives previously notified under aticles 8 and 20 of Regulation (EC) No 1829/2003 on genetically modified food and feed.

The range of uses of this maize for food and feed will be identical to the full range of equivalent uses of traditional maize.

This application does not include import of NK603 into the E.U., which was already authorised under Directive 2001/18/EC in 2004.

c) Intended use of the product and types of users

NK603 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 is substantially equivalent to traditional maize except for its introduced tolerance to glyphosate, which is a trait of agronomic interest. This maize was shown to be as safe and as nutritious as traditional maize. Therefore, NK603 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.

e) Any proposed packaging requirements

NK603 is substantially equivalent to traditional maize (except for the introduced glyphosate-tolerance). Therefore, NK603 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 and derived products.

The applicant and his licencees will sell certified NK603 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.

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

Operators shall be required to label foods and feeds derived from NK603 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 and derived foods and feeds in the E.U. are required to be aware of the legal obligations regarding traceability and labelling of these products. Given that explicit requirements for the traceability and labelling of GMOs and derived foods and feeds are laid down in Regulations (EC) No 1829/2003 and 1830/2003, and that authorized foods and feeds shall be entered in the Community Register, operators in the food/feed chain will be fully aware of the traceability and labeling requirements for NK603.

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

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 is suitable for food and feed 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 is unlikely, as the proposed uses for this maize include all the current uses of traditional maize (except the use for importation which was previously approved). NK603 is substantially equivalent to traditional maize except for the introduced tolerance to glyphosate, which is a trait 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 products are the same as those for traditional maize. No specific conditions are warranted or required for the placing on the market of NK603.

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

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 domestication. 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 soil cultivation practices 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

NK603 was modified by incorporation of a restriction fragment of plasmid DNA, designated as PV-ZMGT32L (see question ***C.2***, Figure 1), into the maize genome using a particle acceleration method.

2. Nature and source of the vector used

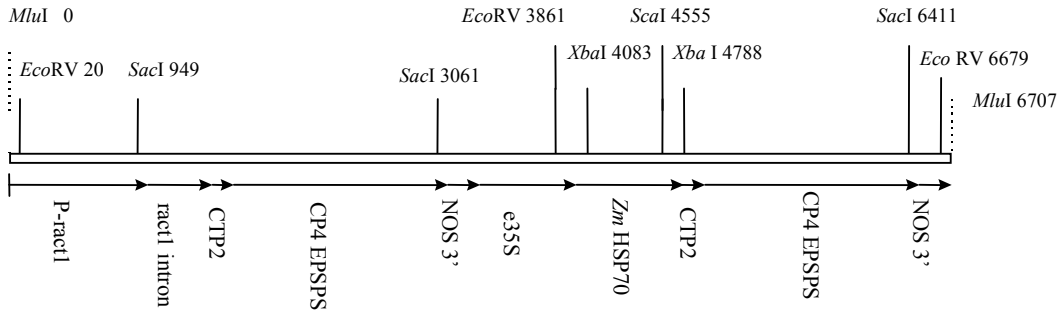
NK603 was produced by a particle acceleration transformation method using a gel-isolated *Mlu*I restriction fragment of plasmid vector PV-ZMGT32 (designated PV-ZMGT32L, Figure 1), containing a 5 enolpyruvylshikimate-3-phosphate synthase (*epsps*) gene from *Agrobacterium* sp. strain CP4 (*cp4 epsps*).

The *cp4 epsps* gene encodes a tolerant form of EPSPS, which confers glyphosate-tolerance to the plant.

The plant expression plasmid vector, PV-ZMGT32 (Figure 2), was developed by Monsanto Company, St. Louis, Missouri (U.S.A.) and contains two adjacent plant gene expression cassettes each containing a single copy of the *cp4 epsps* gene. The vector also contains an *nptII* selectable marker gene, which allowed selection of bacteria containing the plasmid, and an origin of replication (*ori*) necessary for replicating the plasmid in *Escherichia coli*.

