Application for authorization of Event MIR604 maize cultivation in the European Union under Regulation (EC) No 1829/2003

PART II: SUMMARY

This document is complete as of December 2010. Since it is submitted as one part of a regulatory application, which is subject to an on-going regulatory review, it may be subject to later amendment or replacement. The information may also be supplemented with additional material requested by regulatory authorities. As such, it may only be considered properly with reference to those later amendments or supplementary materials and in the context of the dossier as a whole.

A. GENERAL INFORMATION

1. Details of application

a) Member State of application UK
b) Application number Not available at the time of submission
c) Name of the product (commercial and other names) Event MIR604 maize (MIR604 maize)
d) Date of acknowledgement of valid application Not available at the time of submission

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 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 on the market, whether it be the manufacturer, the importer or the distributor, if different from the applicant (Commission Decision 2004/204/EC Art 3(a)(ii)) Event MIR604 maize (MIR604 maize) will be cultivated 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	

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 MIR604 maize is approved for commercial cultivation in the USA, Canada and Japan. MIR604 maize is also approved for import in Korea, China, EU, Australia/ New Zealand, Mexico, Japan, Philippines and Taiwan. A number of other submissions have been made in other 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

MIR604 maize is a genetically modified maize that expresses a modified Cry3A (mCry3A) protein which confers protection against certain coleopteran pests like *Diabrotica virgifera virgifera* (Western corn rootworm; WCRW) and related *Diabrotica* species and, a phosphomannose isomerase protein, which acts as a selectable marker enabling transformed plant cells to utilize mannose as a primary carbon source.

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

This application requests the authorization for production and cultivation of genetically modified Event MIR604 maize in the European Union, including seed production and breeding.

Concurrently, a separate application has been submitted requesting the authorization for production and cultivation of genetically modified Bt11 x MIR604 x GA21 maize in the European Union, including seed production and breeding of the GM maize lines necessary to generate Bt11 x MIR604 x GA21 maize.

c) Intended use of the product and types of users

It is intended that MIR604 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 MIR604 maize and products derived from it are not different from those of its conventional counterpart, apart from the introduced trait of insect tolerance. MIR604 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 MIR604 maize.

e) Any proposed packaging requirements

The characteristics of MIR604 maize and products derived from it are not different from those of its conventional counterpart. MIR604 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. MIR604 maize grain will therefore be labelled as "genetically modified maize" and products derived from it will be labelled as "containing (or produced from) genetically modified maize". Since MIR604 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 MIR604 maize has been assigned in accordance with Commission Regulation (EC) 65/2004: SYN-IR6Ø4-5.

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

MIR604 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 MIR604 maize and products derived from it are not different from those of its conventional counterpart, apart from the intended traits.

MIR604 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 MIR604 maize
f) Common name Maize; corn

2a. Information concerning reproduction

(i) Mode(s) of reproduction *Zea mays* is an allogamous plant that propagates through seed produced predominantly by wind-borne cross-pollination. Self pollination of up to 5% may be observed. Male and female flowers are separated on the plant by about 1–1.3m. *Z. mays* has staminate flowers in the tassels and pistillate flowers on the ear shoots. *Z. mays* is a plant with protoandrous inflorescence; however, decades of conventional selection and breeding have produced varieties of maize with protogyny (Angevin *et al.*, 2008). There is no asexual reproduction in maize.
(ii) Specific factors affecting reproduction The key critical stages of maize reproduction are tasselling, silking, pollination and fertilization. Climatic and drought stress affect pollen viability and silk longevity thus potentially limiting the period of possible cross-pollination. Maize pollen is very sensitive to dehydration as it loses water rapidly. Other factors like rainfall or

irrigation inhibit pollen emission because the anther dehiscence is limited by the mechanical layer. In general, maize pollen is only viable for a few hours after emission. 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 meters. Climatic conditions also affect grain and seed production, especially under drought conditions during flowering, tasseling and silking. If severe drought occurs during these phenological stages, the grain yield is reduced.

