UNEP

Convention on Biological Diversity

Distr.
GENERAL

UNEP/CBD/BS/AHTEG-RA&RM/2/2
5 November 2009

ORIGINAL: ENGLISH

AD HOC TECHNICAL EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT UNDER THE CARTAGENA PROTOCOL ON BIOSAFETY
Second meeting
Ljubljana, 19-23 April 2010

SUBMISSIONS ON THE IDENTIFICATION OF LIVING MODIFIED ORGANISMS OR SPECIFIC TRAITS THAT MAY HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY, TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH

INTRODUCTION

1. At its fourth meeting, the Conference of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP) established an Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management.[1]

2. According to its terms of reference as set out by the Parties, the AHTEG shall, at its second meeting, among other things, consider possible modalities for cooperation in identifying living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

3. To assist the AHTEG in its deliberations, the COP-MOP requested Parties and invited other Governments and relevant organizations to submit scientifically sound information available at that time, on the identification of living modified organisms (LMOs) or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

4. The COP-MOP also requested the Executive Secretary to compile the information received and to prepare a synthesis report for consideration by the AHTEG and the Parties.

5. In light of the above, the Secretariat sent out a notification to Parties, other Governments and relevant organizations on 28 May 2009.[2]

6. Six Parties (Burkina Faso, Colombia, European Commission, Mexico, Norway and United Arab Emirates), two non-Party countries (Australia, United States of America) and two organizations (Global Industry Coalition and Public Research and Regulation Initiative) have submitted their views on this issue as of 2 November 2009.

7. Some submissions included recommendations to the AHTEG while others had a list of scientific publications.

8. A compilation of the full submissions is annexed hereto. Submissions made in a language other than English were translated into English by the Secretariat. These translations are also annexed hereto.

[1] Decision BS-IV/11.

[2] Notification SCBD/BS/MPDM/jh/67587 (2009-056).

/…

SYNTHESIS OF VIEWS

A. *LMOS OR SPECIFIC TRAITS THAT MAY HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY, TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH*

9. In some submissions received by the Secretariat, references were made to LMOs or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health as follows:

LM cotton

10. Burkina Faso noted that the environmental risks of LM cotton are being closely monitored and measures are in place to ensure better risk management.

LM fish

11. Norway recommended caution with regards to LM fish with traits such as cold tolerance, increased growth rate or high tolerance to environmental pollutants.

LM maize

12. Mexico noted that the precautionary approach was applied and, consequently, research and introduction into the environment of LM maize harbouring traits that affect or limit its nutritional qualities were prohibited.

13. The European Community stated that in some risk assessments prior to the authorization of insect-resistant GM maize events in the European Union, the potential for adverse effects, i.e., for promoting the occurrence of resistance against Bt-proteins in pest species, is taken into account by means of a requirement for case-specific monitoring to further investigate this issue after placing on the market of these LMOs.

LM trees

14. Norway noted that the long life-span of trees will be a challenge when assessing the risks of these types of LMOs.

LM viruses

15. Norway advised that caution be taken with regards to LM viruses with altered traits and host specificity.

LMOs for production of pharmaceutical or industrial compounds

16. Mexico cited a reference that the production of pharmaceuticals, pharmaceutical precursors, and industrial compounds (generically known as pharmaceutical crops) in crop species used for food or feed entails a risk because of the possibility that pharmaceutical substances could be introduced into the food chain via grain mixture, pollen gene flow or another type of accidental mixture due to the general inability, currently, to distinguish between food crops and pharmaceutical crops.

17. Norway also expressed concerns about LM pharmaplants entering the food chain.

LMOs with stacked traits or multiple LMOs

18. Norway expressed that combinatorial and synergistic effects must be carefully considered in the development and risk assessment of stacked event LMOs with respect to the implications on biodiversity and evolutionary consequences for crop genetic diversity.

LMOs harbouring antibiotic resistance marker genes

19. The European Community recalled that its directive 2001/18/EC introduced propositions calling for a phase-out of LMOs harbouring certain antibiotic resistance marker genes, which may have adverse effects on human health and the environment.

20. Norway expressed concerns about LMOs harbouring antibiotic resistance marker genes. It mentioned two antibiotic resistance genes (*nptII* and *aadA*) and drew attention to the conclusions from the WHO Expert Group on Critically Important Antimicrobials for Human Health on the categorization of the antimicrobials kanamycin, neomycin and spectinomycin as "Highly Important Antimicrobials" and streptomycin as a "Critically Important Antimicrobial".

Insect tolerance

21. Norway noted that LMOs harbouring *Bacillus thuringiensis* (Bt) Cry endotoxins may cause unintended direct adverse effects on biological diversity, both lethal and sub-lethal, including but not limited to insects, aquatic life, soil microbes, and their food web dynamics, as well as on the sustainable use of biological diversity related to crop plants and their progenitors important for sustainable agricultural production and food security.

Herbicide tolerance

22. Colombia stated some potential direct and indirect adverse effects of LMOs due to the use of herbicides, such as medium- and long-term effects of herbicide use as well as secondary environmental effects arising from the control or elimination of a plant pest.

23. Norway noted that LMOs harbouring genes that confer herbicide tolerance may cause unintended direct effects on the sustainable use of biological diversity related to crop plants and their progenitors important for sustainable agricultural production and food security.

Tolerance to abiotic stress

24. Norway recommended caution with regards to LM plants with tolerance to abiotic stresses such as tolerance to drought and cold.

Modified nutrient uptake

25. Norway recommended caution with regards to LM plants with a more efficient nutritional uptake.

B. OTHER CONSIDERATIONS

26. Some submissions received by the Secretariat also contained other considerations related to LMOs or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health as summarized below.

27. In its submission, Mexico stated that a review of the scientific information available to date revealed no LMOs or specific traits posing risks to the environment or to human health.

28. Australia indicated that, to date, no credible information has arisen, either domestically or internationally, to support a link between LM crops approved for commercial release in Australia and adverse impacts on human health or the environment. Australia also expressed that one type of LM carnation with modified colour is no longer required to be licensed for use in that country.

29. The United States of America recommended that the AHTEG may consider modalities for developing a process to examine existing case-specific risk assessments of LMOs in order to extract any consensus conclusions that have been broadly validated by many countries in risk assessments that have been undertaken in a manner consistent with Annex III of the Protocol.

30. The Global Industry Coalition noted that there is no science-based evidence pointing at potential adverse effects of LM plants commercialized to date. Specifically, the GIC argued that the following LMOs, genes, promoter and proteins are safe: LM maize events 1507, Bt11, Bt176, MON810, MON863, MON863 × MON810, MON863 × NK603 × MON810, NK603 × MON810 and T25; LM oilseed rape events GT73, MS8, MS1 × RF1, MS8 × RF3, RF3, T45 and Topas 19/2; antibiotic resistance genes *nptII*, *hph* and *aadA*; 35S promoter from the Cauliflower Mosaic Virus (CaMV); Bt toxins Cry1Ab, Cry3Bb1, Cry1Ac and Cry1F; and phosphinothricin acetyltransferase (PAT) enzyme.

31. The Public Research and Regulation Initiative (PRRI) stated that, to the best of its knowledge, no authorizations for field trials or commercialization have been denied on the basis of scientifically sound indications of adverse environmental impacts. Moreover, PRRI suggested specific questions that may further assist in this process as detailed in the annex hereto.

Annex

COMPILATION OF SUBMISSIONS ON THE IDENTIFICATION OF LIVING MODIFIED ORGANISMS OR SPECIFIC TRAITS THAT MAY HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY, TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH

CONTENTS

I. SUBMISSIONS FROM PARTIES

A. BURKINA FASO

(original and translation)

MINISTERE DES ENSEIGNEMENTS
SECONDAIRE, SUPERIEUR ET DE
LA RECHERCHE SCIENTIFIQUE

SECRETARIAT GENERAL

AGENCE NATIONALE DE BIOSECURITE

BURKINA FASO

Unité – Progrès – Justice

Identification des organismes génétiquement modifiées ou traits spécifiques pouvant avoir des effets négatifs sur la conservation, l'utilisation durable de la diversité biologique et la santé humaine au Burkina Faso.

1. Informations de base

Au Burkina Faso, à ce jour, seule la technologie ***Bt*** est mise en œuvre. Deux variétés de cotonnier burkinabè (FK et STAM) ont été transformées à travers l'introduction des gènes Cry1Ac et Cry2Ab et ont été autorisées par l'Agence Nationale de Biosécurité. Les différentes phases d'essai ont été concluantes et ces CGM sont passées en phase de commercialisation au cours de la présente campagne agricole 2008 – 2009.

Il faut signaler qu'en dehors du coton Bt, aucune autre autorisation n'a été donnée par l'Agence Nationale de Biosécurité. Une étude de l'état des lieux des OGM au niveau national a débuté. Les premiers résultats font apparaître la présence de certains produits génétiquement modifiés au niveau des légumes. Cette étude est entrain d'être complétée

Il a été rapporté que des produits à base d'OGM sont en vente dans les alimentation, mais n'à jusqu'à ce jour donné aucune autorisation pour d'autres type de produits. Elle a commandé une étude en vue de bâtir un plan de règlementation du commerce des produits dérivés des OGM.

2. Identification des organismes génétiquement modifiés

D'une manière générale, des impacts potentiels en rapport avec l'environnement, la santé humaine et animale, ainsi que sur le plan socio-économique et éthique sont examinés par le Comité scientifique national de biosécurité (CSNB) lors de l'évaluation des dossiers de demandes par l'Agence.

Dans le cas du coton Bt, les risques environnementaux font l'objet d'une attention particulière et des dispositifs de biosécurité sont mis en place au niveau des parcelles pour une meilleure gestion de ces risques (pollinisation croisée et apparition des résistances).

Dans le domaine de la détection des OGM, l'Agence Nationale de Biosécurité ne dispose pas pour le moment d'un système de détection, mais elle s'appuie sur l'Institut National de l'Environnement et de la Recherche Agricole pour ces types de travaux en attendant de bénéficier d'un dispositif plus éprouvé qui est attendu pour l'année 2010.

En effet, le Gouvernement du Burkina Faso a consenti un prêt auprès de la Banque Mondiale pour la mise en place et l'équipement d'un laboratoire national de biosécurité à vocation sous-régionale. L'équipement de ce laboratoire se fera en fonction des méthodes d'identification qui seront privilégiées. Ce dossier est actuellement à l'étude.

Pr. Chantal ZOUNGRANA/KABORE
Chevalier de l'Ordre des Palmes Académiques

MINISTÈRE DES ENSEIGNEMENTS SECONDAIRE, SUPÉRIEUR ET DE LA RECHERCHE SCIENTIFIQUE

SECRÉTARIAT GÉNÉRAL

AGENCE NATIONALE DE BIOSÉCURITÉ

BURKINA FASO

Unité – Progrès – Justice

Determining the genetically modified organisms and specific traits that could have negative impacts on conservation, the sustainable use of biological diversity, and human health in Burkina Faso

1. Background information

The only technology implemented to date in Burkina Faso is ***Bt***. Two varieties of Burkinan cotton (FK and STAM) have been transformed through the introduction of genes Cry1Ac and Cry2Ab and authorized by the Agence Nationale de Biosécurité [national biosafety agency]. The various test phases were conclusive and these GM cottons were commercialized in the current 2008-2009 crop year.

Besides *Bt* cotton, no other GM crop has been approved by the Agence Nationale de Biosécurité. A national GM study is currently underway and early results have signalled the presence of certain genetically modified vegetables.

It was reported that GM goods are sold in grocery stores but, to date, no other types of GM produce have been approved. A study whose results should lead to the determination of future GM product trade regulations has been commissioned.

2. Identifying genetically modified organisms

The potential environmental, human and animal health, socioeconomic and ethical impacts of the implementation of a GM crop are examined by the Comité scientifique national de biosécurité (CSBN) [national scientific committee on biosafety] when assessing applications to the Agence Nationale de Biosécurité.

With regards to *Bt* cotton, the environmental risks are closely monitored. Plot-level biosafety measures have been implemented to ensure better risk management (cross-pollination and resistance development).

The Agence Nationale de Biosécurité does not possess a GMO detection system. Rather, it relies on the support of the Institut National de l'Environnement et de la Recherche Agricole [national environment and agricultural research institute]. Proven measures are expected to be implemented in 2010.

The World Bank has extended a loan to the government of Burkina Faso to build a national sub-regional biosafety laboratory. The choice of equipment will be based on the identification methods that are selected. This project is currently underway.

Professor Chantal ZOUNGRANA/KABORE
Chevalier de l'Ordre des Palmes Académiques

B. COLOMBIA

(original and translation)

Ministerio de Relaciones Exteriores
República de Colombia
Libertad y Orden

BICENTENARIO
de la Independencia de Colombia
1810-2010

TELEFAX
1 514 288 6588

VAM/DAM/CAA No.42990

Bogotá, D.C. 12 de agosto de 2009

Señor
AHMED DJOGGHLAF
Secretario Ejecutivo
Convenio de Diversidad Biológica
Montreal, Canadá

Asunto: Protocolo de Cartagena - Información sobre Organismos Vivos Modificados

Señor Secretario Ejecutivo:

En mi calidad de Punto Focal Político de Colombia ante el Convenio de Diversidad Biológica, me permito dar respuesta a su notificación SCBD/BS/MPDM/jh/67587 del 28 de mayo de 2009, por medio de la cual solicita información basada en criterios científicos sobre la identificación de Organismos Vivos Modificados o rasgos específicos que pueden tener efectos adversos sobre la conservación y uso sostenible de la diversidad biológica, teniendo también en cuenta los riesgos para la salud humana.

En este sentido, me permito adjuntar los insumos elaborados por el Ministerio de Ambiente, Vivienda y Desarrollo Territorial sobre el particular.

Cordialmente,

CLARA INÉS VARGAS SILVA
Directora de Asuntos Políticos Multilaterales
Encargada de las Funciones del
Despacho de la Viceministra de Asuntos Multilaterales

Anexos: Uno (1 oficio)

Criterios y Consideraciones de relevancia a tener en cuenta para la identificación de posibles efectos adversos en la conservación y utilización sostenible de la diversidad biológica que puedan derivarse del uso de OVMs.

Tomando el riesgo como la probabilidad de que una amenaza (para este caso: importación del OVM) se convierta en un desastre dada su vulnerabilidad (en este caso: características propias del medio receptor), acorde con lo establecido para la evaluación de riesgos en el PCB, cada país parte en calidad de receptor de un OVM, debe determinar y evaluar estos posibles efectos adversos. Los criterios que se sugieren analizar se refieren al análisis de aspectos propios del caso, más no del OVM en si o de sus rasgos, ya que en el evento de presentarse un efecto adverso, este se relaciona con la vulnerabilidad del medio receptor y con el manejo que se le dé al OVM, dadas las características del medio receptor:

Especies de parientes silvestres relacionados a los OVM y calidad del medio receptor del OVM: Se recomienda el conocimiento previo de la existencia de parientes silvestres o variedades relacionados con los OVM objeto de movimientos transfronterizos o futuros movimientos transfronterizos; una vez se conozca su existencia, conocer aspectos de su biología, fisiología, reproducción, dinámica poblacional, relaciones ecológicas, distribución específica (considerando si se trata de un Centro de Origen y de diversidad genética), entre otros, con el fin de evaluar la vulnerabilidad en cada país Parte acorde a sus características propias.

Característica del OVM a introducir: Acorde con las característica(s) o modificación(es) introducida(s) y el uso previsto del OVM a importar, se sugiere analizar los posibles efectos directos e indirectos de esta característica(s) en aspectos como:

1. Requerimientos de manejo para su uso efectivo y sus implicaciones: por ejemplo su uso puede implicar la aplicación de un herbicida, lo cual a su vez puede tener efectos adversos en el medio ambiente y sus recursos a largo o mediano plazo; para prevenir este hecho debería haber un conocimiento previo de las posibles consecuencias de manejo/uso/cantidad de ese herbicida, dadas condiciones ambientales específicas del medio receptor.
2. Consecuencia directa e indirecta de su uso: por ejemplo la eliminación o control, parcial o total, localizado o generalizado, de un recurso biológico catalogado como plaga: puede desencadenar otra serie de efectos secundarios como respuesta a la eliminación o control de esa "plaga", como respuesta al desequilibrio en una cadena de relaciones ecológicas.

Articulación con la discusión del Artículo 27 "Responsabilidad y Compensación" del PCB
Esta aproximación de criterios, junto con el desarrollo del Artículo 27 del PCB en el marco de la COP – MOP (en discusión), debería ser objeto de discusión en el Grupo Especial de Expertos Técnicos sobre Evaluación y Manejo de Riesgos, para definir igualmente temas como:

1. Efectos adversos y daño a la conservación y uso sostenible de la biodiversidad
2. Bases metodológicas, guías o protocolos, para la valoración del daño.

Articulación con el Artículo 22 "Creación de capacidad" del PCB
Con el fin de atender en la práctica lo relativo a efectos adversos en la conservación y utilización sostenible de la diversidad biológica, y al establecimiento de criterios científicos sólidos en la materia, los países partes con economías en transición y acorde con el Artículo 22 "Creación de capacidad", requerimos creación de capacitación científica y técnica en el manejo adecuado y seguro de la biotecnología y en el uso de la evaluación de riesgo y de la gestión del riesgo, así como el fomento de la capacidad tecnológica e institucional en materia de seguridad de la biotecnología.

COLOMBIA Bogota, 12 August 2009

Ministry of Foreign Relations

Ref.: · VAM/DAM/CAA No. 42990
· SCBD/BS/MPDM/jh/67587 of 28 May 2009

Subject: **Cartagena Protocol – Information on Living Modified Organisms**

Sir,

As CBD National Focal Point of Colombia, I have the honour to reply hereby to notification SCBD/BS/MPDM/jh/67587 of 28 May 2009, in which Parties and other Governments were requested to submit scientifically sound information regarding the identification of Living Modified Organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

I enclose herewith the input of the Minister of the Environment, Housing and Territorial Development on the matter.

Accept, Sir, the assurances of my highest consideration.

[*sgd*] Clara Inés Vargas Silva
Director for Multilateral Affairs
Responsible for the
Office of the Vice-Minister of Multilateral Affairs

Executive Secretary
CBD
Montreal

Ministry of Foreign Relations
Colombia

Relevant Considerations and Guidelines to be Taken into Account Regarding the Identification of Possible Adverse Effects on the Conservation and Sustainable Use of Biological Diversity Resulting from the Use of LMOs

If we see risk as the probability of a threat (in this case, the import of LMOs) becoming a disaster because of an element of vulnerability (in this case, the characteristics of the receiving environment), in accordance with the CPB's provisions in respect of risk assessment, each State Party, in its capacity as a receiver of LMOs, must determine and assess the possible adverse effects of said LMOs. The guidelines suggested for study refer to the analysis of aspects particular to a case, but not the LMO itself or its traits; in the event of an adverse effect, said effect would be related to the vulnerability of the receiving environment and to the management of the LMO, given the characteristics of the receiving environment.

Wild Relative Species Related to LMOs and Quality of the LMO Receiving Environment

We recommend prior study of the presence of wild relatives or varieties of the LMOs undergoing transboundary movement or subject to future transboundary movement. Once their existence has been confirmed, and in order to assess the vulnerability of each State Party according to its particular characteristics, the biological, physiological, and reproductive aspects of these wild relatives or varieties should be studied; as well, aspects related to their population dynamics, ecological relationships, and specific distribution (consideration of whether a centre of origin and genetic diversity is involved) should also be studied.

Characteristics of the LMO to be Introduced

In accordance with the intended use of the import LMO and its characteristic(s) or modification(s), we suggest the study of the possible direct and indirect effects of the LMO's characteristic(s).

1. *Management requirements for the effective use of the LMO and the associated implications.* The use of an LMO can, for example, involve the application of a herbicide, which, in turn, can have adverse effects on the environment and its resources in the long or medium term. To prevent such an occurrence, the possible consequences of the handling/use of given amounts of the herbicide in question should be studied beforehand, taking into consideration the specific environmental conditions of the receiving environment.

2. *Direct and indirect consequences of LMO use*. The elimination or control (whether partial or total, local or generalized) of a biological resource classified as a pest can have a series of side effects, which arise in reaction to an imbalance in a chain of ecological relationships.

Relevance to Discussion on CPB Article 27 - *Liability and Redress*

These considerations, together with the development of PCB Article 27 within the framework of the COP-MOP (under discussion), should be examined by the Ad Hoc Technical Expert

Group on Risk Assessment and Risk Management so that matters such as the following may be determined:

1. Adverse effects on and damage to conservation and sustainable use of biological diversity;

2. Methodological bases, guides, or protocols for damage assessment.

Relevance to CPB Article 22 – *Capacity-Building*

In order to address, in practice, the issues of adverse effects on conservation and sustainable use of biological diversity, and to address, in practice, the establishment of sound scientific principles on the matter, we the States Parties with economies in transition, in accordance with Article 22 – *Capacity-Building*, call for scientific and technical training in the proper and safe management of biotechnology, and in the use of risk assessment and risk management, and the enhancement of technological and institutional capacities in biosafety.

C. EUROPEAN COMMUNITY

se2009.eu

EUROPEAN COMMISSION

Swedish Presidency
of the European Union

Dr. Ahmed Djoghlaf
Executive Secretary
CBD Secretariat
413 rue Saint Jacques, suite 800
Montréal QC H2Y 1N9
Canada

Stockholm, Brussels, 21 September 2009

Subject: EU response to Notification 2009-056

Dear Dr. Djoghlaf,

On behalf of the European Community and its Member States, please find enclosed the response to Notification 2009-056 in which Parties, other governments and relevant international organisations were invited (according to the COP-MOP/4 decision BS-IV/11) to submit scientifically sound information regarding the identification of Living Modified Organisms (LMOs) or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

Yours sincerely,

Charlotta Sörqvist
Deputy Director
Division for Eco-Management and Chemicals
Ministry of the Environment
Stockholm
Sweden

Hugo-Maria Schally
Head of Unit
Environmental Agreements and Trade Unit
Environment Directorate General
European Commission
Brussels

EU coordinated response to Notification 2009-056: Submission of scientifically sound information regarding the identification of Living Modified Organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health:

According to Decision BS-IV/11, paragraph 8, Parties are invited to submit scientifically sound information available at that time, on the identification of LMOs or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

Parties are also invited in paragraph 5 of the same decision to submit information relevant to the work of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management. According to its terms of reference in the Annex to Decision BS-IV/11 (Paragraph 1) e) (iv)), the AHTEG is instructed to consider possible *modalities for cooperation* in identifying living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

Environmental risk assessments of GMOs in the European Community are carried out according to the Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.

Directive 2001/18/EC introduced propositions calling for a phase-out of LMOs harbouring certain antibiotic resistance marker genes, which may have adverse effects on human health and the environment. It is taken into account that these traits are not essential with regard to the purpose of the respective LMOs and that alternatives for these marker genes are available for newly-developed LMOs.

In some risk assessments prior to the authorization of insect-resistant GM maize events in the EU, the potential for adverse effects, i.e. for promoting the occurrence of resistance against Bt-proteins in pest species, is taken into account by means of a requirement for case-specific monitoring to further investigate this issue after placing on the market of these LMOs.

Regarding the fact that risks of LMOs can differ in different geographical areas, general guidance documents concerning risk assessment procedures also seem relevant in this

context. Most of the documents in the following list have already been mentioned in the European coordinated response to Notification 2008-140 submitted to the Secretariat of the Convention on Biological Diversity on 26 February 2009. The European Food Safety Authority will further develop and update in 2010 its guidance on environmental risk assessment as currently included in the guidance document of 2006 on the risk assessment of genetically modified plants (see fourth indent below).

A. Information on how to determine whether a LMO is potentially dangerous.

- Directive 2001/18/EC of 12 March 2001 on the deliberate release of genetically modified organisms and repealing Council Directive 90/220/EEC, including Annex II (Principles for environmental risk assessment)
- Regulation (EC) No 1829/2003 on genetically modified food and feed (principles for human and animal health).
- Commission Decision 2002/623/EC of 24 July 2002 establishing guidance notes supplementing Annex II (Principles for environmental risk assessment) to Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.
- Guidance document of the Scientific Panel on genetically modified organisms for the risk assessment of genetically modified plants and derived food and feed. EFSA Journal (2006) 99,1-100, updated in 2008.
- Guidance document for the risk assessment of genetically modified microorganisms and their derived products intended for food and feed use by the Scientific Panel on Genetically Modified Organisms (GMO) EFSA Journal (2006) 374, 1-115.
- FAO/WHO Expert Consultation on the Safety Assessment of Foods Derived from Recombinant-DNA Animals, World Health Organization, Headquarters Geneva, Switzerland, 26 February – 2 March 2007 (http://www.who.int/entity/foodsafety/publications/biotech/report_biotech_07_en.pdf)
- Codex Alimentarius. Codex principles and guidelines on foods derived from biotechnology(2003):

  Principles for the risk analysis of foods derived from modern biotechnology, CAC/GL 44-2003.

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

Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants CAC/GL 45-2003, including Annex 1 (Assessment of possible allergenicity), Annex 2 (Food safety assessment of foods derived from recombinant-DNA plants modified for nutritional and health benefits) and Annex 3 (Food safety assessment in situations of low-level presence of recombinant-DNA plant material in food), (2003, Annexes 2 and 3 adopted 2008).

Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA animals, CAC/GL 68-2008.

http://www.fao.org/ag/agn/agns/biotechnology_detection_en.asp

- Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Food and Agriculture Organisation: Rome.
- Communication from the Commisssion on the Precautionary Principle, COM (2000)1 final.

  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52000DC0001:EN:HTML
- An Introduction to the Biosafety Consensus Documents of OECD's Working Group for Harmonisation in Biotechnology No. 32, 2005, ENV/JM/MONO(2005)5
- OECD, 1993. Safety Considerations for Biotechnology: Scale-up of Crop Plants
- Van den Eede et al. (2004): The relevance of gene transfer to the safety of food and feed derived from genetically modified (GM) plants. Food and Chemical Toxicology 42, 1127-1156
- Nelson, K.C.; Banker, M.J. Problem formulation and options assessment handbook. 2007, A publication of the GMO ERA Project
- Cellini et al. (2004): Unintended effects and their detection in genetically modified crops. Food and Chemical Toxicology 42, 1089-1125
- Guidance Document for the risk assessment of genetically modified plants containing stacked transformation events by the Scientific Panel on Genetically Modified Organisms (GMO) EFSA Journal (2007) 512,1-5.
- Final report. Long-term effects of genetically modified (GM) crops on health and the environment (including biodiversity): Prioritisation of potential risks and delimitation of uncertainties.

  http://ec.europa.eu/environment/biotechnology/pdf/beetle_report.pdf

B. Information on risks related to specific traits

- Consolidated presentation of the joint Scientific Opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" and the Scientific Opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants, EFSA Journal (2009) 1108, 1-8.
- Module II: Herbicide Biochemistry, Herbicide Metabolism and the Residues in Glufosinate-Ammonium (Phosphinothricin)-Tolerant Transgenic Plants No. 25, 2002, ENV/JM/MONO(2002)14
- Consensus Document on General Information Concerning the Genes and Their Enzymes that Confer Tolerance to Phosphinothricin Herbicid No. 11, 1999, ENV/JM/MONO(99)13
- Consensus Document on General Information Concerning the Genes and Their Enzymes that Confer Tolerance to Glyphosate Herbicide No. 10, 1999, ENV/JM/MONO(99)9
- Consensus Document on General Information concerning the Biosafety of Crop Plants Made Virus Resistant through Coat Protein Gene-Mediated Protection No. 5, 1996, OCDE/GD(96)162
- Consensus Document on Safety Information on Transgenic Plants Expressing *Bacillus thuringiensis* - Derived Insect Control Protein No. 42, 2007, ENV/JM/MONO(2007)14

D. MEXICO

(original and translation)

Comisión Intersecretarial de Bioseguridad de los Organismos Genéticamente Modificados

CIBIOGEM, MEXICO

En respuesta a la Notificación SCBD/BS/MPDM/jh/67587 en seguimiento a la decisión BS-IV/11 de la Cuarta Conferencia de las Partes que actúa como Reunión de las Partes del Protocolo de Cartagena sobre Seguridad de la Biotecnología (COP-MOP 4) que dice a la letra:

> *Pide a las Partes que presenten, e invita a otros gobiernos y organizaciones pertinentes a que presenten al Secretario Ejecutivo, a más tardar tres meses antes de la primera reunión del Grupo especial de expertos técnicos, la información basada en criterios científicos que esté disponible en ese momento sobre la determinación de los organismos vivos modificados o los rasgos específicos de organismos vivos modificados que puedan tener efectos adversos para la conservación y la utilización sostenible de la diversidad biológica, teniendo también en cuenta los riesgos para la salud humana;*

El Gobierno de México envía la siguiente información.