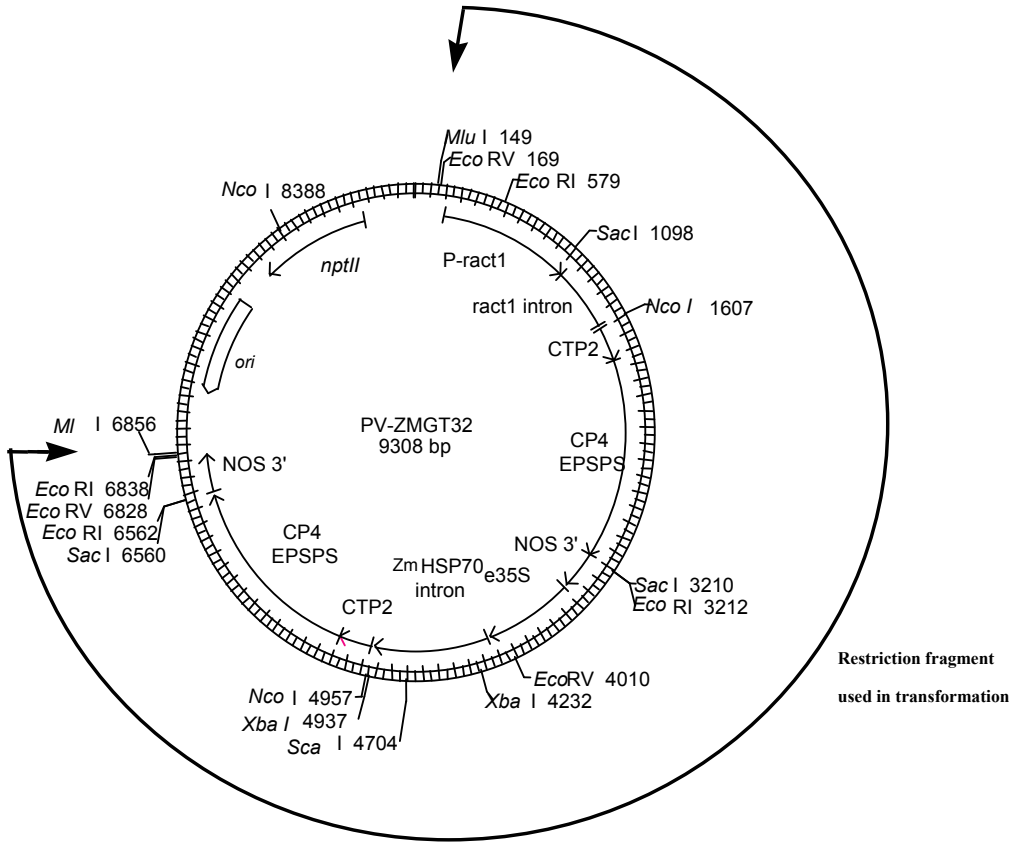
The agarose gel-isolated *Mlu*I restriction fragment of plasmid vector, PV-ZMGT32L, which was utilized for transformation of NK603, contains only the *cp4 epsps* plant gene expression cassettes and does not contain the *nptII* selectable marker gene or origin of replication (Figure 1).

Figure 1. Linear map of PV-ZMGT32L



The DNA fragment PV-ZMGT32L was used to generate NK603 by particle acceleration technology. The dashed lines represent the remaining *Mlu*I sites following digestion of PV-ZMGT32.

Figure 2. Plasmid map of PV-ZMGT32



The plasmid PV-ZMGT32 was used to prepare the *Mlu*I fragment used in the transformation of NK603 by excision and discarding of the origin of replication (*ori*) and antibiotic resistance marker (*nptII*) sequences.

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

All genetic constituents within plasmid vector PV-ZMGT32 are completely known including the gene of interest, *cp4 epsps*, and its function. The size, source and function of the genetic elements present in the plasmid vector PV-ZMGT32 are given in Table 2. The agarose gel-isolated *Mlu*I restriction fragment of the plasmid vector, PV-ZMGT32L, utilized for transformation of NK603, contains only the *cp4 epsps* plant gene expression cassettes and does not contain the *nptII* selectable marker gene or origin of replication (*ori*).