(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.

2b. 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

Compared to other wind-pollinated species, maize pollen grains are relatively large and therefore settle to the ground rapidly and have usually a short flight range. Although vertical wind movements or gusts during pollen shedding can lift pollen up high in the atmosphere and distribute it over significant distances, concentrations of viable pollen considerably decrease with height and distance from the source. Hence, only low levels of cross-pollination could occur over longer distances under suitable climatic conditions.

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

Maize is the world's most widespread cereal with very diverse morphological and physiological traits; it is grown on approximately 161 million hectares worldwide (2008). Maize is distributed over a wide range of conditions: from latitudes 50º North to 50º South, below sea level of the Caspian plains up to 3000m 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.

The EU is the fourth largest grain maize producer in the world, after the USA, China and Brazil. In the EU-27, grain maize was cultivated on about 8.4 million hectares (2009) with a production of 57 million tonnes (2009). Another major maize product is silage maize produced on about 5.1 million hectares (2008).

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

MIR604 maize was produced by transformation of immature maize embryos derived from a proprietary *Zea mays* line *via Agrobacterium tumefaciens*-mediated transformation.

2. Nature and source of the vector used

The plasmid pZM26 was used for transformation. The size, function and donor organism of each element of pZM26 have been provided with the application.

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

MIR604 maize is a genetically modified maize that expresses a modified Cry3A (mCry3A) protein for control of certain coleopteran pests and a phosphomannose isomerase protein, which acts as a selectable marker enabling transformed plant cells to utilize mannose as a primary carbon source.

The region intended for insertion in MIR604 maize contains a modified *cry3A (mcry3A)* gene from *Bacillus thuringiensi*s; this gene is under the control of the maize MTL promoter and the nopaline synthase (NOS) terminator from *Agrobacterium tumefaciens*. It also contains the *pmi* gene (also known as *manA*) from *E.coli* encoding a phosphomannose isomerase; this gene is under the control of the maize polyubiquitin promoter and the NOS terminator from *A. tumefaciens*.

Vector component	Size (bp)	Description
MTL	2556	Promoter derived from the *Zea mays* (maize) metallothionein-like gene.
mcry3A	1797	A modified *cry3A* gene that confers tolerance to western corn rootworm *(Diabrotica virgifera virgifera)* and related *Diabrotica* species.
NOS	253	Polyadenylation region from the nopaline synthase gene from *Agrobacterium tumefaciens.*
ZmUbiInt	1993	Promoter from *Zea may* polyubiquitin genes
pmi	1176	*E. coli pmi* gene encoding the enzyme phosphomannose isomerase (PMI)
NOS	253	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

MIR604 maize is a genetically modified maize that expresses a modified Cry3A (mCry3A) protein which confers protection against certain coleopteran pests like *Diabrotica virgifera virgifera* (Western corn rootworm; WCRW) and related *Diabrotica* species. MIR604 maize also expresses a phosphomannose isomerase (MIR604 PMI) protein as a selectable marker that allows transformed maize cells to utilize mannose as a sole carbon source while maize cells lacking this protein fail to grow.

2. Information on the sequences actually inserted or deleted

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

The insert in MIR604 maize is present at a single locus and inherited as a single gene in a Mendelian fashion.

In addition to sequencing, southern analysis performed demonstrates 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 MIR604 maize were analysed and the results showed that insertion has taken place in the nucleus.

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

Sequencing and southern data have demonstrated that MIR604 maize contains a single DNA insertion with one copy of both the *mcry3A* and the *pmi* genes.

3. Information on the expression of the insert

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

Tissues from maize plants derived from MIR604 maize and near-isogenic conventional maize were analyzed by ELISA to measure the concentrations of mCry3A, and MIR604 PMI.

