European Food Safety Authority

GMO UNIT

SCIENTIFIC PANEL ON GMO

Minutes of the 96th Plenary meeting of the Scientific Panel on GMO

Held on 4–5 March 2015, Brussels

(Agreed on 15 April 2015)

Participants

- **Panel members**:

Salvatore Arpaia, Andrew Nicholas Edmund Birch, Andrew Chesson, Patrick du Jardin, Achim Gathmann, Jürgen Gropp, Lieve Herman, Hilde-Gunn Opsahl Hoen-Sorteberg, Huw Jones, Jozsef Kiss, Gijs Kleter, Martinus Løvik, Antoine Messéan, Hanspeter Naegeli, Kaare Nielsen, Jaroslava Ovesná, Joe Perry, Nils Rostoks, Christophe Tebbe.

- **Hearing experts**:

None.

- **European Commission and/or Member States representatives:**

Dorothée André, Maria Kammenou, Kaja Kantorska, Maria Mirazchiyska, Sabine Pelsser (DG SANTE).

- **EFSA:**

GMO Unit: Herman Broll, Yann Devos, Zoltán Divéki, Antonio Fernández Dumont, Andrea Gennaro, Sylvie Mestdagh, Irina Olaru, Yustina Olshevska Grigorov, Matthew Ramon and Elisabeth Waigmann.

- **Observers (in application of the Guidelines for Observers[1])**: please refer to Annex I.
- **Others:** none.

1. Welcome and apologies for absence

The Chair welcomed the participants.

2. Brief introduction of Panel members and Observers

The Chair welcomed the participants and invited them to introduce themselves.

3. Adoption of agenda

The agenda was adopted without changes.

[1] http://www.efsa.europa.eu/en/stakeholders/observers.html

4. Declarations of Interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[2] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[3], EFSA screened the Annual Declarations of Interest (ADoIs) and the Specific Declarations of Interest (SDoIs) filled in by the experts invited to the present meeting. No conflicts of interest relating to the issues discussed in this meeting were identified during the screening process or in the Oral Declarations of Interest (ODoIs) at the beginning of this meeting.

5. Presentation of the Guidelines for Observers

The Head of the GMO Unit presented the EFSA Guidelines for Observers attending open plenary meetings.

6. Agreement of the minutes of the 95th Plenary meeting held on 21 January 2015, Parma

The minutes of the 95th GMO Plenary meeting held on 21 January 2015 were agreed[4].

7. Scientific outputs submitted for discussion and possible adoption

7.1 Guidance Document for the agronomic and phenotypic characterisation of genetically modified plants (EFSA-Q-2013-00606)

The GMO Panel discussed the comments received during the public consultation and the draft guidance document. Further discussion in the specific Working Group is needed.

7.2 Guidance Document for the risk assessment of the renewal of GM plant products authorised under Regulation (EC) No 1829/2003 (EFSA-Q-2013-00684)

The GMO Panel discussed the comments received during the public consultation and the draft guidance document. Further discussion in the specific Working Group is needed.

7.3 Request to assess maize MON 810 PMEM report for the 2013 cultivation season provided by Monsanto (EFSA-Q-2014-00856)

Following a request from the European Commission, the EFSA GMO Panel assessed the post-market environmental monitoring (PMEM) report for the 2013 growing season of maize MON 810 provided by Monsanto Europe S.A. The EFSA GMO Panel concludes that the data related to insect resistance monitoring does not indicate a significant and consistent decrease in susceptibility of the target pest field populations to Cry1Ab protein in Spain over the 2013 growing season. However, considering that the methodology for insect resistance monitoring remained unchanged compared to previous PMEM reports, the EFSA GMO Panel reiterates its previous recommendations for improvement of the insect resistance management plan of maize MON 810. The EFSA GMO Panel also recommends, as part of general surveillance, the continuation of the screening and discussion of literature on possible adverse effects of maize MON 810 on rove beetles. In the absence of information on

2 http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
3 http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf
4 http://www.efsa.europa.eu/en/events/event/150121a-m.pdf

the general surveillance of maize MON 810 in 2013, the EFSA GMO Panel cannot conclude on potential unanticipated adverse effects due to the cultivation of maize MON 810 in 2013, or on possible changes to the methodology as compared to previous growing seasons.

The opinion was adopted by the Panel and will be published on the EFSA website at: EFSA: Publications.

7.4 Application for authorisation of genetically modified oilseed rape MS8 × RF3 × GT73 for food and feed uses, import and processing submitted under Regulation (EC) No 1829/2003 by Bayer CropScience (EFSA-GMO-NL-2009-75) (EFSA-Q-2009-00890)

The GMO Panel discussed the draft scientific opinion, specifically the sections on molecular characterisation, comparative assessment, food feed safety assessment and environmental risk assessment.

7.5 Application for authorisation of genetically modified maize 5307 for food and feed uses, import and processing submitted under Regulation (EC) No 1829/2003 by Syngenta (EFSA-GMO-DE-2011-95) (EFSA-Q-2011-00310)

The GMO Panel discussed the status of the application.

8. New mandates

8.1 Applications under Regulation (EC) No 1829/2003

- Application for authorisation of genetically modified maize MON 87411 for food and feed uses, import and processing submitted under Regulation (EC) No 1829/2003 by Monsanto Europe S.A./N.V.(EFSA-GMO-NL-2015-124)

8.2 Annual post-market environmental monitoring reports of genetically modified plants

None.

8.3 Other requests and mandates

- Notification for the risk assessment of the genetically modified carnation line SHD-27531-4 from Suntory Holdings Limited for the purpose of import, under Part C of Directive 2001/18/EC (C/NL/13/01)
- Notification for the risk assessment of the genetically modified carnation line FLO-40685-2 from Suntory Holdings Limited for the purpose of import, under Part C of Directive 2001/18/EC (C/NL/13/02)
- Proposal from the GMO Panel for a self-task activity to supplement its previous risk mitigation measures reducing exposure of non-target Lepidoptera to maize MON 810, Bt11 or 1507 pollen.

