MINUTES OF THE 55TH PLENARY MEETING OF THE SCIENTIFIC PANEL ON GENETICALLY MODIFIED ORGANISMS HELD ON 27-28 JANUARY 2010 IN PARMA, ITALY

(ADOPTED ON 10 MARCH 2010)

PARTICIPANTS

GMO Panel:
Hans Christer Andersson, Salvatore Arpaia, Detlef Bartsch, Josep Casacuberta[1], Howard Davies, Gerhard Flachowsky, Patrick du Jardin, Lieve Herman, Huw Jones, Sirpa Kärenlampi, Jozsef Kiss, Gijs Kleter, Harry Kuiper (Chair), Antoine Messéan, Joe Perry, Annette Pöting, Jeremy Sweet, Christoph Tebbe and Jean-Michel Wal.

EFSA: Riitta Maijala[2] (Head of Risk Assessment Directorate), Djien Liem[2] (Head of Scientific Committee and Advisory Forum Unit).

GMO Unit: Per Bergman, Anna Christodoulidou, Yann Devos, Antonio Fernandez Dumont, Andrea Germini, Ana Gomes, Karine Lheureux, Yi Liu, Sylvie Mestdagh, Claudia Paoletti, Nancy Podevin, Ellen Van Haver, Elisabeth Waigmann.

European Commission:
Sabine Pelsser and Michael Walsh (DG SANCO); Ioana Rodica Ispas (DG ENV).

Others:
Miloslava Navratilova[3] (Statni Rostlinolekarska Sprava), Jaroslava Ovesna[3] (VURV), Slavomir Rakousky[3] (Jihoceska Univerzita v Ceskych Budejovicich), Josef Kubicek[3] (Ministerstvo Zivotniho Prostredi Ceske Republiky).

APOLOGIES

GMO Panel:
Kaare Nielsen, Atte Von Wright.

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1. WELCOME AND APOLOGIES FOR ABSENCE

The Chair opened the meeting and welcomed all. Apologies for absence were received from some Panel members as mentioned above.

2. ADOPTION OF THE AGENDA

The agenda was adopted as proposed.

3. DECLARATION OF INTERESTS

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[1] Only present on 28 January

[2] Present on 27 January am, for agenda point 10 only.

[3] Present on 28 January am, for agenda point 7.1 only.

EFSA secretariat screened the ADoI and SDoI filled in by the scientific experts invited at this meeting in accordance with EFSA's Policy on Declarations of Interests.
With regard to this meeting no other interest than those already declared in the ADoI or in a previous SDoI and screened by EFSA in accordance with its Policy on Declarations of Interests and implementing documents thereof was declared by the experts.

4. ADOPTION OF THE MINUTES OF THE 54TH PLENARY MEETING HELD ON 2-3 DECEMBER 2009

The minutes of the 54th Plenary meeting (2-3 December 2009) were adopted and will be published at: http://www.efsa.europa.eu/en/events/event/gmo091202.htm

5. DISCUSSION AND POSSIBLE ADOPTION OF OPINIONS ON:

5.1. Guidance document for the environmental risk assessment of GM plants (EFSA-Q-2008-262)

Introduction

The European Commission and EFSA asked the GMO Panel to further develop and update its guidance for the Environmental Risk Assessment (ERA) of GM plants, submitted within the framework of Regulation (EC) No. 1829/2003 on GM food and feed or under Directive 2001/18/EC on the deliberate release into the environment of GMOs. This document updates the ERA section of the EFSA Guidance document for the risk assessment of GM plants and derived food and feed[4]. The EFSA Guidance document was previously updated with a chapter on general surveillance of unanticipated effects of the GM plant as part of the post-market environmental monitoring (PMEM)[5] and the section on PMEM of this document was not further updated since it was outside the mandate.

Discussion and conclusion

ERA of GM plants involves generating, collecting and assessing information on a GM plant in order to determine its impact on human/animal health and the environment compared to its non-GM conventional counterpart, and thus assessing its relative safety. The document discusses and concludes on the following main issues.

ERA should follow a step-by-step assessment approach. The guidance document elaborates on the six steps for the ERA of GM plants described in Directive 2001/18/EC, starting with (1) a problem formulation including hazard identification; (2) hazard characterisation; (3) exposure characterisation; (4) risk characterisation; (5) risk management strategies and (6) an overall risk evaluation.

