Application for renewal of authorisation of existing products of genetically modified Event GA21 maize, lawfully placed on the market, notified according to Articles 8 and 20 of Regulation (EC) No 1829/2003

PART II: SUMMARY

Updated 17 April 2007

A . GENERAL INFORMATION

1. Details of application

a) Member State of application
b) Application number
c) Name of the product (commercial and other names) Maize Event GA21 In the USA, GA21 is marketed under the product name Agrisure GT[1]
d) Date of acknowledgement of valid application Not available at the time of submission

1 http://www.agrisuretraits.com/Agrisure/AgrisureServlet/PsAgrisureLogin;jsessionid=D5FEE4EAC42BFBA84123E1E9B36152E1?PsAgrisureLogin.hrBroadBand=hrBroadBand&jato.pageSession=

2. Applicant

a) Name of applicant Syngenta Seeds S.A.S on behalf of Syngenta Crop Protection AG, Basel
b) Address of applicant Syngenta Seeds S.A.S. 12, chemin de l'Hobit BP 27 F-31790 Saint-Sauveur France On behalf of Syngenta Crop Protection AG, Basel Switzerland and all 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)) Event 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 An application for the import and use of genetically modified herbicide tolerant maize Event GA21 and all derived products was submitted to EFSA on 29th July 2005 under Regulation (EC) No 1829/2003 (Application EFSA-GMO-UK-2005-19). Additionally, GA21 has been entered on the community register of GM Food and Feed as an Existing product under Article 8 and 20 of Regulation (EC) No 1829/2003.	

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	

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 ☒ By Monsanto	No ☒ By Syngenta
If *yes*, specify Applications for commercial approval were made by Monsanto under Directive 90/220/EEC but have been withdrawn. An application made by Monsanto under Regulation (EC) No 258/97 was approved on 13 January 2006 and the Commission Decision (2006/69/EC) is published in the Official Journal of the European Union.[2] Additionally, GA21 has been entered on the community register of GM Food and Feed as an Existing product under Article 8 and 20 of Regulation (EC) No 1829/2003.	

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

[2] OJ **L34** 7 February 2006 p.29

Yes ☒	No ☐
If *yes*, specify Event GA21 is approved for cultivation in the USA, Canada, Argentina and Japan. It is approved for feed use in USA, Canada, South Africa, Japan, Philippines and China and food use in the EU, USA, Canada, Mexico, Japan, South Africa, Russia, Australia, New Zealand, Korea, Philippines, Taiwan and China.	

8. General description of the product

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

Event GA21 is a genetically modified (GM) maize, which expresses a mutated maize 5-enolpyruvylshikimate-3-phosphate synthase enzyme (mEPSPS). EPSPS is a key enzyme in the shikimic acid pathway, involved in the biosynthesis of aromatic amino acids and is naturally found in all plants, fungi, and bacteria but absent in animals. EPSPS is highly sensitive to herbicide products containing glyphosate. Maize plants transformed with the mutated *epsps* (*mepsps*) gene, such as those derived from Event GA21, synthesize the mEPSPS protein 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 feed and food products containing, consisting or produced from the genetically modified maize Event GA21 including products from inbreds and hybrids obtained by conventional breeding of Event GA21. The application also covers the import and industrial processing of Event GA21 maize for all potential uses as any other maize.

c) Intended use of the product and types of users

Use as any other conventional maize

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 Event GA21 maize and products derived from it are not different from those of its conventional counterpart, apart from the introduced trait of tolerance to herbicide products containing glyphosate. Event GA21 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 Event GA21 maize.

e) Any proposed packaging requirements

The characteristics of Event GA21 maize and products derived from it are not different from those of its conventional counterpart. Event GA21 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

Event GA21 maize grain will be labelled as "genetically modified maize" and products derived from it will be labelled as "containing (or produced from) genetically modified maize". Since Event GA21 maize and products derived from it are not different from those of its conventional counterpart, 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 for Event GA21 has been already assigned in accordance with Commission Regulation (EC) 65/2004: 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

Event 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 Event GA21 maize and products derived from it are not different from those of its conventional counterpart, apart from the intended effect of tolerance to herbicide products containing glyphosate. Cultivation of Event GA21 in the EU is not within the scope of this application. In the unlikely event that small amounts of maize kernels of Event GA21 accidentally found their way into the environment this would

represent extremely low levels of exposure and the survival of these kernels 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 such as cultivation and the use of selective herbicides.