9. Feedback from the Scientific Committee/the Scientific Panel, Working Groups, EFSA and the European Commission

9.1 Scientific Committee and other Scientific Panels

A Vice-Chair of the GMO Panel reported on the issues discussed during the 71st Plenary meeting of the Scientific Committee. These included the life cycle of guidance documents, dealing with divergence over scientific issues between EFSA and Member States and draft guidance documents of the SC Overarching ERA WG.

9.2 EFSA including its Working Groups/Task Forces

9.2.1 Working group on Development of supplementary guidelines for the allergenicity assessment of GM plants

A member of the GMO Unit informed the Panel of the Workshop for stakeholders on the collection of initial feedback on the Allergenicity assessment, scheduled for 17 June 2015, Brussels.

9.2.2 EFSA's 2nd Scientific Conference

The GMO Unit informed the Panel about the EFSA's 2nd Scientific Conference, "Shaping the Future of Food Safety, Together", taking place on 14–16 October 2015, in Milan, in the context of EXPO2015. EFSA's Young researcher initiative[5] was also presented, and participants were encouraged to disseminate the information to potential interested parties.

9.3 European Commission

The European Commission (EC) representatives updated the GMO Panel on applications that are undergoing authorisation procedures and mandates that would be sent to EFSA.

10. Other scientific topics for information and/or discussion

None.

11. Questions from and answers to Observers (in application of the Guidelines for Observers)

Please refer to Annex II.

12. Any other business

None.

13. Closing remarks

The Chair of the GMO Panel thanked the observers for their attendance and active contributions during the meeting.

[5] http://www.efsaexpo2015.eu/young-researcher-initiative/

Annex I

List of observers attending the GMO Panel Plenary meeting

4–5 March 2015

	Last name	First name	Company
1	Apoteker	Arnaud	The Greens/EFA Group in the European Parliament
2	Ball	Louise	DEFRA
3	Bertho	Lieselot	Monsanto Europe S.A.
4	Box	Adrienne	COGEM
5	Carron	Delphine	EuropaBio
6	Cimmarusti	Floriana	SAFE (Safe Food Advocacy Europe)
7	Cotter	Janet	Greenpeace
8	Custers	René	VIB
9	De Buck	Sylvie	IPBO/VIB-UGent
10	de Jong	Philippe	Altius
11	De Schrijver	Adinda	Scientific Institute of Public Health
12	Fuentes Mateos	Angel Manuel	Syngenta
13	Georgieva	Violeta	EuropaBio
14	Glandorf	Boet	RIVM
15	Golstein	Catherine	Haut Conseil des biotechnologies (High Council for Biotechnology)
16	Guillemain	Joël	French Agency for Food, Environmental and Occupational Health & Safety (ANSES)
17	Harrison-Dunn	Annie-Rose	FoodNavigator/NutraIngredients
18	Himanen	Kristiina	University of Helsinki, Department of Agricultural Science
19	Ilegems	Michael	KANAMY Consulting
20	Jensen	Søren Mark	Ministry of Environment
21	Joos	Anouck	VUB
22	Kaiafa	Maria	Demeter International e.V.
23	Leggett	Chris	Mission of Canada to the European Union
24	Legris	Gaston	Dow AgroSciences
25	Nielsen	Louise Lundstrøm	Danish Environmental Protection Agency
26	Pietiäinen	Milla	University of Helsinki, Department of Agricultural Sciences
27	Prater	Donald	US Food and Drug Administration
28	Reichenbecher	Wolfram	Federal Agency for Nature Conservation
29	Renckens	Suzy	Syngenta
30	Ricroch	Agnes	AgroParisTech
31	Schaller	Marek	European Parliament/S&D Group
32	Schmidt	Kerstin	BioMath GmbH
33	Steinmann	Tobias	BASF SE
34	van der Meer	Piet	Ghent University/Free University of Brussels/PRRI
35	Velten	Guido	Bayer CropScience
36	von Kameke	Conrad	Independent

Annex II

Questions from and answers to Observers

Observers were invited to submit questions for the GMO Panel Plenary meeting at the time of registration. These questions, and the corresponding answers, are listed below:

Janet Cotter, Greenpeace:

"1. What is EFSA's opinion on whether, or which, new plant breeding technologies result in a GM organism, specifically ODM and gene editing techniques such as ZfN, TALEN and CRISPR/Cas?

2. Will EFSA be issuing an opinion on these (or some) new plant breeding techniques?

3. If so, on which techniques and when is it expected to be published?"

Marc Fellous, AFBV:

"What is EFSA's position related to new breeding techniques (NBT)?"

Agnes Ricroch, AgroParisTech:

"My question is related to the risk assessment of engineered plants with new methods (nucleases) and the regulation of these edited plants at the European level."

As the written questions submitted by three Observers were all related to the same topic, Elisabeth Waigmann, the Head of the GMO Unit (hereafter referred to as EFSA), indicated that the answer would apply to all of them. She started by indicating that it is outside EFSA's remit to determine whether plants obtained by new breeding techniques (NBTs) are GMOs. In February 2011, EFSA received from EC a request for opinions on the adequacy of EFSA guidelines to perform risk assessment on plants developed through a number of new techniques. The following techniques were proposed by the Competent Authorities for consideration in a first stage by the New Techniques WG of the European Commission: oligonucleotide-directed mutagenesis (ODM); zinc finger nuclease (ZFN) technology (comprising ZFN-1, ZFN-2 and ZFN-3); cisgenesis (comprising cisgenesis and intragenesis); grafting; agro-infiltration; RNA-dependent DNA methylation (RdDM); reverse breeding; and synthetic genomics. This mandate mentioned cisgenesis (comprising cisgenesis and intragenesis) and ZFN-3 as a priority for the GMO Panel.