The EFSA GMO Panel considers seven specific areas of concern to be addressed by applicant and/risk assessors during its evaluation: i) the potential persistence or invasiveness of the plant

[4] http://www.efsa.europa.eu/en/scdocs/scdoc/99.htm

[5] Opinion of the GMO Panel on the Post Market Environmental Monitoring (PMEM) of genetically modified plants (EFSA-Q-2004-061): http://www.efsa.europa.eu/en/scdocs/scdoc/319.htm º

itself, or of its wild relatives, addressed by a "staged approach"; ii) plant to micro-organisms gene transfer; iii) potential interaction of the GM plant with target organisms and iv) with non-target organisms (NTO) including criteria for selection of appropriate NTO species and relevant functional groups for risk assessment; v) potential impact of the specific cultivation, management and harvesting techniques including the consideration of the production systems and the receiving environment(s); vi) effect of biogeochemical processes and vii) potential effects on human and animal health. Each specific area of concern is developed in a systematic way through the six structured steps mentioned above.

ERA should follow a weight-of-evidence approach considering intended and unintended effects.

The ERA should be carried out on a case-by-case basis, so the required information may vary depending on the type of the GM plants and trait(s) concerned, their intended use(s), and the potential receiving environment(s).

There are several general cross-cutting considerations that need to be considered during the ERA of a GM plant including: choice of comparators, receiving environments, general statistical principles, long term effects, stacked events.

Adoption

The draft guidance was adopted by the EFSA GMO Panel and will be presented to the Scientific Committee at their next Plenary meeting before the launch of a two-month public consultation.

5.2. Scientific Opinion on the assessment of potential impacts of GM plants on non-target organisms (EFSA-Q-2008-089)

Introduction

EFSA asked the GMO Panel to establish a self-mandate Working Group with the aim of (1) producing a scientific review of the current guidance of the GMO Panel for Environmental Risk Assessment (ERA), focusing on the potential impacts of GM plants on Non-Target Organisms (NTOs), (2) proposing criteria for NTO selection, and (3) providing advice on standardized testing methodology. This initiative was undertaken in response to a need and request from a wide range of stakeholders, including the European Commission and Member States. It forms an integral part of the draft updated ERA Guidance document referred to in item 5.1 above.

Discussion

In the first instance, the self-mandate Working Group on Non-Target Organisms (EFSA NTO WG) mainly considered impacts of GM plants on invertebrate species, but also took account of ecosystem functions that could be altered.

The EFSA NTO WG considered the necessity for: clear and objective protection goals, for which assessment and measurement endpoints should be developed; the need to initiate the scientific risk assessment by setting testable hypotheses; criteria for appropriate selection of test species and ecological functional groups; appropriate laboratory and field studies to collect relevant NTO data; and the use of statistical techniques integral to experimental design and analysis. The EFSA NTO WG considered the range of approaches and methodologies of ERA of NTOs as described in the current literature. The EFSA NTO WG proposed risk assessment approaches based on selection of functional groups and individual species within a tiered approach.

Conclusion

The present scientific opinion provides guidance to risk assessors for assessing potential effects of GM plants on NTOs, together with the rationale for data requirements in order to complete a comprehensive ERA for NTOs. In this respect, the guidance to applicants as outlined in the present opinion has been inserted in the updated draft guidance document (see 5.1 above) for the ERA of GM plants.

Adoption

The draft opinion was adopted by the EFSA GMO Panel and will be presented to the Scientific Committee at their next Plenary meeting before the launch of a two-month public consultation.

5.3. Scientific Opinion on a notification by Portugal for the prohibition of cultivation of GM Plants in the Autonomous Region of Madeira (EFSA-Q-2009-00851)

Introduction

According to Article 95(5) of the EC Treaty, Portugal notified to the European Commission its intention to declare the Autonomous Region of Madeira as a region free from the cultivation of GM plants. Portugal therefore proposed to introduce a regional decree to prohibit the cultivation of GM seeds and propagating plant material in the Autonomous Region of Madeira. Two reports were provided in support of the national measure. Following the notification of Portugal, the European Commission requested a scientific opinion from the EFSA GMO Panel to investigate whether the information mentioned in the supporting documents contains any new scientific evidence in terms of protection of the environment in the Autonomous Region of Madeira, that would justify such a prohibition of the use of GMOs, including those that have already been authorised under Directive 90/220/EEC or Directive 2001/18/EC.

Discussion and conclusion

In its evaluation, the EFSA GMO Panel only investigated and commented on aspects that relate to the protection of human and animal health and the environment. Socio-economic aspects related to the cultivation of GM plants and the coexistence between cropping systems fall outside the remit of EFSA, and are not addressed in this scientific opinion.