In NK603, the *e35S* promoter utilised in the first plant gene expression cassette, as derived from the cauliflower mosaic virus (CaMV), is well characterised. The safety of the *e35S* promoter is well established and *e35S* does not impart a pathogenic response. The sequence for *epsps* utilised in both cassettes was isolated from *Agrobacterium* sp. strain CP4, while the *NOS 3'* terminator is a 3' non-translated region of the nopaline synthase gene derived from the Ti plasmid of *Agrobacterium tumefaciens*. There is no human or animal pathogenicity known from *Agrobacterium* species, nor is the *cp4 epsps* or *NOS 3'* sequence a determinant of *Agrobacterium* plant pathogenesis.

The *P-ract* promoter and intron, *Zmhsp*70 intron and *ctp2* inserted genetic elements are derived from common plant species including rice, maize and *Arabidopsis*.

In conclusion none of the inserted sequences are known to have any pathogenic or harmful characteristics.

Table 2. Summary of DNA components of the plasmid PV-ZMGT32

Genetic Element	Source	Size (kb)	Function
Genetic elements present in the *Mlu*I restriction fragment, designated PV-ZMGT32L, used for transformation:			
***cp4 epsps* gene cassette (1)**			
P-ract1/ ract1 intron	*Oryza sativa*	1.4	5' region of the rice actin 1 gene containing the promoter, transcription start site and first intron.
ctp 2	*Arabidopsis thaliana*	0.2	DNA sequence for chloroplast transit peptide, isolated from *Arabidopsis thaliana* EPSPS, present to direct the CP4 EPSPS protein to the chloroplast, the site of aromatic amino acid synthesis.
cp4 epsps	*Agrobacterium* sp. strain CP4	1.4	The DNA sequence for CP4 EPSPS, isolated from *Agrobacterium* sp. strain CP4, which imparts tolerance to glyphosate.
NOS 3'	*Agrobacterium tumefaciens*	0.3	A 3' nontranslated region of the nopaline synthase gene from *Agrobacterium tumefaciens* T-DNA which ends transcription and directs polyadenylation of the mRNA.
***cp4 epsps* gene cassette (2)**			
e35S	*Cauliflower mosaic virus*	0.6	The cauliflower mosaic virus (CaMV) promoter with the duplicated enhancer region.
Zmhsp70	*Zea mays L.*	0.8	Intron from the corn *hsp70* gene (heat-shock protein) present to stabilize the level of gene transcription.
ctp 2	*Arabidopsis thaliana*	0.2	DNA sequence for chloroplast transit peptide, isolated from *Arabidopsis thaliana* EPSPS, present to direct the CP4 EPSPS protein to the chloroplast, the site of aromatic amino acid synthesis.
cp4 epsps	*Agrobacterium* sp. strain CP4	1.4	The DNA sequence for CP4 EPSPS, isolated from *Agrobacterium* sp. strain CP4, which imparts tolerance to glyphosate.
NOS 3'	*Agrobacterium tumefaciens*	0.3	A 3' nontranslated region of the nopaline synthase gene from *Agrobacterium tumefaciens* T-DNA which ends transcription and directs polyadenylation of the mRNA.
Genetic Element	**Source**	**Size (kb)**	**Function**
Genetic elements present in the PV-ZMGT32 plasmid backbone, but not present in the *Mlu*I restriction fragment (PV-ZGMT32L) used for transformation:			
ori	*Escherichia coli*	0.65	The origin of replication from the *E. coli* high copy plasmid pUC119.
nptII	*Transposon Tn5*	0.8	The gene for the enzyme neomycin phosphotransferase type II. This enzyme confers resistance to certain aminoglycoside antibiotics and thereby allows for selection of bacteria containing the plasmid.

D. INFORMATION RELATING TO THE GM PLANT

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

NK603 expresses CP4 EPSPS proteins, which impart 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 agricultural 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.

2. Information on the sequences actually inserted or deleted

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

NK603 was modified by incorporating into the maize genome a restriction fragment of plasmid DNA, designated as PV-ZMGT32L (see question ***C.1***, Figure 1), which contains two *cp4 epsps* gene cassettes in tandem. This was done by means of particle acceleration technology.

