Application for authorization of stacked Bt11 x MIR162 x GA21 maize in the European Union under Regulation (EC) No 1829/2003

PART II: SUMMARY

A . GENERAL INFORMATION

1. Details of application

a) Member State of application Germany
b) Application number Not available at the time of submission
c) Name of the products (commercial and other names) Bt11 x MIR162 x GA21 maize
d) Date of acknowledgement of valid application Not available at the time of submission

2. Applicant

a) Name of applicant Syngenta Crop Protection AG, Basel, Switzerland acting on its behalf and through its affiliated companies
b) Address of applicant Syngenta Crop Protection AG, Basel Switzerland acting on its behalf and through its affiliated companies Schwarzwaldallee 215 CH 4058 Basle Switzerland
c) Name and address of the person established in the Community who is responsible for the placing in 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)) Bt11 x MIR162 x GA21 maize will be imported and used as any other maize in the EU by operators currently involved in these processes.

3. Scope of the application

☒ GM plants for food use

☒ Food containing or consisting of GM plants

☒Food produced from GM plants or containing ingredients produced from GM plants

☒GM plants for feed use

☒ Feed containing or consisting of GM plants

☒ Feed produced from GM plants

☒ Import and processing (Part C of Directive 2001/18/EC)

☐ Seeds and plant propagating material for cultivation in Europe (Part C of Directive 2001/18/EC)

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

Yes ☐	No ☒
If *yes*, specify	

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

Yes ☐	No ☒
If *no*, refer to risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC A risk assessment has been performed according to the Directive 2001/18/EC and forms part of this application.	

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

Yes ☐	No ☒
If *yes*, specify	

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

Yes ☒	No ☐
If *yes*, specify Submission covering Bt11 x MIR162 x GA21 maize has been made in third countries around the world and these are at different stages in the approval process.	

8. General description of the product

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

Bt11 x MIR162 x GA21 maize is a stacked genetically modified (GM) product that has been produced by conventional breeding crosses of:

- Event Bt11 maize (Bt11 maize) which produces a truncated Cry1Ab protein for control of certain lepidopteran pests and a phosphinothricin acetyltransferase (PAT) protein that confers tolerance to herbicide products containing glufosinate ammonium.
- Event MIR162 maize (MIR162 maize) which expresses a Vip3Aa20 protein for control of certain lepidopteran pests and a phosphomannose isomerase (PMI) protein, which acts as a selectable marker enabling transformed plant cells to utilize mannose as the only primary carbon source.
- .
- Event GA21 maize (GA21 maize) which produces a modified maize 5-enolpyruvylshikimate-3-phosphate synthase enzyme (mEPSPS) that confers tolerance to herbicide products containing glyphosate.

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

The scope of the application includes all food and feed products containing, consisting or produced from Bt11 x MIR162 x GA21 maize including products from inbreds and hybrids obtained by conventional breeding of this stacked maize product. The application also covers the import and industrial processing of Bt11 x MIR162 x GA21 maize for all potential uses as any other maize.

c) Intended use of the product and types of users

It is intended that Bt11 x MIR162 x GA21 maize will be used as any other conventional maize which is cultivated or imported for all food, feed and industrial purposes.

d) Specific instructions and/or recommendations for use, storage and handling, including mandatory restrictions proposed as a condition of the authorisation applied for The characteristics of Bt11 x MIR162 x GA21 maize and products derived from them are not different from those of their conventional counterparts, apart from the introduced traits of insect tolerance and tolerance to herbicide products containing glufosinate ammonium or glyphosate. Bt11 x MIR162 x GA21 maize has been shown to be as safe and as wholesome as existing varieties of maize. Therefore there are no specific instructions or recommendations for use, storage and handling of Bt11 x MIR162 x GA21 maize.
e) Any proposed packaging requirements The characteristics of Bt11 x MIR162 x GA21 maize and products derived from them are not different to those of their conventional counterparts. Bt11 x MIR162 x GA21 maize has been shown to be as safe and as wholesome as existing varieties of maize. Therefore there are no specific instructions for packaging.
f) A proposal for labelling in accordance with Articles 13 and Articles 25 of Regulation (EC) 1829/2003. In the case of GMOs, food and/or feed containing or 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 A proposal for labelling has been included in the application following the guidance provided by EFSA. This includes the labelling requirements outlined by Regulation (EC) No 1829/2003 and Annex IV of Directive 2001/18/EC. Bt11 x MIR162 x GA21 maize grain will therefore be labelled as “genetically modified maize” and products derived from them will be labelled as “containing (or produced from) genetically modified maize”. Since Bt11 x MIR162 x GA21 maize and products derived from them are not different from those of their conventional counterparts, no additional labelling is required.
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) A unique identifier Bt11 x MIR162 x GA21 maize has been assigned in accordance with Commission Regulation (EC) 65/2004: SYN-BTØ11-1 x SYN-IR162-4 x MON-ØØØ21-9.
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 Bt11 x MIR162 x GA21 maize is suitable for use as any other maize under the terms of the authorisation applied for.

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

Maize is incapable of sustained reproduction outside domestic cultivation and is non-invasive of natural habitats. The characteristics of Bt11 x MIR162 x GA21 maize and products derived from them are not different from those of their conventional counterparts, apart from the intended effect of tolerance to certain lepidopteran insect pests and herbicide products containing glufosinate ammonium or glyphosate. Cultivation of Bt11 x MIR162 x GA21 maize in the EU is not within the scope of this application. In the unlikely event that small amounts of Bt11 x MIR162 x GA21 grain accidentally found their way into the environment, this would represent extremely low levels of exposure and the survival of this grain to produce flowering plants would be very unlikely. In addition, volunteers could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

Bt11 x MIR162 x GA21 maize has been shown to be as safe and as wholesome as existing varieties of maize. Any unintended releases or misuse can be dealt with in the same way as any other conventional maize.

