Application for authorisation to place on the market MON 87419 maize in the European Union, according to Regulation (EC) No 1829/2003 on genetically modified food and feed

EFSA-GMO-NL-2017-140 / EFSA-Q-2017-00263

Part VII

Summary of Application

1. GENERAL INFORMATION

1.1. Details of application

(a) Member State of application

The Netherlands

(b) Application number

Not available at the time of submission

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

The Monsanto development code for this genetically modified maize is MON 87419. It is likely that this product will not be commercialized as a single event; hence, no commercial name will be attributed to this product.

(d) Date of acknowledgement of valid application

Not available at the time of submission.

1.2. Applicant

(a) Name of applicant

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

(b) Address of applicant

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

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
US

(c) Name and address of the representative of the applicant established in the Union (if the applicant is not established in the Union)

See above.

1.3. Scope of the application

(a) Genetically modified food

- ☑ Food containing or consisting of genetically modified plants
- ☑ Food produced from genetically modified plants or containing ingredients produced from genetically modified plants

(b) Genetically modified feed

- ☑ Feed containing or consisting of genetically modified plants
- ☑ Feed produced from genetically modified plants

(c) Genetically modified plants for food or feed uses

- ☑ Products other than food and feed containing of consisting of genetically modified plants with the exception of cultivation
- ☐ Seeds and plant propagating material for cultivation in the Union

The scope of this application covers the import, processing and all uses of MON 87419, as any other maize but excludes cultivation.

1.4. Is the product or the uses of the associated plant protection product(s) already authorised or subject to another authorisation procedure within the Union?

No ☑

Yes ☐ (in that case, specify)

1.5. Has the genetically modified plant been notified under Part B of Directive 2001/18/EC?

Yes ☐

No ☑ (in that case, provide risk analysis data on the basis of the elements of Part B of Directive 2001/18/EC)

The risk assessment presented in the MON 87419 application includes data collected from field trials conducted at multiple US locations covering a range of environmental conditions. A summary of the conclusions of the risk analysis that demonstrate the safety of MON 87419 to humans, animals and the environment, has been presented in the respective sections throughout this summary.

1.6. Has the genetically modified plant or derived products been previously notified for marketing in the Union under Part C of Directive 2001/18/EC?

No ☑

Yes ☐ (in that case, specify)

1.7. Has the product been subject to an application and/or authorised in a third country either previously or simultaneously to this application?

No ☐

Yes ☑ in that case, specify the third country, the date of application and, where available, a copy of the risk assessment conclusions, the date of the authorisation and the scope of the application

MON 87419 has been approved for food and feed uses in Korea and Canada. Further, MON 87419 has been approved for food uses in Australia/New Zealand and Japan. Regulatory submissions and reviews are currently in progress in selected countries around the world.

1.8. General description of the product

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

MON 87419, developed by Monsanto Company through *Agrobacterium*-mediated transformation of maize tissues, contains the *dmo* and *pat* genes derived from *Stenotrophomonas maltophilia* and *Streptomyces viridochromogenes*, respectively. MON 87419 consequently expresses the DMO and PAT proteins, resulting in tolerance to dicamba- and glufosinate-based herbicides, respectively.

(b) Types of products planned to be placed on the market according to the authorisation applied for and any specific form in which the product must not be placed on the market (such as seeds, cut-flowers, vegetative parts) as a proposed condition of the authorisation applied for

The scope of the current application is for authorisation of MON 87419 in the EU for all uses according to Art 3 (1) and 15 (1) of Regulation (EC) No 1829/2003, with the exception of cultivation. The range of uses of this maize will be identical to the full range of equivalent uses of conventional maize.

(c) Intended use of the product and types of users

MON 87419 maize will be used and traded in the EU in the same manner as current commercial maize and by the same operators currently involved in the trade and use of maize.

(d) Any specific instructions and recommendations for use, storage and handling, including mandatory restrictions proposed as a condition of the authorisation applied for

MON 87419 is not different from conventional maize, except for its trait (herbicides tolerance). It was shown to be as safe as conventional maize. Therefore, MON 87419 and derived products will be stored, packaged, transported, handeled and used in the same manner as curent commercial maize. No specific instructions and/or recommendations are considered necessary for the placing on the market of MON 87419 for import, processing and all uses in the EU, as specified in Section 1.8(b) of this document.

(e) If applicable, geographical areas within the Union to which the product is intended to be confined under the terms of the authorisation applied for

MON 87419 is suitable for use throughout the EU as any other maize. The scope of this application covers the import, processing and all uses of MON 87419, as any other maize but excludes cultivation.

(f) Any type of environment to which the product is unsuited

MON 87419 is suitable for use throughout the EU as any other maize. The scope of this application covers the import, processing and all uses of MON 87419 as any other maize but excludes cultivation.

(g) Any proposed packaging requirements

MON 87419 and derived products will be used in the same manner as other maize and no specific packaging is required.

(h) Any proposed labelling requirements in addition to those required by other applicable EU legislation than Regulation (EC) No 1829/2003 and when necessary a proposal for specific labelling in accordance with Article 13(2) and (3), Article 25(2)(c) and (d) and Article 25(3) of Regulation (EC) No 1829/2003. In the case of products other than food and feed containing or consisting of genetically modified plants, a proposal for labelling has which complies with the requirements of point A(8) of Annex IV to Directive 2001/18/EC must be included.

In accordance with Regulations (EC) No 1829/2003 and No 1830/2003, a labelling threshold of 0.9 % is applied for the placing on the market of MON 87419 and derived products.