Molecular analysis was performed to characterise the inserted DNA in NK603. Southern blot analysis was used to determine the insert number (number of integration sites within the maize genome), the copy number (the number of integrated linear DNA fragments used for transformation within one insertion site), the integrity of the inserted promoters, coding regions, and polyadenylation sequences, and the presence or absence of the plasmid backbone sequence. Polymerase chain reaction (PCR) analysis and DNA sequencing were performed to verify the sequences of the insert and the regions flanking the 3' and 5' ends of the insert. Data from the analyses support the following conclusions:

1. the genome of NK603 contains a single insertion of the integrated DNA;
2. adjacent to the insert is a 217 bp fragment of the rice actin promoter and 305 bp with homology to chloroplast DNA;
3. the insert comprises each of the elements present in PV-ZMGT32L (Figure 1) with the second of the two *cp4 epsps* coding regions (designated *cp4 epsps l214p* in the insert) exhibiting two base-pair substitions, one of which results in a single amino acid change in the expressed protein (CP4 EPSPS L214P);
4. the genome of NK603 does not contain any detectable plasmid backbone DNA and does not contain the *ori* or the *nptII* coding sequences;
5. PCR amplification and DNA sequencing confirmed the characterisation of the insert and confirmed that the sequences

flanking the insert are native to the maize genome.

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

Not applicable

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

NK603 contains a single insert in the genome, segregating according to Mendelian genetics. Chi square analysis of the segregation data of NK603 is consistent with a single active site of insertion of the *cp4 epsps* genes (in tandem) into the nuclear genomic DNA, consistent with the molecular characterisation results.

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

The structural organization of the insert in NK603 was analysed by Southern blot analysis. The organization of the inserted material at the insertion site was verified by DNA sequencing.

The results of the molecular characterization established that NK603 contains a single DNA insert, containing one intact copy of the restriction fragment PV-ZMGT32L that was used for transformation. DNA sequencing of the insert showed that two nucleotide changes have occurred in the second of the two *cp4 epsps* coding regions of the plant insert compared to the plasmid, one of which is silent and the other resulting in a single amino acid change in the expressed protein, which is referred to as CP4 EPSPS L214P. Both nucleotide changes have been present in NK603 since its initial transformation. The genome of NK603 does not contain any detectable plasmid backbone DNA. In addition, a 217 bp fragment containing a portion of the enhancer region of the rice actin promoter is inversely linked to the 3' end of the insert. Adjacent to the 217 bp fragment are 305 bp with homology to chloroplast DNA but without homology to known toxins or allergens.

The 5' and 3' ends of the NK603 insert were verified by PCR and DNA sequencing, and the sequences flanking the insert are confirmed as native to the maize genome.

3. Information on the expression of the insert

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

Expression levels of the introduced CP4 EPSPS proteins were measured in tissues from NK603, produced in the field during the 1999 growing season in the E.U. and the 2002 growing season in the U.S.A. These field sites were located within major maize growing regions and provided a variety of environmental conditions.

In 1999, NK603 was produced in field trials at four representative sites in the E.U.: Germignonville (Southern France), Janville (Northern France), L'Isle Jourdain (Northern France) and Bagnarola (Italy). Four replications were used at each of the four sites. CP4 EPSPS levels were

measured in forage and grain from NK603 and control maize because these tissues are most relevant to the assessment of food and feed safety. In forage, the overall mean CP4 EPSPS protein level across the four sites was 48.6 µg/g fresh weight (fw). In grain, the overall mean CP4 EPSPS level across all four sites was 8.4 µg/g fw.

In 2002, further NK603 and control samples were produced in U.S.A. field trials at Benton County (Iowa), Boone County (Missouri), Fayette County (Ohio) and York County (Nebraska). At each site, three replicate plots containing NK603 and the nontransgenic control were planted using a randomized complete block design. Overseason leaf, overseason root, pollen, forage, forage root and grain tissues were collected from each replicated plot at all field sites. On a dry weight basis (dw), the mean CP4 EPSPS levels across four field sites ranged from 300 to 430 µg/g dw for overseason leaf tissues and from 76 to 160 µg/g dw for overseason root tissues (four overseason time points). The mean CP4 EPSPS protein levels across the four field sites for forage, forage root, pollen, and grain tissues were 100, 140, 650, and 14 µg/g dw, respectively.

