SCIENTIFIC PANEL ON GENETICALLY MODIFIED ORGANISMS

167th Plenary meeting

13th – 14th November 2024
10:00 – 18:00 / 9:00 – 13:00
MINUTES - Agreed on 4 December 2024

EUROPEAN FOOD SAFETY AUTHORITY

Location: Parma, EFSA

Attendees

- Panel Members:
Francisco Barro, Josep Casacuberta (Chair), Pilar Cubas (by tele), Ruud de Maagd, Michelle M Epstein, Thomas Frenzel, Jean-Luc Gallois, Frits Koning, Antoine Messéan, F Javier Moreno, Fabien Nogué, Giovanni Savoini, Alan H Schulman, Christoph Tebbe and Eve Veromann.

- Contractors:
Sian Astley (item 7.3); Guillermo Cebrián Auré (item 7.4), Ivano Eberini (item 7.2), Uliano Guerrini (item 7.2), Clare Mills (item 7.3) and Luca Palazzolo (item 7.2)

- European Commission:
Alexandre Huchelmann, Olga Orlova (by tele day 2) and Mara Sgroi (by tele day 1)

- EFSA:
NIF Unit: Ana Afonso, Michele Ardizzone, Giacomo De Sanctis, Agnès De Sesmaisons (item 7.4), Antonio Fernandez Dumont, Arianna Ferrari, Andrea Gennaro, Tilemachos Goumperis, Sara Jacchia, Dafni Maria Kagkli, Silvija Kološevska, Carlotta Leggieri, Paolo Lenzi, Aleksandra Lewandowska, Vania Mendes (item 7.4) Ana Martin Camargo, Franco Maria Neri, Nikoletta Papadopoulou, Pietro Piffanelli, Tommaso Raffaello, Fernando Rivero Pino (item 7.4), Elena Sánchez Brunete, Reinhilde Schoonjans, Francesco Suriano (item 7.4) and Ermolaos Ververis (item 7.4).

MESE Unit: Jose Angel Gomez Ruiz (item 6.6)

ED Chief Scientist Office: Estefania Noriega Fernandez (item 7.4)

FDP Unit: Elena Abenza Bernal and Claudia Parisi

BIOHAW Unit: Simone Baldassa

RAL Unit: Guzman De Gorostegui De Las Rivas, Rodrigo Mendes, Aminata Ndiaye, Pietro Nicolini, Giuseppe Nucera and Riccardo Romagnoli

- Observers:
See Annex I

1. Welcome and apologies for absence

The Chair welcomed the participants and the observers.
Apologies were received from Albert Braeuning.

2. Presentation of the Guidelines for Observers

The NIF Unit presented the guidelines for observers for open plenary meetings.[1]

3. Adoption of agenda

The agenda was adopted without changes.

1 https://www.efsa.europa.eu/sites/default/files/observersguidelines.pdf

4. Declarations of Interest of Panel members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], 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 procedure since the 166th Plenary

5.1 Agreement of the minutes of the 166th Plenary meeting held on 2nd-3rd October 2024

The minutes of the 166th plenary meeting were agreed by written procedure on 14th October 2024.

6. Scientific outputs for discussion and possible adoption

6.1 Application for authorisation of genetically modified maize DAS1131 submitted under Regulation (EC) No 1829/2003 by Corteva Agriscience GMFF-2021-1530 (AP175) (EFSA-Q-2022-00410)

Maize DAS1131 was produced by *Agrobacterium*-mediated transformation using a single transformation vector to introduce genes encoding the Cry1Da2 and DGT-28 EPSPS proteins to confer resistance to certain susceptible lepidopteran pests, as well as tolerance to glyphosate-based herbicides, respectively.

The scope of the application GMFF-2021-1530 is for food and feed uses, import and processing and does not include cultivation in the European Union.

