Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on notification B/BE/19/V1 (maize ATR-Hb^{KO}, ATR-A^{KO} & ATM-Ga^{KO}) from VIB under Directive 2001/18/EC

19 March 2019
Ref. SC/1510/BAC/2019_0242

The notification B/BE/19/V1 has been submitted by the VIB to the Belgian Competent Authority (CA) in January 2019 for a request of deliberate release in the environment of genetically modified higher plants for research and development according to Chapter II of the Royal Decree of 21 February 2005.

The title of the notification is: Scientific field evaluation of maize with an impaired DNA-repair mechanism. The purpose of the release is to assess the phenotype of the ATR^{KO} and ATM^{KO} plants under realistic environmental conditions and assess whether abiotic stress leads to measurable DNA damage.

The notification has been officially acknowledged by the CA on 9 January 2019 and forwarded to the Biosafety Advisory Council for advice.
Within the framework of the evaluation procedure, the Biosafety Advisory Council, under the supervision of a coordinator and with the assistance of its Secretariat, contacted experts to evaluate the dossier. Two experts from the common list of experts drawn up by the Biosafety Advisory Council and the Biosafety and Biotechnology Unit (SBB) answered positively to this request.
The experts assessed whether the information provided in the notification was sufficient and accurate in order to state that the deliberate release of the GM maize lines would not raise any problems for the environment, animal or human health in the context of the intended use.

On 28 February 2019, based on a list of questions prepared by the Biosafety Advisory Council, the CA requested the notifier to provide additional information. Answers to the questions were provided on 07 March 2019.

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For the purpose of the scientific evaluation, the following legislation has been considered:
- Annex II (principles for the risk assessment) and annex III (information required in notifications) of the Royal Decree of 21 February 2005
- Commission Decision 2002/623/EC of 24 July 2002 establishing guidance notes supplementing Annex II to Directive 2001/18/EC.

In parallel to the scientific evaluation, the CA made the dossier available on its website for a one-month public consultation as required in the abovementioned Royal Decree. The CA forwarded the list of questions to the Biosafety Advisory Council. The questions of the public tackling biosafety issues of the GM maize under consideration are taken in consideration in the opinion of the Biosafety Advisory Council. Answers to the questions of the public will be send to the CA.

Summary of the scientific evaluation

1. Information related to the recipient or parental plants

Zea mays is an allogamous plant that propagates through seed produced predominantly by cross-pollination. Maize pollen can be collected by honeybees and other insects, however these pollinating insects play a minor role in the cross-pollination of maize plants which relies mainly on wind for the dispersal of its pollen (OECD, 2003[1]). Data on pollen dispersal in maize demonstrated that the levels of cross-fertilisation drop rapidly over the initial meters around the pollen source and that most of the released pollen is deposited within about 30 m of the source (Devos *et al*., 2005[2]). At distances farther than 30 - 50 m from the source, pollen dispersal is very low but not zero. However, vertical wind movements can lift up pollen and distribute it over distances up to kilometers under suitable climatic conditions. In Belgium (and in Europe) there are no sexually cross-compatible wild relatives with which maize can hybridise and form progeny (OECD, 2003). The only recipient plants that can be cross-fertilised by maize are therefore other cultivated maize varieties.

Seed dispersal of individual kernels of domesticated plants are mainly the result of field operations of harvesting the crop and transporting the grain from the harvested fields to storage facilities. Spilled maize seeds can overwinter, germinate and appear in the field as volunteers. However, maize is incapable of sustained reproduction outside the domestic cultivation area as it has lost its ability to survive in the wild due to its long process of domestication (OECD, 2003). Volunteers will only occur after a warm winter period (with no temperatures lower than 0°C for more than 6 to 8 hours) and will be characterised by a low probability of cross-pollination (Grüber *et al*., 2008[3]; Palaudelmàs *et al*., 2009[4]). Given the Belgium weather conditions, volunteers are not likely to occur.

[1] OECD, 2003. Consensus Document on the biology of *Zea mays* subsp. *Mays* (maize). Series on Harmonisation of Regulatory Oversight in Biotechnology (ENV/JM/MONO(2003)11), No. 27:1-49. http://www.olis.oecd.org/olis/2003doc.nsf/LinkTo/NT0000426E/$FILE/JT00147699.PDF

[2] Devos *et al.*, 2005. The co-existence between transgenic and non-transgenic maize in the European Union: a focus on pollen flow and cross-fertilization. Environmental Biosafety Research 4, 71-87.