The GMO Panel issued scientific opinions on the safety assessment of plants developed by cisgenesis and intragenesis (January 2012) or by ZNF-3 and other site-directed nucleases with similar function (including transcriptor-activator-like effector nucleases (TALENs)) (October 2012). Related to the ZF technology, the Head of the GMO Unit specified that this method is used to introduce genes at pre-defined sites. In both these opinions, the conclusion was that the existing EFSA guidance documents (GDs) for the risk assessment of GMOs are applicable and that fewer data might be required, on a case-by-case basis.

She also indicated that EFSA and its GMO Panel have not assessed other NBT techniques and that EFSA is waiting for further instructions from EC on which NBT to address next.

Regarding the regulation of plants developed by NBTs, Dorothée André, Head of the Biotechnology Unit, EC DG SANTE (hereafter referred to as EC), replied that the EC is currently assessing the legal aspects of NBTs, in order to decide whether they fall under the GMO legal framework and if so, whether they can be considered as exceptions. She explained that biotechnology has evolved significantly since the definitions were included in

the legislation and, therefore, it has to be examined how these new techniques fit into the definitions.

Suzy Renckens, Syngenta:

"1. Would the GMO Panel be willing to review its processes for the assessment of GMO applications (e.g. requirement for standalone applications, single events vs. stacks, resubmission of data packages, regular updating of bioinformatics data during review process, technical challenges) with input from applicants and, of course, without compromising the scientific quality/content of data required for the risk assessment, the independence of EFSA or the integrity of the review process?"

EFSA replied that the process of GMO application assessment is owned by EFSA. EFSA develops and adjusts its processes to reflect the scientific logic of the GMO Panel and the requirements of the legislation. For example, EFSA's completeness check procedure ensures that the minimum requirements are met, as specified in the legislation, which was built on the GD of the Panel.

The Chair of the GMO Panel, Joe Perry, added that the assessment of the single events is a prerequisite for the assessment of stacks, in line with the scientific logic that the assessment of stacks should focus on interactions. Information on the singles is important because the Panel now has to conclude on all sub-combinations of events in a stack, regardless of their origin, as specified in Article 18 of IR503/2013. He presented the following example to illustrate the importance of information on the singles: "Suppose a single event A was characterised using information not from the single event A, but from a three-stack, A×B×C. In this case, the assessment of other stacks containing event A but neither of events B or C (for example, A×D×E×F), and the assessment of their sub-combinations, would contain very little direct evidence for or against the presence of interactions with event A, because the single event A would not have been fully assessed". Therefore, singles should be finalised before the assessment of the stack begins in order to optimise the use of resources—if there is an inconclusive opinion on the single event, the Panel will not be able to conclude on the stack.

EFSA indicated that there are internally developed documents that aim to harmonise the interaction between EFSA panels and applicants. An example would be the document that lists timelines for submission of data packages following a request from a panel[6].

Regarding the involvement of stakeholders in the process of reviewing and updating GDs, stakeholders, including applicants, are constantly involved. A recent example would be the Technical Meeting with Stakeholders on agronomic and phenotypic characterisation of genetically modified plants, held on 18–19 December 2014, where the GMO Panel's Guidance on agronomic and phenotypic characterisation of GM plants was thoroughly discussed by participants. EFSA is striving to be more customer oriented and to strengthen the support it provides to applicants and other stakeholders. One means of communicating with applicants is the annual technical meeting with GMO applicants that EFSA organises, but there are also other opportunities. As part of this initiative, EFSA is inviting hearing experts from industry to WG meetings, when WG experts seek clarifications from applicants, during the risk assessment. One of the GMO Panel's WGs had such a meeting with a hearing expert from industry on 5 February 2015. In addition to all these, applicants regularly contact EFSA scientific staff to enquire about specific applications.

[6] European Food Safety Authority, 2014. Indicative timelines for submitting additional or supplementary information to EFSA during the risk assessment process of regulated products. EFSA Journal 2014; 12(1):3553, 37 pp. doi:10.2903/j.efsa.2014.3553

The Chair of the GMO Panel expressed his personal view on communicating with applicants, while ensuring the independence of the Panel and the integrity of the review process. He emphasised his support for EFSA's policy on transparency and openness and for the idea of improving the efficiency and timeliness of risk assessment through more communication between the Panel and applicants. He noted that EFSA is not able to offer pre-submission meetings with applicants because of resource limitations, but he also expressed his willingness to pursue more communication if it were fully broadcasted via live web-streaming, so that the public and all stakeholders could be assured of the independence of the Panel and of its procedures.

"2. How does the GMO Panel take into account the weight of evidence provided by applicants and available in literature and the anticipated exposure to the GM product in the EU when uncertainties are identified during the risk assessment?"

The Chair of the GMO Panel answered that the weight-of-evidence approach is used by the GMO Panel in the risk assessment of GMOs. The scientific requirements laid down in the guidance document refer to a minimum set of data that should be provided in all cases. Additional data from literature can and do contribute to the evaluation, but the minimum requirements have to be met. He referred to a review by Miguel Sanchez, published in *Nature Biotechnology*, indicating that there are over 30,000 papers dealing with food–feed risk assessment for GMOs, and confirmed the Panel does its best to keep up to date with all relevant important developments. To illustrate the importance of the scientific literature and the extent to which the Panel scrutinises relevant papers, he pointed to the number of references cited in scientific opinions of the GMO Panel, which increased from occupying around 3 pages per opinion in 2004 to more than 15 pages in 2012.

As Regulation (EC) No 178/2002 makes clear, risk is the product of a hazard multiplied by its likelihood of occurrence (alternatively, risk may be represented as an adverse effect multiplied by the exposure of a population to that event). The GMO Panel always considers exposure in evaluating the safety of a GMO. Exposure assessment is one of the crucial six steps of risk assessment—it follows hazard identification and hazard characterisation, and determines, together with hazard characterisation, whether or not there is a risk.

Delphine Carron and Violeta Georgieva, EuropaBio:

"1. What are the status and scope of the EFSA monitoring guidance after the publishing of the report on post-market monitoring (PMM) of food/feed by ADAS 'Review of existing PMM strategies developed for the safety assessment of human and animal health'?"