La autoridad ambiental competente reporta que la revisión de la información científica disponible hasta este momento, no arroja ningún Organismos Vivo Modificado (OVM) o característica particular que presente un riesgo ambiental. Así mismo tomando también en cuenta los riesgos para la salud humana que pueda representar el consumo de OVMs, la autoridad nacional competente reporta que después de haber analizado la información científica disponible hasta el momento en relación a la determinación del riesgo a la salud que pueda representar el consumo de OVMs no ha encontrado argumentos científicos sólidos que demuestren daño por el consumo de los mismos. Ambas conclusiones están basadas en la experiencia acumulada hasta ahora y en la información científica disponible consultada, y considera el enfoque caso por caso de los OVMs.

México, en el caso particular del maíz genéticamente modificado, en su legislación nacional ha aplicado el principio precautorio con respecto a evitar el uso de este cultivo, cuando la modificación afecte o limite sus propiedades alimenticias. Esto es México ha prohibido la experimentación y la liberación al ambiente del maíz genéticamente modificado, cuando la modificación afecte o limite sus propiedades alimenticias. Lo anterior estuvo también fundamentado por la opinión de algunos científicos.

- Nature Biotechnology en su editorial febrero de 2004[1] comunicó que la producción de fármacos, precursores de éstos o productos industriales (denominados genéricamente cultivos farmacéuticos) en especies cultivadas empleadas para la alimentación humana o animal conlleva un riesgo potencial del cual deberíamos estar preocupados como sociedad, siendo que las sustancias farmacéuticas pudieran introducirse en la cadena alimenticia a través de la mezcla de granos o mediante flujo génico por polen o algún otro tipo de mezcla accidental debido a la incapacidad humana de distinguir entre cultivos para alimentos y cultivos para la producción de fármacos.

- La Comisión para la Cooperación Ambiental de América del Norte (CCA) en Noviembre de 2004 emitió el Informe del Secretariado con una serie de recomendaciones sobre los efectos del maíz transgénico[2] en México resultado de un estudio llevado a cabo a petición de varias organizaciones. En dicho informe se reconocen que:

  > *La producción de ciertos fármacos y compuestos industriales no aptos para el consumo humano y animal en cultivos de alimentos entraña riesgos para la salud humana únicos en su género. Esta cuestión reviste particular preocupación en el caso del maíz, que es un alimento básico producido mediante polinización abierta.*

  Derivado de estas conclusiones, el grupo asesor de la CCA emitió varias recomendaciones entre las que se encuentra la siguiente sobre el desarrollo de maíces farmacéuticos:

  > *"... La modificación del maíz para producir fármacos y ciertos compuestos industriales no aptos para el consumo humano y animal deberá prohibirse, en conformidad con las intenciones expresadas por el gobierno mexicano"*

- Una posible alternativa a la producción de fármacos o productos industriales en plantas comestibles podrían ser plantas no comestibles como pudieran ser el tabaco entre otros ampliamente utilizados en investigación científica[3].

---

[1] Nature Biotechnology Vol. 22 Number 2 February 2004, pg. 133

[2] http://www.cec.org/files/PDF//Maize-and-Biodiversity_es.pdf

[3] Ellstrand NC, 2003 Going to "Great Lengths" to Prevent the Escape of Genes That Produce Specialty Chemicals" Plant Physiology, August 2003, Vol 132, pp.1170-1774

Inter-Secretarial Commission on the Biosafety of Genetically Modified Organisms (CIBIOGEM)

MEXICO

In response to Notification SCBD/BS/MPDM/jh/67587, further to Decision BS-IV/11 of the Fourth meeting of the Conference of the Parties serving as the Meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP 4), which

> *"[r]equests Parties and invites other Governments and relevant organizations to submit to the Executive Secretary, not later than three months prior to the first meeting of the Ad Hoc Technical Expert Group, scientifically sound information available at that time, on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health;"*

The Government of Mexico submits the following information.

The competent environmental authority's review of the scientific information available to date revealed no living modified organisms (LMOs) or specific traits posing an environmental risk. The competent national authority's analysis of the scientific information available to date on the risk to human health posed by the consumption of LMOs revealed no sound scientific evidence demonstrating harm resulting from the consumption of LMOs. Both conclusions are based on the experience to date and on the available scientific information consulted; both involve a case-by-case approach to the LMOs in question.

In the particular case of genetically modified corn, Mexican legislation has applied the precautionary principle, providing for the avoidance of this crop if its nutritional properties are affected or limited by modification. That is to say that Mexico has forbidden experimentation with and the release into the environment of genetically modified corn if its nutritional properties have been affected or limited by modification. Some scientific opinion has supported this measure.

- In its editorial, the February 2004[1] issue of *Nature Biotechnology* discussed the production of pharmaceuticals, pharmaceutical precursors, and industrial compounds (generically known as pharmaceutical crops) in crop species used for human food or animal feed. It stated that such production

[1] *Nature Biotechnology*, Vol. 22, Number 2, February 2004, pg. 133.

entails a risk which should concern us as a society because of the possibility that pharmaceutical substances could be introduced into the food chain via grain mixture, pollen gene flow or another type of accidental mixture resulting from human inability to distinguish between food crops and pharmaceutical crops.

- In November 2004, the North American Commission for Environmental Cooperation (CEC) issued its Secretariat Report, containing a series of recommendations related to the effects of transgenic maize[2] in Mexico following a study conducted at the request of various organizations. The report states that

  > *"[p]roducing pharmaceuticals and certain industrial compounds that are incompatible with food and feed in food crops poses unique risks to human health. This is of special concern in maize, which is a staple food produced following open pollination."*

  Based on these conclusions, the CEC's advisory group issued various recommendations, including the following one on the development of pharmaceutical maize:

  > *"The modification of maize to produce drugs and certain industrial compounds not suitable for human and animal consumption should be prohibited, in accordance with the expressed intentions of the Mexican government."*

- A possible alternative to the production of pharmaceuticals or industrial compounds in food plants would be production in non-food plants such as tobacco and other such plants widely used in scientific research[3].

[2] http://www.cec.org/files/PDF//Maize-and-Biodiversity_es.pdf

[3] Ellstrand NC, 2003 Going to "Great Lengths" to Prevent the Escape of Genes That Produce Specialty Chemicals" Plant Physiology, August 2003, Vol 132, pp.1170-1774

E. NORWAY

Attachment 1

Response to the call from the CBD secretariat for "***submission of scientifically sound information regarding the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health*".**

Introduction

Beforehand, there are a number of important considerations with respect to the scientific appraisal that are not only of value to risk assessors, but risk managers, when reviewing this information that we wish to make note of:

First, we wish to note to the CBD secretariat that it would also be useful to also request scientifically sound information that document not only adverse effects, but evidence of safety (as opposed to evidence no effects) for biodiversity and human health.

Second, it is important to acknowledge there are broad uncertainties surrounding the current scientific knowledge on the impacts of novel biologics into complex environments. This includes appraising the relevance empirical data collected within specific time and/or spatial scales under investigation, and especially within particular ecological or management contexts. Further, it must also be kept in mind the difficulty in extrapolation of small-scale experiments, or those using small sample sizes, which often can detect only large differences or effects, to real-world effects. In order to achieve sufficient statistical power, studies utilizing small sample sizes must accept higher levels of Type II error or "false negatives" that would miss effects that may indeed in reality be occurring within the scientific observation.

Clearly, more intensive empirical studies are needed to ascertain the likelihood of field-level impacts to biodiversity and human health. As widely agreed, the case by case approach can best inform what scientific aspects will be important and relevant parameters for the proposed site and conditions of investigation. In sum, the emergent uncertainties should not be equated with risk, but rather incorporated systematically into any risk characterization. That is, the science evidence may or may not be informative under certain scenarios or environments, but can, and should, inform and inspire certain scientific considerations or needed lines of biosafety investigation specific contexts. This kind of scientific information becomes particularly valuable as possible "early warnings", as without such data there exists no basis for opening potentially critical modes inquiry would otherwise be left unexamined, leading to insufficient protection of environmental and human/animal health. This is especially important where a precautionary approach is the desired norm, as stated in the Cartagena Protocol on Biosafety Article 1, which states its objective to be "[I]n accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development".

Thirdly, it should be noted that the request for scientifically sound information also should also follow with a scientifically sound and logical inference when interpreting this information. For example, a common logical fallacy in the interpretation of risk data is

that absence of evidence of harm is the same as evidence of absence of harm. More explicitly, the absence of observable effects *should not be interpreted as evidence safety for any particular effect*. The committees and working groups utilizing this information should not lose sight of this basic logic when drawing conclusions, especially from risk relevant scientific evidence derived from statistical hypothesis testing.

Lastly, and with the above in mind, we wish to call attention to a recent investigative report that appeared in *Nature* magazine (Waltz, September 3, 2009) that document *ad hominem* attacks and other threats towards scientists who have published empirical evidence of potential adverse effects of LMOs. The political fallout from such public controversy creates a kind of scientific silence, where biosafety investigators may fear retribution for merely publishing their experimental work. As one prominent scientist interviewed stated:

"When scientists are even afraid to ask the questions…that's a serious impediment to our progress" (Ibid., 32).

The main point we wish to highlight, is that these troubling developments in the discourse over LMOs likely have led, and will continue to lead to situations where the *adverse effects of LMOs are likely to be under reported, and under investigated.*

Given the often political nature of the scientific debates surrounding the vital issue of food production, many of the studies mentioned in this report are not without their critics. Nevertheless, much of the evidence give compelling insights into the dynamics of novel biologics into complex ecosystems and the difficulty in establishing safety of use of modern biotechnologies in agriculture, medicine, and animal husbandry. Clearly, further research needed to make informed decisions and conclusions. While appropriate policies regarding LMOs are not limited only to scientific considerations, science will play an important role in appraising potential risks.

With respect to scientific information, we wish to submit the following requested scientific information on the two classes of potential effects (A) unintended effects on biodiversity, which includes direct and indirect effects, and (B) unintended effects on human and animal health. Both groupings can be further categorized as direct and indirect effects. Please refer to the end of this report where all scientific studies and reports under discussion are cited.

A. Scientific information on LMOs or traits that "may have adverse effects on the conservation and sustainable use of biological diversity" including direct and indirect effects.

A1.1: Unintended direct adverse effects of Bacillus thuringiensis (Bt) Cry endotoxins on biological diversity, both lethal and sub-lethal, including but not limited to insects, aquatic life, soil microbes, and their food web dynamics

In two meta-analyses of published studies on non-target effects of Bt proteins in insects, Lovei and Arpaia (2005) document that 30% of studies on predators and 57% of studies on parasitoids display negative effects to Cry1Ab transgenic insecticidal proteins. A review by Hilbeck and Schmidt (2006) on all Bt-plants found 50% of studies documenting negative effects on tested invertebrates.

Another quantitative review by Marvier et al, (2007) suggested a reduction in non-target biodiversity in GM in some classes of invertebrates (Bt) cotton fields vs. non-pesticide controls, yet found little reductions in biodiversity in others.

More recent research on aquatic environments has sparked intense interest in the impact of GM (Bt) crops on aquatic invertebrates *Daphnia magna* (Bøhn, 2008), and Trichoptera species (Rosi-Marshall, 2007). These publications warrant future study, given the potential load of novel target proteins that may end up in agricultural runoff and end up in aquatic environments. Further, Douville et al. (2007) present evidence of the persistence of the transgenic insecticidal protein Cry1Ab in aquatic environments and suggest that that sustain release of this bioactive compound in Bt maize production could result in negative impact on aquatic biodiversity.

Impacts on soil microflora and fauna, including earthworms (Zwahlen, 2002), mycrorhizal fungi (Castaldini et al. 2005) and microarthropods in response to Cry endotoxins have also been reported (Wandeler et al 2002, Griffiths et al 2006, Cortet et al 2007).

The significance of tritrophic effects of accumulation of, particularly of insecticidal Cry toxins (Harwood et al 2005, Obrist et al 2006) however is yet to be firmly established. Subchronic dosages of Cry proteins have been demonstrated to affect both foraging behavior and learning ability in non-target bees (Ramirez-Romero et al 2008), and may have indirect effects on recipient populations on other species. The evolutionary implications in terms of fitness are unclear.

A1.2: Unintended direct effects of insect resistance (Bt) and herbicide tolerance genes on the sustainable use of biological diversity related to crop plants and their progenitors, important for sustainable agricultural production and food security

Another important consideration is the adverse effect that certain GM crops may pose for the sustainable use of important crop agrobiodiversity (Gepts and Papas 2003, Quist

2007). Little research to date has been conducted on the evolutionary implications of gene flow from GM crops to wild relatives or landraces. However increased seed production in wild sunflower with introduced Bt genes by Snow et al (2003). that the researchers further found that hybrids of Bt and non-Bt sunflowers had up to 55% more seeds compared to the wild type when the target pest insect was found in the environment, meaning that there was a clear fitness advantage of the potentially weedy hybrid. This shows the potential of Bt-transgenic varieties or hybrids to outcompete native varieties and bring a reduction in diversity from more genetically homogenous domesticated varieties. Outcrossing between Bt and non-Bt plants is also shown in rice in China by Rong et al (2005), the transfer of herbicide tolerance from herbicide tolerate oil seed rape (canola) to weed *Brassica napus* by Mikkelsen (2006) and the expression of Bt and herbicide tolerant proteins in Mexican maize landraces by Dyer et al (2009). This work presents broad evidence of the occurrence of transgene flow. Further, modeling studies by Haygood and Andow (2003) suggest that under recurrent propagule pressure, transgene establishment within a population can occur even under negative selection. With the evidence of broad transgene flow, further work on the evolutionary implications for the sustainable use of biodiversity is warranted.

A2.1 Combinatorial and/or synergistic indirect effects of LMOs with stacked traits or multiple LMOs

The recent development and commercialization of LMOs with multiple transgenic traits has prompted an interest in the possible combinatorial and/or synergistic effects that may produce unintended and undesirable changes to endogenous or introduced traits and functions. The indirect effect of such changes may impact the sustainable development of future LMOs, and comes with high uncertainty of other unintended effects that will need to be monitored in the future.

In the case of simultaneous exposure to different classes of Cry proteins introduced in tandem, despite different modes of insecticidal activity, Tabashnik et al (2009) found evidence of cross reactivity among “pyramided” (stacked events) of Cry1Ac and Cry2B endotoxins in transgenic cotton. The cross reactivity led to higher rates of resistance evolution in pink bollworm, Pectinophora *gossypiella,* in a laboratory setting. Their results suggests that in the case of different Cry protein species, cross reactivity between them may confer increased rates of insect resistance the would alter the efficacy and perhaps biological activity of the LMO.

Then (2009) reviews and discusses the evidence for changes in activity and specificity of Bt proteins dependent on synergisitc interactions with extrinsic features. Such changes may critically influence the bioactivity and hence the potential for unintended effects.

Combinatorial, synergistic effects must be carefully considered in the development and risk assessment of stacked event LMOs with respect to the implications on biodiversity and evolutionary consequences for crop genetic diversity. This will be an important area of investigation for risk research, as multi-trait (stacked) LMOs are poised to replace the current generations of GM crops used in global agriculture. More research in this area is needed.

B Scientific information "taking also into account risks to human health", including direct and indirect effects.

The gaps of knowledge concerning human and animal health impacts of LMOs are quite large (Heinemann and Traavik, 2004). In reality, very few LMOs have been tested on humans (Tayabali et al, 2000). Clinical acute toxicity studies are not the same as chronic exposures likely in the use of GM crops, and may not necessarily uncover undesirable effects. Given the ethical and experimental difficulties in testing of substances on human subjects, other mammal species, such as mice and rats, are often used as surrogates for appraising potential human health impacts of LMOs.

Further, with risk appraisal in mind, one must consider that degree of exposures to GM foods will be different depending on the country. That is, the risk factors for Belgians will be different from say, Zambians, due to large differences consumption patterns of maize.

B1.1 Direct effects of target proteins on animal and human health.

A recent publication by Dona and Arvanitoyannis (2009) reviews the potential health implications of GM foods for humans and animals, including incidences and effects of increased immunogenicity, amounts of anti-nutrients, possible pleiotropic and epigenetic effects, including possible reproductive and developmental toxicity. They conclude that while there is strong evidence for health concerns on many fronts, exposure duration many have not been long enough to uncover important effects and studies should also include subjects with immunodeficiency or exposed to other stress agents.

Bt Cry toxins

A number of studies have raised questions over the possible toxic or immunogenic effects of Cry proteins on mammals (Ito et al 2004, Vázquez-Padrón et al 2000). Further, cytotoxic effects were found in some cases may be tissue specific, meaning effects may be underestimated if the incorrect tissue type is selected for the assay.

Seralini et al. 2007 reviewed data from a feeding trial of MON863 by the producer, which concluded no toxicity, and found evidence for liver and kidney toxicity in rats fed MON863 Bt maize. While the conclusions of Seralini et al were rejected by the developer of the data, the case illustrates that their poor study design, or inappropriate statistical methods applied to scientific evaluations can lead to important effects to go undetected.

Kilic and Akay (2008) report a significant difference (up to 10%) granular degeneration in the kidneys of rats fed Bt vs. non-Bt maize.

Immunological effects have largely focused on potential allergenicity of LMOs, rather than broader suites of immunogenic response. Inhalation studies, rather than oral toxicity are also largely missing from the scientific literature. One study by Kroghsbo et al (2008) found increase antigen-specific antibody response to Bt toxin and PHA-E lectin in a 28 and 90-day study of Wistar rats.

A study by Schroder et al (2007) found a significance difference in white blood cell count and reduced kidney weight among male rats in a 90 day feeding trial with Bt rice.

A team of Austrian researchers conducted feeding trials with a stacked Bt maize event (MON603 x Mon810) and found significant effects vs. non-Bt maize. Along with reports of kidney toxicity, the authors indicate "concluded, that multi-generation studies, especially based on the [reproductive assessment by continuous breeding (RACB)] design are well suited to reveal differences between feeds. The RACB trial showed time related negative reproductive effects of the GM maize under the given experimental conditions. The RACB trial with its specific design with the repeated use of the parental generation is a demanding biological factor for the maternal organism" (p. 4 Velimirov et al., 2008).

In a 2008 feeding trial on mice with MON810 Bt maize, Finamore et al (2008) conclude: "induced alterations in intestinal and peripheral immune response of weaning and old mice. Although the significance of these data remains to be clarified to establish whether these alterations reflect significant immune dysfunctions, these results suggest the importance of considering the gut and peripheral immune response to the whole GM crop, as well as the age, in the GMO safety evaluation" (Ibid, p. 11537).

Herbicide resistance genes

The effects of a GM vs. non-GM soy diet on the liver of mice were empirically tested in two scientific studies by Malatesta et al. The first study (Malatesta et al 2002) found nuclear modifications in DNA processing in liver cells that may be implicated in metabolic function. In a 2-year feeding study, (Malatesta et al 2008) the researchers observed marked changes in features of liver function, including senescence (ageing) markers and reduced metabolic rates in mice fed GM soybean vs. non-GM soy controls. The authors conclude:

"[T]he present work demonstrate that GM soybean intake can influence the liver morpho-functional features during the physiological process of ageing and, although the mechanisms responsible for such alterations are still unknown and some data have been discussed on a speculative basis, there are several findings underlining the importance to further investigate the long-term consequences of a GM-diet and the potential synergistic effects with ageing, xenobiotics and/or stress conditions. " (Ibid. p. 975)

B1.2 Potential bioactive or toxic effects of emerging classes of LMOs

Schubert (2008) reviews the published literature documenting potential risks to human health posed by the impending introduction of nutritionally enhanced LMOs, designed to produce bioactive molecules, into the food supply. Specifically, Schubert highlights the evidence for the potential production of aberrant transgenic molecules may produce toxic effects or those with profound effects on human development. He concludes that "Without proper epidemiological studies, most types of harm will not be detected, and no such studies have been conducted. " (Ibid p.604)

B2.1Adjuvant response to LMOs, including cross-reactive and recombinatorial effects.

The issue of combinatorial and/or synergistic effect of GM proteins either with endogenous host proteins or with other inserted GM traits (e.g. "stacked" events) is an area of nascent scientific inquiry. Several studies that point towards extrinsic factors may modulate Cry (Bt) efficacy and specificity. For example Broderick et al (2009) found that midgut bacterial presence was required for Cry1Ab insecticidal activity gypsy moth (*Lymantria dispar*) only suggesting the intestinal microflora may modulate toxicity in certain target Lepidopteran insect species. Further, research by Soberon et al (2007) suggest that structural changes to the engineered Cry1Ab protein in cotton may lack important oligmerization feature essential to toxin efficacy towards *P. gossypiella*.

Combinatorial or synergistic effects of recombinant proteins acting as adjuvants[1] to immunostimulatory effects, or as potential allergens is also an area of vigorous scientific inquiry. The protein Cry1Ac has been shown to be immunogenic in mice (Vazquez-Padron, 2000), and produces an adjuvant effect on both mucosal and systemic specific antibody responses (Moreno-Fierros et al 2003, Rojas-Hernandez et al. 2004). In investigations with Cry1Ab protein, Guimaraes et al. (2009) did not find a similar type of adjuvant effect elicited against peanut proteins as with Cry1Ac, yet instead found evidence of Cry1Ab acting as an adjuvant leading to early phase production of leukotrienes and increased Th2 and Th17-cytokine production in branchoalveolar lavage fluids after airway exposure. The implications of possible effects of Cry1Ab to produce allergen-induced cytokine responses are an area of investigation warranting further inquiry.

[1] That is, adjuvancy, the ability of a compound to enhance or facilitate an immune response, particularly sensitization to another (food) protein.

References

Birch, A.N.E., Pernin, C., Tabone, E., de Vaufleury, A., Xin, K., Krogh, P.H., 2007. Evaluation of effects of transgenic Bt maize on microarthropods in a European multi-site experiment. Pedobiologia, 51: 207-218.

Bøhn, T. et al. 2008. Reduced fitness of Daphnia magna fed a Bt-transgenic maize variety. Arch Environ Contam Toxicol DOI 10.1007/s00244-008-9150-5

Cortet, J., Griffiths, B.S., Bohanec, M., Demsar, D., Andersen, M.N., Caul, S., Betz, F. S., Hammond, B. G. and Fuchs, R. L. (2000). Safety and Advantages of Bacillus thuringiensis-Protected Plants to Control Insect Pests. Reg. Toxicol. Pharmacol. 32, 156-173.

Douville M, Gagne F, Blaise C, Andre C (2007) Occurence and persistence of Bacillus thuringiensis (Bt) and transgenic Bt corn cry1Ab gene from an aquatic environment. Ecotoxicol Environ Safety 66:195–203

Finamore, A., Roselli, M., Britti, S., Monastra, G., Ambra, R., Turrini, A. and Mengheri, E. (2008). Intestinal and Peripheral Immune Response to MON810 Maize Ingestion in Weaning and Old Mice. J. Ag Food Chem. 56, 11533-11539.

Griffiths, B.S., Caul, S., Thompson, J., Birch, A.N.E., Scrimgeour, C., Cortet, J., Foggo, A., Hackett, C., Krogh, P.H. (2006). Soil microbial and faunal community responses to Bt maize and insecticide in two soils. J. Environ. Qual. 35, 734-741.

Guimaraes VD, Drumare MF, Ah-Leung S, Lereclus D, Bernard H, Creminon C, Wal JM, Adel-Patient K, (2009). Comparative study of the adjuvanticity of Bacillus thuringiensis Cry1Ab protein and cholera toxin on allergic sensitization and elicitation to peanut. Food Agr Immuno. 19(4):325-337.

Harwood, J.D., Wallin, W.G.; Obrycki, J.J. (2005) Uptake of Bt endotoxins by nontarget herbivores and higher order arthropod predators: molecular evidence from a transgenic corn agroecosystem. Molecular Ecology 14, 2815-2823.

Haygood R, Ives AR, Andow DA, 2003. Consequences of recurrent gene flow from crops to wild relatives. Proc. R. Soc. Ser. B.-Bio., 270, 1879–1886.

Gepts, P. and R. Papa (2003). "Possible effects of (trans)gene flow from crops on the genetic diversity from landraces and wild relatives." Environmental Safety Research 2: 89-103.

Hilbeck A, Schmidt JEU (2006) Another view on Bt proteins: how specific are they and what else might they do? Biopestic Int 2(1):1–50

Ito, A., Sasaguri, Y., Kitada, S., Kusaka, Y., Kuwano, K., Masutomi, K., Mizuki, E., Akao, T. and Ohba, M. (2004). A Bacillus thuringiensis crystal protein with selective cytocidal action to human cells. J. Biol. Chem. 279, 21282-21286.

KilIç, A. and Akay, M. T. (2008). A three generation study with genetically modified Bt corn in rats: Biochemical and histopathological investigation. Food Chem. Toxicol. 46, 1164-1170.

Kroghsbo, S., Madsen, C., Poulsen, M., Schroder, M., Kvist, P. H., Taylor, M., Gatehouse, A., Shu, Q. and Knudsen, I. (2008). Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. Toxicol. 245, 24-34.

Lovei GL, Arpaia S (2005) The impact of transgenic plants on natural enemies: a critical review of laboratory studies. Entomol Exp Applic 114:1–14

Malatesta et al., 2002. "Ultrastructural Morphometrical and Immunocytochemical Analysis of Hepatocyte Nuclei from Mice fed on Genetically Modified Soy Bean". Cell Structure and Function 27: 173-18.

Malatesta M, Boraldi F, Annovi G, Baldelli B, Battistelli S, Biggiogera M, Quaglino D (2008) A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol 130:967–977

Mikkellsen, T., J. Jensen, et al. (1996). "Inheritance of oilseed rape (Brassica napus) RAPD markers in a backcross progeny with Brassica camestris." Theoretical & Applied Genetics 92: 492-497.