The GMO Panel revised the draft opinion, and where appropriate, questions were raised and addressed throughout the different sections. It was agreed that the GMO Panel will assess the missing information once it is provided. If no other questions are identified during the assessment, the opinion will be proposed for discussion and possible adoption at one of the upcoming GMO Plenary meetings.

6.2 Mandate on "Protein safety" (EFSA-Q-2023-00664)

Over the last 20 years, the GMO Panel gained considerable experience on the assessment of protein safety. The Panel considers that novel tools and methodologies could be used to strengthen protein safety assessment and that a way forward in this area is possible and necessary. Furthermore, the GMO Panel is facing new challenges related to the protein allergenicity and toxicity assessment of newly expressed proteins. Some applications under assessment by the GMO panel contain numerous newly expressed proteins that in some cases are difficult to assess.

In October 2023, the GMO Panel initiated a self-task mandate to deliver a Scientific Opinion regarding protein safety assessment. For this Scientific Opinion, the GMO Panel considered the experience gained over the last years, new developments in the field, the result of a survey launched on this topic by EFSA at the beginning of 2024 and the outcome of EFSA procurements such as the ones presented in this GMO Plenary meeting under items 7.2, 7.3 and 7.4.

2 http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
3 http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

The progress made on this mandate includes *in silico*, *in vitro* and *in vivo* safety testing. The draft will be proposed for discussion and possible endorsement for public consultation at the upcoming GMO Plenary meeting.

6.3 Mandate on "Mandate on new biotechnology applied to animals (GMA-NGT)" (EFSA-Q-2023-00050)

The GMO Panel, under mandate M-2018-0205, was requested to provide a Scientific Opinion on potential novel hazards and risks from new developments in biotechnology (including synthetic biology and new genomic techniques) applied to animals that may enter the market in the near future, and on the adequacy of the current EFSA risk assessment guidance covering all aspects of molecular characterisation, food/feed safety, welfare and environmental impact. The mandate included the request for a knowledge gathering report to identify known cases of NGT animals for agri/food/feed products. The report is available as EFSA supporting publication (Van Eenennaam, 2023).

The structure of the Scientific Opinion was presented to the GMO Panel. The draft will be proposed for discussion and possible endorsement for public consultation at one of the upcoming GMO Plenary meetings. The mandate deadline for the adoption by the GMO Panel is on the 30th June 2025.

6.4 Application for authorisation of genetically modified MON 94637 soybean in accordance with Regulation (EC) No. 1829/2003 GMFF-2023-21116 (AP188) (EFSA-Q-2024-00054)

Soybean MON 94637 was produced by *Agrobacterium*-mediated transformation using a single transformation vector to introduce genes encoding Cry1A.2 and Cry1B.2 insecticidal proteins conferring protection against lepidopteran pests.

The scope of the application GMFF-2023-21116 is for food and feed uses, import and processing and does not include cultivation in the European Union.

The progress made in the risk assessment by all working groups was presented.

6.5 Application for authorisation of genetically modified sugar beet KWS20-1 in accordance with Regulation (EC) No. 1829/2003 GMFF-2023-14732 (AP184) (EFSA-Q-2023-00378)

Sugar beet KWS20 1 was produced by *Agrobacterium*-mediated transformation using a single transformation vector to introduce genes encoding CP4-EPSPS, DMO and PAT proteins conferring tolerance to glyphosate-, dicamba-, and glufosinate-ammonium-based herbicides respectively.

The scope of the application GMFF-2023-14732 is for import and processing of food and feed produced from sugar beet KWS20-1. The importation of viable material and cultivation in the European Union are not within the scope of this application.

The progress made in the risk assessment by all working groups was presented.