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

1. Complete name

a) Family name Poaceae (formerly Gramineae)
b) Genus *Zea*
c) Species *mays*
d) Subspecies *mays*
e) Cultivar/breeding line or strain A Syngenta proprietary line of maize
f) Common name Maize; corn

2 a. Information concerning reproduction

(i) Mode(s) of reproduction Sexual reproduction: *Zea mays* is an allogamous plant that propagates through seed produced predominantly by cross-pollination and depends mainly on wind borne cross-fertilisation. *Z. mays* is a plant with protandrous inflorescence; however, decades of conventional selection and improvement have produced varieties of maize with protogynous traits. *Z. mays* has staminate flowers in the tassels and pistillate flowers on the ear shoots. Asexual reproduction: there is no asexually reproductive maize.
(ii) Specific factors affecting reproduction The key critical stages of maize reproduction are tasselling, silking, pollination and fertilization. Outcrossing distances are limited by the rapid settling and limited viability of pollen. Most maize varieties are protoandrous with pollen shed preceding silk emergence by up to five days. As maize pollen is large and heavy it tends to be deposited close to the source plant and studies have indicated that most maize pollen falls within 5m of the field's edge. In general, such studies have shown that over 98% of maize pollen remains within a radius of 25-50m of the source, although some grains can travel several hundred metres. Shed pollen typically remains viable for 10 to 30 minutes, but may remain viable longer under refrigerated

and humid conditions.

(iii) Generation time

Maize is an annual crop. The generation time from sowing to harvesting varies according to the genetic background and the climate, it can range 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

Other cultivated plant species: The sexual compatibility of maize with other cultivated plant species is limited to *Zea* species.

Wild plant species*:* No wild relatives of maize are present in Europe. Therefore, maize cannot exchange genes with any other wild species in the EU.

3. Survivability

a) Ability to form structures for survival or dormancy

Maize is an annual crop. Seeds are the only survival structures; they cannot be dispersed without mechanical disruption of the cobs and show little or no dormancy. Natural regeneration from vegetative tissue is not known to occur.

b) Specific factors affecting survivability

Survival of maize is dependent upon temperature, seed moisture, genotype, husk protection and stage of development. Maize cannot persist as a weed. Maize seed can only survive under a narrow range of climatic conditions. Volunteers are killed by frost or easily controlled by current agronomic practices including cultivation and the use of selective herbicides. Maize is incapable of sustained reproduction outside of domestic cultivation and is non-invasive of natural habitats.

4. Dissemination

a) Ways and extent of dissemination

Maize dissemination could occur through seed or pollen dispersal. Seed dispersal does not occur naturally due to the structure of the maize ear.
No wild relatives of maize are present in Europe, therefore, pollen dispersal could only occur to other maize crop plants. Since the scope of this application does not include authorisation for the cultivation of the stacked maize, the likelihood of dissemination of pollen to other plants (including cultivated maize plants) is considered to be negligible.

b) Specific factors affecting dissemination

Maize has a polystichous (arranged in many rows) female inflorescence (group of flowers), called the ear, on a stiff central spike (cob) enclosed in husks (modified leaves). Because of the structure of the ears, seed dispersal of individual kernels does not occur naturally. Maize is non-invasive of natural habitats. The rate of dissemination via pollen will be influenced by the size of pollen, wind direction and speed, other weather conditions such as rainfall, the presence of barriers and the degree of synchrony of flowering. Maize pollen is large and heavy and tends to be deposited close to the source plant. In addition, most maize varieties are protoandrous so pollen shedding precedes silk emergence by up to five days.

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

Maize, which has very diverse morphology and physiology, is grown on approximately 145 million hectares worldwide. It is distributed over a wide range of conditions: from latitudes 50º North and 50º South, below sea level of the Caspian plains up to 3000 m in the Andes Mountains and from semi-arid regions to arid regions. The greatest maize production occurs where the warmest month isotherms range between 21º and 27º C and the freeze-free season lasts 120-180 days.

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 was introduced into Europe in the 15th century by Columbus and is widely grown in the European Union Member States.

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 insect pests, as well as to competition from surrounding weeds. Maize is extensively cultivated and has a history of safe use for human food and animal feed. No significant native toxins are reported to be associated with the genus *Zea*.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Description of the methods used for the genetic modification

The Bt11 x MIR162 x GA21 maize described in this application was produced by crossing insect resistant Bt11 and MIR162 maize and herbicide tolerant GA21 maize through conventional breeding techniques. There was no further genetic modification to produce the stacks.

The Bt11, MIR162 and GA21 maize events maize were produced by genetic modification as follows:

- Bt11 maize was produced using protoplast transformation/regeneration
- MIR162 maize was produced via *Agrobacterium*-mediated transformation
- GA21 maize was produced via microprojectile bombardment of maize suspension culture cells.

2. Nature and source of the vector used

The Bt11 x MIR162 x GA21 maize described in this application was produced by crossing insect resistant Bt11 and MIR162 maize and herbicide tolerant GA21 maize through conventional breeding techniques. The vectors used to produce Bt11, MIR162 and GA21 maize are as follows:

- The *Not*I restriction fragment from the Plasmid pZO1502 was used to produce Bt11 maize. The plasmid is a derivative of the commercially available plasmid pUC18.
- The Plasmid pNOV1300, a binary vector used for *Agrobacterium* mediated plant transformation, was used to generate MIR162 maize.
- The *Not*I restriction fragment from the Plasmid pDPG434, was used to transform GA21 maize via microprojectile bombardment transformation. The plasmid is derived from a pSK- vector which is commonly used in molecular biology and is derived from pUC19.

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

The Bt11 x MIR162 x GA21 maize described in this application was produced by crossing insect resistant Bt11 and MIR162 maize and herbicide tolerant GA21 maize through conventional breeding techniques. There was no further genetic modification to produce the stacked product. The size, source and intended function of each constituent fragment of the regions intended for insertion in each of the single events is described below:

Region intended for insertion from pZO1502 (Event Bt11 maize)

Vector Component	Approx. Size (bp)	Description
Active Ingredient cassette		
35S promoter	509	Promoter from the cauliflower mosaic virus (CaMV).
IVS6-ADH1	471	Intron sequence from the maize (*Zea mays*) alcohol dehydrogenase gene used to enhance gene expression in maize.
cry1Ab	1848	Modified *cry1Ab* gene, which encodes a Cry1Ab protein that confers resistance to certain lepidopteran insect pests. The *cry1Ab* gene was originally cloned from *Bacillus thuringiensis*
NOS	253	Polyadenylation region from the nopaline synthase gene from *Agrobacterium tumefaciens*.
Selectable promoter cassette		
35S promoter	418	Promoter from the cauliflower mosaic virus (CaMV).
IVS2-ADH1	180	Intron sequence from the maize (*Zea mays*) alcohol dehydrogenase gene used to enhance gene expression in maize.
pat	552	*Streptomyces viridochromogenes* gene encoding the selectable marker PAT (phosphinothricin acetyltransferase). PAT confers resistance to herbicides containing glufosinate ammonium
NOS	253	Polyadenylation region from the nopaline synthase gene from *Agrobacterium tumefaciens*.
Vector backbone component		
Component present on the 6.2 kb *Not*I restriction fragment of pZO1502 used for transformation		
ColE1	674	Origin of replication that permits replication of plasmids in *Escherichia coli (E. coli)*.

