Network on Risk Assessment of GMOs
Minutes of the 10th meeting

Held on 18-19 June 2019, Parma

(Agreed on 12 July 2019)[1]

Participants

- **Network Representatives of Member States (including EFTA Countries):**

Country	Name[2]
Austria	Marion Dolezel, Markus Woegerbauer
Belgium	Adinda De Schrijver
Bulgaria	Antoniya Dimitrova, Dimitar Djlianov
Cyprus	-
Croatia	Renata Hanzer, Sanja Miloš
Czech Republic	Miloslava Navratilova
Denmark	Jan W. Pedersen
Estonia	-
Finland	Kirsi Törmäkangas, Annikki Welling
France	Catherine Golstein, Emmanuelle Pic
Germany	Andrea Scheepers, Wolfram Reichenbecher
Greece	Argyrios Boulis, Dionysia Stefanitsi
Hungary	Rita Andorkó, Agota Virag
Ireland	Patrick O'Mahony
Italy	Roberta Onori, Elena Sturchio
Latvia	Lelde Grantina-Ievina
Lithuania	Zygimantas Janeliunas, Odeta Pivoriene
Luxembourg	Luc Schuler
Malta	-
Netherlands	Gijs A. Kleter, Cynthia van Rijn
Poland	Zbigniew Dabrowski, Slawomir Sowa
Portugal	Márcia Reto
Romania	-
Slovak Republic	Zuzana Sevcikova
Slovenia	Boštjan Petelinc
Spain	Carmen Cuadrado, Gema Pérez Farinós
Sweden	Johan Ålander

1 Minutes should be published within 15 working days of the final day of the relevant meeting.

2 Indicate first full name and the surname (John Smith) throughout the document

United Kingdom	Sabrina Roberts, Elspeth Ransom
Norway	Ville Erling Sipinen

- **Hearing Experts**

Michael Eckerstorfer (for item 4.7)

- **Observers**

Ana Velimirovic (Montenegro), Nur Koyncu (Turkey), Aleksej Tarasjev (Serbia), Martin Schrott (Switzerland)

- **European Commission:**

Ilaria Ciabatti and Hans Moons (DG SANTE)

- **EFSA GMO Panel:**

Javier Moreno, Hanspeter Naegeli, Nils Rostoks

- **EFSA**

GMO Unit: Elisabeth Waigmann (Chair), Fernando Álvarez, Giacomo De Sanctis, Yann Devos, Antonio Fernández Dumont, Silvia Federici, Andrea Gennaro, Anna Lanzoni, Ana Martin Camargo, Sylvie Mestdagh, Henna Moilanen, Irina Olaru, Konstantinos Paraskevopoulos, Nikoletta Papadopoulou, and Tommaso Raffaello.

Transformation Services (TS) Unit: Claudia Paoletti.

1. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Tsveta Georgieva (Bulgaria) and Felix Nicolescu (Romania).

2. Adoption of agenda

The agenda was adopted with the following changes:

1) item 4.11 was moved up in the agenda, after item 4.7, and the remaining items kept their order;

2) four AOB items were added: i) confidentiality of GMO applications, proposed by Gijs Kleter (Netherlands); ii) LLP applications, proposed by Emmanuelle Pic (France); iii) 2019 GMO Panel open plenary meeting, proposed by the Chair; and iv) date of the next meeting, proposed by the Chair.

3. Agreement of the minutes of the 9th meeting of the Network on Risk Assessment of GMOs held on 8-9 November 2018, Parma

The minutes were agreed by written procedure and published on the EFSA website[3].

[3] The minutes of the 9th meeting of the GMO Network are available at http://www.efsa.europa.eu/sites/default/files/event/181108-m.pdf

4. Topics for discussion[4]

4.1. Update from EFSA on applications, mandates, and other activities

Irina Olaru, scientific officer of the GMO Unit, presented an overview on EFSA's work on the risk assessment of genetically modified organisms (GMOs), covering four areas: market authorisation applications (hereafter referred to as 'GMO applications'), guidance documents and explanatory notes, external mandates, and grants and procurements. Ms Olaru provided information on: applications received under Regulation (EU) No 1829/2003 (status, types of plant and level of stacking); guidance documents and explanatory notes recently finalised or under development by the EFSA GMO Panel and GMO Unit; external mandates received from the European Commission (EC); and grants and procurements.

