NETWORK ON RISK ASSESSMENT OF GMO
Minutes of the 17th meeting

30-31 May 2024
14:00-18:00 / 09:00-13:00
Minutes agreed on 10 July 2024

Location: Sciensano (Eurostation), Ernest Blerotstraat/Rue Ernest Blerot 1 1070 Brussels

Attendees:

- Network Participants:

Country	Organisation
Austria	Environment Agency Austria (Umweltbundesamt)
Austria	AGES
Belgium	Flanders Institute for Biotechnology (VIB)
Belgium	Sciensano
Bulgaria	Agrobioinstitute
Bulgaria	National Centre of Public Health and Analysis
Bulgaria	Risk Assessment Center on Food Chain, Ministry of Agriculture
Croatia	Croatian Agency for Agriculture and Food
Czech Republic	Ministry of Environment of the Czech Republic
Czech Republic	Ministry of Agriculture
Denmark	National Food Institute, Technical University of Denmark (DTU - Food)
Estonia	Ministry of Environment
Finland	Ministry of Social Affairs and Health
Finland	Finnish Food Safety Authority EVIRA
France	French Agency for Food, Environmental and Occupational Health & Safety (ANSES)
Germany	German Federal Agency for Nature Conservation (BfN)
Germany	Federal Office of Consumer Protection and Food Safety (BVL)
Greece	Ministry of Rural Development and Food
Greece	Independent Public Revenue Authority for; Directorate General of General Chemical State Laboratory
Ireland	Environmental Protection Agency (EPA)
Ireland	Food Safety Authority of Ireland (FSAI)
Italy	Istituto Superiore di Sanità (ISS)
Italy	INAIL-Settore Ricerca Dipartimento Innovazioni Tecnologiche e Sicurezza degli Impianti, Prodotti ed Insediamenti Antropici
Latvia	Institute of Food Safety, Animal Health and Environment BIOR

Lithuania	National Food and Veterinary Risk Assessment Institute
Luxembourg	Luxembourg Veterinary and Food Administration - ALVA
Netherlands	Wageningen Food Safety Research (WFSR)
Netherlands	Institute for Public Health and Environment (RIVM)
Norway	Ministry of Agriculture, Forestry and Food - Administration for Food Safety, Veterinary Sector and Plant Protection
Poland	Plant Breeding and Acclimatization Institute - National Research Institute
Portugal	Faculdade de Farmacia da Universidade do Porto
Romania	National Sanitary Veterinary and Food Safety Authority
Slovenia	Ministry of the Environment and Spatial Planning
Spain	Ministry for the Ecological Transition and the Demographic Challenge, General Directorate of Quality and Environmental Assessment, National Biosafety Commission
Spain	Spanish National Research Council (CSIC) - National Institute for Agricultural and Food Research and Technology (INIA)
Spain	Spanish National Research Council (CSIC) - Center for Biological Research (CIB), Ministry of Science, Innovation and Universities
Sweden	Swedish Food Agency
Sweden	National Board of Agriculture

- Observers:
  Federal Food Safety and Veterinary Office (FSVO) (Switzerland).

- Hearing Experts:
  Fabien Nogue (DAY 1).

- European Commission/Other EU Agencies representatives:
  DG SANTE; EURL-GMFF.

- EFSA:
  NIF Unit: Michele Ardizzone, Giacomo De Sanctis, Antonio Fernandez Dumont, Andrea Gennaro, Aina Gil Gonzalez, Tilemachos Goumperis, Sara Jacchia, Paolo Lenzi, Dafni Maria Kagkli, Franco Maria Neri, Ana Martin Camargo, Nikoletta Papadopoulou, Tommaso Raffaello, Marta Rodrigues, Reinhilde Schoonjas

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Ana Luisa Afonso (EFSA) and Spain (Spanish National Research Council (CSIC) - Center for Biological

Research (CIB), Ministry of Science, Innovation and Universities). Bulgaria (National Centre of Public Health and Analysis), Finland (Ministry of Social Affairs and Health) and The Netherlands (Wageningen Food Safety Research) changed the attendance to online.

2. Adoption of agenda

The agenda was adopted without changes.