Region intended for insertion from pNOV1300 (Event MIR162 maize)

Vector component	Size (bp)	Description
Active Ingredient cassette		
ZmUbiInt	1993	Promoter derived from the maize (*Zea mays*) polyubiquitin gene
vip3Aa19	2370	A modified version of the native *vip3Aa1* gene from *Bacillus thuringiensis* that confers resistance to certain lepidopteran pest species.
iPEPC9	108	Intron from the phosphoenolpyruvate carboxylase gene from maize *(Zea mays).*
35S 3' nontranslated region	70	3' nontranslated region sequence from the 35S DNA from the cauliflower mosaic virus (CaMV).
Selectable marker cassette		
ZmUbiInt	1993	Promoter from the maize (*Zea mays*) polyubiquitin gene
pmi	1176	*E. coli pmi* gene encoding the enzyme phosphomannose isomerase (PMI). This gene is also known as *manA.*
NOS	253	Polyadenylation region from the nopaline synthase gene from *Agrobacterium tumefaciens.*

After insertion in the plant, the *vip3Aa19* gene was designated *vip3Aa20*; the encoded protein was designated Vip3Aa20.

Region intended for insertion from pDPG434 (Event GA21 maize)

Vector Component	Approx. Size (Kb)	Description
Rice actin promoter, exon and intron	1.4	5' region of the rice (*Oryza sativa*) actin 1 gene containing the promoter and first exon and intron provides constitutive expression of the *mepsps* gene in maize.
Optimised transit peptide	0.4	Optimised transit peptide sequence constructed based on transit peptide sequences from sunflower (*Helianthus annus*) and maize (*Zea mays*) ribulose-1,5-bis phosphate carboxylase oxygenase (RuBisCo) genes.
Modified maize EPSPS gene	1.3	Mutated maize (*Zea mays*) *epsps* gene, which confers resistance to herbicide products containing glyphosate.
Nos 3' end	0.3	Polyadenylation region from the nopaline synthase gene from *Agrobacterium tumefaciens*.

D. INFORMATION RELATING TO THE GM PLANT

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

The Bt11 x MIR162 x GA21 maize described in this application was produced by crossing insect resistant Bt11 and MIR162 maize and herbicide tolerant GA21 maize through conventional breeding techniques and produce the following proteins:

- a truncated Cry1Ab protein for control of certain lepidopteran pests.
- a phosphinothricin acetyltransferase (PAT) protein that confers tolerance to herbicide products containing glufosinate ammonium.
- a Vip3Aa20 protein for control of certain lepidopteran pests.
- a phosphomannose isomerase (PMI) protein expressed in MIR162 to act as a selectable marker.
- a modified maize EPSPS (mEPSPS) protein that confers tolerance to herbicide products containing glyphosate.

2. Information on the sequences actually inserted or deleted

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

The Bt11 x MIR162 x GA21 maize described in this application was produced by crossing insect resistant Bt11 and MIR162 maize and herbicide tolerant GA21 maize through conventional breeding techniques.

Bt11 and MIR162 maize each contains one single insert present at one single locus; each insert contains one functional copy of the fragment introduced. The insert in GA21 maize is present at one locus and is comprised of six contiguous regions derived from the 3.49 kb *Not*I restriction fragment from pDPG434 employed in the generation of GA21 maize (copies 1-6). Copy 1 contains the rice actin promoter that has a 5’ deletion of 696 bp, the actin first exon and intron, the optimized transit peptide, the *mepsps* gene and the NOS terminator. Copies 2, 3 and 4 are intact versions of the 3.49 kb *Not*I restriction fragment from pDPG434. Copy 5 contains a complete rice actin promoter, the actin first exon and intron, the optimized transit peptide and the first 288 bp of the *mepsps* gene which ends in a stop codon and does not contain the NOS terminator. Copy 6 contains the rice actin promoter and a truncated actin first exon only and contains no other elements from pDPG434.

In addition to sequencing, southern analysis performed on each of the single events demonstrate the absence of further copies of the insert or vector backbone sequence elsewhere in the genome.

In order to assess the integrity of the insert from each individual event during conventional breeding to produce the stacked maize products, additional Southern analysis was performed. The predicted DNA hybridization pattern from each individual event was confirmed in

Bt11 x MIR162x GA21 maize, demonstrating preservation of the integrity of the transgenic fragment from each individual event to the stacked maize products.

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

Not applicable

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

The inheritance pattern of the inserts in Bt11, MIR162 and GA21 maize were analysed and the results showed that insertions had taken place in the nucleus.

The Bt11 x MIR162 x GA21 maize described in this application has been produced by combining the GM maize events: Bt11, MIR162 and GA21 through conventional breeding techniques. It therefore contains the inserts derived from the single events. The presence of the inserts from Bt11, MIR162 and GA21 maize in the stacked product was confirmed by Southern blot analyses.

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

The Bt11 x MIR162 x GA21 maize described in this application has been produced by combining the GM maize events: Bt11, MIR162 and GA21 through conventional breeding techniques. The organisation of the inserted genetic material in Bt11, MIR162 and GA21 maize is as follows:

Bt11 maize

Sequencing and southern data have demonstrated that Bt11 maize contains a single DNA insertion with one copy of both the *cry1Ab* and the *pat* genes. The sequence analysis confirmed that the insert is intact and that the contiguousness of the functional elements within the insert as intended in pZO1502 has been maintained.

MIR162 maize

Sequencing and southern data have demonstrated that MIR162 maize contains a single DNA insertion with one copy of both the *vip3Aa20* and the *pmi* genes. The sequence analysis confirmed that the insert is intact and that the contiguousness of the functional elements within the insert as intended in pNOV1300 has been maintained.

GA21 maize

Sequencing and southern data have demonstrated that GA21 maize contains a single DNA insertion. The insert is comprised of six contiguous regions derived from the 3.49 kb *Not*I restriction fragment from pDPG434 employed in the generation of Event GA21 (copies 1-6). See section D.2.a for further details.

Molecular comparisons of the Bt11 x MIR162 x GA21 maize with the single maize events Bt11, MIR162 and GA21 have shown that the inserts are preserved in the stacked maize products.