Event GA21 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 Event GA21
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. Pollen dispersal is limited by several factors, including large size (0.1 mm diameter), rapid settling rate and short survivability. Most maize varieties are protoandrous so pollen shedding precedes silk emergence by up to five days. More than 98% of the pollen settles to the ground within a maximum distance of 25-50 meters of its source. 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 can only be accomplished through seed dispersal. Seed dispersal does not occur naturally due to the structure of the ear.
b) Specific factors affecting dissemination

Maize has a polystichous (arranged in many rows) female inflorescence (flower), 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.

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

Maize, which has very diverse morphological and physiological traits, is grown on approximately 147 million hectares worldwide. It is distributed over a wide range of conditions: from 56º N Lat to 40º S Lat, 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

Event GA21 was produced via microprojectile bombardment of maize suspension culture cells.

2. Nature and source of the vector used

A *Not*I restriction fragment from the Plasmid pDPG434, was used to transform Event GA21 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

Event GA21 is a genetically modified (GM) maize tolerant to herbicide products containing glyphosate. The DNA used in the transformation process, which resulted in Event GA21, was contained within a *Not*I restriction fragment and the components are shown below. The *Not*I restriction fragment contains the modified 5-enolpyruvylshikimate-3-phosphate synthase (*mepsps*) expression cassette but does not contain the origin of replication, the *bla* gene or the partial *lacZ* sequence from the plasmid pDPG434.

Vector Component	Approx. Size (Kb)	Description
Rice actin promoter and intron	1.4	5' region of the rice 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 maize and sunflower ribulose-1,5-bis phosphate carboxylase oxygenase (RuBisCo) genes.
Modified maize EPSPS gene	1.3	Mutated *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

Event GA21 maize contains a modified EPSPS enzyme (mEPSPS) 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 entire Event GA21 insert and flanking regions have been sequenced. It has been shown that 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). 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 has been performed to demonstrate the absence of further copies of the insert or vector sequence elsewhere in the genome.

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

Not applicable

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

The inheritance pattern of the insert in Event GA21 was investigated. Statistical analysis confirmed the expected Mendelian inheritance ratio for the *mepsps* gene, showing that insertion had taken place in the nuclear genome.

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

The entire insert and the 5' and 3' flanking regions were sequenced. The organisation of the insert is described in Section D2 (a) above. Based on the flanking sequence data, five putative open reading frames (ORFs) were identified. Two of these were identified solely

within the maize DNA at the 3' of the GA21 insert. Due to the proximity of these putative ORFs with the truncated rice actin first exon, these putative ORFs were examined for homology to known toxins or allergens. No homology with known toxins or allergens in the database could be found. Of the remaining three, two of putative ORFs were identified at the 5' end of the GA21 insert and spanned the maize-insert junction and the other was found at the 3' end, again spanning the maize-insert junction. These putative ORFs were analysed for homology to known toxins or allergens. No homology with known toxins or allergens in the database could be found.

3. Information on the expression of the insert

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

To characterize the range of expression of the mEPSPS protein in maize plants derived from Event GA21, the concentrations of the protein was determined by ELISA at four growth stages (whorl, anthesis, seed maturity and senescence). Quantifiable concentrations of mEPSPS protein were detected in most Event GA21-derived plant tissues. Across all growth stages, mean mEPSPS concentrations measured in leaves, roots and whole plants ranged from below the limit of quantification (<0.2 µg/gfw) to *ca.* 15 µg/gfw (<0.4—71 µg/gdw). Mean mEPSPS concentrations measured in kernels ranged from *ca.* 4—7 µg/gfw(5—10 µg/gdw) and in pollen averaged *ca.* 168 µg/gfw. The concentrations of mEPSPS were generally similar between hybrids for each tissue type at each time point.

b) Parts of the plant where the insert is expressed

To characterize the range of expression of proteins in maize plants derived from Event GA21, the concentrations of these proteins were determined by ELISA in several plant tissues (leaves, roots, kernels, pollen and whole plants). Quantifiable concentrations of mEPSPS protein were detected in most Event GA21-derived plant tissues.