[3] Grüber *et al*., 2008. Post-harvest gene escape and approaches for minimizing it. CAB International 2008 (http://www.cababstractsplus.org/cabreviews)

[4] Palaudelmàs *et al.*, 2009. Effect of volunteers on maize gene flow. Transgenic Res. 18, 583-594

2. Information on the design and management conditions in the field trial

The field trial will be conducted during one growing season (from May 2019 until October 2019). The surface of the area for cultivation will not exceed 345 m^2.

Prior to complete formation, tassels from the GM maize will be removed by hand in order to prevent the dispersal of GM pollen. Some tassels will be covered by a tassel bag. Once the last leave has been formed, monitoring of upcoming tassels will take place three times a week until all tassels have been removed and will be maintained until September 15. Removed tassels will be transported in closed bags and inactivated.

During harvest, cobs of the GM maize plants will be collected by hand and transported in closed bags to the lab. Material will be inactivated if no longer needed for research. Stems and leaves, except for a few which will be harvested, will be shredded on the field. Roots and the lowest part of the stem will be left in the ground.

After the field trial, the field will be left fallow and ploughed during the next spring.

3. Information related to the genetic modification

The GM maize lines ATR-Hb^{KO}, ATR-A^{KO} & ATM-Ga^{KO} obtained by the CRISPR-Cas9 technology (introduced via *Agrobacterium tumefaciens*-mediated transformation), are subject of this field experiment.

The maize lines ATR-Hb^{KO} and ATR-A^{KO} contain a knocked out *ATR* gene. For ATR-Hb^{KO}, this has been achieved by addition of one basepair (bp); for ATR-A^{KO} by a deletion of 1272 bp. The maize line ATM-Ga^{KO} contains a knocked out *ATM* gene, which has been achieved by the insertion of two additional bp. The *ATR* and *ATM* genes encode for proteins involved in the DNA repair mechanism of the plant.

The three maize lines were obtained using a vector containing the CRISPR-Cas9 genes on a T-DNA construct. The T-DNA construct used for transformation also contains a *bar* gene that served as a marker for the selection of transformants after *Agrobacterium tumefaciens*-mediated transformation. The *bar* gene produces the phosphinotricin acetyl transferase (PAT) enzyme, which acetylates phosphinotricin (also known as glufosinate, the active ingredient of the broad spectrum herbicides), thereby rendering it inactive. The vector backbone contains a spectinomycin resistance marker gene.

Transformed plants were selected on the basis of glufosinate and subsequently backcrossed with B104 and finally selfed to obtain homozygous plants solely containing the mutation (and no vector DNA). The homozygous plants included in the field trial (ATR-Hb^{KO}, ATR-A^{KO} & ATM-Ga^{KO}) were tested for the lack of vector sequences, including the antibiotic resistance marker gene, via their glufosinate sensitivity and via qRT-PCR using several construct-specific primers. These tests confirmed the absence of any vector DNA.

4. Potential risks for the environment, animal or human health associated with the release of the GM maize

The intended changes in the characteristics of maize as a result of the *ATR* and *ATM* gene expression (impaired DNA-repair) are not expected to confer a selective advantage to

survivability. Moreover, the measures taken (removal of tassels and manual collection of cobs) rule out the development and survival of the GM maize in the year(s) after the field trial.

Vertical gene transfer through pollen can virtually be ruled out due to the removal of the tassels.

The possibility of horizontal gene transfer between plants and micro-organisms is considered as a rare event under natural conditions (Keese, 2008[5]). In case gene transfer from the GM maize to micro-organisms would take place and gene expression would occur, negative effects on the environment and humans are not expected. The *ATR* and *ATM* genes, expressing proteins involved in DNA repair in eukaryotes, will not confer a selective advantage to micro-organisms.

Further, it is not expected that the GM maize would have significant effects on organisms (invertebrates, vertebrates and soil micro-organisms) and humans, as no trait that could affect the behaviour or development of organisms via contact or feeding has been integrated. Given the restricted scale of the field trial, any potential effect to organisms and biogeochemical processes - if these would occur - will be of a local and temporal nature. As the release of GM pollen in the environment is prevented, a possible altered allergenicity potential of the transgenic pollen (allergy from maize pollen may occur in case of occupational exposure to high amounts of pollen grains, see e.g. Oldenburg *et al*., 2011[6]) does not form a concern for human health.

