RAPPORTO TECNICO

GYM4SID: UN CASO DI TRAINING ESPERIENZIALE IN UN CONTESTO MULTIDISCIPLINARE

di

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1. Introduzione

Il presente rapporto tecnico illustra l'attività di training esperienziale denominata 'Gym4SID', ideata e sviluppata dalle autrici nell'ambito del progetto di scuola pilota **"Co-design di una school4SID"**.

Il rapporto esamina nello specifico la fase della costruzione della proposta di training esperienziale, il contenuto della stessa, nonché la preparazione e lo svolgimento del training ed infine la valutazione ex post dell'intero progetto, soffermandosi sulle indicazioni rilevanti per l'attività in oggetto.

La disamina del processo di costruzione e di realizzazione dell'attività di training esperienziale nonché l'analisi finale del prodotto consente anche di trarre indicazioni utili e prodromiche alla proposizione di azioni analoghe.

Il materiale, in lingua inglese, predisposto per la realizzazione dell'attività e che viene allegato, è da considerare parte integrante del presente rapporto.

L'attività **'**Gym4SID' è stata realizzata nell'ambito della Scuola di Scienza in processi decisionali e negoziazione School4SID (https://school4sid.cnr.it/), ideata e coordinata da Pier Francesco Moretti dell'Ufficio Relazioni Europee e Internazionali del CNR. Si tratta di un modello di formazione che mira a introdurre un nuovo approccio per il supporto scientifico al processo decisionale e alla negoziazione. Il primo corso pilota 'Co-design di una school4SID' è stato tenuto per una comunità diplomatica internazionale composta di membri di delegazioni dei paesi presso l'Unione Europea, referenti di iniziative intergovernative comunitarie e *science diplomats* a Gaeta dal 5 al 7 giugno 2019 in collaborazione con la Fondazione Caboto: https://school4sid.cnr.it/event/pilot-school/.

2. Costruzione della proposta di training esperienziale

Scelta metodologica: la simulazione

La proposta avente per oggetto un laboratorio partecipativo denominato Gym4SID[1] nasce dalla opportunità di proporre un intervento formativo, che, partendo da un tema ben preciso e funzionale alla complessità del progetto pilota School4SID, potesse offrire anche un esercizio di applicazione concreta delle conoscenze trasferite, attraverso il metodo esperienziale.
Pertanto, nell'ottica di introdurre nel progetto pilota elementi aggiuntivi e al tempo stesso complementari, sia da un punto di vista dei contenuti che della metodologia, considerato che tutte le lezioni si svolgevano infatti in modalità frontale, si è deciso di proporre un esercizio di simulazione con le seguenti finalità:

- testare la pratica di un processo decisionale attraverso il coinvolgimento di "scienziati" e diplomatici nel lavoro collaborativo su un caso concreto;
- testare l'approccio multidisciplinare della Scuola;
- affrontare le incertezze scientifiche nel processo decisionale, comprese le loro implicazioni per le conclusioni della valutazione, l'applicazione del principio di precauzione, nonché i temi interconnessi dell'accesso alle informazioni in materia ambientale e della comunicazione dei rischi;
- osservare e comprendere la dinamica del processo, comprese le relazioni interpersonali.

Scelta del tema: il principio precauzionale

In prima battuta, è stata avviata un'attenta analisi delle numerose tematiche[2] proposte dalla scuola quali esempi di consulenza scientifica alle decisioni per interventi a lungo e breve termine.
Al termine di tale analisi, e considerando che questa attività di training veniva associata ad uno degli interventi previsti nella Scuola, cioè all'*International legal aspects*[3], si è ritenuto che il tema più adatto da trattare in questo contesto fosse il principio precauzionale.
Infatti, il principio precauzionale si presta ad essere oggetto di un esame degli aspetti giuridici internazionali ed europei rilevanti ed è, al tempo stesso, un principio generale della dottrina dello sviluppo sostenibile che è molto utilizzato in tutti i settori scientifici e tecnologici, soprattutto negli ambiti di nuove tecnologie e di avanguardia scientifica.
Inoltre, questo principio, già introdotto in molti ordinamenti nazionali, nell'ordinamento europeo così come in molti trattati internazionali, si presta perfettamente ad offrire degli esempi concreti

[1] Il nome del format contiene l'acronimo della Scuola (School4SID) e richiama il senso di esercizio pratico Gym.
[2] Tra le varie tematiche proposte dalla scuola, e oggetto di interventi specifici, si segnalano: fondamenti dei sistemi complessi, la modellazione, i sistemi cognitivi, l'intelligenza artificiale e i diversi approcci a sostegno della politica; il focus finale sulle sfide del Mar Mediterraneo, come uno degli esempi di complessità in termini di sistema socio-ambientale e di governance. Per il programma dettagliato si rinvia a https://school4sid.cnr.it/event/pilot-school/programme.
[3] Si rinvia all'Allegato 3 contenente il PPT della presentazione su International Legal Aspects, dal titolo "International Law: a case study on the precautionary principle".

di gestione del processo di adozione delle decisioni in tutti i casi in cui vi sia incertezza scientifica in relazione all'impatto di un'attività umana sull'ambiente e sulla salute umana.

Una volta scelto il tema che rappresentasse anche una sorta di *trait d'union* tra molti degli interventi programmati, si è deciso di avviare una ricerca della dottrina, delle fonti e del materiale rilevante per costruire il caso che sarebbe stato oggetto della simulazione.

Nella fattispecie, Gym4SID è incentrato su un caso di diritto internazionale ispirato concretamente ad un ricorso presentato davanti alla Corte di giustizia dell'Unione europea da un'organizzazione non governativa per l'annullamento di una decisione della Commissione europea in merito all'autorizzazione concessa a favore di una multinazionale per la commercializzazione di alimenti e mangimi geneticamente modificati.

Il primo elaborato è stato concepito per essere condiviso con il comitato tecnico-scientifico e organizzativo della Scuola come base di discussione per revisioni e integrazioni della proposta, al fine di valutarne la corrispondenza con l'approccio generale. A valle dell'approvazione del razionale riportato di seguito, è stato sviluppato il materiale a supporto, per il passaggio alla fase operativa.

Proposta di training approvata (in inglese)

Rationale and objectives: (Testing) The GYM4SID

The proposed exercise aims at turning into practice decisional process by grouping 'scientists' and 'diplomats' to work together, bringing their expertise while showcasing to what extent the multidisciplinary approach of the School can support the purpose of orienting an informed decision taking, towards the improvement of the objectivity of expert advice.

In this way, the dynamic, including interpersonal, that lays beyond decision-taking can be observed for an *ex-post* analysis to evaluate the feasibility of developing a tailored activity within the School4SID.

The methodology foreseen at first the identification of a suitable while attractive concrete topic chosen to stimulate the discussion and favouring the active participation of players. Teams are pre-formed by the organizers in order to balance the expertise. The 'game' is proposed and explained during the school days without any pre-notice, not to generate any pressure nor additional burden.

In the present case, the exercise is developed in collaboration with one of the scientists, whose intervention focuses on *International law*, and in particular the precautionary principle, setting the scene on the general background of the discipline. The idea is to work on a real case brought before

the Court of Justice of the European Union (and not yet decided), that has been "manipulated" in a creative manner in order to simply the game and render it more attractive.
The main idea is to cope with the precautionary principle's application to the commercialisation of GMOs in the EU territory as well as with the interconnected themes of access to information in environmental matters and risk communication. While the lack of consistent application of this principle adds complexity to the framework, it provides the opportunity to stimulate further discussion at the science-policy interface, e.g. on the environmental and health protection vs innovation and technological progress.

Specifically, the present Gym4SID test aims at:

- favour an objective debate and confrontation on a situation of scientific uncertainty where economic interests faces the application of the precautionary principle (sensu Rio+92) at least for a temporary duration;
- reflect on how the results of such debate are communicated, with particular emphasis on the relevance of 'risk communication', and on its different impacts.

From a legal perspective, it seeks at the same time to tackle the following technical issues:

- the level of jurisdiction on environmental matters (the authorization to commercialize a product is given by countries);
- the environmental standard restrictions;
- the so-called 'reversal of the burden of proof', giving to the organization/company requiring the authorization for commercializing a product the responsibility to evaluate the risks;
- the misuse of international general principles non-binding conventions, e.g. Aarhus.

Disclaimer

The case is inspired by the appeal brought on 14 February 2017 by TestBioTech eV, European Network of Scientists for Social and Environmental Responsibility eV, Sambucus eV against the judgment of the General Court (Fifth Chamber) delivered on 15 December 2016 in Case T-177/13, and modified for the purposes of the exercise. References to real parties are not intended to compromise any actors nor outcomes of the trial. For the smooth and effective running of the exercise, while participants are welcome to deploy different instruments as well as imagination to challenge and convince the Court, compliance with actual jurisdictional rules is deemed necessary for framing the range of application of the exercise. For instance, it has to be duly considered that the case develops in Europe and judged by European Institutions (i.e. recognizing the EU treaty whose main framework is at first economical) where the soybean is commercialized while it is cultivated abroad.

Description of the case

TestBioTech eV brings before the Court of EU an application pursuant to Article 263 Treaty on the Functioning of the European Union (TFEU) for annulment of a decision of the European Commission (the contested decision) which rejected the applicants' requests for Internal Review of the Commission Decision (the authorization decision) granting a market authorization under Regulation No 1829/2003 on genetically modified food and feed to Monsanto Europe SA for its genetically modified soybean "MON 87769 x MON 89788".

The parties

- TestBioTech eV, the applicant, is a not-for-profit association to promote independent research and public debate on the impacts of biotechnology, established in Germany. It is supported by the European Network of Scientists for Social and Environmental Responsibility, established in Germany;
- European Commission, the defendant, is supported by the United Kingdoms and the European Food Safety Authority;
- Monsanto Europe SA, established in Belgium and Monsanto Company, established in Delaware (United States) aa private companies supporting the position of the EC;
- European Court, Fifth Chamber, based in Brussels.

How the exercise is practically developed

The case is presented during the first day dinner, sharing with all participants a brief text including positions, while the groups are communicated the day after the breakfast time in order to favour some discussion during the breaks through the day *(10').*

The exercise is developed after the *International legal aspects* talk in two steps: (1) the Teams works on the case anticipated the night before *(20')* by analysing the background material and discussing internally to formulate a brief argumentation text (500-1000 words). It is important that the group identifies a spokeperson in charge of presenting the argumentation to all Teams *(5' each)*; (2) after hearing the speech of all Teams, each of them works *(15')* to finalize the text providing a final written argumentation to the Court. This might be slightly improved compared to the first version after hearing the presentations of the other Teams. Total duration: 50'.

The decision of the Court is communicated during the dinner *(15')*.

3. Preparazione dell'attività

Dalla lettura e sintesi delle fonti normative, dalla prassi giudiziaria e del materiale tecnico-giuridico rilevante e, grazie al supporto esperto dei colleghi esperti del Dipartimento di Scienze Bioagroalimentari del CNR per l'individuazione di documenti tecnico-scientifici adeguati all'argomento scelto, è stato elaborato un Dossier, contenente i testi normativi e il materiale a supporto per guidare i partecipanti nei rispettivi compiti. Nel paragrafo seguente è riportato, in lingua inglese, l'indice del Dossier, riportato nella sua versione completa nell'Allegato 1. Gli ultimi due passaggi preparatori sono stati l'elaborazione della presentazione delle 'regole' dell'esercizio (Allegato 2) e la pre-composizione ragionata dei gruppi di partecipanti, che comprendono sia i docenti che i discenti della Scuola. L'eterogeneità delle competenze e settori di provenienza in ciascun gruppo è un elemento caratterizzante questo tipo di approccio formativo.

The Dossier (Index)

- Background to the dispute;
- TestBioTech eV comment on the Monsanto SA concerned assessment;
- EFSA Panel on Genetically Modified Organisms (GMO, European Food Safety Authority (EFSA), Parma, Italy, *Scientific opinion on application (EFSA-GMO-NL-2009-73) for the placing on the market of insect-resistant and herbicide-tolerant genetically modified soybean MON 87701 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto*, EFSA Journal 2012;10(2):2560 (Abstract & Summary);
- Marco Mazzara, Encarnacion Luque Perez, Emanuele Grazioni, Guy Van den Eede, *Report on the Verification of the Performance of MON87701 and MON89788 Event-specific Methods on the Soybean Event MON87701 x MON89788 Using Real-time PCR*, European Commission Joint Research Center & European Union Reference Laboratory for GM Food and Feed, 14 Feb 2012;
- Selected Articles of *Regultation No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed* and *Regulation No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies*;
- Ruth Mampuys, COGEM, *Socio-economic Considerations in Regulatory Decision-making on Genetically Modified Crops* (Abstract & Introduction), and Michael Wach, *Risk Communication*, (Abstract), in Ministero dell'Ambiente e della Tutela del Territorio e del Mare (MATTM), International Centre for Genetic Engineering and Biotechnology (ICGEB), Collection of Biosafety Reviews, Vol. 10, 2018.

GYM Teams' composition/suggested subgroups[4]

Team 1, TestBioTech eV: Annabelle Ascher, Salvatore Capasso, Gian Vittorio Caprara, Amedeo Cesta, Eszter Lakos, Sergej Mozina, Fabio Trincardi. Supporting Subteam: European Network of Scientists for Social and Environmental Responsibility eV.

Team 2, the European Commission: Marga Gual Soler, Fausto Guzzetti, Stephan Kuster, Frank Möschler, Roberto Natalini, Andrea Passarella, Alessandro Rossi, Giulia Tercovich. Supporting Subteam 1: EFSA; Supporting Subteam 2: the UK Government.

Team 3, Monsanto SA: Lisa Almesjö, Lorenzo Orsi, Omar Cutajar, Fabio Fiorentino, Cécile Heriard, Petra Manderscheid, Elisa Palazzi, Mario Paolucci, Maurizio Ribera d'Alcalà. Supporting Subteam: in house due diligence officers.

Team 4, the European Court: Gemma Andreone, Emiliano Bruner, Laura Macchi, Pier Francesco Moretti.

References (in addition to the background material)

- European Parliament, The precautionary principle, Definitions, applications and governance, EPRS, European Parliamentary Research Service, Author: Didier Bourguignon, Members' Research Service December 2015 — PE 573.876, ISBN 978-92-823-8480-0, doi:10.2861/821468;
- Kenisha Garnett and David J. Parsons, Multi-Case Review of the Application of the Precautionary Principle in European Union Law and Case Law, Risk Analysis, Vol. 37, No. 3, 2017, DOI: 10.1111/risa.12633.

Acknowledgments

Technical support by the National Research Council Bioagrofood Department: Mauro Gamboni, Rosanna Mabilia, Giada Tassone.

[4] Rispetto alla proposta, ci sono state alcune variazioni e integrazioni alla composizione delle squadre dovute per esempio alla presenza di osservatori che si è deciso di coinvolgere in modo estemporaneo.

4. Svolgimento dell'attività

Di seguito si ripercorrono cronologicamente i vari momenti dell'attività di training esperienziale distribuiti nel corso dei tre giorni di durata del workshop secondo il programma riportato nella tabella di seguito. È opportuno sottolineare che per un siffatto esercizio - basato in gran parte sul raggiungimento di un buon grado di affiatamento all'interno di gruppi composti prevalentemente da perone che non si conoscono e ampiamente focalizzato su dinamiche interpersonali e sull'uso della comunicazione verbale e non verbale nel perseguimento degli obiettivi - occorre diluire il ritmo degli interventi lungo tutto il periodo di formazione concedendo un tempo adeguato, che può essere trovato anche in momenti informali esterni allo spazio delle lezioni come pause, cene, passeggiate.

Programma Pilot School	
05 Giugno 2019, Hotel Serapo 14:00 - 18:00	
14:00 - 14:30 Welcome and introduction	
(13:00 – 14:00 Light Lunch)	
Welcome	Maria Rosa Valente
Rationale and aims of the school	Pier Francesco Moretti
14:30 - 15:30 Short-term and long-term preparedness	
Response and Resiliency to emergencies	Fausto Guzzetti
Mitigation and Adaptation to climate change	Elisa Palazzi
15:30 - 18:00 Predicting the future	
Minds	Emiliano Bruner
Artificial Intelligence	Amedeo Cesta
16:30 – 17:00 Break	
Game Theory	Roberto Natalini
Metrics and statistics	Luigi Mazari Villanova
06 Giugno 2019, Signora del Vento 09:30 - 18:00	
09:30 - 12:30 Support to policy	
Psycology of decisions and statistics for mortals	Laura Macchi
Psycology of political reasoning	Gian Vittorio Caprara
Conflict resolution	Lorenzo D'Orsi
11:00 – 11:30 Break	
Intelligence	Alessandro Rossi
Governance of complexity	Pier Francesco Moretti
12:30 - 14:00 Light Lunch	
14:00 - 16:30 Approaches and instruments	
Computational models of human learning	Mario Paolucci
Multi-Modeling	Massimo Bernaschi

Programma Pilot School	
Economics	Salvatore Capasso
15:30 – 16:00 Break	
International legal aspects	**Gemma Andreone**
16:30 - 18:00 Reflections/exercise	
Towards a Gym4SID: a joint experiment	**Margherita Cappelletto**
07 Giugno 2019, ITS Caboto 09:00 - 13:00	
09:00 - 13:00 Knowledge-based support to management/governance of Seas and Oceans	
Complexity of marine environment	Maurizio Ribera d'Alcalà
Understanding and managing fisheries	Fabio Fiorentino
Maritime Spatial Planning	Alessandro Sarretta
Big data	Federico Falcini
10:30 – 11:00 break	
Cyber-physical convergence	Emilio Fortunato Campana
Regional Approach	Fabio Trincardi
Report of the school and next steps	Pier Francesco Moretti
13:00 – 14:00 Light Lunch	

Tabella 1 – Programma della Scuola pilota School4SID, Gaeta, 5-7 giugno 2019

Presentazione delle 'regole del gioco' e presentazione delle squadre (giorno 1)

In maniera informale, al termine delle sessioni del primo giorno di Workshop ma senza che fosse ufficialmente previsto nel programma (vedi Tabella 1), viene brevemente svelato il contenuto dell'attività indicata in programma per il giorno 2. Si illustrano modalità e tempi di svolgimento e si presentano le squadre (cfr. paragrafo 'GYM Teams' composition/suggested subgroups') precedentemente assortite dagli organizzatori, anche per creare un effetto sorpresa. La presentazione relativa a questa fase è riportata nell'Allegato 2.

Figura 1 – Margherita Cappelletto (CNR-DSSTTA) presenta le 'regole del gioco' (Crediti: Roberto Bellucci, CNR-DSSTTA)

Distribuzione del Dossier alle squadre e identificazione del portavoce (giorno 2)

Poco prima della pausa pranzo del secondo giorno, vengono distribuite alcune copie del Dossier (3 per squadra, cfr. Allegato 1). Per ciascuna squadra viene identificato un portavoce che, oltre a coordinare le attività del gruppo, rappresenterà la squadra in seno alla Corte. I gruppi si mettono subito al lavoro utilizzando anche i momenti informali come dimostrano le seguenti immagini.

Lezione su 'International legal aspects' (giorno 2)

La lezione (https://school4sid.cnr.it/science/why/international-legal-aspects), tenuta da Gemma Andreone (CNR-ISGI) e riportata nell'Allegato 3, affronta il caso studio sul principio precauzionale. Essa è funzionale al trasferimento di contenuti tecnici che connotano il contesto di svolgimento del laboratorio formativo.

Figura 2 – Gym4SID, squadre al lavoro!/1 (Crediti: Pier Francesco Moretti, CNR-UREI)

Figura 3 - Squadre al lavoro!/2 (Crediti: Roberto Bellucci, CNR-DSSTTA)

Figura 4 - Squadre al lavoro!/3 (Crediti: Roberto Bellucci, CNR-DSSTTA)

Udienza (giorno 2)

Con l'intervento 'Towards a Gym4SID: a joint experiment' Margherita Cappelletto (CNR-DSSTTA) sintetizza i contenuti dell'esercizio (presentazione riportata nell'Allegato 4) e avvia il 'conto alla rovescia' per la preparazione da parte di ogni squadra dell'intervento davanti alla Corte. Durante tutti i momenti in cui i gruppi hanno interagito per discutere la propria posizione rispetto al caso e scegliere su quali aspetti puntare per difendere le proprie ragioni, sono stati effettuati interventi estemporanei da parte delle organizzatrici 'di disturbo', volti a introdurre informazioni aggiuntive/distrattive, come verosimilmente accade in casi reali, o semplicemente ad animare la discussione.

Dopo circa un'ora, le parti vengono udite una prima volta e un'occasione di replica è concessa a valle degli interventi di tutti. La Corte, acquisiti tutti gli elementi, si ritira per deliberare.

Figura 5 – Un momento dell'udienza (Crediti: Roberto Bellucci, CNR-DSSTTA)

Figura 6 – La Corte.

Restituzione, la sentenza (giorno 3)

L'ultimo giorno della scuola, il terzo, ritagliando qualche minuto dagli interventi conclusivi, la squadra che rappresentava la Corte pronuncia la sentenza. La scelta di rappresentare l'apparato processuale nelle sue diverse fasi, inclusa la sentenza finale, è legata anche alla dimensione della sfida che in questa tipologia di laboratori 'attoriali' costituisce elemento imprescindibile di stimolo. Di seguito è appunto riportata la sentenza come pronunciata dalla corte a conclusione dell'attività.

Figura 7 – La Corte pronuncia la sentenza. Al centro Gemma Andreone (CNR-ISGI). (Crediti: Roberto Bellucci, CNR-DSSTTA)

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Disclaimer

Role-playing game used as training tool.

The participants to the four teams (1. TestBioTech as the applicant, 2. the European Commission as resistant, 3. Monsanto as intervener, 4. The European Court of Justice) were asked to deploy different instruments and skills as well as imagination to challenge and play the role game.

As far as the content is concerned, the case was inspired by the appeal (still under judgment) brought before the European Court of Justice (ECJ) against the judgment of the General Court (Fifth Chamber) delivered on 15 December 2016 in Case T-177/13, and it was conceived for the purposes of the exercise. References to real parties are not intended to compromise any actors nor

outcomes of the trial. The jurisdictional and legal settings of the role-play game do not reproduce accurately the proceedings before the EU courts.

The European Court of Justice
Final judgment

In the Case C 666,
Among TestBioTech, as the applicant, and the European Commission, as the defendant, and the Monsanto Company, as intervener,
After the hearing, held on 6 June 2019, where the parties presented their oral argument and answered the questions put by the Court;

The Court delivers, by 4 votes to 1, the following judgement that is final and cannot be appealed.
The Court answers, in first place, to the inadmissibility objection raised by the European Commission and states that it cannot be accepted as the Applicant satisfied the criteria set out in art. 11 of the Regulation 1367/2006 and were, therefore, as NGOs for the purpose of that article, entitled to make a request for internal review and thus it also enjoys a legal standing before this Court for asking the annulment of the decision of the European Commission rejecting the request of internal review, also called the contested decision.

Then, the Court rejects the argument of the applicant regarding the suspicious of market distortion that Monsanto would have intentionally generated by using and submitting erroneous scientific data with the aim of gaining an economic advantage since this issue is out of the scope of the present proceedings; thus, it cannot be ruled upon by this Court.

At the same time, the Court favourably acknowledges the efforts that the Company has done, and promised to do in future, for complying with its due diligence obligations, with particular reference to ensuring the level of application of human rights and environmental protection that is provided by European Union legislation and that is expected to be complied with by all multinational enterprises that make business in the European territory when carrying out their economic activity all along the whole production process, as well as the post production and post market phases.

The Court also acknowledges the EFSA statement that “an evaluation of the environmental impacts and the post market environmental monitoring plan was also undertaken”, nevertheless the Court considers that the European Commission didn’t sufficiently substantiated the effectiveness of the existing post market environmental monitoring plan as well as its ability to monitoring, in a comprehensive way, even the short and long-term impact of the Monsanto GMOs on the human and animal health.

* * *

Having considered that Commission is bound by the precautionary principle, which is a general principle of EU law and has to give precedence to the requirements related to the protection of environmental interests over economic interests.

Having considered that the applicant TestBioTech submitted, at the hearing, a new scientific opinion on the effects on animal health of glyphosate residues in feed, that is envisaging a potential threat to human and animal health of using GMOs in food and feed, and the Commission itself in other contexts has shared this hypothesis.

Having considered that this new information seems to giving legitimacy to the suspect of inadequate risk assessment claimed by the applicant in the request for internal review of the authorization decision.

For all these reasons, the Court declares the present action admissible and annul the contested decision.

Before closing the session, I will give the floor to Judge Bruner and Judge Bernaschi for their respective dissenting and separate opinions.