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

a) Reproduction

No changes in the reproduction, dissemination or survivability compared to non-GM maize have been observed in agronomic assessments conducted with Event GA21.

b) Dissemination

No changes in the reproduction, dissemination or survivability compared to non-GM maize have been observed in agronomic assessments conducted with Event GA21.

c) Survivability

No changes in the reproduction, dissemination or survivability compared to non-GM maize have been observed in agronomic assessments conducted with Event GA21.

d) Other differences

No changes in the reproduction, dissemination or survivability compared to non-GM maize have been observed in agronomic assessments conducted with Event GA21.

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

Genetic stability:

Southern analysis of DNA derived from several generations of Event GA21 plants was conducted to confirm a single insertion site. The hybridisation data demonstrate that the insert incorporated into Event GA21 is stable over several generations.

Phenotypic stability:

The stability of mEPSPS protein expression over multiple generations was evaluated. Seed from three backcross generations was grown under greenhouse conditions and leaf material was collected at anthesis for analysis of mEPSPS protein concentrations. Mean mEPSPS concentrations measured across all backcross generations were *ca.* 13—14 µg/gfw (82—96 µg/gdw). Overall, mEPSPS concentrations were similar across the three generations analyzed, demonstrating stable expression of mEPSPS protein across multiple generations.

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, and would occur primarily through homologous recombination in microbes[3]. The *mepsps* gene is under the control of a plant promoter and *epsps* genes are

[3] EFSA, 2004c. Opinion of the Scientific Panel on Genetically Modified Organisms on the use of antibiotic resistance genes as marker genes in genetically modified plants, The EFSAJournal 48, 1-18 http://www.efsa.eu.int/science/gmo/gmo_opinions/384_en.html

ubiquitous in nature. The specific changes present in the *mepsps* gene were introduced to specifically alter two amino acids in the mEPSPS protein. These specific changes confer tolerance to herbicide products containing glyphosate and were not introduced to enhance recombination or gene transfer. Southern analysis of Event GA21 has been performed and has shown that the origin of replication in the original transformation vector has not been transferred to Event GA21. The only sequence of bacterial origin in GA21 is the *nos* terminator, which has been derived from *Agrobacterium tumefaciens*. This sequence is commonly used in the production of genetically modified plants and there is no evidence to suggest that the presence of this sequence enhances the potential of intact horizontal gene transfer from GM plants to bacteria.

b) Plant to plant gene transfer

The genetic modification in Event GA21 is not intended to change any of the typical crop characteristics of maize (except for the tolerance to herbicide products containing glyphosate). Observations from field trials have confirmed that the agronomic characteristics of Event GA21 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 compared to traditional maize. Gene transfer from Event 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 Event GA21 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

Event GA21 was compared with relevant control maize lines that had not been genetically modified. Commercial varieties were also included in the comparison where possible.

7.2 Production of material for comparative assessment

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

To confirm that Event GA21-derived maize plants are substantially equivalent to the non-transgenic isolines, replicate trials of transgenic and corresponding isogenic controls were planted. 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) produced from Event GA21-derived maize plants 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 GA21-derived maize plants and isogenic non-transgenic 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 GA21-derived maize plants and isogenic non transgenic 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 *mepsps* transgene.

These data support the conclusion that Event GA21 maize is compositionally equivalent to conventional maize, apart from the introduced trait of 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.

Event GA21-derived hybrids were grown in the USA during 2004, and in Brazil in 2003. Up to 20 separate agronomic traits were assessed, although not all traits were recorded at all locations. The commercial Event GA21 hybrids and their near isogenic non-transgenic hybrids were compared. While some differences between transgenic and control were found to be significant, there were no consistent trends in the data across locations or hybrids that would indicate that any of these differences were due to the presence of the transgene. These differences were within the normal range of variation experienced in agronomic field trials conducted with transgenic events by Syngenta over the past decade.

These data support the conclusion that Event GA21 maize is agronomically equivalent to conventional maize, apart from the introduced trait of herbicide tolerance.

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 Event GA21 maize and products derived from it are not different from those of its conventional counterpart.

7.6 Effect of processing

Maize from Event GA21 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 mEPSPS protein will influence this processing in any way.

