GENETICALLY MODIFIED ORGANISMS UNIT

SCIENTIFIC PANEL ON GENETICALLY MODIFIED ORGANISMS

MINUTES OF THE 147th MEETING – OPEN TO OBSERVERS

Held on 1-2 December 2021, TELE/WEB

(Agreed on 23 December 2021)

Participants

- Panel Members:

Jean-Louis Bresson, Tamas Dalmay, Ian Dewhurst, Michelle Epstein, Leslie George Firbank, Philippe Guerche, Jan Hejatko, Francisco Javier Moreno, Ewen Mullins, Hanspeter Naegeli, Fabien Nogué, Nils Rostoks, Jose Juan Sanchez Serrano, Giovanni Savoini, Eve Veromann and Fabio Veronesi

- European Commission:

DG SANTÉ : Ilaria Ciabatti, Alexandre Huchelmann, Juliette-Marie Margueritte and Olga Orlova

- EFSA:

GMO Unit: Ana Afonso, Michele Ardizzone, Giuseppe Condorelli, Giacomo De Sanctis, Silvia Federici, Antonio Fernández Dumont, Andrea Gennaro, Paschalina Grammatikou, Dafni Maria Kagkli, Anna Lanzoni, Paolo Lenzi, Aleksandra Lewandowska, Franco Maria Neri, Nikoletta Papadopoulou, Pietro Piffanelli, Tommaso Raffaello and Franz Streissl

DATA Unit: José Ángel Gómez Ruiz

SCER Unit: Yann Devos for item 7.1

- Observers:

Esteban Alcalde (Syngenta); Mary beatty (Corteva Agriscience); Jose Antonio Bouzada (Laboratorio Central de veterinaria); Marjan Bovers (COGEM); Stefano Brizzi (BASF); Hermann Broll (BfR); Daniela Mirela Calutu (County Sanitary Veterinary and Food Safety - Division DOLJ); Mark Cassar (Malta Competition and Consumer Affairs Authority (MCCAA); Filip Cnudde (Corteva Agriscience); Lisa Creato (Private person); Ine Criel (BASF); Fabiola Cuevas (Bayer); Tsveta Georgieva (National Center of Public Health and Analyses, Bulgaria); Marzia De Giacomo (Italian Institute of Health); Mihail Valentin Huciu (Romanian Maize Growers Association (APPR); Adinda de Schrijver (Sciensano); Nicolas de Schrijver (Perseus); Tina Demsar (Slovenian National Institute of Biology, Department of Biotechnology and Systems Biology); Tewodros Duressa (Bayer CropScience); Edyta Gruda (WIORIN); Youssef El Quadrhiri (ANSES); Vincenzo Ferrantelli (Istituto zooprofilattico sperimentale della Sicilia); Iva Fiolic (Croatian Institute of Public Health); Hrvoje Fulgosi (Institute Rudjer Boskovic); Tao Geng (Bayer); Vasiliki Giatrakou (Jotis SA); Taha Hosni (Nuseed); Konstantin

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf

Ivanov (Corteva Agriscience); Margarita Karavangeli (Hellenic Food Authority); Katharina Kawall (Fachstelle Gentechnik und Umwelt); Gijs Kleter (Wageningen Food Safety Research); Petra Kostolaniova (CropLife Europe); Jasna Kureljusic (Institute of Veterinary Medicine of Serbia); Gaston Legris (Corteva Agriscience); Zuzana Malinova (Czech Ministry of Agriculture); Ugo Marchesi (IZSLT); Maica Martinez (BASF); Matteo Lener (ISPRA); Piotr Medrzycki (CREA); Eric Meunier (Inf'OGM); Andrea Moglia (University of Torino); Anna Rita Mosetti (Italian ministry of health); Concepcion Novillo (Bayer CropScience); Simona Pileviciene (NFVRAI); Nancy Podevin (Pioner Overseas Corporation); Bert Popping (FOCOS); Yolande Proroga (IZS Mezzogiorno); Roam Raemaekers (Syngenta); Wolfram Reichnbecher (Federal Agency for Nature Conservation, Germany); Federica Roman (Laemmegroup Srl); Silvio Salvi (University of Bologna); Luc Schuler (Ministry of health, Luxembourg); Valerie Sert (Corteva Agriscience); Greet Smets (Perseus); Joann Sy (POLLINIS); Cynthia van Rijn (National Institute for Public Health and the Environment); Elisa Vendramin (Council for Agricultural Research and Economics, Italy); Kitty Verhoeckx (UMCU); Rong Wang (Bayer); Sasi Wilhelmi (BASF).