6.6 Application for authorisation of LBFLFK canola import in the European Union submitted under Regulation (EC) No 1829/2003 by BASF Agriculture Solutions (EFSA-GMO-DE-2019-157) (EFSA-Q-2019-00394)

Oilseed rape LBFLFK was produced by *Agrobacterium*-mediated transformation using a single transformation vector to introduce genes encoding fatty acid desaturase and elongase proteins to allow for the synthesis of omega-3 long-chain polyunsaturated fatty acids (LC-PUFAs), including EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), from oleic acid, as well

as an AHAS (acetohydroxyacid synthase) protein to confer tolerance to imidazolinone-containing herbicides.

The scope of the application EFSA-GMO-DE-2019-157 is for food and feed uses, import and processing and does not include cultivation in the European Union.

Due to the need to discuss strictly confidential information, this item was closed to observers. The progress made in the risk assessment by all working groups was presented.

7. Scientific topics for discussion

7.1 Development of risk assessment methodology for RNAi-based GMPs (EFSA-Q-2024-00613)

EFSA has established a risk assessment approach in compliance with the Commission Implementing Regulation (EU) No 503/2013 to assess GM plants designed to induce gene silencing through RNA interference (RNAi), based on available scientific evidence (Pačes et al., 2017; Christiaens et al., 2018; Dávalos et al., 2019) In the frame of the developmental project "Review of risk assessment methodology for RNAi-based GM plants" and related mandate M-2024-00157, EFSA investigated whether updates are needed to improve the current risk assessment methodology based on more recent studies and new evidence from the evolution of the scientific knowledge in this area in the last seven years. The Unit updated the Panel on the progress made and informed that a bioinformatic script was developed to identify plant RNAi off-targets and a EFSA guidance (EFSA-Q-2024-00613) is currently being developed, to be published in the first quarter of 2025.

7.2 Procurement on "i*n-silico* Toxicity" (EFSA-Q-2024-00605)

The outcome report of the EFSA procurement (OC/EFSA/GMO/2021/02 – LOT1), published on the EFSA journal and aiming at developing an *in silico* strategy to predict the toxicity of (novel) proteins was presented. Briefly, commercially available tools predicting protein toxicity based on primary structures were evaluated for their accuracy and usability, using a curated dataset of annotated toxins and non-toxins from UniProt. ToxinPred2 and Toxify emerged as the top performers, showing both high accuracy and suitability for integration into an automated pipeline. An Artificial Intelligence (AI)-based consensus pipeline, integrating results from ToxinPred2, Toxify, and our machine learning models was developed. In addition, recommendations provided in the report included future enhancements of the proposed consensus pipeline to create an independent open-source, user-friendly tool for evaluating the safety of (novel) proteins in food and feed; regular updates of the proposed databases and models; incorporation of 3D structures and in general validation of AI and machine learning models for regulatory uses.

7.3 Procurement on "Allergenicity" (EFSA-Q-2024-00292)

The outcome report of the EFSA procurement (OC/EFSA/GMO/2021/04), published on the EFSA journal aiming at developing novel strategies for predicting allergenicity of innovative/novel proteins was presented. Briefly, a systematic review of allergen molecules in foods listed on EU Regulation together with additional foods known to cause IgE-mediated food allergies in a European region with a prevalence of 0.5%, was undertaken. The best-characterised clinically relevant allergens were identified in peanut, hazelnut, cow's milk, fish and crustacean shellfish with data lacking for allergens from foods such as pecan, lupin and melon. Furthermore, an assessment of *in silico* tools allergenicity prediction found that, whilst many were able to correctly predict allergenicity, none were able to provide an output that could be linked to the clinical relevance. An approach for allergenicity risk assessment was developed that brings together elements of exposure

assessment, combining *in silico*, *in vitro*, and *in vivo* methods. The authors considered that novel tools for assessment of risks of cross-reactive allergies are mature and only require refinement to improve the outputs to inform the allergenicity risk assessment process.