* * *

Final recommendation.
As the Judges of this Court participated to the first Science in Diplomacy School, they could, among the other things, understand the complexity of delaying with scientific uncertainty and, at the same time, they understood the need to go further a mere application of the existing laws to sort out of complex conflicts, thus the Court decides
to “condemn” the Parties to cooperate for the next 3 years to find out a peaceful solution to their opposing positions and, to the end of this cooperation, to attend the next Science in Diplomacy schools that will be organised in the next 3 years under the supervision of Pier Francesco Moretti.
The Court would like to thank warmly and deeply Margherita Cappelletto for having projected and successfully organized the proceedings and the Department staff for the precious assistance!

5. Valutazione dell'attività

Al termine della Scuola è stato distribuito un questionario di valutazione dell'intero Workshop customizzato per i docenti, i discenti e gli osservatori al fine di ottenere indicazioni quantitative e qualitative in merito all'organizzazione e ai contenuti, come riportato nella 'Relazione attività e rendicontazione economica progetto pilota Scuola di Diplomazia Scientifica' a cura di Pier Francesco Moretti, Luigi Mazari Villanova, Margherita Cappelletto, Paolo Braico, Roberto Bellucci, Ruggero Casacchia e Gemma Andreone (riferimento Prot. CNR n. 0051375/2019 del 23/07/2019).

Il valore aggiunto dell'attività laboratoriale può essere sintetizzato in questa frase, estrapolata dalla risposta a una domanda del questionario che chiedeva di condividere esperienze di diplomazia scientifica.

> *"Mancanza di conoscenza della diplomazia come un'arte. Il gioco (intendendosi la GYM4SID ndr) è stato l'unico momento in cui ho capito qualcosa".*

Simulazioni, sessioni interattive, casi di studio, lezioni all'aperto sono tutte indicazioni fornite attraverso il questionario circa gli strumenti che possono essere messi in campo per arricchire la scuola. Il format Gym4SID guarda proprio in questa direzione, nel tentativo di sollecitare un processo di conoscenza informale e mutuo apprendimento di quello che significa supporto scientifico alle decisioni.

Se tra i punti di forza possiamo senz'altro annoverare l'organizzazione e la scelta del tema, che ha catturato l'attenzione dei partecipanti e contribuito a vivacizzare la discussione, tra i punti di debolezza non possiamo non sottolineare l'incompletezza della fase di restituzione, che avrebbe dovuto contemplare, successivamente alla fase di risoluzione del caso giuridico, un momento di meta discussione sulle dinamiche sviluppatesi durante il laboratorio ed eventuali elementi di apprendimento come in uso delle principali scuole omologhe (come da input proveniente da un "Diplomat" con esperienza in format analoghi). Si tratta in effetti di un importante suggerimento metodologico circa la necessità di dedicare del tempo alla discussione, dal vivo e a ridosso dell'attività, non soltanto dei contenuti (vedi fase della 'Sentenza') ma anche delle dinamiche interpersonali e delle strategie comunicative messe in atto. In merito, è stata per esempio riscontrata una difficoltà da parte di alcuni esperti e professionisti ad 'uscire dal proprio personaggio', abilità che in alcuni frangenti del confronto diplomatico è sostanziale.

6. Conclusioni e progetti in cantiere

L'esito di Gym4SID è stato molto positivo e ha fatto emergere l'importanza di prevedere *di default* un'attività pratica tra le sessioni di un percorso formativo del genere School4SID.

La preparazione del test di Gaeta, con la possibilità unica all'interno del CNR di avvalersi delle competenze dei colleghi per supportare la comprensione di argomenti tecnici specifici, e l'esperienza diretta dell'attuazione del laboratorio, hanno consentito di acquisire e maturare alcune competenze inerenti la gestione di un'attività piuttosto particolare: pur nei confini dello schema di gioco proposto e tenendo a mente l'obiettivo di provare a 'travasare' i contenuti discussi nelle lezioni in una situazione concreta, completandoli, è necessario approcciare l'esercizio con un elevato grado di flessibilità, data tra le altre cose l'impossibilità di prevedere e pre-organizzare tutti gli aspetti nonché l'importanza dell'elemento spontaneo. L'attitudine alla finzione, quasi attoriale, in primis da parte degli organizzatori, è da annoverare tra le buone pratiche: l'esperienza funziona senz'altro meglio se si riesce ad agire e far agire un processo di immedesimazione, comprensivo dei tratti emotivi.

Per sintetizzare, il successo dal punto di vista partecipativo e formativo, nonché l'analisi *ex post* dei punti di forza e delle criticità, emersi sia dai feedback dei partecipanti che dal processo di valutazione degli organizzatori unito all'esperienza maturata sul campo, hanno portato le ideatrici a proporre un nuovo format denominato *The School4SID Show*. *Understanding by role-playing*, che verrà presentato in occasione della nuova edizione della Scuola, organizzata per un gruppo di assistenti ai parlamentari europei e prevista a Gaeta a novembre 2020, salvo rinvii dovuti all'emergenza Covid.

Allegati

Gym for SID, the Dossier

Background to the dispute

Monsanto submits to the competent authority of the Netherlands, in accordance with Articles 5 and 17 of Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed an application for the **placing on the market of foods, food ingredients and feed** containing, consisting of, or produced from MON 87701 × MON 89788 soybean ('**the modified soybean**'). The application consisting of scientific dossiers including data collection, impact analysis and environmental risk assessment, also covers the placing on the market of the modified soybean as present in products other than food and feed containing or consisting of that soybean for the same uses as any other soybean, **with the exception of cultivation**.

On the basis of the scientific dossiers submitted by Monsanto, the **European Food Safety Authority (EFSA)** issues an overall opinion in accordance with Articles 6 and 18 of Regulation No 1829/2003 ('the overall opinion') [...] explaining that its **Scientific Panel on Genetically Modified Organisms** ('the Scientific Panel') had adopted a scientific opinion on the application concerning the placing on the market of the insect-resistant and herbicide-tolerant modified soybean, for food and feed uses, import and processing under Regulation No 1829/2003 by Monsanto ('the scientific opinion'), finding that **the modified soybean was, in the context of its intended uses, as safe as its non-genetically modified comparator with respect to potential effects on human or animal health or on the environment**. Moreover, the Scientific Panel concluded that the crossing of modified soybean did not, in the context of its intended uses, result in interactions between the events that would affect the safety of the modified soybean with respect to potential effects on human and animal health and on the environment. In the overall opinion, **EFSA concluded that it 'fulfil[led] the requirements** of Articles 6 and 18 [of Regulation No 1829/2003] **for the placing on the market** of [the modified soybean]'. It also underlines that the opinion is based on the verification that the submission procedure by Monsanto was carried out properly.

On the basis of the EFSA overall opinion, the **Commission** authorises the placing on the market of products containing, consisting of, or produced from the genetically modified soybean, with a Decision ('**the authorisation decision**'). By implementing this authorisation decision, the Commission authorises, subject to certain conditions, for the purposes of Article 4(2) and Article 16(2) of Regulation No 1829/2003:

- foods and food ingredients containing, consisting of, or produced from the modified soybean;
- feed containing, consisting of, or produced from the modified soybean;
- the modified soybean present in products other than food and feed 'containing it' or consisting of it, for the same uses as any other soybean, with the exception of cultivation.

Following this authorization decision, **TestBioTech requests** by letter the Commission to carry out an **internal review of the authorisation decision**, pursuant to Article 10 of Regulation (EC) No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies (OJ 2006 L 264, p. 13). TestBioTech, as applicant, put forward four pleas in law in support of their action:

(i) an alleged absence of substantial equivalence between the modified soybean and its conventional counterpart;
(ii) an alleged failure to assess synergistic/combinatorial effects and toxicity;
(iii) an alleged absence of exhaustive immunological assessment; and
(iv) an alleged absence of post-market authorisation monitoring of consumption of products containing the modified soybean.

The Commission (the Commissioner for Health) rejects the TestBioTech request for internal review

by letter (‘**the contested decision’**). It considers indeed that the authorisation decision complied with Regulation No 1829/2003 and rejected the arguments put forward by TestBioTech.

Judicial case

TestBioTech eV, the applicant, a not-for-profit association to promote independent research and public debate on the impacts of biotechnology, established in Germany **brings before the Court of EU an application pursuant to Article 263 Treaty on the Functioning of the European Union (TFEU) for annulment of a decision of the European Commission (the contested decision) which rejected the applicants’ requests for Internal Review of the Commission Decision (the authorization decision) granting a market authorisation under Regulation No 1829/2003 on genetically modified food and feed to Monsanto Europe SA**, established in Belgium, **for its genetically modified soybean “MON 87701 x MON 89788”**.

The **European Network of Scientists for Social and Environmental Responsibility**, established in Germany, the purpose of which is the advancement of science and research for the protection of the environment, biological diversity and human health against the negative impacts of new technologies and their products, supports TestBioTech. It recalls that it should be borne in mind (…), **that the Commission is bound by the precautionary principle, which is a general principle of EU law. It requires the authorities concerned**, in the particular context of the exercise of the powers conferred on them by the relevant rules, to take appropriate measures to prevent specific potential risks to public health, safety and the environment, by **giving precedence to the requirements related to the protection of those interests over economic interests** (case-law cited).

The **European Commission, supported by the UK Government,** is resistant in the procedure and in its defence highlights that:

- the EC is not bounded by EFSA;
- the EC has a broad discretion as to the measures to be taken in the present case and considers that the standard of judicial review should be especially light on the ground that the first applicant is not entitled to seek annulment of the authorisation decision;
- a non-governmental organisation that made the request for internal review of an administrative act under Article 10 of Regulation No 1367/2006 cannot require, at the end of the internal review, that a specific measure be taken by the institution or body concerned. **The choice of measures to be adopted following an internal review is entirely discretionary.**

The **UK adds that**, in the present case, as Monsanto did not seek authorisation for the modified soybean to be cultivated in the European Union, **the environmental risk assessment is therefore limited to a consideration of the likely effects of accidental dissemination into the environment**. That, it contends, greatly reduces the range of environmental risks that must be considered and (…) even the risk of harmful spreading of soybean in the environment would not cause any damage when considering the climatic condition of The Netherlands.

Monsanto contends that judicial review must be limited to manifest errors of assessment that are ‘so serious that even a non-scientist can easily detect and correctly identify them’**.**

International law

The **Aarhus Convention** on access to information, public participation in decision-making and access to justice in environmental matters, signed in Aarhus on 25 June 1998 and approved by the EU, provides for:

- the right of everyone to receive environmental information that is held by public authorities ("access to environmental information"). This can include information on the state of the environment, but also on policies or measures taken, or on the state of human health and safety where this can be affected by the state of the environment;
- the right to participate in environmental decision-making;
- the right to review procedures to challenge public decisions that have been made without respecting the two aforementioned rights or environmental law in general ("access to justice").

Article 9(1) to (4) of the Convention provides:
1. Each Party shall, within the framework of its national legislation, **ensure that any person who considers that his or her request for information under article 4 has been ignored, wrongfully refused, whether in part or in full, inadequately answered**, or otherwise not dealt with in accordance with the provisions of that article, **has access to a review procedure before a court of law** or another independent and impartial body established by law.

2. Each Party shall, within the framework of its national legislation, ensure that **members of the public concerned:**
(a) Having a sufficient interest or, alternatively,
(b) Maintaining impairment of a right, where the administrative procedural law of a Party requires this as a precondition, **have access to a review procedure before a court of law and/or another independent and impartial body established by law**, to challenge the substantive and procedural legality of any decision, act or omission (…).

What constitutes a sufficient interest and impairment of a right shall be determined in accordance with the requirements of national law and consistently with the objective of giving the public concerned wide access to justice within the scope of this Convention. (…)

3. In addition and without prejudice to the review procedures referred to in paragraphs 1 and 2 above, each Party shall ensure that, where they meet the criteria, if any, laid down in its national law, **members of the public have access to administrative or judicial procedures to challenge acts and omissions by private persons and public authorities which contravene provisions of its national law relating to the environment**.

4. In addition and without prejudice to paragraph 1 above, **the procedures** referred to in paragraphs 1, 2 and 3 above **shall** provide adequate and effective remedies, including injunctive relief as appropriate, and **be fair, equitable, timely and not prohibitively expensive**. (…)

EU Law

Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified (GM) food and feed.

Recital 1 indicates that it aims to ensure the **free movement of safe and wholesome food and feed**, which is **an essential aspect of the internal market and contributes significantly to the health and well-being of citizens, and to their social and economic interests**.

Recital 2 states that **a high level of protection of human life and health, animal health and welfare, environment and consumer interests in relation to genetically modified food and feed should be ensured in the pursuit of EU policies**, whilst recital 3 states that genetically modified food and feed undergo a safety assessment before being placed on the market within the European Union.

Recital 32 recognises that, in some cases, **scientific risk assessment alone cannot provide all the information on which a risk management decision of the Commission should be based, and that other legitimate factors relevant to the matter under consideration may be taken into account by it**.

Recital 43 allows account to be taken 'of the international trade commitments of the European [Union] and of the requirements of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity as regards importer obligations and notification'.

Article 5, Application for authorization, states that in the case of **GMOs or food containing or consisting of GMOs, the application shall also be accompanied by**:
(a) the **complete technical dossier** supplying the information required (…);
(b) a **monitoring plan for environmental effects** conforming with Annex VII to Directive 2001/18/EC, including a proposal for the duration of the monitoring plan; this duration may be different from the proposed period for the consent.

According to the Article 18 (Opinion of the Authority),

3. In order to prepare its opinion, **the Authority**:
(d) shall forward to the Community reference laboratory referred to in (omissis), i. e. the Commission Joint Research Center. The Community reference laboratory shall test and validate the method of detection and identification proposed by the applicant;
(e) shall, in verifying the application of Article 13(2)(a), **examine the information and data submitted by the applicant to show that the characteristics of the food are not different from those of its conventional counterpart**, having regard to the accepted limits of natural variations for such characteristics.

4. In the case of GMOs or food containing or consisting of GMOs, **the environmental safety requirements** referred to in Directive 2001/18/EC **shall apply to the evaluation to ensure that all appropriate measures are taken to prevent the adverse effects on human and animal health and the environment which might arise from the deliberate release of GMOs**.

5. **In the event of an opinion in favour of authorising the food, the opinion shall also include the following particulars**:
(e) where applicable, **any conditions or restrictions which should be imposed on the placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements** based on the outcome of the risk assessment **and**, in the case of

GMOs or food containing or consisting of GMOs, **conditions for the protection of particular ecosystems/environment and/or geographical areas**;
(f) **the method**, validated by the Community reference laboratory, **for detection**, including sampling, identification of the transformation event and, where applicable, for the detection and identification of the transformation event in the food and/or in foods produced from it; an indication of where appropriate reference material can be accessed.

EU Regulation No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies.

Recitals 11, 18, 19 and 21 read as follows:

(11) **Administrative acts of individual scope should be open to possible internal review where they have legally binding and external effects**. ...

(18) (…) Provisions on access to justice (according to Article 9(3) of the Aarhus Convention) should be consistent with the Treaty. It is appropriate in this context that this Regulation address only acts and omissions by public authorities.

(19) To ensure adequate and effective remedies, including those available before the Court of Justice of the European Communities under the relevant provisions of the Treaty, it is appropriate that the Community institution or body which issued the act to be challenged […], be given the opportunity to reconsider its former decision, or, in the case of an omission, to act.

(21) **Where previous requests for internal review have been unsuccessful, the non-governmental organisation concerned should be able to institute proceedings before the Court of Justice** in accordance with the relevant provisions of the Treaty.'

Article 2(1)(f) contains a definition of the **term 'environmental law' that includes EU legislative provisions covering the protection of human health and the preservation and protection of the quality of the environment**.

Article 10, headed '**Request for internal review of administrative acts**', stipulates that:

1. Any non-governmental organisation which meets the criteria set out in Article 11 is entitled to make a request for internal review to the Community institution or body that has adopted an administrative act under environmental law or, in case of an alleged administrative omission, should have adopted such an act.

2. The Community institution or body referred to in paragraph 1 shall consider any such request, unless it is clearly unsubstantiated.

3. Where the Community institution or body is unable, despite exercising due diligence, to act in accordance with paragraph 2, it shall inform the non-governmental organisation which made the request as soon as possible and at the latest within the period mentioned in that paragraph, of the reasons for its failure to act and when it intends to do so.

General Technical Information

According to the World Health Organization **Genetic Modified Organisms (GMOs)** are plants, animals or microorganisms in which the genetic material (DNA) has been altered in a way that does not occur naturally by mating and/or natural recombination. The safety assessment of GM foods generally focuses on:

a) direct health effects (toxicity);
b) potential to provoke allergic reaction (allergenicity);
c) specific components thought to have nutritional or toxic properties;
d) the stability of the inserted gene;
e) nutritional effects associated with genetic modification; and
f) any unintended effects which could result from the gene insertion.

As far as concern the environment:

a) the capability of the GMO to escape and potentially introduce the engineered genes into wild populations;
b) the persistence of the gene after the GMO has been harvested;
c) the susceptibility of non-target organisms (e.g. insects which are not pests) to the gene product; 4. the stability of the gene;
d) the reduction in the spectrum of other plants including loss of biodiversity;
e) and increased use of chemicals in agriculture.

[The environmental safety aspects of GM crops vary considerably according to local conditions].

As far as concern the human health the three main issues debated are the potentials to provoke:

a) allergic reaction (allergenicity),
b) gene transfer and
c) outcrossing.

The **European Food Safety Authority's risk assessments of GMO applications**, evaluating the potential impact of GMOs on human health, animal health and the environment, **are based on scientific dossiers presented by applicants** and any other available relevant scientific information. GMO applications must contain adequate information to enable assessment of the potential long-term adverse effects of the GMO on human health, animal health and the environment.

EFSA applies the principles of GMO risk assessment considering the following aspects:

- Molecular characterisation;
- Comparative analysis: comparison of the GM plant with its conventional counterpart. The aim is to detect differences in the plant's observable appearance such as height and colour – phenotypic characteristics – and its agronomic characteristics such as yield.;
- Evaluation of potential toxicity and allergenicity;
- Evaluation of potential environmental impact.

Depending on the outcome of the risk assessment, applicants may be required to carry out additional long-term studies. In other cases, **post-market monitoring** (PMM) of GM food or feed may be considered. **Post-market environmental monitoring (PMEM) activities are obligatory for all GMOs that are put on the EU market**. These mechanisms help in identifying and managing potential long-term adverse effects of GMOs on the environment and/or on organisms that are not meant to be affected by the GMO, the so-called non-target organisms.

TESTBIOTECH Background 18 - 12 - 2018

Testbiotech comment on 'Assessment of genetically modified soybean MON 89788 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-011)' by company Monsanto

Testbiotech e. V.
Institute for Independent Impact Assessment in Biotechnology

Christoph Then & Andreas Bauer-Panskus

Introduction

Ten years after soybean MON89788, which is resistant to glyphosate (EFSA 2018a), was first authorised for import into the EU, the EFSA GMO Panel assessed an application for renewal of authorisation. The EFSA re-assessment completely ignores the fact that there has been a considerable increase in problems with herbicide resistant weeds over the last ten years; and that the number of sprayings and the amount of sprayed complementary herbicide is now higher than it was then. Therefore, new data are needed before any decision is made on the safety of the GE soybean.

1. Molecular characterisation

EFSA should have requested data that takes into account the increased number of times that glyphosate is sprayed because of problems with herbicide resistant weeds (see, for example, Benbrook, 2016). A higher number of applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018).

This aspect, which is the most relevant in regard to the re-assessment of this event, was completely ignored by EFSA. EFSA should have requested that Monsanto submit data from field trials sprayed with the highest dosage of the complementary herbicides that can be tolerated by the plants, also including repeated spraying. The material derived from those plants should have also been assessed using Omics techniques to investigate changes in the gene activity of the transgene and in the natural genome of the plants.

2. Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

There have been huge changes in the last ten years in the way that glyphosate-resistant plants are cultivated. Therefore, new field trials should have been requested from the applicant. Due to the changes in weed populations, it has to be expected that these plants can and will be exposed to higher and repeated dosages of glyphosate. Higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence plant composition and agronomic characteristics. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018).

This aspect, which is the most relevant in regard to this specific event, was completely ignored in the risk re-assessment. The issues of practical conditions prevalent in large scale cultivation and increasing weed occurrence were left aside.

EFSA should have requested that Monsanto submit data from field trials sprayed with the highest dosage of the complementary herbicides that can be tolerated by the plants, also including repeated spraying. The material derived from those plants should have been assessed using Omics techniques to investigate changes in plant composition and agronomic characteristics.

Further, data representing more extreme environmental conditions, such as those caused by climate change, would have been necessary.

New field trials are also necessary since new standards for conducting the trials and assessment of the data are now requested in the EU (see Regulation 503/2013).

Toxicology

Both the EU pesticide regulation and the GMO regulation require a high level of protection for health and the environment. Thus, in regard to herbicide-resistant plants, specific assessment of residues from spraying with complementary herbicides must be considered to be a prerequisite for granting authorisation. In assessing the safety of the products derived from the soybeans, the assessments made by the Pesticide Panel in 2015 (EFSA 2015) and 2018 (EFSA 2018b) have to be taken into account. They state that:

> *«In the framework of the renewal, representative uses were proposed for conventional crops only and residue trials on glyphosate tolerant GM crops were not provided."* (EFSA 2015)
>
> *"For genetically modified crops, data were sufficient to derive MRL for sweet corn (EPSPS modification) and cotton seed (EPSPS modification), noting that MRLs should be tentative pending on the submission of confirmatory methods for enforcement of AMPA and N-acetyl-glyphosate. For sugar beet roots, maize and soybeans (EPSPS modification), soybeans (GAT modification) and rapeseeds (GOX modification), the available data were insufficient to derive MRLs and risk assessment values."* (EFSA 2018b)

The conclusion that has to be taken from these EFSA reports (2015 and 2018 b) is that the existing data are not sufficient to conclude on the overall safety of the soybeans for import.

Further, while the GMO panel considers the assessment of the toxicity of the residues from spraying to be outside its remit, it is the duty of the GMO panel to consider and assess the specific metabolism in the plants and the specific metabolites that might occur in the plants after application of the complementary herbicides. These residues might show a specific pattern or accumulation that only occurs in this specific event. The pesticide panel can only assess the toxicity of these metabolites, if the GMO panel request specific data on metabolism and metabolites, also considering the various formulas, mixtures and combination of the complementary herbicides. So even if it is the case that the pesticide panel only has to assess the toxicity of these metabolites, it is the duty of the GMO panel to request these specific data that are needed to conclude on the safety of the plants.

In addition, as mentioned, higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018). These changes can have a serious impact on health since soybeans are known to produce many bioactive compounds such as allergens and oestrogens.

There are further relevant issues: for example, the potential impact on the intestinal microbiome also has to be considered. Such effects might be caused by the residues from spraying since glyphosate has been shown to have negative effects on the composition of the intestinal flora of

cattle (Reuter et al., 2007) and poultry (Shehata et al., 2013). New research also shows an increase in resistance to antibiotics due to selective pressure caused by exposure to glyphosate (Kurenbach et al. 2018). In general, antibiotic effects and other adverse health effects might occur from exposure to a diet containing these plants (see also EFSA, 2018c); these were not assessed under pesticide regulation.

As a result, the toxicological assessment carried out by EFSA is not acceptable.

Allergenicity
No data were presented to show that plant composition is unchanged in regard to allergenic potential.

As mentioned, higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018). These changes can have serious impacts on health since soybeans are known to produce many allergens.

Consequently, the assessment in regard to allergenicity cannot be regarded as conclusive.

Others
According to Regulation (EU) No 503/2013, the applicant has to ensure that post-market monitoring (PMM) is developed to collect reliable information on the detection of indications showing whether any (adverse) effects on health may be related to GM food or feed consumption (see also EFSA, 2018c). Thus, the monitoring report should at very least contain detailed information on:

i) actual volumes of the GE soybean imported into the EU,
ii) the ports and silos where shipments of the GE soybean were unloaded,
iii) the processing plants where the GE soybean was transferred to,
iv) the amount of the GE soybean used on farms for feed, and
v) transport routes of the GE soybean.

Environmental monitoring should be run in regions where viable kernels of the GE soybean are transported, stored, packaged, processed or used for food/feed. In case of losses and spread of the GE soybean, all receiving environments need to be monitored.

Furthermore, environmental exposure through organic waste material, by-products, sewage or faeces containing the GE soybean during or after the production process, and during or after human or animal consumption should be part of the monitoring procedure (see also EFSA, 2018c).

Conclusions and recommendations
The EFSA risk assessment cannot be accepted.