Operators shall be required to label products containing or consisting of MON 87419 with the words “genetically modified maize” or “contains genetically modified maize” and shall be required to declare the unique identifier in the list of GMOs that have been used to constitute the mixture that contains or consists of this GMO.

Operators shall be required to label foods and feeds derived from MON 87419 with the words “produced from genetically modified maize”. In the case of products for which no list of ingredients exists, operators shall ensure that an indication that the food or feed product is produced from GMOs is transmitted in writing to the operator receiving the product.

Operators handling or using MON 87419 and derived foods and feeds in the EU shall be required to be aware of the legal obligations regarding traceability and labelling of these products. Given that explicit requirements for the traceability and labelling of GMOs and derived foods and feeds are laid down in Regulations (EC) No 1829/2003 and No 1830/2003 and that authorised foods and feeds shall be entered in the EU Register for genetically modified food and feed, operators in the food/feed chain will be fully aware of the traceability and labelling requirements for MON 87419. Therefore, no further specific measures are to be taken by the applicant.

(i) Estimated potential demand

(i) In the EU

There are no anticipated changes to the demand as a result of the introduction of MON 87419 into the maize supply. It is anticipated that the introduction of MON 87419 maize will replace some of the maize in exising food and feed products.

(ii) In EU export markets

There are no anticipated changes to the extent of maize production in exports markets as a result of the introduction of MON 87419 maize. It is anticipated that the introduction of MON 87419 maize will replace some of the maize grain products.

(j) Unique identifier in accordance with Regulation (EC) No 65/2004

The OECD unique identifiers for MON 87419 is MON-87419-8.

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

Because this application is for consent to import, process and all uses of MON 87419 as any other maize, excluding the cultivation in the EU, the only potential means of environmental release would be more likely to occur during import, storage and processing of MON 87419. However, modern methods of grain handling minimize losses of grain, so there is little chance of germination of spilt grain resulting in the development of mature plants of MON 87419 in the EU. Moreover, in the event of incidental spillage, the establishment of volunteer plants would be unlikely, since maize cannot survive without human assistance and is not capable of surviving as a weed. Although maize seed can over-winter in mild conditions and can germinate the following year, the appearance of maize in rotational fields is rare under European conditions. Maize volunteers, if they occur, are usualy killed by frost or could be easily controlled by the use of selective herbicides (other than dicamba and glufosinate based herbicides) or by mechanical means. Moreover, the information presented in this application established that MON 87419 is not different in

composition, nutritional and agronomic characteristics relative to the conventional counterpart, except for its tolerance to dicamba- and glufosinate-based herbicides, and that MON 87419 is unlikely to pose any threat to the EU environment or to require special measures for its containment. Therefore, no special measures are considered to be required in case of misuse or unintended release, and no specific conditions are warranted or required for the placing on the market of MON 87419 for import, processing and all uses as specified in Section 1.8(b).

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

2.1. Complete name

(a) Family name Poaceae (formerly Gramineae)

(b) Genus *Zea*

(c) Species *mays* (2n = 20)

(d) Subspecies N/A

(e) Cultivar/breeding line LH244

(f) Common name Maize / Corn

2.2. Geographical distribution and cultivation of the plant, including the distribution within the Union

Maize is widely grown in the EU and represents a significant portion of global maize production. Significant areas of maize production in Europe include the Danube Basin from southwest Germany to the Black Sea along with southern France through the Po Valley of northern Italy.

2.3. Information concerning reproduction (for environmental safety aspects)

(a) Mode(s) of reproduction

Maize is wind-pollinated, and the distances that viable pollen can travel depend on prevailing wind patterns, humidity, and temperature. Pollen is shed from the tassel and is viable for approximately 20 minutes to 24 hours depending on environmental conditions. Maize plants shed pollen for up to 14 days.

(b) Specific factors affecting reproduction

Maize, as a thoroughly domesticated plant, has lost all ability to disseminate its seeds and relies entirely on the aid of man for its distribution.

(c) Generation time

As maize is a short day plant, time to maturity is strongly influenced by photoperiod. Maize is an annual crop with cultural cycle ranging from as short as 60 to 70 days to as long as 43 to 48 weeks from grainling emergence to maturity.

2.4. Sexual compatibility with other cultivated or wild plant species (for environmental safety aspects)

Potential for cross-pollination with cultivated maize varieties

Maize morphology fosters cross-pollination; therefore, high levels of pollen mediated gene flow can occur in this species. Researchers recognize that (1) the amount of gene flow that occurs can be high because of open pollination; (2) the percent gene flow will vary by population, hybrid or inbred; (3) the level of gene flow decreases with greater distance between the source and recipient plants; (4) environmental factors affect the level of gene flow; (5) maize pollen is viable for a short period of time under field conditions; (6) maize produces ample pollen over an extended period of time; and, (7) maize is wind-pollinated; pollinating insects, especially bees, are occasional visitors to the tassels but rarely visit silks of maize.

Potential for cross-pollination with wild species

Maize and annual teosinte (*Zea mays* subsp. *mexicana*), are genetically compatible, wind-pollinated and hybridize when in close proximity to each other *e.g.*, in areas of Mexico and Guatemala. Outside its center of origin, like the EU, teosinte cannot be regarded as a native wild relative of maize as its presence in Europe is currently limited to agricultural fields where it causes a weed management problem. There are no compatible wild relatives of maize in Europe. In addition, hybridization between maize and teosinte is very unlikely due to a variety of physical factors. If intraspecific hybridization were to happen, literature has demonstrated the process to be asymmetric, favoring teosinte cross-pollinating maize. The lack of relevance of the occurrence of teosinte in maize fields in the EU for the risk assessment of cultivation of several GM maize events has been confirmed by EFSA (EFSA, 2016).