Following investigation of the evidence presented in the Portuguese submission, the EFSA GMO Panel did not identify new scientific information on the environmental or human and animal health impacts of EU approved GM plants. The EFSA GMO Panel therefore concluded that, based on the supporting documents submitted by Portugal, no new scientific evidence, in terms of risk to human and animal health and the environment, was provided that would justify a prohibition of the cultivation of GM plants in the Autonomous Region of Madeira.

Adoption

The opinion was adopted unanimously by the EFSA GMO Panel. The scientific opinion will be published on the following EFSA website: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_ScientificDocuments.htm

5.4. Scientific Opinion on application (EFSA-GMO-NL-2007-39) for the placing on the market of insect resistant and herbicide tolerant GM maize MON 89034 x MON 88017 for food and feed uses, import and processing

The EFSA GMO Panel started a discussion of the Scientific Opinion on EFSA-GMO-NL-2007-39. However, the possible adoption of the opinion was deferred to the next plenary meeting because of time constraints.

6. DISCUSSION OF OPINIONS

None

7. UPDATE ON APPLICATIONS RECEIVED UNDER REGULATION (EC) NO 1829/2003 AND REGULATION (EC) NO 1831/2003

7.1. Regulation (EC) No 1829/2003

The Competent Authority of the Czech Republic has carried out the environmental risk assessment (ERA) of application EFSA-GMO-UK-2008-60 (GA21 maize for cultivation) in accordance with articles 6.3(c) and 19.3(c) of Regulation (EC) No 1829/2003. Representatives of the Competent Authority of the Czech Republic presented their ERA report of application EFSA-GMO-UK-2008-60 to the GMO Panel. The members of the EFSA GMO Panel thanked the Czech experts for their work and presentation. The EFSA GMO Panel will consider this report when assessing GA21 maize, and the report will be included as an annex to the final EFSA overall opinion adopted by the Panel.

7.2. Regulation (EC) No 1831/2003

None

8. NEW REQUESTS TO EFSA: DISCUSSION AND ADOPTION OF MANDATES

None

9. UPDATE ON SELF-MANDATE ACTIVITIES AND GUIDANCE FOR GMO RISK ASSESSMENT

Self-mandate on the choice of comparators. The working group will hold its next meeting on 4 February 2010, the outcome of which will be presented to the Panel at its next Plenary meeting.

Self-mandate for updating the Guidance for risk assessment of GM microorganisms. New *ad hoc* experts have joined the working group. The next meeting is scheduled for 2-3 March 2010.

Environmental risk assessment of GM animals. A workshop on GM fish will be organised by EFSA on 4 February 2010 to review the draft final report provided by the contractor, and to set the basis for a working group that will draft a guidance document on the environmental risk assessment of GM animals. The Panel was also informed about the kick-off meetings with the contractors that have been assigned to the tenders for GM insects and for GM mammals and birds.

Risk assessment of GM animals and derived food/feed. The guidance document is being revised following suggestions from the GMO Panel when the document was presented at their Plenary meeting of 2-3 December 2009. A revised mandate that will request EFSA to address welfare issues in addition to the safety issues is under preparation by the European Commission.

10. FEEDBACK FROM EFSA AND THE SCIENTIFIC COMMITTEE

Riitta Maijala, Head of the Risk Assessment Directorate, gave a presentation on EFSA key priorities for 2010 and their implementation in the field of GMO risk assessment. The Panel was also informed about modified rules for EFSA Panels and Scientific Committee as adopted by the EFSA Management Board[6].

Djien Liem, Head of the Scientific Committee and Advisory Forum Unit presented the Opinion of the Scientific Committee on Transparency in the Scientific Aspects of Risk Assessments carried out by EFSA[7].

11. FEEDBACK FROM THE COMMISSION

The Commission representative informed the EFSA GMO Panel about the status of applications that have been presented to the Standing Committee on the Food Chain and Animal Health (14 December 2009). The final version of the EC guidelines on the risk assessment of genetically modified food and feed will be discussed at the next meeting of the Standing Committee on the Food Chain and Animal Health.

12. DATE AND PLACE OF FUTURE MEETINGS

Meeting dates for 2011 will be presented at the next Plenary meeting.

13. ANY OTHER BUSINESS

The EFSA GMO Panel discussed the outcomes of a recently published article by de Vendômois et al. (2009) regarding a statistical reanalysis of data from three 90-day rat feeding studies already assessed by the GMO Panel. The deliberations of the Panel on this paper are annexed to these minutes (Annex 1).

The EFSA GMO Panel assessed the updated bioinformatic analysis of maize event NK603 (see their assessment in Annex 2 to these minutes), following a comment by Austria on the bioinformatic data evaluated during the assessment of maize event NK603.