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Jose Sanchez Serrano for the 2nd day of the Plenary meeting.

2. Presentation of Guidelines for Observers

The Chair presented the guidelines for observers for open plenary meetings.[2]

3. Adoption of agenda

The agenda was adopted without changes.

4. Declarations of Interest of Panel members

In accordance with EFSA's Policy on Independence[3] and the Decision of the Executive Director on Competing Interest Management[4] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

5. Report on written procedures since the 146th GMO Plenary meeting

Since the 146th Plenary meeting, two outputs have been adopted by written procedure:

5.1 Minutes of the 146th Plenary meeting

[2] https://www.efsa.europa.eu/sites/default/files/observersguidelines.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[4] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

The minutes of the 146th Plenary meeting, held online on 29-30 September 2021 were adopted by written procedure and published on 14 October 2021.[6]

5.2 Application for placing on the market of genetically modified maize NK603xT25xDAS-40278-9, in accordance with Regulation (EC) No 1829/2003 (EFSA-GMO-NL-2019-164)[5]

The draft opinion was submitted for adoption at the 146th Plenary meeting held on 29-30 September 2021.[6] It was agreed to adopt the opinion by written adoption after submission by the applicant of additional information (i.e. clarification on additional data). The text of the scientific opinion was adopted by written procedure on the 28 October 2021. The scientific opinion was published on the EFSA website and in the EFSA Journal.

6. Scientific topics for discussion

6.1 Application for renewing the authorisation for the placing on the market of food and feed products containing, consisting of or produced from genetically modified soybean A5547-127 and products other than food and feed containing or consisting of it with the exception of cultivation, authorised under Regulation 1829/2003 (Commission Decision (2012/81/EU) (EFSA-GMO-RX-020)[7]

Soybean A5547127 was developed to confer tolerance to glufosinate ammonium containing herbicides. Following a thorough risk assessment by EFSA, the placing on the market of soybean A5547127 for products containing, consisting of, or produced from this GM soybean, excluding cultivation in the EU, was authorised by Commission Implementing Decision 2012/81/EU and Commission Implementing Decision (EU) 2019/1195 amending Decision 2012/81/EU. In 2020 the applicant asked the European Commission to renew the authorisation for the placing on the market of soybean A5547127 and submitted application EFSA-GMO-RX-020 in support of their request. The GMO Panel assessed application EFSA-GMO-RX-020 in accordance with Articles 11 and 23 of Regulation (EC) No 1829/2003 and the relevant EFSA guidelines. Additional data requested on DNA sequence quality is still to be submitted by the applicant.
The GMO Panel reviewed the current text, where appropriate. It was agreed that, once the missing information will be provided, the GMO Panel will assess it.

6.2 Scientific opinion on the Evaluation of existing guidelines for their adequacy for the food and feed risk assessment of genetically modified plants obtained through synthetic biology)[8]

The activities of the working group on synthetic biology (SynBio) genetically modified plants (GMPs) – food and feed were presented at the 146th Plenary meeting.[6] The terms of reference and the applied methodology to address the mandate were summarised. The draft opinion covers the risk assessment aspects for the food and feed from GMPs developed via SynBio approach and evaluates the adequacy of the existing food and feed guidelines using case studies. It complements the opinion published in 2021 on Molecular Characterization and environmental risk assessment for synthetic biology genetically modified plants[9]

[5] https://open.efsa.europa.eu/questions/EFSA-Q-2019-00808
[6] https://www.efsa.europa.eu/en/events/event/146th-plenary-meeting-gmo-panel
[7] https://open.efsa.europa.eu/questions/EFSA-Q-2021-00003
[8] https://open.efsa.europa.eu/questions/EFSA-Q-2021-00052
[9] https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2021.6301

The text of the draft opinion was presented and discussed. Minor changes were introduced in the draft text and the GMO Panel endorsed the scientific opinion for public consultation.