EFSA explained that the report mentioned in the question indicated that the largest barriers to conducting PMM of GM food and feed in the EU were found to be the 'unrecognisable' nature of GM traits further down the food and feed supply chain after processing, and the lack of appropriate consumption data at the branded/product level. EU legislation on traceability and labelling of GMOs requires products to carry a 'unique identifier'. However, this information is lost once the product is further processed to become a product 'produced from a GMO'. Consumption data held at a product level by retailers or market research agencies were shown to be more useful for PMM of GM food or feed than data held at the national level by public bodies. The project concluded that several changes would be required in order to conduct comprehensive PMM of GM food and feed in the EU, namely greater detail on traceability requirements of GMOs, a database of which food and feed products contain which GM traits at specific quantities, consumption data at the branded/product level and a system for reporting the relevance and intensity of effects and unintended effects. EFSA has recommended PMM in three cases (the scientific opinions on soybean 305423, soybean 87769 and soybean 87705), specifying that consumption data should be collected to support the nutritional assessment.

EC added that the authorisation proposals for the three GM soybeans mentioned by EFSA include requirements for data in line with EFSA's recommendations and they are currently undergoing the authorisation procedure.

"2. Could EFSA please address the applicants' concerns that the draft guidance for renewal of GM applications deviates from the definition of GMO which is to be authorised/renewed (as it is laid down in Regulation No (EC) 1829/2003, and more specifically Articles 11 and 23, as well as in Directive 2001/18/EC) by requesting the applicants to generate new data on a diverse set of commercialised GM crop varieties?"

EFSA indicated that, since an authorised transformation event is defined by its complete nucleotide sequence (insert and flanking regions), the applicant is requested to confirm the identity of the event for renewal by comparing the full sequence of this event to that of the original authorisation. Therefore, it is not considered to represent new data in support of the risk assessment. This requirement is in line with legislation, as confirmed by EC during the discussions on this GD.

"3. Does EFSA intend to include in the text of the draft guidance document on the agronomic and phenotypic characterisation of GM plants a provision for a period of transition and explicitly specify its duration and scope?"

EFSA replied that the EFSA Legal Services Department is being consulted on the possibility of including in the text a transition period for certain provisions, while others would be implemented immediately after the guidance is published.

"4. How is the announced EFSA's self-task revision of its scientific opinions for three already safety assessed products compatible with the weight-of-evidence approach in risk assessment if it is triggered by just one publication?"

The Chair of the GMO Panel replied that the weight-of-evidence approach can be defined as a process in which all of the evidence considered relevant for a risk assessment is evaluated and weighed. Using its own criteria in the weighing of the evidence for the risk assessment of GMOs, the GMO Panel thoroughly considers all the available data and evaluates all of them for their suitability for the intended purpose.

In this respect, and for completeness of its risk assessments, EFSA and its GMO Panel continuously monitor the scientific literature pertaining to GMOs, to be up to date with scientific development. All the data and information available for the assessment are evaluated, but only those judged to be relevant are used for the risk assessment. This is the case for the publication by Hofmann et al. (2014) on maize pollen deposition over long distances[7]. The GMO Panel pointed out that the findings by Hofmann et al. have potential implications on the results of the modelling exercise to estimate the effects of Bt maize pollen on sensitive non-target *Lepidoptera* and hence on the recommended risk mitigation measures to limit exposure to GM pollen in protected habitats. In accordance with its in-house procedures, EFSA therefore embarked on a self-task activity with the support of risk managers. The Hofmann paper presents results that add to the GMO Panel's previous knowledge and are duly taken into account.

He added that the Scientific Committee of EFSA is currently developing further guidelines on the use of the weight-of-evidence approach for the evaluation of scientific data. The objective is to improve the transparency of risk assessments by better explaining the selection and weighing of individual papers and how the findings have been integrated to reach the final conclusions.

[7] Hofmann F, Otto M and Wosniok W, 2014. Maize pollen deposition in relation to distance from the nearest pollen source under common cultivation – results of 10 years of monitoring (2001 to 2010). Environmental Sciences Europe 2014, 26:24 doi:10.1186/s12302-014-0024-3

Piet van der Meer, Ghent University/Free University of Brussels/PRRI:

"1. Does the GMO Panel concur that in order for an observed unintended change in a GM plant to be considered as a novel 'characteristic linked to the genetic modification' such a change has to be consistent and significant? In how many dossiers did the Panel identify such consistent and significant changes that they were considered as an unintended novel characteristic linked to the genetic modification? Could the Panel give examples of unintended effects that are more likely to happen due to transformation than due to conventional forms of modification? What are the precedents for expecting such types of unintended effects? How big must this unintended effect be in order to reach a concern threshold?"

The Chair of the GMO Panel replied that, whereas so-called 'intended' effects are linked to the intended objective of the genetic transformation (e.g. improved fatty acid profile/oil composition), the unintended effects are all the other effects that go beyond the objective of the genetic modification (e.g. interference with other metabolic pathways).

The EU regulatory framework on GMOs requires the risk assessment of direct, indirect, and delayed adverse effects, as well as intended and unintended adverse effects resulting from the genetic modification. The search for unintended effects involves a generic null hypothesis and therefore entails a scientific challenge, because the methodology to search for 'unknown unknowns' is not straightforward, and it is debatable how much effort is proportionate to seek such effects. As explained in Codex Alimentarius (2003)[8]: "A variety of data and information are necessary to assess unintended effects because no individual test can detect all possible unintended effects or identify, with certainty, those relevant to human health." Since it is difficult to look for all possible unintended effects, decisions must be made about the most relevant endpoints to select for study. Often, such endpoints will relate directly to potential harm; however, it is possible that some will act as general diagnostic endpoints which may, if differences are found, indicate the need for further data to be collected, i.e. follow-up measurements that more directly relate to adverse effects.

Hence, for food/feed safety assessments, there is international agreement concerning methodology: the search for unintended effects proceeds through molecular characterisation of the GMO, followed by compositional, agronomic and phenotypic comparative analyses. OECD recommends this comparative approach, as described in Codex Alimentarius (2003). The OECD approach forms the basis for protocols for the risk assessment of GM food and feed adopted and currently used in the USA, Canada, Australia, New Zealand, many other OECD countries, as well as in the EU (through EFSA's own guidance).