5. Information related to the control, monitoring, post-release and waste treatment

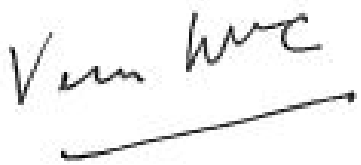
The management measures proposed are considered as sufficient to prevent potential adverse effects to the environment, animal and human health during and after the field trial. The removal (or covering) of any appearing tassel in the transformed line will prevent gene flow by pollen spread. Careful manual harvesting of the cobs and storing them in closed bags will prevent seed dispersal. The seeds and the few collected tassels will be destroyed after analysis.

[5] Keese, P. 2008. Risks from GMOs due to horizontal gene transfer. Environ. Biosafety Res. 7: 123-149.

[6] Oldenburg 2011. Maize pollen is an important allergen in occupationally exposed workers. Journal of Occupational Medicine and Toxicology

Conclusion

Provided that the trials are conducted as described in the dossier, the Biosafety Advisory Council concludes that it is very unlikely that this proposed small scale field trials with GM maize will harm human health, animals or the environment.



Dr. Corinne Vander Wauven
President of the Biosafety Advisory Council

Annex I: Compilation of comments of experts in charge of assessing the dossier B/BE/19/V1 (ref: BAC_2019_0178)

Note on the detection method:

We want to note that the provided protocol is appropriate to detect point mutations via DNA sequencing in ATR-Hb^{KO} and ATM--Ga^{KO} (planted) homozygous material. For the analysis of individual heterozygous plants, e.g. a potential volunteer plant occurring after the field trial, the protocol may raise problems as one needs to rely on a peak shift for the identification of mutants. With this protocol one is unable to verify whether GM pollen from ATR-Hb^{KO} and ATM--Ga^{KO} has contaminated maize occurring in the surroundings. For the latter, usually pooled samples are taken and therefore a more appropriate method that can distinguish with sufficient sensitivity single nucleotide differences needs to be applied (e.g. NGS or digital PCR). Such a type of protocol is not provided.

Compilation of comments of the experts in charge of evaluating notification B/BE/19/V1

Ref. SC/1510/BAC/19_0178

Coordinator: Geert Angenon (VUB)
Experts: Jan Van Doorsselaere (VIVES), Patrick du Jardin (ULg), Nina Papazova (Sciensano, GMOLAB) en Nancy Roossens (Sciensano, GMOLAB)
SBB: Adinda De Schrijver

INTRODUCTION

Dossier **B/BE/19/V1** concerns a notification of the VIB, for deliberate release in the environment of genetically modified higher plants (GMHP) according to Chapter II of the Royal Decree of 21 February 2005.

The notification has been officially acknowledged on 09 January 2019 and concerns a field trial with a maize with an impaired DNA-repair mechanism.

Experts were invited to evaluate the genetically modified organisms considered in the notification as regards their potential impacts on the environment, including human and animal health, and information relating to pre- and post-release treatment of the site.
The comments of the experts are roughly structured as in
- Annex II (principles for the risk assessment) of the Royal Decree of 21 February 2005
- Annex III (information required in notifications) of the Royal Decree of 21 February 2005
- Commission Decision 2002/623/EC of 24 July 2002 establishing guidance notes supplementing Annex II to Directive 2001/18/EC.

Comments sent to the VIB are indicated in grey. It should be noted that all the comments received from the experts are considered in the evaluation of this dossier and in formulating the final advice of the Biosafety Advisory Council.

LIST OF COMMENTS RECEIVED

The comments below have served as a basis for a list of questions that the competent authority forwarded to the notifier with a request to provide additional information. The comments highlighted in grey correspond to the questions/comments selected and sent to the notifier.

1. INFORMATION RELATED TO THE RECIPIENT OR (WHERE APPROPRIATE) PARENTAL PLANTS

(e.g. reproduction, survivability, dissemination, geographic distribution,...)

Have evaluated this section and have no comments/questions: 1 expert

Comment 1

Page 4: it is mentioned that the maize plants will be detasseled; this is in contradiction with p 15 and 17 where it is said that some plants will not be detasseled (G1b and G4). See further

2. INFORMATION RELATED TO THE GENETIC MODIFICATION

(e.g. methods used for the modification, description of the vector,...)