3. Information on the expression of the insert

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

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding techniques. Therefore these maize plants produce the transgenic proteins inherited from these single GM maize events: Cry1Ab, PAT, Vip3Aa20, PMIand mEPSPS.

Tissues from maize plants derived from Bt11, MIR162, GA21 maize and conventional breeding stacks containing these events (Bt11 x MIR162 x GA21) were analyzed by ELISA to compare the concentrations of Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS.

The analyses were performed on key plant tissues collected from transgenic hybrid plants at different sampling times across the growing season. To control for background effects, the corresponding tissues from a non-transgenic, near-isogenic control maize were also analyzed.

Bt11 x MIR162 x GA21 maize

The concentrations of Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS were, in general, statistically similar in the Bt11 x MIR162 x GA21 hybrid and the corresponding individual-event hybrids. Although some minimal significant differences were observed after statistical analysis of all transgenic protein concentrations measured, the results of this study support the conclusion that transgenic protein expression in the Bt11 x MIR162 x GA21 maize hybrid was generally similar to that of the hybrids derived from the individual Bt11, MIR162 and GA21 events.

These results support the conclusion that, as expected, transgenic protein expression in Bt11 x MIR162 x GA21 is not substantially different from that of the Bt11, MIR162 or GA21 single maize events.

b) Parts of the plant where the insert is expressed

To characterize the range of expression of Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS proteins in Bt11 x MIR162 x GA21 maize plants, the concentrations of these proteins were determined by ELISA in several plant tissues (leaves, roots, whole plants, kernels and pollen).

- Quantifiable concentrations of Cry1Ab protein were detected in leaves, roots, whole plants and kernels derived from Bt11 maize and the stacked maize. Very low levels of Cry1Ab expression were detected in the pollen of Bt11 maize and the stacked maize.
- Quantifiable concentrations of PAT protein were detected in leaves, whole plants and roots derived from Bt11 maize and the stacked maize, however no quantifiable levels could be detected in the kernels and in pollen.
- Quantifiable concentrations of Vip3Aa20 protein were detected in leaves, roots, whole plants, kernels and pollen derived from MIR162 maize and the stacked maize.
- Quantifiable concentrations of PMI were detected in all plant tissues analysed in MIR162

maize and Bt11 x MIR162 x GA21 maize. • Quantifiable concentrations of mEPSPS protein were detected in all GA21 maize and the stacked maize plant tissues analysed.

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

a) Reproduction No changes in the reproduction compared to non-GM maize has been observed in the agronomic assessment conducted for Bt11 x MIR162 x GA21 maize.
b) Dissemination No changes in the dissemination compared to non-GM maize has been observed in the agronomic assessment conducted for Bt11 x MIR162 x GA21 maize.
c) Survivability No changes in the survivability compared to non-GM maize has been observed in the agronomic assessments conducted for Bt11 x MIR162 x GA21 maize.
d) Other differences No changes in the reproduction, dissemination or survivability compared to non-GM maize has been observed in the agronomic assessments conducted for Bt11 x MIR162 x GA21 maize.

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

Analyses showed that the traits have been stably integrated into Bt11, MIR162 and GA21 maize.

Bt11 x MIR162 x GA21 maize F_1 seed is produced through conventional breeding involving Bt11, MIR162 and GA21 lines. Bt11 x MIR162 x GA21 maize seed once planted by growers produces grain (F_2) which is harvested for food, feed or industrial use. Such grain or products entering the commodity chain are not kept for further sowing.

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

a) Plant to bacteria gene transfer

The horizontal gene transfer from GM plants to bacteria with subsequent expression of the transgene is regarded as a highly unlikely event under natural conditions, especially in the absence of selective pressure. No changes in the ability of the Bt11 x MIR162 x GA21, Bt11, MIR162 or GA21 maize to transfer genetic material to other organism are expected compared to conventional maize since no sequences have been introduced to allow this to occur.

b) Plant to plant gene transfer

The genetic modification in the single maize events (Bt11, MIR162 and GA21) is not intended to change any of the typical crop characteristics of maize (except for the tolerance to insect and herbicide products).
Observations from field trials have confirmed that the agronomic characteristics of Bt11, MIR162, GA21 and with the higher level stack Bt11 x MIR162 x MIR604 x GA21 maize (in line with the EFSA guidance) have not changed in comparison with isogenic controls, and therefore, there is no increase or decrease in the potential for plant-to-plant gene transfer with the stacked maize products compared to traditional maize.
Gene transfer from Bt11 x MIR162 x GA21 maize to other sexually compatible plant species is not possible since maize has no wild relatives in the EU. In addition, since the scope of this application does not include authorisation for the cultivation of the stacked maize, the likelihood of dissemination of pollen to other plants (including cultivated maize plants) is considered to be negligible.

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 Stacked maize plants containing Bt11, MIR162 and GA21 maize were compared with relevant control maize lines that had not been genetically modified. Commercial varieties were also included in the comparison where possible. The stack study was conducted with the higher level stack Bt11 x MIR162 x MIR604 x GA21 maize. This approach is consistent with the EFSA guidance.

7.2 Production of material for comparative assessment

a) number of locations, growing seasons, geographical spreading and replicates To confirm that the stacked maize plants are equivalent in composition to the non-transgenic, near-isogenic lines, replicate trials of transgenic and corresponding isogenic controls were conducted. The locations of the trial sites were selected to be representative of the range of environmental conditions under which the hybrid varieties are expected to be grown. At each location, three replicate plots of each genotype were planted.
b) the baseline used for consideration of natural variations The levels of multiple nutritive components were compared in maize kernels (grain) or whole plants (forage) from the transgenic and simultaneously grown isogenic control plants. The mean values are also compared with the range of data published in the literature, where data was available.

7.3 Selection of materials and compounds for analysis

Based on guidance of the OECD, grain from transgenic plants and non-transgenic, near-isogenic control plants were analysed for proximates (including starch), minerals, amino acids and selected fatty acids, vitamins, anti-nutrients and secondary metabolites. Forage (whole plants) from transgenic maize plants and isogenic control plants were analysed for proximates and minerals.

No consistent pattern has emerged to suggest that biologically significant changes in composition or nutritive value of the grain or forage had occurred as an unintended result of transformation or expression of the transgenes in the stacked maize.

These data support the conclusion that Bt11 x MIR162 x GA21 maize is compositionally equivalent to conventional maize, apart from the introduced traits of insect and herbicide tolerance.

