Technical background for a complaint under Article 10 of Regulation (EC) No. 1367/2006 against the decision of the EU Commission to give market authorisation to stacked maize MON89034 × 1507 × MON88017 × 59122 (SmartStax)

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Content

Summary

Existing EU regulations provide a high level of protection for consumers and the environment.

- For example, Regulation 1829/2003 states that genetically engineered organisms “should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard.” (Recital 9 of Regulation 1829/2003).
- Annex II of Directive 2001/18 requires the examination of the direct and indirect, the immediate and delayed effects of the GMO on human health or the environment.
- Directive 2001/18 requires post-marketing monitoring “in order to trace and identify any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOS as or in products after they have been placed on the market.”

In November 2013, based upon an EFSA opinion, the EU Commission issued a market authorisation for the genetically engineered maize MON89034 × 1507 × MON88017 × 59122 (hereinafter designated the Maize or “SmartStax”) and its segregating progeny (sub-combinations). Testbiotech examined EFSA´s opinion and the decision of the EU Commission. In this technical background, which is based upon the analysis of the risk analysis that was carried out, we show that EFSA´s opinion and the decision of the Commission do not fulfil the requirements of EU Regulations. This technical background is additionally underpinned by a legal analysis and is based upon scientific findings. It is upon this basis that we elucidate the grounds for the complaint. The grounds for the complaint are:

- EFSA did not require the Applicants to submit evidence based on appropriate comparators and/or it erred in concluding that the Maize is 'substantially equivalent' to that comparator;
- EFSA failed to consider and/or require the Applicants to investigate health impact of the whole food/feed as well as combinatorial effects;
- EFSA particularly failed to require the Applicants to undertake a sufficient assessment of the immunological risks posed by the Maize in issue;
- EFSA generally failed to require sufficiently reliable information from the Applicants fulfilling necessary scientific standards;

- the EU Commission failed to ensure that an appropriate monitoring plan was put in place.

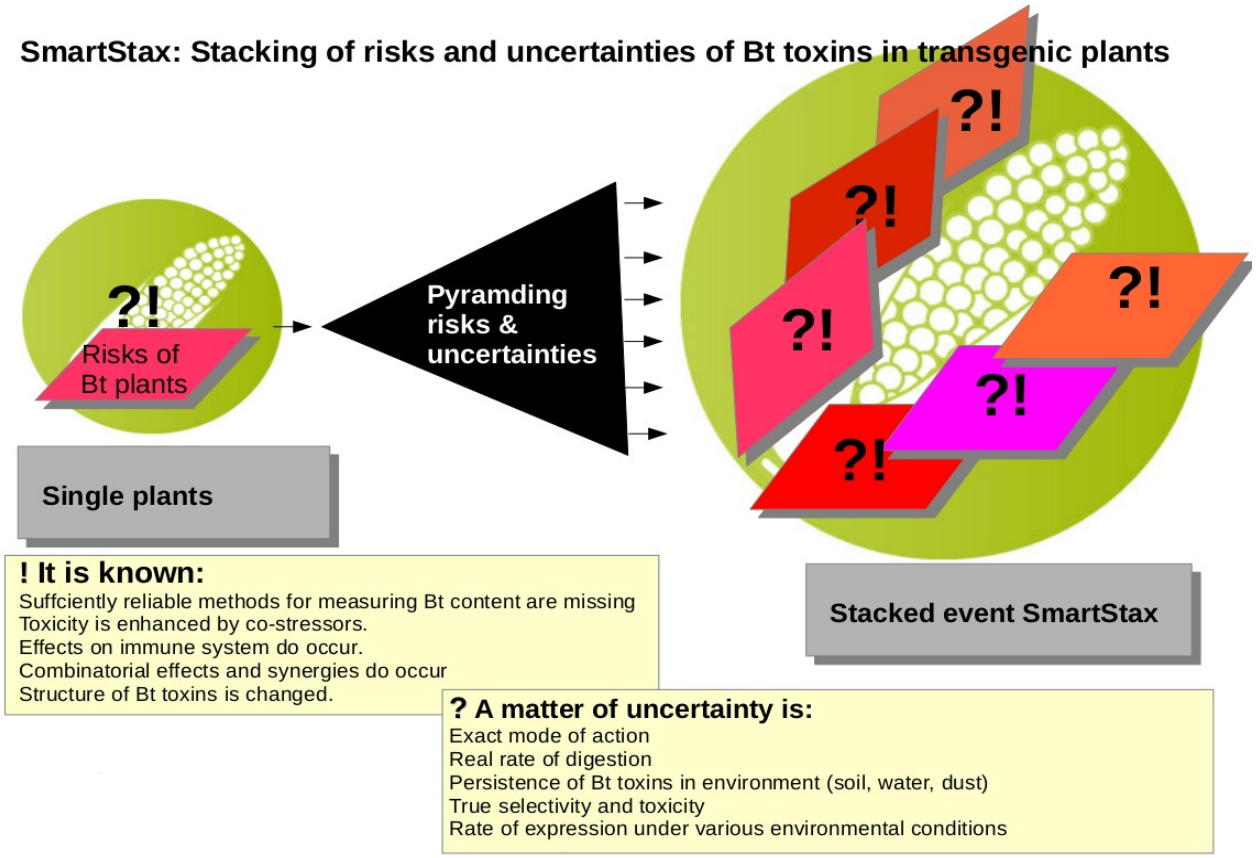
Some of the deficiencies are self evident and crucial to Testbiotech's submission that the overall risk analysis is fundamentally flawed. Some of the relevant deficiencies and failures are:

- Many of the dossiers prepared by industry do not fulfil basic scientific standards (such as Good Laboratory Practice, GLP), and were not reviewed by independent scientists.
- The comparison made between the Maize and conventional plants is flawed because
  > it does not fulfil the Guidance of EFSA,
  > it does not include most relevant regions of maize production and
  > historical data that are known to be unreliable were used to assess the significant differences between the Maize and its comparator.
- The expression rate of the Bt toxin in the plants was not assessed reliably.
- The health impact of the insecticidal protein as produced in the plants and relevant combinatorial effects were not assessed thoroughly.
- The impacts on the immune system (such as adjuvant effects) were not investigated.
- The residues from spraying with the complementary herbicides were not taken into account nor any combinatorial effects with the insecticide or any other combinatorial effects.
- No feeding study was performed with the stacked Maize to investigate potential effects on health, no investigation was carried out to examine the impact of long-term exposure.
- The Commission did not request targeted monitoring of effects on health from the Maize at the stage of consumption.
- The Commission failed to request adequate measures for tracing and identifying the Maize in the market.

Most of the flaws in the Commission's decision and the opinion of EFSA have also been observed in the Parental Plants, so the conclusion that the Maize is safe conflates a whole series of substantial flaws and uncertainties. The Commission's decision and the EFSA opinion clearly arise from pyramiding flaws and uncertainties in previous

opinions and decisions on the Parental Plants. This is shown in Figure 1 summarising some of the risks and uncertainties in regard to the Bt toxins produced in the plants.

Figure 1 Overview of some risks and uncertainties related to Parental Plants (single plants) and the Maize (stacked event SmartStax).



Art. 10 of EU Regulation 1367/2006, allows NGOs active in the field of environmental protection to request re-examination of Commission decisions. Based upon this regulation we request the re-examination of the risk analysis by EFSA and the EU Commission as well as immediate withdrawal of market authorisation for MON89034 × 1507 × MON88017 × 59122 (SmartStax).

The following designations appear in this document:

The Maize: Genetically engineered stacked maize MON89034 × 1507 × MON88017 × 59122 (“SmartStax”) and its segregating subcombinations.

The Parental Plants: Single events of genetically engineered maize MON89034, 1507, MON88017, 59122

The Applicants: Dow AgroSciences Ltd and Monsanto Europe S.A.

1. General Legal Framework

Regulation 1829/2003 on genetically modified food and feed ("the GM Regulation") states that, in order to protect human and animal health, food and feed that consists of, contains, or is produced from genetically modified organisms should undergo a safety assessment before it is placed on the market in the European Union.