The endorsed draft will be launched for public consultation at the beginning of 2022 and will be accessible via the dedicated page[10] on the EFSA website.

6.3 Application for authorisation of genetically modified maize DP-023211-2 in accordance with Regulation (EC) No 1829/2003 by Pioneer Overseas corporation (EFSA-GMO-NL-2019-163)[11]

The scope of the application EFSA-GMO-NL-2019-163 covers the import and processing for all food and feed uses of maize DP-023211-2 in the European Union. DP-023211-2 maize expresses DvSSJ1 double-stranded RNA (dsRNA) and the IPD072Aa protein, both for control of corn rootworm pests, as well as the phosphinothricin acetyltransferase (PAT) protein for tolerance to glufosinate herbicide and the phosphomannose isomerase (PMI) protein as a selectable marker.

Scientific officers of the GMO Unit presented relevant elements of the risk assessment of maize DP-023211-2.

Genetically modified maize DP-023211-2 was developed in 2 sequential transformation steps, which allow for the insertion of the expression cassettes in a precise site in the host genome. This approach is defined as site-specific integration (SSI). During the risk assessment of maize DP-023211-2 all vectors used for both transformation steps were considered and evidence was used by the GMO Panel to confirm that the undesirable genetic elements from both the first and the second transformations were not present in the final event.

The DvSSJ1 dsRNA and the IPD072Aa protein expressed in maize DP-023211-2 confer resistance to certain coleopteran pests. IPD072Aa is a novel insecticidal protein which is not a *Bacillus thuringiensis* (*Bt*) toxin (Cry and Vip) and could mitigate the problem of emerging resistance to *Bt* proteins (Cry and Vip). The mode of action of *Bt* toxins has been extensively described, but there is less information about IPD072Aa to date. During the risk assessment of maize DP-023211-2 the GMO Panel has requested more evidence on the mode of action of IPD072Aa. This information will also be crucial to predict interactions of IPD072Aa protein with other newly expressed proteins as in the case of stacks. The dsRNA DvSSJ1 decreases DVSSJ1 protein translation in the target insects, which leads to intestinal damage, growth inhibition and increased mortality. The preliminary evaluation suggests that the DvSSJ1 dsRNA is specific to insects, there are no chemical modifications that would increase its stability in the human and animal gastrointestinal tract, and similarly to other not coding RNAs commonly introduced by the diet would be rapidly degraded and encounter barriers to cellular uptake.

Further discussion is needed to conclude the risk assessment of this application.

6.4 Scientific Opinion of the GMO Panel with recommendations for future development of allergenicity risk assessment)[12]

The Scientific Opinion on development needs for the allergenicity and protein safety assessment of food and feed products derived from biotechnology was presented to the Panel members for discussion and potential adoption.

The scientific opinion focuses on 1) improving the allergenicity risk assessment for products derived from biotechnology, 2) defining knowledge gaps, 3) determining how new basic research findings and technological developments can improve the current risk assessment methodology, and 4)

[10] https://www.efsa.europa.eu/en/calls/consultations
[11] https://open.efsa.europa.eu/questions/EFSA-Q-2019-00807
[12] https://open.efsa.europa.eu/questions/EFSA-Q-2020-00316

prioritizing basic research funding. The scientific opinion was adopted by the Panel and will be published on the EFSA website and in the EFSA Journal at the beginning of 2022.

7 Feedback from the Scientific Committee/the Scientific Panels, EFSA, the European Commission

7.1 Scientific Committee and other Scientific Panel(s) including their Working Groups

The Chair of the GMO Panel reported on discussions at the last Scientific Committee meeting and ongoing EFSA activities.[13]

The Panel members were also updated on the activities on the EC mandate on plants developed through cisgenesis and intragenesis[14] that are ongoing in the recently established working group.[15]

The Panel members were informed that the CompERA WG[16] is currently working on the EC mandate[17] requesting EFSA to update its technical report (2016)[18] on the 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.