3. Agreement of the minutes of the 16th GMO Network meeting held on 13 December 2024, online

The minutes of the 16th GMO Network meeting had been previously agreed by written procedure on 18 January 2024 and published on the EFSA website.[1]

4. Welcome from the Head of the Scientific Directorate 'Biological Health Risks'

The Head of the Scientific Directorate 'Biological Health Risks' at Sciensano provided information on their work and scientific activities. As a One Health institute, Sciensano combines human and veterinary epidemiology, chemical and biological risk assessment, and infectious disease domains, ensuring mission continuity through applied research, service provision and expertise. The institute advises Belgian national and regional authorities and hold numerous national and international recognitions. Further, Sciensano manages 15 national reference centers for human pathogens and 64 national reference laboratories, including those for GMOs, Capripoxvirus, and foot-and-mouth disease. Sciensano is also a reference lab for WHO on measles, rubella, and influenza. The institute continually improves their surveillance and data strategies, learning from the recent pandemic. Sciensano collaborates closely with the Belgian Biosafety Advisory Council and EFSA, sharing a science-driven approach, transparency, and collaboration values. The meeting mentioned reflects long-term collaboration aimed at improving GMO risk assessment methodologies for food, feed, and the environment. The speaker wished the participants fruitful discussions and thanked the organizing committee of the meeting for their efforts.

5. Update from NIF (GMO) Unit

Abstract

On 1st February 2023, EFSA launched a call for expression of interest for membership of the Scientific Panels and the Scientific Committee. The selection procedure has been recently completed. EFSA communicated the outcome of the procedure for the renewal of the GMO Panel, introduced its composition and summarized the selection process. The process involved multiple evaluation steps as detailed in the report

[1] https://www.efsa.europa.eu/sites/default/files/2024-01/minutes-16th-gmo-v2-network-meetingpdf.pdf

available on the EFSA website.[2] In particular, 104 applications indicating the GMO Panel as fist choice were received. Out of these, 91 were eligible and were further assessed and 59 candidates met the required threshold to be considered eligible. Expertise mapping helped finalizing a draft list of experts, though one candidate was excluded due to a conflict of interest. The final GMO Panel, which will be active from July 2024 till June 2029, includes experts with the various specializations required for the functionality of the GMO Panel. The list is available in the presentation.
The renewed GMO Panel has a significant turnover among panel members. EFSA has provided the new experts with basic information on panel operations. The inaugural plenary, which is scheduled for July 2024, will be structured to contain a general session common for all EFSA Panels and Scientific Committee, followed by the specific Panel activities.
From July to December 2024, additional support and training, including tutoring and webinars, will be provided to new experts. In 2024, the GMO Panel plenary meeting will be held in October and in November, with the latter one being open to observers.

Discussion

Ireland asked if there is a minimum number of Member State experts that must be represented and whether there is a gender or country balance in the GMO Panel composition. EFSA confirmed that, in line with the EFSA Implementing Rule[3] while there is no strict minimum for member state representation, EFSA shall endeavor to avoid over-representation from a single country. The GMO Panel's country distribution was well-balanced. Regarding gender balance, the Implementing Rule also indicates that gender balance shall endeavor to be achieved; although the GMO Panel's gender balance isn't ideal, this was maintained from the initial list of experts to the final selection.

6. Scientific opinion on new developments in biotechnology applied to animals (including synthetic biology and new genomic techniques)

Abstract

EFSA provided an update of the mandate on New Developments in Biotechnology applied to animals. The status of the mandate, its progress and the deadlines were presented. The outcome of the horizon scanning for known cases of NGTs application to animals for food, feed and agricultural use was presented, also focusing on their current "commercial, precommercial and proof-of-concept" status. It was also reminded the importance of participation to the Public Consultation that will be launched around end of 2024, beginning 2025, upon endorsement of the draft scientific opinion by the GMO Panel.

Discussion

Belgium (Flanders Institute for Biotechnology) asked whether animals for sports and animal welfare are considered in this mandate. EFSA clarified that animals for sports are not considered since the mandate covers animals for food and feed and

[2] https://www.efsa.europa.eu/sites/default/files/event/mb97/Item%2005%20-%20doc1%20-%20Report%20panel%20renewal%20-%20mb240321-i1.pdf
[3] https://www.efsa.europa.eu/sites/default/files/2022-10/paneloperation_0.pdf