The GMO Panel acknowledges the difficulty of investigating such effects, in particular those that cannot be anticipated. In order to comply with the request from the legislators and risk managers to assess these possible unintended adverse effects, the GMO Panel considers all the evidence available that characterises the GMO under assessment. Molecular characterisation and compositional, agronomic and phenotypic data are part of a comparative analysis in which the GM is compared to a conventional counterpart. From this comparison, the assessor can determine whether or not an identified unintended effect has resulted from the genetic modification.

Regarding significance, the Chair of the GMO Panel clarified that, when the statistical analysis points to a difference, the biological relevance of that difference is assessed and, based on the analysis, the assessor determines whether or not there is a potential harm. This process is also enshrined in Implementing Regulation (EU) No 503/2013.

[8] Codex Alimentarius, 2003. Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA microorganisms. CAC/GL 46-2003

Regarding consistency, the data supplied by applicants usually come from a single set of trials collected from only one generation and in one genetic background. To assess consistency routinely would require the Panel, in its guidance documents, to request applicants to routinely repeat the set of trials. So far, the Panel has not considered such requests to be proportionate to the risk. Should it be the case that a biologically relevant unintended effect is identified, the Panel may ask the applicant to provide further data on whether or not there is a potential harm.

During its risk assessment of marketing applications, the GMO Panel encountered cases where unintended effects could not be excluded, owing to the differences observed in compositional, agronomic and phenotypic characteristics of the GM crop compared with its comparator (Application 64 for soybean BPS-CV127-9[9] and Application 101 for oilseed rape MON 88302[10]). But there have been also cases where the unintended effect was predictable, based on the newly expressed protein. In those cases, the applicant has performed additional studies, in order to rule out a potential harm (Application 43 for soybean 356043[11] and Application 53 for maize 98140[12]).

"2. Referring to the draft EFSA guidance document for the agronomic and phenotypic characterisation of GM plants, could the Panel discuss some examples of changes in phenotypic and agronomic characteristics presented in that document that would be 'linked to the genetic modification' rather than be the result of typical genetic variability in plants or even the variability that can be generated by merely putting plants through tissue culture, i.e. without the introduction of any new genes?"

EFSA replied that there is a possibility that changes in agronomic/phenotypic characteristics result from modifications of an endogenous metabolic pathway which may require additional comprehensive comparative analyses and subsequent food/feed safety assessment (e.g. a modified seed colour may result from changes in the GM plant's secondary metabolism). It is important to consider the interplay between the molecular characterisation, the agronomic/phenotypic characterisation and the compositional analysis in order to reliably capture the spectrum of differences between the GM plant and the appropriate test materials as a starting point to conduct the risk assessment. An agronomic/phenotypic difference may be indicative of an additional alteration in a food/feed safety related component (e.g. a GM plant exhibiting altered pest resistance might have an altered level of an anti-nutrient or toxicant, or another type of a bioactive constituent).

Agronomic and phenotypic data may provide information relevant to the assessment of the persistence and invasiveness of some GM plants, as some intended and unintended differences may be associated with changes in the plant's biology and/or life cycle characteristics. Therefore, where considered relevant, agronomic and phenotypic data can be part of the weight of evidence that is used in the environmental risk assessment to evaluate whether the GM plant is likely to have significantly altered characteristics indicative of a change in persistence and invasiveness (e.g. in the case of a GM oilseed rape, an increase in seed number (yield/seed weight) can have consequences on its persistence).

"3. Does the Panel concur that a potential adverse effect should only be considered if there is a scientifically plausible scenario that such an effect might occur, including the chain of events that must happen for an unintended effect to survive the breeding process and create a potential risk? Could the Panel discuss some concrete examples of 'magnitude' of the potential consequences of each adverse effect?"

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[9] http://www.efsa.europa.eu/en/efsajournal/doc/3505.pdf
[10] http://www.efsa.europa.eu/en/efsajournal/doc/3701.pdf
[11] http://www.efsa.europa.eu/en/efsajournal/doc/2310.pdf
[12] http://www.efsa.europa.eu/en/efsajournal/doc/3139.pdf

The Chair of the GMO Panel indicated that applicants currently give sufficient information about the breeding process to enable the Panel to determine whether a comparator is appropriate for the GM under assessment.

The EFSA risk assessment process seeks to identify differences between GM and comparators and evaluates those differences with regard to biological relevance. This is in line with international regulatory procedures. To determine what magnitude of difference equates to harm is difficult. The Panel assesses such differences on a case-by-case basis. For food–feed risk assessment, the equivalence concept is helpful in this regard. For environmental risk assessment (ERA), applicants should be able to set 'limits of concern'. The EFSA Scientific Committee's WG on ERA Protection Goals is currently developing an opinion on this topic. This opinion will support risk managers in translating protection goals into specific measurement endpoints and in defining the acceptable magnitude of adverse effects.

Annie Rose Harrison-Dunn, FoodNavigator/NutraIngredients:

"Given the recent discussions around national rights to ban GM crops that have already been approved at an EU level, how does EFSA see its role as a scientific authority developing? Does the recent vote mean science could become irrelevant in the policy-making process?"

EFSA replied that the EFSA GMO Panel is in charge of the risk assessment of GMOs prior to their placing on the market in the European Union. The recently approved regulation amending Directive 2001/18/EC on the deliberate release of GMOs into the environment provides Member States with the option to restrict or prohibit ('opting out') the cultivation, in all or part of their territory, of GMOs that have been authorised at EU level.

It is only on the basis of criteria other than science-based (e.g. socio-economic criteria) that Member States can ask to exclude their territories from the authorisation or ask a company seeking approval for a GM crop to exclude their territories from the scope of the application. Since science-based criteria cannot be used, EFSA's remit remains as before.