7.2 EFSA including its Working Groups/ Task Forces

None

7.3 European Commission

The representatives of the European Commission (EC) informed the GMO Panel on their on-going activities, including approval procedures for applications for which the GMO Panel has delivered a scientific opinion.

8 Other scientific topics for information and/or discussion

8.1 Presentation of the outcome of the contract on "Verification of the compliance to quality standards (GLP and ISO) of studies submitted in GMO dossiers" NP/EFSA/GMO/2020/01

In 2020 EFSA awarded Pharma Quality Europe (PQE) a contract to support the verification of the compliance to GLP and ISO quality standards of studies submitted in Genetically Modified Organism (GMO) dossiers. Two main tasks were requested (1) to provide an overview of the quality of GMOs studies in applications submitted under the Regulation (EU) 503/2013 and (2) to provide recommendations. A representative of PQE reported the main conclusions of their activities that identified how all the assessed studies comply with the expected Quality Standard. The contractor provided recommendations for evaluation of the quality compliance. The PQE report does contain sensitive data related to the assessed application and will not be published.

[13] https://www.efsa.europa.eu/en/events/event/106th-plenary-meeting-scientific-committee
[14] https://open.efsa.europa.eu/questions/EFSA-Q-2021-00361
[15] https://www.efsa.europa.eu/en/science/scientific-committee-and-panels/gmo#working-groups
[16] https://www.efsa.europa.eu/sites/default/files/wgs/gmo/gmocompera2019.pdf
[17] https://open.efsa.europa.eu/questions/EFSA-Q-2021-00557
[18] https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2016.EN-1094

9 Questions from and answers to Observers

Observers were invited to submit questions to the GMO Panel at the time of registration. EFSA received the following questions ahead of the meeting:

NUMBER	QUESTION	ANSWER
1	DP-Ø23211-2 maize was created using site-specific integration (SSI). The use of SSI for targeted transgene insertion has advantages compared to random transformation by allowing the ability to pre-select the insertion location to avoid endogenous gene disruption and pre-test the genomic location for agronomic neutrality. Does EFSA take into account that the SSI approach can simplify risk assessment of the final event intended for commercialization as it concerns potential for insertional effects? Intermediate plant lines used to create SSI events are not intended for commercialization since GM food and feed comes from the final commercial event DP-Ø23211-2 maize.	EFSA GMO Panel conducts the risk assessment applying the principles laid down in the Regulation (EU) 503/2013. Following communication with EC in the case of GM plants obtained by SSI methodology, risk assessment of the information provided by the applicant is carried out regardless of the methodology used to achieve the desired transformation(s). The EFSA GMO Panel has published the SDN3 opinion (2012) where it was highlighted that in such an approach, a targeted integration should allow for a simplified risk assessment, when the insertion is targeted to a genomic site known for not rising safety concerns (i.e. previously characterized as such). In this particular case, the insertion site has not been previously characterized, but even if so, the GMO Panel does not identify any datasets that are not needed for the RA of this application. Therefore, the GMO Panel has to perform a complete risk assessment of the GM plant, considering all genetic elements inserted following both transformation events, according to the guidelines.
2	1) To what extent is the "GMO" in the Panel's name being influenced by the current discussion on the remit of GMO legislation? Could the Panel in future perhaps have to deal with other types of biotechnology not defined as GM? 2) As regards allergenicity, it appears that the methodology applied to newly expressed proteins in GMOs is now being extrapolated to novel foods (e.g., bioinformatics applied to the genome/transcriptome/proteome of novel food organisms, with 100s or 1,000s of new proteins). Is there any cross-talk with the NDA Panel on this?	1) The GMO Panel name is defined in the GFL (reg 178/2002/EC). A possible change of the Panel's name is currently not under discussion. 2) Please let us reassure that cross-talks exist between EFSA Panels. EFSA organised a workshop on allergenicity assessment (prediction) in June 2021 where these and other aspects were discussed. Members of the Working Groups of NDA and GMO Panels participated. Currently the only