The expression levels for forage and grain reported above are in general agreement with the CP4 EPSPS levels measured in forage and grain samples collected from six non-replicated and two replicated field trials conducted in 1998 in the U.S.A., which were previously reported by Monsanto. In the trials from 1998, CP4 EPSPS expression levels ranged from 18.0 to 31.2 µg/g fw for forage and from 6.9 to 15.6 µg/g fw for grain, respectively.

All CP4 EPSPS expression levels were measured using a validated enzyme-linked immunosorbent assay (ELISA) that recognises both CP4 EPSPS proteins contained in NK603.

b) Parts of the plant where the insert is expressed

The expression of the CP4 EPSPS 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

Experience gathered from comparative assessments in the field and from extensive commercial planting of NK603 varieties demonstrates that, except for the introduced tolerance to Roundup herbicide (glyphosate), there are no biologically relevant differences in the reproductive capability, dissemination or survivability of NK603 when compared to traditional maize.

Observational data from comparative assessments in the field using NK603 and experience from commercial plantings in the Americas confirm that no biologically relevant differences exist between NK603 and traditional maize. NK603 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 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 resulting from disease, insect pests or applied pesticides. Importantly, there is no adverse information to indicate that there would be a potential for NK603 to establish, persist and disperse to a greater extent than traditional maize.

b) Dissemination

The introduced herbicide-tolerance trait has 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 has not been altered in its survivability when compared to traditional maize.

d) Other differences

Comparative assessments of a number of phenotypic and agronomic characteristics over several trial seasons did not reveal biologically significant differences between NK603 and traditional maize, except for the introduced glyphosate-tolerance trait.

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

NK603 contains a single insert containing a single copy of the transformed DNA, which is stably integrated into the nuclear maize genome. This has been confirmed by Southern blot analyses and by studies of the inheritance pattern of this trait in maize representing nine generations of NK603 progeny.

The Chi square analysis of the segregation results for the glyphosate-tolerance trait in NK603 progeny are consistent with a single active site of insertion of the tandem *cp4 epsps* cassettes into the nuclear genomic DNA of NK603, segregating according to Mendelian genetics. These results are consistent with the molecular analysis previously discussed.

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 insert in NK603, no changes are to be expected in the ability of the GM plant to transfer genetic material to bacteria.

b) Plant to plant gene transfer

Since reproductive morphology of NK603 is unchanged compared to traditional maize, pollen production and pollen viability are not

expected to be affected by the genetic modification. 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 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

Compositional analyses were conducted on key maize tissues produced from eight U.S.A. trials in 1998 and four E.U. trials in 1999. The study also included compositional analyses of a near-isogenic, non-transgenic control hybrid with similar background genetics as the test product. The analytical results have shown that NK603 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 certain 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 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, the field trials have shown that NK603 is substantially equivalent to traditional maize, with the exception of the expressed CP4 EPSPS proteins.

7.2 Production of material for comparative assessment

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

Compositional analyses were conducted on key maize tissues produced from eight U.S.A. trials in 1998 (two replicated trials in Illinois and Ohio and six non-replicated trial in Iowa, Illinois, Indiana, and Kansas) and from four replicated E.U. trials in 1999 (Germignonville and Janville in Northern France, L'Isle Jourdain in Southern France, and Bagnarola in Italy), together representing the range of typical agricultural environments in which maize is grown. At the non-replicated U.S.A. sites, there were two blocks (treated and untreated): the treated block contained six plots, one each for NK603 and five other test lines tested; the untreated block contained a single plot for the control line. A randomized complete block design was used for the replicated U.S.A. sites with four blocks or replicates per site; each block contained seven plots, one each for the six test lines and the control. For the E.U. sites a randomized complete block design was used for two of the four sites. For the two other sites, the NK603 plots were not in the same block as the non-transgenic control plots due to space limitations and therefore a non-randomized design (incomplete treated/untreated block design) was used for these two sites.

b) the baseline used for consideration of natural

variations

Compositional analyses were made for forage and grain samples from NK603. The study also included analyses of forage and grain collected from concurrent non-transgenic controls and non-transgenic commercial maize hybrids. Finally, also comparisons with baseline data from other Monsanto 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 and non-transgenic counterpart.