Presence of mEPSPS protein was quantitatively analysed in maize grain and standard wet-milled and dry-milled processing fractions, corn oil and corn chips from the maize grain derived from Event GA21 and the corresponding near-isogenic non-transgenic controls.

Concentrations of mEPSPS were below the limit of detection in all of the wet-milled fractions. Quantifiable amounts of mEPSPS were found in the starting grain and all of the dry-milled fractions. The concentration of mEPSPS in both the corn chip and corn oil samples were below the limit of detection.

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 Event GA21 to the conventional maize supply. It is anticipated that Event

GA21 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 been shown to be the case through extensive compositional assessment.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

Maize derived from Event GA21 expresses a modified EPSPS protein (mEPSPS). The mEPSPS protein is derived from *Zea mays* and is greater that 99.3% homologous to maize EPSPS. EPSPS proteins are ubiquitous in nature and will naturally be present in foods derived from plant and microbial sources. To demonstrate the safety of this protein a series of studies were conducted. The data obtained showed that the mEPSPS, is not structurally and functionally related to proteins that have the potential to adversely affect human or animal health. It is sensitive to heat and processing and is rapidly degraded in simulated gastric fluid. It shows no sequence homology with known toxins or allergens. In addition, an acute oral toxicity study of mEPSPS in mice confirmed that the protein is not acutely toxic to mice at the highest dose tested.
Supplemental information was also provided by a 90-day whole food safety study in rodents and a poultry feeding study showing no adverse effects on rats and chickens.

7.8.2 Testing of new constituents other than proteins

Event GA21 has been modified to express the mEPSPS protein. No other new constituents apart from this protein are expected to be produced in Event GA21 and compositional analyses have confirmed the substantial equivalence of GA21 compared to conventional maize. Therefore no testing of any other constituent is considered necessary.

7.8.3 Information on natural food and feed constituents

Maize is a common source of food and feed and has a long history of safe use. 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 in Event GA21 and compared with non-genetically modified 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 transformation process or expression of the transgene.

7.8.4 Testing of the whole GM food/feed

In addition to the compositional analysis, the wholesomeness and safety of maize Event

GA21 was confirmed in a 90-day whole food safety study in rats and a 49-day poultry feeding study.

The 90-day whole food safety study was conducted to observe the effect of Event GA21on rats. The incorporation of Event GA21 transgenic maize grain in diets fed to rats for at least 90 consecutive days produced no deleterious effects that were considered to be attributable to the inclusion of Event GA21 transgenic maize grain in the diet.

The 49-day poultry feeding study was also conducted to evaluate whether standard poultry diets prepared with Event GA21 grain had any adverse effect on male or female broiler chickens as compared to diets prepared with non-transgenic isoline control grain and a commercial source of corn. The study showed that the transgenic corn had no deleterious effects on broiler chickens.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

Maize derived from Event GA21 expresses a modified EPSPS protein (mEPSPS). The mEPSPS protein is derived from *Zea mays* and is greater than 99.3% homologous to maize EPSPS. EPSPS proteins are ubiquitous in nature and will naturally be present in foods derived from plant and microbial sources. To assess the potential for allergenicity of the mEPSPS protein a series of studies were conducted. The data obtained showed that the mEPSPS

- is not derived from a known allergenic source,
- has no homology to known or putative allergens
- is rapidly degraded in simulated gastric fluid
- is sensitive to heat and processing

From these data, it can be concluded that the mEPSPS protein expressed in Event GA21 maize plants is 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 an allergenic food crop and Event GA21 does not express any new proteins with allergenic characteristics.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

Genetically modified Event GA21 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

Genetically modified Event GA21 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 Event GA21 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)

Maize derived from Event GA21 expresses a mEPSPS protein that confers tolerance to herbicide products containing glyphosate. Since the only modified trait expressed by the GA21 maize is that of herbicide tolerance there are no target organisms in this case.

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 maize derived from Event GA21 in the EU is not within the scope of this application. In the unlikely event that small amounts of maize kernels of Event GA21 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 mEPSPS protein does not affect the agronomic characteristics or weediness potential of Event GA21, as demonstrated in field trials conducted to evaluate the agronomic performance of this event 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 probability of the genetically modified plants 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 event into the EU can be considered negligible.