It is with extreme difficulty and special techniques that maize and the closely related perennial species, *Tripsacum* (gamma grass) hybridize. Furthermore, the offspring of the cross show varying levels of sterility and are genetically unstable.

Based on the above, the possibility of gene transfer between cultivated maize and annual teosinte or wild species of *Tripsacum* is highly unlikely.

2.5. Survivability (for environmental safety aspects)

(a) Ability to form structures for survival or dormancy

Although grown extensively throughout the world, maize is not considered a persistent weed or a plant that is difficult to control. Maize, as we know it today, cannot survive in the wild because the female inflorescence (the ear) is covered by a husk thereby restricting seed dispersal. The transformation from a wild, weedy species to one dependent on humans for its survival most likely evolved over a long period of time through plant breeding by the indigenous inhabitants of the western hemisphere.

(b) Specific factors affecting survivability

See Section 2.5.(a).

2.6. Dissemination (for environmental safety aspects)

(a) Ways and extent of dissemination

Maize is not listed as a weed in the major weed references. In addition, maize has been grown throughout the world without any report that it is a serious weed. Modern maize does not survive as a weed because of past selection in the development of maize. During domestication of maize, traits often associated with weediness have been eliminated such as seed dormancy, a dispersal mechanism, and the ability to establish fertile populations outside of cultivation.

(b) Specific factors affecting dissemination

See Section 2.6.(a).

2.7. Geographical distribution within the Union of the sexually compatible species (for environmental safety aspects)

There are no sexually compatible wild relatives of maize in the EU.

2.8. In the case of plant species not normally grown in the Union description of the natural habitat of the plant, including information on natural predators, parasites, competitors and symbionts (for environmental safety aspects)

Not applicable, as maize is grown in Europe.

2.9. Other potential interactions, relevant to the genetically modified 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 (for environmental safety aspects)

There are no known toxic effects of the maize plant to humans, animals or livestock; it has a history of safe use for human food and animal feed. Maize has been a staple of the human diet for centuries, and its processed fractions are consumed in a multitutde of food and animal feed products. A thorough description of the anti-nutrients present in maize has been presented in an OECD consensus document.

3. MOLECULAR CHARACTERISATION

3.1. Information relating to the genetic modification

(a) Description of the methods used for the genetic modification

MON 87419 was developed through *Agrobacterium*-mediated transformation of maize, using transformation plasmid vector PV-ZMHT507801.

(b) Nature and source of the vector used

PV-ZMHT507801 which contains two separate T-DNAs, that are each delineated by Right and Left Border regions. The first T-DNA (T-DNA I) contains the *dmo* and *pat* expression cassettes. The second T-DNA (T-DNA II) contains the *cp4 epsps* expression cassette for selection. During transformation, both T-DNAs were inserted into the maize genome. Subsequently, traditional breeding, segregation, selection and screening were used to isolate plants that contained the *dmo* and the *pat* expression cassettes (T-DNA I) and did not contain the *cp4 epsps* expression cassette (T-DNA II).

The backbone region of PV-ZMHT507801, located outside both of the T-DNAs, contains two origins of replication for maintenance of the plasmid vector in bacteria (*ori V*, *ori-pBR322*), a bacterial selectable marker gene (*aadA*) and a coding sequence for repressor of primer (ROP) protein for the maintenance of the plasmid vector copy number in *Escherichia coli*.

(c) Source of donor nucleic acid(s) used for transformation, size and intended function of each constituent fragment of the region intended for insertion

The genetic elements of PV-ZMHT507801 intended for insertion into the maize genome are comprised between the T-DNA I Border regions. Starting from the Right Border region, the first element intended for insertion is the the *Ubq* promoter (P-*Ubq*), followed by the *Ubq* leader and intron sequences for the ubiquitin gene (L-*Ubq* and I-*Ubq*, respectively), the *pat* coding sequence (CS-*pat*), the *Ara5* transcription termination sequence (T-*Ara5*), the *PClSV* promoter (P-*PClSV*), the *Cab* leader sequence (L-*Cab*), the *Ract1* intron sequence (I-*Ract1*), the *CTP4* targeting sequence (TS-*CTP4*), the *dmo* coding sequence (CS-*dmo*) and the *Hsp17* transcription termination sequence (T-*Hsp17*). These elements together constitute the *dmo* and *pat* expression cassettes. Information relating to the genetically modified plant

3.2. Information relating to the genetically modified plant

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

Monsanto Company has developed herbicides tolerant maize MON 87419 that expresses the DMO and PAT proteins. The DMO protein is derived from *S. maltophilia*, whereas the PAT protein is derived from *S. viridochromogenes*. The DMO and PAT proteins provide tolerance to dicamba- and glufosinate-based herbicides, respectively.

3.2.2. *Information on the nucleic acid(s) sequences actually inserted or deleted*

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

Molecular characterization of MON 87419 demonstrated that a single copy of the intended T-DNA from PV-ZMHT507801 (T-DNA I) containing the *dmo* and the *pat* expression cassettes was integrated at a single locus in MON 87419. This single locus included only sequence from the T–DNA I and was devoid of sequence from the backbone and T-DNA II.

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

A sequence comparison between the PCR product generated from the conventional counterpart and the sequence generated from the 5' and 3' flanking sequences of MON 87419 indicated that there was a 602 bp deletion of genomic DNA at the insertion site in MON 87419. Such changes are common during plant transformation and these changes presumably resulted from double-stranded break repair mechanisms in the plant during the *Agrobacterium*-mediated transformation process.