The compounds analyzed were selected based on OECD guidance. Grain samples were analyzed for proximate (protein, fat, ash, moisture), acid detergent fiber (ADF), neutral detergent fiber (NDF), amino acid, fatty acid, vitamin E, mineral (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc), phytic acid and trypsin inhibitor content. Forage samples were analyzed for proximate, ADF and NDF content. Carbohydrate values in forage and grain were estimated by calculation.

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, 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 the efficacy of the newly introduced agronomic trait have been studied in the field in Germany and France from 2000 to 2002. The variety of trial locations provided a range of environmental and agronomic conditions representative of a major temperate region for maize production. These field trials showed no biologically significant differences between NK603 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 plants to glyphosate. None of the trials were indicative of any changes in selective advantage or fitness between NK603 and traditional maize. The data also support a conclusion of no changes in reproductive parameters or dissemination potential, and no changes in survivability or weed potential of NK603 compared to the control. Overall, by-site comparisons did not indicate differences between NK603 and traditional maize. Where statistically significant differences ($p < 0.05$). were detected, those differences were numerically small and did not show any consistent trend across trials or hybrids tested. Moreover, the results were still within normal biological variability expected for maize. None of the detected statistically significant differences were considered to be of biological significance in terms of pest potential or adverse plant growth and development.

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 is substantially equivalent to traditional maize except for the introduced glyphosate-tolerance trait.

7.5 Product specification

NK603 will be used in the European Union by growers and operators that have traditionally been involved in the production, commerce, processing and use of maize and maize-derived products in the European Union.

The determination of compositional and phenotypic equivalence of NK603 to traditional maize, taken together with 1) the long history of safe use of the host plant (maize) as a common source of animal feed and human food, 2) the data establishing the safety of NK603 and the expressed CP4 EPSPS proteins, and 3) the history of safe use of NK603 since 2001 and of other Roundup Ready crops expressing virtually identical CP4 EPSPS, support the conclusion that NK603 is as safe and nutritious as maize that is used commercially today.

NK603 is detectable in foods and feeds using the insert-specific PCR detection method, previously ring-tested by the European Network of GMO Laboratories under the coordination of the Community Reference Laboratoy (the E.U. Joint Research Centre).

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 is substantially equivalent and as safe and as nutritious as traditional maize, the use of NK603 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 foods and feeds are not expected to be 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 extended presence of NK603 in the maize supply. NK603 is expected to further replace a portion of current maize products such that the intake and use of NK603 will represent some part of the total products derived from maize.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

The human and animal safety of the CP4 EPSPS proteins is based upon the extensive characterisation of CP4 EPSPS and CP4 EPSPS L214P and their relatedness to EPSPS enzymes commonly found in a wide variety of food sources, which have a long history of safe use.

Furhermore, the CP4 EPSPS proteins expressed in NK603 are virtually identical to CP4 EPSPS expressed in other Roundup Ready crops with

a history of safe human and animal consumption (*e.g.* Roundup Ready soybean, MON-Ø4Ø32-6). Maize containing the NK603 insert also has gained a history of safety since the first commercialisation of NK603 varieties in North America in 2001 and its use for food and feed around the world.

The safety of the CP4 EPSPS and CP4 EPSPS L214P proteins is supported by (1) the lack of signs of acute toxicity in a mouse acute gavage study at dose levels orders of magnitude higher than the levels encountered in the human or animal diet, (2) rapid digestion of CP4 EPSPS and CP4 EPSPS L214P proteins in simulated digestive fluids, and (3) lack of any significant homology of CP4 EPSPS and CP4 EPSPS L214P with known protein toxins. Further, the absence of allergenic potential of the CP4 EPSPS and CP4 EPSPS L214P proteins is discussed in Section D.7.9.1.