It should be noted that the new rules would allow Member States to ban GMOs on environmental policy grounds *other than* the risks to health and the environment already assessed by EFSA. Safeguard clauses and emergency measures will still be available to Member States, if a scientific reason is the basis for the proposed ban.

The Chair of the GMO Panel added that Member States have submitted safeguard clauses and emergency measures with little credible scientific justification, which made them seem motivated by politics rather than science, since they usually do not contain any information that has not already been considered by the Panel. He also expressed his hope that, with the new opt-out procedure, this will not be the case in the future.

EC confirmed that EFSA's role is not affected by the opt-out policy, as this allows Member States to ban a GMO based on reasons other than science based ones.

Wolfram Reichenbecher, Federal Agency for Nature Conservation:

"For its opinions and in line with its guidance documents EFSA assumes that good agronomic and agricultural practices are applied when GMOs are cultivated, including that complementary herbicides are used at a certain dosage.

However, conditions may deviate from EFSA's assumptions and, in practice, farmers may overuse complementary herbicides with GMO to fight hard to control weeds, which can influence the plant's composition.

1. Does the presumed discrepancy (e.g. deviation from EFSA's assumptions) have any impact on the validity of EFSA's opinions (and if so in which way)?"

The Chair of the GMO Panel replied that requirements for compositional and agronomic/phenotypic field trials foresee eight locations that should be representative of the receiving environment. Usually, treatments differ between locations, so overall the data will come from plants which had received a variety of treatments. Representativeness, as defined in the latest version of the GD on agronomic and phenotypic characterisation of GM plants, is concerned with ensuring an appropriate diversity of environmental conditions, whilst ensuring suitability and appropriateness. The GM receives over-the-top treatment (conventional and target herbicide). Therefore, overall, the field trial itself can be considered representative of the diverse agronomic practices that occur. The GMO Panel tends to focus on data from trials that are representative of current practices rather than those that are extreme and unrepresentative; experience and the scientific literature suggests that this provides more reliable data for risk assessment purposes.

"Provided EFSA agrees that there is a problem:

2. How does EFSA want to address the problem in the future?"

The Chair of the GMO Panel stated that he did not agree that such a problem existed.

"3. If the above-mentioned deviation is seen as a topic for risk management rather than risk assessment, shouldn't EFSA in its opinions at least note that there is a problem to make the Commission as the risk manager aware of it?"

The Chair of the GMO Panel indicated that, in the case of GM plants cultivated in the EU, there is the applicable legislation (Directive 2009/128/EC establishing a framework for Community action to achieve the sustainable use of pesticides) and Good Agricultural Practices (http://www.fao.org/prods/gap/), which include monitoring the use of herbicides, in order to prevent overuse. He also pointed to the importance that the EFSA GMO Panel gives to assessing properly the indirect effects of herbicides used within GM herbicide-tolerant systems on biodiversity. The scientific opinion on soybean 40-3-2[13] was given as an example of the care taken by the Panel in this regard. He then reminded EC of the discussion that took place at the 94th GMO Panel plenary meeting[14] related to the interplay between pesticides and GMO risk assessment, in which he expressed the Panel's view that the indirect effects of herbicides must continue to be assessed by the GMO Panel in its scientific opinions.

EC replied that the interplay between GMO and pesticides is meant to find a way to avoid duplication of work in these two areas of risk assessment. There are on-going discussions on this topic in the EC, and the result will be a draft proposal that will then be discussed with Member States.

René Custers, VIB:

"Learning from experience: the reason why stacks need to go through an authorisation process is because we want a pre-market evaluation to check on any unwanted interactions between the different modifications. By experience we know that herbicide tolerance and insect resistance do not interact. At what moment will the GMO Panel take on board this experience, update their guidance on stacks on this point, and advise the European Commission to no longer require dossiers for stacks of traits of which we know that they do not interact?"

[13] http://www.efsa.europa.eu/en/efsajournal/doc/2753.pdf
[14] http://www.efsa.europa.eu/en/events/event/141203b-m.pdf

EFSA replied that the principles for the risk assessment of stacked GM events are laid down in Implementing Regulation (EU) No 503/2013, which came into force on 8 December 2013, and is mandatory for applications submitted under Regulation (EC) No 1829/2003.

The risk assessment of GM plants containing stacked events requires the risk assessment of the GM plants containing these events independently (i.e. GM plants containing single events). For GM plants containing a combination of transformation events (stacked events) the primary concern for risk assessment is to establish that the combination of events is stable, and that no interactions occur between the stacked events that may give rise to safety concerns compared with the single events. The risk assessment of GM plants containing stacked events focuses on issues related to stability of the inserts, expression of the introduced genes and their products and potential synergistic or antagonistic effects resulting from the combination of the events.

Depending on the outcome of this analysis, further toxicological and nutritional information may be required. The risk assessment of a GM plant containing stacked events should address all sub-combinations occurring by natural segregation from the GM plant. Whenever relevant, sub-combinations produced by targeted breeding approaches, which can combine any of the events in all possible permutations, should also be assessed. The risk assessment of these sub-combinations should take into account the different exposure levels covered by the scope of the application. Applicants should provide appropriate data to enable the risk assessment of the sub-combinations.

As risk assessment is an evidence-based process, applicants should provide data covering the aspects mentioned above.

The statement that “herbicide tolerance and an insect resistance do not interact” may be correct in specific cases for import and processing applications relating to food–feed safety, but the Panel would not make such an all-encompassing statement without data and must work on a case-by-case basis.

For cultivation applications the statement “herbicide tolerance and an insect resistance do not interact” is questionable. The Perry et al. paper[15] gave details of a specific interaction which have not yet been refuted.

Joel Guillemain, French Agency for Food, Environmental and Occupational Health & Safety (ANSES):

“1. Renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003: the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) made comments during the public consultation on the Draft Guidance launched by EFSA in November 2014. This item will be treated under point 7.2 of the Agenda, but we would appreciate to have the opportunity to interact with the EFSA GMO Panel about some of our comments in Section 2.3 on PMM/PMEM and Section 2.5 on Additional documents and studies (in particular, why some elements of the EFSA 2006 Guidance (EFSA Journal (2006) 435, 1–4) are not present in this new guidance).”