9.2 Selective advantage or disadvantage

Event GA21 plants have been modified to contain a modified *mepsps* gene to confer tolerance to herbicide products containing glyphosate. Maize is a highly domesticated plant and cannot survive without human intervention. Therefore, tolerance to herbicide products containing glyphosate would not increase the chances of maize survival under European conditions and would not confer any selective advantage.

It is important to emphasise that cultivation of Event GA21 in the EU is not within the scope of this application. In the unlikely event that small amounts of maize kernels of Event GA21 accidentally found their way into the environment, this would represent extremely low levels of exposure and the survival of these kernels would be very unlikely for the reasons stated above. In addition, they could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

In summary, the potential risk of the expression of the mEPSPS protein in Event GA21 maize resulting in a selective advantage to the plants under the scope of this application can be considered negligible.

9.3 Potential for gene transfer

Gene transfer from Event 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 Event GA21 maize to other maize could occur through pollen dispersal during the cultivation of the crop. Maize is predominantly wind pollinated. Plants produce pollen for 10-13 days and shed pollen typically remains viable only a short time. 98% of pollen settles to the ground within 25-50 meters of its source. Cultivation of maize Event GA21 is not within the scope of this application. It is therefore highly unlikely that this maize could grow in any significant quantity in the EU. In the unlikely event that small amounts of grain from maize Event GA21 could accidentally find their way into the environment this would represent extremely low levels of exposure and the survival of these grain would be very unlikely for the reasons stated above. In addition, they could be easily controlled using any of the current agronomic measures taken to control other commercially available maize. Therefore maize derived from Event GA21 is extremely unlikely to flower and fertilise other varieties of maize in Europe.

In summary, the potential for gene transfer between Event 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

Since the scope of this application does not include cultivation of maize plants of Event GA21, there will not be significant direct or indirect interactions with target organisms.

In addition as the only modified trait expressed by the GA21 maize is that of herbicide tolerance there are no target organisms in this case.

9.5 Interactions of the GM plant with non-target organisms

Since the scope of this application does not include cultivation of maize plants of Event GA21, direct or indirect interactions with non-target organisms are highly unlikely. In the unlikely event that small amounts of grain from maize Event GA21 accidentally found their way into the environment this would represent extremely low levels of exposure and the survival of these grain would be very unlikely since any germinating grain could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

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

9.6 Effects on human health

Event GA21 imported in the EU could enter the food chain. Human exposure to this maize could therefore occur though food consumption. However, the recipient organism, maize, has a history of safe use throughout the world. Event GA21 expresses a mEPSPS protein conferring tolerance to herbicide products containing glyphosate. Studies comparing the composition of Event GA21 maize plants and non-modified maize have been performed. These studies lead to the conclusion that this maize is substantially equivalent to conventional maize. mEPSPS is sensitive to processing and heat and rapidly degraded in simulated gastric fluids. It shows no sequence homology with known toxins or allergens.

In addition, the acute oral toxicity study conducted with mEPSPS in mice, confirmed that the protein is not acutely toxic to mice at the highest dose tested. No test substance related mortalities occurred during the study and no clinical signs attributable to the test substance were observed. There were no treatment related effects on body weight, food consumption or organ weights, nor were any treatment related effects observed following macroscopic or microscopic examination of tissues.

An allergenicity assessment has been conducted showing that this protein is unlikely to be allergenic.

The inserted DNA and the flanking regions have been sequenced. A detailed open reading frame analysis could find no evidence for sequences of ORFs with homology to known toxins

or allergens

The wholesomeness and safety of maize Event GA21 was confirmed in a 90-day toxicity study in rats and a poultry feeding study, where no treatment related effects were observed and no differences with the non-GM controls were detected.

In summary, it can be concluded that grain from maize Event GA21 is safe for food consumption and no differences in wholesomeness are expected with comparable non-GM maize varieties.

9.7 Effects on animal health

Event GA21 will be imported in the EU and could enter the feed chain. Animal exposure to this maize could therefore occur though feed consumption. However, the recipient organism, maize, has a history of safe use throughout the world. Event GA21 expresses a mEPSPS protein conferring tolerance to herbicide products containing glyphosate. Studies comparing the composition of Event GA21 maize plants and non-modified maize have been performed. These studies lead to the conclusion that this maize is substantially equivalent to conventional maize. The mEPSPS protein is sensitive to processing and heat and rapidly degraded in simulated gastric fluids. It shows no sequence homology to known toxins or allergens.