7.4 Procurement on "Processing of protein" (EFSA-Q-2023-00659)

The outcome of the procurement on the processing of novel proteins in food and feed risk assessment, recently published on the EFSA Journal was presented. The safety of novel proteins is routinely evaluated in various regulated areas of the food and feed chain, including genetically modified (GM) crops and novel foods (NFs). This project aimed at mapping food and feed products containing protein from the main GM crops, relevant food categories falling under the NF Regulation, and unconventional feed, together with their production processes and to discuss the effect of these processes on the safety of the corresponding novel proteins. A scoping literature review, an open online survey and a stakeholder workshop were the basis to map products and processes, also including operational conditions for each processing step. Moreover, a systematic literature review, carried out within the project, assisted in the identification of the available evidence on the impact of processing on protein safety.

8. New Mandates

8.1 Applications

- Soybean DBN9004 × DBN8002 GMFF-2024-24650 (AP189)
- (EFSA-Q-2024-00326)
- Soybean GMB151 × DAS-44406-6 GMFF-2024-21774 (AP190)
- (EFSA-Q-2024-00330)
- Maize Bt11 x MIR162 x 1507 x NK603 GMFF-2024-22091 (AP191)
- (EFSA-Q-2024-00558)
- Soybean COR23134 GMFF-2023-21132 (AP192)
- (EFSA-Q-2024-00570)
- Maize MON 87427 × MON 89034 × MIR162 × MON 95275 × MON 88017 GMFF-2024-27058 (AP193)
- (EFSA-Q-2024-00592)
- Maize Bt11 x MIR162 x MZIR098 x DP4114 x NK603 GMFF-2024-22152 (AP194)
- (EFSA-Q-2024-00635)

8.2 Mandates

- Request to provide scientific and technical assistance for a regular horizon scanning to assess new scientific data on plants, animals, microorganisms and products thereof obtained by new genomic techniques. (EFSA-Q-2024-00643)

9. Feedback from the Scientific Committee/ Scientific Panels/EFSA/ EC

9.1 Scientific Committee

The Chair of the GMO Panel reported the discussions at the last Scientific Committee meeting and ongoing EFSA activities.[4] The Chair also informed that the upcoming Scientific Committee will be open to observers.[5]

9.2 European Commission

[4] https://www.efsa.europa.eu/en/events/121st-plenary-meeting-scientific-committee
[5] https://www.efsa.europa.eu/en/events/122nd-plenary-meeting-scientific-committee-open-observers

The representatives of the EC informed the GMO Panel on their ongoing activities, including approval procedures for applications for which the GMO Panel has delivered a scientific opinion.

9.3 Scientific Panel(s) including their Working Groups

The GMO Panel was updated on discussions of transversal relevance that took place in the last working groups molecular characterisation (MC), comparative risk assessment and ERA (CompERA) and food and feed (FF).

10. Any other business

None

11. 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	How does the GMO Panel plan to address the potential environmental impacts of genetically modified organisms, particularly in relation to biodiversity and ecosystem health.	EFSA issued guidance documents on the environmental risk assessment (ERA) of GM plants, GM microorganisms and GM animals. The risk assessment takes into account the level and routes of environmental exposure to the GMO (e.g. for GM plants in relation to the scope of the application: cultivation in the EU vs. import and processing). Several opinions implementing the EFSA approach for cultivation have been released (herbicide tolerance and insect resistance, some examples of GM crops for cultivation maize Bt11 or maize GA21) So far, the only authorised GM plant for cultivation is EU is maize MON810 and no applications for the cultivation of GM plants in EU have been received in the last over 10 years. Maize MON810 is subject to an annual post market environmental monitoring (2022 PMEM report maize MON810) No application for the release of GM microorganisms or GM animals in the environment have been received so far.
2	With a view on the European Commission's upcoming review on innovation and biotechnology, does the Panel also consider possible biogases applications of GMOs?	So far, the GMO Panel did not consider nor received biogas applications. EFSA has not been mandated by EC on this type of GMO applications.
3	Regarding TOP 7.1: How is EFSA addressing the requirement for good quality reference genomes for reliable bioinformatic off-target analyses? Who should provide such data, e.g. EFSA, the applicants?	EFSA is currently developing a guidance document that will cover multiple aspects of risk assessment of RNAi-based GM plants, including the off-target analysis. The exact recommendations for the query sequences that the applicants shall use for these bioinformatic analyses are