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SCIENTIFIC OPINION

Scientific opinion on application (EFSA-GMO-NL-2009-73) for the placing on the market of insect-resistant and herbicide-tolerant genetically modified soybean MON 87701 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

This scientific opinion is an evaluation of a risk assessment for placing on the market the genetically modified (GM) insect-resistant and herbicide-tolerant soybean MON 87701 × MON 89788 for food and feed uses, import and processing. Soybean MON 87701 × MON 89788 was produced by conventional crossing methods, and the F_1 plant is hemizygous for all newly introduced traits. The soybean contains the *Cry1Ac* and CP4 *epsps* genes conferring resistance against certain lepidopteran target pests and tolerance to glyphosate-based herbicides. No biologically relevant differences were identified in the composition or agronomic and phenotypic characteristics of soybean MON 87701 × MON 89788, as compared with its comparator, except that it expresses the Cry1Ac and CP4 EPSPS proteins. The safety assessment identified no concerns regarding the potential toxicity and allergenicity of soybean MON 87701 × MON 89788. There are no indications of an increased likelihood of establishment and spread of feral soybean plants. Considering its intended use as food and feed, environmental risks associated with an unlikely but theoretically possible horizontal gene transfer from soybean MON 87701 × MON 89788 to bacteria have not been identified. Potential interactions of soybean MON 87701 × MON 89788 with the biotic and abiotic environment were not considered to be an issue owing to the low level of exposure. The monitoring plan and reporting intervals are in line with the intended uses of soybean MON 87701 × MON 89788. In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87701 × MON 89788 addresses the scientific comments raised by Member States and that the soybean MON 87701 × MON 89788, as described in this application, is as safe as its comparator with respect to potential effects on human and animal health and the environment, in the context of its intended uses.

[1] On request from the Competent Authority of the Netherlands for an application (EFSA-GMO-NL-2009-73) submitted by Monsanto, Question No EFSA-Q-2009-00761, adopted on 26 January 2012.

[2] Panel members: Hans Christer Andersson, Salvatore Arpaia, Detlef Bartsch, Josep Casacuberta, Howard Davies, Patrick du Jardin, Gerhard Flachowsky, Lieve Herman, Huw Jones, Sirpa Kärenlampi, Jozsef Kiss, Gijs Kleter, Harry Kuiper, Antoine Messéan, Kaare Magne Nielsen, Joe Perry, Annette Pöting, Jeremy Sweet, Christoph Tebbe, Atte Johannes von Wright and Jean-Michel Wal. Correspondence: gmo@efsa.europa.eu

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KEY WORDS

GMO, soybean (*Glycine max*), MON 87701 × MON 89788, insect-resistant, herbicide-tolerant, human and animal health, import and processing, Regulation (EC) No 1829/2003.

SUMMARY

Following the submission of an application (EFSA-GMO-NL-2009-73) under Regulation (EC) No 1829/2003[4] from Monsanto, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) was asked to deliver a scientific opinion on the safety of insect-resistant genetically modified (GM) soybean MON 87701 × MON 89788 (Unique Identifier MON-877Ø1-2 × MON-89788-1) for food and feed uses, import and processing.

In delivering its scientific opinion, the EFSA GMO Panel considered the application EFSA-GMO-NL-2009-73, additional information supplied by the applicant, scientific comments submitted by the Member States and relevant scientific publications. Further information from applications for placing on the market under European Union regulatory procedures the single soybean events MON 87701 and MON 89788 was taken into account. The scope of application EFSA-GMO-NL-2009-73 is for food and feed uses, import and processing of soybean MON 87701 × MON 89788 within the EU in the same way as any non-GM soybean but excludes cultivation in the EU. The EFSA GMO Panel evaluated soybean MON 87701 × MON 89788 with reference to the intended uses and appropriate principles described in its guidance documents of the Scientific Panel on Genetically Modified Organismsfor the risk assessment of genetically modified plants and derived food and feed (EFSA 2006) and for the risk assessment of GM plants containing stacked transformation events (EFSA 2007). The scientific evaluation of the risk assessment included molecular characterisation of the inserted DNA and expression of the corresponding proteins. An evaluation of the comparative analysis of the composition and phenotypic and agronomic characteristics was undertaken, and the safety of the new proteins and the whole food/feed was evaluated with respect to potential toxicity, allergenicity and nutritional wholesomeness. An evaluation of the environmental impacts and the post-market environmental monitoring plan was also undertaken.

The single soybean events MON 87701 and MON 89788 were the subject of separate earlier risk assessment evaluations by the EFSA GMO Panel. The EFSA GMO Panel concluded that they are unlikely to have any adverse effect on human and animal health and the environment, in the context of their intended uses (EFSA 2008, 2011a). The placing on the market of products containing, consisting of or produced from genetically modified soybean MON 89788 was authorised pursuant to Regulation (EC) No 1829/2003.[5] No new genes, in addition to those occurring in soybean MON 87701 and MON 89788, have been introduced in soybean MON 87701 × MON 89788. Soybean MON 87701 × MON 89788 was produced by conventional crossing of the single soybean events to combine in the same stack resistance against certain lepidopteran target pests and tolerance to glyphosate-based herbicides.

Molecular analysis has confirmed that soybean MON 87701 and MON 89788 inserts are present and that their structures are retained in soybean MON 87701 × MON 89788. The result of the updated bioinformatic analyses of the flanking sequences and the open reading frames spanning the insert–plant DNA junctions did not reveal a safety concern. The overall levels of the Cry1Ac and CP4 EPSPS proteins were comparable to those of the corresponding single soybean events MON 87701 and MON 89788.

The EFSA GMO Panel compared the composition and phenotypic and agronomic characteristics of soybean MON 87701 × MON 89788 with its comparator (A5547), assessed all statistically significant differences identified, and came to the conclusion that no biologically relevant differences were identified in the composition or phenotypic and agronomic characteristics of soybean MON 87701 × MON 89788 as compared with its comparator (A5547) and that the composition fell within the range of non-GM soybean varieties, except that soybean MON 87701 × MON 89788 expressed the CP4 EPSPS and Cry1Ac proteins. A small increase in final stand count in soybean MON 87701 × MON 89788 was observed, but no safety issues were identified linked to this increase. The risk assessment included an analysis of data from analytical and bioinformatics studies, as well

[4] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Official Journal of the European Communities, L268, 1–23.

[5] Commission decision of 4 December 2008 authorising the placing on the market of products containing, consisting of or produced from genetically modified soybean MON 89788 (MON-89788-1) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council. Official Journal of the European Union L 333/7–10.

as in vitro and in vivo studies. The EFSA GMO Panel concluded that soybean MON 87701 × MON 89788 is as safe as its comparator and that the overall allergenicity of the whole plant has not changed.

Potential interaction between the soybean events with respect to an effect on human and animal health were the focus of the assessment on food/feed issues. On the basis of the known functional characteristics and modes of action of the newly expressed proteins (Cry1Ac and CP4 EPSPS), the EFSA GMO Panel considers it unlikely that interactions between these proteins would occur that would raise any safety concerns. Thus, the Panel is of the opinion that soybean MON 87701 × MON 89788 is as safe and as nutritious as its comparator and commercial soybean varieties, in the context of its intended uses.

The application EFSA-GMO-NL-2009-73 concerns food and feed uses, import and processing. Therefore, there is no requirement for scientific information on possible environmental effects associated with the cultivation of soybean MON 87701 × MON 89788. There are no indications of an increased likelihood of the establishment and spread of feral soybean plants in the event of the accidental release into the environment of viable soybean MON 87701 × MON 89788 grains during transport and processing for food and feed uses, except under conditions of infestation by the specific lepidopteran pests or the application of glyphosate-based herbicides. Taking into account the scope of the application, both the rare occurrence of feral soybean plants and the low levels of exposure to the environment indicate that the risk to target and non-target organisms is extremely low. The unlikely but theoretically possible transfer of the recombinant gene from soybean MON 87701 × MON 89788 to environmental bacteria does not raise concern owing to the lack of a selective advantage in the context of its intended uses. The scope of the post-market environmental monitoring plan provided by the applicant is in line with the intended uses of soybean MON 87701 × MON 89788. Furthermore, the EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in its general surveillance plan.

In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87701 × MON 89788 addresses the scientific issues indicated by the guidance document of the EFSA GMO Panel and the scientific comments raised by the Member States, and that soybean MON 87701 × MON 89788 is as safe as its comparator with respect to potential effects on human and animal health or the environment in the context of its intended uses. In addition, the EFSA GMO Panel is of the opinion that crossing of single soybean events MON 87701 and MON 89788 to produce soybean MON 87701 × MON 89788 does not result in interactions between the events that would affect the safety of soybean MON 87701 × MON 89788 with respect to potential effects on human and animal health and on the environment, in the context of its intended uses.

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BACKGROUND

On 27 August 2009, EFSA received from the Dutch Competent Authority an application (Reference EFSA-GMO-NL-2009-73) for authorisation of genetically modified (GM) soybean MON 87701 × MON 89788 (Unique Identifier MON-877Ø1-2 × MON-89788-1) submitted by Monsanto within the framework of Regulation (EC) No 1829/2003 on GM food and feed. After receiving the application EFSA-GMO-NL-2009-73, and in accordance with Articles 5(2)(b) and 17(2)b of Regulation (EC) No 1829/2003, EFSA informed the Member States and the European Commission, and made the summary of the application publicly available on the EFSA website. EFSA initiated a formal review of the application to check compliance with the requirements laid down in Articles 5(3) and 17(3) of Regulation (EC) No 1829/2003. On 8 December 2009, EFSA declared the application as valid in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003.

EFSA made the valid application available to Member States and the EC and consulted nominated risk assessment bodies of the Member States, including the national Competent Authorities within the meaning of Directive 2001/18/EC[6], following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003, to request their scientific opinion. Member States had three months after the date of receipt of the valid application (until 8 March 2010) within which to make their opinion known.

The EFSA Scientific Panel on Genetically Modified Organisms (EFSA GMO Panel) carried out an evaluation of the scientific risk assessment of the GM soybean MON 87701 × MON 89788 for food and feed uses, import and processing, in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003. The EFSA GMO Panel carried out the safety evaluation in accordance with the appropriate principles described in the guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA 2006). In addition, the scientific comments of the Member States, additional information provided by the applicant and relevant scientific publications were taken into consideration.

On 26 February 2010, 8 July 2010, 26 August 2011, 13 October 2011 and 2 December 2011, the EFSA GMO Panel requested additional information from the applicant. The applicant provided the requested information on 9 April 2010, 5 September 2011, 3 November 2011 and 6 December 2011.

In giving its opinion on soybean MON 87701 × MON 89788 to the EC, the Member States and the applicant, and in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003, EFSA has endeavoured to respect a time limit of six months from the acknowledgement of the valid application. As additional information was requested by the EFSA GMO Panel, the time limit of 6 months was extended accordingly, in line with Articles 6(1), 6(2), 18(1) and 18(2) of Regulation (EC) No 1829/2003. According to Regulation (EC) No 1829/2003, this scientific opinion is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation and thus will be part of the EFSA overall opinion in accordance with Articles 6(5) and 18(5).

TERMS OF REFERENCE

The EFSA GMO Panel was requested to carry out a scientific assessment of soybean MON 87701 × MON 89788 for food and feed uses, import and processing, in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003. Where applicable, any conditions or restrictions that should be imposed on its placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements based on the outcome of the risk assessment and, in the case of GMOs or food/feed containing or consisting of GMOs, conditions for the protection of particular ecosystems/environment and/or geographical areas, should be indicated in accordance with Articles 6(5)(e) and 18(5)e of Regulation (EC) No 1829/2003.

The EFSA GMO Panel was not requested to give a scientific opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the EFSA GMO Panel did also not consider proposals for labelling and

[6] 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. Official Journal of the European Communities, L106, 1–38.

methods of detection (including sampling and the identification of the specific transformation event in the food/feed and/or food/feed produced from it), which are matters related to risk management.

ASSESSMENT

1. INTRODUCTION

The GM soybean MON 87701 × MON 89788 (Unique Identifier MON-877Ø1-2 × MON-89788-1) was evaluated with reference to its intended uses, taking account of the appropriate principles described in the guidance documents of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA 2006) and for the risk assessment of GM plants containing stacked transformation events (EFSA 2007). The evaluation of the risk assessment presented here is based on the information provided in the application, as well as additional information from the applicant, scientific comments submitted by the Member States and relevant scientific publications.

2. ISSUES RAISED BY MEMBER STATES

The issues raised by the Member States are addressed in Annex G of the EFSA overall opinion[7] and have been considered in this scientific opinion.

3. MOLECULAR CHARACTERISATION

3.1. Evaluation of relevant scientific data

3.1.1. Method of production of soybean MON 87701 × MON 89788

Conventional breeding methods were used to develop soybean MON 87701 × MON 89788, and no new genetic modification was involved[8]. The two inserts that are present in soybean MON 87701 × MON 89788 were derived from soybean lines containing two independent events: MON 87701 and MON 89788. Genetically modified soybeans MON 89788 and MON 87701 were the subjects of earlier safety evaluations (EFSA 2008, 2011a). Soybean MON 87701 × MON 89788 combines resistance to certain lepidopteran pests with tolerance to glyphosate-based herbicide.

3.1.2. Summary of the evaluation of the single events

3.1.2.1. MON 87701

Soybean MON 87701 was developed through *Agrobacterium*-mediated transformation and, as a result, expresses the *cry1Ac* gene, under the control of *Arabidopsis thaliana rbcS4* promoter, to confer resistance to specific lepidopteran insects. Molecular characterisation data have established that MON 87701 contains a single insert with one copy of the intact Cry1Ac expression cassette at a single locus and that vector backbone sequences are absent. A comparison with the pre-insertion locus of the parental soybean A5547 indicated that a 32-bp fragment of endogenous DNA has been deleted in soybean MON 87701, and 14 bp have been introduced immediately 5′ to the insertion site. The results of bioinformatic analysis did not indicate the interruption of a soybean coding sequence(s) with known function in the MON 87701 event. The analysis of cryptic open reading frames (ORFs) in the MON 87701 event did not indicate any alignment that would meet or exceed the Codex Alimentarius (2009) threshold for potential allergenicity, and no relevant similarities to known toxic proteins other than Bt proteins (Cry1Ac) were found. The *cry1Ac* gene was shown to be stably inherited and the inheritance followed a Mendelian segregation pattern. A more detailed evaluation of the MON 87701 event can be found in a previous EFSA opinion (EFSA 2011a).

3.1.2.2. MON 89788

Soybean MON 89788 was developed through *Agrobacterium*-mediated transformation and, as a result, expresses the CP4 *epsps* gene, conferring tolerance to glyphosate-based herbicides, under the control of the chimeric promoter consisting of enhancer sequences from the 35S promoter of the figwort mosaic virus and the promoter from the *Tsf1* gene of *Arabidopsis thaliana*. Molecular characterisation data established that MON 89788

[7] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2009-00761
[8] Technical Dossier/Section C

contains a single insert with one copy of the intact CP4 *epsps* expression cassette at a single locus and that vector backbone sequences are absent. Similarity searches revealed that the flanking regions of the insert in soybean MON 89788 show significant level of identity to soybean genomic DNA sequences and indicated that the pre-insertion locus was preserved except for the deletion of 40 bp. Bioinformatic analysis confirmed that no known endogenous soybean ORFs or regulatory sequences have been disrupted by the insert. The bioinformatic analysis revealed no biologically relevant similarities to allergens or toxins for any of the putative (poly)peptides that might be produced from ORFs spanning the junction regions. Southern analysis of MON 89788 and maintenance of the phenotype indicated genetic and phenotypic stability of the event over multiple generations. A more detailed evaluation of the MON 89788 event can be found in a previous EFSA opinion (EFSA 2008).

3.1.3. Transgenic constructs in MON 87701 × MON 89788

The integrity of the individual inserts present in this soybean was investigated using Southern analyses[9]. This involved the use of DNA probes specific for MON 87701 and MON 89788 inserts and the use of restriction enzymes that allowed the structures of the inserts, including the junction regions, to be determined within the stack. The predicted DNA hybridisation patterns from each single event were retained in the MON 87701 × MON 89788 stack, demonstrating that integrity of the inserts was maintained.

3.1.4. Information on the expression of the insert

The levels of newly expressed proteins Cry1Ac and CP4 EPSPS of soybean MON 87701 × MON 89788 were analysed by enzyme-linked immunosorbent assay (ELISA)[10]. Tissue samples for analysis were collected from five field trials conducted in Argentina during 2007/2008. The trials were located in major soybean-growing regions of Argentina and provided a variety of environmental conditions. Each trial included appropriate comparators (MON 89788 and MON 87701 as positive controls, and a conventional soybean variety with a genetic background similar to soybean MON 87701 × MON 89788 as a negative control). Over-season leaf (OSL 1–4), forage, root and seed tissues were collected from each replicated plot at all field sites.

The scope of the application covers food and feed uses and import and processing, therefore protein expression data related to the seeds are considered most relevant and are summarised in Table 1. Levels of proteins in the stacked line were comparable to levels in the single events. Although some statistically significant differences were found, these differences were small or not consistent across the growing season.

[9] Technical Dossier/Section D.2.
[10] Technical Dossier/Section D.3.

Table 1 Summary of protein levels in seeds of soybean MON 87701 × MON 89788 (µg/g dry weight)

		MON 87701 × MON 89788	MON 87701	MON 89788
Cry1Ac	Mean	7.9	5.1	N/A
	Range	4.5–12	3.6–6.7	
CP4 EPSPS	Mean	160	N/A	160
	Range	74–300		38–300

N/A, not assayed.

3.1.5. Inheritance and stability of inserted DNA

The genetic stability of the inserted DNA in events MON 89788 and MON 87701 has been demonstrated previously (EFSA 2008; 2011a). In soybean MON 87701 × MON 89788 the two inserts are combined. The Southern data show that the integrity of the inserts present in the single events is retained in MON 87701 × MON 89788. Furthermore, each of the traits has been conserved in this soybean.

3.2. Conclusion

As conventional breeding methods were used in the production of soybean MON 87701 × MON 89788, no additional genetic modification was involved. Southern analyses demonstrated that the integrity of the inserts in the MON 87701 and MON 89788 events was retained in soybean MON 87701 × MON 89788. The levels of Cry1Ac and CP4 EPSPS proteins in the seeds (and all other tissues examined) of soybean MON 87701 × MON 89788 have been demonstrated to be comparable with those in the single events. The EFSA GMO Panel concludes that the molecular characterisation does not indicate a safety concern.

4. COMPARATIVE ANALYSIS

4.1. Evaluation of relevant scientific data

4.1.1. Summary of the previous evaluation of the single events

4.1.1.1. MON 87701

The EFSA GMO Panel has already given an opinion on the insect-resistant soybean MON 87701 (EFSA 2011a). In the compositional studies, the GM soybean MON 87701 was compared with the Asgrow variety A5547, which is a non-GM soybean variety with background genetics similar to MON 87701. The compositional seed and forage data for these soybean materials were collected in field trials in the USA (2007) and Argentina (2007/2008), each season/year at five different geographical sites. Each field trial included soybean MON 87701, the conventional counterpart (A5547) and four different commercial non-GM soybean varieties per field trial site. In total, 20 commercial soybean varieties were used as reference lines to provide data on the natural variation in the composition of this food and feed plant. The results of the compositional analysis of materials from these field trials have been published (Berman et al. 2009). A summary of these studies is given below.

The constituents analysed were the same as in the study of soybean MON 87701 × MON 89788 (see section 4.1.3). In both years/seasons of field trials, analysis of the data across sites revealed no statistically significant differences in the level of analysed constituents in forage between soybeans MON 87701 and A5547. In the corresponding analysis of data from seeds, 15 statistically significant differences were observed in the material from the field trials in 2007 in the USA (the proximates protein and carbohydrates; the amino acids alanine, glycine, histidine, isoleucine, leucine, lysine, serine, threonine and valine; the fatty acid behenic acid; vitamin E; trypsin inhibitor; and daidzein), whereas the level of only four of the constituents differed between seeds of soybean MON 87701 and A5547 in material from the Argentinian field trials in the season 2007/2008 (the amino acid tryptophan, the fatty acid linolenic acid, vitamin E and stachyose). Apparently, the increase in the nine amino acids in the field trials in the USA reflected the increased protein content of the seed. Nevertheless, the

statistically significant differences between soybean MON 87701 and its conventional counterpart were usually small and inconsistent (observed at a few of the field trial sites), and measured levels were with one exception (a single low lectin value) within the range defined by the commercial non-GM varieties included in the studies or reported by the ILSI database (2006) or the USDA-ISO (2006) isoflavone database. Thus, the only constituent for which the difference was consistent (four of the five field trial sites in the USA and five of the five sites in Argentina) and reached some level (around 25%) was vitamin E. When statistically analysed over all field trial sites each growing season, vitamin E levels were increased both in 2007 (7.69 vs 6.24 mg/100 g dry weight) and in the season 2007/2008 (4.40 vs 3.42 mg/100 g dry weight). Although the vitamin E level was increased by on average around 25 % in soybean MON 87701, the level is still within the range of values commonly observed in conventional commercial non-GM soybean varieties, as defined by the reference lines, and by the ILSI crop composition database (ILSI 2006). The applicant provided information on the agronomic performance and phenotypic characteristics of soybean MON 87701 and soybean A5547 (conventional counterpart) from 16 field trial sites in the USA in 2007 and eight field trial sites in Argentina in the season 2007/2008. These field trials also included several commercial non-GM soybean varieties (four per site) used as reference material to estimate the range in baseline values for the studied phenotypic and agronomic parameters in commercial soybean varieties. All materials were grown under normal agronomic conditions for the geographical region; all maintenance chemicals were commercially registered products and were applied at label rates. In the field trials performed in the USA, no significant differences were detected between soybean MON 87701 and the conventional counterpart regarding the phenotypic and agronomic parameters investigated. In the field trials performed in Argentina, early stand count (96.9 vs 105.9 plants in defined rows) and seed moisture content (11.0 % vs 11.6 %) were reduced in soybean MON 87701, and test weight (171.3 vs 169.2 g/250 ml) increased, but these significant differences were found at only two, five, and three, respectively, out of the eight field trial sites in the season 2007/2008. Whereas seed moisture content and test weight were within the range of values defined by the commercial non-GM soybean varieties, the early stand count for soybean MON 87701 (96.9 plants) was slightly below the range for the reference varieties (103.8–204.0 plants). The applicant gave a plausible explanation in that the lower early stand count, which did not influence yield and final stand count, could be due to the different climatic conditions under which the seeds used for the present field trials were produced (MON 87701 seeds were produced in the USA and the A5547 seeds in Puerto Rico). Separate studies have revealed no difference in the percentage of viable pollen produced, pollen diameter and pollen morphology between soybean MON 87701 and its conventional counterpart A5547. Nor were any relevant alterations in germination characteristics observed between soybeans MON 87701 and A5547.

Compositional equivalence between soybean MON 87701 in a different genetic background than in that under consideration here and commercial non-GM soybean varieties has been confirmed in studies on forage and seeds harvested in Brazil (Berman et al. 2010).

The EFSA GMO Panel considered the total set of compositional, phenotypic and agronomical data supplied, and the statistically significant differences between soybean MON 87701 and its conventional counterpart A5547, and concluded that soybean MON 87701 is not different compositionally from its conventional counterpart, except that is has an increased vitamin E content and expresses the Cry1Ac protein. Other than the latter attribute, soybean MON 87701 is compositionally equivalent to commercial non-GM soybean varieties. Regarding agronomic performance and phenotypic characteristics, the Panel identified no difference between soybean MON 87701 and its conventional counterpart and a large set of non-GM soybean varieties that is likely to be biologically relevant.

4.1.1.2. MON 89788

The EFSA GMO Panel has already given an opinion on the glyphosate-tolerant soybean MON 89788 (EFSA 2008). In the compositional studies, the GM soybean MON 89788 was compared with the Asgrow variety A3244, which is a conventional non-GM soybean variety with background genetics similar to MON 89788. Soybean MON 89788 was treated with glyphosate-based herbicides at the recommended dose for commercial use, and the conventional counterpart A3244 and 12 commercial non-GM soybean varieties (included in the study to establish the natural variation in the level of soybean constituents) were treated with other commercial herbicides. The field trials were carried out in Argentina in the season 2004/2005 and in the USA in 2005 at five

different geographical sites each season/year. The results of the compositional analysis of materials from these field trials have been published (Lundry et al. 2008). A summary of these studies is given below.