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 near-isogenic control maize were also analyzed.

mCry3A protein was quantifiable in all tissues of MIR604 plants analyzed, with the exception of pollen, where no mCry3A was detected. Concentrations of MIR604 PMI were quantifiable in leaves, roots, pollen, and kernels of MIR604 maize plants.

b) Parts of the plant where the insert is expressed

Quantifiable concentrations of mCry3A protein were detected in leaves, roots and kernels derived from MIR604 maize. No mCry3A expression was detected in pollen.

Quantifiable concentrations of MIR604PMI protein were detected in all MIR604 maize derived plant tissues.

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

a) Reproduction

No changes in the reproduction compared to near-isogenic conventional maize have been observed in agronomic assessments conducted with MIR604 maize.

b) Dissemination

No changes in the dissemination compared to near-isogenic conventional maize have been observed in agronomic assessments conducted with MIR604 maize.

c) Survivability

No changes in the survivability compared to near-isogenic conventional maize have been observed in agronomic assessments conducted with MIR604 maize.

d) Other differences

No changes in the reproduction, dissemination or survivability compared to near-isogenic conventional maize have been observed in agronomic assessments conducted with MIR604 maize.

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

Molecular analyses showed that the insert has been stably integrated into the plant's genome in MIR604.

MIR604 maize F_1 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 MIR604 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 MIR604 maize is not intended to change any of the typical crop characteristics of maize (except for the intended traits). Observations from field trials have confirmed that the agronomic and phenotypic characteristics of MIR604 maize have not changed in comparison with near-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 MIR604 maize to other sexually compatible plant species is not possible since maize has no wild relatives in the EU.

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

MIR604 maize plants were 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 evaluate whether biologically significant changes in composition occurred in MIR604 maize plants compared to near-isogenic conventional maize, replicate trials were planted at a range of locations in the USA and the EU. 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.

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 MIR604 maize and near-isogenic conventional maize plants grown concurrently. The mean values were 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 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 relevant changes in composition or nutritive value of the grain or forage have occurred as an unintended result of the transformation or resulting from expression of the transgenes in MIR604 maize.

These data support the conclusion that MIR604 maize is compositionally equivalent to conventional maize, apart from the intended traits. .

7.4 Agronomic traits

MIR604 maize plants were grown concurrently with near-isogenic conventional maize plants in a series of trials across the USA and the EU. Selected agronomic and phenotypic traits were assessed and compared. The results of these trials showed that MIR604 maize is agronomically and phenotypically 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 MIR604 maize and products derived from it are not different from those of its conventional counterpart.

7.6 Effect of processing

MIR604 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 (mCry3A and MIR604 PMI) 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 MIR604 maize to the conventional maize supply. It is anticipated that the introduction of MIR604 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 as confirmed by the results obtained from the extensive compositional assessment.

7.8 Toxicology

7.8.1 Safety assessment of newly expressed proteins

MIR604 maize produces two newly expressed proteins: mCry3A and MIR604 PMI. Potential adverse effects to human and animal health arising from mCry3A and MIR604 PMI have previously 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.
- mCry3A and MIR604 PMI have no significant amino acid homology to known mammalian protein toxins.
- mCry3A and MIR604 PMI are unlikely to be allergenic
- mCry3A and MIR604 PMI are readily degraded in *in vitro* digestibility assays.
- mCry3A and MIR604 PMI 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. MIR604 maize has been modified to produce mCry3A and MIR604 PMI. No other new constituents apart from these proteins are expected to be produced in MIR604 maize and compositional analyses have confirmed the compositional equivalence of MIR604 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 relevant 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, the wholesomeness and safety of MIR604 maize was confirmed in rat and poultry feeding studies.

7.9 Allergenicity

7.9.1 Assessment of allergenicity of the newly expressed protein

The allergenic potential arising from mCry3A and MIR604 PMI have previously been assessed and it was concluded that the allergenic potential to humans and animals of these proteins could be considered negligible. In summary:

- None of the transgenic proteins produced by MIR604 (mCry3A and MIR604 PMI) come from donors known to be a significant cause of food allergy.
- mCry3A and MIR604 PMI have no biologically significant amino acid homology to known allergens
- mCry3A, and MIR604 PMI are readily degraded in *in vitro* digestibility assays.