7.4 Agronomic traits

The scope of the application does not include cultivation, however measurement and observation of agronomic characteristics can add to the assessment of unintended effects of the genetic modification. The stack study was conducted with the higher level stack Bt11 x MIR162 x MIR604 x GA21 maize. This approach is consistent with the EFSA guidance.

The agronomic performance of Bt11 x MIR162 x MIR604 x GA21 maize was evaluated in a series of trials. Up to 18 separate agronomic traits were assessed, although not all traits were recorded at all locations. The Bt11 x MIR162 x MIR604 x GA21 maize and their near-isogenic hybrids were compared. Results of these trials support the conclusion that Bt11 x MIR162 x MIR604 x GA21 and Bt11 x MIR162 x GA21 maize are agronomically equivalent to conventional maize, apart from the introduced traits.

7.5 Product specification

Maize as a product has a history of safe use for human food and animal feed. No significant native toxins are reported to be associated with the genus *Zea*. The information presented in this application confirms that Bt11 x MIR162 x GA21 maize and products derived from them are not different from those of their conventional counterparts.

7.6 Effect of processing

Bt11 x MIR162 x GA21 maize will be produced and processed in the same way as any non-GM maize and there is no evidence to suggest that the expression of the proteins produced by this maize (Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS) will influence this processing in any way.

7.7 Anticipated intake/extent of use

There are no anticipated changes to the intake/extent of use of maize as a result of the introduction of Bt11 x MIR162 x GA21 maize to the conventional maize supply. It is anticipated that the introduction of Bt11 x MIR162 x GA21 maize will replace some of the maize in existing food and feed products. However, the genetic modification was not intended to change any of the compositional parameters in food and feed and this has been shown to be the case through extensive compositional assessment.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding and therefore it produces the proteins inherited from the single GM maize events. Potential adverse effects to human and animal health arising from Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS have been assessed and it was concluded that the potential toxic effects to humans and animals of these proteins could be considered negligible. A summary is provided below:

- The recipient organism, maize, has a history of safe use throughout the world.
- None of the gene sequences or their donors are known to be pathogenic to humans and no pathogenic sequences have been introduced.
- Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS have no significant amino acid homology to known mammalian protein toxins.
- Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS are unlikely to be allergenic
- Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS are readily degraded in *in vitro* digestibility assays.
- Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS mEPSPS show no acute oral toxicity in mammalian studies

7.8.2 Testing of new constituents other than proteins

Maize is a common source of food and feed and has a long history of safe use. Bt11 x MIR162 x GA21 maize produces the Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS proteins. No other new constituents apart from these proteins are expected to be produced in

Bt11 x MIR162 x GA21 maize and compositional analyses have confirmed the substantial equivalence of the stacked maize compared to conventional maize. Therefore no testing of any other constituent is considered necessary.

7.8.3 Information on natural food and feed constituents

The presence and levels of natural food and feed constituents such as macro- and micronutrients, secondary plant metabolites as well as natural toxins and antinutritional factors have been analysed and compared with non-GM isolines and data from the literature.

These analyses showed that the levels of the components measured had not changed beyond the natural variation in maize. No consistent patterns emerged to suggest that biologically significant changes in composition or nutritive value of the grain or forage had occurred as an unintended result of the expression of the transgenes.

7.8.4 Testing of the whole GM food/feed

In addition to the compositional analysis with Bt11 x MIR162 x GA21 maize, the wholesomeness and safety of the stacked products was confirmed in a broiler feeding study with the higher level stack Bt11 x MIR162 x MIR604 x GA21 maize. This approach is consistent with the EFSA guidance.
The study showed that the transgenic corn had no deleterious effects on broiler chickens. These data support the conclusion that grain from Bt11 x MIR162 x MIR604 x GA21 and Bt11 x MIR162 x GA21 maize is safe for food and feed consumption and no differences in wholesomeness are expected with comparable non-GM maize variety.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding and therefore express the proteins inherited from the single GM maize events. Potential allergenic potential arising from Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS have been assessed and it was concluded that the allergenic potential to humans and animals of these proteins could be considered negligible. A summary is provided below:

- None of the transgenic proteins produced by the stacked maize (Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS) come from donors known to be a significant cause of food allergy.
- The Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS proteins have no biologically significant amino acid homology to known allergens
- Susceptibility of the transgenic proteins to proteolytic degradation supports the conclusion that Cry1Ab, PAT, Vip3Aa20, PMI PMI and mEPSPS proteins will be readily digested as conventional dietary protein under typical mammalian gastric conditions.

From these data, it can be concluded that the Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS proteins produced by Bt11 x MIR162 x GA21 maize plants are highly unlikely to be allergenic.

7.9.2 Assessment of allergenicity of the whole GM plant or crop

Maize has been extensively cultivated and has a history of safe use for human food and animal feed. Maize is not considered to be a food crop which causes significant food allergy and Bt11 x MIR162 x GA21 maize produces transgenic proteins that are very unlikely to be allergenic.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

Bt11 x MIR162 x GA21 maize is not intended to change the nutritional status of individuals of populations or to be processed in products with enhanced functionality. Compositional analysis and whole food safety tests have demonstrated that no unexpected alterations in nutrients and other food components have occurred and that no nutritional imbalances were introduced.

7.10.2 Nutritional assessment of GM feed

Bt11 x MIR162 x GA21 maize is not intended to change the nutritional status of livestock animals. Compositional analysis and whole food safety tests have demonstrated that no unexpected alterations in nutrients and other food components have occurred and that no nutritional imbalances were introduced.

7.11 Post-market monitoring of GM food/feed

As described in sections 7.1 to 7.10 above, the presence of Bt11 x MIR162 x GA21 maize in food and feed will not result in any nutritional changes, therefore post-market monitoring is not considered necessary.

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

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding. Therefore Bt11 x MIR162 x GA21 maize plants produce the transgenic proteins inherited from each of the single GM maize events: Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS. The Cry1Ab and Vip3Aa20 proteins confer protection against certain lepidopteran pests and are known for the specificity to insects from the order Lepidoptera. The other transgenic proteins produced by the stacked maize, PAT, PMI and mEPSPS are not known to have any effects on organisms. Therefore the target organisms for Bt11 x MIR162 x GA21 maize are limited to certain species of Lepidoptera.

The cultivation of Bt11 x MIR162 x GA21 maize is not within the scope of this application, therefore plant interactions with target organisms are highly unlikely in the EU. In the unlikely event that small amounts of Bt11 x MIR162 x GA21 maize grain could accidentally find their way into the environment this would represent extremely low levels of exposure and the survival of this grain would be very unlikely. Any plants germinating from this grain could be easily controlled using any of the current agronomic measures taken to control other commercially available maize. Therefore Bt11 x MIR162 x GA21 maize is extremely unlikely to germinate and survive outside agricultural environments and its potential to interact with target species is very low.