Giacomo De Sanctis, scientific officer of the GMO Unit, presented in detail the procurement on non-target Lepidoptera. The objectives of this procurement are i) to develop a spatially and temporally-explicit model able to provide realistic predictions in terms of risks to NT Lepidoptera for Bt-maize events, and ii) to provide risk assessors and risk managers with tools to estimate risks to NT Lepidoptera, accounting for the characteristics of the receiving environments relevant to their region. The timeline of this procurement was also presented, and GMO Network members were encouraged to test the web-interface that would result from this activity.

Slawomir Sowa (Poland) and Adinda De Schrijver (Belgium) asked about the type of applications that have been withdrawn recently, and whether the rationale for withdrawal had been communicated. EFSA replied that these were import-processing applications (excluding cultivation), and that applicants are not required to justify the withdrawal; nevertheless, in these recent cases, communication from applicants listed the lack of commercial interest as reason.

4.2. Follow-up on EFSA consultation of national Competent Authorities on GMO applications

Sylvie Mestdagh, scientific officer and Coordinator of Applications of the GMO Unit, presented an overview of the consultation held with MS Competent Authorities on GMO applications, as a follow-up to the discussion held at the previous GMO Network meeting. The key messages passed by EFSA at the 2018 meeting were two-fold, i.e. (1) calling for scientific comments of relevance for the risk assessment of GMOs, and (2) drawing the attention of MS to the efforts of the EFSA GMO Unit to lean the work related to handling MS comments in the Annex G[5].

At the present meeting, following the request from several MSs to provide guidance on comments to submit or not, EFSA exemplified the main types of MS comments contributing to the assessment of applications, focusing on the comments that are out of scope. For the latter, the following types were identified: comments falling outside the remit of EFSA (e.g. on detection methods, labelling proposals, implementation of PMEM) or the GMO Panel (on residues of pesticides), statements not supported by rationale or evidences, and

[4] The presentations given during this meeting are available on the meeting page: http://www.efsa.europa.eu/en/events/event/190618

[5] The presentations given at the 2018 GMO Network meeting can be found at http://www.efsa.europa.eu/en/events/event/181108

comments on single events reiterated in the frame of applications for stacked events. For an optimized use of resources on both EFSA and MS side, Ms Mestdagh encouraged MS experts to submit risk assessment-targeted comments.

In addition Ms Mestdagh continued the discussion on the reporting started last year and informed MS that EFSA is reconsidering the format of the aforementioned Annex G, without undermining the level of scrutiny of the comments and in full compliance with Regulation (EC) No 1829/2003.

During the general discussion that followed the presentation, Jan Pedersen (Denmark) and Wolfram Reichenbecher (Germany) asked for further clarifications about comments that would be considered out-of-scope by EFSA, and about the reporting on the comments, included in Annex G of EFSA overall opinion. Marion Dolezel (Austria) emphasized that comments on the methodology of the monitoring plan should be considered by EFSA and that cross-checking between the monitoring plan proposed by the applicant and the implementation of this plan is necessary in order to ensure that PMEM plans are operational. EFSA clarified that comments pertaining to the methodology and the scientific quality of the PMEM plan are within EFSA remit whereas comments on the implementation of the PMEM provisions should be handled by risk managers. To the question on reporting, EFSA confirmed that it will be streamlined but that all relevant comments are considered during the risk assessment.