agricultural purposes, while animal welfare was part of the previous mandate when EFSA (2012) guidance was developed. EFSA also informed that several concepts in animal welfare have evolved since then. EFSA clarified that the main purpose for this mandate is to conclude whether the previous EFSA guidances are still applicable or not.
Czech Republic (Ministry of Agriculture) commented on the interest of animal breeders and whether the risk assessment of animals developed via NGTs would be performed by EFSA, considering that the new regulation regards plants. EFSA staff clarified that breeders are in fact very interested in these technologies which can shorten the developmental time avoiding for instance the need of multiple animal generations to fix the genetic modification. Commission also explained that NGT animals are regulated as GMO and that any applications for GM animal will be subject to the EU rules on GMO. Moreover, the Commission clarified that the mandate was sought to gather additional information on NGT animals and their safety, in line with the conclusion of the 2021 Commission study on new genomic techniques.
Poland (Plant Breeding and Acclimatization Institute - National Research Institute) commented on the low interest on publishing about NGT animals in EU, given the very few publications retrieved in the presented study, and why countries such as Argentina, Canada and Brazil don't have publications, although they seem to have legislations in place and products on the market. On the contrary, many publications are reported for China but there are no products being commercialized. Indeed, EFSA staff confirmed that is not aware of the activities taking place in China, contrary to what is shared by other countries that actively participate in a mutual exchange of information and updates, being part of an active international network. EFSA also confirmed that there are very few publications in Europe where there is some activity on fish and some mammals, though. EFSA also confirmed that the geographical distribution was made on the authors' affiliation. Belgium (Flanders Institute for Biotechnology) noted that the research carried out in industry may not be reported in publications.
Slovenia (Ministry of the Environment and Spatial Planning) confirmed the distribution of publications is rather similar to what obtained in their previous activity on synthetic biology. Slovenia also asked whether the public consultation included input/information from industry and whether EFSA considers that the NGT animals could be categorized as Commission proposed for plants. EFSA confirmed that the information from industry was also gathered in this mandate. However, regarding the possible categorization of NGT animal the work is still ongoing therefore this question cannot be answered now.
EFSA added some more considerations on the environmental release of NGT animals. For example, some species have a higher risk of escaping, compared to others, like fish, which would require specific considerations for the environmental risk assessment.
The Netherlands (Wageningen Food Safety Research) noted that cultured meat may be produced with NGTs and part of EFSA guidance may be applicable to these products. EFSA clarified that indeed the inclusion of these type of products was discussed with Commission at the start of the activity but these products would be included in this work according to the interpretation of the mandate's ToR.

7. Scientific opinion on new developments in biotechnology applied to microorganisms

Abstract

EFSA presented an update on the mandate on new developments in biotechnology applied to microorganisms, specifically Categories 3 and 4 as defined in the EFSA GMO Panel Guidance (2011). The draft scientific opinion underwent a public consultation from February to April 2024, receiving 398 comments from stakeholders, including NGOs, public authorities, academia, and industry representatives. EFSA thanked the Member States who actively and constructively contributed to this public consultation.
The GMO Network has been informed of the progress of this mandate and scientific opinion on several occasions. During the 15th meeting in June 2023, an update focused on the horizon scanning was given. During the 16th meeting in December 2023, EFSA presented the scientific opinion which was to be endorsed by the GMO Panel before the public consultation. In that occasion all Member States were invited to contribute to the public consultation and disseminate the information further.
Stakeholders provided detailed feedback on the Terms of Reference of the Mandate. All comments were taken into consideration and the text was amended accordingly when needed. In several occasions the public consultation provided very useful feedback, like in the case of the inclusion of gene-drive like systems, the need to assess presence/absence of CRISPR-Cas system when it is meant to be removed.
The EFSA GMO Panel concluded that EFSA guidances are "partially applicable", therefore on a case-by-case basis for specific NGT-Ms fewer requirements may be needed. Some of the EFSA guidances are "not sufficient" and updates are recommended. Because possible hazards relate to genotypic and phenotypic changes introduced and not to the method used for the modification, the EFSA GMO Panel recommended that any new guidance should take a consistent risk assessment approach for strains/products derived from or produced with microorganisms obtained with conventional mutagenesis, EGTs or NGTs.
The presentation emphasized ongoing collaboration and updates to refine risk assessment methodologies to keep pace with the evolving landscape of biotechnology. It underscored the importance of aligning guidelines with new technological developments to ensure comprehensive and accurate safety evaluations for genetically modified microorganisms.

Discussion

Belgium (Flanders Institute for Biotechnology) commented that in addition to the GMO regulation, other sectorial regulations may apply to the risk assessment of GM microorganisms. EFSA clarified that with the current regulatory framework, products containing category 3 and 4 GMM would be assessed by the GMO panel as well as another panel depending on the use of the product, e.g., food/feed additive etc. leading to double-dossiers. For such double dossiers, the different EFSA panels would closely collaborate to apply the same risk assessment principles. However, EFSA pointed out, that this was not subject of the current mandate, but goes beyond the scientific question presented. Overall, EFSA reminded that the regulatory framework is not determined by EFSA and EFSA performs the risk assessment based on the current legislations.