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

The Chi (χ^2) square analysis of the segregation pattern, according to Mendelian genetics, was consistent with a single site of insertion into maize nuclear DNA.

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

Molecular characterization of MON 87419 confirmed the organization and intactness of the full T-DNA I and all expected elements within the insert, with the exception of incomplete Right and Left Border sequences that do not affect the functionality of the *dmo* and *pat* expression cassettes.

(e) In case of modifications other than insertion or deletion, describe function of the modified genetic material before and after the modification, as well as direct changes in expression of genes as a result of the modification

Not applicable.

3.2.3. *Information on the expression of the insert*

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

DMO and PAT proteins expression levels were determined by a validated enzyme-linked immunosorbent assay (ELISA) in treated and untreated MON 87419 tissues collected during 2013 US growing season.

(b) Parts of the plant where the insert is expressed

In terms of food and feed safety assessment of MON 87419, forage and grain are the most relevant tissues.

3.2.4. *Genetic stability of the insert and phenotypic stability of the genetically modified plant*

MON 87419 contains a single copy of the T-DNA I sequence and was integrated into a single chromosomal locus of the maize genome. The inserted DNA is inherited in a Mendelian fashion and is stably maintained through multiple generations of breeding.

3.2.5. *Information (for environmental safety aspects) on how the genetically modified plant differs from the recipient plant in:*

(a) Mode(s) and/or rate of reproduction

Phenotypic and agronomic as well as environmental interaction data were collected from field trials conducted in 2013, 2014 and 2016 in major US maize growing regions. In each of the assessments MON 87419, either treated or not with dicamba and glufosinate, was compared to an appropriate conventional counterpart which has a genetic background similar to MON 87419 but does not possess the *dmo* and *pat* expression cassettes. In addition, multiple commercial references were included to provide a range of comparative values that are representative of existing commercial references for each measured phenotypic, agronomic, and environmental interaction characteristic.

Results of this field study showed that there are no unexpected changes in the phenotype or ecological interactions indicative of increased pest or weed potential of MON 87419 compared to the conventional counterpart.

It is therefore possible to conclude that no differences in the mode or rate of reproduction, dissemination, survivability or other agronomic, phenotypic or environmental interaction characteristics are expected in MON 87419 and that MON 87419 shows no difference to the conventional counterpart in its phenotypic and agronomic behaviour, except for its herbicides tolerance trait.

(b) Dissemination

See Section 3.2.5 (a).

(c) Survivability

See Section 3.2.5 (a).

(d) Other differences

See Section 3.2.5 (a).

3.2.6. *Any change to the ability of the genetically modified plant to transfer genetic material to other organisms (for environmental safety aspects)*

(a) Plant to bacteria gene transfer

None of the genetic elements in MON 87419 has a genetic transfer function. Therefore, no changes are expected in the ability of this maize to transfer genetic material to bacteria.

(b) Plant to plant gene transfer

Not applicable, the scope of the current application does not include the cultivation of MON 87419 in the EU.

4. COMPARATIVE ANALYSIS

4.1. Choice of the conventional counterpart and additional comparators

MON 87419 was compared to a conventional counterpart with background genetics similarto MON 87419, as well as with other commercially available maize.

4.2. Experimental design and statistical analysis of data from field trials for comparative analysis

Field trials for comparative analysis were conducted in several field sites in major growing areas of the US during 2013, 201 and/or 2016 field seasons. Additionally, conventional references were included at each field site to provide reference substances representative for their respective growing regions. Field sites were representative of commercial maize growing areas and were distributed to reflect a variety of agronomic practices, soils and climatic factors. Difference and equivalence tests were conducted using statistical models provided in EFSA guidance and according to the 2010 EFSA Scientific Opinion on Statistical considerations for the safety evaluation of GMOs.

4.3. Selection of material and compounds for analysis

The key nutrients and other nutritionally important components that were selected for analysis in the compositional study were chosen on the basis of internationally accepted guidance (OECD, 2002).

Certain characteristics together with environmental interactions were studied to assess for a potential indicator of phenotypic changes.

4.4. Comparative analysis of agronomic and phenotypic characteristics

The assessment of the phenotypic, agronomic and environmental interactions of MON 87419 compared to conventional maize demonstrated that there are no unexpected changes in the phenotype or ecological interactions indicative of increased plant weed or pest potential of MON 87419 compared to the conventional conterpart (*see* also Section 3.2.5).

4.5. Effect of processing

MON 87419 has been shown not to be different from conventional maize, except for its herbicides tolerance trait. The processing of MON 87419 is therefore not expected to be any different from that of conventional maize.

5. TOXICOLOGY

(a) Toxicological testing of newly expressed proteins

The the *dmo* and *pat* genes are the only genes expressing novel proteins in MON 87419. Therefore, the safety assessment of the newly expressed proteins is focused on the DMO and PAT proteins expressed in MON 87419.

Following the guidelines adopted by the Codex Alimentarius Commission an assessment of potential toxicity of introduced proteins has been conducted. This assessment demonstrated that it is unlikely that the MON 87419 DMO and PAT proteins will cause toxicity concerns due to the following considerations:

- These proteins have a history of safe use and pose negligible risk to human and animal health. They are derived from the bacterial species *S. maltophilia* and *S. viridochromogenes*, respectively, which have also a long history of safe use and are ubiquitous in the environment with widespread human exposure and no adverse safety reports.
- These proteins do not share sequence similarities with any known toxins or other biologically active proteins with adverse effects.
- These proteins are rapidly digested by proteases found in the human gastrointestinal tract (pepsin and pancreatin) under physiological conditions.