		internationally accepted threshold used for bioinformatics analysis is the one defined by Codex Alimentarius (2003-2009). Some authors argue that the current approach is highly conservative and appears to lead to a high number of false-positive identifications. While others point that there are also studies reporting experimental IgE cross-reactivity between proteins despite a very low sequence identity, even below thresholds defined by Codex Alimentarius. In the near future, more recent advanced bioinformatic tools will provide new opportunities to develop novel approaches that reduce uncertainties and improve allergenicity prediction.
	3) Food flavours appear to be the 1st commercial synthetic biology food products from microorganisms but could fall outside the scope of GM food legislation. Is the Panel aware of this novelty?	3) Item 6.2 in draft agenda of the GMO Panel is on the assessment of adequacy of existing EFSA Guidance to cover food and feed risk assessment aspects plants developed through synthetic biology (SynBio). This mandate is a part of an overarching activity covering not only SynBio plants but also GM microorganisms. EFSA did not receive any application of this type so far.

In addition to the questions referred to above, observers could also pose questions during the meeting. Questions received (exact quote from web-streamers) and replies given by Panel member or GMO Unit staff are reported in the table below.

AGENDA ITEM	QUESTION	EFSA/EC REPLY
6.1	This is one out of many GMOs with PAT-based herbicide tolerance as newly introduced trait. What prospects are there for a "light" version of the (re-)assessment of such very familiar modifications?	Although the trait expressed by the product to be renewed has been assessed in many other applications, the applicant is requested to submit data in according to Regulation (EU) No 503/2013, the EFSA guidance for renewal applications of genetically modified food and feed (EFSA GMO Panel, 2015)[19] and the EFSA submission guidance on renewal applications (EFSA, 2019)[20].

[19] https://www.efsa.europa.eu/en/efsajournal/pub/4129
[20] https://www.efsa.europa.eu/en/supporting/pub/en-1668

6.2	The suggestion to choose a safe chassis early in the development aligns with the "safe by design" approach (as also discussed in a Dutch proposal to the 2 OECD Working Parties on biosafety of biotechnology). Would the EFSA GMO panel & unit staff be available for any activities to instil a "safety culture" amongst developers and other stakeholders involved?	Selecting safe-by-design organisms and genetic constructs is a strategy encouraged by EFSA during various interactions with stakeholders, e.g. during applicant meetings.
6.2	For the gluten-adjusted wheat example, I am not aware this was complex nor that modelling was utilized (merely standard bioinformatic tools), so can it be clarified why this is considered SynBio.	The gluten-free wheat is one of the case studies identified by the GMO Panel during the activities on the EC mandate on the evaluation of existing guidelines for their adequacy for the molecular characterisation and environmental risk assessment of genetically modified plants obtained through synthetic biology (EFSA GMO Panel, 2021).[21] This case study was selected because it is likely to require synthetic biology approaches to correctly identify all gliadins and glutenins in the hexaploid genome of bread wheat and to identify an engineering strategy that introduced mutations of the correct nature and positions in each gene. Although plants with a small number of mutations have already reached the market, the large number of mutations required to achieve such gluten-free wheat is far beyond any plant previously assessed.
6.2	Following up on the vitamin B12 maize case study: To what extent is the possibility considered that with many genes involved there will also be greater chance of a mutation occurring e.g. in the enzymes catalyzing intermediate biosynthesis. For example, could the toxicity of the intermediate be an issue?	Aspects related to the molecular characterisation of this case study were previously addressed (EFSA GMO Panel, 2021). The GMO Panel considered relevant this case study to address food and feed risk assessment aspects for its complexity, including: the multiplicity of newly introduced genes and consequently the number of enzymes newly expressed; the complexity of the introduced metabolic pathway and the potential impact of such enzymes (and their combination) on the plant metabolic pathways; and the *de novo* presence of Vitamin B12 as compared to conventional maize. The high number of proteins newly expressed in this case study would challenge the current strategy for the