8. Some recent trends in agri-food biotechnology and their possible implications for food & feed safety, regulation,

and enforcement (results of desk research at WFSR, Netherlands)

Abstract

The Dutch delegation presented several examples of recent literature research on new biotechnological developments performed by Wageningen Food Safety Research for the Dutch government (NB these do not represent viewpoints of the latter). The studies looked into the following technological trends and their implications for the current safety assessment approach, regulation, and traceability and detection:

- Plant molecular farming, *i.e.,* the production of animal proteins in transgenic crops for food use. There have been concerns over potential allergic reactions to the animal proteins expressed in these crops in unwitting allergy patients if accidentally commingled with the mainstream of the host crop. In many aspects, these crops are to be treated in the same way as other transgenic crops.
- Random mutagenesis innovations: Space breeding (exposure of plant materials to, *e.g.*, cosmic radiation and microgravity) and the use of ion-particle beams as mutagen are relatively new forms of random mutagenesis applied to genetic crop improvement. Whereas the frequencies of mutations may at times differ from the more traditional forms of random mutagenesis, their nature is not different. As for the traditional methods, the breeding practices of *e.g.,* backcrossing and selection provide an additional safety net against unwanted effects.
- The use of GM micro-organisms for bioethanol production from starchy and cellulosic substrates, as well for gas fermentation to create biomass from industrial exhausts. Side streams have to be authorized if to be used as GM animal feed.
- Null-segregants derived from temporarily genetically modified crops: These might originate from future technologies applied to crop breeding such as reverse breeding, synthetic apomixis etc., to speed up breeding, amongst others. Detection and traceability of these crops will be challenging as they won't contain any remnants of GM material.

Discussion

Czech Republic (Ministry of Agriculture) noted that it might be challenging to standardize the production of animal proteins in plant molecular farming since plants may experience differences in their composition and/or physiology due to diverse growing conditions. Netherlands (Wageningen Food Safety Research) agreed with the comment informing that these plants are currently grown in greenhouses to guarantee the product quality. Czech Republic (Ministry of Agriculture) also mentioned that in EU a product is considered GM if DNA is present. Netherlands confirmed this observation but in other jurisdiction a product is considered GM only in case viable cells are present. Germany (German Federal Agency for Nature Conservation) considered that the environmental aspects (like gene-environment interaction) should be considered in plant farming and mechanisms of protein translation may be different in different organisms. Netherlands agrees that plant post transcriptional modifications may be indeed different from those in animals, but risk assessment aspects would still be covered by available guidances. The

Netherlands (Wageningen Food Safety Research) also informed that the newly produced proteins may not need to be purified but rather the plant material would be used as whole feed for example with the newly proteins already incorporated in the feed material. Ireland (Food Safety Authority of Ireland) reminded that back in 2006, the Commission clarified GMOs in fermentation, classifying a GMO and its products as GMOs if viable cells remain in the product. If the product is secreted and purified away from the GMO, it is considered a processing aid. This includes residual, non-harmful DNA fragments, while full-length antibiotic resistance genes pose a hypothetical risk. The term "precision fermentation" has since emerged, with DNA fragments now considered at risk. Many GM products on the market are harmless and assessed by EFSA and Member States, and not all DNA fragments render a food a GM food. EFSA asked how can plants producing, for instance milk proteins, be regulated as they would have to the listed as allergen and cross-contamination can be a problem. Netherlands (Wageningen Food Safety Research) replied that it's been repeatedly stated by FDA that companies should be responsible for this labelling, moreover geographical isolation of these GM crops used for molecular farming may help minimize cross-contamination issues. Slovenia (Ministry of the Environment and Spatial Planning) commented that the Netherlands suggested to track the developments in this area but this monitoring may be challenging. Netherlands (Wageningen Food Safety Research) replied that this work was performed by his institute as a contractor for the Dutch government but acknowledged that there are also other Dutch institutions carrying out similar projects. The Netherland suggested that collaborating is important, also with other Member States, to avoid work duplication. Poland (Plant Breeding and Acclimatization Institute - National Research Institute) asked about the legislation applied to the offspring of the GM plants that do not contain genetic constructs anymore. Netherlands answered that for some non-EU countries, null-segregants are not considered a GMO.

9. Improvement of PMEM plans for import and processing applications

Abstract

EFSA presented the activity on the potential improvement of the Post-Market Environmental Monitoring (PMEM) plans required under Directive 2001/18/EC. The Directive mandates notifiers to implement PMEM plans for the duration of the authorization. PMEM plans consist of Case-Specific Monitoring (CSM) in case potential adverse effects or critical uncertainties are identified during Environmental Risk Assessment (ERA), and General Surveillance (GS) to monitor unanticipated adverse effects. General surveillance is mandatory for all applications.
EFSA highlighted critical aspects of the PMEM plans proposed by applicants. Member States (MS) have expressed concerns over the lack of detail in the proposed methodologies for GS. The GMO Panel's CompERA Working Group (WG), which assesses the adequacy of PMEM plans, has noted that, while the current PMEM plans are proportionate to the scope of the application, they lack transparency in the proposed methodology. In response to these shared concerns, EFSA initiated a dialogue with MS and applicants aimed at improving the transparency on the methodology of PMEM plans. This initiative is supported by the European Commission.