Moreno-Fierros, L., Garcia, N., Gutierrez, R., Lopez-Revilla, R., and Vazquez-Padron, R.I. 2000. Intranasal, rectal and intraperitoneal immunization with protoxin Cry1Ac from Bacillus thuringiensis induces compartmentalized serum, intestinal, vaginal and pulmonary immune responses in Balb/c mice. Microbes and infection, 2: 885-890.

Moreno-Fierros L, Ruiz-Medina EJ, Esquivel R, López-Revilla R, Piña-Cruz S., 2003. Intranasal Cry1Ac protoxin is an effective mucosal and systemic carrier and adjuvant of Streptococcus pneumoniae polysaccharides in mice. Scand J Immunol., 57: 45-55.

Obrist, L.B., Dutton, A., Albajes, R., Bigler, F. (2006) Exposure of arthropod predators to Cry1Ab toxin in Bt maize fields. Ecological Entomology 31, 143-154.

Quist D. 2007. “Vertical (trans)gene flow: Implications for crop diversity and wild relatives”. In: Lim Li Ching and Terje Traavik (Editors in Chief). 2007. Biosafety First: Holistic Approaches to Risk and Uncertainty in Genetic Engineering and Genetically Modified Organisms. Tapir Academic Press, Trondheim, Norway, pp 205-217.

Ramirez-Romero R, Desneux N, Decourtye A, Chaffiol A and M.H. Pham-Delegue (2007) Does Cry1Ab protein affect learning performances of the honey bee Apis mellifera L. (Hymenoptera, Apidae)? Ecotox Env Safety 70:327-333.

Rojas-Hernández S, Rodríguez-Monroy MA, López-Revilla R, Reséndiz-Albor AA, Moreno-Fierros L., 2004. Intranasal coadministration of the Cry1Ac protoxin with amoebal lysates increases protection against Naegleria fowleri meningoencephalitis. Infect Immun., 72:4368-4375.

Schroder M., Poulsen M., Wilcks A., Kroghsbo S., Miller A., Frenzel T., Danier J., Knudsen I. A 90-day safety study of genetically modified rice expressing Cry1Ab protein (Bacillus thuringiensis toxin) in Wistar rats (2007) Food and Chemical Toxicology, 45 (3), pp. 339-349.

Schubert, D (2008). The problem with Nutritionally Enhanced Plants. J Med Food 11(4): 601-605.

Snow, A. A., D. Pilson, L. H. Rieseberg, M. Paulsen, N. Pleskac, M. R. Reagon, D. E. Wolf, and S. M. Selbo. 2003. A Bt transgene reduces herbivory and enhances fecundity in wild sunflowers. Ecological Applications 13:279–286.

Tayabali, A. F. and Seligy, V. L. (2000). Human cell exposure assays of Bacillus thuringiensis commercial insecticides: production of Bacillus cereus-like cytolytic effects from outgrowth of spores. Environ. Health Pers. 108, 919-930.

Traavik T. and Heineman J. Genetic Engineering (GE) and omitted health research: still no answers to ageing questions. (2005). Pp. 245-253 In: Faissner K (editor): Gefahr Gentechnik, Irrweg and Ausweg. Concord-Verlag, Mariahof, 2005 (ISBN 3-9501887-1-1).

Vázquez-Padrón, Gonzáles-Cabrera, J., García-Tovar, C., Neri-Bazan, L., Lopéz-Revilla, R., Hernández, M., Moreno-Fierro, L. and de la Riva, G. A. (2000). Cry1Ac protoxin from Bacillus thuringiensis sp. kurstaki HD73 binds to surface proteins in the mouse small intestine. Biochem. Biophys. Res. Comm. 271, 54–58.

Velimirov, A., Binter, C. and Zentek, J. (2008). Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice. Bundesministerium für Gesundheit, Familie und Jugend, Sektion IV.

Wandeler, H., Bahylova, J. Nentwig, W. (2002). Consumption of two Bt and six non-Bt corn varieties by the woodlouse Porcellio scaber. Basic Appl. Ecol. 3, 357-365.

Zwahlen C,Hilbeck A,Howald R,Nentwig W. (2003). Effects of transgenic Bt

corn litter on the earthworm Lumbricus terrestris.Molecular Ecology 12: 1077–1086.

Attachment 2

This input was submitted to the Norwegian CP-FP and BCH-FP in Norwegian. The key paragraphs have been translated

→ … the advisory board wishes to emphasise that negative effects on biodiversity is somewhat different from negative environmental effects. There is substantial scientific documentation that indicates negative effects of certain LMOs on the environment, e.g. negative effects of Bt-maize on non-target insects. This is not the same as documenting that the use of such LMOs has a negative effect on the functionality of ecosystems, or the total biodiversity. The advisory board experiences uncertainty, broad interpretations and extensive debates with regards to scientific literature and what it tells us about possible effects on biodiversity. Long term studies are also lacking.

The advisory board will not present and discuss the relevant literature but wish to point out that in the recent years a number of relevant scientific studies have introduced new elements for consideration. One example is the work of Ramirez-Romero *et al*. (2008) indicating that when honeybees are exposed to the Cry1Ab toxin through their natural diet (exposure through pollen from GM-plants) this may lead to reduced capacity for learning and altered pattern of feeding. It is therefore not a direct lethal effect but a more subtle effect that may have ecological consequences and an effect on biodiversity due to a possible reduced survival of the species.

When risk assessing LMOs the advisory board wishes to point out that the context of the evaluation is important and that it is necessary to routinely assess the alternatives to any given LMO. Existing agricultural practices with the use of mono cultures and efficient pesticide regimes have had a clear negative effect on biodiversity both past and present. Less weeds, fewer small mammals and reduced access to seeds in the fields have had large consequences for biodiversity – even before LMOs entered the market. An example is the reduction of bird populations which is well studied and documented in Great Britain. When the use of a certain LMO is to be related to biodiversity it is important to consider the consequences of an already established practice and if the LMO contributes to an existing negative trend, if it has a positive effect or if it introduces new elements of risk.

As opposed to many of the existing LMOs on the market there are a number of “new” LMOs that have a large probability of negative impact on biodiversity if released into the environment. These LMOs must therefore undergo a thorough risk assessment. The advisory board would advise caution with regards to:

- GM-viruses with altered traits and host specificity

- GM-fish with cold tolerance/increased growth rate/high tolerance environmental pollutions
- Stress tolerant GM-plants (drought tolerant/cold tolerant)
- GM-plants with a more efficient nutritional uptake
- Pharma plants

Even though these organisms may have what appears to be very useful traits for purposes of production they may also have selective advantages in nature. This could lead to increased invasiveness and change in ecosystem functionality with the consequence that the number of species drop dramatically or that the balance is altered in other undesirable ways. One scenario is the displacement of locally adapted species through spread of stress tolerant GM forage grasses adapted to marginal habitats/growth areas. Another example is the possible consequences of a GM-fish tolerant to higher concentrations of environmental pollutants leading to higher accumulations of pollutants in the food chain which may in turn have negative health effects.

Both in Norway and the rest of the world the case by case approach is a central principle for LMO risk assessment. The advisory board believes this is an important requirement in order to understand the characteristics of each LMO and reveal the possible effects of the intended use. We would in that respect underline the challenges that risk assessors face when dealing with several of the newer LMOs such as GM-trees (long generation span), GM-viruses (may be difficult to control, risk of mutation) and pharmaplants (risk of entering the food chain).

References

Ramirez-Romaro *et al.* (2008) Does Cry1Ab protein affect learning performances of the honey bee *Apis mellifera* L. (Hymenoptera, Apidae)? Ecotoxicology and Environmental Safety 70 327-333.

Attachment 3

Antibiotic resistance marker genes (ARMG)

Relevant scientific reports on the topic of ARMG:

- **EFSA Scientific Opinion (2009)**: Consolidated presentation of the joint Scientific Opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" and the Scientific Opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants". EFSA Journal

(2009). http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902569520.htm

With regards to the 2009 EFSA report we would like to make the following comments:

- There are geographical differences in the distribution of the antibiotic resistance genes *nptII* and *aadA* in naturally occurring bacteria and the distribution patterns are often unknown
- We would draw the attention to the mentioned conclusions from the WHO Expert Group on Critically Important Antimicrobials for Human Health regarding the categorization of the antimicrobials kanamycin, neomycin and spectinomycin as 'Highly Important Antimicrobials' and streptomycin as a 'Critically Important Antimicrobial'
- The EFSA opinion had two minority opinions that should be noted

- **VKM (2005)**. An assessment on potential long-term health effects caused by antibiotic resistance marker genes in genetically modified organisms based on antibiotic usage and resistance patterns in Norway. http://www.vkm.no/dav/23de90b2ff.pdf

F. UNITED ARAB EMIRATES

UNITED ARAB EMIRATES
MINISTRY OF ENVIRONMENT & WATER

الإمارات العربية المتحدة
وزارة البيئة والمياه

Our Ref: 3885
Date:15/9/2009

Dear Mr. Dioghlaf
Executive Secretary
Secretariat of the Convention on Biological Diversity

SUBJECT: SUBMISSION OF SCIENTIFICALLY SOUND INFORMATION REGARDING THE IDENTIFICATION OF LIVING MODIFIED ORGANISMS OR SPECIFIC TRAITS THAT MAY HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY,TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH

Reffering to your letter Ref : SCBD/MPDM/jh/67587 regarding the above subject. we would like to inform you that for the recent time these information is not avaliable ,and we promise to send whenever it is prepared .

Please accept the assurance of my highest consideration

Regards,
Seif Alshra
Executive Director / Water Resources & Nature Conservation
Ministry of Environment and Water
E-mail: Saif Mohammed AlShara (smalshara@moew.gov.ae)
Tel:00971 4 2958161
Fax:00971 4 2957766

II. SUBMISSIONS FROM OTHER GOVERNMENTS

G. AUSTRALIA

AUSTRALIAN GOVERNMENT SUBMISSION – SEPTEMBER 2009

Notification SCBD/BS/MPDM/JH/67587

Invitation for Parties, other Governments and relevant organisations to submit to the Executive Secretariat scientifically sound information on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking into account risks to human health.

In Australia, the Gene Technology Regulator (the Regulator) is responsible for protecting human health and safety and the environment, by identifying and managing risks posed by or as a result of gene technology. Risk assessments are science-based and are carried out on a case-by-case basis and involve extensive consultation with experts.

The Regulator has issued over 70 licences authorising the release of LMOs into the Australian environment, comprising 10 commercial release licences and more than sixty licences for the limited and controlled release of LMOs for experimental purposes (field trials). The LMOs authorised for commercial release in Australia include several varieties of GM cotton and canola and a GM rose. The Regulator concluded that LMOs approved for commercial release in Australia, are as safe as conventional varieties and are able to be used in the same manner as their conventional counterparts. One LMO, colour modified carnations, is no longer required to be licensed and has been placed on the GMO Register. Dealings are entered on the GMO Register when the Regulator is satisfied that risks posed by the dealings are minimal and it is not necessary for anyone conducting the dealings to be covered by a licence in order to protect the health and safety of people or the environment.

It is a condition of a licence that the licence holder inform the Regulator as soon as possible if the licence holder becomes aware of additional information as to any risks to the health and safety of people or the environment or, of any unintended effects of the dealings authorised by the licence. Information may be supplied by other persons covered by a licence or by any other organisation or individual. In addition, the Office of the Gene Technology Regulator (OGTR) continues to monitor the scientific and other literature for any new information in relation to GM crops, and assess this information for its potential to impact on any existing regulatory approvals.

GM cotton currently comprises the majority of the Australian cotton crop and insect resistant 'Bt cotton' has been grown commercially in Australia since 1996. To date, the OGTR has not received any reports of adverse effects on human health or the environment associated with Bt cotton. Similarly, no credible information has arisen, either domestically or internationally, to support a link between GM crops approved by the Regulator for commercial release in Australia and adverse impacts on human health or the environment.

Australia considers that all LMOs should be assessed according to the case-by-case, science based risk assessments called for under the Protocol and that information regarding LMOs be considered in regard to the consensus of opinion in the scientific literature. Assessment should be undertaken in the context of existing production

practices in conjunction with the consideration of effective risk treatments for identified risks.

Australia notes that where competent authorities have not approved the release of a LMO the reasons given often relate to uncertainty as to risk, either in terms of consequence or likelihood of an adverse effect on biological diversity. There are a number of different types of uncertainty (incertitude, variability, descriptive uncertainty or cognitive uncertainty). Risk assessments would benefit from a more precise discussion of the type of uncertainty that is causing concern. Australia has developed a *Risk Analysis Framework* (RAF) which provides guidance on how the Regulator, and staff in the OGTR approach the risk analyses of LMOs. The RAF includes guidance on how to characterise and deal with uncertainty and is available at http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1.

H. UNITED STATES OF AMERICA

United States Department of State

Washington, D.C. 20520

To:
Dr. Ahmed Djoghlaf
Executive Secretary
Convention on Biological Diversity
Montreal, Canada

Re: Notification No 2009-103

September 14, 2009

Dear Dr. Djoghlaf,

The United States appreciates this opportunity to provide information relevant to the 28 May 2009 notification from the Secretariat entitled "Submission of scientifically sound information regarding the identification of Living Modified Organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health."

This question was part of the 2008 notification from the Secretariat, and we commented on this issue in our submission to the Secretariat in January of 2009. Below we reiterate the relevant points in response to this most recent request from the Secretariat.

1. Decisions about the suitability of an LMO should take into account a case-specific risk assessment. In decision BS-IV/11, the Parties asked the AHTEG to "consider possible modalities for cooperation in identifying living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health."

The United States believes that undertaking this task as an *a priori* exercise would violate the established principle set out in Annex III that case-by-case analyses should be used to make decisions about an LMO. The United States notes that Annex III sets out general principles, methodological steps, and points to consider in the conduct of risk assessment. The general principles include, among others, the concepts that:

- Risk assessment should be carried out in a scientifically sound and transparent manner;
- Lack of scientific knowledge or scientific consensus should not necessarily be interpreted as indicating a particular level of risk, an absence of risk, or an acceptable risk;
- Risks should be considered in the context of risks posed by the non-modified recipients or parental organisms; and that
- Risks should be assessed on a case-by-case basis.

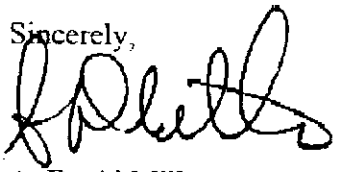
As noted above, the methodology described in Annex III of the Protocol follows the conventional risk assessment paradigm, beginning with identification of a potential hazard, such as characteristics of an LMO, which may have an adverse effect on biodiversity. Risks are then characterized based on combined evaluation of the likelihood of adverse effects, and the consequences should those effects be realized.

Therefore, the task of identifying such LMOs (i.e. "that may have adverse effects on the conservation and sustainable use of biological diversity...") in fact contradicts the very foundation that risk assessment plays in providing scientifically sound assessments to decision makers, regardless of whether the decisions are being made under the Protocol or under a national biosafety legal system. It is not possible to reach valid conclusions on hypothetical LMOs, because there is no real information to analyze, and this analysis would not take into account the particularities of different receiving environments as well as differences in how a particular LMO might be used. Furthermore, it is unclear how such a list of LMOs would relate to Parties' obligations under the Protocol. In addition, such a list would not remove the obligation to make decisions on transboundary movements.

2. The United States supports an alternative approach to making lists of LMOs. Under this alternative approach, the AHTEG might consider modalities for developing a process to examine existing case-specific risk assessments of LMOs in order to extract any consensus conclusions that have been broadly validated by many countries in risk assessments that have been undertaken in a manner consistent with Annex III. Such reviews may be able to identify broad-based consensus on LMOs whose transboundary movement are unlikely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. There are now quite a few LMOs that have been subjected to multiple assessments by different countries, in various receiving environments, and it may be useful for other countries to be aware of the extent of agreement across these risk assessments. This approach would provide a basis for a decision of the Parties as described in Article 7 paragraph 4.

> "The advance informed agreement procedure shall not apply to the intentional transboundary movement of living modified organisms identified in a decision of the Conference of the Parties serving as the meeting of the Parties to this Protocol as being not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health."

Sincerely,



A. David Miller
Division Chief
National Focal Point
Biosafety Protocol

III. SUBMISSIONS FROM RELEVANT ORGANIZATIONS

I. GLOBAL INDUSTRY COALITION

15 September 2009

VIEWS ON THE IDENTIFICATION OF LIVING MODIFIED ORGANISMS THAT MAY HAVE AN ADVERSE EFFECT ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY

GLOBAL INDUSTRY COALITION

The Global Industry Coalition (GIC)[1] is submitting the following information in relation to the request for scientifically sound information on "the identification of living modified organisms (LMOs) or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health". This request from the Secretariat is one of the provisions of the medium-term programme of work, decision BS-I/12 paragraph 4 (b) (iii), and is further elaborated in decision BS-IV/11 adopted by the fourth Meeting of the Conference of the Parties to the Convention on Biological Diversity serving as the Meeting of the Parties to the Cartagena Protocol on Biosafety (Bonn, 12-16 May 2008).

Paragraphs II.8 and 9 of BS-IV-11 explicitly state:

> *8. Requests Parties and invites other Governments and relevant organizations to submit to the Executive Secretary, not later than three months prior to the first meeting of the Ad Hoc Technical Expert Group, scientifically sound information available at that time, on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health;*
>
> *9. Requests the Executive Secretary to compile the information received and to prepare a synthesis report for consideration by the Ad Hoc Technical Expert Group and the Parties;*

The private sector strongly believes that after all submitted information is appropriately analyzed, the conclusion will be that there is no scientifically based evidence that the plant-based LMOs currently marketed have any potential for increased adverse effects on the conservation and sustainable use of biological diversity, when compared to their conventional counterparts in line with the General Principles for Risk Assessment as provided in Annex III to the Protocol.

[1] The Global Industry Coalition (GIC) for the Cartagena Protocol on Biosafety receives input and direction from trade associations representing thousands of companies from all over the world. Participants include associations representing and companies engaged in a variety of industrial sectors such as plant science, seeds, agricultural biotechnology, food production, animal agriculture, human and animal health care, and the environment.

The GIC wishes to note in this submission that UNEP/CBD/BS/COP-MOP/4/10 presented a misleading overview to Parties on the potential for LMOs to have adverse effects on the conservation and sustainable use of biodiversity. It was based almost exclusively on a review of notifications to the European Commission from five Member States (Austria, France, Germany, Greece and Hungary) without consideration of the subsequent reviews by the European Food Safety Authority (EFSA), which concluded that each country's actions had no scientific merit. As such, UNEP/CBD/BS/COP-MOP/4/10 confused politically motivated decisions with validated science-based assessments. The GIC points out in this submission that the actions taken by the five Member States were merely attempts to inappropriately use scientific argumentation to mask what in fact were political positions, which were subsequently unable to withstand rigorous scientific scrutiny by EFSA. The other examples in UNEP/CBD/BS/COP-MOP/4/10 are also readily explained by factors other than evidence of risk to the conservation and sustainable use of biodiversity.

With regard to paragraph 8 in BS-VI-11 and the specific request for information, it is important to recall that:

- The request for information on "the identification of living modified organisms (LMOs) or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health" must be restricted to those LMOs for which there is scientifically sound risk assessment information and that are likely to be subject to transboundary movement. Only those LMOs that have been subject to risk assessment according to Annex III and where information from those assessments is available to Parties through the BCH are within scope. Opinions derived from theoretical speculation and conjecture based on actions taken such as withdrawn applications should not be considered as scientifically sound evidence of adverse effects. Furthermore, it would be inappropriate to conclude that the decision in paragraph 8 of BS-IV-11 is applicable to research materials for which information is too scarce to make valid risk characterizations. Cases where applicants have requested withdrawal of their application are usually inspired by very practical motives, such as a change in research and development interest, the availability of improved material or the need to perform additional studies.

- Cases where applications for field trials or commercial use have been rejected may provide interesting grounds for speculation, but there can be several reasons leading to such decisions. For instance, an Authority may deem the available information insufficient to perform an appropriate risk assessment and to decide on adequate risk management measures. This illustrates the importance of addressing uncertainty but does not *per se* point to a potential adverse impact.

- Cases where permits have been suspended or products have been prohibited also require further investigation of the rationale for such decisions, including the scientific validity of the arguments. Isolated findings, without overarching perspective of the body of scientific evidence in support of a product approval and without confirmation by other studies, should be interpreted with great care.

As noted above, this submission is intended to provide scientifically sound information to Parties on specific allegations made by a very small number of countries, most of which are opposed to GM crops on a political basis. The information on the few cases is organized in a manner to address each allegation clearly and in detail, and in the following scientific framework:

Molecular characteristics

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids containing event MON810. One of the areas of concern documented by Greece related to the molecular characterization of MON810 and the presence of certain sequences.

In their review of this request, the EFSA GMO Panel provided the following comments (EFSA, 2006c) with respect to concerns around the molecular characterization of MON810 maize:

- The Greek submission questioned the molecular characterization of MON810 maize, in particularly stressing the potential for unintended effects due to the so-called 'genome scrambling'. The GMO Panel elaborated on the information regarding the molecular characterization that applicants are required to provide for the transgene locus. This includes the DNA sequence of the inserts and flanking regions that allow for the identification of unintended sequences, if any, and potential re-arrangements of the transgene locus. After having analyzed all the data, no specific risk was identified by the GMO Panel due to the possibility of genome scrambling.

- As the *cry1Ab* gene in MON810 maize is driven by the CaMV 35S promoter, Greece was concerned that the CaMV 35S promoter may be transferred, possibly integrated, and might influence the expression of other bacterial genes, and genes in viruses and mammalian tissue. In their comments, EFSA noted that suggestions that the CaMV 35S promoter could result in an inadvertent activation of plant genes or endogenous viruses, promote horizontal gene transfer, or might even recombine with mammalian viruses with unexpected consequences (Ho *et al*., 1999; Ho *et al*., 2000) had been previously considered in reviews of the safety of CaMV 35S promoter (Hull *et al*., 2000; ACRE, 2002; EFSA, 2003). The GMO Panel was of the opinion that the conclusions of the ACRE study regarding the safety of the CaMV 35S promoter were still valid.

- ***"The GMO Panel concludes that the Greek submission provided no new scientific data or information in support of their particular concerns on molecular characterization" (EFSA, 2006c).***

Antibiotic resistance marker genes

The potential for increased resistance to antibiotics in humans, animals and in organisms in the wider environment as a result of horizontal gene transfer has been raised as a concern with respect to the presence of antibiotic resistance marker (ARM) genes in GM plants.

The use of ARM genes in GM plants has been the subject of several reviews (Gay and Gillespie, 2005; Goldstein *et al*., 2005; Miki and McHugh, 2004; Nap *et al*., 1992; Nielsen *et al*., 1998; Ramessar *et al*., 2007) and expert consultations: Working Party of the British Society for Antimicrobial Chemotherapy (Bennett *et al*., 2004), FAO/WHO Consultation on Foods Derived from Biotechnology (FAO/WHO, 2000), Scientific Steering Committee of the European Commission (SSC, 1999) Zentrale Kommission für die Biologische Sicherheit, Germany (ZKBS, 1999), and the Advisory Committee on Novel Foods and Processes, UK (ACNFP, 1996). These reports confirm that the frequencies of horizontal gene transfer from plants to bacteria are likely to be extremely low [see Keese (2008) for a recent review on the subject of horizontal gene transfer]. It has been concluded that such a rare event would not contribute effectively to the extant abundance of ARM genes in bacteria in the environment (soil, plants, water and human and animal guts) and that the presence of ARM genes, and in particular the *nptII* gene, in GM plants does not pose a relevant risk to human or animal health or to the environment.

Some authorities have opted to implement policies discouraging the use of ARM genes in GMOs but have further specified these as referring to genes expressing resistance to antibiotics in use for medical or veterinary treatment (e.g., European Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC).

The EFSA GMO Panel has evaluated the potential risks associated with specific ARM genes taking into account the factors that impact on the likelihood of any adverse effects on humans or the environment of ARM genes used in GM plants (EFSA, 2004b), in particular:

- Their current usage in clinical and veterinary medicine;
- The likely occurrence of horizontal gene transfer from GM plants to microbes; and
- The potential impact of horizontal gene transfer where naturally occurring resistance to the relevant antibiotics exists in the microbial gene pool.

The GMO Panel considered the frequency of horizontal gene transfer from GM plants to other organisms as very low for all ARM genes considered. With respect to clinical importance, the Panel categorized ARM genes into three groups with different potentials for compromising human health and the environment. ARM genes in the first group include genes conferring resistance to kanamycin (e.g., *nptII*) and hygromycin (e.g., *hph*). The GMO Panel was of the opinion that with regard to safety, there was no rationale for inhibiting or restricting the use of genes in this category, either for field experimentation or for the purpose of placing on the market. The use of ARM genes in the second or third group was proposed to be respectively restricted or prohibited in view of the importance of the related antibiotics in clinical usage.

In a subsequent statement (EFSA, 2007a), the GMO Panel agreed with the European Medicines Agency (EMEA) that the preservation of the therapeutic potential of the aminoglycoside group of antibiotics is important. The Panel confirmed its opinion that the therapeutic effect of these antibiotics will not be compromised by the presence of the *nptII* gene in GM plants, given:

- The extremely low probability of gene transfer from plants to bacteria and its subsequent expression;
- That the presence of the *nptII* gene in GM plants is very unlikely to change the existing widespread prevalence of this antibiotic resistance gene in bacterial sources in the environment; and
- The evidence indicating that integration of the *nptII* gene would only be one of many mechanisms by which bacteria could become resistant to aminoglycosides such as kanamycin.

In 2009, a joint opinion (EFSA, 2009a) of the GMO Panel and the Panel on Biological Hazards (BIOHAZ) was published focusing on two ARM genes that are present in GM plants for which an application has been submitted to EFSA. One is functional in the plant (*nptII*, kanamycin/neomycin resistance) and the other gene (*aadA*; streptomycin/spectinomycin resistance) is not expressed in the GM plants as the expression is regulated by a bacterial promoter not active in plants. The joint opinion indicated that adverse effects on human health and the environment resulting from the possible transfer of these two antibiotic resistance genes from GM plants to bacteria, associated with use of GM plants, were unlikely.

Bt176 maize (C/F/94/11-03) was authorized for all uses in the European Union by Commission Decision 97/98/EC of 23 January 1997 (EC, 1997) and final consent was granted by the French competent authority on 4 February 1997. On 14 February 1997, **Austria** invoked Article 16 of Directive 90/220/EEC partly based on the fact that in their opinion the impact of a potential gene transfer of the **β-lactamase** encoding *bla* gene and a potential induction of resistance in bacteria on the therapy of humans and animals with antibiotics remained not fully conclusive.

Upon reviewing the additional arguments:

- The Scientific Committee for Animal Nutrition (SCAN, 1997) confirmed that there was no evidence indicating that the use in animal feeding of the genetically modified maize (Bt176) would give rise to any adverse effect on animal health. SCAN thereby reinforced its initial assessment of 1996 (SCAN, 1996).

- The Scientific Committee on Food confirmed to have been aware of and took into account the available scientific knowledge concerning the unexpectedly long survival of DNA in the environment and the persistence of fragments of DNA in the human body following the consumption of food. The likelihood of a possible horizontal gene transfer to microorganisms in the intestinal tract under specific conditions was also known and taken into consideration. The potential hazard arising from the original transformation of maize by the use of the pUC plasmid harbouring the gene encoding ß-lactamase was given particular attention and was even the major topic of the *ad hoc* expert meeting organized jointly by the SCF and SCAN on 6 December 1996. In its opinion expressed on 13 December 1996, SCF made reference to the widespread presence in the intestine and in

the environment of bacteria that harbour the naturally occurring genes encoding ß-lactam resistance, and concluded that the possibility that the product would add significantly to the already widespread occurrence of ampicillin resistant bacteria in animals and man was remote (SCF, 1996). The SCF noted that none of its conclusions concerning the toxicology, nutritional value, allergenicity and secondary changes were affected by the Austrian arguments.