We note that a description of these safety aspects of the CP4 EPSPS proteins and of NK603 was given in the earlier applications for use of NK603 under Directive 2001/18/EC and Regulation (EC) No 258/97, which were reviewed by the Competent Authorities of the E.U. Member States and by the European Food Safety Authority in 2003 (http://www.efsa.eu.int/). In 2004, NK603 was approved for import, processing, and food and feed use in the E.U. (Commission Decisions 2004/643/EC and 2005/448/EC).

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 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 and traditional maize were established by compositional analysis. In addition, the wholesomeness and safety of NK603 have been confirmed in a 42-day feeding study using broiler chickens and a 90-day toxicology study in laboratory rats, which did not indicate adverse effects associated with the repeated administration of NK603 in the diet.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

The CP4 EPSPS proteins are present at very low levels in NK603. 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 allergenic potential, it was concluded that the use of NK603 for cultivation and for food and feed does not lead to an increased risk for allergenic reactions compared to the equivalent uses of traditional maize.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

The introduced glyphosate-tolerance is a trait of agronomic interest and does not change the nutritional aspects of this maize. Hence this maize is not expected to be more or less attractive for cultivation, or use for food or feed. Therefore, anticipated dietary intake of maize-derived foods and feeds is not expected to be altered and no nutritional imbalances are expected as a result of the extended use of NK603.

7.10.2 Nutritional assessment of GM feed

A confirmatory feeding study in broiler chickens was conducted to compare the nutritional value of NK603 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-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, the non-transgenic hybrid, and commercially available reference maize hybrids. The NK603-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, which showed that there were no biologically relevant differences in nutritional and compositional properties relative to control and reference maize hybrids. These data support the conclusion that NK603 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 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 use of NK603 demonstrates that the risks of consumption of NK603 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)

Not applicable. NK603 is herbicide-tolerant and does not have any target organisms.

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

9.1 Persistence and invasiveness

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

9.2 Selective advantage or disadvantage

Compared with traditional maize, the presence of the introduced trait in a NK603 volunteer would only confer a meaningful advantage where plants would be treated with glyphosate herbicide and if no other, more important factors limiting the volunteer's establishment in the environment would be present. The risk of the glyphosate-tolerance in NK603 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 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, 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

Not applicable. NK603 is herbicide-tolerant and does not have any target organisms.

9.5 Interactions of the GM plant with non-target organisms

The introduced CP4 EPSPS proteins present a negligible hazard to 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 would possess biological activity towards any non-target organisms. As a consequence, there is negligible risk for harmful effects of NK603 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 this maize in the Americas. No evidence has been brought forward by the many farmers and operators handling NK603 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 for human health were summarized in Sections D.7.1 to D.7.11. Based on the extensive characterization of the inserted trait and the safety demonstrated for the expressed CP4 EPSPS proteins, 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 plants would be any different from traditional maize regarding their direct influence on biogeochemical processes or nutrient levels in the soil, as NK603 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 non-target organisms in the vicinity of a release of this maize are not likely to cause hazardous effects on the biogeochemical processes in the soil as the CP4 EPSPS proteins belong to the class of EPSP synthases that are ubiquitous in the natural environment.

9.9 Impacts of the specific cultivation, management and harvesting techniques

No specific cultivation techniques are required to grow NK603. 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. 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, which are well-established 'baseline' practices in agriculture. 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. Glyphosate was previously found safe for use in glyphosate-tolerant crops under the prevailing Directive 91/414/EEC.

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 is substantially equivalent to traditional maize, with the exception of the introduced glyphosate-tolerance, which is imparted by the expression of CP4 EPSPS proteins in the plant. CP4 EPSPS proteins do not have known negative interactions with the abiotic environment. The CP4 EPSPS proteins belong to the class of EPSP synthases, which are enzymes with a history of safety that are present in algae, micro-organisms and higher plants.