The CompERA WG discussed what additional documentation could help improve transparency in PMEM plans. The additional information initially considered included gathering/requesting more detail on the methodologies for GS, the identification of locations of potential high exposure in the EU (i.e. transportation nodes and processing plants dealing with high volumes of GM material), and critical steps in processing GM materials where environmental exposure is more likely. After discussions on the feasibility and added value of the different documents, the CompERA WG concluded to recommend applicants to provide more detail on the proposed monitoring activities to detect unforeseen adverse effects and their expected outcome.
EFSA highlighted the steps taken so far, including the public release of recommendations to applicants, discussions with MS and applicants, and ongoing consultations to refine and implement the proposed enhancements. These discussions include how applicants should provide additional details in PMEM plans and the amount of detail required, considering factors like crop specificity and the balance between prescriptiveness and flexibility.
The presentation emphasizes the importance of coordination between risk assessors and managers to effectively implement PMEM plans.

Discussion

Austria (Environment Agency Austria) requested clarification on the reasons why the identification of areas with higher potential exposure to GM material was considered unfeasible. EFSA indicated that several Member States were contacted to retrieve information such as the processing facilities where the GM crops are processed or the transportation nodes dealing with high volumes of GM imports. However, such info was not readily available in all Member States. Following these initial investigations and consulting with the European Commission, the identification of these hotspot areas would be unfeasible. France (ANSES) asked whether a reflection was conducted on what should be done in case of spillage of GM seeds, like France reported last year when the French agency was mandated to check the adequacy of the measures to address such spillage in an incident that led to the identification of feral GM oilseed rape plants. France also sought information on whether the ANSES report evaluating this incident had contributed to the EFSA CompERA WG discussions. EFSA clarified that the report was indeed discussed with the WG experts and indicated that prevention of seed spillage and control of feral plants that may emerge from these incidents is addressed in the PMEM plans proposed by the applicants.
Germany (German Federal Agency for Nature Conservation) asked how long the area would be controlled when spillage occurs, since seeds may become dormant and may germinate at later stage. EFSA replied that the PMEM, including the eradication of feral plants, is in place as long as the authorization for that GM event is valid.
Poland (Plant Breeding and Acclimatization Institute - National Research Institute) noted that EFSA mentioned that there is not enough transparency in the PMEM plan which casts doubts on the implementation of such PMEM. EFSA replied that the applicants are not detailed in the specific monitoring activities proposed, including the specific measures to put in place in case of spillage.

10. Request for a scientific opinion on recent studies on the proposal for a regulation of the European Parliament and of the Council on plants obtained by certain new

genomic techniques and their food and feed, and amending Regulation (EU) 2017/625

Abstract

EFSA presented the mandate received by the European Parliament (EP) to deliver a scientific opinion on the analysis by French Authority ANSES on the Annex I of the EC proposal for a regulation on plants obtained by certain NGTs and their food and feed, and amending Reg (EU) 2017/625 (EC proposal). EFSA provided a summary of the content of the ANSES's analysis which focused on the need for clarifications regarding several aspects and definitions included in Annex I of the EC proposal. The structure of the scientific opinion was presented. The working group of the GMO Panel addressed the points raised by ANSES including clarifications on terms and definitions used in the EC proposal, the scientific rationale of the criteria in Annex I which were set to determine whether a given NGT plant is equivalent to conventional bred plants, and the potential risks from plants under category 1 NGT. The opinion is proposed for adoption at the 164th GMO Panel meeting in June.

Discussion

Czech Republic (Ministry of Agriculture) asked how many mutations can be obtained in random mutagenesis and how the number of 20 modifications can be scientifically justified and be related to the safety. EFSA replied that the number 20 was extensively discussed with the experts in the frame of this mandate. Random mutagenesis may lead to a much higher number of mutations than 20, but calculating the exact number is difficult and may also depends on the genome size and species ploidy for example. Czech Republic commented that plants obtained by random mutagenesis with a lot more than 20 mutations, but dramatic changes can be obtained with only one mutation. EFSA did agree regarding this point. However, EFSA confirmed that less than 20 modifications can also be achieved by conventional breeding methods, so the experts concluded that setting 20 modifications as a threshold to determine whether an NGT plant can also be achieved by conventional breeding methods is, in this respect, justified.

Netherlands (Wageningen Food Safety Research) agreed with the approach followed by the GMO Panel experts, but requested clarification on the mandate and the follow up activities once the mandate will be finalized, for example whether a presentation of the scientific opinion at the European Parliament would be foreseen. EFSA clarified that presentation at the Parliament could be a possibility but the follow up activities are not defined yet and will depend on the Parliament's decisions.