In a subsequent opinion (EFSA, 2006b) the GMO Panel specifically addressed the presence of the *bla* gene in Bt176 and T25 maize. They stated that ampicillin and its derivatives are antibiotics of clinical importance but the resistance conferred by the *bla* gene is common on mobile genetic elements in a range of bacteria present in the environment, as discussed in detail in a 2004 opinion of the GMO Panel (EFSA, 2004d). Therefore, the GMO Panel agreed with the previous safety assessments carried out by the Scientific Committee on Plants on Bt176 (SCP, 1999a; 2000) and on T25 (SCP, 1998c; 2001a,b,c), stating that the likelihood of adverse effects due to the presence of the ARM genes in Bt176 and in T25 maize was extremely low. It is also noted that T25 maize contains only a partial *bla* gene, which is, therefore, non-functional (SCP, 1998a).

On 16 July 2008, **Austria** notified to the European Commission a national safeguard clause on GM maize event **MON863**, which had been approved for import into the EU. Data provided from Austria indicated the spread of **kanamycin resistance** in human food-borne pathogens at a frequency of *ca*. 1%. The GMO Panel (EFSA, 2009d) reviewed the specifics of the resistance, the use of the particular antibiotics, the likelihood for horizontal gene transfer, and the prevalence of the resistance in the environment. In their comments, the GMO Panel noted that:

> ***"The transfer of ARM genes from GM plants to bacteria has never been shown to occur under laboratory or natural conditions in the absence of sequence identity. If transfer of ARM genes from GM plants to bacteria occurs at all, its frequency is below the limit of detection. The process is therefore considered unlikely to impact on the occurrence of antibiotic resistance in humans, animals and the environment" (EFSA, 2009d).***

The GMO Panel concluded that even in the unlikely event of the transfer of the *nptII* gene from MON863 maize to bacteria, its contribution to the existing pool of kanamycin resistance in bacteria would be negligible.

Toxicology and allergenicity related safety evaluations

Bt176 maize (C/F/94/11-03) was authorized for all uses in the European Union by Commission Decision 97/98/EC of 23 January 1997 (EC, 1997) and final consent was granted by the French competent authority on 4 February 1997. On 14 February 1997, Austria invoked Article 16 of Directive 90/220/EEC. In February 2004, Austria provided additional information to support the national safeguard measures partly based on the fact, that in their opinion, the toxicology and allergenicity of the genetically modified plants and derived products destined for human and/or animal consumption were insufficiently covered.

Originally the Scientific Committee on Food (SCF, 1996) had drawn the following conclusions:

- The transgenic maize was, except for the inserted traits, substantially equivalent to maize available on the market;
- Animal feeding studies with the genetically modified maize supported its substantial equivalence to the parent plant;
- No nutritional concerns were associated with the use of this transgenic maize;
- It was unlikely that the genetic changes introduced any new potential for allergenicity;
- No human toxicological concerns arose regarding the inserted traits based upon the toxicological and digestibility data considered; and
- The possibility that the product would add significantly to the already widespread occurrence of ampicillin resistant bacteria in animals and man was remote.

In a subsequent opinion (SCF, 1997) the SCF noted that none of its conclusions concerning the toxicology, nutritional value, allergenicity and secondary changes were affected by the Austrian arguments.

The three reports submitted by Austria in 2004 (Spök *et al*., 2003a; Spök *et al*., 2003b; Spök *et al*., 2003c) were related to procedures and requirements for toxicity and allergenicity safety evaluations. In responding to these reports (EFSA, 2004c), the GMO Panel reiterated its support of a comparative approach to safety assessment of GMOs, stating that:

> ***"The underlying assumption of this comparative assessment approach for GMOs is that traditionally-cultivated crops have a history of generally accepted safe use with regard to human and animal consumption and the environment. These crops therefore serve as baseline comparators for the risk assessment of GMOs. This comparison is the starting point for the safety assessment which then focuses on the impact of any intended or unintended differences identified" (EFSA, 2004c).***

The EFSA GMO Panel concluded that: ***"The three reports do not provide any new scientific data to indicate adverse affects on human and animal health or the environment of the maize events Bt176, MON 810 and T25" (EFSA, 2004c).***

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France

ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids containing event MON810. One of the areas of concern documented by Greece consisted of accepting that safety studies of Cry proteins are performed with proteins produced in bacteria, as the nucleotide sequence of the corresponding genes integrated into GM crops may not be precisely the same as the nucleotide sequence of the bacterial gene.

The GMO Panel (EFSA, 2006c) commented that an analysis of the suitability of bacterially produced proteins had already been carried out by the Competent Authorities of France and the Scientific Committee on Plants in their original assessment (SCP, 1998a). The GMO Panel confirmed that the altered sequence of the *cry1Ab* gene in MON810 maize had been assessed by the GMO Panel in previous opinion (EFSA, 2005c).

Another area of concern submitted by Greece was the impact of MON810 maize on human health. The GMO Panel (EFSA, 2006c) reviewed all of the documents provided and came to the conclusion that most were not relevant for the case. Although not mentioned explicitly by the Greek Authority, the GMO Panel identified that there seemed to be a concern that transgenic DNA from GM food, including MON810 maize, is transferred to cells of the consumer and could give rise to adverse effects. The Panel reviewed information on the detection of DNA in animal tissues and food products such as meat, milk and eggs concluding that these observations confirm that transgenic DNA does not behave in a different way to DNA occurring in conventional food and feed products. Furthermore, according to the GMO Panel:

> ***"...the presence of such gene fragments has never shown any adverse effects on animals. Incorporation of functional plant gene fragments from consumed plant material into mammalian cells in vivo has never been observed and is considered extremely improbable" (EFSA, 2006c).***

In conclusion, ***"The GMO Panel therefore affirms its conclusions that, on the basis of current scientific knowledge, MON810 maize is unlikely to have adverse effects on human and animal health or on the environment in the context of its intended uses" (EFSA, 2006c).***

On 13 September 2007, **Greece** notified to the European Commission a ministerial decision concerning the extension of validity and amendment of an existing safeguard measure invoked to provisionally prohibit the cultivation of MON810 on its territory (EFSA, 2008c). One of the areas documented by Greece consisted of a toxicological concern related to the animal feeding studies justified by a SANCO note to EFSA of 15.03.2007 on MON863 rat feeding studies and a publication by Séralini *et al*. (2007).

The study by Séralini and co-workers on MON863 maize, to which the Greek authorities refered, had been extensively considered by the GMO Panel and commented on in a statement (EFSA, 2007b). Maize MON863 considered in this study contained a different Cry toxin from maize

MON810 and the GMO Panel advised that conclusions on MON863 were not relevant to MON810. In summarizing their review of Séralini *et al*. (2007), the GMO Panel stated that:

> ***"In the absence of any indications that the observed differences in test parameters are indicative of adverse effects, the GMO Panel does not consider that the publication by Séralini et al. (2007) raises new issues which are toxicologically relevant" (EFSA, 2007b).***

The GMO Panel (EFSA, 2008c) further referred to a 90-day feeding study with MON810 maize that had been provided in the dossier on GM maize MON863 x MON810 and that had also been published in peer-reviewed literature (Hammond *et al*., 2006). The GMO Panel considered that the results of the 90-day sub-chronic rodent study did not indicate adverse effects from consumption of maize MON810 and the GMO Panel concluded that there were no concerns over its safety (EFSA, 2005e). In more general terms, the issue of safety testing of GM products in animals has been addressed by a working group of the EFSA GMO Panel (EFSA, 2008d).

On 9 February 2008, **France** notified to the European Commission an Order suspending the cultivation of seed varieties derived from the maize event MON810 and submitted an information package comprised of different supporting documents.

One of the areas of concern consisted of food and feed safety issues. France provided various arguments as to why they considered the safety testing performed with MON810 maize and the Cry1Ab protein had not been sufficient and referred specifically to the following:

- The proteins produced by *Bacillus thuringiensis* and that produced by MON810 did not have the same primary sequences;
- The protein produced by MON810 could be modified in its spatial conformation by addition of elements, which could have important consequences for its functional characteristics and its potential pathogenic capacity;
- The duration of the toxicological tests was insufficient and should have been conducted in multiple animal models; and
- The toxicological tests performed for the assessment of transgenic plants did not cover the new domains of health (prion disease, oncology).

Interestingly, the AFSSA ("l'Agence Française de Sécurité Sanitaire des Aliments", the French authority on food safety) opinion of 30 April 2008 (AFSSA, 2008), which also stated that, taking into consideration the updated data and published scientific literature provided in the dossier, maize containing the transformation event MON 810, and derived products, present the same level of safety as conventional maize varieties and their derived products.

The GMO Panel reviewed all relevant and most recent scientific literature and publications, such as the scientific advice of AFSSA (2008) and COGEM (2008), as well as the risk assessment approach recommended by the internationally harmonized Codex alimentarius (Codex alimentarius, 2003) and the EFSA Guidance Document (EFSA, 2006a).

In its evaluation, the GMO Panel addressed the following concerns (EFSA, 2008e):

- **Allergenicity:** France claimed there were indications that Cry1Ab protein triggers an immune response in the rat model (Kroghsbo *et al*., 2008). The GMO Panel confirmed that during the safety assessment of GMOs, potential allergenicity of a GMO is considered and that no indications had been found for the Cry1Ab protein that would raise concerns over any potential allergenicity. With regard to the experiment described by Kroghsbo *et al*. (2008), it is not uncommon for a protein to act as an antigen. The authors themselves noted that *"It is well documented that introduction of a new or 'foreign' protein by the oral route will induce an antigen-specific immune response"*.

  "This information could therefore not be taken by the GMO Panel as an indication of any allergic response to the Cry1Ab protein" (EFSA, 2008e).

- **Toxicity:** It was pointed out by France that: (1) the Cry1Ab protein had not been tested according to current methods in the domain of research on prions; and (2) the toxicological studies should have considered research on oncogenes.

  The GMO Panel countered that, in accordance with the EFSA Guidance Document (EFSA, 2006a) and the Codex alimentarius guidelines (Codex alimentarius, 2003), characteristics of proteins, including structure and functionality, various other relevant physico-chemical and biochemical properties, and potential toxicity and allergenicity, are routinely included as part of the assessment for GMOs. The GMO Panel was of the opinion that arguments raised by the French authorities were highly speculative and did not reveal any new insights that the Cry1Ab protein could act as a prion, particularly the prion involved with TSE/BSE.

  Furthermore, the GMO Panel did not agree that information provided by France indicated a potential for transgenic DNA within MON810 maize to have oncogenic properties. They further stated that:

  "Moreover, neither is the cry1Ab gene a known oncogene, nor does the function and origin of the cry1Ab transgene in maize MON810 indicate any role as an oncogene in plants or humans/animals" (EFSA, 2008e).

- **Long-term toxicity tests:** France provided comments on the 90 day rodent study on MON810 based on Séralini *et al*. (2007). They also indicated that testing for a longer period on multiple generations of animals, and on multiple mammalian species, was required.

  The GMO Panel considered that the data provided by the French authorities did not contain any data or other indications for hazards specifically posed by MON810 maize. Performance of the 90-days rat study with whole GM crop products was not a standard requirement and had to be considered on a case-by-case basis. The basis was formed by an extensive comparative assessment in which the GM crop is compared to its counterpart with regard to molecular characteristics, composition (macronutrients, micronutrients, anti-nutrient, toxins, allergens), and agronomic/phenotypic characteristics in accordance with internationally harmonized guidelines of Codex alimentarius (Codex alimentarius,

2003) and the EFSA Guidance Document (EFSA, 2006a). Based upon the biologically relevant changes in characteristics of the GM crop thus identified, further testing may be required. Details including the assessment of long-term effects can be found in the recently published report of the GMO Panel's Working Group on Animal Feeding Trials (EFSA, 2008d).

The GMO Panel further referred to a statement on the Séralini *et al*. (2007) publication (EFSA, 2007b), concluding that these data do not cause it to deviate from its previous opinions. As summarized by the GMO Panel:

"The data presented by the French 'Comité de préfiguration' neither provide any new scientific information nor give any other indications that maize MON810 would pose a risk" (EFSA, 2008e).

- **Characteristics of the Cry1Ab protein:** In reacting to France's claim that post-translational modifications of the Cry1Ab protein in plants have been inadequately considered, the GMO Panel replied that the data provided by France did not point to a hazard that can specifically be linked to the Cry1Ab protein and did not provide any new information on this protein either. The information referenced by France pertained to the functionality and post-translation modifications of proteins other than Cry1Ab. In addition, it implies that the safety assessment of the Cry1Ab protein would be limited to a consideration of its similarity to the protein produced naturally by *Bacillus thuringiensis*. On this matter, the GMO Panel concluded that:

  "None of the data on the Cry1Ab protein and similar Cry proteins that have been assessed by the GMO Panel for their safety have indicated any modifications with potential adverse health effects" (EFSA, 2008e).

On 10 June 1999 and on 8 May 2000, **Austria** provisionally prohibited the placing on the market of the authorized genetically modified (GM) maize events **MON810** and **T25**, respectively, on its territory. In their respective scientific opinions, both the Scientific Committee on Plants (SCP, 1999a, 2000) and the EFSA GMO Panel (EFSA, 2004c) concluded that, based on the information submitted by Austria, MON810 and T25 maize did not constitute a risk to human and animal health or the environment.

On 21 November 2007, Austria provided to the European Commission an Austrian study entitled "Supplementary risk assessment on GMO maize MON810 (with consideration of maize T25)". The aim of the Austrian study was to summarize Austria's arguments in response to the decision of the World Trade Organisation Panel 'European Communities – Measures affecting the approval and marketing of biotech products', because part of the measures dealt with the Austrian safeguards concerning the import and use of maize MON810 and T25. Subsequently, the Austrian delegation presented published data on a reproduction study with mice fed NK603xMON810 maize (Velimirov *et. al*., 2008) and a study on the intestinal immune system in rats fed MON810 maize (Finamore *et al*., 2008).

Austria claimed that there were shortcomings in the comparative, the toxicological and the allergenicity assessment of MON810. The GMO Panel reviewed the arguments for each assessment and concluded (EFSA, 2008e) that:

- The arguments provided by the Austrian authorities did not indicate that a specific risk had been identified in MON810 maize since its approval under Directive 90/220/EC, which was preceded by an evaluation of the safety of MON810 by the Scientific Committee on Plants in 1998 (SCP, 1998a).
- The Austrian authorities indicated that additional details of the compositional analysis of maize MON 810 and the background data should have been provided. However, the publications that Austria mentioned appeared after the approval of MON810 maize, including the OECD consensus document, and would not have been available at the time of the application.
- The GMO Panel had evaluated safety data on various stacked events containing the maize event MON810 combined with other transgenic events, including MON863xMON810 (EFSA, 2005e), MON863xNK603xMON810 (EFSA, 2005f) and NK603xMON810 (EFSA, 2005h). These data included compositional analysis of these stacks, MON810, and other comparators. The evaluations were carried out according to the GMO Panel's principles as has also been laid out in its Guidance Document (EFSA, 2006a). The evaluated data did not indicate any adverse effects.
- With regard to the data published by Velimirov *et al*. (2008), the methods used for these investigations were not routinely used for the safety assessment of whole foods and feeds, and that therefore neither experience with these models nor data on background variability in the tested parameters existed. Moreover, the GMO Panel identified various deficiencies in data reporting, methodologies and statistical calculations, which did not allow any interpretation.

- ***"Therefore, the GMO Panel considers that these data do not invalidate the conclusions of the GMO Panel on the safety of MON810 maize" (EFSA, 2008e).***

Austria claimed that for T25 maize the risk assessment provided by the applicant did not take in to account all relevant issues according to the state-of-the-art of scientific knowledge, referring to details and references to the scientific literature given in Dolezel *et al*. (2007). The GMO Panel referred to the safety assessment of T25 maize as carried out by the applicant and evaluated by the Scientific Committee on Plants in 1998 (SCP, 1998c). The Panel also concluded that the Austrian authorities had not provided evidence of health risks associated with T25 maize. The GMO Panel had previously evaluated the safety data of a number of other GM crops (maize, oilseed rape, cotton, rice, soy) containing a similar genetic modification as T25, i.e. the introduction of the phosphinothricin acetyltransferase (PAT) enzyme conferring tolerance to glufosinate-ammonium-based herbicides. For none of these crops did the evaluation by the GMO Panel indicate any effect linked to products of this modification that could raise concerns for human and animal health.

On 27 July 2007, **Austria** notified to the European Commission a national safeguard clause on GM oilseed rape event **GT73** which had been approved for import in the EU (notification C/NL/98/11). The GMO Panel (EFSA, 2009c) observed that the two publications related to toxicological and allergenicity aspects of the risk assessment quoted by Austria (Spök *et al*., 2004, 2005) did not provide new data specific on the safety of oilseed rape GT73. Furthermore, Austria referred to various arguments that had already been addressed in the previous EFSA

GMO Panel opinion on oilseed rape GT73 (EFSA, 2004a). The EFSA GMO Panel concluded that the toxicological and allergenicity information provided by Austria were not new and had already been considered in the respective opinions of the EFSA GMO Panel.

On 15 July 2008, **Austria** notified to the European Commission a national safeguard clause on GM oilseed rape events **MS8, RF3 and MS8xRF3**, which had been authorized for import in the EU. The argumentation was similar to what had been submitted before for GT73. The reply by the GMO Panel (EFSA, 2009e) reflected the same argumentation as developed for the safeguard clause on GT73, confirming that there was no new evidence that would suggest any risk.

On 16 July 2008, **Austria** notified to the European Commission a national safeguard clause on GM maize event **MON863**, which had been approved for import in the EU. Austria submitted comments on a number of details of toxicological and nutritional studies with MON863 maize, which are cited by an article by Hammond *et al*. (2006) describing the outcomes of the 90-day rat oral toxicity study with MON863 maize. The GMO Panel (EFSA, 2009d) concluded that no new data had been presented by the Austrian authorities that could be considered evidence of potential toxic effects on MON863 maize and its transgenic components on humans and animals. In the absence of such evidence, the EFSA GMO Panel could not follow the Austrian recommendation for requiring additional toxicity tests for subchronic, chronic, developmental, and reproductive toxicity of MON863 maize.

Bt in soil and effect on soil

Bt176 maize (C/F/94/11-03) was authorized for all uses in the European Union by Commission Decision 97/98/EC of 23 January 1997 (EC, 1997) and final consent was granted by the French competent authority on 4 February 1997.

On 14 February 1997, **Austria** invoked Article 16 of Directive 90/220/EEC partly based on the fact that in their opinion the effect of the Bt toxin in soil was insufficiently covered. The SCP (1997) concluded that based on the available information, soil exposure from the GMO maize plants would be less than the exposure resulting from a single conventional spray application including the run-off from plants. Only trace amounts of the toxin can be detected in the roots of the maize and furthermore, normal agricultural practice would involve removal of the greater part of the plant at harvest. The residual plant materials are often shredded and transformed into silage for use as animal feed at a later stage. Bt toxin concentration can be increased as a result of binding and adsorption by soils, but argumentation was provided showing that transgenic plant material did not persist at a high level in the soil. Considering the exposure in the soil ecosystem including exposure to earthworms and *Collembola*, the Committee noted that these issues were addressed satisfactorily in the dossier submitted by the notifier.

The SCP did not find that the information provided by Austria required an adaptation of its earlier assessment (SCP, 1996)

In February 2004, Austria provided additional information to support the national safeguard measures. This information included the three peer-reviewed papers:

- Zwahlen *et al*. (2003a) reporting a 200-day study investigating the impact of transgenic Bt maize event Bt11 (expressing Cry1Ab Bt toxin) on immature and adult *Lumbricus terrestris* in a single worst-case laboratory study and in a single small scale field test.

  "Due to the experimental design, the authors were unable to exclude that possibility that the weight loss of earthworms fed with Bt maize in the laboratory test was due to other factors. Consequently, the authors themselves conclude: 'Further studies are necessary to see whether or not this difference in relative weight was due to the Bt toxin or other factors discussed in the study'" (EFSA, 2004c).

- Zwahlen *et al*. (2003b) published the results of two field studies in the temperate maize-growing region of Switzerland with regard to the degradation of Cry1Ab toxin in transgenic Bt maize leaves during autumn, winter and spring periods.

- Saxena *et al*. (2002) found that the release of Cry1Ab proteins by roots is a common phenomenon with transgenic maize.

The GMO Panel (EFSA, 2004c) reviewed the documents, put the findings in perspective of other additional studies and concluded that none of the cited papers contained scientific information that would alter the risk assessment of the maize events.

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 –

Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 21 January 2005, **Hungary** invoked Article 23 (safeguard clause) of Directive 2001/18/EC to provisionally prohibit the production, use and distribution of seeds derived from the authorized genetically modified maize line MON810. The Hungarian submission referred to research carried out in Hungary allegedly showing that the long-term presence of the plant in the ecosystem may have adverse effects on biological soil activity through accumulation of Bt toxin. The supporting documents were abstracts of reports presented at scientific conferences which summarize results of research studies but do not contain any data that can be evaluated on a scientific basis.

The GMO Panel (EFSA, 2005d) reviewed the information as well as other publications on release of Bt via exudation and decaying material from plants, incorporation into and persistence of Bt in soil, absence of effects on earthworms and nematodes, and absence of negative effects on soil microbial communities. The Panel concluded that in general, there were no published data on the impact of Bt maize on biological soil functions which indicate the need for a change in the original environmental risk assessment that was conducted by the SCP in 1998 (SCP, 1998a). As noted by the GMO Panel:

> ***"Considering the available information on potential effects of Bt plants on the soil environment and in particular on soil non-target organisms, adverse effects due to slightly altered decomposition rates are unlikely" (EFSA, 2005d).***

In April 2008, Hungary forwarded additional studies to the European Commission and requested that the four submitted reports be considered as confidential information:

- Report #1: On the results of the tender entitled "Assessment of the soil biological effects of genetically modified organisms" (No. NTA-1030/2006) Part 1. Confidential (51 pages) as referenced in EFSA (2008b);
- Report #2: On the results of the tender entitled "Assessment of the soil biological effects of genetically modified organisms" (No. NTA-1030/2006) Part 2. Confidential (5 pages) as referenced in EFSA (2008b);
- Report #3: Research Report entitled "Data on ecological risk assessment in Hungary of MON810 maize varieties producing Cry1Ab toxin that can be applied against European corn borer (*Ostrinia nubilalis*) larvae" (No. NTE-725/2005). Confidential (64 pages) as referenced in EFSA (2008b); and
- Report #4: Closing Report entitled "Supplementary ecological impact assessments concerning the MON810 maize varieties I. Biological studies involving MON810 pollen and DIPEL, as well as protected and rare butterflies living on stinging nettle" (No. NTE-1436/2005). Confidential (80 pages) as referenced in EFSA (2008b).

Hungary reported a decomposition study of Bt-maize and data on degradation of Cry1Ab protein in soil. In addition Hungary raised concerns on the persistence of Cry1Ab protein in soil due to the cultivation of maize MON810. The GMO Panel (EFSA, 2008b) confirmed that the issue of

decomposition of MON810 had been extensively addressed in its previous opinion (EFSA, 2005d). The GMO Panel further evaluated the data presented by Hungary and agreed with the conclusions drawn by the authors: *"In the current stage of our studies and based on the available techniques we have no data at all concerning whether the differences found in some cases in the decomposition of organic material are a consequence of differences in the chemical composition of the two maize strains or of the presence of Bt-toxin"* (Hungarian report #3). In addition the GMO Panel reviewed other studies on the decomposition and persistence of Bt-maize and concluded that the concerns on Cry1Ab protein persistence in soil raised by Hungary were not substantiated by the available scientific data.

The GMO panel also concluded that the variation in microbial communities observed in the Hungarian study was similar to that observed in other studies performed with plants expressing Cry proteins from *Bacillus thuringiensis* and other GM crops (references in EFSA, 2008b), and that the study therefore provided no new information about the effects of Bt-plants on soil microorganisms.

Finally, the GMO Panel considered that there was no evidence presented supporting the conclusion of rearrangements of nematode populations due to MON810 maize and concluded that no new data were presented to show that MON810 maize would pose a risk to nematode populations in Hungary.

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids with the genetic modification MON810.

One of the areas of concern documented by Greece consisted of environmental impacts of MON810 maize, particularly in relation to soil. The GMO Panel (EFSA, 2006c) commented on the Greek presentation of scientific literature and statements as follows:

- **Potential higher lignin content in MON810 maize:** The Panel reviewed data on lignin content and related decomposition of different plant species expressing Bt. Generally, Bt plants showed less decomposition than non-Bt plants. However, this effect was not clearly related to lignification or reduced microbial activity in soil. According to the GMO Panel:

  "Considering the available information on potential effects of Bt plants on the soil environment and in particular on soil non-target organisms, the GMO Panel concluded that adverse effects due to slightly altered lignin contents are unlikely" (EFSA, 2006c).

- **Potential effects of MON810 maize residues on soil function and soil organisms:** The published results from laboratory and field trials (references in EFSA, 2006c) showed that on short to medium time scales (up to 3 years) and under field conditions, the effects of Cry1Ab-expressing maize on soil functions and biodiversity did not exceed "natural" variability. No conclusive evidence had been presented that currently approved Cry1Ab-expressing GM crops were causing significant direct effects on the soil environment. The effects of Cry1Ab-expressing maize in these experiments were small, if they existed at all. In addition, the available data did not indicate a chain of events that might result in long-term effects.

  "There have been no reports of soil function problems in countries where Cry1Ab-expressing crops have been cultivated continuously for several years. The GMO Panel is

thus of the opinion that the risk of MON810 maize to soil function and soil organisms is negligible" (EFSA, 2006c).

- **<u>Potential adverse effects of MON810 maize on *Collembola*</u>:** The review paper of Losey *et al*. (2004) referred to a website of the U.S. Environmental Protection Agency for a study that might have shown a significantly higher mortality and reduced reproduction rate in the soil-dwelling collembolan, *Folsomia candida*, exposed to the Bt176 maize event. The GMO Panel considered the accessible information as well as other studies in which MON810 maize had shown no negative effects on the collembolan, *Protaphorura armata* (Heckmann *et al*., 2006). Furthermore, no adverse effect of Cry1Ab-expressing maize on *Collembola* was observed in an intensive field study with Bt176 maize (Candolfi *et al*., 2004).

  "The GMO Panel concludes that no adverse effect of Cry1Ab-expressing maize on Collembola has been reported" (EFSA, 2006c).

Bt and non-target organisms

Bt176 maize (C/F/94/11-03) was authorized for all uses in the European Union by Commission Decision 97/98/EC of 23 January 1997 (EC, 1997) and final consent was granted by the French competent authority on 4 February 1997.