Comment 1

C1 Page 7: off target analysis; provide info about in silico analysis to guarantee specificity. Are there ATR and/or ATM homologues?

C2 Page 9: plasmid; provide a legend and info on the guides

Where are the guides situated? Provide scheme of the gene (exons/introns) and position guides.
The deletion in ATRA is unusual big (1200 bp): did VIB use two guides?

Comment 2

As pointed out by the SBB/BAC, this is the first dossier with CRISPR/Cas9 modified plants and, to the best of my knowledge, no European guidelines are available for the molecular characterization and risk assessment of such genetically-modified plants. However, taking into account the principles and requirements of transgenic plants, the following information might be relevant for the risk assessment of such plants:

1) The risk assessment needs to consider both intended and unintended effect of the genetic modification. Regarding CRISPR/Cas9 edited plants, the design of the guide-RNAs is a critical step to minimize off-target mutations. Little information is provided at this level. The applicant claims that the guide-RNAs were designed in such a way to minimize possible matches with other sites of the maize genome, but which stringency criteria were applied and with which results are worth describing in the dossier. For instance, whether and which possible secondary targets were identified by the bioinformatic analysis would be interesting to know. In case such sites are identified, targeted sequencing in the final GM events could be performed. Discussing possible off targets is of relevance from the point of view of the aim and justification of the trial (probably more than for identifying possible hazards and risks).
2) Out-segregation of the effector molecules Cas9 and guide-RNAs needs to be confirmed. In this dossier both phenotypic characterization via linked herbicide resistance marker

(glufosinate in this dossier) and molecular characterization by PCR allowed to rule out the persistence of these sequences in the final GM plants conducted to the field trialling.

3) Description of the mutation and of the likely expressed peptides resulting from the genetic modification. In two out of the three mutations introduced, single nucleotide additions have been obtained. The consequences of such additions depend on their location in the mutated gene (/ORF). New polypeptides are likely to result from frameshift mutations. As these changes are intentionally introduced into the GM plants, they could be detailed by the application. The same holds true for the intended deletion caused by the third mutation. In case new peptides are produced, bioinformatic analysis could provide insight into their potential allergenicity and toxicity, as it is done for the newly expressed polypeptides in transgenic GMOs. However, extensive bioinformatic analysis of the newly expressed peptides is not required within the scope of field trials, hence this information should not be demanded for CRISPR/Cas9-edited plants.

Comment 3:
In order to allow detection of the modified lines, it would be relevant to know if the induced mutations occur naturally in maize.

Note SBB: We want to note that for 'ordinary' Part B notifications, one

1. needs to give an estimation of the copy number. In line with this, we think it is worthwhile to ask for information on the number of ATR and ATM (homologue) genes in maize.
2. does not need to analyse which maize genes have been interrupted due to the insertion of a new DNA construct. In line with previous field trial evaluations we consider that information on which off-target mutations have occurred (through targeted sequence analysis), should not be asked in the early stages of development.

3. INFORMATION RELATED TO THE GENETICALLY MODIFIED PLANT

3.1. Information related to the traits and characteristics, which have been introduced or modified

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
We are dealing here with a special case, where the intended modification is to enhance the rate of stress-induced mutations. In other words, the intended effect of the targeted mutations is to enhance the rate of non-targeted mutations. However, as described by the applicant, previous in vitro experiments have indicated that reduced growth is observed upon chemical treatments diminishing the rate of DNA replication, but not in greenhouse conditions, suggesting that detrimental effects become evident in specific conditions only. Overall, the available information suggests a possible reduction of fitness of the GM plant, as compared with the parental genotype, but no increase that might impact the persistence and invasiveness of the plant, which is a key issue in the environmental risk assessment.

3.2. Information on the molecular characteristics of the final GMO

(e.g. number of copies of the transgenes,...)

Comment 1
D1 and D2: it is mentioned that no donor material is present in the crispr cas lines.

It is mentioned in Bijlage 2 that (q)PCR was performed to demonstrate absence of backbone; these data are not shown/ Please provide data demonstrating the absence of donor material.

Comment 2
Many of the characteristics of transgenic GM plants subjected to molecular analysis (e.g. copy number, integrity, expression of the introduced sequences) are not applicable to edited GM plants.

3.3. Information on the expression (of the insert)

(e.g. parts of plants where the insert is expressed, (expected) expression of the insert during the lifecycle of the plant,...)