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

9.1 Persistence and invasiveness

Cultivation of Bt11 x MIR162 x GA21 maize in the EU is not within the scope of this application. In the unlikely event that small amounts of grain of Bt11 x MIR162 x GA21 maize accidentally found their way into the environment their survival would be very unlikely as maize is highly domesticated and cannot survive without human intervention, especially under normal European climatic conditions. The expression of the Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS does not affect the agronomic characteristics or weediness potential of Bt11 x MIR162 x GA21 maize, as demonstrated in field trials conducted to evaluate the agronomic performance in comparison with the isogenic control. In the unlikely event that these maize plants were to survive they could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

In summary, the likelihood that Bt11 x MIR162 x GA21 maize becoming more persistent than the recipient or parental plants in agricultural habitats or more invasive in natural habitats as a result of importing maize kernels of this maize into the EU can be considered negligible.

9.2 Selective advantage or disadvantage

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding. No new genetic modification has therefore taken place in Bt11 x MIR162 x GA21 maize and, as intended, the plants produce the transgenic proteins inherited from the single GM events: Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS.

Expression of Cry1Ab and Vip3Aa20, conferring resistance to certain species of Lepidoptera, in areas of Europe where these are important maize pests, could be considered an advantage over conventional maize. However maize is a highly domesticated plant and cannot survive without human intervention, even in areas without pressure from these target pests. Therefore, expression of Cry1Ab and Vip3Aa20 will not increase the chances of maize survival under European conditions and would not confer any selective advantage.

Expression of PAT and mEPSPS could confer advantage to maize plants when herbicide products containing glufosinate ammonium or glyphosate are applied. However this rarely happens outside agricultural environments. Therefore, expression of PAT and mEPSPS is highly unlikely to confer selective advantage to maize plants.

Expression of PMI (in MIR162) could only confer an advantage to maize plants growing under conditions where mannose was the only primary source of carbon, conditions that are highly unlikely in normal soils. Therefore, expression of PMI cannot be considered a factor that would confer selective advantage to maize.

Cultivation of Bt11 x MIR162 x GA21 maize in the EU is not within the scope of this application. In the unlikely event that small amounts of grain from Bt11 x MIR162 x GA21 maize could accidentally find their way into the environment in the EU, the survival of this grain would be very unlikely for the reasons stated above. In addition, any plants germinating from this grain could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

In summary, the likelihood that the expression of the Lepidoptera pest protection traits, the herbicide tolerant traits or the selectable marker in Bt11 x MIR162 x GA21 maize will result in a selective advantage or disadvantage compared with conventional maize, under the scope of this application, can be considered negligible.

9.3 Potential for gene transfer

Gene transfer from Bt11 x MIR162 x GA21 maize to other sexually compatible plant species is not possible since there are not any maize wild relatives in the EU.

Gene transfer from Bt11 x MIR162 x GA21 maize to other maize could occur through pollen dispersal during the cultivation of the crop. However, cultivation of Bt11 x MIR162 x GA21 maize is not within the scope of this application. It is therefore highly unlikely that this maize could grow in significant quantities in the EU. In the unlikely event that small amounts of grain from Bt11 x MIR162 x GA21 maize accidentally found their way into the environment in the EU, this would represent extremely low levels of exposure, and the survival of the grain would be very unlikely. In addition, plants resulting from spilled grain could be easily controlled using any of the current agronomic measures taken to control other commercially-available maize. Therefore Bt11 x MIR162 x GA21 maize is extremely unlikely to flower and fertilise other varieties of maize in Europe.

In summary, the potential for gene transfer between Bt11 x MIR162 x GA21 maize plants and other maize plants or sexually compatible wild relatives in the EU can be considered negligible under the scope of this application.

9.4 Interactions between the GM plant and target organisms

The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize in the EU, therefore interactions between Bt11 x MIR162 x GA21 maize and target organisms are highly unlikely.

Bt11 x MIR162 x GA21 maize was produced by combining Bt11 and MIR162 and GA21 maize through conventional breeding and therefore Bt11 x MIR162 x GA21 maize produces the transgenic proteins inherited from the single GM maize events: Cry1Ab, PAT, Vip3Aa20 PMI and mEPSPS. The Cry1Ab and Vip3Aa20 proteins confer protection against certain lepidopteran pests and are known for specificity to insects from the order Lepidoptera. The other proteins produced by Bt11 x MIR162 x GA21 maize: PAT, PMI (from MIR162) and mEPSPS are not known to have adverse effects on organisms.

In summary, immediate or delayed effects in the environment due to direct or indirect interactions between Bt11 x MIR162 x GA21 maize plants and target organisms can be considered highly unlikely under the scope of this application.

9.5 Interactions of the GM plant with non-target organisms

The scope of this application does not include the cultivation of Bt11 x MIR162 x GA21 maize in the EU, therefore interactions between Bt11 x MIR162 x GA21 maize and non-target organisms are highly unlikely.

Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding and therefore Bt11 x MIR162 x GA21 maize produces the transgenic proteins inherited from the single GM maize events: Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS. The Cry1Ab and Vip3Aa20 proteins confer protection against certain lepidopteran pests and are known for its specificity to insects from the order Lepidoptera. The other proteins produced by Bt11 x MIR162 x GA21 maize: PAT, PMI (from MIR162) and mEPSPS are not known to have adverse effects on organisms.

In the unlikely event that small amounts of Bt11 x MIR162 x GA21 maize grain accidentally found their way into the environment this would represent extremely low levels of exposure and the survival of this grain would be very unlikely. Any plants germinating from this grain could be easily controlled using any of the current agronomic measures taken to control other commercially available maize. Therefore Bt11 x MIR162 x GA21 maize is extremely unlikely to germinate and survive outside agricultural environments and its potential to interact with non-target species is very low.

In summary, immediate or delayed effects in the environment due to direct or indirect interactions between Bt11 x MIR162 x GA21 maize plants and non-target organisms can be considered highly unlikely under the scope of this application.

9.6 Effects on human health

The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize in the EU, therefore exposure to this maize is most likely to occur through ingestion of food containing Bt11 x MIR162 x GA21 maize.
Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding. The potential for adverse effects on human health of these single events has been assessed in risk assessments and it has been concluded that the potential for adverse effects on human health from consumption of Bt11, MIR162 or GA21

maize are negligible.