The constituents analysed for soybean seeds and forage were the same as in the study of soybean MON 87701 × MON 89788 (see section 4.1.3). Statistical differences in the level of analysed constituents between soybeans MON 89788 and A3244 across field trial sites were observed for four constituents in one of the two seasons. These constituents were the moisture content of the forage and the levels of daidzein, glycitein and vitamin E in the seeds. Differences relative to the control were small (–1.6 %, –7.4 %, –10.6 % and 7.4 %, respectively), and were well within the natural variation calculated from the occurrence of these constituents in the 12 commercial non-GM soybean varieties. They also fell within the natural variation of these constituents in soybeans described in the USDA-ISO (2006) isoflavone database. When statistically analysed per site, the level of the first three of these four constituents was significantly altered at one of the five trial sites, whereas for the fourth, vitamin E, the level was not significantly altered at a single site. The statistical analysis of compositional data of soybean MON 89788 and A3244 within sites showed no consistent alteration in the level of the studied components between sites or between growing seasons. Furthermore, the differences were generally small and fell within the range of natural variation calculated from the occurrence of these constituents in conventional soybean varieties.

The applicant also supplied data from field trials in the USA in 2006 (eight sites) and 2007 (two sites), in which soybean MON 89788 sprayed with glyphosate-based herbicides was compared with unsprayed MON 89788 in order to confirm that the spraying regime had no unexpected influence on the soybean composition. No non-GM controls were included in these field trials. The only soybean constituent the level of which was statistically significantly different between unsprayed and sprayed soybean MON 89788 in both years of these field trials was stachyose. However, sprayed plants contained higher levels in 2006 and reduced levels in 2007.

Harrigan et al. (2010) have discussed some of the compositional data obtained from soybean MON 89788, its conventional counterpart and commercial non-GM soybean varieties in more detail. The EFSA GMO Panel concluded that soybean MON 89788 is compositionally equivalent to the conventional counterpart soybean A3244 and other conventional soybean varieties, except that it expresses the introduced trait (EFSA 2008).

The applicant provided information on the agronomic performance and phenotypic characteristics of soybean MON 89788 and soybean A3244 (control) from 17 field trials performed in the USA in 2005. These studies also gave information on reproduction, dissemination and survival of these soybeans, as well as on three or four commercial non-GM soybean varieties for each trial site (in total 23 varieties for all trial sites). The only difference between soybeans MON 89788 and A3244, confirmed by statistical analysis over all trial sites, was plant height, which was lower in soybean MON 89788 than in the control (77.9 vs 82.0 cm). This reduction in plant height was noted at four of the seven sites but was always within the natural variation of the commercial soybean varieties (48.8 to 108.2 cm). As the magnitude of the difference was small (around 5.3 %), the plant height fell within the normal variation and no ecological risks could be linked to the reduction in height, the Panel found this difference to be of no biological importance. No difference in pollen morphology and viability was observed.

Compositional equivalence between soybean MON 89788 in genetic backgrounds other than in the original application and commercial non-GM soybean varieties has been confirmed in studies on forage and seeds harvested in Brazil (Berman et al. 2010). In addition, De Vries and Fehr (2011) studied a selection of compositional and agronomic parameters in 27 back-crossed MON 89788 glyphosate-tolerant lines and 27 back-crossed glyphosate-sensitive lines obtained from populations segregating from soybean MON 89788 in three genetic backgrounds and grown at four field trial sites in the USA. Although statistically significant differences in the mean values for some of the studied parameters were observed between soybean MON 89788 and its non-GM comparator in some of the genetic backgrounds, these differences were small, not consistent over the various genotypes and considered not to be biologically relevant. The investigators concluded that it would be possible to select glyphosate-tolerant (MON 89788) and glyphosate-sensitive lines with comparable performance from soybean populations developed by crossing a glyphosate-sensitive parent with a glyphosate-tolerant parent carrying the MON 89788 event (De Vries and Fehr 2011).

The EFSA GMO Panel considered soybean MON 89788 and its non-GM counterpart to be compositionally and agronomically equivalent to conventional soybean lines, except that soybean MON 89788 expresses the CP4 EPSPS protein rendering the plant glyphosate tolerant. The comparative analysis of soybean MON 89788 with the non-GM variety A3244 and other conventional soybean varieties provided no indication of unintended effects resulting from the genetic modification. Data published on soybean MON 89788 after the EFSA GMO Panel gave its opinion on this GM crop confirm the interpretation of the Panel.

4.1.2. Choice of comparator and production of material for the compositional assessment[11]

The application EFSA-GMO-NL-2009-73 for food and feed use, import and processing of soybean MON 87701 × MON 89788 within the EU presented compositional data from seed and forage material collected in field trials in the USA (2007) and Argentina (2007/2008). These field trials compared the composition of soybean MON 87701 × MON 89788 with a comparator having a comparable genetic background. The comparator was the Asgrow variety A5547, which was the commercial soybean variety originally used in the transformation to establish transformation event MON 87701.

In both years/seasons, the field trials were performed at five separate sites, all of which were representative of the soybean cultivation areas of the countries. The plots designed to supply material for comparative compositional studies included soybean MON 87701 × MON 89788 treated with glyphosate-based herbicides (and, in addition, maintenance pesticides) and the comparator (A5547) and four different commercial non-GM soybean varieties treated with required maintenance pesticides (referred to as untreated). On average, glyphosate was applied at a later stage of soybean growth in the South American field trials than in the North American field trials. The plots designed for agronomic, phenotypic and ecological studies were not sprayed with glyphosate. Altogether 20 commercial non-GM soybean varieties[12] were the reference lines used to provide data on the natural variation in composition of this food and feed plant. The reference lines were checked for natural contamination with the MON 87701 and MON 89788 events. One of the replicates of A5547 at one of the field trial sites in the USA and Argentina contained unacceptably high levels of unintended traits and was excluded from the study. At each field trial site, soybean MON 87701 × MON 89788, the comparator and the commercial non-GM lines were planted following a randomised complete block design with three replicates at each site. Whereas all replicates of soybean MON 87701 × MON 89788 and its comparator were chemically analysed for selected soybean constituents, only one of the replicates of the commercial non-GM varieties was analysed.

As there were no compositional data on soybean MON 87701 × MON 89788 treated with maintenance pesticides other than glyphosate to be compared with soybean A5547 treated with maintenance pesticides, and no agronomic and phenotypic analysis of soybean MON 87701 × MON 89788 treated with glyphosate and maintenance pesticides to be compared with soybean A5547 treated with maintenance pesticides, the EFSA GMO Panel requested additional data on the composition, agronomic and phenotypic characteristics and ecological interaction of soybean MON 87701 × MON 89788 compared with its comparator A5547. The applicant supplied compositional data on soybean MON 87701 × MON 89788 and its comparator not treated with glyphosate from the field trial performed in Argentina in 2007/2008 (similar data were not available from the field trials in the USA in 2007) and agronomic and phenotypic data for soybean MON 87701 × MON 89788 and its comparator treated and not treated with glyphosate from field trials in the USA in 2009[13]. The latter studies also used eight commercially available soybean varieties[14] as reference materials.

[11] Technical dossier/Section D7.2

[12] The commercial non-GM varieties in the field trials in the USA were A5843, A5959, CMA5804AOC, H6686, UA 4805, Ozark, Anand, Hornbeck C5894, A5560, CMC5901COC, A5403, LEE 74, A4922, H4994, H5218, A5427, DP 5989, Hutcheson, Fowler, and USG 5601T. The same commercial non-GM varieties were used in the field trials in Argentina, except for H6686, for which USG 5002T was substituted.

[13] Additional information, November 2011.

[14] The commercial non-GM varieties used in the field trials in the USA in 2009 were Ozark, Anand, H5218, A5427, Teejay, Jake Fowler and USG 5601T.

4.1.3. Compositional analysis[15]

Soybean seeds were harvested and analysed for proximates (protein, fat, ash and moisture), carbohydrates by calculation, fibre fractions (acid detergent fibre (ADF) and neutral detergent fibre (NDF)), amino acids, fatty acids, the micronutrient vitamin E, anti-nutrients (i.e. phytic acid, trypsin inhibitor, lectins, stachyose and raffinose) and other secondary metabolites (isoflavones). Forage was analysed for proximates, carbohydrates by calculation and fibre fractions (ADF, NDF). In total, 64 different compounds, including those recommended by OECD (2001), were analysed in the material harvested in field trials in the USA, 57 in seeds and seven in forage. The data on each analyte were statistically analysed for potential difference in levels between soybean MON 87701 × MON 89788 and its comparator within site and across sites (sites of the trial combined). Nine of the fatty acids analysed in material from the field trials in the USA and 11 in the material from Argentina were minor constituents and frequently occurred at levels below the limit of quantification; when this occurred in more than 50 % of the samples, the analyte was omitted from the statistical analysis. In cases in which constituent levels were statistically significantly different between seeds of soybean MON 87701 × MON 89788 and its comparator, the level was compared with the levels occurring in the commercial non-GM soybean varieties included in the study, as well as with ranges of soybean constituent levels published in the scientific literature and in the ILSI crop composition database (ILSI 2006).

When the compositional data for seed samples from the field trials in the USA (soybean MON 87701 × MON 89788 sprayed with glyphosate, the comparator untreated) were evaluated across sites, a statistically significant difference between soybean MON 87701 × MON 89788 and its comparator was found for 20 analytes: the proximate protein; the amino acids alanine, aspartic acid, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, proline, serine, threonine and valine; the fatty acids palmitic acid, stearic acid, linolenic acid and arachidic acid; and lectin, daidzein and genistein. For forage only the level of total protein differed significantly between soybean MON 87701 × MON 89788 and its comparator. Apparently, the increase in the 12 amino acids reflected the increased protein content of the seed. The evaluation per site revealed that not all of the differences observed for the across-site analysis occurred at all of the individual sites. The statistically significant differences between soybean MON 87701 × MON 89788 and its comparator were usually small, and in all cases, except one, the levels detected were within the range found in the commercial non-GM varieties included in the study. The exception was a single lectin value in one of the three replications of soybean MON 87701 × MON 89788 at a single field trial site. The EFSA GMO Panel concluded that this was an incidental deviation not reflecting the characteristics of soybean MON 87701 × MON 89788. Also, the 26 additional statistically significant differences identified in the per-location statistical analysis of other soybean constituents were small and did not raise concern.

The statistical evaluation of compositional data of seed samples from field trials in Argentina across sites, revealed statistically significant differences between glyphosate-sprayed soybean MON 87701 × MON 89788 and its untreated comparator for 11 analytes: the proximate ash; the two amino acids glutamic acid and leucine; the fatty acids stearic acid, linoleic acid and arachidic acid; and vitamin E, stachyose, daidzein and genistein. The evaluation per site illustrated that, among the 11 constituents that were significantly different in soybean MON 87701 × MON 89788 and the comparator in the across-site analysis, four showed a statistically significant difference at one site, three at two sites, two at three sites and one at four of the five sites. Only the level of acid detergent fibre differed significantly between soybean MON 87701 × MON 89788 and its comparator in forage. The statistically significant differences between soybean MON 87701 × MON 89788 and its comparator were usually small and inconsistent, and in all cases the levels registered were within the range described by the commercial non-GM varieties included in the study and the range reported by the ILSI database (2006) or the USDA-ISO (2006) isoflavone database. In addition, the 16 additional statistically significant differences identified in the per-location statistical analysis of other soybean constituents were small, and all but two were within the range defined by the 20 soybean non-GM reference varieties. Both individual values lying outside the range defined by the non-GM varieties were slightly higher moisture contents of seeds of the comparator A5547: 10.22 % and 10.97 % fresh weight, compared with the range in moisture content of the reference lines (6.88–10.06 % fresh weight). Thus, the statistical analysis comparing compositional data from forage and seeds of

[15] Technical dossier/Section D7.1

glyphosate-treated soybean MON 87701 × MON 89777 and the untreated comparator harvested in field trials in the USA and Argentina, respectively, identified 20 differences between the genetically modified soybean and its comparator in 2007 and 11 in 2007/2008. Six constituents were altered in both growing seasons. These were glutamic acid (altered in one of the ten field sites), leucine (two sites), stearic acid (eight sites), arachidic acid (five sites), daidzein (five sites) and genistein (four sites). However, the levels of these seed constituents were not consistently different across individual field trial sites (figures given within brackets above) and were within the range of values commonly observed in conventional soybean varieties, as defined by the commercial non-GM varieties. There were no consistent statistically significant differences in forage parameters between soybean MON 87701 × MON 89777 and the comparator. Furthermore, the statistically significant differences between these materials observed in only one of the seasons of field trials were small and levels were within the range observed in the commercial non-GM varieties. As the protein content of soybean MON 87701 × MON 89788 was higher than in its comparator (being statistically significant in one of the growing seasons), the difference in glutamic acid and leucine could be foreseen. The level of individual fatty acids varies considerably depending on environmental conditions, as is demonstrated by the wide range in content of the various fatty acids in the commercial non-GM material. This is also the case for the flavonoids daidzein and genistein (USDA-ISO 2006). The approximately 25 % increased level of vitamin E observed in one of the parental soybean events, MON 87701 in the A5547 background (EFSA 2011a), was not observed in soybean MON 87701 × MON 89788.

On request from the EFSA GMO Panel, the applicant supplied compositional data from forage and seed samples from the field trials in Argentina 2007/2008 in which both soybean MON 87701 × MON 89788 and its comparator were not treated with glyphosate (sprayed with maintenance pesticides only)[16]. Analysis of the seed data across sites revealed statistically significant differences between the two soybean materials for 12 analytes: the proximates moisture and ash; the amino acid tryptophan; the fatty acids stearic acid, oleic acid, linoleic acid and arachidic acid; and vitamin E, raffinose, stachyose, daidzein and genistein. The evaluation per site illustrated that among these 12 constituents, four showed statistically significant differences at one site, three at two sites, two at three sites and three at four of the five sites. Again in this case the statistically significant differences between soybean MON 87701 × MON 89788 and its comparator were small (never above 20 %) and in all cases within the range found in the commercial non-GM varieties included in the study and the range reported by the ILSI database (2006) or the USDA-ISO (2006) isoflavone database. The level of none of the constituents analysed in forage differed between soybean MON 87701 × MON 89788 and its comparator.

In conclusion, the only statistically significant differences across locations between soybean MON 87701 × MON 89788 and its comparator that were consistently observed in both the USA and Argentina across the seasons were changes in the level of some fatty acids and increased levels of daidzein and genistein. These differences were small and not considered biologically relevant. Moreover, the values reported fell within the range defined by the natural variation of these constituents in commercial non-GM soybean varieties grown in the same field trials.

The EFSA GMO Panel considered the total set of compositional data supplied and the observed statistically significant differences between soybean MON 87701 × MON 89788 and its comparator, in the light of the field trial design, measured biological variation and the level of the studied compounds in commercial non-GM soybean varieties, and concluded that no biologically relevant differences were identified in the compositional characteristics of soybean MON 87701 × MON 89788 in comparison with its comparator soybean A5547 and that its composition fell within the range of non-GM soybean varieties, except that is expresses the CP4 EPSPS and Cry1Ac proteins.

4.1.4. Agronomic traits and GM phenotype[17]

The applicant performed a comparative assessment of the phenotypic and agronomic characteristics of soybean MON 87701 × MON 89788 and its comparator (A5547) based on field trials at eight sites in Argentina in the season 2007/2008. At each site a randomised complete block design was used, with four replications at three of the sites and three replications at the other five sites. These field trials also included several commercial non-GM

[16] Additional information November 2011.
[17] Technical dossier/Section D4.

soybean varieties[18] (four per site) used as reference material to estimate a range of baseline values among commercial non-GM soybean varieties for each studied phenotypic and agronomic parameter. All materials were grown under normal agronomic conditions for the geographical region; glyphosate-based herbicides were not used. The phenotypic and agronomic characteristics evaluated were early stand count, seedling vigour, plant growth stages, days to 50 % flowering, flower colour, plant pubescence, plant height, lodging, pod shattering, final stand count, seed moisture content, 100-seed weight, test weight (g/250 ml) and yield. In the phenotypic comparison around half of the parameters studied differed between soybean MON 87701 × MON 89788 and A5547. Early stand count (140.6 vs 105.9 plants in defined rows), final stand count (130.0 vs 97.1 plants in defined row), test weight (171.8 vs 169.2 g/250 ml) and yield (2.8 vs 2.5 t/ha) were increased, whereas lodging (2.4 vs 3.3 scale points), grain moisture content (10.9 % vs 11.6 % fresh weight) and 100-seed weight (15.3 vs 16.0 g) were decreased. Of these differences early and final stand count were significantly higher at seven out of the eight field trial sites studied. Test weight was increased at six of eight sites and yield at three of eight sites. A reduction in seed moisture content was observed at seven of eight sites, a lower 100-seed weight at four of eight sites, and reduced lodging at five of eight sites. As the measured endpoint for all parameters showing a statistically significant difference between soybean MON 87701 × MON 89788 and its comparator was within the range in levels of these constituents in soybean reference varieties in the combined site analysis, the applicant argued that no biologically relevant difference in terms of increased potential for the soybean to become a weed between soybean MON 87701 × MON 89788 and its comparator was identified, except the expected difference in tolerance to glyphosate. No developmental differences in categorical parameters (flower colour, plant pubescence and plant growth stage) were observed between soybean MON 87701 × MON 89788 and its comparator.

In the field trials conducted in Argentina in the season 2007/2008, plant response to abiotic stressors and the effects of disease damage were measured four times during the growing season at all eight field trial sites, whereas arthropod damage and abundance were evaluated 15 and nine times, respectively, during the growing season at three of the eight sites. The stressors were defined by experts at each field trial site and varied between sites. A difference between soybean MON 87701 × MON 89788 and its comparator was noted in one of the 192 comparisons made for abiotic stress and plant disease damage. This was caused by soybean mosaic virus at one of the field trial sites during observation 2 (MON 87701 × MON 89788 none vs A5547 slight). This disease damage category was within the range of damage observed among the reference soybean varieties. Regarding arthropod damage, no statistical significant difference was detected between soybean MON 87701 × MON 89788 and the comparator for 23 out of 32 comparisons. In eight of the nine cases in which a difference was detected, it was the result of reduced damage in soybean MON 87701 × MON 89788 caused by lepidopteran pests, which was expected as this GM soybean carries an insect protection trait targeted against lepidopteran pests. The other difference detected was reduced damage by stink bugs in soybean MON 87701 × MON 89788 than in A5547; however, notably in this case the stink bug damage was within range in the reference soybean varieties and observed on only one occasion. There was no difference in arthropod abundance between soybean MON 87701 × MON 89788 and its comparator regarding several investigated species.

On request from the EFSA GMO Panel for additional agronomic and phenotypic data, the applicant supplied data from field trials in the USA in 2009 in which soybean MON 87701 × MON 89788 sprayed with glyphosate and maintenance pesticides[19], or sprayed with maintenance pesticides only[20], was compared with the comparator A5547 sprayed with maintenance pesticides. Of the five field trials initiated in the soybean-growing regions of the USA, one site (Arkansas) was dropped from the study owing to poor germination and emergence as a result of excessive rain. Differences were observed in two agronomic characteristics between the glyphosate-sprayed soybean MON 87701 × MON 89788 and the comparator, namely seedling vigour and final stand count. The differences, however, were not large, and measured values fell within the range found in commercial non-GM soybean varieties grown in the same field trials.

[18] A total of 20 commercial reference varieties were evaluated (USG 5002T, Asgrow A5427, Hornbeck C5894, Asgrow A5959, Hartz H5218, Asgrow A5403, CMA 5804A0C, DP 5989, Ozark (5.2), Annand (5.4), Asgrow A5843, CMC 5901C0C, UA 4805, A5560, LEE 74, A4922, H4994, Hutcheson, USG 5601T, Fowler).
[19] Additional information November 2011.
[20] Additional information November 2011.

When plants were not treated with glyphosate, one statistically significant difference was observed between soybean MON 87701 × MON 89788 and its comparator – and that was a higher stand count. The increased mean values in stand count were within the range observed in commercial non-GM soybean varieties grown in the same field trials.

It is concluded that crossing insect-resistant soybean MON 87701 with glyphosate-tolerant soybean MON 89788 to produce the stacked soybean MON 87701 × MON did not result in any consistent changes in phenotypic and agronomic characteristics, as compared with its comparator, with the exception of a small increase in final stand count which is not considered biologically relevant by the EFSA GMO Panel.

4.2. Conclusion

The EFSA GMO Panel concludes that no biologically relevant differences were identified in the composition or agronomic and phenotypic characteristics of soybean MON 87701 × MON 89788, as compared with the comparator soybean A5547, and that the composition of soybean MON 87701 × MON 89788 fell within the range observed in non-GM soybean varieties, except that it expresses the CP4 EPSPS and Cry1Ac proteins. Based on the assessment of the data available, the EFSA GMO Panel is of the opinion that crossing soybean MON 87701 and soybean MON 89788 to produce soybean MON 87701 × MON 89788 does not result in interactions that cause compositional, agronomic or phenotypic changes that would raise safety concerns.

5. FOOD/FEED SAFETY ASSESSMENT

5.1. Evaluation of relevant scientific data

5.1.1. Summary of the previous evaluation of the single events

5.1.1.1. MON 87701

The EFSA GMO Panel has already given an opinion on the safety assessment of soybean MON 87701 (EFSA 2011a). In short, soybean MON 87701 expresses a Cry1Ac protein from an introduced gene (*cry1Ac*) derived from *Bacillus thuringiensis* subsp. *kurstaki*. An *Escherichia coli*-produced Cry1Ac protein was used for safety studies after it had been demonstrated experimentally that it was structurally similar and physicochemically/functionally equivalent to the Cry1Ac protein extracted from soybean event MON 87701. No toxicity of the Cry1Ac protein was observed up to the highest doses tested (1460 mg/kg body weight in males and 1290 mg/kg body weight in females) in an acute oral toxicity study in mice. The Cry1Ac protein was shown to be quickly degraded in simulated gastric fluid, and all transiently appearing fragments were quickly degraded on subsequent exposure to simulated intestinal fluid. Bioinformatics studies demonstrated that the Cry1Ac protein showed homology only with other Cry proteins not toxic to mammals. The newly expressed Cry1Ac protein was shown to be unlikely to be an allergenic protein and the whole GM soybean MON 87701 unlikely to differ in allergenic potential from that of commercial non-GM soybeans. Two 90-day feeding studies in rats with diets including 15 % or 30 % toasted and defatted soybean meal prepared from soybean MON 87701 or the conventional counterpart (A5547) indicated no toxicity. In addition, a 42-day broiler chicken feeding study identified no relevant difference in broiler performance, carcass yield or meat composition between chickens fed diets containing extracted soybean meal produced from soybean MON 87701 and the conventional counterpart or other commercial non-GM soybean varieties.

5.1.1.2. MON 89788

The EFSA GMO Panel has already given an opinion on the safety assessment of soybean MON 89788 (EFSA 2008). In short, soybean MON 89788 expresses the CP4 EPSPS protein. An *E. coli*-produced CP4 EPSPS protein was used for safety studies after it had been demonstrated experimentally that the microbially produced protein is structurally similar and physicochemically/functionally equivalent to the CP4 EPSPS protein extracted from soybean event MON 89788. No toxicity of the CP4 EPSPS protein was observed up to the highest dose tested (572 mg/kg body weight) in an acute oral toxicity study in mice. The CP4 EPSPS was shown to be quickly degraded in simulated gastric fluid, and a little less quickly degraded in simulated intestinal fluid. A quick

degradation of the CP4 EPSPS protein in simulated gastrointestinal fluids has been confirmed (Shim et al. 2010). Bioinformatics studies demonstrated that the CP4 EPSPS protein show no homology to known toxic or allergenic proteins. A 90-day feeding study in rats with diets including 5 % or 15 % processed meal of soybean MON 89788 or the conventional counterpart (A3244) indicated no toxicity. In addition, a recently published study showed that feeding a diet containing about 38 % soybean flour from MON 89788 (for 182 days) to male Wistar rats had comparable responses to feeding a diet containing the same amount of flour from soybean A3244 (Tutelyan et al. 2010; Tyshko et al. 2010). The original application contained a 42-day feeding study on broiler chickens, which has now been published and shows that soybean MON 89788 is as nutritionally wholesome as the conventional counterpart and commercial non-GM soybean varieties (Taylor et al. 2007). Using extracts from soybean MON 89788, the conventional counterpart (A3244), and commercial non-GM soybean varieties, and sera from non-allergic and soybean-allergic patients, it was demonstrated that it is unlikely that the overall allergenicity of the whole GM soybean MON 89788 is different from that of conventional soybeans.