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
Not applicable.

3.4. Information on how the GM plant differs from the recipient plant

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
See comments in 3.1.

3.5. Genetic stability of the insert and phenotypic stability of the GMHP

Comment 1
Page 12 D5 and page 13 D10: it is mentioned that the lines do not show a “fenotype” in the greenhouse; this is contradictory with page 15 F1 which states that … that VIB wishes to investigate whether the lines show the same modified phenotype as in the greenhouse….

Comment 2
The applicant explains that no genetic instability is expected for the introduced genetic modification, which should behave like any other mutations. It is also mentioned that the phenotypic stability will be studied during the field trial. I do not understand which phenotypic traits will actually be followed. If we refer to section D4a), no phenotype distinguishing the GM plant from the reference line B104 is well established, a delay of flowering being the only expected phenotype based on greenhouse observations. The trial can hardly study at the same time which phenotypic trait characterizes the GM plant and how stable is this property. Furthermore, whether the genetic/phenotypic stability can be studied at all in only one generation of field-trialled material is questionable. The applicant should clarify these issues.

Note SBB and coordinator: Information on which phenotypic characteristics will be measured in the field, is not a risk assessment-related question.

3.6. Any change to the ability of the GMHP to transfer genetic material to other organisms

Have evaluated this section and have no comments/questions: 2 experts

3.7. Information on any toxic, allergenic or other harmful effects on human health arising from the genetic modification

Comment 1
Page 13 D7: effect of environmental stress at DNA level; see further

Comment 2
The increased rate of mutations expected in the GM plants potentially leads to new peptides and the accumulation of intermediate metabolites, both raising potential safety issues. However, this corresponds to an increased frequency of events which spontaneously happen in the maize genome and have not raised any safety issues so far. Furthermore, the field trial is a fundamental research aiming at quantifying the impact of environmental stress on the frequency of mutations and the role of the knocked-out genes at that level. In conclusion, no further information on the potential toxic or allergenic constituents of the GM plant seems necessary.

3.8. Information on the safety of the GMHP to animal health, particularly regarding any toxic, allergenic or other harmful effects from the genetic modification, where the GMHP is intended to be used in animal feedstuffs

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
See comments under 3.7 above.

3.9. Mechanism of interaction between the genetically modified plant and target organisms (if applicable)

Have evaluated this section and have no comments/questions: 2 experts

3.10. Potential changes in the interactions of the GMHP with non-target organisms resulting from the genetic modification

Have evaluated this section and have no comments/questions: 1 expert

3.11. Potential interactions with the abiotic environment

Have evaluated this section and have no comments/questions: 1 expert

3.12. Description of detection and identification techniques for the GM plant

Have evaluated this section and have no comments/questions: 1 expert

Comment 1:
We want to note that the provided protocol only allows detection of nucleotide modifications in (planted) homozygote material. With this protocol one is unable to check heterozygous material for nucleotide modifications, if requested. For example, one will not be able to verify whether GM pollen have contaminated maize occurring in the surroundings. For the latter, more appropriate methods that can distinguish with sufficient sensitivity single nucleotide differences need to be applied (e.g. NGS or digital PCR). We welcome any feedback on this observation.

Annex 9 gives the sequences of the oligonucleotide primers proposed for the PCR detection of the modified ATR and ATM genes, but the exact map locations of these primers are not indicated. The position of the primers and their targets have to be illustrated by a figure. Further, the amplicon sequence should be provided to be able to analyse the sequence. Finally, data should be provided to demonstrate that the method is working (e.g. PCR with gel and visualisation of the PCR fragment, sequencing results and analysis, such as a BLAST or other type of sequence alignment).

3.13. Information about previous releases of the GM plant, if applicable

Have evaluated this section and have no comments/questions: 1 expert

4. INFORMATION RELATING TO THE SITE OF RELEASE

(e.g. description of the site ecosystem, presence sexually compatible species, proximity of protected areas, ...)

Have evaluated this section and have no comments/questions: 2 experts

5. INFORMATION RELATING TO THE RELEASE

(e.g. purpose of release, dates and duration of the release, methods for preparing and managing the release site, number of plants, ...)

Comment 1

Purpose of the release:

It is mentioned that the aim of the trial is to monitor the GMO plants in the field.