In addition, compositional analysis with Bt11 x MIR162 x GA21 maize and broiler feeding studies with the higher level Bt11 x MIR162 x MIR604 x GA21 maize (this approach is consistent with EFSA guidance) have confirmed that the Bt11 x MIR162 x GA21 maize is equivalent in composition to conventional maize and as safe and nutritious as conventional maize.

There is no reason to anticipate that conventional breeding of Bt11, MIR162 and GA21 maize would result in a stacked product that differs in toxicity or allergenic potential to humans. None of the proteins produced by Bt11, MIR162 and GA21 maize are known to be toxic or allergenic to humans and there are no known precedents where interactions between non-toxic proteins lead to toxic effects. Throughout all the tests conducted by Syngenta with Bt11 x MIR162 x GA21 maize no evidence of interaction between the transgenic proteins produced by these plants (Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS) has been observed.

In summary, no adverse effects on human health or adverse consequences for the food chain are expected following consumption of food consisting or containing Bt11 x MIR162 x GA21 maize.

9.7 Effects on animal health

The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize in the EU, therefore exposure to these maize is most likely to occur through ingestion of feed containing Bt11 x MIR162 x GA21 maize. Bt11 x MIR162 x GA21 maize was produced by combining Bt11, MIR162 and GA21 maize through conventional breeding. The potential for adverse effects on animal health of each of the single GM maize events (Bt11, MIR162 and GA21) has been assessed in risk assessments and it has been concluded that the potential for adverse effects on animal health from consumption of Bt11, MIR162 or GA21 maize are negligible.

In addition, compositional analysis with Bt11 x MIR162 x GA21 maize and broiler feeding studies with the higher level Bt11 x MIR162 x MIR604 x GA21 maize (this approach is consistent with EFSA guidance) have confirmed that the Bt11 x MIR162 x GA21 maize is equivalent in composition to conventional maize and as safe and nutritious as conventional maize.

There is no reason to anticipate that conventional breeding of Bt11, MIR162 and GA21 would result in a stacked product that differs in toxicity or allergenic potential to animals. None of the proteins produced by these single GM maize events (Bt11, MIR162 and GA21) are known to be toxic or allergenic to animals and there are no known precedents where interactions between non-toxic proteins lead to toxic effects. Throughout all the tests conducted by Syngenta with Bt11 x MIR162 x GA21 maize plants, no evidence of interaction between the transgenic proteins produced by these plants (Cry1Ab, PAT, Vip3Aa20, PMI and mEPSPS) has been observed.

In summary, no adverse effects on animal health or adverse consequences for the feed chain

are expected following consumption of feed consisting or containing Bt11 x MIR162 x GA21 maize.
9.8 Effects on biogeochemical processes The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize in the EU. Interactions with target or non-target organisms that could lead to effects on biogeochemical processes are therefore highly unlikely. In the unlikely event that small amounts of grain of Bt11 x MIR162 x GA21 maize accidentally found their way into the EU environment, their survival would be very unlikely, as maize is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. Moreover, these plants could be easily controlled using any of the current agronomic measures taken to control other commercially available maize. In the unlikely event that some Bt11 x MIR162 x GA21 maize plants survived, the potential effects on biogeochemical processes as a result of interactions with target and non-target organisms are likely to be the same as those effects resulting from cultivation of non-modified maize. In summary, the risk of adverse effects on biogeochemical processes resulting from interactions of Bt11 x MIR162 x GA21 maize and target or non-target organisms can be considered negligible under the scope of this application.
9.9 Impacts of the specific cultivation, management and harvesting techniques The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize plants in the EU; therefore there are no specific cultivation, management and harvesting techniques for the use of Bt11 x MIR162 x GA21 maize in the EU.

10. Potential interactions with the abiotic environment

The scope of this application does not include cultivation of Bt11 x MIR162 x GA21 maize in the EU; therefore interactions of Bt11 x MIR162 x GA21 maize with the abiotic environment are highly unlikely. In the unlikely event that small amounts of grain of Bt11 x MIR162 x GA21 maize accidentally found their way into the EU environment, their survival would be very unlikely, as maize is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. Moreover, these plants could be easily controlled using any of the current agronomic measures taken to control other commercially available maize. In the unlikely event that some Bt11 x MIR162 x GA21 maize plants survived, the potential effects on the abiotic environment are likely to be the same as those effects resulting from cultivation of non-modified maize.

In summary, environmental impacts as a result of interactions between Bt11 x MIR162 x GA21 maize and the abiotic environment can be considered negligible within the scope of this application.

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 required by Article 5(5)(b) and 17(5)(b) of Regulation (EC) No. 1829/2003 the proposed monitoring plan for Bt11 x MIR162 x GA21 maize has been developed according to the principles and objectives outlined in Annex VII of Directive 2001/18/EC and Decision 2002/811/EC establishing guidance notes supplementing Annex VII to Directive 2001/18/EC. The structure of the monitoring plan also takes into account the guidance on presentation of applications provided in the Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed.

An environmental risk assessment (ERA) for each of the individual GM maize used to produce Bt11 x MIR162 x GA21 maize has been conducted. These risk assessments were conducted as recommended by the Guidance document of the Scientific Panel of Genetically Modified Organisms for the risk assessment of GM plants and derived food and feed. The conclusion of these risk assessments was that the adverse effects to the environment arising from the import and use of either Bt11, MIR162 or GA21 maize could be considered as negligible as those from any other commercial maize.

A risk assessment for the stacked Bt11 x MIR162 x GA21 maize has also been conducted following the same Guidance document and taking into account the recent Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of GM plants containing stacked transformation events. Risk assessment concepts described in recent publications have also been used.

The conclusions of the ERA confirm that the effects to the environment arising from the use of Bt11 x MIR162 x GA21 maize will be no different to those from any other commercial maize.

11.2 Interplay between environmental risk assessment and monitoring

In general two types of environmental monitoring can be described:

a. case-specific monitoring, designed to evaluate potential adverse effects linked to the genetic modification, identified in the environmental risk assessment (ERA)
b. general surveillance, which is aimed to identify adverse unforeseen effects that were not anticipated in the environmental risk assessment.