Furthermore, the low concentrations of the DMO and PAT proteins in tissues that are consumed provide additional assurance for their safety.

It should be further noted that the safety of the DMO and PAT proteins and their donor organisms was reviewed by the numerous global regulatory agencies, including the EFSA (EFSA, 2009, 2013a, 2013b, 2013c, 2017a, 2017b) in the context of various applications for food and feed uses and no safety concerns were identified.

Based on this weight of evidence, it is possible to conclude that the MON 87419 DMO and PAT proteins are safe and pose no concerns for humans, animals and the environment.

(b) Testing of new constituents other than proteins

The components analysed in MON 87419 were compositionally similar compared to conventional maize. Therefore, no testing of any constituent other than the introduced proteins is required.

(c) Information on natural food or feed constituents

No relevant changes in the composition of MON 87419 were detected compared to conventional maize. Therefore, the levels of food and feed constituents in MON 87419 have not been altered.

(d) Testing of the whole genetically modified food and feed

The safety assessment demonstrates that MON 87419 is as safe as conventional maize for food and feed use through the compositional assessment of MON 87419 harvested forage and grain to harvested forage and grain from conventional maize already on the market. The safety for humans and animals of the DMO and PAT proteins has been demonstrated on the basis of extensive characterization, history of safe use, lack of structural similarities with known protein toxins and allergens, absence of acute toxicity in oral gavage studies in rodents and rapid digestion in simulated digestive fluids. Moreover, the history of safe use

of the introduced proteins and the familiarity of the host organisms from which the genes are derived have been demonstrated.

Based on this weight of evidence, no more data is required to demonstrate that MON 87419 is as as safe as conventional maize from a food and feed perspective and therefore it can be concluded that there was no evidence of any adverse effects on human or animal health.

Nonetheless, inspite not being scientifically justified, in accordance with Commission Implementing Regulation (EU) No 503/2013, a 90-day feeding study with maize grain from MON 87419 in rats was performed. As expected, the study supports the conclusion that MON 87419 is as safe as conventional soybean from a food and feed perspective.

6. ALLERGENICITY

(a) Assessment of allergenicity of the newly expressed protein

The the *dmo* and *pat* genes are the only genes expressing novel proteins in MON 87419. Therefore, the safety assessment of the newly expressed proteins is focused on the DMO and PAT proteins expressed in MON 87419.

Following the guidelines adopted by the Codex Alimentarius Commission an assessment of potential allergenicity of introduced proteins has been conducted. This assessment demonstrated that it is unlikely that the MON 87419 DMO and PAT proteins will cause allergenic concerns due to the following considerations:

- These proteins are from a non-allergenic source;
- These proteins do not share sequence similarities with any known allergens
- These proteins are rapidly digested by proteases found in the human gastrointestinal tract (pepsin and pancreatin) under physiological conditions.

It should be further noted that the safety of the DMO and PAT proteins was reviewed by the numerous global regulatory agencies, including the EFSA (EFSA, 2009, 2013a, 2013b, 2013c, 2017a, 2017b) in the context of various applications for food and feed uses and no safety concerns were identified.

Based on this weight of evidence, it is possible to conclude that the MON 87419 DMO and PAT proteins are safe and pose no concerns for humans, animals and the environment.

(b) Assessment of allergenicity of the whole genetically modified plant

Maize is not considered a common allergenic food. Therefore a possible overexpression of any endogenous protein, which is not known to be allergenic, would be unlikely to alter the overall allergenicity of the whole plant or the allergy risk for consumers. MON 87419 is comparable to and as safe as conventional maize. Further, as the introduced proteins in MON 87419 do not have any allergenic potential, it was concluded that the use of MON 87419 for food and feed does not lead to an increased risk for allergenic reactions compared to the equivalent range of food and feed uses of conventional maize.

7. NUTRITIONAL ASSESSMENT

(a) Nutritional assessment of the genetically modified food

Detailed compositional and nutritional comparisons of MON 87419, a conventional counterpart and commercially available references confirmed that MON 87419 is compositionally not different from conventional maize.

(b) Nutritional assessment of the genetically modified feed

See Section 7 (a).

8. EXPOSURE ASSESSMENT – ANTICIPATED INTAKE/EXTENT OF USE

The exposure assessment in humans and animals indicates that there is minimal dietary exposure to DMO and PAT proteins from consumption of foods and feed derived from MON 87419. There are no anticipated changes in the intake and/or extent of use of maize or derived products for use as or in food or feed as a result of the addition of MON 87419 to the maize supply. MON 87419 is expected to replace a portion of current maize such that its intake or use will represent some fraction of the total products derived from maize.

9. RISK CHARACTERISATION

Based on the information provided in this application, it can be concluded that MON 87419 is as safe as conventional maize. The molecular characterization of MON 87419 did not raise any safety concern and did not show any evidence of unintended changes in MON 87419. Detailed compositional comparisons of MON 87419, its conventional counterpart and conventional references demonstrated that MON 87419 is compositionally similar to the conventional counterpart and that MON 87419 is not a contributor to compositional variability in maize. The assessed phenotypic and agronomic characteristics of MON 87419 were within the range expected for maize and did not show any phenotypic changes indicative of increased plant weed/pest potential of MON 87419 compared to conventional maize. An extensive characterisation of the DMO and PAT proteins expressed in MON 87419 confirmed that these proteins are safe for human and animal consumption. Additionally, the exposure assessment in humans and animals did not indicate any safety concerns.