[6] http://www.efsa.europa.eu/en/aboutefsa/keydocs.htm

[7] http://www.efsa.europa.eu/en/scdocs/scdoc/1051.htm

Annex 1

GMO Panel deliberations on the paper by de Vendômois et al. (2009, A Comparison of the Effects of Three GM Corn Varieties on Mammalian Health, International Journal of Biological Sciences, 5: 706-726)

The EFSA GMO Panel has considered the paper by de Vendômois *et al.* (2009, A Comparison of the Effects of Three GM Corn Varieties on Mammalian Health, *International Journal of Biological Sciences*, 5: 706-726), a statistical reanalysis of data from three 90-day rat feeding studies already assessed by the GMO Panel (EFSA, 2003a,b; EFSA 2004a,b; EFSA 2009b,c). The GMO Panel concludes that the authors' claims, regarding new side effects indicating kidney and liver toxicity, are not supported by the data provided in their paper. There is no new information that would lead it to reconsider its previous opinions on the three maize events MON810, MON863 and NK603, which concluded that there were no indications of adverse effects for human, animal health and the environment.

The GMO Panel notes that several of its fundamental statistical criticisms (EFSA, 2007a,b) of the authors' earlier study (Seralini *et al*., 2007) of maize MON863 are also applicable to the new paper by de Vendômois *et al.* In the GMO Panel's extensive evaluation of Seralini *et al*. (2007), reasons for the apparent excess of significant differences found for MON863 (8%) were given and it was shown that this raised no safety concerns. The percentage of variables tested reported by de Vendômois *et al*. that were significant for NK603 (9%) and MON810 (6%) were of similar magnitude to that for MON863. The GMO Panel considers that de Vendômois *et al.:* (1) make erroneous statements concerning the use of reference varieties to provide estimates of variability that allow equivalence testing to place statistically significant results into biological context as advocated by EFSA (2008, 2009a); (2) do not use the available information concerning normal background variability between animals fed with different diets, to place observed differences into biological context; (3) do not present results using their False Discovery Rate methodology in a meaningful way; (4) give no evidence to relate well-known gender differences in response to diet to claims of effects due to the respective GMOs; (5) estimate statistical power based on inappropriate analyses and magnitudes of difference.

The significant differences highlighted by de Vendômois *et al.* have all been considered previously by the GMO Panel in its previous opinions on the three maize events MON810, MON863 and NK603. The study by de Vendômois *et al*. provides no new evidence of toxic effects. The approach used by de Vendômois *et al*. does not allow a proper assessment of the differences claimed between the GMOs and their respective counterparts for their toxicological relevance because: (1) results are presented exclusively in the form of percentage differences for each variable, rather than in their actual measured units; (2) the calculated values of the toxicological parameters tested are not related to the normal range for the species concerned; (3) the calculated values of the toxicological parameters tested are not compared with ranges of variation found in test animals fed with diets containing different reference varieties; (4) the statistically significant differences did not show consistency patterns over endpoint variables and doses; (5) the inconsistencies between the purely statistical arguments of de Vendômois *et al.,* and the results for these three animal feeding studies which relate to organ pathology, histopathology and histochemistry, are not addressed. Regarding claims made by de Vendômois *et al*. concerning the inadequacy of the experimental design of these three animal feeding studies, the GMO Panel notes that they were all carried out to agreed internationally-defined standards consistent with OECD protocols.

References

EFSA, 2003a. Opinion of the Scientific Panel on genetically modified organisms (GMO) on a request from the Commission related to the safety of foods and food ingredients derived from herbicide-tolerant genetically modified maize NK603, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/9.htm

EFSA, 2003b. Opinion of the Scientific Panel on genetically modified organisms (GMO) on a request from the Commission related to the Notification (Reference CE/ES/00/01) for the placing on the market of herbicide-tolerant genetically modified maize NK603, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/10.htm

EFSA, 2004a. Opinion of the Scientific Panel on genetically modified organisms (GMO) on a request from the Commission related to the Notification (Reference C/DE/02/9) for the placing on the market of insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/49.htm

EFSA, 2004b. Opinion of the Scientific Panel on genetically modified organisms (GMO) on a request from the Commission related to the safety of foods and food ingredients derived from insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/50.htm

EFSA, 2007a. EFSA review of statistical analyses conducted for the assessment of the MON 863 90-day rat feeding study. http://www.efsa.europa.eu/en/scdocs/scdoc/19r.htm