It is advisable that VIB provides information on the “fenotype observed in the greenhouse”, the methods that will be used to analyze the plants from the trial (NGS for mutations?). It is not clear which information VIB wants to obtain from this trial. Also mentions … a modified phenotype while it was stated several times that the lines do not show a phenotype as compared to WT plants.

The effect of …. environmental pollution effects and extreme weather conditions … (page 15 F1)

Environmental pollution: the GMO maize will be planted in a classic non-polluted field. What does VIB mean by environmental pollution? This needs more explanation. Also VIB is hoping for “extreme weather conditions”? This cannot be controlled in the field, while in the greenhouse, conditions such as light and drought and other stresses can be well regulated.

Note SBB and coordinator: The specific analyses and methodologies that will be used during the trial and the information the applicants want to obtain from this trial, are not relevant for risk assessment; consequently, there is no need to ask for further clarification.

Comment 2

The applicant proposes to cultivate the plot with commercial maize the year after the trial, based on the absence of any regrowth of GM maize following previous releases since 2012. However, I have no access to the information about the post-release operations in the previous trials and on how the monitoring of the possible regrowth was performed, hence it is difficult to validate the claims of the applicant.

Note SBB: The monitoring reports of B/BE/11/V4 and B/BE/14/V2 state that no volunteers were found in years following the trial.

6. INFORMATION RELATED TO THE RISKS FOR THE ENVIRONMENT

6.1. Information on the likelihood for the GMHP to become more persistent than the recipient or parental plants or more invasive

Have evaluated this section and have no comments/questions: 2 experts

6.2. Information on the selective advantage or disadvantage conferred to the GMHP

Have evaluated this section and have no comments/questions: 2 experts

6.3. Information on potential of gene transfer to other sexually compatible plant species under conditions of planting and its consequences

Have evaluated this section and have no comments/questions: 2 experts

6.4. Information on the environmental impact resulting from direct and indirect interactions of the GMHP with target organisms

Have evaluated this section and have no comments/questions: 2 experts

6.5. Information on the environmental impact resulting from direct and indirect interactions of the GMHP with non-target organisms, including herbivores, parasites, symbionts...

Have evaluated this section and have no comments/questions: 2 experts

6.6. Information on possible effects on human health resulting from potential direct and indirect interactions of the GMHP and persons working with, coming into contact with or living in the vicinity of the GMHP release

Have evaluated this section and have no comments/questions: 2 experts

6.7. Information on possible effects on animal health and consequences for the food/feed chain resulting from consumption of the GMO and any product derived from it, if it is intended to be used as animal feed

Have evaluated this section and have no comments/questions: 2 experts

6.8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s)

Have evaluated this section and have no comments/questions: 2 experts

6.9. Information on environmental impact of the specific cultivation, management and harvesting techniques used for the GMHP where these are different from those used for non-GMHPs

Have evaluated this section and have no comments/questions: 2 experts

7. INFORMATION RELATED TO CONTROL, MONITORING, POSTRELEASE AND WASTE TREATMENT

7.1. Precautions taken

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
G1b page 16 and G4 page 17: why will some plants not be detasseld? (… paper bag…). Is there a reason to assume that the lines will not produce pollen?
Referee suggests to detassel all plants (in order to avoid dispersal of pollen)

7.2. Information on methods for post release treatment of site

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
See previous comment under section 5.

7.3. Information on post release treatment methods for the GM plant material, including wastes

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
Page 17 G3: it is mentioned that … stem and leaves are not reproductive and therefore not GMO….; according to EU legislation stems and leaves are considered as GMO (due to the method used to generate the plants) but it can be said that these plant residues do not pose harm for the environment since these plant residues will break down.

7.4 Information related to monitoring plans and the detection techniques

Have evaluated this section and have no comments/questions: 2 experts

7.5. Information on the emergency plan(s) proposed by the notifier

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
The only information resembling and “emergency plan” is section 7. “Afwijkingen” in Bijlage 5. “Proefprotocol” but I consider this as sufficient.

7.6. Information on methods and procedures to protect the site

Have evaluated this section and have no comments/questions: 1 expert

Comment 1
I could not find this information in the dossier.

Note SBB: information can be found in G.6

8. OTHER INFORMATION

Comment 1
guidelines for the risk assessment of CRISPR-edited GM plants are lacking. It might be useful to see whether such information is available from other competent authorities in EU (and/or from EFSA or ISPRA JRC?).