From these data, it can be concluded that mCry3A and MIR604 PMI produced by MIR604 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 the newly expressed proteins in MIR604 maize are very unlikely to be allergenic.

7.10 Nutritional assessment of GM food/feed

7.10.1 Nutritional assessment of GM food

MIR604 maize is not intended to change the nutritional status of individuals of populations or to result 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

MIR604 is not intended to change the nutritional status of livestock animals. Compositional analysis and whole food and feed safety tests have demonstrated that no unexpected alterations in nutrients and other food or feed 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 MIR604 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)

MIR604 maize is resistant to maize pests such as *Diabrotica virgifera virgifera* (Western Cornrootworm; WCRW). Resistance to WCRW is achieved through the expression of mCry3A, an insecticidal protein with specific activity to insects from the order Coleoptera. The other transgenic protein produced by MIR604 maize, MIR604 PMI, is not known to have any effects on organisms. Therefore the target organisms for MIR604 maize are limited to certain species of Coleoptera.

Interactions of the target pest with MIR604 maize have been described in the application and an insect resistance management (IRM) plan has been included.

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

9.1 Persistence and invasiveness

Potential changes in persistence and invasiveness in MIR604 maize compared to conventional maize have been assessed. For the comparative assessment of phenotypic and agronomic characteristics of MIR604 maize and its corresponding near-isogenic conventional maize, multiple field trials were grown in the USA and in the EU. One of the aims of these trials was to test the hypothesis of no greater persistence or invasiveness of MIR604 maize compared with conventional maize. The endpoints measured in these trials were selected to study significant unintended changes in seed dispersal or other traits that might affect the ability of maize to survive without human intervention (such as seedling emergence, plant height, failure to produce an ear, dropping of ears before harvest, grain yield and disease incidence).

These investigations showed that, while some differences between MIR604 maize and near-isogenic controls for some of the measured endpoints were statistically significantly different at some locations, 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 transgenes. Therefore the results indicate that MIR604 maize will not be more persistent or invasive than conventional maize.

In summary, the likelihood that MIR604 maize would become more persistent than the recipient or parental plants in agricultural habitats or more invasive in natural habitats can be considered negligible.

9.2 Selective advantage or disadvantage

MIR604 maize expresses the proteins mCry3A and MIR604 PMI. Expression of mCry3A, conferring resistance to certain pest species of Coleoptera, 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 mCry3A will not increase the chances of maize survival under European conditions and would not confer any selective advantage.

Expression of MIR604 PMI could only confer an advantage to maize plants growing under conditions where mannose was the only source of carbon, conditions that are highly unlikely in normal soils. Therefore, expression of MIR604 PMI cannot be considered a factor that would confer selective advantage to maize.

In summary, the likelihood that the expression of the Coleoptera pest protection trait, or the selectable marker in MIR604 maize will result in a selective advantage or disadvantage compared with conventional maize can be considered negligible.

9.3 Potential for gene transfer

MIR604 maize expresses the proteins mCry3A and MIR604 PMI. Given the characteristics of the genes inserted and the constructs used, the likelihood that genes from MIR604 maize would become established in the genome of microorganisms in the environment or human and animal digestive tract is very low. In the very unlikely event that such a horizontal gene transfer would take place, no adverse effects on human and animal health or the environment are expected.

Gene transfer from MIR604 maize to other sexually compatible plant species is not possible since there are no wild relatives of maize in the EU.

9.4 Interactions between the GM plant and target organisms

As described in Section D.8 interactions of the target pests with MIR604 maize have been described in the application and an insect resistance management (IRM) plan has been included.