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 includes the use of NK603 for 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 was conducted as required by Articles 5(5) and 17(5) of Regulation (EC) No 1829/2003. Analysis of the characteristics of NK603 has shown that the risk for potential adverse effects on human health and the receiving environment, resulting from the proposed use of NK603 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 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 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 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 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 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

The NK603 insert is detectable in food and feed using the validated, insert-specific PCR method for detecting the introduced DNA present in NK603. Further information is provided at http://gmo-crl.jrc.it.

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

Monsanto notifications under Part B of the Directive 2001/18/EC or Directive 90/220/EEC in the E.U.-15: B/FR/99/04/06; B/IT/99/17; B/BE/00/WSP13; B/FR/00/03/05; B/DE/00/115; B/ES/00/06; B/FR/01/01/01; B/ES/01/05; B/IT/02/01; B/ES/02/03; B/DE/03/148; B/FR/04/02/02; B/ES/04/17; B/ES/04/19. In addition, NK603 has been notified for regulated field releases in some of the new E.U. Member States under their national regulatory schemes.

b) Conclusions of post-release monitoring

The E.U. field trials with NK603 which were conducted to date, relate to the assessment of agronomic performance, growth and developmental, morphological and other phenotypic characteristics, yield potential, residues determination, protein expression, compositional analysis and variety testing. 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 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

Maize containing the NK603 insert has been planted commercially on millions of hectares in the U.S.A. and Canada since 2001. In 2004, NK603 varieties were commercialised for the first time in Argentina, and since 2005 also other countries in the Americas and Asia are cultivating this maize.

In addition, NK603 and derived products are approved for import and consumption in an increasing number of countries around the world, including the E.U.-25.

Prior to its commercialisation, NK603 has been tested extensively at multiple locations in the field in a broad range of environments around the world.

b) Authority overseeing the release

The authority overseeing the first field release was the United States Department of Agriculture (USDA). NK603 was later deregulated in the U.S.A. and approved for commercial use in many more countries around the world.

c) Release site

All major maize growing regions in North America and increasingly in other countries around the world, as decribed in Section E.2.(a).

d) Aim of the release

Commercial release for all uses as traditional maize.

e) Duration of the release

Commercial 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, indicating that a requirement for post-release monitoring would not be appropriate.

In addition, NK603 is commercialized alongside stewardship 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 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 NK603 or derived products would be the cause of 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

NK603 was approved for import, processing and feed use in the E.U.-25 on 19 July 2004 (see Commission Decision 2004/643/EC). NK603 has also been approved for food use in the E.U.-25 under Regulation (EC) No 258/97 (see Commission Decision 2005/448/EC).

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 any still pending Monsanto dossiers.

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 publicly accessible Initial Assessment Reports (IAR) under Directive 2001/18/EC, including the IAR from the Spanish Lead Member State for Monsanto's notification C/ES/00/01 for import, processing and feed use of NK603.

c) EFSA opinion

Favourable safety opinions by EFSA regarding the import, processing, and food and feed use of NK603 are posted at http://www.efsa.eu.int/science/gmo/gmo_opinions/catindex_en.html.

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

http://europa.eu.int/comm/food/dyna/gm_register/index_en.cfm

e) Molecular Register of the Community Reference

	Laboratory/Joint Research Centre Information on the validated detection method for NK603 foods and feeds is posted at http://gmo-crl.jrc.it/statusofdoss.htm
f)	**Biosafety Clearing-House (Council Decision 2002/628/EC)** The publicly accessible portal site of the Biosafety Clearing-House (BCH) can be found at http://bch.biodiv.org/.
g)	**Summary Notification Information Format (SNIF) (Council Decision 2002/812/EC)** The JRC website http://gmoinfo.jrc.it/gmc_browse.asp provides a link to the publicly accessible SNIF summaries of Monsanto's notifications for NK603 under Directive 2001/18/EC. Further, EFSA provides a link to the publicly accessible summary of this application for NK603 under Regulation (EC) No 1829/2003 at http://www.efsa.eu.int/science/gmo/gm_ff_applications/catindex_en.html.