EFSA referred to the discussion held under point 7.2 of the agenda, where it was explained how the comments received during the public consultation were taken into consideration.

“2. Post-market monitoring (PMM): we would like to know how EFSA plans to go ahead on this topic, especially how it will exploit the external scientific reports “Strategy support for the Post-Market Monitoring (PMM) of GM plants: Review of existing PMM strategies developed for the safety assessment of human and animal health” from ADAS (EFSA supporting

[15] Perry J et al, 2012. Estimating the effects of the Cry1F Bt-maize pollen on non-target Lepidoptera using a mathematical model of exposure. Journal of Applied Ecology, 2012, 49, 29-37

publication 2015:EN-739) and “Use of farmer/producer associations/federations to form sentinel surveillance networks for adverse events in primary production” from BioMath GmbH (supporting publication 2014:EN-543). Indeed, it seems that there has been no real technical discussion on which information should be provided when the first PMM were adopted with the authorisations of soybeans MON 87705, 305423 and MON 87769.”

EFSA replied that in the scientific opinions on soybeans with altered fatty acid profile there is a recommendation for a post-market monitoring (PMM) plan to be provided by the applicant. EFSA recommends that the PMM plan should include the collection of consumption data for the European population.

“3. Demand to have the flanking sequences in the case of stacked events: we would like to have the opinion of the EFSA GMO Panel on our demand to have the flanking regions sequenced in the stacked events. In our opinion, this information is a cheap and easy way to check that the sequences of the parents are effectively conserved in the stacked events (after several generations of crosses). If differences are observed, then the risk assessment on potential new ORF encoding proteins that could be toxins or allergens should be performed on the stacked event and not inferred from the sequence data of its parents. Additionally, any modification in the flanking sequences could have consequences on the performances of the PCR detection methods (we guess for the same reasons explain why the Draft Guidance for Renewal Applications of Genetically Modified Food and Feed authorised under Regulation (EC) No. 1829/2003 states that “The data should be generated from a representative number of current varieties of GM plants from different geographical areas that typically export to the European Union.” (lines 132 to 134)).”

EFSA clarified that the requirement to sequence insert and flanking regions of stacks is laid down in Implementing Regulation (EU) No 503/2013 (Annex I, Part II Scientific information, Section 1.2.2.4).

Kristiina Himanen, University of Helsinki, Department of Agricultural Sciences:

“1. Why is GMO evaluation focused on risk assessment without consideration of benefits?”

The Chair of the GMO Panel replied that the scientific opinions of EFSA’s GMO Panel are generated following requests from the EC to assess the safety of GMOs, in line with current legislation. Consideration of benefits is not in EFSA’s remit. The GMO Panel cannot legally discuss benefits in its opinions; the Panel’s function is restricted to the assessment of risk. According to the EU’s definition and operation of the precautionary principle, it is risk managers who have the responsibility to do a full cost–benefit analysis.

“2. What would be required to introduce risk/benefit assessment to GMO legislation?”

EC replied that analysis of benefits falls outside EFSA’s remit, according to current GMO legislation. It is the JRC’s European GMO Socio-Economics Bureau that works on proposing a toolbox to Member States to assess the implications of the cultivation of GMOs. The recently adopted ‘opt-out’ procedure implies that Member States will be able to use socio-economic considerations when deciding on cultivation of EU approved GMOs.

Adinda De Schrijver, Scientific Institute Public Health, and **Boet Glandorf, RIVM**:

“1. Could EFSA update us on which comments received during the public consultation have been taken into account in the update of the Guidance on the Agronomic and Phenotypic Characterisation of Genetically Modified Plants?

2. Could EFSA update us on which comments received during the public consultation have been taken into account in the update of the Guidance for Renewal Applications of Genetically Modified Food and Feed Authorised under Regulation (EC) No. 1829/2003?”

EFSA referred to the discussion held under points 7.1 and 7.2 of the agenda, where it was explained how the comments received during the public consultation were taken into consideration.

Louise Ball, DEFRA:

"1. Draft guidance on renewals: the need for re-sequencing in a representative number of current varieties from different geographical areas is a controversial requirement on both legal and scientific grounds. Would EFSA please explain how it has resolved the issue?"

EFSA referred to the discussion held under point 7.2 of the agenda, where it was explained how the comments received during the public consultation were taken into consideration.

"2. Guidance on agro/pheno characterisation: At the stakeholder meeting in Parma, we had an interesting discussion, which established that EFSA considers hazard identification to be outside of problem formulation. EFSA clarified that it is looking to identify unintended differences and reasons for those differences in this first step. How does EFSA stop this from being an open-ended exercise? Does it look at what regulators in other parts of the world require? We would be very interested to hear what changes have been made to the first draft and what the rationale behind those changes is."

The Chair of the GMO Panel welcomed the opportunity to clarify several issues. He challenged the idea that EFSA considers hazard identification to be outside problem formulation. The EFSA ERA Guidance Document (2010) makes it clear that problem formulation includes hazard identification; problem formulation (PF) cannot be done properly without it. The identified hazards are characterised in step 2 of the ERA, followed by step 3, which is characterisation of exposure. The ERA GD mentions that differences (some possibly unintended) identified within the comparative analysis of a GM and its conventional counterpart are then assessed initially within the problem formulation step, to focus the risk assessment on potential consequences.

The process of ERA begins with foreknowledge of the results of molecular characterisation and of agronomic, phenotypic and compositional comparative analysis. For all applications, meaning both cultivation and import-processing applications, the PF step considers any difference identified in these first four analyses—these may indicate hazards that need to be taken into account of in the ERA. The PF step also seeks to identify further hazards, other than the already identified ones, by consideration of the GM trait, the plant and any other relevant information.