9.5 Interactions of the GM plant with non-target organisms

MIR604 maize expresses the proteins mCry3A and MIR604 PMI. mCry3A is a protein which displays insecticidal activity against certain coleopteran species. One of the concerns associated with the cultivation of GM crops expressing Bt proteins is the possibility that non-target organisms that play an important function in the agro ecosystem may be adversely affected. In order to assess the potential adverse effects of MIR604 maize cultivation on non-target organisms in the EU a tiered testing approach was followed.

The potential exposure of non-target organisms to mCry3A following cultivation of MIR604 maize was determined, and the hypothesis that such exposure is not harmful was tested. The hypothesis was tested rigorously by making worst-case or highly conservative assumptions about exposure, along with Tier I laboratory testing for hazards using species taxonomically related to the target pest and species representing non-target organisms expected to have high exposure to mCry3A, or both. Further rigour was introduced by study designs incorporating long exposures and measurements of sensitive endpoints. No adverse effects were observed in any study, and in most cases exposure to mCry3A in the study was higher than the worst-case or conservative expected exposure. These results indicate minimal risk of MIR604 maize to non-target organisms.

9.6 Effects on human health

Potential adverse effects to humans and animals of the newly expressed proteins mCry3A and MIR604 PMI were previously evaluated as part of the risk assessments conducted to support the MIR604 import application (EFSA-GMO-

UK-2005-11) which is now approved. The conclusions reached by the EFSA GMO Panel were that there are no safety concerns to mammals arising from exposure to the proteins mCry3A and MIR604 PMI.

In summary, the risk to human or animal health as a result of exposure to MIR604 maize is negligible.

9.7 Effects on animal health

Potential adverse effects to humans and animals of the newly expressed proteins mCry3A and MIR604 PMI were previously evaluated as part of the risk assessments conducted to support the MIR604 import application (EFSA-GMO-UK-2005-11) which is now approved. The conclusions reached by the EFSA GMO Panel were that there are no safety concerns to mammals arising from exposure to the proteins mCry3A and MIR604 PMI.

In summary, the risk to human or animal health as a result of exposure to MIR604 maize is negligible.

9.8 Effects on biogeochemical processes

The potential effects of MIR604 maize to soil NTOs have been assessed and the conclusions from this assessment are that the cultivation of MIR604 maize will not result in harmful effects on soil organisms either in MIR604 maize fields or in surrounding environments. Given the specificity of mCry3A to Coleoptera, the lack of adverse effects on soil organisms, the low levels of exposure in soil and the rapid degradation of these proteins in soil, the risk that MIR604 cultivation will result in adverse effects on soil organisms or soil processes can be considered low.

9.9 Impacts of the specific cultivation, management and harvesting techniques

The likelihood that cultivation of MIR604 maize in the EU results in management practices different to those currently used in conventional maize that could result in adverse environmental effects has been assessed. The intended effect of MIR604 maize is the protection of maize from pests such as WCRW. The conclusion from the ERA conducted is that cultivation, management and harvesting techniques used for MIR604 maize in the EU will not result in harmful environmental effects.

10. Potential interactions with the abiotic environment

The genetic modification introduced in MIR604 maize is not intended to change any of the maize crop characteristics. The comparative safety assessments conducted for MIR604 maize showed that the composition, phenotypic and agronomic characteristics are comparable to those of conventional maize apart from the intended traits. The potential adverse effects of these traits on non-target organisms and biogeochemical processes have also been assessed and the conclusions are that the risks will be low. Therefore, given the specificity and mode of action of the newly expressed proteins, the lack of adverse effects on non-target organisms and soil organisms, the low levels of exposure in soil and the rapid degradation of these proteins in soil, the risk that interactions between MIR604 maize with the abiotic environment result in adverse effects to the environment can be considered low.

11. Environmental monitoring plan (not if application concerns only food and feed)

The scope of this application covers the production and cultivation of genetically modified Event MIR604 maize in the European Union, including seed production and breeding.