4.3. Updated explanatory note on literature searching

Yann Devos, scientific officer of the GMO Unit, presented the updated explanatory note on literature searching, which was published in April 2019[6]. In 2017, EFSA published an explanatory note on literature searching conducted in the context of GMO applications for (renewed) market authorisation and annual post-market environmental monitoring (PMEM) reports on GMOs authorised in the EU market[7]. This explanatory note: (1) clarifies the scope and methodology for literature searching; and (2) provides detailed recommendations on how to conduct and report systematic/extensive literature searches, and present the results of any scoping reviews, thereby complementing previous guidance of EFSA and its GMO Panel. Specific recommendations are given for: (1) formulating review questions and clarifying their purpose; (2) searching for/identifying relevant publications; (3) selecting publications; (4) extracting high level data from the relevant publications, where appropriate; and (5) summarising and reporting the data, and considering the implications of the findings. The explanatory note aims to: (1) assist applicants to perform consistent and sensitive literature searches; (2) ensure that as many relevant publications as possible are retrieved to minimise biases such as publication bias; and (3) ensure that sufficient detail about the search process and its results are provided to promote transparency, facilitate appraisal and enable reproducibility.

In view of the experience gained in the application of the 2017 explanatory note, EFSA has updated it to provide further guidance on specific issues (e.g., search strategies through case studies, eligibility/inclusion criteria to establish relevance, approaches to identify search terms and subject indexing terms,

[6] Available at http://www.efsa.europa.eu/en/supporting/pub/en-1614
[7] Available at https://www.efsa.europa.eu/en/supporting/pub/en-1207

reference publications, reviewers, reporting, search updates), or to relax former provisions/requirements (e.g., eligibility/inclusion criteria to establish relevance, searches of internet pages of key organisations), where appropriate. The presentation addressed the key revisions of the note.

During the general discussion that followed the presentation, Adinda De Schrijver (Belgium) asked whether applicants are requested to submit a scoping review upon submission of an application, and an updated scoping review that covers the risk assessment period from submission onwards when the application is close to finalisation, to which EFSA answered positively. Emmanuelle Pic (France) reported on her organisation's experience with the appraisal of literature searches. Slawomir Sowa (Poland) indicated that substantial resources (trained personnel and time) are required for the appraisal of literature searches.

4.4. Update from EFSA's Gene drive WG

Yann Devos, scientific officer of the GMO Unit, gave an update on EFSA's activities on gene drive modified organisms. The presentation covered the mandate received from the European Commission, the Working Group established by EFSA to address this activity, and the two-step consultation with stakeholders – at the beginning of the process, in the context of a stakeholder Workshop on the problem formulation for the environmental risk assessment of gene drive modified insects[8], held in Brussels on 15 May 2019, and at the end of the process, through an online public consultation. The stakeholder workshop represented a new model of engagement with stakeholders that needs to be fine-tuned further. Consequently, the presentation also focused on the lessons learnt and feedback received from the workshop participants.

During the general discussion that followed the presentation, Zbigniew Dabrowski (Poland) suggested to consider the tsetse fly (genus *Glossina*) as an additional case study, and supported the selection of *Drosophila suzukii* as case study. Following a clarification question from Gijs Kleter (Netherlands), it was confirmed that *Wolbachia* is considered. Aleksej Tarasjev (an observer from Serbia) asked whether epigenetics would be covered by the mandate, to which EFSA replied negatively. Related to the workshop, Marion Dolezel (Austria), Rita Andorkó (Hungary), and Adinda De Schrijver (Belgium) provided positive feedback on the organisation and format of the workshop, but agreed with EFSA's analysis that more time would have been welcomed to discuss such a complex topic. For future similar workshops, Catherine Golstein (France) suggested to operate in several steps, allowing the scientific community to work separately from, and in interaction with, stakeholders, and underlined the importance of making sure the related socio-economics issues are addressed by a relevant body to supplement EFSA's mandate for the complete information of the European Commission.