In summary, there are no signs of adverse or unanticipated effects observed in a number of safety studies and the pre-market risk characterisation for food and feed use of MON 87419. The consumption of food and feed derived from MON 87419 is as safe as the consumption of its conventional counterpart. It can be concluded that the food derived from MON 87419 is not nutritionally disadvantageous for the consumer compared to the food which is intended to replace. Finally, it can also be concluded that the feed derived from MON 87419 does not harm or mislead the consumer by impairing distinctive features of the animal products compared to conventionally produced feed.

10. POST-MARKET MONITORING ON THE GENETICALLY MODIFIED FOOD OR FEED

As demonstrated in this application, there are no intrinsic hazards related to MON 87419. No data have emerged to indicate that MON 87419 is less safe than its conventional counterpart. The pre-market risk characterisation for food and feed use of MON 87419 demonstrates that the risks of consumption of MON 87419 or its derived products are no different from the risks associated with the consumption of conventional maize and maize-derived products. As a consequence, specific risk management measures are not indicated and post-market monitoring of the use of this maize for food and feed is not considered necessary.

11. ENVIRONMENTAL ASSESSMENT

11.1. Mechanism of interaction between the genetically modified plant and target organisms

No target organisms are associated with this event. As a consequence, an assessment of the potential resistance development in target organisms resulting from import, processing and all uses as any other maize, but excluding the cultivation of MON 87419 in the EU is not relevant for this submission.

11.2. Potential changes in the interactions of the genetically modified plant with the biotic environment resulting from the genetic modification

The scope of this application covers the import, processing and all uses as any other maize, but excludes the cultivation of MON 87419 in the EU. Therefore, no deliberate release of viable plant material in the EU environment is expected, and interactions of MON 87419 with the biotic environment will be limited.

(a) Persistence and invasiveness

Results from the assessment support the conclusion that the abilities of MON 87419 to persist in agricultural fields or invade non-agricultural habitats are comparable to those of conventional maize in the EU. Thus, MON 87419 is not more likely to represent an agronomic problem in agricultural fields or become more invasive in natural habitats and no adverse effects on ecological functions within agricultural production fields or on biodiversity is expected as a result of the import, processing and all uses as any other maize.

(b) Selective advantage or disadvantage

Compared with conventional maize, the introduced herbicides tolerance trait in MON 87419 confers a selective advantage only under specific conditions (*i.e.* following treatment with dicamba and/or glufosinate), which are short in duration. This advantage is of purely agronomic interest and presents negligible risk to the non-agricultural environments, because of the poor survival characteristics of maize under most European conditions. Therefore, it is concluded that the potential hazard is negligible.

(c) Potential for gene transfer

Given the low likelihood of occurrence of horizontal gene transfer and lack of adverse consequences if it were to occur, the import, processing, and food and feed use of MON 87419 in the EU is not likely to adversely impact human, animal, or environmental health, and poses negligible risk.

(d) Interactions between the genetically modified plant and target organisms

An assessment of the potential resistance development in target organisms resulting from the import, processing and all uses as any other maize of MON 87419 in the EU is not relevant for this application.

(e) Interactions of the genetically modified plant with non-target organisms

Given the low levels of environmental exposure combined with low hazard from exposure of MON 87419 to non-target organisms (NTOs), the likelihood of adverse effects to NTO communities that perform in-field ecological functions and NTO communities outside of the field from import of MON 87419, is negligible.

(f) Effects on human health

Given the low levels of environmental exposure combined with the negligible hazard occurring from the contact with MON 87419 grain, the likelihood for any adverse effects on humans and animals handling MON 87419 import and processing in the EU is negligible.

(g) Effects on animal health

See Section 11.2.(f).

(h) Effects on biogeochemical processes

Given the low level of environmental exposure combined with a lack of hazard, the import, processing and all uses of MON 87419 as any other maize in the EU is not likely to adversely impact soil micro-organisms that perform ecological functions in-field or in non-agricultural habitats, and therefore poses negligible environmental risk.

(i) Impacts of the specific cultivation, management and harvesting techniques

Cultivation of MON 87419 in the EU is not included in the scope of this application. An assessment of the impacts of specific cultivation, management and harvesting techniques of MON 87419 is therefore not relevant for this application.

11.3. Potential interactions with the abiotic environment

MON 87419 carries a trait of agronomic interest: herbicides tolerance. As MON 87419 was shown not to be different from conventional maize (with the exception of the introduced trait, imparted by the expression of the DMO and PAT proteins), with respect to its composition and agronomic and phenotypic characteristics, there is no evidence that this maize would be any different from conventional maize with regard to its baseline interactions with the abiotic environment.

Although the DMO and PAT proteins are expressed in maize, they already have a safe history of use and they have no known negative interactions with the abiotic environment.

In addition, because this application is for import, processing and all uses as any other maize in the EU, but excludes cultivation, interactions of MON 87419 with the environment will be limited. Moreover, no negative impact of MON 87419 on the abiotic environment is expected to result from the import, processing and all uses as any other maize in the EU.

11.4. Risk characterization

Results from the environmental risk assessment which takes into consideration the risk characterization and includes results described above addressing risk hypotheses for the specific areas of assessment laid down in EFSA (2010) guidance, support a conclusion that the import, processing and all uses in the EU (excluding cultivation) of MON 87419, as any

other maize, represents negligible risk to human and animal health and the environment, and poses no greater risk than the import and processing of conventional maize. Because no immediate adverse effects are expected, the probability of long-term adverse effects is also negligible. Based on the conclusions formulated for MON 87419 and maize being a segregant crop, there is no reason to expect that any sub-combination of the single events would represent a risk to human and animal health or the environment.