Environmental exposure to MIR604 maize could occur through cultivation and in the event that small amounts of grain of MIR604 maize found their way into the environment in the EU. However, the survival of grain or seed outside of an agricultural environment 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 (ERA) has been conducted taking into account the scope of this application. Comparison of MIR604 maize with conventional maize has been used as a baseline.

The conclusions of this ERA confirm that the effects to the environment arising from the use of MIR604 maize can be considered as negligible as those from any other commercial maize.

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 MIR604 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 ERA for MIR604 maize has previously been conducted as part of the application for the import and use under Regulation (EC) No 1829/2003. The conclusion of this risk assessment was that the adverse effects to the environment arising from the import and use of MIR604 maize can be considered as negligible as those from any other commercial maize. An environmental risk assessment (ERA) has been conducted also taking into account the scope of this application. Comparison of MIR604 maize with conventional maize has been used as a baseline. The conclusions of this ERA confirm that the effects to the environment arising from the cultivation of MIR604 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 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 MIR604 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 MIR604 maize can be considered negligible. Therefore, a case-specific monitoring plan is not considered necessary under the scope of this application.

Although Syngenta considers that the potential for development of resistance to target insects is not an environmental risk, Syngenta understands that this would represent a threat to the technology; therefore Syngenta has developed an IRM plan for MIR604 maize to delay the development of resistance in target pests.

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)

The main objective of case-specific monitoring is to determine the significance of any adverse effects identified in the ERA. The ERA conducted for MIR604 maize, confirmed that the potential for adverse effects on human and animal health or the environment can be considered negligible.

The EFSA GMO Panel has identified the possible development of resistance of target organisms to mCry3A proteins as a potential risk due to large scale cultivation and/or long term exposure. Although Syngenta considers that the potential for development of resistance to target insects is not an environmental risk, Syngenta understands that this would represent a threat to the technology; therefore IRM plans to delay the development of resistance in target pests.

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 includes cultivation and seed production of MIR604 maize.

It is intended that MIR604 maize will be used as any other maize in the EU, hence background information relating to conventional practices in the cultivation have been considered in the development of the monitoring plan. In relation to the cultivation of MIR604 maize, farmers are considered to be the most valuable source of information because they are regularly in contact with that part of the receiving environment occupied by the GM crop.

The majority of cultivated MIR604 maize 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 MIR604 maize.

Syngenta is committed to inform farmers, traders, processors and the European feed and food industry with details on the safety of MIR604 maize 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, 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 applicant/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 applicant 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 MIR604 based on a real-time quantitative TaqMan® PCR for specific detection of the genomic DNA was submitted to the DG JRC-EURL and has been validated. The validation report can be found on the DG-JRC EURL website

http://gmo-crl.jrc.ec.europa.eu/summaries/MIR604_validated_Method.pdf

and

http://gmo-crl.jrc.ec.europa.eu/summaries/MIR604_val_report.pdf

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 of MIR604 maize in Spain, Czech Republic and Romania.

a) Notification number

Spain: B/ES/08/33, B/ES/09/40

Czech Republic: B/CZ/09/01

Romania: B/RO/08/01, B/RO/09/13

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 have been observed or reported during these releases

The results of these field trials confirm the safety of the deliberate release of MIR604 maize 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 have 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

a) Release country

MIR604 is approved for cultivation in the USA, Canada and Japan. Syngenta has conducted research field trials with this maize in the USA and Argentina.

b) Authority overseeing the release

US EPA, USDA, 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 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 The occurrence of volunteers after planting MIR604 field trials was no different to other maize
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 has 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 MIR604 under the Directive 2001/18/EC has not been made by Syngenta.
c) EFSA opinion An EFSA opinion on MIR604 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.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 MIR604 maize under Directive 2001/18/EC has not been made by Syngenta, however a link to this Summary and the Summary supplied as part of the Application EFSA-GMO-UK-2005-11 under Regulation (EC) No 1829/2003 may be found at:

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