Whilst it is clear that potential intended or anticipated unintended effects of a genetic modification can be identified through the PF step, leading to specific hypotheses that can be tested, it is also the case that those unintended effects that are unanticipated still need to be ruled out with sufficient certainty. This involves a generic null hypothesis and therefore entails a scientific challenge, because the methodology to search for 'unknown unknowns' is not straightforward and it is debatable how much effort is proportionate to seek such effects.

The EFSA GMO Panel is aware that risk assessment is not research, that data informing risk assessment should be restricted to questions based on 'the need to know', that research questions are broader and based on what is 'nice to know', and that there is a need for data requirements for risk assessment to be proportionate. Equally, EFSA is often called upon to defend the conclusions in its scientific opinions and to justify precisely how the data submitted have allowed those conclusions to be reached. The EC has been taken to court in actions that claim that EFSA has not followed its own GDs. Hence, it is important to gather sufficient evidence to rigorously identify potential unintended effects. The GMO Panel is often unwilling to conclude in the absence of what it regards as sufficient evidence. In practice, this balance is often struck in two ways: (i) the development of guidance which specifies what

endpoints to request and what standards of quality of information should be adhered to; and (ii) the posing of questions to applicants requesting clarifications and/or further data.

The GMO Panel is aware of some stakeholders' opinions on the need to make a transition from the present EU process-based regulation to a trait-based regulatory system, like the one employed by Canada. However, it should be noted that no regulatory authority (including Canada) neglects to test for unintended effects, because to do so would leave risk assessments inconclusive and subject to considerable unresolved uncertainty. The Chair of the GMO Panel cited from the Health Council of Canada's guidance: "The starting point for the safety assessment of novel foods is the evaluation of these foods relative to conventional counterparts that have a history of safe use. This approach takes both intended and unintended effects into account. […] As more complex or layered genetic modifications are attempted through recombinant DNA techniques, for instance to introduce both improved nutritional traits and agronomic traits into the same organism, these could increase the potential for unintended effects compared to simpler modifications. By the same token, other methods of genetic modification could also introduce multiple changes." The Health Council of Canada's guidance requires the traditional analyses: molecular characterisation compositional, agronomic and phenotypic comparisons—all four of these analyses are associated with generic, not specific, hypotheses. The Health Council of Canada's guidance states: "The safety criteria for the assessment of novel foods outlined in the current document were derived from internationally established scientific principles and guidelines developed through the work of the OECD, FAO, WHO and the Codex Alimentarius. The application of genetic modification through either traditional breeding or genetic engineering is not considered to increase or decrease the inherent risk associated with consuming the organism as a food. However, the wide variety of manipulations possible through genetic modification, and the potential for the introduction of toxic compounds, unexpected secondary effects and changes in the nutritional and toxic characteristics of the food product may give rise to safety concerns".

After having answered the written questions submitted by Observers upon registration, the Chair of the GMO Panel opened the floor for further questions.

Louise Ball asked where to draw the line when it comes to asking for information from applicants. She indicated that observed differences do not automatically translate into harm.

A Panel member replied that the current requirements of the Agro-pheno GD are for fewer endpoints than usually submitted by applicants. He also pointed to previous questions on unintended effects and to challenges imposed by looking for unintended effects.

Another Panel member added that an observed difference will inform the risk assessment, but whether that difference will be a harm or not cannot be predetermined.

Boet Glandorf asked whether the agro-pheno guidance includes distinct requirements for single and stacked GM events.

A Panel member reminded the audience of the answer provided by EFSA to the question on the risk assessment of stacked GM events. He stressed that the GMO Panel has the legal obligation to assess stacks and their sub-combinations. The Chair of the GMO Panel added that, for some sub-combinations, there are limited or no data available to support the risk assessment, which makes concluding on all sub-combinations difficult.

René Custers followed with a question related to the risk assessment of stacked GM events, asking whether it would be possible for certain events to have authorisations that would automatically include the crosses between them.

A Panel member replied that the data packages are already reduced for stacked GM events in comparison with single events. One of the differences between singles and stacks is the

requirement for toxicological studies, such as the 90-day study. The assessment of stacked GM events uses the weight-of-evidence approach. He also indicated that the authorisation is not in the remit of EFSA.

Another Panel member added that the risk assessment of stacks relies on two pillars: (i) the previously assessed single events and (ii) the additional data specific for the stacked GM event. He supported the statement that requirements for stacks are already reduced compared with the singles, and he could not see any need to further reduce them.

Conrad von Kameke asked whether the GMO Panel intends to apply the principle of proportionality in its GDs.

A Panel member replied that the GMO Panel endeavours to be proportionate in its evaluation of products and guidance development.

Piet van der Meer pointed to the growing requirements of the GMO Panel's GDs, and indicated that it is difficult for public research institutes to comply with these requirements, should they try to submit applications for GMOs. He expressed his hope that the requirements for data would have lowered in time, as the element of novelty linked to GMOs disappeared, but this never happened.

A Panel member acknowledged budget limitations of public institutions, but clarified that science evolves, therefore it is normal that the requirements for data change over time. Another Panel member added that the requirements of the GMO Panel also have to be in line with the applicable legislation.

Catherine Goldstein asked from which application the IR 503/2013 would be applicable and how Article 5 paragraph 2 would be applied.

EFSA replied that IR 503/2013 applies to applications received after the date of its entry into force, i.e. 8 December 2013. The first application received after that date was Application 121.

Regarding Article 5, paragraph 2, EFSA indicated that it will accept a justification for cases when data cannot be provided for technical reasons. However, this paragraph cannot be used as a justification for not performing field trials.

EC confirmed EFSA's answer by indicating that this paragraph was indeed introduced for cases where data cannot be provided because of technical limitations.

Suzy Renckens commented that it is difficult for applicants to comply with constantly increasing requirements and with GDs that do not foresee a transition period. She also asked whether the GMO Panel takes into consideration scientific papers which support the claim that the null segregant is an adequate comparator for GMOs, to which EFSA replied that Regulation (EC) No 1829/2003 clearly defines the conventional counterpart to be used in the comparative assessment and the null segregant falls outside this definition.