In addition, the acute oral toxicity study conducted with mEPSPS in mice, confirmed that the protein is not acutely toxic to mice at the highest dose tested. No test substance related mortalities occurred during the study and no clinical signs attributable to the test substance were observed. There were no treatment related effects on body weight, food consumption or organ weights, nor were any treatment related effects observed following macroscopic or microscopic examination of tissues.

The inserted DNA has been sequenced. A detailed open reading frame analysis could find no evidence for ORFs which showed homology to known toxins or allergens.

The wholesomeness and safety of maize Event GA21 was confirmed in a 90-day toxicity study in rats and a poultry feeding study, where no treatment related effects were observed and no differences with the non-GM controls were detected.

In summary, it can be concluded that grain from maize Event GA21 is safe for feed consumption and no differences in wholesomeness are expected with comparable non-GM maize varieties.

9.8 Effects on biogeochemical processes

Since the scope of this application does not include cultivation of maize plants of Event GA21, effects on biogeochemical processes are highly unlikely. In the unlikely event that small amounts of maize kernels of Event GA21 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. Moreover, if these 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, effects on biogeochemical processes resulting from the use of Event GA21 under the scope of this application are highly unlikely.

9.9 Impacts of the specific cultivation, management and harvesting techniques

The scope of this application does not include cultivation of maize plants of Event GA21 in the EU.

10. Potential interactions with the abiotic environment

The scope of this application does not include cultivation of Event GA21 maize in the EU, therefore interactions of maize Event GA21 with the abiotic environment are highly unlikely. In the unlikely event that small amounts of maize kernels of event GA21 accidentally found their way into the environment these plants will not have different interactions with the abiotic environment to similar non-GM plants. They will not be able to survive under European climatic conditions, and if they would, they could easily be controlled using conventional agronomic measures normally used on commercial maize 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)

The scope of this application does not include cultivation of Event GA21 maize in the EU. Environmental exposure to Event GA21 could only occur in the unlikely event that small amounts of grain of maize Event GA21 accidentally found their way into the environment in the EU. However, the survival of this grain would be very unlikely as maize is a highly domesticated plant and cannot survive without human intervention, especially under normal European climatic conditions. This grain, if germinated could be easily controlled using any of the current agronomic measures taken to control other commercially available maize.

An environmental risk assessment (e.r.a.) has been conducted as recommended by the Guidance document of the EFSA Scientific Panel of Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. According to this guidance the e.r.a. should follow the principles outlined in Directive 2001/18/EC (Annex II). The risk assessment is described as *"a process of evaluation, including the identification of the attendant uncertainties, of the likelihood and severity of an adverse effect(s)/event(s) occurring to man or the environment following exposure under defined conditions to a risk source(s)"*. This risk assessment has been conducted taking into account the scope of this application, which covers the import of grain for use as any other conventional maize grain,

but does not include the cultivation of Event GA21. A sequential approach to the e.r.a., as recommended by Commission Decision 2002/623/EC has been followed, so the characteristics of Event GA21 that may cause an adverse effect have been identified, their potential consequences evaluated, the likelihood of their occurrence assessed and the overall risk posed by each characteristic identified. Comparison of Event GA21 maize with conventional maize has been used as a baseline.

The conclusions of this e.r.a. confirm that the effects to the environment arising from the use of Event GA21 can be considered as negligible as those from any other commercial maize, under the scope of this application.

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 e.r.a.
b. general surveillance, which is aimed to identify adverse unforeseen effects that were not anticipated in the environmental risk assessment.

An environmental risk assessment (e.r.a.) has been conducted in accordance with Annex II of Directive 2001/18/EC to evaluate potential adverse effects of Event GA21 on human and animal health and the environment. The conclusions of this e.r.a. confirm that the potential risks to human and animal health or the environment arising from the placing on the market of Event 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 is outlined below.