On 14 February 1997, **Austria** invoked Article 16 of Directive 90/220/EEC partly based on the fact that in their opinion the effect of the Bt toxin on non-target organisms was insufficiently covered. In its response (SCP, 1997) to the supporting information provided by Austria the European Scientific Committee for Pesticides recognized the complexity of comparing the exposure of a pest to GM plants, where exposure may be prolonged and maintained, and conventionally applied pesticides, with shorter and repeated exposure. The Committee noted that in the case of GM maize, the effect of the genetically incorporated toxin is more targeted than in the case of a spray application, which involves a range of Bt toxins. The exposure scenario in the case of GM maize is comparable to multiple applications of insecticides, but the impact of the Bt-genetically incorporated toxin on the environment is considerably lower than traditionally applied pesticides.

The SCP did not find that the information provided by Austria required an adaptation of its earlier assessment (SCP, 1996)

In a subsequent opinion of the GMO Panel (EFSA, 2004c) it was further specified that [for references see EFSA (2004c)]:

- Previous worst-case scenario tests on Bt maize reporting potential adverse effects on non-target organisms have been proven irrelevant in laboratory and environmental field tests;
- Bt toxin (Cry1Ab) has no direct effect on larvae of the green lacewing;
- A substantial number of other entomophagous arthropods are not sensitive to Cry1Ab;
- Ecological field tests in France have shown no effects on non-lepidopteran species; and
- The impact of Bt corn pollen from current commercial hybrids on monarch butterfly populations is negligible.

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 21 January 2005, **Hungary** invoked Article 23 (safeguard clause) of Directive 2001/18/EC to provisionally prohibit the production, use and distribution of seeds derived from the authorized GM maize line MON810. The Hungarian submission referred to research carried out in Hungary allegedly showing that the long-term presence of the plant in the ecosystem may have adverse effects on non-target and endangered caterpillars (Darvas *et al*., 2004).

EFSA (2005d) commented on the presented data and put them in perspective to other scientific publications [references in EFSA (2005d)] concluding that in consideration of the toxicity and exposure of Cry1Ab, the risk of exposure of non-target Lepidoptera to harmful toxin concentrations via MON810 maize pollen was negligible and that adverse impacts on populations were very unlikely. They further confirmed that no conclusive evidence had been presented that the released transgenic Bt crops were causing significant direct effects on the environment and concluded that, overall, the evidence presented by Hungary contained no new scientific information on the environmental or human health impacts of the specified GM maize event.

In April 2008, Hungary forwarded additional studies to the European Commission and requested that the four submitted reports be considered as confidential information. Two of these reports referenced a publication by Bakonyi *et al*. (2006). The paper described preference tests with *Collembola* on one maize MON 810 variety and its near-isogenic counterpart. In analyzing these data and reviewing additional publications, the GMO Panel (EFSA, 2008b) noted that: ***"Different varieties have been shown previously to elicit various responses related to their background genetic composition and not to the GM event or its products"*** and that differences in consumption of Bt maize ***"may be due to nutritional differences, as suggested by the C/N ratio."*** Overall, the GMO Panel concluded that no new data were presented which demonstrated that MON810 maize would pose a risk to *Collembola*.

Two reports submitted by Hungary summarized data on butterfly species potentially occurring in maize field margins in Hungary, shed maize pollen and on estimated pollen densities on host plant leaves. Data from these Hungarian studies allegedly demonstrated a potential hazard for certain non-target caterpillars consuming high amounts of maize MON810 pollen on host plants.

The GMO Panel reviewed the information and concluded that the data presented by Hungary:

- Were collected under conditions of high pollen exposure where pollen was synthetically adhered to host plant leaves. This is unlikely to occur in the field where environmental factors (e.g., rain, wind) decrease the exposure of lepidopteran larvae to pollen (e.g., Pleasants *et al*., 2001; Gathmann *et al*., 2006a); and
- Did not examine exposure of butterfly populations. There was no indication of the proportion of butterfly populations that would be exposed to toxic levels of Bt-maize pollen in Hungary. Other factors influencing butterfly populations in agricultural landscapes should be considered (Gathmann *et al*., 2006b), such as butterfly phenology, crop rotation, other pesticide usage, refuge areas and cultivation.

The GMO Panel concluded that there were no new data presented which demonstrated that MON810 maize would constitute a risk for non-target butterfly populations.

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids with the genetic modification MON810. One of the areas of concern documented by Greece consisted of environmental impacts of MON810 maize, particularly in relation to biodiversity, ecosystem stability and potential adverse effects on non-target fauna, taking into account the specific climatic and agricultural conditions in Greece.

The GMO Panel (EFSA, 2006c) commented on the Greek presentation of scientific literature and statements as follows:

- **Potential effects of MON810 maize on lepidopteran pests:** MON810 maize varieties expressing Cry1Ab protein are not only protected against *Ostrinia nubilalis*, the European Corn Borer (ECB), but are also used to control other lepidopteran pest species, such as *Sesamia nonagrioides*. The GMO Panel considered that low infestation levels of *Ostrinia nubilalis* and other lepidopteran pests in maiz*e* in Greece did not alter the environmental risks associated with MON810 cultivation.

- **Potential adverse effects of MON810 maize on non-target Lepidoptera:** The GMO Panel confirmed that it is well documented that a range of lepidopteran species may be affected by Cry1Ab proteins and some of these species may be present in maize fields. However, the exposure of any populations of Lepidoptera to the protein is restricted to those consuming the Cry1Ab plant or its products. Taking into account the available literature data, the GMO Panel was of the opinion that the risk of MON810 pollen to silkworm and other non-target lepidopteran species was negligible due to its low Cry1Ab content and the low levels of exposure of wild species to maize pollen.

- **Potential effects of MON810 maize on Coleoptera:** The GMO Panel analyzed a study of Wold *et al*. (2001) and found that there was insufficient evidence to conclude that Cry1Ab protein had any adverse effect on beneficial insects including Coleoptera in the field.

- **Potential effects of MON810 maize on green lacewings:** Cry1Ab protein does not show specific binding *in vitro* to brush border membrane vesicles from the midgut of *Chrysoperla carnea* larvae, which is a prerequisite for toxicity. The GMO panel summarized the evidence refuting allegations on Bt acting on lacewings, confirming that no negative effects on these predators had been documented in the field.

- **Potential unanticipated adverse effects of MON810 maize on parasitoids:** The GMO panel noted that some higher tier studies indicated that populations of specific natural enemies of *Ostrinia nubilalis* are less abundant in Cry1Ab-expressing maize fields than in non-Bt maize fields. This is not thought to be due to the direct effects of the Cry1Ab protein consumed while predating or parasitizing *Ostrinia nubilalis* but to decreased availability of specific prey.

- **Potential impact of MON810 maize on biodiversity:** The GMO Panel referred to available data on the long-term ecological and biodiversity effects of Cry1Ab-expressing maize (e.g., Dutton *et al*., 2003 a,b; Rauschen *et al*., 2004 ; Lövei and Arpaia, 2005; O'Callaghan *et al*., 2005; Romeis *et al*., 2006 ; Eckert *et al*., 2006 ; Eizaguirre *et al*., 2006; Gathmann *et al*., 2006a). The GMO Panel agreed with Mendelsohn *et al*. (2003) that MON810 maize poses no specific significant risk to the environment or to human health compared with other maize types.

- **Potential food-chain effects of MON810 maize:** The GMO Panel agreed that tri-trophic effects on non-target organisms (like maize lepidopteran pest) are an important issue to consider during the environmental risk assessment (ERA). However, the overall data for

effects of MON810 maize on biodiversity indicate that the environmental risks to non-target species are negligible.

The GMO Panel considered that the environmental impact MON810 maize would be similar to comparable non-GM maize cultivars. In addition, reports and reviews of studies of the effects of the Cry1Ab protein on biodiversity, including the abundance of non-target and biocontrol species, indicated that significant adverse environmental effects due to Cry1Ab-expressing maize cultivation were unlikely (Amman, 2005; Clark *et al*., 2005; Dolezel *et al*., 2006; Eizaguirre *et al*., 2006; Rodrigo-Simon *et al*., 2006; Romeis *et al*., 2006).

On 9 February 2008, **France** notified to the European Commission an Order suspending the cultivation of seed varieties derived from the maize event MON810 and submitted an information package made of different supporting documents.

One of the areas of concern consisted of exposure and impacts on non-target fauna. France referred to new evidence allegedly confirming:

- The possibility of long-term toxic effects in earthworms, isopods, nematodes and monarch butterflies;
- Presence of Bt toxin in the food chain and persistence in water, in sediment draining from a plot, in contact with roots and in the soil, with exposure of insect populations higher up the food chain.; and
- An effect on some families of invertebrates, although these effects were smaller than those related to treatment with insecticides.

The GMO Panel (EFSA, 2008e) reviewed all relevant scientific literature and publications, such as the scientific advice of COGEM (2008), as well as those considered specific for French receiving environments. This led to the opinion that the information and documents provided by France did not provide any new or additional scientific evidence that would invalidate the previous risk assessments of maize MON810 for the non-target organisms. The detailed review included following topics:

- **Persistence of Bt-proteins in soil: Exposure assessment** – According to the GMO Panel the review of the literature indicated that the possible exposure of non-target soil organisms to the Cry1Ab protein was likely to be variable and case-specific. In an assessment of environmental risks, therefore the exposure has to be combined with a hazard assessment. In this respect, the focus of the GMO Panel was on the assessment of the susceptibility of non-target soil fauna to the Cry1Ab protein, effects on microorganisms and impacts on soil organism diversity and functions. These aspects are discussed in the following sections.

- **Biological effects in soil: impact assessment** – The GMO Panel referred to multi-year experiments conducted across European climatic zones showing that no or only few effects on snails, microarthropods or mycorrhizal fungi could be attributed to Bt-maize (event MON810). Bt-maize does not have adverse effects on soil biota, since effects

observed were most likely to be caused by season, soil type, tillage, crop type or variety. Similarly, effects on soil microbial community structure, microarthropods and larvae of a non-target root-feeding Dipteran (*Delia radicum*) observed in a glasshouse experim*ent* were most likely due to soil type and plant growth stage, rather than Bt-maize (event MON810).

- **Non-target soil organisms: impact assessment on earthworms** – The GMO Panel cited several scientific findings confirming that although earthworms can be exposed to the Cry1Ab protein through root exudates and decomposing plant material, no adverse effect had been revealed on earthworm survival, growth and reproduction following protein ingestion.

- **Non-target soil organisms: impact assessment on isopods** – Reference was made to laboratory feeding studies with woodlice (*Porcellio scaber*), considered a model decomposer organism, for detecting potential adverse impacts related to exposure to plant material from Cry1Ab expressing maize. No adverse effects of the Cry1Ab protein on consumption, survival and growth of *P. scaber* were observed when fed plant material of Bt-maize expressing the Cry1Ab protein and non-Bt-maize. The survival and growth of *Trachelipus rathkii* and *Armadillidium nasatum*, two abundant isopods in maize growing regions, were not adversely affected after exposure to the purified Cry1Ab protein or leaves of Bt-maize (events Bt11 and MON810) under laboratory conditions for 8 weeks.

- **Non-target soil organisms: impact assessment on nematodes** – The GMO Panel reviewed several studies conducted on the exposure of different isolated species as well as natural nematode communities to Bt plants. They concluded that current scientific information indicated that possible changes in the nematode community structure associated with Bt-maize and their products were likely to be minor compared with effects of agricultural practices, environmental stresses, or differences between localities and maize varieties. Rearrangements of nematode populations, which are normally associated with several sources of variation in the agricultural environment, occur frequently and are not necessarily an indication of environmental harm.

- **Microbiological effects: impact assessment** – Upon a detailed review of information on the effect of root exudates of Bt maize and decomposing plant parts on mycorrhizal fungus, on rhizosphere heterothrophic bacteria and mycorrhizal colonization, and on soil microbial community structure, the GMO Panel was of the opinion that potential effects on soil microorganisms due to maize MON810 if they occur, would be transient, minor and localized in different field settings and were likely to be within the range currently caused by a range of other agronomic and environmental factors.

- **Presence of *cry1Ab* gene and Bt-proteins in water: exposure and impact assessment in aquatic environments** – The GMO Panel indicated that DNA presence alone is not considered a reliable indicator of toxicity to non-target organisms. A more reliable indicator of toxicity to non-target organisms would be the presence and concentrations of the Cry1Ab protein in surface water and sediment. It had been reported that the presence of the Cry1Ab protein in water bodies was either absent or just above the detection limit

(Douville *et al*., 2005), suggesting that Cry1Ab protein concentrations would remain far below any toxic level.

Recent reports by Rosi-Marshall *et al*. (2007) and Bøhn *et al*. (2008) suggested that Bt-maize by-products (e.g., pollen, detritus) are transported to downstream water bodies and may result in potential toxic effects to non-target aquatic organisms following consumption. The GMO Panel was of the opinion that important background information was missing and considered that the conclusions made by Rosi-Marshall *et al*. (2007) were not supported by the data presented in the paper. The GMO Panel (EFSA, 2007c) and other scientists (ACRE, 2007; Beachy *et al*., 2008; Parrott, 2008) provided arguments why this study was incomplete and stated that conclusions on environmental impacts could not be made. This discussion was further elaborated in a subsequent GMO Panel opinion (EFSA, 2008f). In a laboratory experiment, Bøhn *et al*. (2008) concluded that *Daphnia magna* fed with a Bt-maize flour-containing suspension (event MON810) had a higher mortality and a lower proportion of females reached sexual maturity as compared to the non-Bt-maize treatment. The authors suggested that the results were due to toxic effects of Bt-maize. However, since maize flour is not part of the natural diet of *Daphnia*, the unusual delays in development of *Daphnia* fed non-Bt-maize might have been caused by nutritional deficiencies related to a maize-based diet. Moreover, internationally accepted guidelines for toxicity and reproduction testing of *Daphnia* were not followed. Due to these methodological weaknesses, the GMO Panel doubted that any substantive conclusion on potential risks of maize MON810 could be drawn from the study.

- **Exposure and impacts on non-target lepidopteran organisms** – Although maize is not considered an important source of food for indigenous lepidopteran species in the EU, larvae of lepidopteran species consuming the Bt-plant or its products can be exposed to the Cry1Ab protein. In the vicinity of Bt-maize fields, larvae can be exposed to the Bt-protein when feeding on host plant leaves naturally dusted with pollen and anthers of Bt-maize during anthesis. The anticipated effects of Bt-maize on secondary lepidoptera pests largely depend upon the maize event, its expression pattern, the type of ingested plant material, and the phenology of the species in field conditions.

  An extensive study of field experiments conducted in the US reported that the risk of Bt maize pollen on monarch butterfly populations is likely to be negligible for MON810 maize. Lethal and sublethal effects were only observed when monarch butterfly larvae consumed a very high level of MON810 maize pollen. Because the proportion of the monarch butterfly larvae population exposed to levels of Bt-pollen sufficiently high to have toxic effects is small (e.g., due to the lack of temporal overlap between larval development and pollen shed) and the amount of toxin contained in MON810 maize pollen is low as compared to maize Bt176, it was concluded that impacts on *D. plexipus* populations are negligible. The GMO Panel furthermore concluded that intact Bt-anthers alone or in combination with Bt-pollen were not likely to pose a significant risk to monarch butterflies, and that no new scientific data regarding exposure of non-target lepidopteran species to MON810 maize were presented in the application that would alter risk assessment of this event.

- **Global analysis of non-target entomofauna** – The GMO Panel reviewed several papers reviewing the results and experience obtained while cultivating Cry1Ab maize, including:
  - Nine years of experience of Cry1Ab maize cultivation in Spain revealing no adverse effects on non-target arthropods (de la Poza *et al*., 2005; Pons *et al*., 2005; Eizaguirre *et al*., 2006; Farinós *et al*., 2008).

  - Field monitoring study performed in Germany from 2000 to 2005 on field pairs (half-fields) planted with Bt-maize (event MON810) and a conventional maize variety were followed to determine densities of taxa on plants, activity densities and diversity of ground-dwelling arthropods (Schorling and Freier, 2006). Density comparisons of different taxa (such as aphids, thrips, heteropterans, aphid specific predators, spiders and carabids) revealed a few significant differences for specific taxa between Bt and conventional maize fields, but no general tendencies over the six years.

  - No effects due to the growing of maize MON810 on non-target communities including lepidopteran larvae were observed during a field study performed in Germany over three consecutive years (Gathmann *et al*., 2006a; Eckert *et al*., 2006; Toschki *et al*., 2007).

  - Monitoring of foliage-dwelling spiders was carried out in another study in Bt-maize fields (event Bt176) and adjacent margins over three successive years in Germany as compared to non-Bt-maize fields. Results revealed no consistent adverse effects on individual numbers, species richness and guild structure of spiders due to the cultivation of Bt-maize (Ludy and Lang, 2006).

  - Results of a meta-analysis of 42 independent field experiments carried out across different continents by Marvier *et al*. (2007) indicated that non-target invertebrates are generally more abundant in near isogenic control fields where no insecticide treatments are applied than in fields cropped with Bt-cotton or Bt-maize (events MON810, Bt176 and MON863) mainly due to a lower abundance of Bt-susceptible (target) pest species, which are prey/hosts for natural enemies. However, when non-Bt-cotton or maize fields are managed conventionally with the application of insecticides, non-target taxa were shown to be less abundant than in fields cropped with Bt-cotton or maize.

  - A more recent meta-analysis (Wolfenbarger *et al*., 2008) of published field studies on non-target effects of Bt-crops made the differentiation among functional guilds of non-target arthropods. Thereby, the abundance of predators, parasitoids, omnivores, detritivores and herbivores was compared under scenarios where the non-Bt-crops alone, Bt and non-Bt-crops together or no plots received insecticide treatments and showed different effects of Bt-maize among functional guilds of non-target arthropods. As expected, fewer specialist parasitoids of the target pest occurred in Bt-maize fields, as compared to unsprayed non-Bt-controls, but no significant reduction was detected for other parasitoids. In comparison to sprayed non-Bt-controls, numbers of predators and herbivores were higher in Bt-crops, with the magnitude of the difference being influenced by the type of insecticide.

The use of and type of insecticides influence the magnitude and direction of observed effects, and insecticide effects were reported to be larger than those of Bt-crops.

- **Trophic chain effects on predators:** Invertebrate predators can be exposed to the Cry1Ab protein through their prey organisms. Levels of Bt-toxin have been observed within non-target herbivores and their natural enemies such as spiders and predatory insects under field conditions, showing that significant quantities of the Cry1Ab protein can move into higher trophic levels. Some studies showed that the Cry1Ab protein from Bt-maize passed along trophic chains up to the third trophic level, and that in some cases it accumulated in concentrations that were higher than on leaves.

  The uptake of the Cry1Ab protein by predators will not only occur by direct feeding on Bt-expressing plant material (such as pollen), but also indirectly through the consumption of arthropod prey that contains the Bt-protein, especially for species preying on spider mites. The exposure to the Cry1Ab protein might be thus very different between predatory taxa due to variability in phenology and feeding habits.

  Potentially toxic effects on predators fed with preys containing levels of the Cry1Ab protein might occur when predators are sensitive to the protein. Data on the susceptibility of several groups of natural enemies are available in the literature and have been reviewed. Romeis *et al*. (2006) suggested that there are little or no indications of direct adverse effects of Cry1Ab expressing maize on natural enemies. In this respect, several studies confirmed that the Cry1Ab protein is not toxic to non-target organisms less closely related to targeted pests. Meissle *et al*. (2005) related the adverse effects on the generalist predator, *Poecilus cupreus*, fed *S. littoralis* larvae, which had been raised on Bt-maize (event MON810) to the nutritional quality of the prey and not to the direct effect of the Cry1Ab protein.

- **Trophic chain effects on parasitoids:** In general, invertebrate parasitoids appear to be more sensitive to diets that contain Cry proteins than predators, though effects are possibly associated with the poor quality of their hosts. It is likely that slower developing hosts might not provide sufficient nutrients for the normal development of parasitoid larvae. Direct toxic effects seemed unlikely due to the specificity of the Cry 1Ab protein. Yet, one study suggested that the Cry1Ab protein present in the host, *Spodoptera frugiperda*, fed Bt-maize may have a direct effect on *C. marginiventris* (Ramirez-Romero *et al.*, 2007). These authors observed that the exposure to Cry1Ab protein via hosts fed Bt-maize tissue affected parasitoid developmental times, adult size, and fecundity, but not cocoon-to-adult mortality and sex ratio. The authors were also able to prove the importance of the plant in causing negative effects at the third trophic level, since negative results were not observed when pure protein-containing diet was used in the tritrophic experiments.

  By contrast, the performance of *C. marginiventris* fed aphid honeydew was observed to increase due to positive effects of Bt-maize (events Bt11, MON810 and Bt176) on the performance of the maize leaf aphid, *Rhopalosiphim maidis* (Faria *et al*., 2007). With the larger colony densities of aphids on Bt-maize, more honeydew was produced, in turn

increasing parasitoid longevity and rate of parasitism. Based on the observations made, Faria *et al*. (2007) concluded that as a long as aphid numbers do not reach pest status, the increase in Bt-maize susceptibility to aphids may pose an advantage in maintaining beneficial insect fauna in Bt-maize.

In summing up their review of the foregoing literature, the GMO Panel was of the opinion:

> ***"...that the information and documents provided by France do not provide any new or additional scientific evidence that would invalidate the previous risk assessments of maize MON810 for the non-target organisms" (EFSA, 2008e).***

In a scientific opinion requested by the **European Commission,** the GMO Panel (EFSA, 2008f) reviewed a set of scientific publications, published after the adoption of the complemented scientific opinions on maize Bt11 and 1507. In relation to this section the following papers are discussed:

- **Prasifka *et al.* (2007):** The authors suggested that monarch butterfly larvae exposed to Bt-anthers behave differently and that ingestion may not be the only way Bt can affect non-target insects like the monarch butterfly. However, they pointed out that it is unclear whether the changed behavioural measures (increased time spent off leaf disks and increase frequency of larvae moving off leaf disks) would translate into changes in behaviour on intact insect host plants in the field as larvae might have the option of moving to the underside of the host milkweed leaf (which would not receive deposits of anthers).

  The GMO Panel further referred to an examination of anthers in and near maize fields showing that toxic levels of anthers are uncommon (Anderson *et al*., 2004). In addition, larvae can move to the underside of leaves where they would avoid any contact with anthers (Pleasants *et al*., 2001; Jesse and Obrycki, 2003).

- **Hilbeck and Schmidt (2006):** The authors discussed in more detail potential direct effects reported from a laboratory Bt-toxin feeding study, to document the sensitivity of green lacewing, *Chrysoperla carnea*, larvae to purified Cry protein concentrations or via Bt-maize (presumably Bt176) raised lepidopteran larvae fed to the lacewing predator. The original datasets were previously published by Hilbeck *et al*. (1998 a,b; 1999). The GMO Panel reviewed in detail a wide range of publications concerning the safety of Bt-maize, including the original data presented by Hilbeck *et al*. (EFSA, 2005 a,c), concluding:

  - Absence of specific binding of Cry1Ab protein in vitro to brush border membrane vesicles from the midgut of *C. carnea* larvae, which is a prerequisite for toxicity (Rodrigo-Simón *et al*., 2006);
  - Lack of clear identification of the cause of the higher mortality in Bt-exposed lacewings in the laboratory studies by Hilbeck *et al*. (1998 a,b; 1999) which are more likely to be a consequence of the lepidopteran prey apparently being of lower nutritional quality (Romeis *et al*., 2006);

- Data showing that *C. carnea* larvae are unaffected when feeding on non-susceptible *Tetranychus urticae* containing large amounts of biologically active Cry1Ab protein (Dutton *et al*., 2002);
- Knowledge that *C. carnea* larvae in the field are known to feed mainly on aphids, whereas lepidopteran larvae are not considered an important prey;
- Continuous exposure of *C. carnea* to diets exclusively based on lepidopteran larvae is unlikely under field conditions (Canard, 2001; Dutton *et al*., 2003a);
- Demonstration that adults of *C. carnea* are not affected by Bt-maize pollen and are not sensitive to the Cry1Ab and Cry3Bb1 proteins at concentrations exceeding those observed in pollen of Bt-maize (Li *et al*., 2008); and
- No observation of negative effects on *C. carnea* in the field; sampling from Cry1Ab expressing maize fields has not shown a decline in their abundance (Bourguet *et al*., 2002; Eckert *et al*., 2006).

On 10 June 1999 and on 8 May 2000, **Austria** provisionally prohibited the placing on the market of the authorized GM maize events MON810 and T25, respectively, on its territory. In their respective scientific opinions, both the Scientific Committee on Plants (SCP, 1999a, 2000) and the EFSA GMO Panel (EFSA, 2004c) concluded that, based on the information submitted by Austria, MON810 and T25 maize did not constitute a risk to human and animal health or the environment.

On 21 November 2007, the Permanent Representation of Austria provided to the European Commission an Austrian study entitled "Supplementary risk assessment on GMO maize MON810 (with consideration of maize T25)". The aim of the Austrian study was to summarize Austria's arguments in response to the decision of the World Trade Organisation Panel 'European Communities – Measures affecting the approval and marketing of biotech products', because part of the measures dealt with the Austrian safeguards concerning the import and use of MON810 and T25 maize.

Austria cited comments and supporting literature similar to concerns raised before at other occasions, on interactions of the GM plant with non-target organisms (Lepidoptera, entomofauna, predators, parasitoids, Hymenoptera, water-dwelling insects and soil organisms). No new information was provided. The GMO Panel (EFSA, 2008g) elaborated as indicated above on other occasions and confirmed that no new information had been provided that would invalidate the previous determination of safety of MON810.

In April 2009, **Germany** prohibited the cultivation of MON810 maize in Germany (BVL, 2009) based on so-called new evidence, including publications by Rosi-Marshall *et al*. (2007), Bøhn *et al*. (2008), Schmidt *et al*. (2009), Hofmann (2007), and Hofmann *et al*. (2009).

Three reactions to this prohibition, and the arguments used to justify it, have been noted:

- The first is a critical examination by Ricroch *et al*. (2009) of two papers describing laboratory force-feeding trials on ladybirds and daphnia, and previous data on Lepidoptera, aquatic and soil organisms. They demonstrated that the suspension was based on an incomplete list of references, ignored the widely accepted case-by-case

approach, and confused potential hazard and proven risk in the scientific procedure of risk assessment. Furthermore, they did not find any justification for this suspension in an extensive survey of the scientific literature regarding possible effects under natural field conditions on nontarget animals. The vast majority of the 41 articles published in 2008 and 2009 indicated no impact on these organisms; and only these two articles indicated a minor effect, which was either inconsistent during the planting season or represented an unexplained indirect effect. Publications from 1996 to 2008 (376 publications) and recent meta-analyses provide strong scientific evidence against the action where the authors are from a broad cross-section of stakeholders. On the contrary, the meta-analysis demonstrated that Bt maize has generally a lower impact than insecticide treatment, and also demonstrates that available meta-knowledge on Cry1Ab expressing maize was ignored by the German government which instead used selected individual studies.

- The position from the ZKBS (German Central Commission for Biological Safety). The ZKBS is one of the advisory bodies to the German competent authority and is constituted by experts in the field of bacteriology, virology, plant breeding, medicine and ecology, as well as industrial and environmental safety. In its position of July 2009 (ZKBS, 2009), the ZKBS remarks that they were not consulted before the prohibition was decided at political level. The ZKBS also provided a critical review of the different papers and concluded that on the basis if the available scientific literature the cultivation of MON 810 did not present any environmental risk.