4.5. Update from EFSA's Synthetic biology WG

Nikoletta Papadopoulou, scientific officer of the GMO Unit, provided an update on EFSA's activities on synthetic biology (SynBio). The presentation covered the background, the mandate's terms of reference and scope, and the relevant guidelines and legislation for the topic. This activity will be conducted by two

[8] More information on this event is available at http://www.efsa.europa.eu/en/events/event/190515

working groups, one focused on plant SynBio environmental risk assessment (ERA) and one on microorganisms SynBio ERA. For plant SynBio ERA, Ms Papadopoulou presented the outcome of a procurement for a scientific literature search mapping plant SynBio developments in the agri-food sector likely to reach the market in the next 10 years; the outcome indicated that SynBio in plants is still rare compared to microorganisms, therefore commercialisation is difficult to predict. Nevertheless, the plant SynBio WG experts who also mapped the current plant SynBio developments, chose three case studies that are being used by the WG, to test the adequacy of the EFSA guidelines and regulatory documents. EFSA will deliver in a first phase, by 31 March 2020, an endorsed draft opinion (for public consultation) on the adequacy of the guidance for Category 4 GMMs for molecular characterisation and environmental aspects, and an endorsed draft opinion (for public consultation) on the adequacy of the guidance for environmental risk assessment of GM plants, including molecular characterisation.

During the general discussion that followed the presentation, Jan Pedersen (Denmark) commented that the test-cases chosen are not very different from complex GMOs that are received now in applications, to which EFSA replied that the choice was made based on the results of mapping the likely applications of synthetic biology that would reach the market in the next 10 years. Slawomir Sowa (Poland), Gijs Kleter (Netherlands) and Michael Eckerstorfer (invited hearing expert from Austria) asked whether bioremediation products, SynBio animals, or *de novo* domesticated plants were considered in this exercise, to which EFSA replied that these products were either not identified by the mapping as likely candidates to reach the market, or would be considered at a later stage of the mandate (SynBio animals).

4.6. New mandate on SDN-1&2 and ODM

Tommaso Raffaello, scientific officer of the GMO Unit, presented the mandate recently received from the European Commission on site-directed nucleases 1 and 2 (SDN-1&2), and oligonucleotide-directed mutagenesis (ODM). The terms of reference of this mandate request EFSA i) to advise whether section 4 of the 2012 EFSA scientific opinion on the safety assessment of plants developed using SDN-3[9] may be applicable, in whole or in part, to plants developed with SDN-1, SDN-2 and with ODM; and, if the answer to i) is positive, ii) to advise whether the conclusions of the EFSA 2012 scientific opinion on plants developed using SDN-3 are valid, in whole or in part, to plants developed with SDN-1, SDN-2 and ODM. The topic will be dealt with by the GMO Panel's Molecular Characterisation (MC) WG and the draft scientific opinion will be ready for a first reading at the January 2020 GMO Panel plenary meeting; comments and suggestions from the GMO Panel will be then considered and incorporated in the opinion, which will be brought to the April 2020 plenary meeting for adoption.

After the presentation, Gijs Kleter (Netherlands) and Wolfram Reichenbecher (Germany) asked about the flexibility and coverage of the definition of SDN-1 (i.e. improved versions of Cas9 and other nucleases with high precision, multiplexing and consecutive applications), since there are new technologies constantly developed, to which Nils Rostocks, the Chair of the GMO Panel's MC WG, and EFSA replied that the opinion cannot cover all technologies and

[9] Available at http://www.efsa.europa.eu/en/efsajournal/pub/2943

therefore has to be practical and cover products that are likely to enter the market in the next 10 years.

4.7. Biosafety considerations for plants developed by genome editing and other new genetic modification techniques (nGMs)