"Genetically modified organism" is defined in Article 2(2) of Directive 2001/18 as "an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination", where an "organism" is defined in Article 2(1) as "any biological entity capable of replication or of transferring genetic material".

Food and/or feed that consists of, contains, or is produced from, genetically modified organisms must not:

- "have adverse effects on human health, animal health or the environment": Articles 4(1)(a) and 16(1)(a) GM Regulation; or
- be placed on the market "unless it is covered by an authorisation granted in accordance with" the GM Regulation: Articles 4(2) and 16(2) GM Regulation.

In order to gain an authorisation, an application must be made to the competent authority of a Member State: Articles 5(2) and 17(2) GM Regulation. That application should include, among other things:

- "a copy of the studies, including, where available, independent, peer-reviewed studies, which have been carried out and any other material which is available to demonstrate that the food complies with the criteria referred to in Article 4(1) [/16(1)]": Articles 5(3)(e) and 17(3)(e) GM Regulation; and
- "either an analysis, supported by appropriate information and data, showing 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 and to the criteria specified in Article 13(2)(a), or a proposal for labelling the food…": Articles 5(3)(f) and 17(3)(f) GM Regulation.

The European Food Safety Authority was established by Regulation 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety ("the Food Safety Regulation").

Chapter II Section 1 of the Food Safety Regulation makes clear the "General Principles of Food Law" upon which European measures, such as the GM Regulation, should be based. These include:

- The "General Objective" of "a high level of protection of human life and health and the protection of consumers' interests": Article 5 of the Food Safety Regulation (reflected in Recital (3) ;
- The principle of "Risk Analysis". According to Article 6 of the Food Safety Regulation:

"(1) In order to achieve the general objective of a high level of protection of human health and life, food law shall be based on risk analysis except where this is not appropriate to the circumstances or the nature of the measure.

(2) Risk assessment shall be based on the available scientific evidence and undertaken in an independent, objective and transparent manner."

The GM Regulation was adopted with a view to achieving these General Principles by giving special weight to the precautionary principle. Recitals (2), (3) and (9) make clear:

> "(2) A high level of protection of human life and health should be ensured in the pursuit of [Union] policies.
>
> (3) In order to protect human and animal health, food and feed consisting of, containing or produced from genetically modified organisms...should undergo a safety assessment through a [Union] procedure before being placed on the market within the [Union].
>
> (9) The new authorisation procedures for genetically modified food and feed should...make use of the new framework for risk assessment in matters of food safety set up by [the Food Safety Regulation]. Thus, genetically modified food

and feed should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard, to be undertaken under the responsibility of the European Food Safety Authority (Authority), of any risks which they present for human and animal health and, as the case may be, for the environment. This scientific evaluation should be followed by a risk management decision by the Community, under a regulatory procedure ensuring close cooperation between the Commission and the Member States."

In the context of these General Principles, the European Food Safety Authority is mandated to issue guidance on the manner in which it will assess applications for authorisations under the GM Regulation. In particular:

- Under Article 23(b) of the Food Safety Regulation, one of its tasks is that it must "promote and coordinate the development of uniform risk assessment methodologies in the fields falling within its mission";

- Under Articles 5(8) and 17(8) GM Regulation, it "shall publish detailed guidance to assist the applicant in the preparation and presentation of the application";

It has issued two Guidance documents of particular relevance to the present application. These are the "Guidance on the submission of applications for authorisation of genetically modified food and feed and genetically modified plants for food or feed uses under Regulation (EC) No 1829/20031" (EFSA 2006, including draft updated document 2008), and the "Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants containing stacked transformation events", adopted on 16 May 2007 ("EFSA Guidance (2007)").

These guidance documents outline the European Food Safety Authority's own view of how, in practice, it will discharge its obligation to conduct a "scientific evaluation of the highest possible standard" (Recital (9) GM Regulation), and to do so using a 'uniform methodology' (Article 23(b) Food Safety Regulation) and "based on the available scientific evidence and... in an independent, objective and transparent manner" (Article 6(2) Food Safety Regulation).