- In the same period, the GMO Panel debated the renewal of the authorizations for MON810. In the opinion adopted on 15 June 2009, the GMO Panel (EFSA, 2009b) considered that the information available for maize MON810 addressed the scientific comments raised by Member States and that maize MON810 is as safe as its conventional counterpart with respect to potential effects on human and animal health. The EFSA GMO Panel also concluded that MON810 maize is unlikely to have any adverse effect on the environment in the context of its intended uses, especially if appropriate management measures are put in place in order to mitigate possible exposure of non-target Lepidoptera. Moreover, the EFSA GMO Panel advised that pest resistance management strategies continue to be employed.

The above examples are based on actual actions taken by authorities and risk assessment bodies. In addition, there have been several well-publicized responses to certain peer-reviewed publications that need to be recognized for a balanced discussion. As an example we refer to Lövei *et al*. (2009) and the rebuttal by Shelton *et al*. (2009).

Lövei *et al*. (2009) based their findings on an analysis of 55 laboratory studies of Cry proteins and 27 studies of proteinase inhibitors (PIs; including lectins) that were published through mid-2007 and conclude that these proteins *"often have non-neutral effects on natural enemies"*. They further concluded that *"parasitoids were more susceptible than predators to the effects of both (toxins)"* and that *"conclusions that Bt…gene products have no harm to natural enemies are currently overgeneralized and premature"*. Shetlon *et al*. (2009) pointed out that these conclusions were in conflict with those of several recent comprehensive reviews and meta-analyses (e.g., O'Callaghan *et al*., 2005; Romeis *et al*., 2006; Marvier *et al*., 2007; Wolfenbarger *et al*., 2008; Naranjo, 2009). Furthermore they provided arguments demonstrating that the paper

by Lövei *et al*. (2009) "*advocates inappropriate summarization and statistical methods, a negatively biased and incorrect interpretation of the published data on non-target effects, and fails to place any putative effect into a meaningful ecological context*". They concluded that "*such erroneous analyses do not serve the scientific or regulatory communities"*.

Bt and pollinators (bees)

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids with the genetic modification MON810. One of the areas of concern documented by Greece consisted of the potential impact of MON810 maize on the large-scale beekeeping.

Greece expressed concerns over adverse effects of MON810 maize pollen to bee health due to the observation that bees may visit the male flowers for pollen collection and transport the collected pollen to their hives for feeding. In a review, Malone (2004) concluded: *"Evidence available so far show that none of the GM plants currently commercially available have significant impacts on honey bee health"*. The GMO Panel (EFSA, 2006c) agreed with this statement for MON810 maize and did not see the need for further risk assessment concerning the direct exposure of bees to MON810 maize. Following their review of the submission and other literature, the GMO Panel noted that:

> ***"Also considering the low concentration of Cry1Ab protein in MON810 pollen, it is likely that larvae will be exposed to very low concentrations of the protein. The literature cited in the submission does not alter this conclusion and therefore the GMO Panel considers that the low exposure level combined with the selective activity of Cry1Ab is unlikely to result in any adverse effects on bees" (EFSA, 2006c).***

In concluding, the GMO Panel stated that: ***"...the Greek submission provided no new scientific data or information in support of an adverse effect of MON810 maize on the large-scale beekeeping industry in Greece"*** (EFSA, 2006c).

On 13 September 2007, Greece notified to the European Commission a ministerial decision concerning the extension of validity and amendment of an existing safeguard measure invoked to provisionally prohibit the cultivation of MON810 on its territory. One of the areas documented by Greece consisted of an environmental concern related to potential impact on bee colonies justified with a set made of the following documents:

- Study on colony collapse disorder by Paschalis Harizanis;
- Florida Workshop on colony collapse disorder;
- US national bee colony loss survey; and
- Sierra Club – Bee colony collapse disorder.

Colony Collapse Disorder (CCD) of bee colonies had been indicated as a serious problem of which the cause was unknown. In the information provided by Greece, the GMO Panel (EFSA 2008c) saw no indication that the CCD was likely to be related to the presence of GM crops in the area. The GMO Panel reviewed additional scientific literature and indicated that CCD symptoms (e.g., low number of adult bees in the hives which still held food supplies and immature bees) do not resemble those expected in Bt intoxicated organisms (where immature stages are much more sensitive than adults). They pointed out that the American working group on CCD was concentrating on the following three hypotheses considered to be the more likely causes of bee colony loss in the USA:

- Reemerging pathogens responsible for CCD;
- Stresses working together to weaken bee colonies and allowing stress-pathogens to cause final collapse; and
- Environmental chemicals (especially neonicotinoids) causing the immuno-suppression of bees and triggering CCD.

A recent publication by Johnson *et al*. (2009) provided even more evidence against the speculation that GM crops have some causal relationship with CCD. Their data make allegations of potential effects of Bt maize in particular and Bt crops in general on CCD even more implausible.

The GMO Panel provided references supporting their consideration that low exposure level of bees to maize pollen combined with the low toxicity of the Cry1Ab protein in MON810 maize was unlikely to result in any adverse effects on bees. Therefore, the GMO Panel concluded that the Greek submission provided no new scientific data or information in support of an adverse effect of MON810 maize on the beekeeping industry in Greece and that would justify a national safeguard measure concerning this product.

Of note, Higes *et al*. (2009) recently described the clinical features of two professional bee-populations affected by CCD. Anamnesis, clinical examination and analyses support that the depopulation in both cases was due to the infection by *Nosema ceranae* (Microsporidia), an emerging pathogen of *Apis mellifera*. No other significant pathogens or pesticides (neonicotinoids) were detected and the bees had not been foraging in corn or sunflower crops. The treatment with fumagillin avoided the loss of surviving weak colonies.

On 9 February 2008, **France** notified to the European Commission an Order suspending the cultivation of seed varieties derived from maize event MON810 and submitted an information package made of different supporting documents.

One of the areas of concern consisted of exposure and impacts on pollinating insects. France submitted that impact studies needed to be carried out on bees in hives kept under normal apiculture conditions, to analyze the cumulative effects. The GMO Panel (EFSA, 2008e) presented a detailed review of impact as well as exposure studies and concluded that:

- The low exposure level of Cry1Ab containing pollen combined with its low toxicity was unlikely to result in any adverse effects on honeybees under normal apicultural conditions;

- Available scientific evidence gathered from laboratory and semi-field studies did not demonstrate impacts of MON810 maize pollen on honeybees; and

- The claims and documents provided by France did not provide any new or additional scientific evidence that would invalidate previous risk assessments of MON810 maize.

In a scientific opinion requested by the **European Commission**, the GMO Panel (EFSA, 2008f) reviewed a set of scientific publications, published after the adoption of the complemented scientific opinions on maize Bt11 and 1507. In relation to this section, the paper by Rose *et al*. (2007) is highlighted. Laboratory feeding studies performed by Rose *et al*. (2007) showed no effects on the weight and survival of honeybees feeding on Cry1Ab-expressing sweet maize Bt11 pollen for 35 days. Colonies foraging in sweet maize plots and fed Bt-pollen cakes for 28 days were not affected by the Cry1Ab protein, as no adverse effects on bee weight, foraging activity, and colony performance were observed. Brood development was not shown to be affected by exposure to Bt-pollen but was reduced significantly by the positive insecticide control. The authors reported that the number of foragers returning with pollen loads, pollen load weight, and forager weight were the most consistent endpoints as indicators of foraging activity.

The GMO Panel agreed with the conclusion of the Rose *et al*. (2007) study in which no adverse effects on honeybee weight, foraging activity, and colony performance were observed. Furthermore the GMO Panel referred to a meta-analysis Duan *et al*. (2008) of 25 independent laboratory studies assessing direct effects on honeybee survival of Cry proteins from currently commercialized Bt-crops, concluding that the assessed Cry proteins did not negatively affect the survival of either honeybee larvae or adults in laboratory settings.

In concluding their review of Rose *et al*. (2007), the GMO Panel noted that:

> ***"...in terms of risk to human and animal health and the environment, the provided information in Rose et al. (2007) does not present new scientific evidence that would invalidate the previous risk assessments of maize Bt11 and 1507" (EFSA, 2008f).***

Resistance development of target pest species

Bt176 maize (C/F/94/11-03) was authorized for all uses in the European Union by Commission Decision 97/98/EC of 23 January 1997 (EC, 1997) and final consent was granted by the French competent authority on 4 February 1997. On 14 February 1997, Austria invoked Article 16 of Directive 90/220/EEC partly based on the fact that in their opinion the risk of resistance development as well as the management of such a risk were insufficiently covered.

The Scientific Committee for Pesticides (SCP) has addressed the topic in its initial opinion (SCP, 1996) indicating that the possible development of insect resistance to the Bt-toxin cannot be considered an adverse environmental effect, as existing agricultural means of controlling such resistant species of insects will still be available. Nevertheless SCP pointed out that resistance management strategies are needed during the years of use of any pesticide, Bt sprays included.

In response to the Austrian arguments (SCP, 1997), the SCP drew attention once again to the need for effective resistance management, including monitoring on agronomic grounds, to prolong the effectiveness of Bt toxin both in conventional sprays and in genetically modified maize. It also felt that the submission of a satisfactory monitoring and resistance management programme should be a requirement for the authorization to use genetically modified maize seeds expressing Bt-toxin.

In a subsequent opinion, the GMO Panel (EFSA, 2004c) took into account the results of resistance monitoring performed in Spain, concluding that no consistent shifts in susceptibility were found after 5 years of Bt maize cultivation.

In February 2004, Austria provided additional information to support the national safeguard measures. This information included a paper by Morin *et al*. (2003) reporting that field populations of pink bollworm (*Pectinophora gossypiella*), a major cotton pest, harbours three mutant alleles of a gene encoding cadherin which are linked with resistance to Bt toxin Cry1Ac and survival on transgenic Bt cotton.

The GMO Panel (EFSA, 2004c) concluded that this manuscript had no relevance to transgenic maize lines MON810 and Bt176 expressing Bt toxin Cry1Ab and providing resistance to the target European pest species *Ostrinia nubilalis* and *Sesamia nonagrioides* as the crop, Cry protein, target insects and conditions in this study were not relevant for these GMOs.

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 21 January 2005, **Hungary** invoked Article 23 (safeguard clause) of Directive 2001/18/EC to provisionally prohibit the production, use and distribution of seeds derived from the authorized GM maize line MON810. In April 2008, Hungary forwarded additional studies to the European

Commission and requested that the four submitted reports be considered as confidential information.

One Hungarian report considered resistance development in target organisms as a matter of concern. The EFSA GMO Panel had previously identified this issue as a potential risk with Bt-maize cultivation, and had therefore recommended case-specific monitoring and management measures (EFSA, 2005 b,c).

On 29 March 2006, the European Commission received a request from **Greece** related to a national ban of the marketing in Greece of maize hybrids with the genetic modification MON810. One of the areas of concern documented by Greece was the impact of MON810 maize on the agricultural environment due to resistance development in target insects.

The GMO Panel (EFSA, 2006c) confirmed that it had recommended that monitoring for resistance is a requirement for all Bt crops cultivated in the EU and that the risk to the agricultural environment due to resistance development in target insects and the specific conditions prevailing in Greece mentioned in the Greek statement was currently low. The GMO Panel concluded that the evidence provided by Greece to support its concern could be adequately addressed by implementing case-specific monitoring as was being conducted in Spain.

On 9 February 2008, **France** notified to the European Commission an Order suspending the cultivation of seed varieties derived from the maize event MON810 and submitted an information package made of different supporting documents.

One of the areas of concern consisted of resistance development in lepidopteran target pests. France stated that there was *"No new evidence on the principal insect pests (no demonstrated resistance) but selection of a resistant strain in two secondary target Lepidoptera."*

The GMO Panel (EFSA, 2008e) reviewed all relevant and most recent scientific literature and publications, such as the scientific advice of the COGEM (2008), as well as those considered specific for French receiving environments. They concluded that the large scale cultivation of MON810 maize over several years would increase the selection pressure on corn borers, which could result in the potential development of resistance. Even though an analysis of global monitoring data, collected in Australia, China, Spain and the US, revealed an increased frequency of resistance alleles in some field populations of both *Helicoverpa zea* (a pest of cotton) to the Cry1Ac protein and *S.frugiperda* (a pest of maize) to the Cry1F protein, no field-evolved resistance has been reported to Bt-proteins for other lepidopteran pests (*Helicoverpa armigera, H. virescens, O. nubilalis, Pectinophora gossypiella* and *S. nonagrioides*). The GMO Panel considered that the likelihood of occurrence was low in corn borer populations if appropriate resistance management was implemented.

On 10 June 1999 and on 8 May 2000, **Austria** provisionally prohibited the placing on the market of the authorized GM maize events MON810 and T25, respectively, on its territory. In their respective scientific opinions, both the Scientific Committee on Plants (SCP, 1999a, 2000) and the EFSA GMO Panel (EFSA, 2004c) concluded that, based on the information submitted by Austria, MON810 and T25 maize did not constitute a risk to human and animal health or the environment.

On 21 November 2007, the Permanent Representation of Austria provided to the European Commission an Austrian study entitled "Supplementary risk assessment on GMO maize MON810 (with consideration of maize T25)". The aim of the Austrian study was to summarize Austria's arguments in response to the decision of the World Trade Organisation Panel 'European Communities – Measures affecting the approval and marketing of biotech products', because part of the measures dealt with the Austrian safeguards concerning the import and use of MON810 and T25 maize.

In the Austrian report, it was stated that "*the insect resistance management plan is insufficient because there is no information on baseline data, a lack of information regarding the implementation and a questionable assumption with regard to the adoption speed of GM maize MON810 in the European Union, which was estimated to be unrealistically low"*.

Andow (2008) identified resistance development in target pests as a potential risk, and indicated that this risk can be managed. To delay or prevent the potential development of insect resistance to Bt crops, a resistance management tactic, relying on a 'high dose/refuge strategy', has been endorsed in the US and EU (Bates *et al*., 2005; Andow, 2008; Bravo and Soberón, 2008).

The GMO Panel (EFSA, 2008g) concluded that the likelihood of resistance development was low in corn borer populations if appropriate resistance management was implemented. The GMO Panel considered that the available scientific data support and validate the 3 assumptions on which the high dose/refuge strategy is based:

(1) Resistance alleles are rare;

(2) Mating occurs between resistant insects emerging in Bt-crops and susceptible insects preserved on non-Bt-crops (refuge) at sufficient levels; and

(3) Resistance alleles are recessive.

For each of these, references were provided. The GMO Panel therefore agreed with the insect-resistance management plan proposed by the applicants' EU working group on insect resistance management.

Therefore, the GMO Panel also advised that the potential development of resistance in target pests continues to be monitored in order to detect potential changes in resistance levels in pest populations. Applicants are generally requested to monitor resistance development in target pests under case-specific monitoring as part of their insect resistance management requirements (Alcalde *et al*., 2007) and to consider it under general surveillance through farmer questionnaires (Tinland *et al*., 2007; Schmidt *et al*., 2008).

Establishment of feral populations

Topas 19/2 spring oilseed rape was authorized for import, storage and processing in the European Union by commission Decision (98/291/EC) of 22 April 1998 (EC, 1998a). The **Greek** Competent Authority informed the Commission in a letter dated 3 November 1998, of its decision to prohibit the importation into Greece partly based on the loss of seed during transportation and the establishment of viable modified rape plants in the environment. The SCP (1999b) confirmed that the potential for the loss of seed during transport and the possible establishment of feral plants in uncultivated habitats e.g., roadside verges was considered in the initial risk assessments carried out by the SCP (1998b). Where there is no use of glufosinate ammonium to apply selective pressure, modified rape is no more invasive than unmodified rape plants.

In March 2004, Greece provided additional information (Wilkinson *et al*., 2003; OGTR, 2002a; Eastham and Sweet, 2002; Strid and Tan, 2002; Inomata, 1993; Ramsay *et al*., 2003; Squire *et al*., 2003a) to support the national safeguard measures related with the potential of out-crossing from oilseed rape to other *Brassicaceae*. The EFSA GMO panel reviewed the information and concluded (EFSA, 2004d) that:

- The presence of hybrids between transgenic spring oilseed rape and other *Brassicaceae* is not a hazard in itself and does not imply inevitable ecological damage;
- The likelihood for unintended environmental effects due to the establishment and spread of herbicide tolerant oilseed rape will not be different from that of traditionally bred oilseed rape; and
- The scientific evidence presented by Greece contained no new generic or uniquely local scientific information on the environmental or human health impacts of the GM oilseed rape events.

In a subsequent opinion (EFSA, 2006b), the GMO Panel responded to a consultation concerning the consequences of accidental spillage of **Topas 19/2, Ms1xRf1** and **GT73** oilseed rape and subsequent establishment of GM oilseed rape plants. This consultation was triggered by a report in February 2005 of the Japanese Environmental Studies Institute on the presence of oilseed rape genetically modified for tolerance to an herbicide around Japanese port facilities. The GMO Panel confirmed its previous opinion that the presence of transgenic spring oilseed rape volunteers or feral plants is not a hazard in itself and is not likely to cause ecological damage compared with conventional oilseed rape (EFSA, 2004a; 2005g). The GMO Panel concluded that the likelihood for unintended environmental effects due to the establishment and spread of herbicide-tolerant oilseed rape would not be different from that of traditionally bred oilseed rape.

On 27 July 2007, **Austria** notified to the European Commission a national safeguard clause on genetically modified (GM) oilseed rape event **GT73** which had been approved for import in the EU (notification C/NL/98/11).

Austria stressed the importance of the environmental impact of feral population supported by a study by Pascher *et al*. (2006). In line with its previous scientific opinions on herbicide tolerant oilseed rape GT73 (EFSA, 2004a), MS8xRF3 (EFSA, 2005g) and T45 (EFSA, 2008a), the GMO

Panel (EFSA, 2009c) confirmed that in regions where oilseed rape is grown and/or where oilseed rape seeds are imported and transported, feral oilseed rape populations are likely to occur in non-natural disturbed ecosystems (such as ports, processing facilities, margins of agricultural fields, roadside verges, railway lines, and wastelands). The EFSA GMO Panel was aware that if feral oilseed rape plants derived from spilled seeds remain uncontrolled and reproduce, they may survive, outcross and eventually disperse genes to cross-compatible plants such as *Brassica rapa* and *Raphanus raphanistrum*. In this respect, the scientific information provided in the Austrian safeguard clause notification did not give any new information regarding increased likelihood of establishment or survival of feral oilseed rape plants in case of accidental release into the environment of oilseed rape GT73 seeds during transportation and processing.

In reviewing the available literature, the GMO Panel noted that:

> ***"...there are no compelling data to suggest that the presence of an herbicide tolerance trait in a wild relative changes the behaviour of the wild relative. In the absence of glyphosate-containing herbicides, hybrids or wild relatives containing the herbicide tolerance trait do not show any enhanced fitness and behave as conventional plants. Thus escaped plants and genes dispersed to other cross-compatible plants would not create additional environmental impacts" (EFSA, 2009c).***

Furthermore, it was concluded that there was no evidence that the herbicide tolerance trait introduced by genetic engineering resulted in increased invasiveness of oilseed rape GT73, except when glyphosate containing herbicides would be applied. As such, escaped plants and genes dispersed to other cross-compatible plants would not create additional agronomic or environmental impacts. This – together with the assessment that oilseed rape GT73 and hybridising relatives have no enhanced fitness or invasiveness characteristics (except in the presence of glyphosate containing herbicides) – confirmed earlier conclusions of the EFSA GMO Panel.

On 15 July 2008, **Austria** notified to the European Commission a national safeguard clause on GM oilseed rape events **MS8, RF3 and MS8xRF3**, which had been authorized for import in the EU. The argumentation was similar to what had been submitted before for GT73. The reply by the GMO Panel (EFSA, 2009e) reflected the same argumentation as developed for the safeguard clause on GT73, confirming that there was no new evidence that would suggest any risk.

On 16 July 2008, **Austria** notified to the European Commission a national safeguard clause on GM maize event **MON863**, which had been approved for import in the EU. The intended uses of MON863 maize specifically exclude cultivation, so the environmental exposure is mainly limited to exposure through manure and faeces from the gastrointestinal tracts mainly of animals fed MON863 maize, as well as to accidental release into the environment of MON863 grains during transportation and processing and subsequently to potential occurrence of sporadic feral plants.

The GMO Panel (EFSA, 2009d) considered it very unlikely that volunteers of this GM maize, or its progeny, would differ from conventional maize varieties in their ability to survive until subsequent seasons, or to establish feral populations under European environmental conditions. Since studies in Europe and elsewhere with MON863 maize have shown no altered survival, multiplication or dissemination characteristics except in the presence of the specific target

organisms, the GMO Panel reiterated its previous opinion ***"that the likelihood of unintended environmental effects as a consequence of spread of genes from this maize will not differ from that of conventional maize varieties"*** (EFSA, 2009d). The GMO Panel further concluded that:

> ***"...the Austrian submission provided no new scientific data or information in support of an adverse effect of maize MON863 on the environment and that would justify a national safeguard measure concerning this product" (EFSA, 2009d).***

The case of **Australia** dealing with a GM cotton mentioned in UNEP/CBD/BS/COP-MOP/4/10 also deserves more careful examination.

As corrected by UNEP/CBD/BS/COP-MOP/4/10/Corr.2, the Office of the Gene Technology Regulator authorized in 2002 the unrestricted commercial release of two types of genetically modified cotton in southern Australia (OGTR, 2002b). Commercial release in northern Australia remained pending awaiting further information on the selective advantage the insecticidal genes may confer on cotton including feral cotton populations in northern Australia. In 2006, the Regulator subsequently authorized the same genetically modified cotton in northern Australia following scientific demonstration that caterpillar pests are not the major factor controlling cotton growth in that area and confirming that GM cotton is as safe as non-GM cotton in northern Australia (OGTR, 2006).

Pollen flow and hybridization with related species

Topas 19/2 spring oilseed rape was authorized for import, storage and processing in the European Union by commission Decision (98/291/EC) of 22 April 1998 (EC, 1998a). The Greek Competent Authority informed the Commission in a letter dated 3 November 1998, of its decision to prohibit the importation into Greece partly based on the potential for hybridization with other *Brassicaceae*.

The SCP (1999b) confirmed that the risk of genetic escape was considered by the SCP to be small and that information submitted by the Greek authorities did not change the initial assessment (SCP, 1998b). In the absence of commercial production, the population of GM rape would be restricted to that derived from seeds accidentally lost during transport and handling. The possibility of genetic escape from this extremely limited population to wild Brassica spp. collected for human consumption was correspondingly very small. Should this occur, there were, in the view of the SCP, no implications for human health.

MON810 maize (C/F/95/12-02) was authorized in the European Union for all uses with the exception of food by Commission Decision 98/294/EC on 22 April 1998 (EC, 1998b) and France ratified the Commission Decision on 3 August 1998. According to Regulation (EC) 258/97 – Art. 5, the notification for food use of maize derivatives was forwarded to Member States on 5 February 1998 based on an opinion on substantial equivalence by the UK Advisory Committee on Novel Foods and Processes (EC, 2009).

On 9 February 2008, **France** notified to the European Commission an Order suspending the cultivation of seed varieties derived from the maize event MON810 and submitted an information package made of different supporting documents.

One of the areas of concern consisted of environmental impacts of vertical (pollen-mediated) gene flow. France alluded to new evidence concerning the characterization of pollen dispersal over large distances (kilometres) showing that it was not possible to exclude cross-pollination between GMO fields and GMO-free fields at the local scale (small agricultural region).

In its risk assessment and in addition to the information package supporting the French national measure on MON810 maize, the GMO Panel reviewed all relevant and most recent scientific literature and publications, such as the scientific advice of the COGEM (2008), as well as those considered specific for French receiving environments. The GMO Panel (EFSA, 2008e) summarized that pollen dispersal and consequent cross-pollination were not considered as environmental hazards in themselves. The primary concern is to assess the environmental consequences of transgene flow on ecosystems by assessing the spread and fitness of hybrids and backcross progeny as well as exposure to non-target organisms. Studies conducted by the applicant, published literature on the cultivation of numerous varieties of MON810 maize and monitoring observations in France and Spain indicated that this maize behaved like non-GM maize and was unlikely to establish volunteers or survive over subsequent seasons or to establish feral populations under European environmental conditions.

On 10 June 1999 and on 8 May 2000, **Austria** provisionally prohibited the placing on the market of the authorized GM maize events **MON810** and **T25**, respectively, on its territory. In their respective scientific opinions, both the Scientific Committee on Plants (SCP, 1999a, 2000) and the EFSA GMO Panel (EFSA, 2004c) concluded that, based on the information submitted by Austria, MON810 and T25 maize did not constitute a risk to human and animal health or the environment.

On 21 November 2007, the Permanent Representation of Austria provided to the European Commission an Austrian study entitled "Supplementary risk assessment on GMO maize MON810 (with consideration of maize T25)". The aim of the Austrian study was to summarize Austria's arguments in response to the decision of the World Trade Organisation Panel 'European Communities – Measures affecting the approval and marketing of biotech products', because part of the measures dealt with the Austrian safeguards concerning the import and use of MON810 and T25 maize.

In the Austrian report, it was concluded that "*data indicate that gene flow from GM maize MON810 (or GM maize T25 respectively) through outcrossing to neighbouring non-modified varieties is likely and has relevant environmental and agricultural consequences in Austria. A likely decrease in the income of organic and conventional farmers is caused by out-crossing from GM-maize fields and the consequentially decreased value of their harvest*".

The GMO Panel (EFSA, 2008g) confirmed that:

- Substantial literature shows that vertical gene flow characteristics of MON810 maize are similar to those of non-GM maize;
- The GMO Panel did not consider pollen dispersal and consequent cross-pollination as environmental hazards in themselves. It is an agricultural management and coexistence issue; and
- The primary concern was with assessing the environmental consequences of transgene flow on ecosystems by assessing the spread and fitness of hybrids and backcross progeny as well as exposure to non-target organisms.

Studies conducted by the applicant, published literature on the cultivation of numerous varieties of MON810 maize and monitoring observations indicated that this maize behaved like non-GM maize in its ability to establish volunteers or survive over subsequent seasons, and was very unlikely to establish feral populations under European environmental conditions. The GMO Panel was of the opinion that the information and arguments supplied by Austria, including regional conditions for maize cultivation in Austria, did not provide new or additional scientific evidence on pollen or seed dispersal and its consequences that would alter the previous risk assessments of MON810 maize.

Ecological impact of herbicide tolerance

Topas 19/2 spring oilseed rape was authorized for import, storage and processing in the European Union by commission Decision (98/291/EC) of 22 April 1998 (EC, 1998a). The Greek Competent Authority informed the Commission in a letter dated 3 November 1998, of its decision to prohibit the importation into Greece. In March 2004, Greece provided additional information to support the national safeguard measures partly based on information dealing with crop management and agronomic consequences of cultivation of genetically modified herbicide-tolerant oilseed rape (Champion *et al*., 2003; Squire *et al*., 2003b; Haughton *et al*., 2003; Hawes *et al*., 2003; DEFRA, 2003).

The EFSA GMO panel stated (EFSA, 2004d) that:

- The ecological impact of herbicide tolerance genes in transgenic plants depended largely on the use of herbicide and not on the transgenic event;
- The herbicide tolerant oilseed rape, in general, could lead to cultivation practices that may alter in-field biodiversity as demonstrated in the UK Farm Scale study;
- Any sustainable cultivation of herbicide tolerant oilseed rape would depend on appropriate management measures; and
- Since Topas 19/2 spring oilseed rape was authorized for import, storage and processing only and no cultivation had been granted in the EU, the supporting documents were not appropriate in this case.