Michael Eckerstorfer, senior scientific officer at Environment Agency Austria, presented a paper addressing biosafety considerations for plants developed by genome editing and other new Genetic Modification Techniques (nGMs)[10]. Such considerations are required to implement appropriate risk assessment approaches for nGM products according to Directive 2001/18/EC, including products developed by genome editing regulated for biosafety. The question whether nGM plants might result in non-negligible negative effects for the environment and/or health is also significant for the ongoing discussion concerning future regulatory developments. The considerations and conclusions presented in the paper are based on a survey of the scientific literature to identify recent applications of nGMs for plant development. The results indicate that a holistic perspective is required to analyse nGM-plants for hazards associated either (i) with their (intended) traits and their use, e.g. in agriculture or (ii) with unintended changes resulting from the nGMs or other biotechnological methods applied during breeding. Some of the currently developed traits are complex and/or novel and the underlying physiological mechanisms are not sufficiently elucidated yet. Therefore, it cannot be assumed that all nGM plants will be safe as a default. Also, the characteristics of nGMs such as genome editing, e.g. a small extent of genomic sequence change and a high level of precision, cannot be considered an indication of safety per se. All nGMs considered in this study can result in unintended (genetic) changes of different types and frequencies. Such unintended effects may impact the safety of products under specific conditions, such as e.g. a high complexity of the developed trait(s) and/or high uncertainty regarding their effects, linkage of intended and unintended genetic changes or fast product development with limited downstream crossbreeding, e.g. as with direct modification of elite lines. It was concluded that legislation needs to provide a framework for an appropriate case-specific premarket risk assessment for nGM plants. This risk assessment should be based on a proper problem formulation and an appropriate molecular and phenotypic characterization to identify unintended effects.

During the discussion that followed the presentation, Jan Pedersen (Denmark) commented that introducing many techniques in the discussion lead to additional complexity, to which Mr Eckerstorfer replied that the intention was to include as many techniques as possible, in order to have a complete overview of the process. Slawomir Sowa (Poland) commented that not all off-target effects are linked to a safety issue, and that risk assessment should be triggered by safety issues, not simply by legislation. Mr Eckerstorfer replied that there is a general agreement that with respect to unintended effects precision is linked to safety, but there are also other considerations for risk assessment, e.g. with respect to the newly established trait(s); he added that most if not all regulatory frameworks are not consistently addressing the perspective of overall risks of products , to which Mr Sowa replied that the lack of international agreement on

[10] Available at https://www.frontiersin.org/articles/10.3389/fbioe.2019.00031/full

the risk assessment of these techniques will lead to asynchronous authorisation of products.

4.8. General Food Law – the ART Programme

Claudia Paoletti, programme manager of the ART Programme, gave a presentation on the priorities of the programme and the main changes of the General Food Law[11]. The ART Programme aims to prepare EFSA for the implementation of the updated General Food Law and related new requirements from the European Commission, to close critical gaps in EFSA Strategy 2020, to lean all EFSA core and enabling processes, to adapt risk assessment methods to the development of a digital society. Ms Paoletti summarised the revisions of the General Food Law under four areas of interest: 1) transparency and confidentiality, 2) engagement and risk communication, 3) scientific value, and 4) governance. She explained the challenges laying ahead for EFSA in this transformation process, but also the benefits for external scientists such as Network experts, including EFSA's open collaboration with other institutions, and transparent procedures for stakeholders' engagement in the risk assessment process.

After the presentation, Gijs Kleter (Netherlands) asked whether the confidentiality of data submitted in GMO applications will be assessed by EFSA, under these new legal provisions, to which EFSA replied positively Adinda De Schrijver (Belgium) asked whether the accessibility of the public to the dossiers will impact the current public consultations held by EFSA. EFSA clarified that the current procedures will still apply.

4.9. 90-day studies – GMO Network representatives' perspective

Adinda De Schrijver (Belgium) and Gijs Kleter (Netherlands) gave a presentation on the scientific rationale behind the 90-day feeding study requirement as laid down in Regulation (EU) No 503/2013.The objectives of the presentation were to provide an overview of the current situation at scientific, legal and risk assessment level, to discuss whether the outcomes of the GRACE[12] and G-TwYST[13] projects have influenced the risk assessors' view on the need for a 90-day study, to increase mutual understanding on the scientific need of 90-day studies, and to share information.