5.1.2. Product description and intended use[21]

The scope of application EFSA-GMO-NL-2009-73 is for food and feed use, import and processing of soybean MON 87701 × MON 89788 within the EU. Thus, soybean MON 87701 × MON 89788 will be imported into the EU mixed with other soybean varieties and used as food or feed or for the production of a large number of derived products, in the same way as any commercial soybean variety. The main product for human use is soybean oil. Around 10 % of the heat-processed (toasted) defatted soybean meal goes into soybean products for human consumption, including flours, soybean protein concentrates and various textured products simulating meats, seafoods and cheeses. The rest of the toasted defatted soybean meal goes into animal feed, mainly for poultry, pigs and cattle in the EU (OECD 2001). Whole soybeans are used to produce soy sprouts and baked and roasted soybeans. There is also a limited direct use for soybeans as animal feeds. The genetic modification events present in soybean MON 87701 × MON 89788 result in the expression of two new proteins, one being the Cry1Ac protein, which confers protection against lepidopteran pests such as velvet bean caterpillar (*Anticarcia gemmatalis*), soybean looper (*Pseudoplusia includens*), bean shoot borer (*Epinotia aporema*) and sunflower looper (*Rachiplusia nu*), and the other being the CP4 EPSPS enzyme, which is less sensitive to glyphosate (which inhibits the synthesis of aromatic amino acids) than the endogenous plant EPSPS enzyme and, therefore, allows soybean MON 87701 × MON 89788 to produce aromatic amino acids and grow normally in the presence of glyphosate herbicides. Thus, the genetic modifications are intended only to improve agronomic performance and are not intended to influence the nutritional aspects, the processing characteristics and the overall use of soybean as a crop.

5.1.3. Effects of processing[22]

Soybean MON 87701 × MON 89788 will be used for production and manufacturing of food and feed products in the same ways as any other commercial soybean variety. Taking into account the compositional analysis, providing no indication of relevant compositional changes except for the stacked soybean expressing the CP4 EPSPS and Cry1Ac proteins, the Panel has no reason to assume that the characteristics of soybean MON 87701 × MON 89788, and derived processed products, would be any different from those of the corresponding products derived from soybean MON 87701, soybean MON 89788 and conventional soybean varieties. The processing of soybean MON 87701 × MON 89788 will be no different from the processing of conventional soybeans. Thus, solvent extraction, hard pressing and extrusion result in various types of soybean oil products used as food, soybean meal for animal feed, protein products usually used as feed but to some extent also as food, and various specialised products such as lecithin. Heat treatment of soybean MON 89788 (190 ºC for 30 min), simulating the process used in commercial soybean processing, reduced the amount of immune-detectable CP4 EPSPS protein present in soybean MON 89788 to levels below the limit of detection, thus representing a more than 97 % reduction in the quantity of detectable CP4 EPSPS compared with the unheated MON 89788 sample. A similar study on heat-treated soybean MON 87701 (190 ºC for 15.5 min) reduced also the quantity of immune-detectable Cry1Ac protein to levels below the limit of detection, corresponding to a reduction of at least 94 % compared with the unheated MON 87701. It was suggested that the losses are likely to

[21] Technical dossier/Section D7.7.
[22] Technical dossier/Section D7.6.

be due to protein degradation and/or aggregation into an insoluble complex as a result of the heat treatment. The EFSA GMO Panel finds it likely that similar heat treatments of soybean MON 87701 × MON 89788 will result in corresponding reductions in the amount of immune-detectable CP4 EPSPS and Cry1Ac protein in the heat-treated product.

5.1.4. Toxicology[23]

5.1.4.1. Toxicological assessment of expressed novel proteins in soybean MON 87701 × MON 89788

No new genes, in addition to those occurring in the parental soybean varieties, have been introduced in soybean MON 87701 × MON 89788. The CP4 EPSPS protein expressed in soybean MON 89788 has been evaluated for its safety previously (EFSA 2008), and no safety concerns were identified. This was confirmed in an updated bioinformatics study in which the amino acid sequence of the CP4 EPSPS protein was compared with amino acid sequences available in databases containing toxic proteins. The EFSA GMO Panel is not aware of any other new information that would change this conclusion. The Cry1Ac protein expressed in soybean MON 87701 was more recently evaluated for its safety (EFSA 2011a), and in this case too no safety concerns for humans or animals were identified. Quantification of expression levels of the Cry1Ac and CP4 EPSPS proteins in various tissues of soybean MON 87701 × MON 89788, MON 87701 and MON 89788 revealed comparable expression levels in the stacked hybrid as compared with the expression levels in the parental events (at most a twofold difference).

The EFSA GMO Panel has reviewed all the data available for soybean MON 87701 × MON 89788, both for the single events and for the newly expressed proteins Cry1Ac and CP4 EPSPS, including information provided by the applicant in response to questions from the Panel, and considers that interactions between the single events that might impact on food and feed safety are unlikely.

5.1.4.2. Toxicological assessment of new constituents other than proteins

No new constituent, other than the Cry1Ac and CP4 EPSPS proteins, is expressed in soybean MON 87701 × MON 89788, and no relevant changes in the composition of soybean MON 87701 × MON 89788 were detected by the compositional analysis.

5.1.4.3. Toxicological assessment of the whole GM food/feed

Both soybeans MON 89788 and MON 87701 have previously been found as safe for human and animal consumption as their corresponding conventional counterparts and commercial non-GM soybean varieties (EFSA 2008, 2011a).

A molecular characterisation undertaken on soybean MON 87701 × MON 89788 identified no altered stability of the single soybean events (see section 3.1.5) when these were brought together by crossing, and expression analysis of the Cry1Ac and CP4 EPSPS proteins revealed no relevant change in expression levels in soybean MON 87701 × MON 89788 compared with the single soybean events MON 87701 and MON 89788, respectively (see section 3.2). As no biologically relevant differences were identified in the compositional characteristics of soybean MON 87701 × MON 89788 in comparison with non-GM soybean varieties, except that it expresses the CP4 EPSPS and Cry1Ac proteins, and an assessment found no indication for interaction between the single events that could influence the safety of soybean MON 87701 × MON 89788 for humans and animals, the EFSA GMO Panel is of the opinion that no additional animal safety studies are required.

5.1.5. Allergenicity[24]

The strategies used when assessing the potential allergenic risk focus on the characterisation of the source of the recombinant protein, the potential of the newly expressed protein to induce sensitisation or to elicit allergic

[23] Technical dossier/Section D7.8.
[24] Technical dossier/Section D7.9

reactions in already sensitised persons, and whether the transformation may have altered the allergenic properties of the modified food.

5.1.5.1. Assessment of allergenicity of the newly expressed proteins

A weight-of-evidence approach is recommended when assessing the potential allergenicity of a newly expressed protein, taking into account all of the information obtained with various test methods, as no single experimental method yields decisive evidence for allergenicity (Codex Alimentarius 2009; EFSA 2010).

The CP4 EPSPS protein present in soybean MON 89788 and the Cry1Ac protein present in soybean MON 87701 have been evaluated previously within the assessment of the single events, and it was found unlikely that they are allergenic (EFSA 2008, 2011a). Nonetheless, the applicant supplied a bioinformatics-supported comparison of the amino acid sequence of the CP4 EPSPS protein with amino acid sequences of known allergens collected in an updated proprietary database. This study confirmed the hypothesis that CP4 EPSPS is unlikely to be an allergen. The EFSA GMO Panel has, thus, concluded that it is unlikely that these newly expressed proteins are allergenic.

5.1.5.2. Assessment of allergenicity of the whole GM plant or crop

Soybeans are common allergenic foods. Therefore, new genetically modified soybeans are assessed in order to assure that the allergenicity of the whole GM plant has not been increased by the genetic modification. Such assessments have already been performed for soybeans MON 89788 and MON 87701 (EFSA 2008, 2011a), and it was concluded that the overall allergenicity of the whole soybeans MON 89788 and MON 87701 is unlikely to be different from that of their corresponding conventional counterparts and commercial soybean varieties. On request from the EFSA GMO Panel, the applicant supplied additional data to demonstrate that the overall allergenicity of soybean MON 89788 × MON 89788 was not altered when compared with the overall allergenicity of its comparator A5547[25]. The applicant separated proteins from extracts of soybeans MON 87701 × MON 89788 and A5547 by one- or two-dimensional gel electrophoresis and identified bands of major allergenic proteins and spots of less abundant allergens by tandem mass spectrometry. On visual inspection of the intensities of the bands of the abundant α′, α, and β subunits of glycinin beta-conglycinin, the acidic and basic chains of glycinin and trypsin inhibitor on the one-dimensional gel and the less abundant spots Gly m Bd30k (P34), Gly m Bd28k and Gly m 4(SAM22) on the two-dimensional gel in soybeans MON 87701 × MON 89788 and A5547 no differences were observed. Thus, the requested study confirmed that bringing together the single soybean events MON 87701 and MON 89788 by conventional crossing to form the stacked soybean MON 87701 × MON 89788 does not result in any observable differences in allergen content between soybeans MON 87701 × MON 89788 and its comparator.

The EFSA GMO Panel considers it unlikely that potential interactions will occur in soybean MON 87701 × MON 89788 that might change the allergenicity of the whole crop.

5.1.6. Nutritional assessment of GM food/feed[26]

The applicant provided a 42-day broiler chicken feeding study (Cobb × Cobb 500) performed according to generally accepted guidelines (ILSI 2003), and consisting of nine treatment groups, all with different types of soybean meal. One group received meal of soybean MON 87701 × MON 89788, one soybean MON 87701 (not considered in this context), another soybean A5547 (a non-GM soybean with comparable background genetics to MON 87701 × MON 89788), and the other six groups meals of different commercial non-GM soybean varieties[27].

Each treatment group consisted of 60 male and 60 female broilers (in pens of 12 chickens/pen being reduced at day 7 to 10 birds/pen), which were fed starter diets (days 0–21) containing about 33 % (32.3–33.5 %) soybean meal and grower/finisher diets (days 21–42) containing 30–31 % soybean meal. The various soybean meals were

[25] Additional information November 2011.
[26] Technical dossier/Section D7.10.
[27] The non-GM soybean varieties used were Anand, Ozark, NK S38-T8, H437, NC+2A86, and NK25-J5.

characterised regarding 89 constituents before adjusted diets were formulated based on the energy and nutrient requirements for broilers according to NRC (1994). Diets were controlled for their quality with respect to pesticide and mycotoxin content, which in all cases were below threshold levels of concern for feeding studies.

The animals were weighed at the beginning of the study and after 42 days of feeding. On days 43 (males) and 44 (females), animals were sacrificed and processed for body analyses. Statistical analyses of the experimental results were performed by two-factorial analysis of variance (factors were diet and sex).The mortality rates in the different treatment groups during the first 7 days were between 0.8 % and 4.2 % (average 2.3 %; soybean MON 87701 × MON 89788 2.5 %), and were mainly due to bacterial infection and dehydration. During the remainder of the study, days 7–42, mortality rates (due to ascites and sudden death syndrome) were on average 0.6 %, ranging from 0 % to 2.0 % across the treatment groups (soybean MON 87701 × MON 89788 0 %). Surviving birds were in good health during the study. No significant effect on performance was noted. Thus, weight at the start (around 38 g) and end of the study (average 2.511–2.547 kg; soybean MON 87701 × MON 89788 2.545 kg), feed intake, weight gain and adjusted feed conversion rate (average 1.528–1.560; soybean MON 87701 × MON 89788 1.528) were comparable in broiler chickens fed diets with soybean meal from MON 87701 × MON 89788 and A5547. No relevant effects were observed on the various parameters of carcass yield or of fat, protein and moisture content of breast and thigh meat.

In conclusion, the broiler feeding study identified no relevant difference in broiler performance, carcass yield or meat composition between chickens fed diets containing soybean meal produced from soybean MON 87701 × MON 89788, the comparator A5547, or the six commercial non-GM soybean varieties. Thus, these data demonstrate that diets formulated with soybean MON 87701 × MON 89788 are as nutritious as those formulated with commercial non-GM soybean varieties.

5.1.7. Post-market monitoring of GM food/feed

The risk assessment concluded that no data have emerged to indicate that soybean MON 87701 × MON 89788 is any less safe than its comparator A5547. In addition, soybean MON 87701 × MON89788 is as nutritious as conventional soybeans. Therefore, and in line with the guidance document (EFSA 2006), the EFSA GMO Panel is of the opinion that post-market monitoring of the GM food/feed is not necessary.

5.2. Conclusion

The CP4 EPSPS protein expressed in soybean MON 89788 and the Cry1Ac protein expressed in soybean MON 87701 have been evaluated previously, and no safety concerns were identified. Given all the information provided, the EFSA GMO Panel considers that interactions between the single events that might impact on food and feed safety are unlikely. The Panel also noted that the nutritional properties of soybean MON 87701 × MON 89788 are not different from those of commercial soybean varieties. The EFSA GMO Panel considers that soybean MON 87701 × MON 89788 is as safe and as nutritious as its comparator A5547 and that it is unlikely that the overall allergenicity of the whole plant is changed.

6. ENVIRONMENTAL RISK ASSESSMENT AND MONITORING PLAN

6.1. Evaluation of relevant scientific data

The scope of this application EFSA-GMO-NL-2009-73 is for food and feed uses, import and processing, and does not include cultivation. Considering the intended uses of soybean MON 87701 × MON 89788, the environmental risk assessment is concerned with the exposure through the manure and faeces from animals fed soybean MON 87701 × MON 89788 and with the accidental release into the environment of viable grains of soybean MON 87701 × MON 89788 during transport and processing. Soybean MON 87701 × MON 89788 has been developed for tolerance to glyphosate-based herbicides and protection against certain lepidopteran pests (i.e. *A. gemmatalis*, *P. includens*, *E. aporem* and *R. nu*, which are not present in European fauna). Herbicide tolerance is conferred by the expression of the CP4 EPSPS protein. Insect resistance is achieved by the expression of the *B. thuringiensis*-derived Cry1Ac protein. As the scope of the present application excludes

cultivation, environmental concerns in the EU related to the use of glyphosate herbicides on the GM soybean do not apply.

6.1.1. Evaluation of the single events

In a previous scientific opinion, the EFSA GMO Panel was of the opinion that the single soybean events MON 87701 and MON 89788 are as safe as conventional soybean with respect to potential effects on human and animal health or the environment in the context of their intended uses (EFSA 2008, 2011a). Furthermore, post-market environmental monitoring plans, including general surveillance, were proposed by the applicant and accepted by the EFSA GMO Panel for soybeans MON 87701 and MON 89788.

6.1.2. Environmental risk assessment

6.1.2.1. Unintended effects on plant fitness due to the genetic modification[28]

Cultivated soybean (*Glycine max* (L.) Merr.) is a species in the subgenus *Soja* of the genus *Glycine*. The species originated from eastern Asia and is a highly domesticated crop (Lu 2005). The major worldwide soybean producers are Argentina, Brazil, China, North Korea, South Korea and the USA. In the EU, soybean is mainly cultivated in Austria, France, Italy, Hungary and Romania (Dorokhov et al. 2004).[29] Cultivated soybean seeds rarely display any dormancy characteristics, and only under certain environmental conditions grow as volunteers in the year following cultivation (OECD 2000). In soybean fields, seeds usually do not survive during the winter due to predation, rotting, germination resulting in death, or due to management practices prior to planting the subsequent crop (Owen 2005). The herbicide tolerance trait can be regarded as providing only a potential agronomic and selective advantage for this GM soybean plant where and when glyphosate-based herbicides are applied. Similarly, insect resistance against certain lepidopteran target pests provides a potential agronomic advantage where plants are cultivated under an infestation of the target pests. However, survival of soybean plants outside cultivation where glyphosate herbicides are applied is mainly limited by a combination of low competitiveness, absence of a dormancy phase, and susceptibility to plant pathogens and cold climatic conditions. As these general characteristics are unchanged in soybean MON 87701 × MON 89788, herbicide tolerance and insect resistance are not likely to provide a selective advantage outside cultivation or other areas where the herbicides are applied. Even if herbicides are applied to these plants, it will not change their ability to survive over seasons. Therefore, it is considered very unlikely that soybean MON 87701 × MON 89788 will differ from conventional soybean varieties in its ability to survive until subsequent seasons or to establish feral populations under European environmental conditions.

Field trials with soybean MON 87701 × MON 89788 were carried out by the applicant across eight locations in Argentina in 2007/2008 and across five locations in the USA in 2009 as described in section 4.1.4. As mentioned above, the combined site analysis of the 2007/2008 field data identified seven statistically significant differences in early and final stand count, test weight, yield, lodging, grain moisture content and 100-seed weight. The combined site analysis of the 2009 field data identified two statistically significant differences in seedling vigour and final stand count. The EFSA GMO Panel considers that the differences observed are unlikely to affect the overall fitness, invasiveness or weediness of the GM soybean, except under conditions of infestation by the specific lepidopteran pests or application of glyphosate-based herbicides.

In addition to the data presented by the applicant, the EFSA GMO Panel is not aware of any scientific report of increased spread and establishment of GM soybean and any change in its survival capacity, including overwintering (Dorokhov et al. 2004; Owen 2005; Bagavathiannan and Van Acker 2008, Lee et al. 2009). The EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects of the soybean MON 87701 × MON 89788 in Europe will not be different from that of conventional soybean varieties.

[28] Technical dossier/sections D4, D9.1 and D9.2 and additional information, November 2011,
[29] http://epp.eurostat.ec.europa.eu/portal/page/portal/agriculture/data/database

6.1.2.2. Potential for gene transfer[30]

A prerequisite for any gene transfer is the availability of pathways for the transfer of genetic material, either through horizontal gene transfer of DNA or vertical gene flow via seed dispersal and cross-pollination.

(a) Plant-to-bacteria gene transfer

Genomic DNA is a component of many food and feed products derived from soybean. It is well documented that DNA present in food and feed becomes substantially degraded during digestion in the human or animal gastrointestinal tract. However, a low level of exposure of fragments of ingested DNA, including the recombinant fraction of such DNA, to microorganisms present in the digestive tract of humans, domesticated animals and other animals feeding on soybean MON 87701 × MON 89788 is expected.

Current scientific knowledge of recombination processes in bacteria indicates that horizontal transfer of non-mobile, chromosomally located DNA fragments between unrelated organisms (such as plants to microorganisms) is not expected to occur at detectable frequencies under natural conditions (see EFSA 2009 for further details).

A successful horizontal transfer would require stable insertion of the transgene sequences into a bacterial genome and a selective advantage conferred to the transformed host. The only known mechanism that facilitates horizontal transfer of non-mobile, chromosomal DNA fragments into bacterial genomes is homologous recombination. This requires the presence of stretches of DNA sequences that are similar in the recombining DNA molecules and, in addition to substitutive gene replacement, facilitates the insertion of non-homologous DNA sequences if their flanking regions share sequence similarity with bacterial sequences in the recipient.

The hybrid soybean MON 87701 × MON 89788 contains genetic elements with identity or high similarity to those of bacteria. These are from MON 87701 the coding sequence of Cry1Ac, a synthetic gene that is highly similar to corresponding genes from Cry1Ac producing *B. thuringiensis*, and from MON 89788 a codon-optimised synthetic sequence of CP4 *epsps* from *Agrobacterium tumefaciens*. The flanking regions of the *cry1Ac* and CP4 *epsps* gene inserts both contain on their right border an approximately 40-bp-long sequence and on their left border for CP4 *epsps* a 150-bp-long and for *cry1Ac* a 264-bp-long sequence of the Ti-plasmid of *A. tumefaciens.*

Neither *A. tumefaciens* nor *B. thuringiensis* is considered to be prevalent in the main receiving environment, that is the gastrointestinal tract of humans or animals. Both occur in soil, and, in addition, *B. thuringiensis* has been frequently isolated from the guts of insects (Jensen et al. 2003). However, occurrence of the recombinant genes outside their immediate receiving environment in the habitats of both bacterial species cannot be ruled out (Hart et al. 2009) and is therefore also considered here.

On a theoretical basis (i.e. without any study providing experimental evidence for horizontal gene transfer in the case of GM food and feed derived from soybean MON 87701 × MON 89788 or any other GM plant) it can be assumed that, as an extremely rare event, homologous recombination may occur in the environment between the recombinant *cry1Ac* or CP4 *epsps* genes and their natural variants as they may occur in *B. thuringiensis* (for *cry1Ac*) and *A. tumefaciens* (for CP4 *epsps*). Such recombination events would only replace natural variants (substitutive recombination) and are therefore unlikely to provide any new property connected to a selective advantage for the recipient organisms (EFSA 2009). Double homologous recombination of the flanking regions with those on natural Ti-plasmids of *A. tumefaciens* would result in gene replacement, by which a *cry1Ac* or CP4 *epsps* gene would substitute genes for crown gall formation (loss of auxin-, cytokinin- and opine-synthesising genes). This event is limited by the short lengths of the DNA-flanking regions providing DNA homologies (Brigulla and Wackernagel 2010)In addition to homology-based recombination processes, illegitimate recombination that does not require DNA similarity between the recombining DNA molecules is theoretically possible. However, the transformation rates for illegitimate recombination are considered to be 10^{10}-fold lower

[30] Technical dossier/section D6

than for homologous recombination (Hülter and Wackernagel 2008; EFSA 2009). Illegitimate recombination events have not been detected in studies that have exposed bacteria to high concentrations of GM plant DNA (EFSA 2009). Thus, this process, in comparison with homologous recombination, is not considered to significantly contribute to horizontal gene transfer events. In comparison with the above described homology-facilitated recombination processes, the contribution of illegitimate recombination is extremely low.Both protein-encoding genes from bacteria are regulated in soybean MON 87701 × MON 89788 by promoters optimised for expression in plants: the *cry1Ac* gene by a promoter derived from the *A. thaliana RbcS4* gene and the CP4 *epsps* gene by a synthetic promoter derived from the promoter of the figwort mosaic virus and the *A. thaliana Tsf1* gene. The expression of the *prRBCS4–cry1ac* and P-*FMV/Tsf1*–CP4 *epsps* constructs in bacteria is unknown, but generally the expression level of eukaryotic promoters in bacteria is inefficient (Warren et al. 2008).In a worst-case scenario, considering the possibility of expression, an *A. tumefaciens* recipient would become capable of producing an insecticidal Cry1Ac protein or a plant codon-optimised CP4 EPSPS protein. However, the exposure of bacterial communities to the recombinant genes in soybean MON 87701 × MON 89788 must be seen in the context of the natural occurrence and level of exposure to alternative sources of similar genes to which bacterial communities are continually exposed. The protein encoded by CP4 *epsps* is an enzyme involved in the biosynthesis of chorismate, the common precursor of numerous aromatic compounds in bacteria, fungi and plants. It can therefore be expected that both sequence-similar and -different *epsps* genes are widely distributed in gut and other microorganisms occurring in the receiving environments. Owing to its specific lifestyle as a soil bacterium and plant pathogen, in contrast to the lifestyle of *B. thuringiensis*, which colonizes insect guts and infects specific target insects, the EFSA GMO Panel considers it unlikely that *A. tumefaciens* would gain selective advantage from such horizontal gene transfer by double homologous recombination.The EFSA GMO Panel concludes that the *cry1Ac* or CP4 *epsps* genes from soybean MON 87701 × MON 89788 may, on a theoretical basis, be transferred by double homologous recombination to *A. tumefaciens*. This event is highly limited by the short lengths of the DNA-flanking regions providing DNA homologies and also by the fact that *A. tumefaciens* is not a gut bacterium and thus not a member of the microbial community in the main receiving environment. Owing to the natural occurrence of *cry1Ac* and CP4 *epsps* in the environment, a low-level gene transfer to *A. tumefaciens* (for CP4 *epsps* and *cry1Ac*) or *B. thuringiensis* (for *cry1Ac*) is not regarded as conferring a new trait and selective advantage. Considering its intended use as food and feed and the above assessment, in agreement with its previous opinions on the single events, the EFSA GMO Panel has therefore not identified any concern associated with horizontal gene transfer from soybean MON 87701 × MON 89788 to bacteria.*(b) Plant-to plant-gene transfer*

Considering the intended uses of soybean MON 87701 × MON 89788 and the physical characteristics of soybean seeds, a possible pathway of gene dispersal is from seed spillage and pollen of occasional feral GM soybean plants originating from accidental seed spillage mainly during transport and/or processing.The genus *Glycine* is divided into two distinct subgenera: *Glycine* and *Soja*. Soybean is in the subgenus *Soja*. The subgenus *Glycine* contains 16 perennial wild species, while the cultivated soybean, *G. max*, and its wild and semi-wild annual relatives, *G. soja* and *G. gracilis*, are classified in the subgenus *Soja* (OECD 2000). Owing to the low level of genomic similarity among species of the genus *Glycine*, *G. max* can cross only with other members of *Glycine* subgenus *Soja* (Hymowitz et al. 1998; Lu 2004). Hence, the three species of the subgenus *Soja* are capable of cross-pollination, and the hybrid seed that is produced can germinate normally and produce plants with fertile pollen and seed (Abe et al. 1999; Nakayama and Yamaguchi 2002). However, since *G. soja* and *G. gracilis* are indigenous to Australia, China, Japan, Korea, the Philippines, the far eastern region of Russia, the South Pacific and Taiwan, and since they have not been reported in other parts of the world where the cultivated soybean is grown (Dorokhov et al. 2004; Lu 2005), the plant-to-plant gene transfer from soybean is restricted to cultivated soybean in the EU.