Germany (Federal Office of Consumer Protection and Food Safety) noted that EFSA stated in the discussion that category 1 NGT plants are risk neutral but, later on, these plants were described as having no additional risks compared to conventional breeding. EFSA informed that in almost every mandate recently received on NGTs, GMO Panel experts had to compare NGTs with established genomic techniques and to conventional breeding, only at the technique level, hence additional risks would mean a new risk that is manifested due to the new genomic technique used. In this respective, EFSA reminded that the Panel concluded that no additional risks were identified for NGTs compared to the techniques used in conventional breeding and random mutagenesis. Germany emphasized that the core issue lies in this discussion, pointing out that while conventional breeding carries risks and remains

unregulated, new genomic techniques (NGTs), which entail fewer risks, are subject to regulation.
Poland (Plant Breeding and Acclimatization Institute - National Research Institute) suggests providing more detailed explanations about the 20 genetic modifications. For example, one interpretation is that introducing a new trait in a given species may require at least 20 modifications to be successful. This contrasts with conventional breeding, which results in thousands of modifications to obtain the desired trait. Poland emphasizes the need for clarity on how this number of modifications was determined, as additional explanations would benefit many Members States. The Commission clarified that the justification regarding the number of modifications can be found in the EC technical paper (link). Belgium (Flanders Institute for Biotechnology) considered that talking about uncertainties could be more appropriate than risks and, when it comes to targeted and random mutagenesis, the former implies much less uncertainties than the latter.
Germany (German Federal Agency for Nature Conservation) asked whether the Commission would engage in a discussion with the member States following the completion of this mandate. The Commission clarified that this mandate was an initiative of the European Parliament and that follow-up discussion should be held with the European Parliament.
Czech Republic (Ministry of Agriculture) emphasized that Annex I criteria are not clearly understood by many scientific experts and should be clarified more. EFSA took note of the comment but reminded that the outcome of the mandate is a GMO Panel scientific opinion on the ANSES's report and not a direct analysis of the Annex I criteria.

11. ANSES' collective appraisal on risk evaluation of NGT plants

Abstract

Following a mandate from the French ministries in charge of agriculture and environment, ANSES conducted an expert appraisal on new genomic techniques (NGTs). ANSES' experts studied the risks associated with plants obtained using NGTs, particularly those resulting from site-directed mutagenesis using the CRISPR-Cas system. Experts concluded that the current framework for assessing health and environmental risks of genetically modified plants was only partially suitable for the assessment of these new plants, but that some of the risks identified for NGTs are not radically different from those arising from transgenesis techniques. Nevertheless, the level of exposure to the plants obtained could be much higher considering the diversity of possible applications. ANSES therefore proposed a case-by-case assessment taking into account both the precision of the technique used and the characteristics of the plant obtained once the genome has been modified. The agency developed a decision tree adapted to a graduated approach to risk, and proposes a simplified risk assessment framework in cases where the mutation reproduces a modification of the genome observed in nature or already obtained by traditional techniques, and for which no risk has been identified. ANSES also stressed the importance of post-marketing surveillance and recommended setting up a comprehensive mechanism to monitor NGT plants and derived products for health and environmental effects, as well as to observe changes in cultivation practices associated with these plants. Lastly, on the basis of the regulatory requirements that

will ultimately be decided, ANSES called for common guidelines to be drawn up in order to limit differences in interpretation of risk assessment between the countries of the European Union. Anses' opinion is publicly available and has been translated into English (https://www.anses.fr/fr/system/files/BIORISK2021SA0019EN.pdf).

Discussion

Czech Republic (Ministry of Agriculture) requested clarification on why ANSES concluded that the EC proposal would have a negative impact on organic production. France (ANSES) responded that, auditions were organized with representatives of organic farming. These producers were concerned not to be informed on the nature of the crop they would buy and on the difficulties due to the coexistence of these sectors.

Regarding the undesired effects potentially harboured by NGT plants, Belgium (Flanders Institute for Biotechnology) noted that the information available in the literature may not be representative of what will be placed on the market. Indeed, the selection process would remove products with undesired effects before they reach the market. France (ANSES) agreed and noted that this is indeed what is also reported in the document. Belgium (Sciensano) requested clarification on the 'adapted molecular characterization´ proposed in the document. France (ANSES) clarified that the terms mean to perform a complete characterization of the modified site but also to look at possible undesired effects.

Poland (Plant Breeding and Acclimatization Institute - National Research Institute) emphasized the importance of clarifying the possible two meanings of the terms 'undesired effects'. These terms could be interpreted as modifications of the DNA sequence (e.g., off-targets) and/or new undesired traits that should be removed before placing the new variety on the market. France (ANSES) clarified that 'undesired effects' identified in the literature are undesired modifications in the genome other than the intended targeted modification.