Gijs Kleter (Netherlands) presented the outcome of the GRACE and G-TwYST projects and indicated that the recommendations resulting from these projects were as follows: studies should not be conducted in the absence of a hypothesis; there is no basis for mandatory 90-day feeding studies; and there is no value of extension from 90 days to long-term trials. The presentation included an overview of the answers collected by Ms De Schrijver from GMO Network representatives[14] from European countries on two questions linked to conducting

[11] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety

[12] http://www.grace-fp7.eu/

[13] https://www.g-twyst.eu/

[14] With a focus on representatives of the GMO Network's Food and Feed section, where available (the list of Member Organisations is available at http://www.efsa.europa.eu/sites/default/files/assets/gmonetworklist.pdf); not all GMO Network representatives were reached for the survey.

90-day feeding studies. The first question asked whether 90-day studies should be requested only on a case-by-case basis, when a hypothesis for testing has been formulated, to which consulted GMO Network representatives from 20 countries agreed, while GMO Network representatives from five countries were of the opinion that these studies should be requested even in the absence of such a hypothesis; GMO Network representatives from seven countries could not provide their answer on this point in advance of the meeting. The second question asked whether 90-day studies for single events previously assessed by EFSA need to be re-assessed in the context of GM stacked events, to which GMO Network representatives from 21 countries replied negatively.

Ms De Schrijver concluded the presentation with a reference to Regulation (EU) No 503/2013, which indicates that the requirement for 90-day feeding studies would be reviewed depending on the outcome of the GRACE project. The presenters from Belgium and Netherlands indicated that they appreciated the valuable feedback received and would like to continue discussions on this topic with the network members after the meeting.

The presentation was followed by a general discussion. Elisabeth Waigmann (EFSA) and Hanspeter Naegeli, the Chair of the EFSA GMO Panel, reminded the GMO Network experts that Regulation (EU) No 503/2013 requires 90-day feeding studies for GM events as singles or as part of stacked events, therefore EFSA requires and assesses these data and asks for additional information, if needed. Mr Naegeli also recalled that EFSA already expressed its scientific view in the GMO Panel 2011 Guidance for risk assessment of food and feed from GM plants[15], where 90-day studies are required on a case-by-case basis, if indicated by preceding analyses.

Wolfram Reichenbecher (Germany) indicated that, coming from an ERA organisation, toxicology is not the main focus, but as 90-day studies are also about unintended effects in general, he would like to comment. Since the comparative assessment is not comprehensive, this study is requested as a screening step involving a test animal, to detect unintended effects of the genetic modification; in the case of stacked GM events, it can provide useful information on combinatorial effects of residues when events conferring herbicide tolerance and insect resistance are stacked. Mr Reichenbecher also noted that he had not received the questions in advance of the meeting. For the point related to 90-day studies for stacked GM events, Rita Andorkó (Hungary) expressed her support and noted that the Hungarian GMO Network members did not receive the questionnaire before the meeting probably due to personel changes. She added that the official opinion regarding this issue has not been changed in Hungary.

Emmanuelle Pic (France) commented that, in the absence of a positive control, no conclusion can be drawn from the 3 projects, GRACE, G-TwYST and GMO90+, about the added value or interest of the 90-day study. Ms Pic added that, in the past, the 90-day study was often the first study required when there was a doubt about the safety of a GMO, this being one of the reasons why it was made mandatory in Regulation (EU) No 503/2013; she also indicated that, as far as she knows, there is currently no alternative ready to replace the 90-day study.

[15] Available at https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.2150

Andrea Scheepers (Germany), who represents the German FF organisation to the GMO Network, shared her opinion via the instant messaging tool for online participants and commented in writing during the meeting that she supports the view that there are many comprehensible reasons that contradict the mandatory requirement to perform a 90-day rodent feeding study (e.g. results and conclusions from GRACE and G-TwYST; 3R principle which is fixed in Directive 2010/63/EU). Therefore, from a scientific point of view, the conduct of such a study should be a case-by-case decision and not a standard requirement.

Slawomir Sowa (Poland) commented that 90-day studies can provide useful information only if a clear hypothesis has been formulated.