Soybean is an annual mostly self-pollinating plant which has a percentage of cross-pollination in field crops usually lower than 1 % (Weber and Hanson 1961; Caviness 1966; Ray et al. 2003; Lu 2005; Yoshimura et al. 2006; Abud et al. 2007). Soybean pollen dispersal is limited because the anthers mature in the bud and directly pollinate the stigma of the same flower (OECD 2000). However, cross-pollination rates as high as 6.3 % have been reported for closely spaced plants (Ray et al. 2003), suggesting the potential for some within-crop gene flow in soybean. These results indicate that natural cross-pollination rates can fluctuate significantly among different soybean varieties under particular environmental conditions such as a favourable climate for pollination

and an abundance of pollinators (Gumisiriza and Rubaihayo 1978; Kikuchi et al. 1993; Ahrent and Caviness 1994; Ray et al. 2003; Lu 2005).

Plant-to-plant gene transfer could therefore occur under the following scenarios: imports of soybean MON 87701 × MON 89788 seeds (although most soybean MON 87701 × MON 89788 seeds will be processed in the country of production), processing outside importing ports, transport in regions of soybean production in Europe, spillage of GM seeds mainly during transport, germination and development of spilled seeds within soybean fields or in very close vicinity to cultivated soybean fields, overlap of flowering periods, and environmental conditions favouring cross-pollination. The likelihood of all these conditions occurring and thereby resulting in cross-pollination between GM soybean plants and cultivated soybean is extremely low. Apart from seed production areas, GM plants and plants derived from outcrossing with this GM soybean will not persist over time. Dispersal of soybean seeds by animals is not expected owing to the characteristics of the seed, but accidental release into the environment of seeds may occur (e.g. during transport and processing for food, feed and industrial uses). However, cultivated soybean seeds rarely display any dormancy characteristics and grow only under certain environmental conditions as volunteers in the year following cultivation (OECD 2000). Even in soybean fields, seeds usually do not survive during the winter because of predation, rotting, germination resulting in death, or management practices prior to planting the subsequent crop (Owen 2005).

The EFSA GMO Panel takes into account the fact that this application does not include cultivation of the soybean within the EU, so that likelihood of cross-pollination between cultivated soybean and occasional soybean plants resulting from seed spillage is considered to be extremely low. However, in countries cultivating this GM soybean and producing seed for export, there is a potential for admixture in seed production and thus the introduction of GM seeds through this route.

In conclusion, as soybean MON 87701 × MON 89788 has no altered survival, multiplication or dissemination characteristics, the EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects as a consequence of spread of genes from soybean MON 87701 × MON 89788 in Europe will not differ from that of conventional soybean varieties.

6.1.2.3. Potential interactions of the GM plant with target organisms[31]

Owing to the intended uses of soybean MON 87701 × MON 89788, which exclude cultivation, and the low level of exposure to the environment, potential interactions of the GM plant with target organisms were not considered an issue by the EFSA GMO Panel.

6.1.2.4. Potential interactions of the GM plant with non-target organisms[32]

Owing to the intended uses of soybean MON 87701 × MON 89788, which exclude cultivation, and the low level of exposure to the environment, potential interactions of the GM plant with non-target organisms were not considered an issue by the EFSA GMO Panel.However, the EFSA GMO Panel evaluated whether the Cry1Ac protein might potentially affect non-target organisms by entering the environment through manure and faeces from animals fed this GM soybean. Cry proteins are degraded by enzymatic activity in the gastrointestinal tract, meaning that only a very small quantity would remain intact to pass out in faeces. This was demonstrated for Cry1Ab (Einspanier et al. 2004; Lutz et al. 2005; Lutz et al. 2006; Wiedemann et al. 2006; Guertler et al. 2008; Paul et al. 2010) and Cry1Ab/Ac fusion protein (Xu et al. 2009). There would, subsequently, be further degradation of the protein in the manure and faeces as a result of microbiological proteolytic activity.In addition, there will be further degradation of Cry proteins in soil, reducing the possibility for the exposure of potentially sensitive non-target organisms. While Cry proteins may bind to clay minerals and humic substances in soil, thereby reducing their availability to microorganisms for degradation, there are no indications of persistence and accumulation of Cry proteins from GM crops in soil (reviewed by Icoz and Stotzky 2008). The EFSA GMO Panel is not aware of evidence of released Cry proteins from GM plants causing significant negative effects on soil micro- or macroorganisms. Considering the scope of the application, it can be concluded that the exposure of

[31] Technical dossier/sections D8 and D9.4.
[32] Technical dossier/section D9.5.

potentially sensitive non-target organisms to the Cry1Ac protein is likely to be very low and of no biological relevance.

6.1.2.5. Potential interactions with the abiotic environment and biogeochemical cycles[33]

Owing to the intended uses of soybean MON 87701 × MON 89788, which exclude cultivation, and the low level of exposure to the environment, potential interactions with the abiotic environment and biogeochemical cycles were not considered an issue by the EFSA GMO Panel.

6.1.3. Post-market environmental monitoring[34]

The objectives of a monitoring plan according to Annex VII of Directive 2001/18/EC are (1) to confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO, or its use, in the environmental risk assessment are correct and (2) to identify the occurrence of adverse effects of the GMO, or its use, on human health or the environment that were not anticipated in the environmental risk assessment. Monitoring is related to risk management, and thus a final adoption of the monitoring plan falls outside the mandate of EFSA. However, the EFSA GMO Panel gives its opinion on the scientific content of the monitoring plan provided by the applicant (EFSA 2011b). The potential exposure to the environment of soybean MON 87701 × MON 89788 would be through manure and faeces from animals fed soybean MON 87701 × MON 89788 or through accidental release into the environment of GM soybean seeds (e.g. during transport and processing). The scope of the monitoring plan provided by the applicant is in line with the intended uses. As the environmental risk assessment did not cover cultivation and identified no potential adverse environmental effects, no case-specific monitoring is necessary.

The general surveillance plan proposed by the applicant includes (1) the description of an approach involving operators (federations involved in soybean import and processing) reporting to the applicant via a centralised system any observed adverse effect(s) of GMOs on human health and the environment; (2) a coordinating system established by EuropaBio for the collection of the information recorded by the various operators; and (3) the use of networks of existing surveillance systems (Lecoq et al. 2007; Windels et al. 2008). The applicant proposes to submit a general surveillance report on an annual basis and a final report at the end of the consent.

The EFSA GMO Panel is of the opinion that the scope of the monitoring plan proposed by the applicant is in line with the intended uses of soybean MON 87701 × MON 89788 as the environmental risk assessment did not cover cultivation and identified no potential adverse environmental effects. In addition, the EFSA GMO Panel acknowledges the approach proposed by the applicant to put in place appropriate management systems to restrict environmental exposure in the case of accidental release of viable seeds of soybean MON 87701 × MON 89788. The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in the general surveillance plan.

6.2. Conclusion

The scope of the application is for food and feed uses, import and processing of soybean MON 87701 × MON 89788 and excludes cultivation. Considering the intended uses, the environmental risk assessment is concerned with indirect exposure mainly through manure and faeces from animals fed seeds produced by soybean MON 87701 × MON 89788 and with the accidental release into the environment of viable seeds of soybean MON 87701 × MON 89788 (e.g. during transport and processing).In the case of accidental release into the environment of viable seeds of soybean MON 87701 × MON 89788 there are no indications of an increased likelihood of establishment and spread of feral soybean MON 87701 × MON 89788 plants, except under conditions of infestation of specific lepidopteran pests or the application of glyphosate-based herbicides. The low levels of environmental exposure of these GM soybean plants indicate that the risk to non-target organisms is extremely low. The unlikely but theoretically possible transfer of the recombinant gene from soybean MON 87701 × MON 89788 to environmental bacteria does not raise concern owing to the lack of a selective advantage

[33] Technical dossier/sections D9.8 and D10.
[34] Technical dossier/section D11.

in the context of its intended uses. The scope of the post-market environmental monitoring plan provided by the applicant and the reporting intervals are in line with the intended uses of soybean MON 87701 × MON 89788 and the guidance document of the EFSA GMO Panel on post-market environmental monitoring of GM plants (EFSA 2011b). In addition the EFSA GMO Panel acknowledges the approach proposed by the applicant to put in place appropriate management systems to restrict environmental exposure in cases of accidental release of viable seeds of soybean MON 87701 × MON 89788. The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in the general surveillance plan.

OVERALL CONCLUSIONS AND RECOMMENDATIONS

The EFSA GMO Panel was requested to carry out an evaluation of a scientific risk assessment of the soybean MON 87701 × MON 89788 for food and feed uses, import and processing in accordance with Regulation (EC) No 1829/2003. The EFSA GMO Panel evaluated MON 87701 × MON 89788, which has been produced by conventional crossing of soybean lines containing the single events MON 87701 and MON 89788. Both single events have already been evaluated by the EFSA GMO Panel (EFSA 2008 2011a). In evaluating soybean MON 87701 × MON 89788 the EFSA GMO Panel considered the application EFSA-GMO-NL-2009-73, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications. Further information from applications for placing the single soybean events MON 87701 and MON 89788 on the market under the EU regulatory framework was taken into account.

The EFSA GMO Panel is of the opinion that the molecular characterisation data provided for soybean MON 87701 × MON 89788 are sufficient. The results of the bioinformatic analyses of the inserted DNA and the flanking regions of the single events MON 87701 and MON 89788 do not raise a safety concern. The levels of Cry1Ac and CP4 EPSPS proteins in soybean MON 87701 × MON 89788 have been sufficiently analysed, and the stability of the genetic modification has been demonstrated. The EFSA GMO panel considers that the molecular characterisation does not indicate a safety concern.

Previous evaluations of the single soybean events MON 87701 and MON 89788 showed that they do not differ in composition or agronomically and phenotypically from their corresponding conventional counterparts, except for the introduced traits and soybean MON 87701 having an increased vitamin E content. Both single events were within the ranges of commercial non-GM soybean varieties, except for the introduced traits. The results of the comparative analysis indicated that no biologically relevant differences were identified in the composition or phenotypic and agronomic characteristics of soybean MON 87701 × MON 89788 and its comparator soybean A5547, and that its composition fell within the range of non-GM soybean varieties, except for the presence of the newly expressed CP4 EPSPS and Cry1Ac proteins. A small increase in final stand count in soybean MON 87701 × MON 89788 was observed, but no safety issues were identified linked to this increase. Based on the assessment of the data available, the EFSA GMO Panel is of the opinion that crossing soybean MON 87701 and soybean MON 89788 to produce soybean MON 87701 × MON 89788 does not result in interactions that cause changes in composition or agronomic or phenotypic characteristics that would raise a safety concern.

The safety of the Cry1Ac protein expressed in MON 87701 and the CP4 EPSPS protein expressed in MON 89788 has been assessed previously, and no safety concerns were identified for humans and animals. In addition, the EFSA GMO Panel considers that it is unlikely that the overall toxicity and allergenicity of the whole soybean MON 87701 × MON 89788 has been changed. A feeding study with broiler chickens confirmed that the nutritional properties of soybean meal obtained from soybean MON 87701 × MON 89788 are not different from those of soybean meal from commercial non-GM soybean varieties. Potential interactions between the soybean events with respect to an effect on human and animal health were the focus of the assessment on food/feed issues. On the basis of the known functional characteristics and modes of action of the newly expressed proteins (Cry1Ac and CP4 EPSPS), the EFSA GMO Panel considers it unlikely that interactions between these proteins would occur that would raise any safety concerns. Thus, the EFSA GMO Panel concludes that soybean MON 87701 × MON 89788 is as safe and as nutritious as its comparator and commercial soybean varieties in the context of its intended uses.

Considering the intended uses of soybean MON 87701 × MON 89788, which exclude cultivation, there is no requirement for scientific assessment on possible environmental effects associated with the cultivation of this GM soybean. In the case of accidental release into the environment of viable seeds of soybean MON 87701 × MON 89788 (e.g. during transport and processing), there are no indications of an increased likelihood of establishment and spread of feral soybean plants, except under conditions of infestation of the specific lepidopteran pests or application of glyphosate-based herbicides. The low levels of environmental exposure of these GM soybean plants indicate that the risk to non-target organisms is extremely low. The unlikely but theoretically possible transfer of the recombinant gene from soybean MON 87701 × MON 89788 to environmental bacteria does not raise concern owing to the lack of a selective advantage in the context of its

intended uses. The scope of the post-market environmental monitoring plan provided by the applicant and the reporting intervals are in line with the intended uses of soybean MON 87701 × MON 89788 and the guidance document of the EFSA GMO Panel on post-market environmental monitoring of GM plants (EFSA 2011b). In addition, the EFSA GMO Panel acknowledges the approach proposed by the applicant to put in place appropriate management systems to restrict environmental exposure in the case of accidental release of viable seeds of soybean MON 87701 × MON 89788.

In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87701 × MON 89788 addresses the scientific issues indicated by the guidance document of the EFSA GMO Panel and the scientific comments raised by the Member States, and that the soybean MON 87701 × MON 89788 is as safe as its comparator with respect to potential effects on human and animal health or the environment in the context of its intended uses. In addition, the EFSA GMO Panel is of the opinion that crossing of single soybean events MON 87701 and MON 89788 to produce soybean MON 87701 × MON 89788 does not result in interactions between the events that would affect the safety of soybean MON 87701 × MON 89788 with respect to potential effects on human and animal health and on the environment, in the context of its intended uses.

DOCUMENTATION PROVIDED TO EFSA

1. Letter from the Competent Authority of the Netherlands, received 1 September 2009, concerning a request for placing on the market soybean MON 87701 × MON 89788, submitted by Monsanto under Regulation (EC) No 1829/2003.

2. Acknowledgement letter, dated 17 September, from EFSA to the Competent Authority of the Netherlands (Ref. CGL/PB/KL/mt (2009) 4258912).

3. Letter from EFSA to applicant, dated 8 December 2009, delivering the 'Statement of Validity' for application EFSA-GMO-NL-2009-73 soybean MON 87701 × MON 89788, submitted by Monsanto under Regulation (EC) No 1829/2003 (Ref. PB/CE/lg (2009) 4497410).

4. Letter from EFSA to applicant, dated 26 February 2010, requesting additional information and stopping the clock (Ref. PB/KL/JA/lg (2010) 4675210).

5. Letter from applicant to EFSA, received 9 April 2010, providing additional information.

6. Letter from EFSA to applicant, dated 8 July 2010, requesting additional information and maintaining the clock stopped (Ref. PB/KL/lg (2010) 4982465).

7. Letter from EFSA to applicant, dated 8 July 2010, restarting the clock (Ref. PB/KL/CE/mt (2011) 5866844).

8. Letter from EFSA to applicant, dated 26 August 2011, requesting additional information and maintaining the clock stopped (Ref. EW/JA/AG/mt (2011) 5932927).

9. Letter from applicant to EFSA, received 5 September 2011, providing additional information.

10. Letter from EFSA to applicant, dated 13 October 2011, requesting additional information and maintaining the clock stopped (Ref. EW/ZD/JA/AG/mt (2011) 6025366).

11. Letter from applicant to EFSA, received 3 November 2011, providing additional information.

12. Letter from EFSA to applicant, dated 2 December 2011, requesting additional information and maintaining the clock stopped (Ref. EW/ZD/JA/AG/shv (2011) 6106761).

13. Letter from applicant to EFSA, received 6 December 2011, providing additional information.

14. Letter from EFSA to applicant, dated 20 January 2012, restarting the clock (Ref. EW/ZD/AG/shv (2012) 6190466).

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JRC VALIDATED METHODS, REFERENCE METHODS AND MEASUREMENTS

Report on the Verification of the Performance of MON87701 and MON89788 Event-specific Methods on the Soybean Event MON87701 x MON89788 Using Real-time PCR

Verification Report

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Joint Research Centre
Institute for Health and Consumer Protection
Molecular Biology and Genomics Unit

Executive Summary

The European Union Reference Laboratory for GM Food and Feed (EU-RL GMFF), established by Regulation (EC) No 1829/2003, has carried out an in-house verification study to assess the performance of two quantitative event-specific methods on the soybean event MON87701 x MON89788 (unique identifier MON-877Ø1-2 x MON-89788-1) which combines the MON87701 and the MON89788 transformation events. The two methods have been validated individually on single-trait events, to detect and quantify each event in soybean samples. This study was conducted according to internationally accepted guidelines [1, 2].

In accordance to Regulation (EC) No 1829/2003 of 22 September 2003 on genetically modified food and feed and to Regulation (EC) No 641/2004 of 6 April 2004 on detailed rules for the implementation of Regulation (EC) No 1829/2003, Monsanto Company provided the detection methods and the control samples: genomic DNA from homogenised seeds of MON87701 x MON89788 soybean and from homogenised seeds of conventional soybean. The EU-RL GMFF prepared the verification samples (calibration samples and blind samples at different unknown GM percentages [DNA/DNA]).

The results of the verification study were evaluated with reference to ENGL method performance requirements (http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm) and to the validation results on the individual parental events (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm)

The results of this EU-RL GMFF in-house verification studies are made publicly available at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm

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Report on Steps 1-3 of the Validation Process

Monsanto submitted the detection methods and control samples of the soybean event MON87701 x MON89788 (unique identifier MON-877Ø1-2 x MON-89788-1) under Articles 5 and 17 of Regulation (EC) No 1829/2003 of the European Parliament and of the Council "on genetically modified food and feed".

The European Union Reference Laboratory for GM Food and Feed (EU-RL GMFF), following reception of the documentation and material including control samples (step 1 of the validation process), carried out the scientific assessment of documentation and data (step 2) in accordance with Commission Regulation (EC) No 641/2004 "on detailed rules for the implementation of Regulation (EC) No 1829/2003 of the European Parliament and of the Council as regards the application for the authorisation of new genetically modified food and feed, the notification of existing products and adventitious or technically unavoidable presence of genetically modified material which has benefited from a favourable risk evaluation" and according to its operational procedures ("Description of the EU-RL GMFF Validation Process", http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm).

The scientific assessment focused on the method performance characteristics assessed against the method acceptance criteria set out by the European Network of GMO Laboratories (ENGL) and listed in the "Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing" (http://gmo-crl.jrc.ec.europa.eu/doc/Method%20requirements.pdf) (see Annex 1 for a summary of method acceptance criteria and method performance requirements). During step 2, a scientific assessment of the detection method for soybean MON87701 x MON89788 was positively concluded in September 2009.

The event-specific detection methods for the two soybean lines hosting the single events MON87701 and MON89788 were validated by the EU-RL GMFF following the conclusion of the respective international collaborative studies and the publication of the validation reports (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm). Hence, the detection methods applied on the soybean event MON87701 x MON89788 did not undergo a full validation process. The EU-RL GMFF performed an in-house verification of the detection methods to assess whether they exhibit a comparable performance on samples of event MON87701 x MON89788 combining the two traits (as provided in accordance to Annex I.2.C.2 of Commission Regulation (EC) No 641/2004).

In March 2010, the EU-RL GMFF concluded the verification of the method characteristics (step 3, experimental testing of the samples and methods) by quantifying, with each specific method, five blind GM levels within the range 0.085%-8.10% on a genome copy number basis. The experiments were performed under repeatability conditions and demonstrated that the PCR efficiency, linearity, trueness and repeatability of the quantification were within the limits established by the ENGL.

A Technical Report summarising the results of tests carried out by the EU-RL GMFF (step 3) is available on request.

Content

1. Introduction

Monsanto Company submitted the detection methods and control samples of the soybean event MON87701 x MON89788 (unique identifier MON-877Ø1-2 x MON-89788-1) under Articles 5 and 17 of Regulation (EC) No 1829/2003 of the European Parliament and of the Council "on genetically modified food and feed".

The European Union Reference Laboratory for GM Food and Feed (EU-RL GMFF), established by Regulation (EC) 1829/2003, carried out an in-house verification of the two event-specific methods for the detection and quantification of MON87701 and MON89788 in the MON87701 x MON89788 soybean event combining the two traits. The single methods had been previously validated by international collaborative studies on the single-trait soybean events (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm).

Upon reception of methods, samples and related data (step 1), the EU-RL GMFF carried out the assessment of the documentation (step 2) and the in-house evaluation of the methods (step 3) according to the requirements of Regulation (EC) 641/2004 and following EU-RL GMFF procedures. The EU-RL GMFF method verification was concluded in March 2010.

A method for DNA extraction from soybean seeds, submitted by the applicant, was evaluated by the EU-RL GMFF in order to confirm its performance characteristics. The protocol for DNA extraction is available at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm.

The operational procedure of the in-house verification included the following module:

- ✓ Quantitative real-time PCR (Polymerase Chain Reaction). The methodology consists of two event-specific real-time quantitative TaqMan® PCR procedures for the determination of the relative content of events MON87701 and MON89788 DNA to total soybean DNA in the MON87701 x MON89788 soybean event. The procedures are simplex systems, in which the events MON87701 and MON89788 were quantified in reference to a soybean *Le1 (lectin*) endogenous gene.

The study was carried out in accordance to the following internationally accepted guidelines:

- ISO 5725: 1994. (1)
- The IUPAC "Protocol for the design, conduct and interpretation of method-performance studies". (2)

2. Materials

For the verification of the quantitative event-specific methods, control samples consisted of:

- genomic DNA extracted from homogenised seeds of MON87701 x MON89788 soybean, and
- genomic DNA extracted from homogenised seeds of conventional soybean.

Samples were provided by the applicant, in accordance to the provisions of Regulation (EC) No 1829/2003, Art 2.11 [control sample defined as "the GMO or its genetic material (positive sample) and the parental organism or its genetic material that has been used for the purpose of the genetic modification (negative sample)"].

Samples containing mixtures of 100% MON87701 x MON89788 and non-GM soybean genomic DNA at different GMO concentrations were prepared by the EU-RL GMFF in a constant amount of total soybean DNA, using the control samples provided.

The protocols (reagents, concentrations, primer/probe sequences) followed in the in-house verification are those already published as validated methods for the individual MON87701 and MON89788 events and are available at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm.

Table 1 shows the five GM levels of unknown samples used in the verification of the MON87701 and MON89788 methods.

Table 1. MON87701 and MON89788 GM contents in soybean event MON87701 x MON89788.

MON87701 GM% (GM DNA / Non-GM DNA x 100)	**MON89788 GM%** (GM DNA / Non-GM DNA x 100)
0.085	0.1
0.26	0.4
0.90	0.9
2.70	4.0
8.10	8.0

3. Experimental design

Eight runs for each event-specific method were carried out. In each run, samples were analysed in parallel with both the GM-specific system and the reference system (*Le1*). Five GM levels per run were examined and two replicates for each GM level were analysed. PCR analysis was performed in triplicate for all samples. In total, for each method (MON87701 and MON89788), the quantification of the five GM levels was performed as an average of sixteen replicates per GM level. An Excel spreadsheet was used for determination of GM%.

4. Method

Description of the operational steps

For specific detection of events MON87701 and MON89788 in soybean event MON 87701 x MON 89788, two specific fragments, of 89-bp and 139-bp respectively, of the integration regions of the constructs inserted into the plant genome (5′ insert-to-plant junction) are amplified using specific primers. PCR products are measured during each cycle (real-time) by means of target-specific oligonucleotide probes labelled with two fluorescent dyes: FAM (6-carboxyfluorescein) is used as reporter dye at its 5′-end and TAMRA (6-carboxytetramethylrhodamine) as a quencher dye at its 3′-end.

For relative quantification of events MON87701 and MON89788, a soybean-specific reference system amplifies a 74 bp fragment of the soybean endogenous gene *Le1* (*lectin*), using two *Le1* gene-specific primers and a *Le1* gene-specific probe labelled with FAM and TAMRA.

Standard curves are generated for each GM specific system (MON87701 and MON89788), by plotting Ct values of the calibration standards against the logarithm of the DNA copy numbers of MON87701 or MON89788, and by fitting a linear regression into these data. Thereafter, the normalised Ct values of the unknown samples are measured and the relative amount of MON87701 or MON89788 DNA, respectively, is estimated using the regression formula.

For detailed information on the preparation of the standard curve calibration samples please refer to the protocols of the validated methods at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm.

5. Deviations reported

No deviations have been reported.

6. Summary of results

PCR efficiency and linearity

The values of the slopes of the standard curves, from which the PCR efficiency is calculated using the formula $[10^{(-1/slope)} - 1] \times 100$, and of the R^2 (expressing the linearity of the regression) reported for all PCR systems in the eight runs, are presented in Tables 2 and 3 for MON87701 and MON89788 methods, respectively.

