European Food Safety Authority

GMO UNIT

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BILATERAL TECHNICAL MEETING BETWEEN MEMBERS OF THE EFSA PANEL ON GENETICALLY MODIFIED ORGANISMS AND THE BELGIAN BIOSAFETY ADVISORY COUNCIL

According to Article 30.2 of the Regulation (EC) No 178/2002

UPDATED GUIDANCE DOCUMENT FOR THE RISK ASSESSMENT OF GM PLANTS AND DERIVED FOOD AND FEED

Agreed Meeting report of the meeting on 10 December 2008

The below report does reflect the common understanding of EFSA and the delegation of the Belgian Biosafety Advisory Council of the meeting. This report is not, and cannot be regarded as, representing the position, the views or the policy of the European Food Safety Authority or of any national or EU Institution, agency or body.

Participants

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	Rene Custers	BAC, Flanders Interuniversity Institute for Biotechnology
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EFSA GMO Food/Feed Working Group members:	Anderson Christer, Annette Poeting, Gerhard Flachowsky, Gijs Kleter, Harry Kuiper, Ilona Kryspin Soerensen, Jean-Michel Wal, Willem Seinen	
EFSA GMO Unit:	Andrea Germini, Anna Christodoulidou, Claudia Paoletti, Elisabeth Waigmann, Yi Liu	

1. Welcome

The chair of the EFSA GMO Panel welcomed the Belgian Delegation. The objective of the meeting, which was initiated by the Belgian Biosafety Advisory Council (BAC), was to enter into a dialogue with scientific experts of the Belgian Delegation on several topics addressed in the draft Updated Guidance Document for the Risk Assessment of GM Plants and Derived Food and Feed. EFSA has continuously liaised with various parties on the contents of this guidance document, also in the frame of the public consultation on the draft

document that took place during the summer 2008. This meeting serves as a specific opportunity to further discuss selected issues.

The Belgian Delegation explained that part of their questions was formulated by BAC experts, and part was formulated by independent experts who are consulted in the context of dossier evaluations, but who are not BAC members.

2. Issues discussed:

Substantial Equivalence

Substantial equivalence is one of the main concepts in risk assessment of GMOs. Upon request of the Belgian Delegation, the experts of the Food/feed Working Group of EFSA GMO Panel explained how equivalence is assessed: a large number of assessment endpoints is compared between the GMO and its appropriate non-GM comparator. Potential differences are then evaluated taking into account natural variation. The baseline for 'natural variation' is defined by the range of variation observed in conventional varieties. The larger the number of parameters analyzed, the more likely is it that differences are observed. However, the observed differences may not be biologically relevant. Therefore GMO Panel focuses on differences that are consistently observed. This holds true for both compositional analysis and for animal trials where animals are fed with material obtained in field trials across several sites and seasons. Based upon experience, differences observed in animal trials are frequently without biological relevance. Nonetheless, whenever statistically significant differences are observed, these differences must be evaluated with respect to background variation. Furthermore, the GMO Panel Working Group on Statistics is elaborating a report that details an approach to assess background variation based on the inclusion of reference lines into the experimental design.

Experiments addressing substantial equivalence are therefore not the end of the risk assessment process, but the starting point for further evaluation.

Nutritional issue

The Belgian Delegation raised the issue that measurement of dietary fibre is standard for assessment of food products. However, the GMO Panel in its risk assessment currently assesses acid detergent fibre (ADF) and neutral detergent fibre (NDF), which is different from assessment of dietary fibre. There have been no indications of changes in ADF/NDF/crude fiber indicating relevant changes from a health perspective.

The Food/feed Working Group acknowledged this comment. For crops, OECD consensus documents recommend specific parameters, which are also considered by the EFSA GMO Panel, those parameters include also ADF/NDF. As stated in OECD consensus document, for food use the concept of dietary fibre is preferred, although different definitions and methods of analysis are being used. Within Codex Alimentarius, the discussion on which methods to be used to quantify dietary fibre is still ongoing. A further consideration in this context is that changes in dietary fibre are not expected to result in health impacts. The Food/feed Working Group also acknowledged that the BCA has previously posed this question. The Food/feed Working Group experts confirmed that if information on dietary fibre is provided in a dossier, it will be assessed.

Power of statistical analysis

The Belgian Delegation found the new report of the EFSA GMO Statistics Working Group is helpful. It addresses two of their concerns: the question of statistical power, and the question of multiple endpoints versus a single endpoint for certain parameters. The Food/feed Working Group explained that the Statistics Working Group has specifically considered the Belgian comments on this matter. The statistics report strikes a balance

between adequate power requirements and realistically obtainable amount of data. Currently these requirements for statistical power are not yet compulsory in dossiers. The report provides a limited introduction to the possible application of statistical methods for comparative risk assessment on multiple endpoints. Substantial more work on this subject is needed.

Additional animal studies for stacked events

The discussion addressed whether animal trials could be used to screen for unintended effects due to interaction between traits. Currently, potential interactions between traits in stacked events are assessed by the Panel using compositional data, molecular characterization, and data on the functionality. Based on the outcome of this assessment, the GMO Panel decides if further studies are needed, including animal studies. Indeed, in several cases additional animal studies were requested.

The Belgian Delegation asked how potential interaction between traits is practically examined and if gene expression microarrays would be a feasible method. The Food/feed Working Group explained that potential interaction is primarily assessed by considering any indications based on the functionality of the different introduced gene products, molecular characterization and extensive compositional analysis. The Food/feed Working Group recognized that microarrays may provide some useful indication on potential interactions The Belgian Delegation and the Food/feed Working Group experts consider the 90-day animal feeding study as a possibility to detect adverse effects resulting from a potential interaction, although it is relatively insensitive.