12. ENVIRONMENTAL MONITORING PLAN

(a) General (risk assessment, background information)

As required by Article 5(5)(b) and 17(5)(b) of Regulation (EC) No 1829/2003 the proposed Post-Market Environmental Monitoring (PMEM) plan for MON 87419 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 PMEM also takes into account the Scientific Opinion on guidance on the Post-Market Environmental Monitoring of genetically modified plants (EFSA, 2011).

(b) Interplay between environmental risk assessment and monitoring

The scope of this application is the authorisation of MON 87419 for import, processing, food and feed use in the European Union (EU) under Regulation (EC) No 1829/2003. The scope of the application does not include authorisation for the cultivation of MON 87419 seed products in the EU.

An environmental risk assessment (e.r.a.) was carried out for MON 87419 according to the principles laid down in Annex II to Directive 2001/18/EC and Decision 2002/623/EC establishing guidance notes supplementing Annex II to Directive 2001/18/EC. The scientific evaluation of the characteristics of MON 87419 in the e.r.a. (Section 5 of Part II – Scientific information) has shown that the risk for potential adverse effects on human and animal health or the environment is negligible in the context of the intended uses of MON 87419.

(c) Case-specific genetically modified plant monitoring (approach, strategy, method and analysis)

The scientific evaluation of the characteristics of MON 87419 in the e.r.a. has shown that the risk for potential adverse effects on human and animal health or the environment is negligible in the context of the intended uses of MON 87419. It is therefore considered that there is no need for case-specific monitoring.

(d) General surveillance of the impact of the genetically modified plant (approach, strategy, method and analysis)

Any potential adverse effects of MON 87419 on human health and the environment, which were not anticipated in the e.r.a., can be addressed under the general surveillance. General surveillance is largely based on routine observation and implies the collection, scientific evaluation and reporting of reliable scientific evidence, in order to be able to identify whether unanticipated, direct or indirect, immediate or delayed adverse effects have been caused by the placing on the market of a GM crop in its receiving environment. In order to allow detection of the broadest possible scope of unanticipated adverse effects, general surveillance is performed by either selected, existing networks, or by specific company stewardship programmes, or by a combination of both. The consent holder will ensure that appropriate technical information on MON 87419 and relevant legislation will be available

for the relevant networks, in addition to further relevant information from a number of sources, including industry and government websites, official registers and government publications.

Following the approval of this maize in the EU, the consent holder will approach key stakeholders and key networks of stakeholders of the product (including international grain traders, maize processors and users of maize grain for animal feed) and inform them that the product has been authorised. The consent holder will request key stakeholders and networks for their participation in the general surveillance of the placing on the market of this maize, in accordance with the provisions of Directive 2001/18/EC and the consent. Key stakeholders and networks will be requested to be aware of their use of this maize and to inform the consent holder in case of potential occurrence of any unanticipated adverse effects to health or the environment, which they might attribute to the import or use of this product. Appropriate technical information on MON 87419 will be provided to them.

Where there is scientifically valid evidence of a potential adverse effect (whether direct or indirect), linked to the genetic modification, then further evaluation of the consequence of that effect should be science-based and compared with available baseline information. Relevant baseline information will reflect prevalent use practices and the associated impact of these practices on the environment. Where scientific evaluation of the observation confirms the possibility of an unanticipated adverse effect, this would be investigated further to establish a correlation, if present, between the use of MON 87419 and the observed effect. The evaluation should consider the consequence of the observed effect and remedial action, if necessary, should be proportionate to the significance of the observed effect.

(e) Reporting the results of monitoring

In accordance with Regulation (EC) No 1829/2003, the authorisation holder is responsible to inform the EC of the results of the general surveillance. If information that confirms an adverse effect of MON 87419 and that alters the existing risk assessment becomes available, the authorisation holder will immediately investigate and inform the EC. The authorisation holder, in collaboration with the EC and based on a scientific evaluation of the potential consequences of the observed adverse effect, will define and implement management measures to protect human and animal health or the environment, as necessary. It is important that the remedial action is proportionate to the significance of the confirmed effect.

The authorisation holder will submit an annual monitoring report including results of the general surveillance in accordance with the conditions of the authorisation. The report will contain information on unanticipated adverse effects, if any, that have arisen from handling and use of viable MON 87419.

The report will include a scientific evaluation of the confirmed adverse effect, a conclusion of the safety of MON 87419 and, as appropriate, the measures that were taken to ensure the safety of human and animal health or the environment. The report will also clearly state which parts of the provided information are considered to be confidential, together with a verifiable justification for confidentiality in accordance with Article 30 of Regulation (EC) No 1829/2003. Confidential parts of such report shall be submitted in separate documents.

13. DETECTION AND EVENT-SPECIFIC IDENTIFICATION TECHNIQUES FOR THE GENETICALLY MODIFIED PLANT

The presence of the *dmo* and *pat* genes and the DMO and PAT proteins can be identified by employing different techniques. PCR can identify the inserted nucleotide sequence, while the DMO and PAT proteins can be detected, by optimised tissue extraction, standardised electrophoretic blotting and immunodetection methodologies.

A MON 87419-specific PCR-based assay allowing the identification and quantification of MON 87419 has been provided to the Joint Research Centre (JRC)[1], acting as the European Union Reference Laboratory for GM Food and Feed (EU-RL-GMFF).