On 10 June 1999 and on 8 May 2000, **Austria** provisionally prohibited the placing on the market of the authorized GM maize events MON810 and T25, respectively, on its territory. In their respective scientific opinions, both the Scientific Committee on Plants (SCP, 1999a, 2000) and the EFSA GMO Panel (EFSA, 2004c) concluded that, based on the information submitted by Austria, MO810 and T25 maize did not constitute a risk to human and animal health or the environment.

On 21 November 2007, the Permanent Representation of Austria provided to the European Commission an Austrian study entitled "Supplementary risk assessment on GMO maize MON810 (with consideration of maize T25)". The aim of the Austrian study was to summarize Austria's arguments in response to the decision of the World Trade Organisation Panel 'European Communities – Measures affecting the approval and marketing of biotech products', because part of the measures dealt with the Austrian safeguards concerning the import and use of MON810 and T25 maize.

Austria indicated that changes in weed management were to be expected with introduction of GM maize T25, possibly resulting in a shift in weed communities. They also claimed that long term effects of the herbicide tolerant plant could not be evaluated independently from the respective herbicide use, and effects of glufosinate-ammonium in combination with T25 maize on weed communities needed to be addressed.

Like any other extensively used weed management approach, herbicide regimes used with genetically modified herbicide tolerant (GMHT) crops have the potential to alter the composition,

richness and diversity of weed communities. The GMO Panel (EFSA, 2008g) reviewed different management schemes and concluded that the impact would vary depending on the application regime but also the baseline against which the comparison was made.

In their conclusions, the GMO panel encouraged:

> ***"...both applicants and appropriate competent authorities in Member States establish and implement herbicide management systems for GMHT crops that do no more environmental harm than conventional systems and which are consistent with the environmental protection goals and biodiversity action plans in each Member State" (EFSA, 2008g).***

The case of **Belgium** dealing with a GM oilseed rape mentioned in UNEP/CBD/BS/COP-MOP/4/10 also deserves more careful examination.

In 1996, the dossier C/BE/96/01 'A new hybridization system in oilseed rape *(Brassica napus* L.) - Application for consent to market genetically modified organisms (MS8xRF3)' was submitted to the Belgian Competent Authority. The notification covered a spring variety of oilseed rape which had been genetically modified to introduce a pollination control system (hybrid system) linked to a herbicide tolerance trait, intended for cultivation and import in the EU for all uses (food, feed and industrial uses) as any other oilseed rape.

The risk assessment of the initial dossier was carried out by the experts of the Belgian Biosafety Advisory Council. Based on a positive advice of the Biosafety Advisory Council, the Belgian Minister of Agriculture issued a consent supporting the placing on the market of GM oilseed rape MS8xRF3. In 1998, the Scientific Committee on Plants (SCP, 1998d) of the EC also gave a favourable opinion concluding that there was no evidence to indicate that the placing on the market of GM oilseed rape MS8xRF3, with the purpose to be used as any other oilseed rape, was likely to cause adverse effects on human health and the environment.

When the results of the UK Farm-Scale Evaluation trials were announced, the involved scientists, ACRE and DEFRA pointed out that the conclusions only applied to the management regime used in the farm scale evaluations and that alternative management strategies may have different impacts. For example, there may be viable mitigation measures that could be used by farmers to offset any adverse effects. Consequently, the Belgian experts raised a number of additional questions relating to management practices as well as specific monitoring requirements in relation to the cultivation of the GM plant. As this would have required additional studies and in view of imminent imports from other areas in the world where the GM oilseed rape was already cultivated, the applicant accepted that while the request for import of seeds for processing, food and feed use would proceed, cultivation would not be supported at that time and should be resubmitted when additional information is available. On this basis, the Belgian Competent Ministers took the decision to support granting consent for import and processing of the transgenic oilseed rape MS8, RF3 and MS8xRF3, but not consent for cultivation. This eventually led to Decision 2007/232/EC (EC, 2007) for the placing on the market of the genetically engineered oilseed rape.

References

ACNFP (1996). The use of antibiotic resistance markers in genetically modified plants for human food. The Advisory Committee on Novel Foods and Processes, UK.

ACRE (2002). Advisory Committee on Releases of GM crops into the Environment. ACRE's response to concerns raised in written representations and submissions associated with the CHARDON LL public hearing and to statements made at ACRE's open hearing relating to the safety assessment of T25 GM maize conducted under Directive 90/220/EEC. http://webarchive.nationalarchives.gov.uk/20080727101330/http://www.defra.gov.uk/environment/acre/advice/advice20.htm

ACRE (2007). Minutes of the 116th of ACRE at the University of Essex, Colchester, Thursday 6th December 2007, Point 9 Research paper: toxins in transgene crop by-products may affect headwater stream ecosystems ACRE/07/P31. http://webarchive.nationalarchives.gov.uk/20080727101330/http://www.defra.gov.uk/environment/acre/meetings/07/min071206.htm

AFSSA (2008). Avis de l'Agence française de sécurité sanitaire des aliments relatif à une demande de renouvellement de mise sur le marché du maïs génétiquement modifié MON810, résistant aux lépidoptères, pour l'importation, la transformation, ainsi que l'utilisation en alimentation humaine et animale de ses produits dérivés, au titre du règlement (CE) n°1829/2003, http://www.afssa.fr/Documents/BIOT2008sa0043.pdf

Alcalde, E., Amijee, F., Blache, G., Bremer, C., Fernandez, S., Garcia-Alonso, M., Holt, K., Legris, G., Novillo, C., Schlotter, P., Storer, N. and Tinland, B. (2007). Insect resistance monitoring for Bt maize cultivation in the EU: proposal from the industry IRM working group. *Journal of Consumer Protection and Food Safety* **2**(S1): 47–49.

Amman, K. (2005). Effects of biotechnology on biodiversity: herbicide-tolerant and insectresistant GM crops. *Trends in Biotechnology* **23**: 388–394.

Anderson, P.L., Hellmich, R.L., Sumerford, D.V. and Lewis, L.C. (2004). Effects of Cry1Ab expressing corn anthers on monarch butterfly larvae. *Environmental Entomology* **33**: 1109–1115.

Andow, D.A. (2008). The risk of resistance evolution in insects to transgenic insecticidal crops. *Collection of Biosafety Reviews* **4**: 142–199.

Bakonyi, G., Szira, F., Kiss, I., Villányi, I., Seres, A. and Székács, A. (2006). Preference tests with collembolas on isogenic and Bt-maize. *European Journal of Soil Biology* **42**: S132–135.

Bates, S.L., Zhao, J.-Z., Roush, R.T. and Shelton, A.M. (2005). Insect resistance management in GM crops: past, present and future. *Nature Biotechnology* **25**: 57–62.

Beachy, R.N., Fedoroff, N.V., Goldberg, R.B. and McHughen, A. (2008). The burden of proof: A response to Rosi-Marshall *et al*. *PNAS USA* **105**: E9.

Bennett, P.M., Livesey, C.T., Nathwani, D., Reeves, D.S., Saunders, J.R. and Wise, R. (2004). An assessment of the risks associated with the use of antibiotic resistance genes in genetically modified plants: report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J. Antimicrob. Chemother.* **53**: 418–431.

Bøhn, T., Primicerio, R., Hessen, D. and Traavik, T. (2008). Reduced fitness of *Daphnia magna* fed a Bt-transgenic maize variety. *Archives of Environmental Contamination and Toxicology* **55**: 584–592.

Bourguet, D., Chaufaux, J., Micoud, A., Delos, M., Naibo, B., Bombarde, F., Marque, G., Eychenne, N. and Pagliari, C. (2002). *Ostrinia nubilalis* parasitism and the field abundance of non-target insects in transgenic *Bacillus thuringiensis* corn (*Zea mays*). *Environmental Biosafety Research* **1**: 49–60.

Bravo, A. and Soberón, M. (2008). How to cope with insect resistance to Bt toxins? *Trends in Biotechnology* **26**: 573–579.

BVL (2009) Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL) letter on suspension of MON810 cultivation in Germany
http://www.bvl.bund.de/cln_027/DE/08__PresseInfothek/00__doks__downloads/mon__810__bescheid,templateId=raw,property=publicationFile.pdf/mon_810_bescheid.pdf

Canard (2001). Natural food and feeding habits of lacewings. *In:* McEwen, P.K., New, T.R., Whittington, A.E. (Eds.), Lacewings in the crop environment. Cambridge University Press, Cambridge, UK, pp. 116-129.

Candolfi, M.P., Brown, K., Grimm, C., Reber, B. and Schmidli, H. (2004). A faunistic approach to assess potential side-effects of genetically modified Bt-corn on non-target arthropods under field conditions. *Biocontrol Science and Technology* **14**: 129–170.

Champion, G.T., May, M.J., Bennett, S., Brooks, D.R., Clark, S.J., Daniels, R.E., Firbank, L.G., Haughton, A.J., Hawes, C., Heard, M.S., Perry, J.N., Randle, Z., Rossall, M.J., Rothery, P., Skellern, M.P., Scott, R.J., Squire, G.R. and Thomas, M.R. (2003). Crop management and agronomic context of the Farm Scale Evaluations of genetically modified herbicide-tolerant crops. *Phil. Trans. R. Soc. Lond*. B 358: 1801–1818.

Clark, B.W., Philipps, T.A. and Coats, J.R. (2005). Environmental fate and effects of *Bacillus thuringiensis* (Bt) proteins from transgenic crops: a review. *Journal of Agricultural and Food Chemistry* **53**: 4643–4653.

Codex alimentarius (2003). Principles for risk analysis and guidelines for safety assessment of foods derived from modern biotechnology.
ftp://ftp.fao.org/codex/Publications/Booklets/Biotech/Biotech_2003e.pdf

COGEM (2008). Response by COGEM to the French Opinion on MON810, CGM/080131-04.
http://www.cogem.net/ContentFiles/CGM08013-04%20advice%20MON810%20-%20English.pdf

Darvas, B., Csóti, A., Gharib, A., Peregovits, L., Ronkay, L., Lauber, E. and Polgár, L.A. (2004). Data for the risk analysis in Hungary of Bt maize pollen and larvae of protected butterfly species. *Növényvédelem (Plant Protection)* **40**(9): 441–447 (with English translation).

de la Poza, M., Pons, X., Farinós, G.P., López, C., Ortego, F., Eizaguirre, M., Castañera, P. and Albajes, R. (2005). Impact of farm-scale Bt maize on abundance of predatory arthropods in Spain. *Crop Protection* **24**: 677–684.

DEFRA (2003). GMO Research Programme - Reports: Modelling the effects on farmland food webs of herbicide and insecticide management in the agricultural ecosystem Ref EPG 1/5/188.
http://webarchive.nationalarchives.gov.uk/20081023141438/http://www.defra.gov.uk/environment/gm/research/pdf/epg_1-5-188.pdf

Dolezel, M., Heissenberger, A. and Gaugitsch, H. (2006). Ecological effects of genetically modified maize with insect resistance and/or herbicide tolerance. Literature research report on behalf of the Bundesministerium für Gesundheit und Frauen, Wien, Austria. 64 pp.

Dolezel, M., Eckerstorfer, M., Gaugitsch, H., Heissenberger, A. and Spök, A. (2007). Review of scientific evidence including latest findings concerning Austrian Safeguard measures for GM maize lines MON810 and T25, BMGF, Forschungsberichte der Sektion V, Band 1, 2007.

Douville, M., Gagné, F., Masson, L., McKay, J. and Blaise, C. (2005). Tracking the source of *Bacillus thuringiensis* Cry1Ab endotoxin in the environment. *Biochemical Systematics and Ecology* **33**: 219–232.

Duan, J.J., Marvier, M., Huesing, J., Dively, G. and Huang, Z.Y. (2008). A meta-analysis of effects of Bt crops on honey bees (Hymenoptera: Apidae). *PLoS ONE* **3**: 1–6 (e1415).

Dutton, A., Klein, H., Romeis, J. and Bigler, F. (2002). Uptake of Bt-toxin by herbivores feeding on transgenic maize and consequences for the predator *Chrysoperla carnea*. *Ecological Entomology* **27**: 441–447.

Dutton A., Klein H., Romeis J.and Bigler F. (2002). Uptake of *Bacillus thuringiensis* spray on the predator *Chrysoperla carnea*. *Ecological Entomology* **27**: 441–447.

Dutton, A., Romeis, J. and Bigler, F. (2003a). Assessing the risks of insect resistant transgenic plants on entomophagous arthropods: Bt-Maize expressing Cry1Ab as a case study. *BioControl* **48**: 611–636.

Eastham, K. and Sweet, J. (2002). Genetically modified organisms (GMOs): The significance of gene flow through pollen transfer EEA Environmental issue report No 28

http://reports.eea.eu.int/environmental_issue_report_2002_28/en

EC (1997). Commission Decision 97/98/EC of 23 January 1997 concerning the placing on the market of genetically modified maize (*Zea mays* L.) with the combined modification for insecticidal properties conferred by the Bt-endotoxin gene and increased tolerance to the herbicide glufosinate ammonium pursuant to Council Directive 90/220/EEC. *Official Journal of the European Communities* **L031**: 69–70.

EC (1998a). Decision 98/291/EC of 22 April 1998 concerning the placing on the market of genetically modified spring oilseed rape (*Brassica napus L. spp. oleifera*), pursuant to Council Directive 90/220/EEC. *Official Journal of the European Communities* **L131**: 26–31.

EC (1998b). Commission Decision 98/294/EC of 22 April 1998 concerning the placing on the market of genetically modified maize (*Zea mays* L. line MON810), pursuant to Council Directive 90/220/EEC. *Official Journal of the European Communities* **L131**: 32–33.

EC (2007). Commission Decision Of 26 March 2007 concerning the placing on the market, in accordance with Directive 2001/18/EC of the European Parliament and of the Council, of oilseed rape products (*Brassica napus* L., lines Ms8, Rf3 and Ms8xRf3) genetically modified for tolerance to the herbicide glufosinate-ammonium . *Official Journal of the European Union* L **100**: 20–24.

EC (2009). Community register of genetically modified food and feed. – Event Mon810 http://ec.europa.eu/food/dyna/gm_register/gm_register_auth.cfm?pr_id=11

Eckert, J., Schuphan, I., Hothorn, L.A. and Gathmann, A. (2006). Arthropods on maize ears for detecting impacts of Bt maize on nontarget organisms *Environ. Entomol*. **35**: 554–560.

EFSA (2003). Opinion of the Scientific Panel on Genetically Modified Organisms 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. *The EFSA Journal* **10**: 1–13.

EFSA (2004a). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the Notification (Reference C/NL/98/11) for the placing on the market of herbicide-tolerant oilseed rape GT73, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. *The EFSA Journal* **29**: 1–19.

EFSA (2004b) .Opinion of the Scientific Panel on Genetically Modified Organisms on the use of antibiotic resistance genes as marker genes in genetically modified plants *The EFSA Journal* **48**: 1–18.

EFSA (2004c). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the Austrian invoke of Article 23 of Directive 2001/18/EC. *The EFSA Journal* **78**: 1–13.

EFSA (2004d). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the Greek invoke of Article 23 of Directive 2001/18/EC. *The EFSA Journal* **79**: 1–8.

EFSA (2005a). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the notification (Reference C/ES/01/01) for the placing on the market of insect-tolerant genetically modified maize 1507, for import, feed and industrial processing and cultivation, under Part C of Directive 2001/18/EC from Pioneer Hi-Bred International/Mycogen Seeds. *The EFSA Journal* **181**: 1–33.

EFSA (2005b). Opinion of the Scientific Panel on Genetically Modified Organisms on an application (reference EFSA-GMO-NL-2004-02) for the placing on the market of insect-tolerant genetically modified maize 1507, for food use, under Regulation (EC) No 1829/2003 from Pioneer Hi-Bred International/Mycogen Seeds. *The EFSA Journal* **182**: 1–22.

EFSA (2005c). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the notification (Reference C/F/96/05.10) for the placing on the market of insect resistant genetically modified maize Bt11, for cultivation, feed and industrial processing, under Part C of Directive 2001/18/EC from Syngenta Seeds. *The EFSA Journal* **213**: 1–33.

EFSA (2005d). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safeguard clause invoked by Hungary according to Article 23 of Directive 2001/18/EC. *The EFSA Journal* **228**: 1–14.

EFSA (2005e). Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-DE-2004-03) for the placing on the market of insect-protected genetically modified maize MON863 x MON810, for food and feed use, under Regulation (EC) No 1829/2003 from Monsanto. *The EFSA Journal* **252**: 1–23.

EFSA (2005f). Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-BE-2004-07) for the placing on the market of insect-protected glyphosate-tolerant genetically modified maize MON863xMON810xNK603, for food and feed uses, and import and processing under Regulation (EC) No 1829/2003 from Monsanto. *The EFSA Journal* **256**: 1–25.

EFSA (2005g). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the application (Reference C/BE/96/01) for the placing on the market of glufosinate-tolerant hybrid oilseed rape Ms8 x Rf3, derived from genetically modified parental lines (Ms8, Rf3), for import and processing for feed and industrial uses, under Part C of Directive 2001/18/EC from Bayer CropScience. *The EFSA Journal* **281**: 1–23.

EFSA (2005h). Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-UK-2004-01) for the placing on the market of glyphosate-tolerant and insect-resistant genetically modified maize NK603xMON810, for food and feed uses under Regulation (EC) No 1829/2003 from Monsanto. *The EFSA Journal* **309**: 1–22.

EFSA (2006a). Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. *The EFSA Journal* **99**: 1–100.

EFSA (2006b). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to genetically modified crops (Bt176 maize, MON810 maize, T25 maize, Topas 19/2 oilseed rape and Ms1xRf1 oilseed rape) subject to safeguard clauses invoked according to Article 16 of Directive 90/220/EEC. *The EFSA Journal* **338**: 1–15.

EFSA (2006c). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safeguard clause invoked by Greece according to Article 23 of Directive 2001/18/EC and to Article 18 of Directive 2002/53/EC. *The EFSA Journal* **411**: 1–26.

EFSA (2007a). Statement of the Scientific Panel on Genetically Modified Organisms on the safe use of the *nptII* antibiotic resistance marker gene in genetically modified plants adopted on 22-23 March 2007.
http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620775641.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) adopted on 25 June 2007.
http://www.efsa.europa.eu/cs/BlobServer/Statement/GMO_statement_MON863.pdf?ssbinary=true

EFSA (2007c). Minutes of the 37th plenary meeting of the Scientific Panel on Genetically Modified Organisms held on 22-23 November 2007 in Brussels, Belgium (adopted on 18 December 2007).
http://www.efsa.europa.eu/cs/BlobServer/Event_Meeting/GMO_Minutes_37th_plenmeet.pdf

EFSA (2008a). Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-UK-2005-25) for the placing on the market of glufosinate-tolerant oilseed rape T45 for food and feed uses, import and processing and renewal of the authorization of oilseed rapt T45 as existing products, both under Regulation (EC) 1829/2003 from Bayer CropScience. *The EFSA Journal* **635**: 1–22.

EFSA (2008b). Request from the European Commission related to the safeguard clause invoked by Hungary on maize MON810 according to Article 23 of Directive 2001/18/EC. Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **756**: 1–18.

EFSA (2008c). Request from the European Commission related to the safeguard clause invoked by Greece on maize MON810 according to Article 23 of Directive 2001/18/EC Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **757**: 1–12.

EFSA (2008d). Safety and nutritional assessment of GM plants and derived food and feed: The role of animal feeding trials Report of the EFSA GMO Panel Working Group on Animal Feeding Trials. *Food and Chemical Toxicology* **46**: S2–S70.

EFSA (2008e). Request from the European Commission related to the safeguard clause invoked by France on maize MON810 according to Article 23 of Directive 2001/18/EC and the emergency measure according to Article 34 of Regulation (EC) No 1829/2003 - Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **850**: 1–45.

EFSA (2008f). Request from the European Commission to review scientific studies related to the impact on the environment of the cultivation of maize Bt11 and 1507 Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **851**: 1–27.

EFSA (2008g). Request from the European Commission related to the safeguard clause invoked by Austria on maize MON810 and T25 according to Article 23 of Directive 2001/18/EC Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **891**: 1–64.

EFSA (2008h). Working document of the GMO Panel on the interplay between Directive 2001/18/EC (GMOs) and Directive 91/414/EEC (Plant Protection Products), http://www.efsa.europa.eu/cs/BlobServer/DocumentSet/gmo_working_document_en.pdf

EFSA (2009a). Statement of EFSA on the consolidated presentation of opinions on the use of antibiotic resistance genes as marker genes in genetically modified plants. *The EFSA Journal* **1108**: 1–8.

EFSA (2009b). Scientific Opinion of the Panel on Genetically Modified Organisms on applications (EFSA-GMORX-MON810) for the 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. *The EFSA Journal* **1149**: 1–84.

EFSA (2009c). Request from the European Commission related to the safeguard clause invoked by Austria on oilseed rape GT73 according to Article 23 of Directive 2001/18/EC Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **1151**: 1–16.

EFSA (2009d). Request from the European Commission related to the safeguard clause invoked by Austria on maize lines MON863 according to Article 23 of Directive 2001/18/EC Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **1152**: 1–18.

EFSA (2009e). Request from the European Commission related to the safeguard clause invoked by Austria on oilseed rape MS8, RF3 and MS8xRF3 according to Article 23 of Directive 2001/18/EC. Scientific Opinion of the Panel on Genetically Modified Organisms. *The EFSA Journal* **1153**: 1–16.

Eizaguirre M., Albajes R., López C., Eras J., Lumbieres B. and Pons X. (2006). Six years after the commercial introduction of Bt maize in Spain: field evaluation, impact and future prospects. *Transgenic Research* **15**: 1–12.

FAO/WHO (2000). Safety aspects of genetically modified foods of plant origin. Report of a Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology, World Health Organization.

Faria, C.A., Wäckers, F.L., Prichard, J., Barrett, D.A. and Turlings, T.C.J. (2007). High susceptibility of Bt maize to aphids enhances the performance of parasitoids of lepidopteran pests. *PLoS ONE* **2**: 1–11 (e600).

Farinós, G.P., de la Poza, M., Hernández-Crespo, P., Ortego, F. and Castañera, P. (2008). Diversity and seasonal phenology of aboveground arthropods in conventional and transgenic maize crops in Central Spain. *Biological Control* **44**: 362–371.

Finamore, A., Roselli, M., Britti, A., Monastra, G., Ambra, R., Turrini, A. and Mengheri, E. (2008). Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. *Journal of Agricultural Food and Chemistry* **56** (23): 11533–11539.

Gathmann, A., Wirooks, L., Eckert, J. and Schuphan, I. (2006b). Spatial distribution of *Aglais urticae* (L.) and its host plant *Urtica dioica* (L.) in an agricultural landscape: implications for Bt maize risk assessment and post-market monitoring. *Environmental Biosafety Research* **5**: 27–36.

Gathmann, A., Wirooks, L., Hothorn L.A., Bartsch D. and Schuphan, I. (2006a). Impact of Bt maize pollen (MON810) on lepidopteran larvae living on accompanying weeds. *Molecular Ecology* **15**: 2677–2685.

Gay, P.B. and Gillespie, S.H. (2005). Antibiotic resistance markers in genetically modified plants: a risk to human health? *Lancet Infect. Dis*. **5**: 637–646.

Goldstein, D.A., Tinland, B., Gilbertson, L.A., Staub, J.M., Bannon, G.A., Goodman, R.E., McCoy, R.L. and Silvanovich, A. (2005). Human safety and genetically modified plants: a review of antibiotic resistance markers and future transformation selection technologies. *J. Appl. Microbiol*. **99**: 7–23.

Hammond, B.G., Dudek, R., Lemen, J.K. and Nemeth, M.A., (2006). Results of a 90-day safety assurance study with rats fed grain from corn borer-protected corn. *Food and Chemical Toxicology* **44**: 1092–1099.

Haughton, A.J., Champion, G.T., Hawes, C., Heard, M.S., Brooks, D.R., Bohan, D.A., Clark, S.J., Dewar, A.M., Firbank, L.G., Osborne, J.L., Perry, J.N., Rothery, P., Roy, D.B., Scott, R.J., Woiwod, I.P., Birchall, C., Skellern, M.P., Walker, J.H., Baker, P., Browne, E.L., Dewar, A.J.G., Garner, B.H., Haylock, L.A., Horne, S.L., Mason, N.S., Sands, R.J.N. and Walker, M.J. (2003). Invertebrate responses to the management of genetically modified herbicide-tolerant and conventional spring crops. II. Within-field epigeal and aerial arthropods. *Phil. Trans. R. Soc. Lond*. B **358**: 1863–1877.

Hawes, C., Haughton, A.J., Osborne, J.L., Roy, D.B., Clark, S.J., Perry, J.N., Rothery, P., Bohan, D.A., Brooks, D.R., Champion, G.T., Dewar, A.M., Heard, M.S., Woiwod, I.P., Daniels, R.E., Young, M.W., Parish, A.M., Scott, R.J., Firbank, L.G. and Squire, G.R. (2003). Responses of plants and invertebrate trophic groups to contrasting herbicide regimes in the Farm Scale Evaluations of genetically modified herbicide-tolerant crops, *Phil. Trans. R. Soc. Lond*. B **358**: 1899–1913.

Heckmann, L.H., Griffiths B.S., Caul, S., Thompson, J., Pusztai-Carey, M., Moar, W.J., Andersen, M.N. and Krogh, P.H. (2006). Consequences for *Protaphorura armata* (Collembola: Onychiuridae) following exposure to genetically modified *Bacillus thuringiensis* (Bt) maize and non-Bt maize. *Environmental Pollution* **142**: 212–216.

Higes M., Martín-Hernández, R., Garrido-Bailón, E., González-Porto, A., García-Palencia, P., Meana, A., del Nozal, M., Mayo, R. and Bernal, J. (2009). Honeybee colony collapse due to *Nosema ceranae* in professional apiaries. *Environmental Microbiology Reports* **1**(2): 110–113.

Hilbeck, A. and Schmidt, J.E.U. (2006). Another view on Bt proteins - How specific are they and what else might they do? *Biopesticides International* **2**: 1–50.

Hilbeck, A., Baumgartner, M., Fried, P.M. and Bigler, F. (1998a). Effects of transgenic *Bacillus thuringiensis* corn-fed prey on mortality and development time of immature *Chrysoperla carnea* (Neuroptera: Chrysopidae). *Environmental Entomology* **27**: 480–487.

Hilbeck, A., Moar, W.J., Pusztai-Carey, M., Filippini, A. and Bigler, F. (1998b). Toxicity of *Bacillus thuringiensis* Cry1Ab toxin to the predator *Chrysoperla carnea* (Neuroptera: Chrysopidae). *Environmental Entomology* **27**: 1255–1263.

Hilbeck, A., Moar, W.J., Pusztai-Carey, M., Filippini, A. and Bigler, F. (1999). Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator *Chrysoperla carnea*. *Entomologia Experimentalis et Applicata* **91**: 305–316.

Ho, M.-W., Ryan, A. and Cummins, J. (1999). Cauliflower mosaic viral promoter - a recipe for disaster. *Microbial Ecology in Health and Disease* **11:** 194–197.