Czech Republic (Ministry of Agriculture) commented that France studied the social economic effect of the NGTs and asked whether a small company would be able to afford the risk assessment as proposed by France. France (ANSES) clarified that the report contains a detailed analysis of the socio-economic impact, including for example the patentability.

Slovenia (Ministry of the Environment and Spatial Planning) underlined that France recommended traceability and control of the NGT plants and questioned whether the current system would be able to cope with this requirement. France (ANSES) replied that there are two aspects to consider: the first is that the WG experts recommended traceability and control because monitoring is also recommended; the second point is from the consumer's point of view where consumers were really keen on knowing what they are consuming, according to the auditions performed to collect information on this aspect.

Ireland (Food Safety Authority of Ireland) commented that France mentioned that NGT plants retain some of the known risks of GMO plants, and asked whether any real evidence regarding this aspect were identified in the literature or whether such identified risks are still hypothetical. France (ANSES) clarified that the identified risks are the same as those taken into consideration by the current regulation on GMOs.

EFSA reflected on the difference between the definition of 'history of safe use' and 'prior knowledge', the latter being introduced in the report. France (ANSES) clarified that 'history of safe use' and 'prior knowledge' may both refer to the product rather than to the technique.

12. Update from the Subgroup on NGTs

Abstract

EFSA introduced the Terms of Reference (ToR) and the overall objectives of the Subgroup on NGTs. The establishment of the Subgroup on NGTs was approved by the EFSA Advisory forum in March 2024. The AF consists of representatives from 27 EU Member States, Iceland, Norway, Switzerland, seven pre-accession countries, and the European Commission as observers. Its primary functions include advising EFSA on work programs and priorities, ensuring collaboration between national bodies and EFSA, resolving contentious scientific issues, avoiding duplication of efforts, and increasing scientific cooperation.
The subgroup's main objective is to foster knowledge sharing on NGTs, including their development and application to plants, animals, and microorganisms, and jointly address RA challenges.
Members should have expertise in NGTs and experience in molecular characterization, food and feed, and/or environmental RA of GMOs. Member States can appoint one participant and one alternate. The subgroup will meet at least once a year, either physically or virtually, and the working language will be English.
EFSA informed that the Subgroup on NGTs is currently composed by 30 participants and alternate from 19 Member States, while 9 Member States have not nominated any expert. The proceedings of the subgroup's meetings will be documented and published on the EFSA website.
EFSA provided at the end a summary of the discussion that took place at the 1st Subgroup on NGTs meeting on the 29th May 2024.

Discussion

Slovenia (Ministry of the Environment and Spatial Planning) suggested that there should be a continuous horizon scan for rapidly developing fields to prepare for the future, potentially modifying existing legislation and scientific approaches. There's concern about gaps between completed projects and the start of new ones, emphasizing the need to connect existing knowledge and ensure continuity in knowledge gathering. Another key question is determining the leading institution at the EU level to manage this knowledge. Member states, the European Commission, EFSA, JRC, and/or other organizations like WHO and OECD should be involved in this network. The first step is to clarify these roles among ourselves. The Netherland (Institute for Public Health and Environment) acknowledged that there are different concurrent projects even within the same country. EFSA informed that there are examples from EFSA projects where horizon scans are continuously performed. However, it was acknowledged that the issue is often the lack of coordination to avoid duplication of activities. Slovenia (Ministry of the Environment and Spatial Planning) highlighted the importance of achieving information flow and information sharing. Additionally, EFSA reminded the availability of Teams channels to keep the Network informed and updated Poland (Plant Breeding and Acclimatization Institute - National Research Institute) that there are available databases for knowledge sharing which are the results of collaborations between EU institutions in the areas of GMOs and also NGTs (e.g. Euginius). Germany (German Federal Agency for Nature Conservation) suggested that there might be a need to bring this discussion to the attention of the Advisory Forum.

13. Mandate on protein safety

Abstract

EFSA provided an update related to the current status and next steps of the protein safety assessment mandate. In particular, Member States were informed on the extension of deadline for the endorsement (end of 2024) and publication of the Scientific Opinion (middle 2025). EFSA also communicated on the engagement activities on this topic at international level and the possibility for organizing a workshop at OECD level in 2025. This event would be highly beneficial to the activity ensuring that all issues related to protein safety assessments within and outside Europe are considered by the EFSA GMO Panel. EFSA also summarized the feedback received from the survey launched beginning of 2024. Finally, Member States were asked to provide views on a series of key questions posed, e.g., what is considered a safe protein? What is a hazard in protein safety? How similar is similar in structure and functional analysis of proteins? Is *in vitro* testing ready to be used when needed? Or how can exposure be considered in protein safety within the weight-of-evidence approach?