It was concluded that further scientific debate is needed. However, the legal frame is set by Regulation (EU) No 503/2013, and any discussion of the legal frame is out of the remit of the GMO Network and needs to be conducted at the appropriate forum.

4.10. In silico tools for protein tox: presentation and feedback/initiatives

Konstantinos Paraskevopoulos, scientific officer of the GMO Unit, gave a presentation on future perspectives on *in silico* tools for the toxicity assessment of proteins. The current in silico investigations on newly expressed proteins (NEPs) in GMO dossiers are based on comparing the protein sequence to company in-house databases, but this approach has limitations, since sequence similarity cannot be used as sole criterion for characterising a protein as a toxin. However, extensive information is becoming available in public databases, thus allowing the development of *in silico* tools to determine the potential for protein toxicity based on 3D structures, biological function, molecular pathways, and specific motifs or domains. EFSA has an on-going procurement for a literature search exploring such methods that could support the risk assessment.

During the discussion that followed the presentation, Gijs Kleter (Netherlands) asked whether the outcome of ILSI's Task Force on Protein toxicity has been considered, to which EFSA replied that various sources of information are explored by the contractor at this point, as a first step towards an *in silico* approach to protein toxicity. The possibility of replacing *in vivo* studies with *in silico* tests was welcomed by Jan Pedersen (Denmark). Emmanuelle Pic (France) indicated that *in silico* information concerning the NEPs is useful but not sufficient, and that animal testing remains necessary, since it can cover unintended effects of the genetic modification and the overall toxicity of the whole plant, while *in silico* approach would restrict the toxicity assessment to the NEPs. EFSA clarified that indeed the *in vivo* studies up for discussion for possible reduction are the 28-day toxicity studies on purified NEP, that are conducted on a case-by-case basis. Ms Pic also asked whether a similar exercise would be initiated for allergenicity assessment, to which EFSA replied that this option would need to be explored further.

4.11. Adjuvanticity/immunogenicity/allergenicity assessment of proteins, Cry proteins as a case study

Antonio Fernández Dumont, scientific officer of the GMO Unit, presented the case study on Cry proteins, in the context of adjuvanticity/ immunogenicity assessment of proteins. The guidelines for prediction of immune adverse reactions to proteins were listed and the weight-of-evidence approach used by EFSA in allergenicity assessment was briefly described. The presentation focused

on the assessment of Cry proteins, in particular Cry1Ab and Cry1Ac, for which the potential for adjuvanticity/immunogenicity/allergenicity has been investigated. Scientific literature for these two proteins provides contrasting evidence, which may be due to differences in aminoacid sequence, dose, route of administration, animal models, experimental protocols, and/or matrices used. It was highlighted that testing adjuvant and allergenic potential of proteins requires stronger and fit-for-purpose standardised study design, and that future studies should consider limitations of current models, using relevant routes and methods of administration, doses, appropriate control proteins, and realistic exposure regimes.

The general discussion was initiated with a comment from Patrick O'Mahony (IE) on the fact that allergenicity is not linked exclusively to the properties of a protein, but varies between individuals and even populations, therefore risk assessment models must take into account specific characteristics of individuals and/or population, to which EFSA agreed. Slawomir Sowa (Poland) asked about the grouping of protein Cry1Ab with Cry1Ac in the report. EFSA replied that despite the fact that these two proteins share over 90% identity, there is a great controversy with regard to the outcome from the animal models where they have been tested, raising the need for a fit-for-purpose study design. In addition, no information on the topic is currently available for other Cry proteins.

4.12. Celiac disease assessment

Antonio Fernández Dumont, scientific officer of the GMO Unit, gave an update on current stage and future needs on celiac disease assessment. The stepwise approach to assess the capacity of proteins to cause celiac disease was described. Mr Fernández Dumont explained that certain aspects of the topic may require additional discussion, such as i) elaboration of additional examples including further assessment criteria; ii) development of a robust, publicly-available database; iii) the HLA-DQ-peptide modelling step, which will be the subject of an EFSA procurement; and iv) *in vitro* digestion testing of proteins. Related to the HLA-DQ-peptide modelling procurement, it was highlighted that GMO Network members will be informed of the launch and encouraged to disseminate the information to the relevant institutions and scientists.