Ho, M.-W., Ryan, A. and Cummins, J. (2000). Hazards of transgenic plants containing the cauliflower mosaic viral promoter. Authors' reply to critiques of "The cauliflower mosaic viral promoter – a recipe for disaster? *Microbial Ecology in Health and Disease* **12**: 6–11.

Hofmann F. (2007). Kurzgutachten zur Abschätzung der Maispollendeposition in Relation zur Entfernung von Maispollenquellen mittels technischem Pollensammler PMF. BfN, Bonn. www.bfn.de/fileadmin/MDB/documents/themen/agrogentechnik/07-05-31_Gutachten_Pollendeposition_end.pdf

Hofmann F. Janicke L., Janicke U., Wachter R. and Kuhn U. (2009). Modellrechnung zur Ausbreitung von Maispollen unter Worst-Case-Annahmen mit Vergleich von Freilandmessdaten. BfN Bonn.

http://www.bfn.de/fileadmin/MDB/documents/service/Hofmann_et_al_2009_Maispollen_WorstCase_Modell.pdf

Hull, R., Covey, S.N. and Dale, P.J. (2000). Genetically modified plants and the 35S promoter: assessing the risks and enhancing the debate. *Microbial Ecology in Health and Disease* **12**: 1–5.

Inomata, N. (1993). Crossability and cytology of hybrid progenies in the cross between *Brassica campestris* and three wild relatives of *B. oleracea*, *B. bourgeaui*, *B. cretica* and *B. montana*. *Euphytica* **69**: 7–17.

Jesse, L.C.H. and Obrycki, J.J. (2003). Occurrence of *Danaus plexippus* L. (*Lepidoptera* : Danaidae) on milkweeds (*Asclepias syriaca*) in transgenic Bt corn agroecosystems. *Agriculture, Ecosystems & Environment* **97**: 225–233.

Johnson, R.M., Evans, J.D., Robinson, G.E. and Berenbaum, M.R. (2009). Changes in transcript abundance relating to colony collapse disorder in honey bees (*Apis mellifera*). *PNAS USA* **105**(35): 14790–14795.

Keese, P. (2008). Risks from GMOs due to horizontal gene transfer. *Environ. Biosafety Res.* **7**: 123–149.

Kroghsbo, S., Madsen, C., Poulsen, M., Schrøder, M., Kvist, P., Taylor, M.L., Gatehouse, A., Shu, Q.Y. and Knudsen, I. (2008). Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. *Toxicology* **245**: 24–34.

Li, Y., Meissle, M. and Romeis, J. (2008). Consumption of Bt maize pollen expressing Cry1Ab or Cry3Bb1 does not harm adult green lacewings, *Chrysoperla carnea* (Neuroptera: Chrysopidae). *PLoS ONE* **3**: 1–8 (e2909).

Losey, J.E., Obrycki, J.J. and Hufbauer, R.A. (2004). Biosafety Considerations for Transgenic Insecticidal Plants: Non-Target Herbivores, Detritivores, and Pollinators. Encyclopedia of Plant and Crop Science, Marcel Dekker Inc., 153–155.

Lövei, G.L. and Apaia, S. (2005). The impact of transgenic plants on natural enemies: a critical review of laboratory studies. *Entomol. Exper. Appl.* **116**: 31–41.

Lövei, G.L., Andow, D.A. and Arpaia, S. (2009). Transgenic insecticidal crops and natural enemies: a detailed review of laboratory studies. *Environ Entomol* **38**: 293–306.

Ludy, C., and Lang, A. (2006). A 3-year field-scale monitoring of foliage-dwelling spiders (Araneae) in transgenic Bt maize fields and adjacent field margins. *Biological Control* **38**: 314–324.

Malone, L. A. (2004). Potential effects of GM crops on honey bee health, *Bee World* **85**(2): 29–36.

Marvier, M., McCreedy, C., Regetz, J. and Kareiva, P. (2007). A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. *Science* **316**: 1475–1477.

Meissle, M., Vojtech, E. and Poppy, G.M. (2005). Effects of Bt maize-fed prey on the generalist predator *Poecilus cupreus* L. (*Coleoptera* : Carabidae). *Transgenic Research* **14**: 123–132.

Mendelsohn, M., Kough, J., Vaituzis, Z. and Matthews, K. (2003). Are Bt crops safe? *Nature Biotechnology* **21**: 1003–1009.

Miki, B. and McHugh, S. (2004). Selectable marker genes in transgenic plants: applications, alternatives and biosafety. *J. Biotechnol*. **107**: 193–232.

Morin, S., Biggs, R.W., Sisterson, M.S., Shriver, L., Ellers-Kirk, C., Higginson, D. Holley, D, Gahan, L.J., Heckel, D.G., Carrie, Y., Dennehy, T.J., Brown, J.K. and Tabashnik, B.E. (2003). Three cadherin alleles associated with resistance to *Bacillus thuringiensis* in pink bollworm. *PNAS USA* **100**: 5004–5009.

Nap, J.P., Bijvoet, J. and Stiekema, W.J. (1992). Biosafety of kanamycin-resistant transgenic plants. *Transgenic Res*. **1**: 239–249.

Naranjo, S.E. (2009). Impacts of Bt crops on non-target invertebrates and insecticide use patterns. CAB Rev Perspect Agric Vet Sci Nutrit Nat Resour 4(11): 23.
http://www.cababstractsplus.org/cabreviews

Nielsen, K.M., Bones, A.M., Smalla, K. and Van Elsas, J.D. (1998). Horizontal gene transfer from transgenic plants to terrestrial bacteria--a rare event? *FEMS Microbiol. Rev*. **22**: 79–103.

O'Callaghan, M., Glare, T.R., Burgess, E.P.J. and Malone, L.A. (2005). Effects on plants genetically modified for insect resistance on nontarget organisms. *Annu. Rev. Entomol*. **50**: 271–292.

OGTR (2002a). The biology and ecology of Canola (Brassica napus), Office of the gene technology Regulator (July 2002).
http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/canola-3/$FILE/brassica.pdf

OGTR (2002b). Application for licence for dealings involving an intentional release into the environment DIR 012/2002 Commercial release of Bollgard II cotton.
http://www.health.gov.au/internet/ogtr/publishing.nsf/Content/dir012-3/$FILE/dir012finalrarmp.pdf

OGTR (2006). Risk Assessment and Risk Management Plan for DIR 066/2006 Commercial release of GM herbicide tolerance and/or insect resistant cotton lines north of latitude 22°South.
http://www.health.gov.au/internet/ogtr/publishing.nsf/Content/dir066-3/$FILE/dir066rarmp2.pdf

Parrot, W. (2008). Study of Bt impact on caddisflies overstates its conclusions: Response to Rosi-Marshall *et al*. *PNAS USA* **105**: E10.

Pascher, K., Narendja, F. and Rau, D. (2006). Feral oilseed rape – Investigations on its potential for hybridisation, Studie im Auftrag des Bundesministeriums für Gesundheit und Frauen, Forschungsberichte der Sektion IV, Band 3/2006;

Pleasants, J.M., Hellmich, R.L., Dively, G.P., Sears, M.K., Stanley-Horn, D.E., Mattila, H.R., Foster, J.E., Clark, P.L. and Jones, G.D. (2001). Corn pollen deposition on milkweeds in or near cornfields. *PNAS USA* **98**: 11919–11924.

Pons, X., Lumbierres, B., Lopez, C. and Albajes, R. (2005). Abundance of non-target pests in transgenic Bt-maize: A farm scale study. *European Journal of Entomology* **102**: 73–79.

Prasifka, P.L., Hellmich, R.L., Prasifka, J.R. and Lewis, L.C. (2007). Effects of Cry1Ab expressing corn anthers on the movement of monarch butterfly larvae. *Environmental Entomology* **36**: 228–233.

Ramessar, K., Peremarti, A., Gomez Galera, S., Naqvi, S., Moralejo, M., Muñoz, P., Capell, T. and Christou, P. (2007). Biosafety and risk assessment framework for selectable marker genes in transgenic crop plants. A case of the science not supporting the politics. *Transgenic Res*. **16**: 261–280.

Ramirez-Romero, R., Bernal, J.S., Chaufaux, J. and Kaiser, L. (2007). Impact assessment of Bt-maize on a moth parasitoid, *Cotesia marginiventris* (Hymenoptera: Braconidae), via host exposure to purified Cry1Ab protein or Bt-plants. *Crop Protection* **26**: 953–962.

Ramsay, G., Thompson, C. and Squire, G. (2003). Quantifying landscape-scale gene flow in oilseed rape. Final report of DEFRA Project RG0216: An experimental and mathematical study of the local and regional scale movement of oilseed rape transgene. http://webarchive.nationalarchives.gov.uk/20081023141438/http://www.defra.gov.uk/environment/gm/research/pdf/epg_rg0216.pdf

Rauschen, S., Eckert, J., Gathmann, A. and Schuphan, I. (2004). Impact of growing Bt-maize on cicadas: Diversity, abundance and methods. IOBC/WPRS Bulletins "Ecological risk of GMOs" **27**(3): 137–142.

Ricroch, A., Bergé, J.B. and Kuntz, M. (2009). Is the German suspension of MON810 maize cultivation scientifically justified? Transgenic Res. http://www.springerlink.com/content/r6052757667ng364/fulltext.pdf .

Rodrigo-Simón, A., de Maagd, R.A., Avilla, C., Bakker, P.L., Molthoff, J., González-Zamora, J.E. and Ferré, J. (2006). Lack of detrimental effects of *Bacillus thuringiensis* Cry toxins on the insect predator *Chrysoperla carnea*: a toxicological, histopathological, and biochemical analysis. *Applied and Environmental Microbiology* **72**: 1595–1603.

Romeis, J., Meissle, M. and Bigler, F. (2006). Transgenic crops expressing *Bacillus thuringiensis* toxins and biological control. *Nature Biotechnology* **24**: 63–71.

Rose, R.I., Dively, G.P. and Pettis, J. (2007). Effects of Bt corn pollen on honey bees: emphasis on protocol development. *Apidologie* **38**: 368–377.

Rosi-Marshall, E.J., Tank, J.L., Royer, T.V., Whiles, M.R., Evans-White, M., Chambers, C., Griffiths, N.A., Pokelsek, J. and Stephen, M.L. (2007). Toxins in transgenic crop by products may affect headwater stream ecosystems. *PNAS USA* **104**: 16204–16208.

Saxena, D., Flores, S. and Stotzky, G. (2002). Bt toxin is released in root exudates from 12 transgenic corn hybrids representing three transformation events. *Soil Biology and Biochemistry* **34**: 133–137.

SCAN (1996). Opinion of the Scientific Committee for Animal Nutrition on the safety for animals of certain genetically modified maize lines notified by Ciba Geigy in accordance with Directive 90/220/EEC for feedingstuff use.
http://ec.europa.eu/food/fs/sc/oldcomm6/other/13_en.pdf

SCAN (1997). Opinion of the Scientific Committee for Animal Nutrition on the supplementary question 88 concerning new data submitted by Austrian authorities on the safety for animals of certain genetically modified maize lines notified by Ciba Geigy in accordance with Directive 90/220/EEC for feedingstuff use.
http://ec.europa.eu/food/fs/sc/scan/out133_en.pdf

SCF (1996). Opinion of the Scientific Committee on Food Opinion on the potential for adverse health effects from the consumption of genetically modified maize (*Zea mays* L).
http://ec.europa.eu/food/fs/sc/oldcomm7/out02_en.html

SCF (1997). Opinion of the Scientific Committee on Food on the additional information from the Austrian Authorities concerning the marketing of Ciba Geigy Maize.
http://ec.europa.eu/food/fs/sc/oldcomm7/out01_en.html

Schmidt, J.E.U., Braun, C.U., Whitehouse, L.P. and Hilbeck, A. (2009). Effects of activated Bt transgene products (Cry1Ab, Cry3Bb) on immature stages of the ladybird *Adalia bipunctata* in laboratory ecotoxicity testing. *Arch. Environ. Contam. Toxicol*. **56**: 221–228.

Schmidt, K., Wilhelm, R., Schmidtke, J., Beißner, L., Mönkemeyer, W., Böttinger, P., Sweet, J. and Schiemann, J. (2008). Farm questionnaires for monitoring genetically modified crops: a case study using GM maize. *Environmental Biosafety Research* **7**: 163–179.

Schorling, M. and Freier, B. (2006). Six-year monitoring of non-target arthropods in Bt maize (Cry 1Ab) in the European corn borer (*Ostrinia nubilalis*) infestation area Oderbruch (Germany). *Journal of Consumer Protection and Food Safety* **1**(S1): 106–108.

SCP (1996). Opinion of the Scientific Committee for Pesticides on the Use of Genetically Modified Maize Lines Notified by Ciba-Geigy.
http://ec.europa.eu/food/fs/sc/scp/gmo96-97/out01_en.html

SCP (1997). Further Report of the Scientific Committee for Pesticides on the Use of Genetically Modified Maize Lines.

http://ec.europa.eu/food/fs/sc/scp/gmo96-97/out02_en.html

SCP (1998a). Opinion of the Scientific Committee on Plants regarding the genetically modified, insect resistant maize lines notified by the Monsanto Company.
http://ec.europa.eu/food/fs/sc/scp/out02_en.html

SCP (1998b). Opinion of the Scientific Committee on Plants Regarding the Genetically Modified, Glufosinate-Tolerant Rape Notified by the Agrevo Company (Notification C/UK/95/M5/1)
http://ec.europa.eu/food/fs/sc/scp/out03_en.html

SCP (1998c). Opinion of the Scientific Committee on Plants Regarding "Submission for Placing on the Market of Glufosinate Tolerant Corns (*Zea mays*) Transformation Event T25" by the Agrevo Company
http://ec.europa.eu/food/fs/sc/scp/out04_en.html

SCP (1998d). Opinion of the Scientific Committee on Plants regarding the Glufosinate tolerant, hybrid rape derived from genetically modified parental lines (MS8 x RF3) notified by Plant Genetic Systems (notification C/B/96/01) (Submitted by the Scientific Committee on Plants, 19 May 1998
http://ec.europa.eu/food/fs/sc/scp/out09_en.html

SCP (1999a). Opinion of the Scientific Committee on Plants on Bt-resistance monitoring.
http://ec.europa.eu/comm/food/fs/sc/scp/out35_en.html

SCP (1999b). Opinion of the Scientific Committee on Plants, adopted on 18 May 1999, on the Invocation by Greece of Article 16 ('safeguard' clause) of Council Directive 90/220/EEC with respect to a genetically modified oilseed rape notification C/UK/95/M5/1 (Agrevo) - (SCP/GMO/148-final)
http://ec.europa.eu/food/fs/sc/scp/out36_en.html

SCP (2000). Opinion of the Scientific Committee on Plants on the invocation by Germany of Article 16 of Council 90/220/EEC regarding the genetically modified BT-MAIZE LINE CG 00256-176 notified by CIBA-GEIGY (now NOVARTIS), notification C/F/94/11-03.
http://ec.europa.eu/comm/food/fs/sc/scp/out78_gmo_en.html

SCP (2001a). Opinion of the Scientific Committee on Plants on the invocation by Austria of Article 16 of Council Directive 90/220/EEC regarding a genetically modified maize line T25 notified by AGREVO FRANCE (now AVENTIS CROPSCIENCE, REF. C/F/95/12-07).
http://ec.europa.eu/comm/food/fs/sc/scp/out109_gmo_en.pdf

SCP (2001b). Opinion of the Scientific Committee on Plants regarding "submission for placing on the market of glufosinate tolerant maize (Zea mays) transformation event T25" by the Agrevo company (now Aventis Cropscience).
http://ec.europa.eu/comm/food/fs/sc/scp/out108_gmo_en.pdf

SCP (2001c). Opinion of the Scientific Committee on Plants on the invocation by the United Kingdom of Article 16 of Council Directive 90/220/EEC regarding genetically modified maize line T25 notified by Agrevo (now Aventis Cropscience, ref. C/F/95/12-07). http://ec.europa.eu/food/fs/sc/scp/out110_gmo_en.pdf

Séralini, G.E., Cellier, D, and Spiroux de Vendomois, J. (2007). New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. *Archives of Environmental Contamination and Toxicology* **52**: 596–602.

Shelton, A., Naranjo, S., Romeis, J., Hellmich, R., Wolt, J., Federici, B., Albajes, R., Bigler, F., Burgess, E., Dively, G., Gatehouse, A., Malone, L., Roush, R., Sears, M. and Sehnal, F. (2009). Setting the record straight: a rebuttal to an erroneous analysis on transgenic insecticidal crops and natural enemies. *Transgenic Res* DOI 10.1007/s11248-009-9260-5

Spök, A., Gaugitsch, H., Laffer, S., Pauli, G., Saito, H., Sampson, H., Sibanda, E., Thomas, W., Van Hage, M. and Valenta, R. (2005). Suggestions for the assessment of the allergenic potential of genetically modified organisms. *International Archives of Allergy and Immunology* **137**: 167–180.

Spök, A., Hofer, H., Lehner, P., Valenta, R., Stirn, S. and Gaugitsch, H. (2004). Risk assessment of GMO products in the European Union. *Umweltbundesamt Wien. Berichte, Band* 253. July 2004.

Spök, A., Hofer, H., Valenta, R., Kienzl-Plochberger, K., Lehner, P. and Gaugitsch, H. (2003a). Toxikologie und Allergologie von GVO-Produkten – Teil 1: Empfehlungen zur Standardisierung der Sicherheitsbewertung von gentechnisch veränderten Pflanzen auf Basis der Richtlinie 90/220/EWG (2001/18/EG). *Umweltbundesamt Wien, Monographien Band* **109**: 214 pages.

Spök, A., Hofer, H., Valenta, R., Kienzl-Plochberger, K., Lehner, P., Stirn, S. and Gaugitsch, H. (2003b). Toxikologie und Allergologie von GVO-Produkten – Teil 2a: Untersuchung zur Praxis und Empfehlungen zur Standardisierung der Sicherheitsbewertung von gentechnisch veränderten Lebensmitteln. *Umweltbundesamt Wien, Monographien Band* **164A**: 359 pages.

Spök, A., Karner, S., Stirn, S. and Gaugitsch, H. (2003c). Toxikologie und Allergologie von GVO-Produkten – Teil 2b: Untersuchung zur Sicherheitsbewertung von gentechnisch veränderten Lebensmitteln in der EU und den USA. *Umweltbundesamt Wien Monographien Band* **164B**: 163 pages.

Squire, G.R., Beeg, G.S. and Askew, M. (2003a). The potential for oilseed rape feral (volunteer) weeds to cause impurities in later oilseed rape crops. Final report of the DEFRA project: Consequences for Agriculture of the Introduction of Genetically Modified Crops, RG0114. http://webarchive.nationalarchives.gov.uk/20081023141438/http://www.defra.gov.uk/environment/gm/research/pdf/epg_rg0114.pdf

Squire, G.R., Brooks, D.R., Bohan, D.A., Champion, G.T., Daniels, R.E., Haughton, A.J., Hawes, C., Heard, M.S., Hill, M.O., May, M.J., Osborne, J.L., Perry, J.N., Roy, D.B.,

Woiwod, I.P. and Firbank, L.G. (2003b). On the rationale and interpretation of the Farm Scale Evaluations of genetically modified herbicide-tolerant crops, *Phil. Trans. R. Soc. Lond*. B **358**: 1779–1799.

SSC (1999). Opinion of the Scientific Steering Committee on Antimicrobial Resistance. European Commission. Directorate-General XXIV.

Strid, A. and Tan, K. (2002). *Flora Hellenica*, p. 280-286.

Tinland, B., Delzenne, P. and Pleysier, A. (2007). Implementation of a post-market monitoring for insect-protected maize MON 810 in the EU. *Journal of Consumer Protection and Food Safety* **2**(S1): 7–10.

Toschki, A., Hothorn, L.A. and Roß-Nickoll, M. (2007). Effects of cultivation of genetically modified Bt maize on epigeic arthropods (Araneae; Carabidae). *Environmental Entomology* **36**: 967–981.

Velimirov, A., Binter, C. and Zentek, J. (2008). Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice. Veterinary University of Vienna and Research Institute for Organic Agriculture, Vienna, Austria, 105 pp.

Wilkinson, M.J., Elliott, L.J., Allainguillaume, J., Shaw, M.W., Norris, C., Welters, R., Alexander, M., Sweet, J. and Mason, D.C. (2003). Hybridization between *Brassica napus* and *B. rapa* on a national scale in the United Kingdom. *Science* **302**: 457–459.

Wold, S. J., Burkness, E. C., Hurchison, W. D., and Venette, R. C. (2001). Infield monitoring of beneficial insect populations in transgenic corn expressing a *Bacillus thuringiensis* toxin. *J. Entomol. Sci*. **36**(2): 177–187.

Wolfenbarger, L.L., Naranjo, S.E., Lundgren, J.G., Bitzer, R.J. and Watrud, L.S. (2008). Bt crop effecs on functional guilds of non-target arthropods: a meta-analysis. *PLoS ONE* **3**: 1–11 (e2118).

ZKBS (1999). Stellungnahme der ZKBS zur Biologischen Sicherheit von Antibiotika-Resistenzgenen im Genom gentechnisch veränderter Pflanzen. Zentrale Kommission für die Biologische Sicherheit, Bundesgesundheitsblatt: 975–978.

ZKBS (2009). Stellungnahme der ZKBS zur Risikobewertung von MON810 – Neue Studien zur Umweltwirkung von MON810.
http://www.bvl.bund.de/cln_027/nn_1208608/DE/06__Gentechnik/093__ZKBS/01__Allg__Stellungnahmen/04__pflanzen/Mon810-Neubewertung-Juli09.html

Zwahlen, C., Hilbeck, A., Gugerli, P. and Nentwig, W. (2003b). Degradation of the Cry1Ab protein within transgenic *Bacillus thuringiensis* corn tissue in the field. *Molecular Ecology* **12**: 765–775.

Zwahlen, C., Hilbeck, A., Howald, R. and Nentwig, W. (2003a). Effects of transgenic Bt corn litter on the earthworm *Lumbricus terrestris*. *Molecular Ecology* **12**: 1077–1086.

J. PUBLIC RESEARCH AND REGULATION INITIATIVE

Public Research & Regulation Initiative
Secretariat
Julianalaan 67
2628BC Delft
The Netherlands
Phone: +31-15-278-9289
Email: info@pubresreg.org
Website: www.pubresreg.org

To:
Dr. Ahmed Djoghlaf
Executive Secretary
Convention on Biological Diversity
Montreal, Canada
Fax: +1.514.288-6588

Re: Notification No. 2009-103

14 September 2009

Dear Dr. Djoghlaf,

On behalf of the Steering Committee of the Public Research and Regulation Initiative (PRRI) I hereby send you our response to the request for scientifically sound information regarding the identification of living modified organisms (LMOs) or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

PRRI very much welcomes this kind of forward-looking explorations by the MOP. Having said that, PRRI also believes that some distinctions need to be made in order to help focus the next discussions in the MOP.

The overall objective of the Cartagena Protocol on Biosafety (CPB) is "to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health".

An important phrase in this objective is ***"that may have adverse effects"***. This wording is quite different from the more specific language of article 8g of the CBD, which states that Parties shall establish and maintain national biosafety systems to control the use and release of LMOs that ***are likely to have adverse environmental impacts*** that could affect the conservation and sustainable use of biological diversity, taking also into account the risks to human health. This difference in wording is understandable, because while it is quite feasible for a country to identify for its own national situation which LMOs are likely or unlikely to have adverse environmental effects, the qualifications "likely" and "unlikely" cannot always be extrapolated directly to the situation in other countries. This is why article 19.3 of the CBD and article 1 of the CPB speak of LMOs "that may have adverse effects". Relevant in this context is also article 7.4 of the CPB, which says that the procedures of the CPB shall not apply to LMOs identified by the MOP as "being not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health".

One of the major benefits of the CPB is that it contains an internationally agreed methodology of risk assessment through which receiving countries can assess whether LMOs are likely or unlikely to have adverse effects. In this context, PRRI participates with enthusiasm in the work on the "Road Map" of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (AHTEG), of which we hope that it will assist risk assessors in reaching their goal without unnecessary detours.

A key task of all biosafety regulations, including the CPB, is to identify in a scientifically sound and transparent manner which types of LMOs are likely to have adverse effects and which LMOs are unlikely to have adverse effects. For this task we can make use of the methodology of the risk assessment in the CPB as well as of data on the actual experiences with releases of LMOs.

We therefore advise that for the benefit of the discussions at MOP5 the question " which LMOs or specific traits may have adverse effects"? be split in a number of specific questions:

1. Are there LMOs or traits that *have caused adverse effects*?
2. Are there LMOs or traits of which experience shows that they *are unlikely to cause adverse effects*?
3. Are there LMOs or traits of which risks assessment has shown that they are *likely to cause adverse effects*?
4. Are there LMOs or traits of which risks assessments suggest that they *are unlikely to cause adverse effects*?

In addition, it is also important to bear in mind what is meant by '*adverse effects*'. An overarching general principle of the risk assessment as laid down in the CPB is that risk assessment is comparative, i.e. any identified risks should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment. This is why conclusions on risk assessment in the field of biosafety typically refer to whether or not the assessed LMO is "as safe as its conventional counterpart with respect to potential effects on the environment, taking also into account human health".

In this perspective, PRRI offers the following observations in answer to the above four questions:

1. Are there LMOs or traits that have caused adverse effects?

No. Since the first application of genetic modification in the 80s, many thousands of field trials have been conducted with GM organisms (to date mostly plants), and since 1996 many hundreds of millions of hectares have been planted with GM crops by many millions of farmers and consumed by hundreds of millions of consumers in developed and developing countries, without any verifiable reports of adverse effects on the environment or human or animal health.

In fact, taking a broader look, experience with those GM crops has shown environmental and socio-economic benefits in terms of increases in yield, significant reductions in use of pesticides, fossil fuels and soil erosion, less mycotoxins in grains, as well as increased farmers health and income.

2. Are there LMOs or traits of which experience shows that they are unlikely to cause adverse effects?

The above mentioned experience with the GM crops that have been commercialized thusfar and grown on a large scale, over a long period and by many farmers, suggests that these GM crop plants are unlikely to have adverse effects on the environment, human or animal health. Given that substantive experience shows that these GM crop plants (mainly soybeans, maize, cotton, and oilseed rape, with introduced pest resistance or herbicide tolerance, or a combination of both traits), are unlikely to have adverse effects, they could be eligible for exemption in accordance with article 7.4 of the CPB.

3. Are there LMOs or traits of which risks assessment suggests that they are likely to cause adverse effects?

Prior to the field trials and large scale commercial planting of GM organisms referred to above, many risk assessments have been conducted in many countries. To the best of our knowledge, in no case have authorisations for field trials or commercialisation been denied on the basis of scientifically sound indications of adverse environmental impacts.

4. *Are there LMOs or traits of which risks assessments suggest that they are unlikely to cause adverse effects?*

Bearing in mind that the method of transformation itself is neutral, i.e. that there are no risks related to process of transformation, PRRI believes that there are several types of LMOs and traits for which - on the basis of the characteristics of the host plant, the functioning of the inserted genes and experience with the resulting GMO - it can be concluded that they are as safe as its conventional counterpart with respect to potential effects on the environment, taking also into account human health.

PRRI stands ready to expand on the points made in this letter.

Yours sincerely,

Em. Prof. Marc van Montagu
Chairman of the Steering Committee of the Public Research and Regulation Initiative