An ERA has been conducted in accordance with Annex II of Directive 2001/18/EC and takes into account the recent Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of GM plants containing stacked transformation events to evaluate potential adverse effects of Bt11 x MIR162 x GA21 maize on human and animal health and the environment. The conclusions of this ERA confirmed that the potential risks to human and animal health or the environment arising from the placing on the market of Bt11 x MIR162 x GA21 maize can be considered negligible. Therefore, a case-specific monitoring plan is not considered necessary under the scope of this application. However, a general surveillance plan based on Annex II of the Directive 2001/18/EC has been developed by EuropaBio and is outlined below.

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

An environmental risk assessment (ERA) has been conducted in accordance with Annex II of Directive 2001/18/EC to evaluate potential adverse effects of Bt11 x MIR162 x GA21 maize on human and animal health and the environment. The conclusions of this ERA confirm that the potential risks to human and animal health or the environment arising from the placing on the market of Bt11 x MIR162 x GA21 maize can be considered negligible, under the scope of this application. Therefore, a case-specific monitoring plan is not considered necessary under the scope of this application. However, a general surveillance plan based on Annex II of the Directive 2001/18/EC has been developed by EuropaBio and is outlined below.

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

In accordance with Council Decision 2002/811/EC, general surveillance is not based on a particular hypothesis and it should be used to identify the occurrence of unanticipated adverse effects of the viable GMO or its use for human and animal health or the environment that were not predicted in the ERA.

Exposure to the environment will be limited to unintended release of Bt11 x MIR162 x GA21 maize, which could occur for example via substantial losses during loading/unloading of the viable commodity including Bt11 x MIR162 x GA21 maize destined for processing into animal feed or human food products. However, such exposure is highly unlikely to give rise to an adverse effect and can be easily controlled by clean up measures and the application of current practices used for the control of any adventitious maize plants, such as manual or mechanical removal and the application of herbicides (with the exception of herbicides containing glyphosate or glufosinate ammonium). Furthermore, unintended environmental effects due to the unintended release of Bt11 x MIR162 x GA21 maize will be no different than that of other commercial maize.

However and in order to safeguard against any adverse effects on human and animal health or the environment that were not anticipated in the ERA, general surveillance on Bt11 x MIR162 x GA21 maize will be undertaken for the duration of the authorisation. The general surveillance will take into consideration, and be proportionate to, the extent of imports of Bt11 x MIR162 x GA21 maize and use thereof in the Member States.

In order to increase the possibility of detecting any unanticipated adverse effects, a monitoring system will be used, which involves the authorisation holder and operators handling and using viable Bt11 x MIR162 x GA21 maize. The operators will be provided with guidance to facilitate reporting of any unanticipated adverse effect from handling and use of viable Bt11 x MIR162 x GA21 maize.

11.5 Reporting the results of monitoring

In accordance with Regulation (EC) No 1829/2003, the authorisation holder is responsible to inform the European Commission of the results of the general surveillance.

If information that confirms an adverse effect of Bt11 x MIR162 x GA21 maize and that alters the existing risk assessment becomes available, the authorisation holder will immediately investigate and inform the European Commission. The authorisation holder, in collaboration with the European Commission and based on a scientific evaluation of the potential consequences of the observed adverse effect, will define and implement management measures to protect human and animal health or the environment, as necessary. It is important that the remedial action is proportionate to the significance of the observed effect.

The authorisation holder will submit an annual monitoring report including results of the general surveillance in accordance with the conditions of the authorisation. The report will contain information on any unanticipated adverse effects that have arisen from handling and use of viable Bt11 x MIR162 x GA21 maize.

The report will include a scientific evaluation of the confirmed adverse effect, a conclusion of the safety of Bt11 x MIR162 x GA21 maize and, as appropriate, the measures that were taken to ensure the safety of human and animal health or the environment.

The report will also clearly state which parts of the provided information are considered to be confidential, together with a verifiable justification for confidentiality in accordance with Article 30 of Regulation (EC) No. 1829/2003.

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

The Bt11 x MIR162 x GA21 maize described in this application has been produced by combining the GM maize events: Bt11, MIR162 and GA21 through conventional breeding techniques. There was no further genetic modification to produce the stack. As such the detection methods developed for the single events should be appropriate for use on the stacked event.

Methods for detection of Bt11, MIR162 and GA21 maize have been developed by Syngenta. The proposed methods are real-time quantitative TaqMan® PCR based on specific detection of the genomic DNA of these events. The methods for detection of Bt11 and GA21 maize have been validated by the DG JRC-CRL. A method for detection of MIR162 maize has been submitted to the DG JRC-CRL for validation. In addition, information relating to the applicability of the single event methods for use on the stacked products has been submitted to the DG JRC-CRL.

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

Syngenta has not previously carried out field trials of Bt11 x MIR162 x GA21 maize in the EU.

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

a) Release country

Syngenta has conducted research field trials with this maize in the USA and Argentina.

b) Authority overseeing the release

US: EPA, USDA and for Argentina: Conabia.

c) Release site

Various release sites across the USA and Argentina.

d) Aim of the release

Research and development.

e) Duration of the release

Varied depending on the aim of the trial.

f) Aim of post-releases monitoring

To confirm the management procedures for example in the control of volunteers.

g) Duration of post-releases monitoring

Varied depending on the aim of the trial, typically one year.

h) Conclusions of post-release monitoring

Ongoing.

i) Results of the release in respect to any risk to human health and the environment No evidence of adverse effects to human health or the environment have been found.

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

a) Status/process of approval The status and process of approval can be found on the EFSA website: http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_GMOApplications.htm
b) Assessment Report of the Competent Authority (Directive 2001/18/EC) An application for approval of and Bt11 x MIR162 x GA21 maize under the Directive 2001/18/EC has not been made by Syngenta.
c) EFSA opinion An EFSA opinion on Bt11 x MIR162 x GA21 maize was not available at the time of submission. EFSA opinions, once available can be found at http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_GMOApplications.htm
d) Commission Register (Commission Decision 2004/204/EC The Commission register of GM Food and Feed can be found at http://ec.europa.eu/food/food/biotechnology/authorisation/index_en.htm
e) Molecular Register of the Community Reference Laboratory/Joint Research Centre The Community Reference Laboratory webpage is http://gmo-crl.jrc.ec.europa.eu/
f) Biosafety Clearing-House (Council Decision 2002/628/EC) Information relating to the Biosafety clearing house can be found at: http://bch.biodiv.org/

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

An application for approval of Bt11 x MIR162 x GA21 maize under the Directive 2001/18/EC has not been made by Syngenta, however a link to this Summary under Regulation (EC) No 1829/2003, should be found at:

http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_GMOApplications.htm.