Table 2. Values of standard curve slope, PCR efficiency and linearity (R^2) for the MON87701 method on event MON87701 x MON89788.

Run	MON87701			*lec*		
	Slope	PCR Efficiency (%)	R^2	Slope	PCR Efficiency (%)	R^2
1	-3.48	94	1.00	-3.33	100	1.00
2	-3.40	97	1.00	-3.41	96	1.00
3	-3.44	95	1.00	-3.34	99	1.00
4	-3.40	97	1.00	-3.33	100	1.00
5	-3.51	93	1.00	-3.35	99	1.00
6	-3.38	98	1.00	-3.32	100	1.00
7	-3.43	96	1.00	-3.37	98	1.00
8	-3.48	94	1.00	-3.33	99	1.00
Mean	-3.44	95	1.00	-3.35	99	1.00

Table 3. Values of standard curve slope, PCR efficiency and linearity (R^2) for the MON89788 method on event MON87701 x MON89788.

Run	MON89788			*lec*		
	Slope	PCR Efficiency (%)	R^2	Slope	PCR Efficiency (%)	R^2
1	-3.38	98	1.00	-3.36	99	1.00
2	-3.44	95	1.00	-3.32	100	1.00
3	-3.43	96	1.00	-3.33	100	1.00
4	-3.37	98	1.00	-3.32	100	1.00
5	-3.42	96	1.00	-3.38	98	1.00
6	-3.43	96	1.00	-3.36	98	1.00
7	-3.46	95	1.00	-3.33	100	1.00
8	-3.44	95	1.00	-3.33	100	1.00
Mean	-3.42	96	1.00	-3.34	99	1.00

The mean PCR efficiencies of the GM and species-specific systems are above 90% (95% and 99% for MON87701 and 96% and 99% for MON89788, respectively). The linearity of the methods (R^2) is 1.00 for both systems in all cases. Overall, data reported in Tables 2 and 3 confirm the appropriate performance characteristics of the two methods tested on MON87701 x MON89788 soybean samples in terms of PCR efficiency and linearity.

7. Method performance requirements

The results of the in-house verification study for the MON87701 and MON89788 detection methods applied to soybean event MON87701 x MON89788 DNA are reported in Tables 4 and 5, respectively. Results were evaluated with respect to the method acceptance criteria, as established by ENGL and adopted by the EU-RL GMFF (http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm, see also Annex 1). In addition, Tables 4 and 5 report the trueness and precision for each GM level and for all methods.

Table 4. Estimates of trueness (expressed as bias %) and relative repeatability standard deviation (RSD_r %) of the MON87701 method on event MON87701 x MON89788 soybean DNA.

MON87701					
Unknown sample GM%	**Expected value (GMO%)**				
	0.085	**0.26**	**0.90**	**2.70**	**8.10**
Mean	0.088	0.25	0.97	2.68	8.25
SD	0.01	0.01	0.05	0.20	0.59
RSD_r (%)	13	5.1	4.7	7.5	7.2
Bias (%)	3.0	-2.8	7.9	-0.9	1.9

Table 5. Estimates of trueness (expressed as bias %) and relative repeatability standard deviation of the MON89788 method on event MON87701 x MON89788 soybean DNA.

MON89788					
Unknown sample GM%	**Expected value (GMO%)**				
	0.1	**0.4**	**0.9**	**4.0**	**8.0**
Mean	0.10	0.40	0.93	3.89	8.06
SD	0.01	0.01	0.05	0.23	0.51
RSD_r (%)	7.0	3.5	4.9	5.9	6.3
Bias (%)	3.9	1.0	3.4	-2.7	0.8

The trueness of the method is estimated using the measurements of the method bias for each GM level. According to the ENGL acceptance criteria and method performance requirements, the trueness of the method, measured as bias from the accepted value, should be ± 25% across the entire dynamic range. As shown in Tables 4 and 5, the values range from -2.8% to 7.9% for MON87701 and from -2.7% to 3.9% for MON89788. Therefore, the two methods satisfy the above mentioned requirement throughout their respective dynamic ranges.

Tables 4 and 5 further document the relative repeatability standard deviation (RSD_r) as estimated for each GM level. As indicated by ENGL ("Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing", http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm), the EU-RL GMFF requires the RSD_r values to be below 25%. As it can be observed from Tables 4 and 5, the values range between 4.7% and 13% for MON87701 and between 3.5% and 7.0% for MON89788. Therefore, the two methods satisfy this requirement throughout their respective dynamic ranges.

8. Comparison of method performance between event MON87701 x MON89788 and the single trait events

A comparison of the method performances assessed by the EU-RL on the soybean event MON87701 x MON89788 and the single trait events is shown in Tables 6 and 7. The performance of the methods on the single lines was previously assessed through international collaborative trials.

Table 6. Trueness (bias %) and relative repeatability standard deviation (RSD_r %) of the MON87701 detection method on event MON87701 x MON89788 and on event MON87701.

Trueness and repeatability of MON87701 quantification on MON87701 x MON89788			**Trueness and repeatability of MON87701 quantification on single event MON87701***		
GM%	**Bias (%)**	**RSD_r (%)**	**GM%**	**Bias (%)**	**RSD_r (%)**
0.085	3.0	13	**0.085**	8.6	18
0.26	-2.8	5.1	**0.26**	6.4	21
0.90	7.9	4.7	**0.90**	5.2	15
2.7	-0.9	7.5	**2.7**	5.6	14
8.1	1.9	7.2	**8.1**	0.1	10

*method validated in inter-laboratory study (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm)

Table 7. Trueness (bias %) and relative repeatability standard deviation (RSDr %) of the MON89788 detection method on event MON87701 x MON89788 and on event MON89788.

Trueness and repeatability of MON89788 quantification on MON87701 x MON89788			**Trueness and repeatability of MON89788 quantification on single event MON89788***		
GM%	**Bias (%)**	**RSD_r (%)**	**GM%**	**Bias (%)**	**RSD_r (%)**
0.1	3.9	7.0	**0.1**	-14	16
0.4	1.0	3.5	**0.4**	-5.0	22
0.9	3.4	4.9	**0.9**	-0.9	15
4.0	-2.7	5.9	**4.0**	11	13
8.0	0.8	6.3	**8.0**	2.8	12

*method validated in inter-laboratory study (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm)

For trueness, the MON87701 even-specific method (Table 6) shows generally lower bias when applied to event MON87701 x MON89788 compared to the single trait event, except for the 0.9% and 8.1% GM levels where similar and higher values are observed, respectively. The MON89788 event-specific method (Table 7) shows in general significantly lower bias when is applied to the stack event than the single line event, with an only slightly higher value at the 0.9% GM level. In all cases, the trueness of the two event-specific methods when applied to the

stacked event is within the acceptance range set by ENGL (± 25%) for the whole dynamic ranges studied.

For relative repeatability standard deviation (RSD_r %), the two event-specific methods (Tables 6 and 7) show significantly higher precision when applied to the stacked event than to the single trait events. In all cases, the relative repeatability standard deviations (RSD_r %) of the two event-specific methods when applied to the stacked event are below the ENGL maximum acceptance level established (25%).

Therefore, the in-house method verification has demonstrated that the MON87701 and MON89788 detection methods developed to detect and quantify the single events can be equally applied for the quantification of the respective events combined in event MON87701 x MON89788.

9. Conclusions

The overall method performance of the two event-specific methods for the quantitative detection of events MON87701 and MON89788 combined in soybean event MON87701 x MON89788 has been evaluated with respect to the method acceptance criteria and the method performance requirements recommended by the ENGL (as detailed under http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm), and to the validation results obtained for the single trait events (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm).

The results obtained during the present verification study indicate that the analytical modules of the methods submitted by the applicant comply with ENGL performance criteria. The methods are therefore applicable to the control samples provided (see paragraph 3 "Materials"), in accordance with the requirements of Annex I-2.C.2 to Commission Regulation (EC) No 641/2004.

10. Quality assurance

The EU-RL GMFF operates according to ISO 9001:2008 (certificate number: CH-32232) and technical activities under ISO 17025:2005 [certificate number: ACCREDIA 1172, (Flexible Scope for DNA extraction and qualitative / quantitative PCR) – Accredited tests available at http://www.accredia.it/accredia_labsearch.jsp?ID_LINK=293&area=7]

11. References

1. International Standard (ISO) 5725:1994. Accuracy (trueness and precision) of measurement methods and results. International Organization for Standardization.

2. Horwitz W., 1995. Protocol for the design, conduct and interpretation of method performance studies, *Pure and Appl. Chem*, 67: 331-343.

12. Annex 1: method acceptance criteria and method performance requirements as set by the European Network of GMO Laboratories (ENGL)

Method Acceptance Criteria should be fulfilled at the moment of submission of a method (Phase 1: acceptance for the collaborative study).

Method Performance Requirements should be fulfilled in a collaborative study in order to consider the method as fit for its purpose (Phase 2: evaluation of the collaborative study results).

Method Acceptance Criteria

Applicability

Definition: The description of analytes, matrices and concentrations to which the method can be applied.

Acceptance Criterion: The applicability statement should provide information on the scope of the method and include data for the indices listed below for the product/s for which the application is submitted. The description should also include warnings to known interferences by other analytes, or inapplicability to certain matrices and situations.

Practicability

Definition: The ease of operations, the feasibility and efficiency of implementation, the associated unitary costs (e.g. cost/sample) of the method.

Acceptance criteria: The method should generally be practicable in line with other methods for a similar purpose. More specifically the method is deemed unacceptable, unless suitable justification is supplied, if:

- it requires a new type of apparatus (not generally available) or expensive equipment; or
- the resources required to perform the method (time, workload, reagents, costs) are considerably higher than the resources required to perform other methods for similar purpose.

Other practicability considerations may also deem the method impracticable.

DNA Extraction and Purification

The aim of a DNA extraction procedure is to provide DNA of suitable quality for subsequent analysis. DNA quality depends on the average length, structural integrity and chemical purity of the extracted DNA.
It is recognised that highly fragmented DNA and co-extracted impurities of a DNA preparation may hinder the correct process of detecting and quantifying genetically modified DNA. Food and feed made of various ingredients may exert a matrix effect, depending on the DNA extraction method employed, and impair the sensitivity of the following analytical approach. For this purpose, critical steps of DNA extraction and purification should be clearly highlighted in the technical documentation accompanying a method and acceptance criteria are established to allow objective determination of PCR quality of DNA

extracts which can be considered suitable for subsequent detection experiments (e.g. qualitative and/or quantitative PCR).
DNA extraction procedures should result in repeatable recovery, fragmentation profile, concentration and PCR quality of DNA extracts. As such, it is recommended to process the given DNA extraction protocol on different days (e.g. 3 days) with an adequate number of test portions (e.g. 6 per day).
In agreement with international guidelines (e.g. EN ISO 21571, EN ISO 24276) the following criteria are used to assess method performance.

a) DNA concentration

Definition: amount of an analyte per unit volume of solution

Acceptance criterion: The DNA extraction method employed shall be appropriate to obtain the quantity of nucleic acid required for the subsequent analysis. The DNA concentration measured as weight of the analyte/volume of solution should be higher than the working concentration described in the protocol of the detection method.
Example: if the RT-PCR protocol indicates 40 ng/µL as the DNA concentration of the DNA solution to be added to the master-mix, the concentration of the DNA extract should be > 40 ng/µL.

b) DNA fragmentation state

Definition: Breakage of genomic (high molecular weight) DNA into smaller DNA fragments

Acceptance criterion: For quantitative (real time-based) analysis, the molecular weight of the extracted DNA sample should be at least higher than the amplicon size produced by the event specific and the taxon specific reference systems as established by comparison with a reference nucleic acid marker.
For qualitative analysis, in case of DNA suspensions to be used in qualitative analysis, the presence of a certain proportion of DNA molecules of molecular weight lower than the amplicon size produced by the method may be considered acceptable.

c) Purity of DNA extracts

Definition: the absence of co-extracted compounds in a DNA sample impairing the efficiency of the PCR reactions and leading to a delay in the onset of the exponential phase of the amplification profile

Acceptance criterion: The difference (ΔCt) average between the measured Ct value and the extrapolated Ct value of the first diluted sample of the inhibition test should be <0.5. [(measured Ct – extrapolated Ct)] <0.5 and the slope of the inhibition curve should be within -3.6 and -3.1.
The preferred PCR assay for the inhibition test is the internal control assay (e.g. the taxon specific reference system). The total DNA amount in the first sample of the dilution series should be not less than the total DNA amount used in the submitted method (e.g. the DNA amount indicated in the PCR protocol of the taxon specific reference system).

Specificity

Definition: Property of a method to respond exclusively to the characteristic or analyte of interest.

Acceptance Criterion: The method should not produce amplification signals with target sequences different for the target sequence for which the method was developed. This should be demonstrated by similarity searches against databases (e.g. EMBL, GenBank, Patent, etc.) and with empirical results from testing the method with non-target transgenic events and non-transgenic material.
For detection of specific GM events, the target sequence shall be event specific.
For taxon specific target sequences (target sequence), the absence of allelic and copy-number variation across a globally representative and diverse sample of the species variety shall be demonstrated. Allelic and/or copy-number variation in other lines shall be reported if such variation is known by the applicant.
The specificity of the target sequence shall be verified by *in silico* studies against publicly available sequence databases (e.g. EMBL, GenBank, etc.) and experimentally by demonstrating the absence of amplification products when the target sequence specific assay is applied to individual PCRs of pure genomic DNA of a representative sample of the closest relatives to the target taxa as well as of the most important food crops.

Dynamic Range

Definition: The range of concentrations over which the method performs in a linear manner with an acceptable level of trueness and precision.

Acceptance Criterion: The dynamic range of the method should include the 1/10 and at least 5 times the target concentration. Target concentration is intended as the threshold relevant for legislative requirements. The range of the standard curve(s) for real-time PCR should allow testing of blind samples throughout the entire dynamic range, including the lower (10%) and upper (500%) ends.
Example: 0.09% and 4.5% for a 0.9% GMO concentration or 50 and 2500 genome copies if the target is 500 copies.

Trueness

Definition: The closeness of agreement between the average value obtained from a large series of test results and an accepted reference value. The measure of trueness is usually expressed in terms of bias.

Acceptance Criterion: The trueness shall be within ±25% of the accepted reference value over the whole dynamic range.

Amplification Efficiency

Definition: The rate of amplification that leads to a theoretical slope of –3.32 with an efficiency of 100% in each cycle. The efficiency of the reaction can be calculated by the following equation:

$$Efficiency = 10^{\left(\frac{-1}{slope}\right)} - 1$$

Acceptance Criterion: The average value of the slope of the standard curve shall be in the range of (-3.1 ≥ slope ≥ -3.6)

R^2 Coefficient

Definition: The R^2 coefficient is the correlation coefficient of a standard curve obtained by linear regression analysis.

Acceptance Criterion: The average value of R^2 shall be ≥0.98.

Precision - Relative Repeatability Standard Deviation (RSDr)

Definition: The relative standard deviation of test results obtained under repeatability conditions. Repeatability conditions are conditions where test results are obtained with the same method, on identical test items, in the same laboratory, by the same operator, using the same equipment within short intervals of time.

Acceptance Criterion: The relative repeatability standard deviation should be ≤25% over the whole dynamic range of the method.
Note: Estimates of repeatability submitted by the applicant should be obtained on a sufficient number of test results, at least 15, as indicated in ISO 5725-3**Error! Reference source not found.**.

Limit of Quantification (LOQ)

Definition: The limit of quantification is the lowest amount or concentration of analyte in a sample that can be reliably quantified with an acceptable level of precision and accuracy.

Acceptance Criterion: LOQ should be less than $1/10^{th}$ of the value of the target concentration with an RSD_r ≤25%. Target concentration should be intended as the threshold relevant for legislative requirements.
Example: For a 0.9% nominal value LOQ <0.09%.

Limit of Detection (LOD)

Definition: The limit of detection is the lowest amount or concentration of analyte in a sample, which can be reliably detected, but not necessarily quantified, as demonstrated by single-laboratory validation.

Acceptance Criterion: LOD should be less than $1/20^{th}$ of the target concentration. Experimentally, quantitative methods should detect the presence of the analyte at least 95% of the time at the LOD, ensuring ≤5% false negative results. Target concentration should be intended as the threshold relevant for legislative requirements.
Example: For a 0.9% nominal value LOD <0.045%.

Robustness

Definition: The robustness of a method is a measure of its capacity to remain unaffected by small, but deliberate deviations from the experimental conditions described in the procedure.
The adequacy of the robustness testing needs to be demonstrated on a method-by-method basis. For instance, for a real-time PCR method, the following factors and their origin/source shall be taken into account: different thermal cycler models, DNA polymerase, uracyl-n-glycosylase, magnesium chloride

concentration, primer forward and reverse concentration, probe concentration, temperature profile, time profile, dNTP including dUTP concentrations.

Acceptance Criterion: The response of an assay with respect to these small changes shall not deviate more than ±30%.
Alternatively, robustness can be demonstrated through the application of formal robustness tests using factorial designs such as those published by Plackett Burman [1] or Yuden[2]

Method Performance Requirements

Precision - Relative Reproducibility Standard Deviation (RSDR)

Definition: The relative standard deviation of test results obtained under reproducibility conditions. Reproducibility conditions are conditions where test results are obtained with the same method, on identical test items, in different laboratories, with different operators, using different equipment. Reproducibility standard deviation describes the inter-laboratory variation.

Acceptance Criterion: The relative reproducibility standard deviation RSD_R should be <35% over the whole dynamic range. However, at concentrations <0.2% then RSD_R values <50% are deemed acceptable.

Trueness

Definition: The closeness of agreement between the average value obtained from a large series of test results and an accepted reference value. The measure of trueness is usually expressed in terms of bias.

Acceptance Criterion: The trueness should be within ±25% of the accepted reference value over the whole dynamic range.

---

1) R.L. Plackett and J.P. Burman, "The Design of Optimum Multifactorial Experiments", Biometrika 33 (4), pp. 305-25, June 1946.

2) Statistical Manual of the AOAC, W.J. Youdens and E.H. Steiner, 1987.

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European Commission
EUR 25485 EN – Joint Research Centre – Institute for Health and Consumer Protection

Title: Report on the Verification of the Performance of MON87701 and MON89788

Event-specific Methods on the Soybean Event MON87701 x MON89788

Using Real-time PCR

Author(s): Marco Mazzara, Encarnacion Luque Perez, Emanuele Grazioni, Guy Van den Eede

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Abstract

The European Union Reference Laboratory for GM Food and Feed (EU-RL GMFF), established by Regulation (EC) No 1829/2003, has carried out an in-house verification study to assess the performance of two quantitative event-specific methods on the soybean event MON87701 x MON89788 (unique identifier MON-877Ø1-2 x MON-89788-1) which combines the MON87701 and the MON89788 transformation events. The two methods have been validated individually on single-trait events, to detect and quantify each event in soybean samples. This study was conducted according to internationally accepted guidelines (1, 2).

In accordance to Regulation (EC) No 1829/2003 of 22 September 2003 on genetically modified food and feed and to Regulation (EC) No 641/2004 of 6 April 2004 on detailed rules for the implementation of Regulation (EC) No 1829/2003, Monsanto Company provided the detection methods and the control samples: genomic DNA from homogenised seeds of MON87701 x MON89788 soybean and from homogenised seeds of conventional soybean. The EU-RL GMFF prepared the verification samples (calibration samples and blind samples at different unknown GM percentages [DNA/DNA]).

The results of the verification study were evaluated with reference to ENGL method performance requirements (http://gmo-crl.jrc.ec.europa.eu/guidancedocs.htm) and to the validation results on the individual parental events (http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm)

The results of this EU-RL GMFF in-house verification studies are made publicly available at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm

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Socio-economic Considerations in Regulatory Decision-making on Genetically Modified Crops

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Abstract

The growing adoption of genetically modified (GM) crops worldwide can have socio-economic benefits for society and farmers, including increased farm profitability, income stability and ease of operation, along with decreased labour and pesticide use, crop losses, and exposure to toxic chemicals. Thus, in addition to national and international regulations on biosafety, countries are increasingly aware of the importance of formalising the inclusion of socio-economic considerations (SECs) into regulatory decision-making. In practice, the complex and varied character of SECs can lead to technical and procedural challenges. Market introductions of biotechnology products have inherent microeconomic and competitive benefits and drawbacks. Socio-economic impacts can be positive or negative: in most cases, both occur but are not necessarily specific to GM crops. Socio-economic analyses generally compare the resources used or gained by a project with either (1) the prevailing situation or (2) an alternative scenario to determine the better option. SECs are highly dependent on context, especially the type of GM crop, the geographical location of use and the type of users. The distribution of benefits and costs amongst growers, consumers, food manufacturers, retailers and technology developers can make impact assessment rather complex. Modern biotechnology and its regulation are subject to public and political debate in many parts of the world. On top of environmental safety assessments, socio-economic assessments can contribute to balanced decision-making on market releases, future investments in research and development, and technology deployment. However, systematic and clearly outlined procedures and data/information gathering are needed to guide policy formulation and decision-making on biotechnology applications. This article (1) reviews the role of SECs in biosafety decision-making and (2) discusses the opportunities and challenges of integrating SECs into regulatory decision-making.

Keywords: biosafety, genetically modified crops, GMO regulatory framework, impact assessment, international, SECs, socio-economic considerations, technology introduction.

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1. INTRODUCTION

Regulation has been fundamental to the debate on the use of agricultural biotechnology because of: (1) the possible safety implications for the environment and human health; and (2) non-safety implications such as socio-economic considerations (SECs). Effective and useful regulation ensures an adequate level of safety while enabling access to safe products that will benefit society in general and local communities in particular. As such, regulation aims to obtain a balance between costs and benefits: costs can be economic but can also include risks to humans and the environment; and benefits can be profit but can also include welfare, quality of life or environmental improvement. Apart from identifying and measuring the costs and benefits, the distribution of each is also very important: who bears the costs and who incurs the benefits? Many of these are classified as socio-economic considerations (SECs).

National and international regulations increasingly acknowledge the importance of formalising the inclusion of SECs in decision-making (Secretariat of the CBD, 2010). Currently, most commercial biotechnology applications relate to agricultural products (i.e. genetically modified [GM] crops); thus, SECs in this area tend to focus on factors that influence the food supply chain as a whole. SECs include both economic and social effects at the farm level, on the supply chain and on the end user (i.e. the consumer). The wide range of SECs covers everything considered socio-economically relevant; this can complicate their implementation and operationalisation in regulatory decision-making. It is therefore important to set out a clear framework indicating what is meant by SECs and how they can be measured. The assessment and inclusion of socio-economic impacts in regulatory decision-making for GM crops is complex but the amount of research and data on SECs is increasing (Smale *et al.,* 2009; Hall *et al.,* 2013; Brookes & Barfoot, 2017). Over the years, the methodologies used for socio-economic impact assessments have improved with increasing experience of GM crops (Morris, 2011; Garcia-Yi *et al.,* 2014; Kathage *et al.*, 2016).

This article reviews the use of SECs in regulatory decision-making, either in parallel to or as part of biosafety decision-making. First, a brief introduction to the international legal provisions for including SECs within regulatory decision-making will explore the most commonly used categories of SECs for GM crop cultivation. Next, the different aspects and challenges of measuring, implementing and using SECs in regulatory frameworks will be explored. Many countries recognise the importance of SECs and have mentioned them in their biosafety regulations. However, relatively few have formally implemented them into the actual assessment of genetically modified organisms (GMOs). This review aims to provide greater insight into both the opportunities and challenges of integrating SECs into regulatory decision-making.

Risk Communication

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Abstract

Although risk communication is considered an integral part of the risk analysis process for genetically modified crops, many, if not most, regulatory authorities struggle with the tasks of engaging stakeholders in the regulatory process and effectively exchanging information with them. The situation is made more complicated by controversial issues impacting the regulation of these crops and the fact that stakeholders perceive risks differently from regulators. This article provides some practical suggestions to implementing a more effective risk communication approach within the context of assessing risks from genetically modified crops.

Keywords: mass media, risk communication, risk perception, regulatory decision-making, regulatory transparency, social media, stakeholder engagement.

Riassunto

Sebbene la comunicazione del rischio sia considerata parte integrante del processo di analisi del rischio per le colture geneticamente modificate, molte, se non la maggior parte, delle autorità che si occupano delle normative incontrano difficoltà nel coinvolgere le parti interessate nel processo normativo e nell'efficace scambio di informazioni con esse. Questa situazione è resa più complicata dalle controversie che hanno un impatto sulla regolamentazione di queste colture e dal fatto che le parti interessate percepiscono i rischi in modo diverso dalle autorità di regolamentazione. Questo articolo fornisce alcuni suggerimenti pratici per implementare un approccio di comunicazione del rischio più efficace nel contesto della valutazione dei rischi derivanti da colture geneticamente modificate.