		currently under discussion and will be described in the guidance.
4	If the COM regulatory proposal for NGT plants comes into force, certain RNAi-based GMPs expressing potentially insecticidal, edited miRNA may fall into NGT category 1 and would not be risk assessed nor monitored (see Bohle et al. 2024, https://doi.org/10.3389/fgeed.2024.1377117). Are such potential applications discussed by EFSA regarding TOP 7.1. and if so what are the scientific arguments to potentially regulate RNAi-based GMPs (NGT vs. transgene derived) differently, despite a same mode of action?	The aim of mandate M-2024-00157 is to develop a guidance document or recommendations on the risk assessment of RNAi-derived plants which fall under the current European Union applicable GMO legal framework (Commission's implementing regulation 503/2013, Directive 2001/18, Regulation 1829/2003). The EC proposal for a new regulation of plants obtained by NGTs is still under discussion by the policymakers and is outside the scope of this specific mandate. EFSA has already discussed the risks related to NGTs and has confirmed the scientific basis for considering certain NGT-based plants as equivalent to conventional ones, defined as NGT category 1 (EFSA GMO Panel 2020, EFSA 2024).
5	How can the allergen ranking be used in determining inclusion or exemption from allergenicity data requirements?	Ranking of allergens with a correlation to clinical relevance is a step forward for future developments of more fit-for-purpose databases in risk assessment. Ranking of allergens will help developers of in silico tools to refine their outputs and improve their relevance for risk assessment. In risk assessment, future strategies could involve the development of databases where allergen ranking is associated with specific risk assessment follow-up actions depending on the clinical relevance of the findings

Questions received during the meeting.

Item	Question	Answer
6.1	To what extent could the evidence supporting the safety and the non-necessity of a 28-day study with the newly expressed EPSPS protein also feed into your work on more elaborate guidelines for protein toxicity in general?	Experience gained on the assessment of this protein and other recently cases will be included in the protein safety mandate that the GMO Panel is drafting (see item 6.2 of this GMO Panel agenda). This particular case presented is a perfect example showing that alternative robust approaches for protein safety assessment without the use of animal studies are possible.
7.2	What distinction can be made between toxins requiring short primary or secondary structures (e.g., bradykini-potentiating peptides of 4 or more amino acids, natriuretic peptides) as compared to proteins with multiple 3D domains required	Limitations to the approaches described in this procurement included the lack of appropriate bioinformatics tools for peptides shorter than 20 amino acids.

	for toxic activity (receptor binding, cellular uptake, toxic activity)?	
7.4	Besides any potential novelty, does non-inclusion into the OECD schemes (included into these consensus documents as background) suggest a potential change in exposure to newly expressed and other proteins? I remember that the renewal of a particular GM canola included the scenario of protein-meal-derived food protein (previously only a source of animal feed).	Human and animal dietary exposure assessment is performed according to EFSA statements. Apart from OECD documents, novel products are considered on a case-by-case basis, such as oilseed rape powder and protein isolates e.g. for the assessment of oilseed rape MON 94100 (EFSA-GMO-NL-2020-169). EFSA will review the novel products identified by the procurement and consider them in the exposure assessment if this is not done already.
8.2	To what extent will the search strategy focus on those publications discussing actual hazards and risks?	In frame of the mandate M-2024-00147 EFSA will develop and validate a search strategy that will identify any studies relevant for safety, risk assessment and other considerations examined by EFSA in its relevant scientific opinions concerning NGTs applied to plants, micro-organisms and animals. The inclusion and exclusion criteria will be defined accordingly. Publications discussing specific hazards and risks will be highly relevant for this activity.