Pesticide residues

The Belgian Delegation raised the question which comparisons have to be provided for the compositional analysis of herbicide-resistant crops. The issue regarding compositional analysis of herbicide-tolerant crops is being addressed in the new legal framework. At the end, the Belgian Delegation had come to a clear understanding of what regimes of materials should be tested: the treated GM should be compared with the conventionally treated non-GM.

Allergenicity

The Belgian Delegation raised two issues which in their opinion is not addressed sufficiently: 1) allergenicity assessment is currently mainly based on bioinformatics, with sometimes limited data on the method and databases used; 2) route of exposure may differ between products (e.g. pollen, food), 3) there is limited value of in vitro digestion. The Food/feed Working Group explained that the Panel's assessment on allergenicity relies on the guidance, Codex alimentarius and OECD. Individual tests such as bioinformatic analysis, stability of the protein, are informative but not sufficient on its own. The technical requirements for the databases are being described in more detail in the new legal framework. In summary, the GMO Panel assesses all available information by following the weight of evidence approach. The combined assessment of all tests may indicate a low likelihood of allergenicity. Currently a self-tasking Working Group on Allergenicity is in the final stages of completing a draft report on the issue of assessment (e.g. requirements for methods and databases) of potential allergenicity of GMOs.

The Belgian comments also pertain to the assessment of allergenicity of the whole GM crop. The Food/feed Working Group explained that a food produced from a non-allergenic crop expressing a trait without an indication of allergenicity can be considered low risk. This differs for foods produced from known allergenic crops, which explains why the Panel has required additional information in these cases on sera-testing. However, the availability of human sera may be limited and may be constrained by ethical considerations. If possible and feasible, such data are provided.

The Belgian Delegation asked what the borderline between common and uncommon food allergens could be. The Food/feed Working Group explained that there is a list of food allergens available in the frame of the EU regulations regarding labelling of foods, which is subject to regular updates. This list currently contains 14 food families (e.g. cereals, soybean, peanut, nuts). Rice, maize, potato, tomato and cotton are not on the list.

Omics analytical technologies

The Belgian Delegation mentioned that transcriptomics could be a method to study effects on gene expression. The Belgian Delegation commented that regarding complexity, there is a general trend towards more complex biological models, such as microarrays. The Food/feed Working Group explained that the Panel critically reviews transcriptomics data published in literature and elsewhere. For example, a recently web published report on reproductive assessment of NK603 x MON810 maize by (Velimirov et al. 2008, www.bmgfj.gv.at/cms/site/attachments/3/2/9/CH0810/CMS1226492832306/forschungsbericht_3-2008_letztfassung.pdf) was critically reviewed by the GMO Panel (http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902199319.htm).

The Food/feed Working Group indicated that “omics” could be used to test for unintended effects.

Reproductive animal studies

In light of the recently published reproductive study by (Velimirov et al. 2008), the Belgian Delegation asked about the view of the Panel on the use of reproductive toxicity studies in the context of food safety assessment. The Food/feed Working Group explained that reproductive toxicity assessment was originally developed to test pesticides (FDA). In the EU, this is not a commonly used approach to assess food safety, in particular not for testing whole food. With reference to the reproductive study by (Velimirov et al. 2008), it should be noted that the experimental protocol used in this study is a modified version of the original protocol (FDA).

Suboptimal Dossier Data

The Belgian Delegation indicates that sometimes it appears that sub-optimal data are included in the dossiers. The Food/feed Working Group explained that the Panel never accepts suboptimal studies. All information submitted by applicants is assessed by the Panel, and studies are assessed on a case-by-case basis. The Panel always requires better data if the quality of data presented in the dossier is not acceptable.

General points raised by Belgian experts on comments to dossiers

The Belgian Delegation indicated that dossiers usually contain more data than just those related to compositional and phenotypic/agronomic analysis, especially data on animal feeding trials can be found in dossiers where they were not strictly required by the EFSA guidance. They raised the question whether this implies that the principle of substantial equivalence is being abandoned. Experts of the Food/feed Working Group of the EFSA GMO Panel explained that animal feeding trials are nutritional studies, rather than toxicological studies. They are required on a case-by-case basis. Whenever data of the animal feeding trials are provided in the dossiers, the working group has always assessed them.

The Belgian Delegation addressed the topic of public comments on applications, and the answers received from EFSA. The experts of the Food/feed Working Group remarked that frequently comments do not distinguish between general guidance and the risk assessment specific to an application. However, comments on general issues cannot be addressed in the frame of a specific application and should be dealt with separately from single applications. The Belgian Delegation remarked that concerns about a safety issue, even in a more general context, should be raised. This may be useful for the identification of new issues that require follow-up. Even if some comments are not relevant for specific

applications they may still be valuable in the context of general guidance. The experts of the EFSA Food/feed Working Group expressed that it would be useful to have an academic exchange with national experts on the risk assessment strategy.

3. Concluding remarks

The Belgian Delegation acknowledged the usefulness and quality of this meeting. Further scientific interactions would be welcome. Regarding bilateral meetings with Member States, EFSA is willing to host such events. It was suggested to hold dedicated meetings with Member States on specific dates to discuss current scientific topics.

EFSA closed the meeting by thanking the Belgian delegates for the fruitful discussions and for the suggestion to communicate on general issues, and is looking forward to further scientific interactions.