14. INFORMATION RELATING TO PREVIOUS RELEASES OF THE GENETICALLY MODIFIED PLANT (FOR ENVIRONMENTAL SAFETY ASPECTS)

14.1. History of previous releases of the genetically modified plant notified under Part B of Directive 2001/18/EC or under Part B of Directive 90/220/EEC by the same notifier

(a) Notification number

There is no history of release of MON 87419 in the EU.

(b) Conclusions of post-release monitoring

Not applicable

(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)

Not applicable

14.2. History of previous releases of the genetically modified plant carried out outside the Union by the same notifier

(a) Release country

MON 87419 has been field tested in the US and Puerto Rico since 2011, in Argentina in 2014, in Chile since 2013 and in Brazil since 2015.

(b) Authority overseeing the release

US and Puerto Rico: United States Department of Agriculture (USDA)

Argentina: Secretary of Agriculture, livestock, fishery and feed (SAGPyA) – National Advisory Commission on Agricultural Biotechnology (CONABIA)

Chile: Agriculture and Livestock Service (SAG)

Brazil: National Biosafety Technical Commission (CTNBio)

[1] Joint Research Centre, European Union Reference Laboratory for GM Food and Feed; http://gmo-crl.jrc.ec.europa.eu/ - Accessed on 27 March 2017.

(c) Release site

US: In major maize growing regions

Puerto Rico: Aguadilla, Isabela, Juana Diaz

Argentina: Entre Ríos, Córdoba, Santa Fe, Buenos Aires

Chile: Rengo, San Fernando, Rancagua

Brazil: Cachoeira Dourada-MG, Luis Eduardo Magalhães-BA, Não-Me-Toque-RS, Petrolina-PE, Rolândia-PR, Santa Cruz das Palmeiras-SP and Sorriso-MT

(d) Aim of the release

US/Puerto Rico/Argentina/Chile/Brazil: Regulatory trials, efficacy, yield, breeding and product development.

(e) Duration of the release

US/Puerto Rico/Argentina/Chile/Brazil: One growing season.

(f) Aim of post-releases monitoring

US/Puerto Rico/Argentina/Chile/Brazil: Assessment of volunteers.

(g) Duration of post-releases monitoring

US/Argentina/Puerto Rico: 12 months.

Chile: 6 months.

Brazil: 4 months (irrigated) - 6 months (without irrigation)

(h) Conclusions of post-release monitoring

US/ Puerto Rico/Argentina/Chile/Brazil: In general, no volunteers have been observed since maize is an annual crop. If volunteers occur, practice is to eliminate them manually or chemically to prevent occurrence in subsequent crops.

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

Field-testing provided no evidence that MON 87419 or derived products would be the cause of any adverse effects to human health or to the environment.

REFERENCES

EFSA, 2009. Application (EFSA-GMO-RX-1507) for renewal of authorisation for the continued marketing of existing products produced from maize 1507 for feed use, under Regulation (EC) No 1829/2003 from Pioneer Hi-Bred International, Inc./Mycogen Seeds. The EFSA Journal (2009), 1138, 1-11.

EFSA, 2010. Guidance on the environmental risk assessment of genetically modified plants. The EFSA Journal, 8(11):1879, 1-111.

EFSA, 2011. Guidance on the post-market environmental monitoring (PMEM) of genetically modified plants. The EFSA Journal, 9 (8):2316, 1-40.

EFSA, 2013a. Scientific Opinion on an application from Pioneer Hi-Bred International and Dow AgroSciences LLC (EFSA-GMO-NL-2005-23) for placing on the market of genetically modified maize 59122 for food and feed uses, import, processing and cultivation under Regulation (EC) No 1829/20031 EFSA Panel on Genetically Modified Organisms (GMO). The EFSA Journal, 11(10):3135, 1-104.

EFSA, 2013b. Scientific Opinion on application EFSA-GMO-NL-2011-93 for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. EFSA Panel on Genetically Modified Organisms (GMO). The EFSA Journal, 11(10):3355, 1-30.

EFSA, 2013c. Scientific opinion on applications EFSA-GMO-RX-T25 and EFSA-GMO-NL-2007-46 for the renewal of authorisation of maize T25,1 and for the placing on the market of herbicide-tolerant genetically modified maize T25,2 both for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Bayer CropScience AG. EFSA Panel on Genetically Modified Organisms (GMO). The EFSA Journal, 11(10):3356, 1-30.

EFSA, 2016. Relevance of new scientific evidence on the occurrence of teosinte in maize fields in Spain and France for previous environmental risk assessment conclusions and risk management recommendations on the cultivation of maize events MON810, Bt11, 1507 and GA21. The EFSA Journal, 1-13.

EFSA, 2017a. Scientific Opinion on an application by Dow AgroSciences LLC (EFSA-GMO-NL-2011-91) for the placing on the market of genetically modified herbicide-tolerant soybean DAS-68416-4 for food and feed uses, import and processing under Regulation (EC) No 1829/2003. The EFSA Journal, 15(3): 4719, 1-31.

EFSA, 2017b. Scientific opinion on an application by Dow AgroSciences LLC (EFSA-GMO-NL-2012-106) for the placing on the market of genetically modified herbicide-tolerant soybean DAS-44406-6 for food and feed uses, import and processing under Regulation (EC) No 1829/2003. The EFSA Journal, 15(3): 4738, 1-33.

OECD, 2002. Consensus document on compositional considerations for new varieties of maize (*Zea mays*): key food and feed nutrients, anti-nutrients and secondary plant metabolites. Organization of European Cooperation and Development, Series on the Safety of Novel Foods and Feeds, OECD ENV/JM/MONO (2002) 25, 1-42.