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http://icgeb.org/biosafety/publications/collections.html

1. INTRODUCTION

Before genetically modified (GM)[1] crops can be cultivated or used in food and feed, every country (except the few with moratoria in place) requires that risks to environmental resources and human health should be assessed and appropriately managed. Both risk assessment and risk management are science-based processes involving the collection and evaluation of highly technical, and frequently voluminous, data to inform regulatory decision-making. To date, environmental risk assessments and food safety assessments have been issued on almost 500 different GM crop varieties (ISAAA, 2018), representing thousands of individual regulatory decisions. Ostensibly, all of these decisions have been made using internationally approved methods and standards (see, for example, OECD, 1986; 1993; 2007; 2010; Secretariat of the Convention of Biological Diversity, 2000). However, when it comes to communicating with stakeholders about these regulatory decisions, there seems to be no consistent method followed. For example, some regulatory authorities, such as those in Australia (OGTR, 2018; FSANZ, 2018), Canada (CFIA, 2018; Health Canada, 2018), the European Union (EFSA, 2018), and the United States of America (APHIS-USDA, 2018; USEPA, 2018; USFDA, 2018), publish their decisions regarding GM crops as well as the associated environmental risk or food safety assessments. Other countries, such as Sudan (National Biosafety Council, 2015), publish the decision document but not the assessment underlying the decision, whereas yet others, such as China (Biosafety Management Office of Agricultural GMOs, 2008), publish an announcement that a decision has been made but provide neither the assessment nor the decision document itself.

Typically, the volume of information released by any regulatory authority at the end of the decision-making process for a particular risk assessment reflects the amount of information that was exchanged with stakeholders during the deliberative process preceding the final decision. Unfortunately, this exchange of information, commonly called “risk communication”, is challenging for many regulatory authorities for a host of reasons, such as a lack of resources, lack of training or lack of political will; consequently, some governments do risk communication badly or not at all. Even those governments that expend considerable time and resources to communicate with stakeholders throughout the deliberation process for a GM crop may be hard-pressed to claim that they do it “well”; they can only say they do it as best they can.

This article will attempt to explain what risk communication is, what role it plays in assessing and managing the risks posed by GM crops and how a risk communication

[1]Genetically modified crops are those produced through modern biotechnology. “Modern biotechnology” means the application of: (a) *In vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or (b) Fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection (Secretariat of the Convention of Biological Diversity, 2000).

programme can be built in a series of manageable steps. It will also attempt to convey the fundamental challenge of risk communication: that it is not an analytical process, which is something that risk assessors have been trained to master, but instead a personal process.

2. THE IMPORTANCE OF RISK COMMUNICATION

In order to make sound decisions regarding the assessment and management of risks posed by the development and use of GM crops, regulators must have high quality, relevant information (Fischhoff & Kadvany, 2011). Risk communication is the process which provides, exchanges or obtains such information and facilitates engagement with stakeholders regarding risk (National Academy of Sciences, 2016). Risk communication is integral to the assessment and management of risks associated with the development, importation and use of GM crops. Risk assessment involves evaluating the probability that a particular hazard will cause harm to a valued resource, such as biodiversity or human health. During the assessment process, risk communication ensures that the scope and boundaries of the assessment are clearly described, the criteria used to make decisions about risk are clearly defined, stakeholder interests are considered and feedback is provided. Although risk communication has an educational component, it does not attempt to change basic values and beliefs (Gough, 1991); instead, regulators acknowledge the existing values and beliefs and incorporate them, when appropriate, into regulatory decision-making (Lofstedt, 2004).

Risk communication also includes explaining to stakeholders how the regulatory system works, how regulatory decisions are made and what the decisions mean (OECD, 2002). For any regulatory system, including one for genetically modified organism (GMOs), building trust involves demonstrating regulatory rigour: specifically that the regulations are strictly enforced and that breaching the regulations results in an appropriate penalty. Moreover, risk communication must reinforce the fact that regulators are neither proponents for nor opponents of modern biotechnology but impartial observers who are required to communicate to both the government and the public on matters relating to the risk assessment and risk management of GMOs. Regulators should also strive to demonstrate openness by listening to stakeholders and holding themselves accountable for errors. The regulatory system must be as transparent as possible, especially because the technology behind GM crops is difficult for most stakeholders to fully understand. By providing stakeholders with a transparent view of the regulatory process, risk communication efforts also build trust in the process and the people behind it (Renn, 2006; National Academy of Sciences, 2016). As such, risk communication is an expression of the social contract that a government has with its stakeholders (Fischhoff & Kadvany, 2011) and can therefore be considered integral to the regulatory oversight of GM crops (OECD, 2002; WHO, 2008; OGTR, 2009; Jansen Van Rijssen *et al.,* 2015).

(TOWARDS THE) GYM FOR SID

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Scope

Practicing a decisional process by grouping ‘scientists’ and ‘diplomats’ to work together on a concrete case developed in collaboration with one of the scientist and focusing on *International law.* The game takes inspiration by one case brought before the General Court of Justice of the European Union.

Testing the multidisplinary approach of the School.

Coping with scientific uncertainties in decision-taking, including their implications for assessment conclusions, the application of precautionary principle as well as with the interconnected themes of access to information in environmental matters and risk’s communication.

Observing the process dynamic, including interpersonal

Rules

3 Teams + the Court = a non-for-profit Association; the European Commission; a private Company. Teams are pre-formed by the organizers.

2 Steps = The exercise is developed after the related talk on “International law”

(1) Each Team receives a brief description of the case and some background materials to be analysed and discussed internally (**no internet consultation allowed**); it organizes itself internally and identifies a spokeperson; it formulates a brief argumentation text (500-1000 words) defending its own position (**25’**). The **spokeperson presents the argumentation** on behalf of its Team to all Teams (**5’ each**).

(2) after hearing the presentation by all Teams, each of them works (**20’**) to finalize the text, providing a final written argumentation to the Court, possibly including a reply to the positions of the other Teams, that might be improved compared to the first version after hearing the presentations of the other Teams. The final text is then submitted to the Court.

1 Decision = Communicated by the Court is after the dinner, based on the argumentations and considerations on the dynamic of the whole process (**10’**).

Disclaimer

The case is inspired by the appeal (still under judgment) brought before the European Court of Justice (ECJ) against the judgment of the General Court (Fifth Chamber) delivered on 15 December 2016 in Case , and it has been conceived for the purposes of the exercise. References to real parties are not intended to compromise any actors nor outcomes of the trial. For the smooth and effective running of the exercise, *while participants are welcome to deploy different instruments as well as imagination to challenge and convince the Court, compliance with actual jurisdictional rules is deemed necessary for framing the range of application of the exercise*.

The Teams

Team 1, the non-for-profit Association: Annabelle Ascher, Salvatore Capasso, Gian Vittorio Caprara, Amedeo Cesta, Eszter Lakos, Luca Moretti, Sergej Mozina, Fabio Trincardi, Maria Rosa Valente.

Team 2, the European Commission: Federico Falcini, Marga Gual Soler, Fausto Guzzetti, Stephan Kuster, Frank Möschler, Roberto Natalini, Alessandro Rossi, Alessandro Sarretta, Giulia Tercovich.

Team 3, the private Company: Lisa Almesjö, Emilio Fortunato Campana, Omar Cutajar, Lorenzo D'Orsi, Fabio Fiorentino, Cécile Heriard, Petra Manderscheid, Elisa Palazzi, Mario Paolucci, Maurizio Ribera d'Alcalà.

Team 4, the European Court: Gemma Andreone, Massimo Bernaschi, Emiliano Bruner, Laura Macchi, Pier Francesco Moretti.

International LAW

CASE STUDY ON THE PRECAUTIONARY PRINCIPLE

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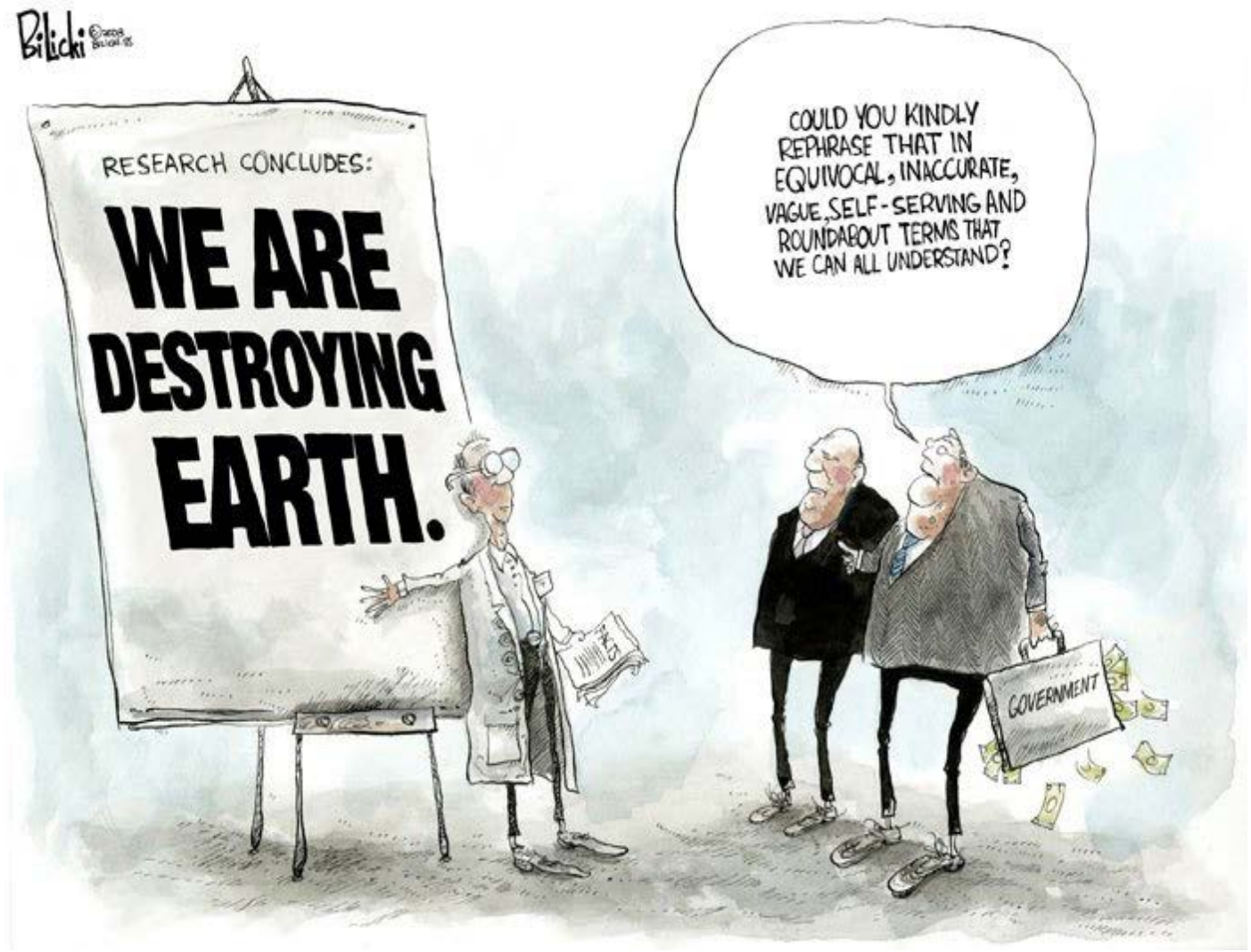

Case Study The Precautionary Principle

OUTLINE

- Meaning of the principle
- Genesis of the principle and its appearance in International law
- Definition and Content of the norm under international, EU and national legal orders
- Functioning of the principle and its impact on scientific progress
- Law Cases in which it has been applied

From a preventive approach to precaution

- **New technological activities** may have harmful impact on environment or human and animal health
- Prevent harm to or negative on the environment on the basis of the **best available scientific information**
- When scientists **do not agree or are uncertain** about the consequences of a new activity, decision makers and judges still has to take decisions

*The precautionary principle or «precautionary approach to risk management» states that, if an activitiy or policy has a suspected risk of causing harm to the public or to the environment, in **the absence of scientific consensus** that the activity or policy is not harmful, the decision makers can adopt precautionary measures rectricting or interdicting that activity/policy*

The Precautionary Principle In International Law

Genesis of the principle and **disruption** with previous approaches

- Before: limits to human activities were only based on ethical and technological issues/gaps; Resources were perceived as unlimited; No concern and respect for future generations; Environment considered antithetic to development
- Then:1972 UN Stockholm Conference on the Human Environment: first time these 2 words are together (environment and development) in **art. 21** of the Final Declaration → Preventive action

- 1992 UN Rio Conference on Environment and Development: **Agenda 21** contained in the Rio Declaration: Doctrine of sustainable development
- Today: many new principles introduced or consolidated - polluter pays, intergenerational equity, common but differentiated responsibilities and → Precautionary principle

Definitions of the principle

different definitions in treaties and national legal orders

- Art.15 of the Rio Declaration 1992

Where there are threats of **serious or irreversible damage**, **lack of full scientific certainty** shall **not** be used as a reason for **postponing cost-effective measures** to prevent environmental degradation.

- Preamble Convention on Biological Diversity 1992

Where there is **a threat of significant reduction or loss of biological diversity**, lack of full scientific certainty should not be used as a reason for postponing **measures to avoid or minimize such a threat.**

- Art. 3, para. 3 Framework Convention on Climate Change 1992

- The parties should take precautionary measures to anticipate, prevent, or minimize the causes of climate change and mitigate its adverse effects. Where there are **threats of serious or irreversible damage**, lack of full scientific certainty should not be used as a reason for postponing such measure, **taking into account that policies and measure to deal with climate change should be cost-effective so as to ensure global benefits at the lowest possible cost.**

HARD AND SOFT LAW IN INT.L LAW

- status of the principle in international law: soft law or hard law
- international customary norm: non written, binding and applicable to all States - highly difficult to determine the exact content
- features of the environmental obligations:
  - erga omnes nature = common and protection of fundamental values

INTERPLAY AMONG DIFFERENT LEGAL ORDERS

- Relevant norms providing for the precautionary principle
  - national legal orders, binding in the territory and on the nationals outside the territory
  - and treaties (EU included), binding for the Parties to each treaty (States, IOs and individuals)
  - international customary norm?
    - flexibility of international norms
    - enforceability of international law depends mainly on national judges
    - international judges do not have enforcement powers

The precautionary principle in intern.l case law

- International Arbitral Tribunal
  - Trail Smelter Case (US v. Canada) - 1940 (burden and standard of proof before the development of the precautionary principle)

- **International Tribunal for the Law of the Sea (ITLOS)**
- Bluefin Tuna Cases (N.Z. v. Japan, Austi. v. Japan), **Provisional Measures** - **1999**
- MOX Plant Case (Ir. v. U.K.), Provisional Measures - 2001
- Responsibilities and obligations of States sponsoring persons and entities with respect to activities in the Area, **Opinion** - **2011**

- **World Trade Organization (WTO)**
  - Appellate Body Report, EC Measures Concerning Meat and Meat Products (Hormones) - 1998
  - Appellate Body Report, Japan **-** Measures Affecting the Importation of Apples - 2003
  - Panel Report, EC Measures Affecting the Approval and Marketing of Biotech Products - 2006

- **International Court of Justice (ICJ)**
  - Nuclear Tests (N.Z. v. Fr.) - 1995
  - Legality of the Threat or Use of Nuclear Weapons (United Nations) - 1996
  - Gabdikovo-Nagymaros Project (Hung. v. Slovk.) - 1997
  - Pulp Mills on the River Uruguay (Arg. v. Uru.) - 2010

The functioning of the principle

DIFFICULT TO BE USED AS LEGAL PRINCIPLE

- DEPENDENT ON THE POLITICAL WILL/DISCRETION OF DECISION MAKERS
- BROAD OR WEAK APPLICATION BY JUDICIAL AUTHORITES DEPENDS ON SEVERAL ASPECTS

THE PRECAUTIONARY PRINCIPLE USUALLY SHIFTS THE BURDEN OF PROOF– REVERSAL OF THE BURDEN

- IT'S UP TO WHOEVER WANTS TO INITIATE AN ACTIVITY TO PROVIDE INFORMATION TO THE DECISION MAKER AND PROVE THE SAFETY OF THE ACTIVITY AND NOT UP TO WHOM IS CLAIMING FOR HIGHER PROTECTION

SCIENTIFIC UNCERTAINTY SHOULD BE REGULARLY REVIEWED

FLEXIBLE AND DEMOCRATIC DECISION MAKING PROCESS

In the absence of scientific consensus that an activity or policy is not harmful, the burden of proof that it is not harmful falls on those taking an action

The precautionary principle in the EU

- **Article 191 of the Treaty on the Functioning of the European Union** (Maastricht Treaty 1992). The PP is introduced among the principles underpinning EU environmental policy. Like the other principles, **it is not defined in the treaty.**
- The principle has also been incorporated into a number of measures of **EU secondary legislation** (i.e. Regulations and Directives)

Comunication from the Commission on the precautionary principle, European Commission, COM(2000)

'Whether or not to invoke the precautionary principle is a decision exercised where scientific information is insufficient, inconclusive, or uncertain and where there are indications that the possible effects on the environment, or human, animal or plant health may be potentially dangerous and inconsistent with the chosen level of protection.'

References for further and general information: European Parliament, The precautionary principle, Definitions, applications and governance, EPRS, European Parliamentary Research Service, December 2015 and European Commission publication, FUTURE BRIEF: The precautionary principle: decision-making under uncertainty September 2017, Science for Environmental Policy, Issue 18 http://ec.europa.eu/environment/integration/research/newsalert/pdf/precautionary_principle_decision_making_under_uncertainty_FB18_en.pdf

Precautionary principle in the EU legislation

Environmental Chemicals

- PCBs
- Halocarbons (including CFCs)
- TBT antifoulants
- Booster biocides
- Mercury
- Cigarette smoke
- Tetrachloroethylene
- DBCP
- DDT
- Vinyl chloride
- Bisphenol A

Ecosystems

- Resilience of ecosystems
- Great Lakes contamination
- Acid rain
- Declining bee populations
- Invasive alien species
- Flooding
- Climate change
- Fisheries

Feed additives

- BSE (mad cow disease)
- Growth hormones (beef)
- Antimicrobials (antibiotics) as growth promoters

Technology

- Nanotechnology
- GMOs

Pharmaceuticals

- Contraceptive pills
- Diethylstilbestrol (DES)

Occupational exposure to chemicals

- Asbestos
- Beryllium

Fuel additives

- Benzene
- MTBE
- Lead

Radiation

- X-rays
- Mobile phones
- Nuclear accidents

Sources: adapted from Late lessons from early warnings: the precautionary principle 1896-2000 and Late lesson from early warnings: science, precaution, innovation, European Environment Agency, 2002 and 2013.

EU Case Law

- The European Union Courts on precautionary principle:
  - the **transmissibility of bovine spongiform encephalopathy or 'Mad cow disease'** to humans - the Court of Justice specified that the precautionary principle also applied to the *protection of human health*.
  - the **transfer of resistance to antibiotics from animals to humans** and the authorisation of medicines for human use - the Court of Justice found that the competent public authorities could be obliged to actively adopt precautionary measures.
  - **nature conservation** - broad interpretation of the precautionary principle providing for authorisation only on the condition that 'the competent national authorities are convinced that it will not adversely affect the integrity of the site concerned'
  - **waste water treatment** - a degree of *probable causality* was sufficient to require Member States to adopt protection measures
  - **Genetically modified organisms** - the General Court recently (2018) accepted a wider interpretation of the relevant directives – *risk assessment is not limited to environment but extended to health and safety*
    - *GMOs and the reversal of burden of proof are still under judgment before the Court of Justice*

Scientific uncertainty between law and policy

- Balancing different interests
- Precautionary measures should be **cost effective** or ensuring global benefits at the lowest possible cost? Political decision
- **Socially** acceptable levels of risk for a given hazard
- Access to justice and to environmental informations and more **democratic decision** making
- **Common procedural framework** for the assessment of collective risk – harmonisation of precautionary principle's application through cooperation

International legal aspects
Basic course: 12 hours

Learning unit	Hours	Knowledge
The interplay of International, European and national legal orders	2	X
Sources of International Law. Hard and soft law	1	X
Responsibility of States, International Organizations and Non-State actors in a changing international community	2	X
State sovereignty and State's powers allocation on land, at sea, in space and over polar regions.	3	X
Erga omnes obligations in the environmental and human rights frameworks	3	X
International Cooperation: harmonization vs. decentralization	1	X

GYM FOR SID

BY MARGHERITA CAPPELLETTO & GEMMA ANDREONE

TECHNICAL SUPPORT BY CNR BIOAGROFOOD DEPARTMENT:

MAURO GAMBONI, ROSANNA MABILIA, PAOLA TASSONE

Description of the case

TestBioTech eV brings before the Court of EU an application pursuant to Article 263 Treaty on the Functioning of the European Union (TFEU) for annulment of a decision of the European Commission (**the contested decision**) which rejected the applicants' requests for Internal Review of the Commission Decision (**the authorization decision**) granting a market authorisation under Regulation No 1829/2003 on genetically modified food and feed to Monsanto Europe SA for its genetically modified soybean "MON 87701 x MON 89788".

The Parties

TestBioTech eV, the applicant, is a not-for-profit association to promote independent research and public debate on the impacts of biotechnology, established in Germany. It is supported by the European Network of Scientists for Social and Environmental Responsibility, established in Germany, the purpose of which is the advancement of science and research for the protection of the environment, biological diversity and human health against the negative impacts of new technologies and their products.

European Commission, the defendant, is supported by the United Kingdoms and the European Food Safety Authority.

Monsanto Europe SA, established in Belgium (branch of the Monsanto Company established in the United States), supports the position of the EC.

European Court, Fifth Chamber, based in Brussels.

The Teams

Team 1, TestBioTech eV: Annabelle Ascher, Salvatore Capasso, Gian Vittorio Caprara, Amedeo Cesta, Eszter Lakos, Luca Moretti, Sergej Mozina, Fabio Trincardi, Maria Rosa Valente. **Supporting Subteam: European Network of Scientists for Social and Environmental Responsibility eV**.

Team 2, the European Commission: Federico Falcini, Marga Gual Soler, Fausto Guzzetti, Stephan Kuster, Frank Möschler, Roberto Natalini, Alessandro Rossi, Alessandro Sarretta, Giulia Tercovich. **Supporting Subteam 1**: **EFSA**; **Supporting Subteam 2: the UK Government**.

Team 3, Monsanto Company: Lisa Almesjö, Emilio Fortunato Campana, Omar Cutajar, Lorenzo D'Orsi, Fabio Fiorentino, Cécile Heriard, Petra Manderscheid, Elisa Palazzi, Mario Paolucci, Maurizio Ribera d'Alcalà. **Supporting Subteam: in house due diligence officers**.

Team 4, the European Court: Gemma Andreone, Massimo Bernaschi, Emiliano Bruner, Laura Macchi, Pier Francesco Moretti.

Dossier for consultation

- Background to the dispute;
- Selected Articles of (i) Aarhus Convention, (ii) *Regultation No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed* and (iii) *Regulation No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies*;
- General technical info on Genetically Modified Organisms (GMOs) and assessments' applications;
- Testbiotech comment on 'Assessment of genetically modified soybean MON 89788 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMORX-011)' by company Monsanto, TESTBIOTECH Background 18/12/2018;
- EFSA Panel on Genetically Modified Organisms (GMOs), European Food Safety Authority (EFSA), Parma, Italy, *Scientific opinion on application (EFSA-GMO-NL-2009-73) for the placing on the market of insect-resistant and herbicide-tolerant genetically modified soybean MON 87701 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto,* EFSA Journal 2012;10(2):2560 (Abstract & Summary);
- Marco Mazzara, Encarnacion Luque Perez, Emanuele Grazioni, Guy Van den Eede, *Report on the Verification of the Performance of MON87701 and MON89788 Event-specific Methods on the Soybean Event MON87701 x MON89788 Using Real-time PCR*, European Commission Joint Research Center & European Union Reference Laboratory for GM Food and Feed, 14 Feb 2012 (Executive Summary);
- Ruth Mampuys, COGEM, *Socio-economic Considerations in Regulatory Decision-making on Genetically Modified Crops* (Abstract & Introduction), and Michael Wach, *Risk Communication*, (Abstract & Introduction), in Ministero dell'Ambiente e della Tutela del Territorio e del Mare (MATTM), International Centre for Genetic Engineering and Biotechnology (ICGEB), Collection of Biosafety Reviews, Vol. 10, 2018.