Discussion

Ireland (Food Safety Authority of Ireland) informed that the EFSA Novel Food Panel assesses the safety of novel products such as new plants, new insects, or new microorganisms. Therefore, their knowledge may help answering the questions on what is considered safe. A discussion took place on differences/similarities between GMO and novel food safety assessment of proteins. EFSA highlighted that new applications received in the GMO area are moving towards the expression of many different proteins which might render the GMO assessment issues closer to those in Novel Foods. Additionally, Novel Foods area is restricted to human safety only, whereas GMO risk assessment also evaluates the safety of feed.

Czech Republic (Ministry of Agriculture) highlighted that determining the safe intake levels for proteins can be challenging. Proteins can be allergenic and toxic, requiring feeding studies to ensure safety in some cases. Guidelines on protein safety exist, but gathering all necessary information is complex. Environmental conditions affect protein expression, complicating safety assessments. The burden of conducting these studies and collecting data often falls on companies, raising questions about costs and responsibilities. EFSA highlighted that exposure to newly expressed proteins is not always the case, as for example certain products to be placed on the market may not contain proteinaceous part (e.g. oil).

Ireland (Food Safety Authority of Ireland) commented that EFSA Panel on Novel Foods assesses lots of 'unknowns'. They evaluate available data, mainly history of safe use from other regions, while GMO assessment includes more data such as bioinformatics, animal feeding studies, etc. This process involves assessing allergenicity and potential cross-reactivity. While dealing with few specific proteins like in GMOs might be easier than evaluating a whole new organism, the EFSA Panel on Novel Foods may provide some views on how to risk assess complex GMO products.

Belgium (Sciensano) reminded that the issue of protein safety assessment was also raised in the discussion with the Subgroup on NGTs. Also, non-transgenic proteins may still require safety evaluation. Questions arose on how to assess these proteins and whether the Novel Foods regulation addresses such issues. Belgium highlighted

the need for an exchange of information with other regulatory bodies. Moreover, Belgium (Flanders Institute for Biotechnology) suggested to look into the chemical compound safety assessments which can inform protein safety evaluation. Advanced methods, such as artificial intelligence and AlphaFold, offer sophisticated tools for designing proteins and predicting properties, helping identify and mitigate unwanted characteristics in proteins. However, these new tools are not yet commonly used in risk assessment and further criteria on how to interpret/assess them is needed.

14. Request for placing on the market of Soy Leghemoglobin produced from genetically modified Pichia pastoris (EFSA-GMO-NL-2019-162) – update

Abstract

The network hosted a presentation and subsequent discussion regarding the assessment of Soy Leghemoglobin protein produced by genetically modified yeast. This product, developed and imported from outside of the EU, is intended for use in meat analogues to provide a meat-like taste and appearance due to the iron haem group within the Soy Leghemoglobin protein. The GMO panel has conducted a thorough assessment covering molecular characterization, compositional analysis, and the impact of the genetic modification. The collaboration with the Food Additive and Flavourings (FAF) Panel, who has already assessed the final product for use as food additive, focused on ensuring the safety of the product in its intended use, considering both the genetic modification and the final food product itself. The process also includes the consideration of any potential allergenicity, toxicity, nutritional and environmental impact with specific reference to the GMO legislation and its requirements. Several aspects have been scrutinized, such as the potential presence of viable cells and DNA, product specifications, exposure estimation, and a detailed safety assessment. The panels have also investigated the history of safe use, sequence similarities with other hemoglobins and the needs for additional information. The Member States' comments on the original GMO dossier were duly considered. This complex and collaborative regulatory process involving multiple panels and experts is continued to ensure the safety and compliance of this ingredient intended for use in food.

Discussion

Czech Republic (Ministry of Agriculture) asked about the history of safe use of leghemoglobin. EFSA replied that the WG concluded that there is no history of safe use and no data on consumption related to this were present in the dossier. Belgium (Sciensano) asked whether, in a future application on GMO that involves the risk assessment carried out by two Panels, the GMO Panel would still look at all aspects needed for the risk assessment of GMO, or whether the dossier would be divided among the Panels involved, where the GMO Panel would look more into the molecular aspects while the FAF Panel would assess the nutritional and compositional analysis. EFSA clarified that this would have to be agreed with all involved parties. EFSA also clarified that in this case the applications were received at different points in time, therefore both Panels were involved and EFSA took the decision how to proceed with both applications. France (ANSES) asked whether the FAF Panel had accessed the MS comments submitted for the GMO application. EFSA clarified that the comments were

shared and experts of both Panel where informed about the relevant scientific comments.

15. End of the meeting

The Chair thanked the GMO Network members for their active participation and the fruitful discussion.

The Chair informed that the draft minutes will be shared with the participants and published on the EFSA website together with the presentations.

The meeting was closed at 13:00.