12. Next meeting

The next meeting will be held on 11th December 2024 online.

Annex III List of Observers

Online: 87 registered online observers, (62 attended)

Observer	Organization
Esteban Alcalde	Syngenta
Ignacio Alvarez	University of Zaragoza
Ana Paula Arévalo	National Biosafety Authority – Uruguay
Kwame Dei Asamoah-Okyere	National Biosafety Authority – Uruguay
Natalia Bacchino	National Biosafety Authority – Uruguay
Laura Barre	ESPOL
Finja Bohle	Federal Agency for Nature Conservation
Alexandra Chanoca	Corteva Agriscience LLC
Alessandra Crisa'	Consiglio per La Ricerca in Agricoltura e l'Analisi dell'Economia Agraria (CREA)
Fabiola Cuevas	Corteva Agriscience Belgium BV
Lucas Cutri	Sugarcane Technology Center
Hanne Decuypere	Bayer Cropscience
Pascale Delzenne	Bayer Cropscience
Marion Dolezel	Environment Agency Austria
Malak Elbassuny	National Food Safety Authority – Egypt
Alvaro Eseverri Sabate	BASF
Alejandra Ferenczi	National Biosafety Authority – Uruguay
Paul Finglas	European Food Information Resource
Carmen García	National Biosafety Authority – Uruguay
Tao Geng	Corteva
Aina Gil	University Of Copenhagen
Ana Granados	European Forum Of Farm Animal Breeders
Ana Guillem Amat	Syngenta
María Gutiérrez	University Of Zaragoza
Taha Hosni	Nuseed
Lin Huixin	Bayer Crop Science
Krasimira Ivanova	Executive Environment Agency, Sofia , Bulgaria
Hana Jirakova	Ministry Of The Environment

Gijs À. Kleter	Wageningen Food Safety Research
Sonja Krone-Wolf	Feed And Additives Gmbh
Gerasimos Maniatis	Hellenic Ministry Of Rural Development And Food
Maica Martinez Parrilla	Corteva
Andrés Mas	Technical Secretary Of The National Biosafety System
Natalie Merlinski	National Biosafety Authority Uruguay
Matthew Merrell	Corteva Agrisciences
Fabiola Montero	Techlink Global Solutions
Luísa Nora	Äio Tech Oü
Concepción Novillo	Bayer Cropscience
Federica Orsenigo	The University of Surrey, Guildford
Stavroula Panagea	Region Of Attica
Paula Pescador	Biosafe Ltd Oy
Eva-Theresa Pyl	Federal Office Of Consumer Protection And Food Safety (BVL)
Romaan Raemaekers	BEBR
Mariana Richero	National Biosafety Authority Uruguay
Lilette Robles	Symrise
Marta Rodrigues	None
Diego Rodriguez	Corteva Agriscience
Scott Saracco	Bayer Crop Science
Berlian Purnama Sari	Pt. Bio-Teknika Sukses Abadi
Luc Schuler	Alva
Valerie Sert	Corteva Agriscience
Megan Shaw	Nuseed
Anxhela Shima	Ministry Of Agriculture And Rural Development
Ewelina Swora-Cwynar	Institute Of Natural Fibres & Medicinal Plants
Eirini Tatsi	Hellenic Ministry of Rural Development and Food Head of the Directorate General of Agriculture
Thomas van Boxmeer	Bayer Cropscience
Julie Vanderstraeten	Bio Base Europe Pilot Plant
Antonio Vicent	Instituto Valenciano De Investigaciones Agrarias (IVIA)
Rong Wang	Bayer Cropscience

Gonca Yildirim	Toros University
Krasimira Zaharieva	Risk Assessment Center on Food Chain
Luise Zühl	Federal Agency for Nature Conservation, Germany

Onsite:
Five registered onsite observers (2 attended)

Observer	Organization
Valerie Sert	Corteva Agrisciences
Maica Martinez Padilla	Corteva Agrisciences