(a) Particular provisions of Directive 2001/18[1]

Directive 2001/18[2] requires that the placing on the market of a genetically modified organism (GMO) as or in a product may only take place after written consent by the competent authority has been given (Article 19). The application for such consent (notification, Article 13) must be accompanied by an environmental risk assessment, by other information, and by a monitoring plan (Article 13(2.b, 2.a, and 2.e)).

The environmental risk assessment

Recital (19) of Directive provides that "[a] case-by-case environmental risk assessment should always be carried out prior to a release. It should also take due account of potential cumulative long-term effects associated with the interaction with other GMOs in the environment." Moreover, "[n]o GMOs, as or in products, intended for deliberate release are to be considered for placing on the market without first having been subjected to satisfactory field testing at the research and development stage in ecosystems which could be affected by their use."

Recital 33 of the Directive indicates that the environmental risk assessment submitted as part of the notification procedure has to be "full". Recital 55 stresses the importance of following "closely" the development and use of GMOs.

Article 13 (2.b) provides that the notification shall be accompanied by "the" environmental risk assessment and the conclusions required in Annex II, section D. Annex II section D provides that information on the points listed in sections D1 or D2 should be included, as appropriate, in notifications with a view to assisting in drawing conclusions on the potential impact from the release or the placing on the market of GMOs. This information is to be based on the environmental risk assessment carried out in accordance with the principles laid down by sections B and C of Annex II to the Directive.

Accordingly, the principles with which environmental risk assessments should comply are laid down in Annex II to the Directive. Annex II indicates that the environmental impact assessment is not limited to an examination of the effects of genetically

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1 These chapters are mostly derived from Ludwig Krämer Dossier, 2012, attached

2 Directive 2001/18/EC of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC, OJ 2001, L 106 p.1. ("the Directive").

modified products containing GMO on the natural environment, it must also examine the effects on human health. This follows from the general objective of Directive 2001/18 as laid down in Article 1 – "[i]n accordance with the precautionary principle, the objective of this Directive is...to protect human health and the environment"[3], in Recital 5 of the Directive, and the reference to "human health or the environment" in Annex II itself, where this reference appears five times in the introductory remarks and in each of the four parts A to D of that Annex. Further, section A of Annex II states that:

> "The objective of an [environmental risk assessment] is, on a case by case basis, to identify and evaluate potential adverse effects of the GMP, either direct, indirect, immediate or delayed, on human health and the environment which the deliberate release or the placing on the market of GMOs may have. The [environmental risk assessment] should be conducted with a view to identifying if there is a need for risk management and if so, the most appropriate methods to be used."

Finally, it is to be noted that it follows from Article 191(1) TFEU (The Treaty of the Functioning of the European Union) that in EU law, the "protection of the environment" includes the protection of human health[4].

The introductory remarks to Annex II of the Directive state: "A general principle of environmental risk assessment is also that an analysis of the 'cumulative long-term effects' relevant to the release and the placing on the market is to be carried out. 'Cumulative long-term effects' refers to the accumulated effects of consents on human health and the environment". Thus, the continued consumption of genetically modified plants, where herbicide residues might be present, should be submitted to risk assessment as a matter of course.

Section B sets out the general principles governing the performance of an environmental risk assessment, which include "identified characteristics of the GMP and its use which have the potential to cause adverse effects should be compared to

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[3] The importance of the protection of human health is reinforced by the multiple references to it in the Directive – see: Article 13(6), in Recital 5 of the Directive, and the reference to "human health or the environment" in Annex II itself, where this reference appears five times in the introductory remarks and in each of the four parts A to D of that Annex.

[4] Article 191(1) TFEU: " *Union policy on the environment shall contribute to the pursuit of the following objectives:... – protecting human health..."*

those presented by the non-modified organism from which it is derived and its use under corresponding situations."