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

An environmental risk assessment (e.r.a.) has been conducted in accordance with Annex II of Directive 2001/18/EC to evaluate potential adverse effects of Event GA21 on human and animal health and the environment. The conclusions of this e.r.a. confirm that the potential risks to human and animal health or the environment arising from the placing on the market of Event 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 is outlined below.

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

The objective of general surveillance is to identify unforeseen adverse effects of the GM plant or its use, on human health and the environment, which were not predicted in the risk

assessment. The scope of this application is limited to import of Event GA21 and excludes cultivation practices. Cultivation outside the EU is accompanied by stewardship and surveillance programmes which include the provision of information to traders and processors of bulk mixtures of grain.

The provisions concerning traceability and labelling for placing on the market of Event GA21 maize will allow the prompt identification of products containing or consisting of this maize, and thus enable any unanticipated adverse effects to be effectively traced.

The majority of imported Event GA21 material will be used for feed purposes. Therefore, traders and processors as well as the European feed industry serve as a good focal point to address questions related to any unanticipated effects that might be associated with the use of Event GA21.

Syngenta is committed to inform traders, processors and the European feed and food industry with details on the safety of Event GA21 and to establish a communication network where unforeseen effects can be reported. If unusual observations are reported, more focussed in-depth studies can be carried out in order to determine cause and relationship with the specific event. Final decisions on whether any identified effects are significant can only be made if causality is clear and endpoints are determined.

Although not a formal part of the surveillance plan, it is appropriate to note that there is an extensive information network, with global reach, which will provide additional information on possible adverse effects arising from the use of GM crops. These include new and rapid means of access to information from across the globe through telecommunications, the media and Internet access. Through these means, many groups, including agronomists, ecologists, health professionals, and the general public now have unprecedented access to reports on the use world-wide of GM crops. In addition, electronic discussion sites, for example those of WHO, OECD, FAO, and consumer organisations, are valuable sources of information and communication for professionals and, in many cases, the general public.

11.5 Reporting the results of monitoring

The notifier/consent holder is responsible, under Regulation (EC) No 1829/2003, to inform the Commission of the results of the surveillance. Consistent with the EFSA guidance, the notifier will submit a General Surveillance Report containing information related to the monitoring on an annual basis.

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

A method for detection of Event GA21 has been developed by Syngenta. The proposed method is a real-time quantitative TaqMan® PCR based on specific detection of Event GA21 genomic DNA.

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 carried out field trials in 2006 of Event GA21 in Spain, Czech Republic and France. We have also carried out field trial in Romania in 2006.
a) Notification number Spain: B/ES/06/04 France: B/FR/06/01/12 Czech Repuplic: B/CZ/05/02 Romania: 108378/20.12.2005/64265/A.B./20.12.2005.
b) Conclusions of post-release monitoring No unexpected effects or observations have been detected to date. No adverse effects on human health or the environmental has been observed or reported during these releases The results of these field trials confirm the safety of the deliberate release of Event GA21 into the environment in the E.U.
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) No unexpected effects or observations have been detected. No adverse effects on human health or the environmental has been observed or reported during these releases Final reports of the releases can be found at the JRC web page http://gmoinfo.jrc.it/

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

Event GA21 is approved for cultivation in the USA, Canada, Argentina and Japan. Syngenta has grown Event GA21 commercially in the USA and Canada since 2005. Additionally Event

GA21 field trials have been carried out in South Africa and Brazil.

. 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.eu.int/science/gmo/gm_ff_applications/catindex_en.html
b) Assessment Report of the Competent Authority (Directive 2001/18/EC) An application for approval of Event GA21 under the Directive 2001/18/EC has not been made by Syngenta.
c) EFSA opinion An EFSA opinion on Event GA21 was not available at the time of submission. EFSA opinions, once available can be found at http://www.efsa.eu.int/science/gmo/gmo_opinions/catindex_en.html
d) Commission Register (Commission Decision 2004/204/EC) The Commission register of GM Food and Feed can be found at http://europa.eu.int/comm/food/dyna/gm_register/index_en.cfm
e) Molecular Register of the Community Reference Laboratory/Joint Research Centre The Community Reference Laboratory webpage is http://gmo-crl.jrc.it/
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 Event GA21 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.eu.int/science/gmo/gm_ff_applications/more_info/catindex_en.html.