EFSA, 2007b. Statement on the analysis of data from a 90-day rat feeding study with MON 863 maize by the Scientific Panel on genetically modified organisms (GMO). http://www.efsa.europa.eu/en/scdocs/scdoc/753.htm

EFSA, 2008. Updated guidance document for the risk assessment of genetically modified plants and derived food and feed. Annex A. http://www.efsa.europa.eu/en/scdocs/scdoc/293r.htm

EFSA, 2009a. Statistical considerations for the safety evaluation of GMOs. http://www.efsa.europa.eu/en/scdocs/scdoc/1250.htm

EFSA, 2009b. Applications (references EFSA-GMO-NL-2005-22, EFSA-GMO-RX-NK603) for the placing on the market of the genetically modified glyphosate tolerant maize NK603 for cultivation, food and feed uses, import and processing and for renewal of the authorisation of maize NK603 as existing products, both under Regulation (EC) No 1829/2003 from Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/1137.htm

EFSA, 2009c. Applications (EFSA-GMO-RX-MON810) for renewal of authorisation for the continued marketing of (1) existing food and food ingredients produced from genetically modified insect resistant maize MON810; (2) feed consisting of and/or containing maize MON810, including the use of seed for cultivation; and of (3) food and feed additives, and feed materials produced from maize MON810, all under Regulation (EC) No 1829/2003 from Monsanto. http://www.efsa.europa.eu/en/scdocs/scdoc/1149.htm

Seralini, G.E., Cellier D., de Vendômois J.S. 2007. New analysis of a rat feeding study with genetically modified maize reveals signs of hepatorenal toxicity. Arch. Environ. Contam. Toxicol., 52: 596-602.

Annex 2

GMO Panel risk assessment of an updated bioinformatic analysis of maize event NK603

The EFSA GMO Panel discussed a comment by Austria on the bioinformatic data evaluated during the assessment of maize event NK603. Regarding the bioinformatic analysis of the genomic flanking regions in maize event NK603, the GMO Panel is aware of data submitted in the context of application for a triple hybrid containing event NK603, EFSA/GMO/NL/2009/65, (Tu and Silvanovich, 2009) using the same query sequence and BLAST search parameters as in the study performed for the analysis of the single event NK603 in application EFSA/GMO/NL/2005/22 (McClain and Silvanovich, 2008). As opposed to the data in McClain and Silvanovich (2008) that report no hits, results in Tu and Silvanovich (2009) indicate the existence of several homologous nucleotide sequences when a blastn analysis is performed on ESTs and non-redundant nucleotide databases. The difference between the two reports might be explained (i) by the use of databases which differ from one another, not only by the dates of release, but also from the nature of the deposited sequences: "GenBank CDNA nucleotide database" in McClain and Silvanovich (2008) and "GenBank EST and non-redundant nucleotide databases" in Tu and Silvanovich (2009) ; (ii) by the used algorithms which were "publicly available BLAST algorithms" in the first study and "publicly available BLAST algorithms + algorithms downloaded from the National Center for Biotechnology Information (NCBI)" in the latter. Owing to the progress in bioinformatic tools and databases available, the importance of these analyses in the risk assessment has increased and therefore, currently, the GMO Panel requests a more extended bioinformatic analysis which includes a more detailed description of the versions and characteristics of the databases used.

The results of Tu and Silvanovich (2009) are in agreement with the analysis of the Austrian experts and point to the existence of several homologous nucleotide sequences when a blastn analysis is performed on ESTs and non-redundant nucleotide databases. In order to evaluate the relevance of these matches and whether they may indicate the interruption of endogenous protein-coding genes raising possible safety concerns, the following observations must be taken into account:

- Although the total length of the query sequence corresponding to the re-constructed insertion site is 808 bp, the length of the nucleotide regions matching database entries is always less than 195 bp;
- The blastn analysis identified a homologous database entry corresponding to a gene sequence coding for the *Zea mays* P2 protein, a *myb*-related transcription factor (Zhang *et al.* 2000, The Plant Cell, 12:2311); however, the aligned interval is limited to 109 bp of the query sequence and the alignment is located outside the protein-coding part of the P2 gene sequence deposited in GenBank; this is in line with the blastx analysis which failed to identify any known protein from maize.
- The blastx analysis failed to identify any known polypeptide from *Zea mays* and the top alignment only displays 23% identity in a window of 95 amino acids with a hypothetical protein from rice (E-Score of 0.33).

Altogether, these results are not indicative of the interruption of any known endogenous protein-coding sequences and do not raise a safety concern. This conclusion is in line with the observed agronomic and compositional equivalence between NK603 maize and its conventional counterparts.