[21] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2021.6301

		toxicological assessment of new proteins, calling for new strategies and methods to overcome issues and strengthen the overall assessment (e.g. *in silico* toxicity predictive tools and *in vitro* studies). The GMO Panel considers that the existing guidelines would be adequate to assess the impact of vitamin B12 on food and feed safety and nutrition, and to identify possible unintended effects induced by the genetic modification. The GMO Panel also remarks that information from the SynBio product design and optimization could support the identification of potentially hazardous unintended effects.
6.2	Production of vitamin B12 occurs at an industrial level via the use of bacteria. Can anything be learned from this experience, in particular to assess the safety of the novel proteins produced by the GM maize? Has this been considered?	The safety and nutritional assessment of vitamin B12 is addressed *per se* as indicated in the existing guidelines, taking into account the knowledge on this compound, its biological role and dietary intake considerations. However, reconstructing the vitamin B12 pathway in a plant is a highly complex task likely to integrate multiple SynBio approaches to select the most promising iterations; optimising the expression level of each gene including the use of conditional switches to maintain the desired levels and patterns of expression within the plant; metabolic modelling of the cell to identify endogenous genes that prevent the accumulation of the end product. Regarding the newly expressed proteins, information on the use of the gene source organisms in technological processes and on the consumption of the proteins themselves can support the History of Safe Use (HoSU). On the basis of the available information for the vitamin B12 case study, there are insufficient elements supporting a HoSU of both the genes' sources and the newly expressed proteins. The introduced genes in the SynBio plant derive from bacteria (e.g. *Pseudomonas denitrificans*, *Rhodobacter capsulatus*) found primarily in soil and/or surface water. There is no evidence that humans or other animals considered in the food and feed assessments have any significant exposures to these organisms via the diet or other routes.

6.3	Does the precision of the insertion make the assessment lighter on this point. For example, is there lower likelihood of unintended effects? Does this also chime with the conclusions for the SDNs and Synbio opinions?	See reply to question 1 received ahead of the Plenary.
6.3	To the Corteva question: as less unintended effects due to insertional effects are expected which is normally evaluated in the comparative assessment, could this be streamlined	The GMO Panel is required to follow the guidelines laid in the implementing regulation (EU) 503/2013, even though fewer issues related to insertional effects are expected. See reply to question 1. A full bioinformatic dossier is also required, including bioinformatic updates.
6.3	In point 8.1 of the report of the 145th GMO Panel Meeting EFSA highlights the need to treat the products of double transformations with a specific approach. Is this dossier considered as such a double transformation? And can it be clarified what is meant with 'a specific approach'?	This is the first application where the event under assessment has been integrated into the recipient genome using two sequential transformation steps. The event will be assessed as a single event however a specific approach is needed because both transformation steps need to be risk -assessed. The GMO Panel also reminds that the first transformation product might be subsequently used for inserting other events in the landing pads, so it is important to rule out any safety issues at this stage.
6.4	What are the prospects of these recommendations being picked up by research-funding organizations? For example, will EFSA itself initiate research calls and/or will it make the case for their uptake into topics within future Horizon Europe calls?	The opinion will be presented to the EFSA Scientific Committee. EFSA will continue to launch procurement calls related to allergenicity risk assessment aspects. EFSA also provides recommendations for future research to the European Commission to be considered for research funding actions.
6.4	The sliding window approach comes from FAO/WHO 2001 while Codex 2003 and EFSA 2010 allow alternative methods such as full FASTA to be used. What is the scientific rationale to keep on requesting a sliding window approach (EFSA 2010 text: the added value of initial amino acid sequence segmentation into overlapping 80-mers prior to alignment is questionable Codex 2003: more than 35% identity in a segment of 80 or more amino acids (FAO/WHO 2001) or other scientifically justified criteria)	At the moment the sliding window approach is embedded in Codex Alimentarius (2003-2009) and the EFSA guidance documents and regulation, so EFSA is required to use it during risk assessment. However, some authors argue that this approach is very stringent/conservative and prone to false positives. While others point that there are also studies reporting experimental IgE cross-reactivity between proteins despite a very low sequence identity. In the near future, more recent advanced bioinformatic tools will provide new opportunities to develop novel approaches that reduce uncertainties and improve allergenicity prediction.