During the discussion that followed the presentation, Gijs Kleter (Netherlands) commented whether there are other proteins than gluten that have a motif which binds to T-cells, to which EFSA replied that current sequences in available databases dealing with celiac disease are those linked to gluten. According to the EFSA guidance on allergenicity[16], knowledge on the protein in question can be used to calibrate the safety assessment. If there is sufficient information to support the lack of adverse effects with the consumption of a specific protein, the safety assessment can be stopped at this step.

[16] EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Naegeli H,Birch AN, Casacuberta J, De Schrijver A, Gralak MA, Guerche P, Jones H, Manachini B, Messean A,Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal J-M, Eigenmann P, Epstein M,Hoffmann-Sommergruber K, Koning F, Lovik M, Mills C, Moreno FJ, van Loveren H, Selb R and Fernandez Dumont A, 2017. Guidance on allergenicity assessment of genetically modified plants. EFSA Journal2017;15(5):4862, 49 pp.

5. Any Other Business

5.1. Confidentiality of GMO applications

Gijs Kleter (Netherlands) indicated that, during the last couple of years, Monsanto has claimed several dossiers as completely confidential. This is not in line with EU regulation. Article 30 (3) of (EC) 1829/2003 states which information shall not be considered as confidential information. The Dutch Competent Authority is therefore of the opinion that dossiers under 1829/2003 cannot be claimed as completely confidential and proposes that EFSA checks whether these dossiers comply to the requirements of article 30 (2) of (EC) 1829/2003 of as part of their completeness check.

A representative of the European Commission replied that this issue has been discussed in the PAFF meeting of 11 September 2018 and confirmed that confidentiality claims must refer to specific parts of the application and be accompanied by verifiable justification. EFSA added that confidentiality claims limit the access of the public, not of MS Competent Authorities, and that, before publication of scientific opinions, EFSA requests a public version of the application and checks that no confidential information is displayed in the published scientific opinion.

5.2. LLP applications

Emmanuelle Pic (France) asked whether EFSA had received any applications for GMO to be placed on the market at low levels, that would be in the scope of the EFSA guidance document (2017)[17], to which EFSA replied negatively and indicated that such applications would be sent by applicant through the European Commission. The representative of the European Commission confirmed that no such applications have been submitted to EC.

5.3. 2019 GMO Panel open plenary meeting

Irina Olaru, scientific officer of the GMO Unit, informed the GMO Network that the 2019 GMO Panel open plenary meeting would take place on 27-28 November, in Parma. The GMO Network experts will be informed when the registration to observe the meeting is open.

5.4. Date of the next meeting

Irina Olaru, scientific officer of the GMO Unit, informed the GMO Network that EFSA is considering organising the next meeting in May-June 2020. Once set, the meeting date will be communicated to experts by email.

6. Conclusions (s)

The Chair thanked the GMO Network experts for the active participation and the fruitful discussion, the speakers for the interesting topics proposed and excellent presentations, the GMO Panel members for contributing to the scientific exchange, and EFSA staff for organising and contributing to the meeting.

7. Closure of the meeting

[17] Available at http://www.efsa.europa.eu/en/efsajournal/pub/5048

Abbreviations

Bt	Bacillus thuringiensis
EFSA	European Food Safety Authority
EFTA	European Free Trade Association
ERA	Environmental risk assessment
GMM	Genetically modified microorganism
GMO	Genetically modified organism
ILSI	International Life Sciences Institute
MC	Molecular characterisation
MS	Member State
NEP	Newly expressed protein
nGMs	New genetic modification techniques
NT	Non-target
ODM	Oligonucleotide-directed mutagenesis
PMEM	Post-market environmental monitoring
SDN	Site-directed nucleases
SynBio	Synthetic biology
WG	Working Group