6.4	Industry welcomes the initiative to modernize the allergenicity assessment. However, given the broader scope of allergenicity assessment (i.e. not only for biotech plants), would it not be more appropriate to frame it under the scope of novel food schemes providing that likely sources of novel food will not be biotech plants?	EFSA agrees that allergenicity assessment is a cross-cutting issue, relevant not only to the work of the GMO but also other Panels. However, different regulated products have specific safety requirements set by relevant regulations. Cross-talks between EFSA Panels exist, e.g. during the recently organised workshop on allergenicity assessment and at ad-hoc working group level.
6.4	Only 1-3% of population carries HLA DQ2 or DQ8 genes has CD. Will the knowledge gap of CD biology be included in the research interest or how the clinic relevance research help?	The prevalence of celiac disease is estimated to be comparable to Ig-related food allergies. Knowledge gaps in the biology of celiac disease should be also of interest. For the clinical relevance, EFSA has recently launched a procurement call as new approaches can be taken into consideration for the ranking of allergens and the development of improved novel strategies for the allergenicity assessment.
7.1	In the previous opinion, it was clear that cisgenic plants are GMOs. Do I understand it correctly that the current mandate is asking what would be proportionate as a RA (when cisgenic plants would not fall under GM legislation)	As specified in the terms of reference of the cisgenesis mandate, the aim is to identify any potential risks related to cisgenic plants, compared to plants obtained through conventional breeding. EFSA will investigate to what extent the current guidelines for GMO risk assessment are applicable for cisgenic plants.
8.1	Would these outcomes & recommendations be amenable to a new self-task for the Panel to develop supplementary instructions to applicants on these issues?	The outcome and recommendations will be taken on board in light of continuous improvement on the quality legal requirements set by Regulation (EU) No. 503/2013. The outcomes and recommendations could be communicated to EFSA Application Desk (APDESK) and the European Commission, so that the instructions for applicants might be improved. However, the report will not be published because it contains sensitive data related to applications.
8.1	How is this exercise connected with the EFSA GLP monitoring programme?	This exercise is under the umbrella of EFSA's GLP -related activities but is not formally a part of the EFSA GLP monitoring programme, which focuses on *a posteriori* monitoring of closed dossiers. In case an issue is identified, the affected studies of the dossier might be subjected to auditing.
8.1	GLP studies performed in the EU are performed in Test Facilities under the GLP monitoring of the National GLP authorities.	Reg (EU) No 503/2013 sets the frame for the quality of studies submitted in GMO dossiers. The presented procurement

	Those authorities are auditing Test Facilities and studies, with specific outcomes and findings. How the outcome of this exercise is or is not connected to that?	supports the GMO Panel in evaluating the compliance to such legal requirement, and to identify possible issues. The previously mentioned EFSA GLP monitoring programme regularly is horizontal to EFSA and involves National GLP authorities on closed dossiers. In addition, EFSA can ask for ad hoc quality assessment of a study by National competent authorities during the risk assessment if quality issues are identified.
9	Was the environmental risk assessment considered in an appropriate way? I can see some underestimated issues like: 1) insecticidal gene expression in the pollen and the risk to pollinators 2) risk of gene drift to wild species and subsequent risks to the stability of ecosystems	The scope of application EFSA is currently assessing is for import, processing, and food and feed uses within the European Union and does not include cultivation in the EU. The environmental risk assessment of GM plants which excludes cultivation focuses on (1) the exposure of microorganisms to recombinant DNA in the gastrointestinal tract of animals fed GM material and of microorganisms present in environments exposed to faecal material of these animals (manure and faeces); and (2) the accidental release into the environment of viable seeds during transportation and/or processing. The issues considered in the questions are more relevant in case of application for cultivation. Moreover, the update on the current activities on Teosinte (see item 7.1) demonstrates how the environmental risk assessment for events authorised for cultivation is carefully considered.

10 Adoption of the minutes and next meeting

The minutes of the current meeting will be adopted by written procedure and will be published at: https://www.efsa.europa.eu/en/events/event/147th-plenary-meeting-gmo-panel-open-observers

The 148th GMO Plenary meeting will be held on 26-27 January 2022 online.