Section C.2 of Annex II describes the "Steps in the environmental risk assessment". As a first step, that part requires the identification of characteristics that may cause adverse effects, and gives a general indication of what has to be done, noting that "it is important not to discount any potential adverse effect on the basis that it is unlikely to occur". Section C.2 then alerts to "Potential adverse effects of GMOs will vary from case to case and may include: - disease to humans including allergenic or toxic effects…" Finally, Section C.2 outlines the steps involved in reaching an overall assessment of the risk posed by a genetically modified plant. These include the evaluation of the potential consequences of the adverse effects (for which the evaluation should assume that such an effect will occur), the evaluation of the likelihood of and the risk posed the occurrence of each potential adverse effect, and the identification of risk management strategies.

The conclusions of the risk assessment shall be part of the notification, in order to allow the competent authority to draw its own conclusions (Annex II, part D). The conclusions on the risk assessment shall include "Possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMOs [GMHP] and persons working with, coming into contact with or in the vicinity of the GMO [GMHP] release(s)"[5].

It follows from these provisions that the environmental risk assessment has to include all effects which the placing of a GMO on the market may have on human health, including any possible cumulative effects. This also includes the potential effects of the use of herbicides or pesticides on the GMO plant or product. Of particular importance is the fact that the assessment of a particular potential adverse effect may not be excluded from the overall assessment on the basis that it is considered it is unlikely to occur. Although the likelihood of a potential adverse effect is one factor of the evaluation, the magnitude of its potential consequences and the risks it would pose to the environment and human health must still be assessed, and both of these elements should be taken into account in the overall risk assessment.

[5] Directive 2001/18, Annex II, part D1 no.6 and part D2 no.6. Part D1 refers to GMOs other than higher plants, part D2 to genetically modified higher plants (GMHP). For reasons of simplification the two sections D1 no. 6 and D2 no. 6 were assembled in one text.

Other information

"Other information" which has to accompany every notification under Article 13 of Directive 2001/18, shall include "considerations for human health and animal health, as well as plant health: (i) toxic or allergenic effects of the GMO and/or their metabolic products[6], furthermore "identification and description of non-target organisms which may be adversely affected by the release of the GMO, and the anticipated mechanisms of any identified adverse interaction"[7]and, as a catch-all formula "other potential interactions with the environment"[8]. For genetically modified higher plants (GMHP), Annex IIIB applies, this requires the notifier to supply, with his notification, the following information: "Information on any toxic, allergenic, or other harmful effects on human health arising from the genetic modification"[9]; "Information on the safety of the GMHP to animal health, particularly regarding any toxic, allergenic or other harmful effects arising from the genetic modification, where the GMHP is intended to be used in animal feedstuffs"[10]; and "Potential interactions with the abiotic environment"[11].

This wording with regard to the "other information" is thus again very broad and tries to cover all effects that the GMO product might have on human health or animal health. The choice of the terms "arising from the genetic modification" clarifies that information is to be supplied not only on the effects caused directly by the GMO, but also on all other harmful effects on human or animal health and which are, in one way or another, related to the genetically modified plant.

The monitoring plan

According to Article 13(2.(e), a monitoring plan has to accompany the notification; the plan shall be established in accordance with Annex VII to the Directive. Its objectives are underlined by recital 43 of Directive 2001/18 which states: "it is necessary to introduce into this Directive an obligation to implement a monitoring plan in order to trace and identify any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOS as or in products after they have been placed on the market". The use of the word "any" both in the Recital 43 and in Annex VII itself demonstrates that the purpose of the monitoring plan is to discover all

6 Directive 2001/18, Annex III A, section II, C.2(i)

7 Directive 2001/18, Annex IIIA, section IV B12.

8 Directive 2001/18, Annex IIIA, section IV B.16.

9 Directive 2001/18, Annex IIIB, section D no.7.

10 Directive 2001/18, annex IIIB, section D no.8.

11 Directive 2001/18, annex IIIB, section D no11.

possible impacts of adverse effects of GMOs, including those effects not foreseen in the environmental risk assessment ("unforeseen").

This interpretation is confirmed by the provisions in Annex VII on the design of the monitoring plan: the plan has to

1. be detailed on a case by case basis (Annex VII, C.1);
2. take into account the relevant environmental conditions where the GMO is expected to be released (C.2);
3. incorporate general surveillance for unanticipated adverse effects (C.3);
4. provide for case-specific monitoring, though routine surveillance practices that "were already established" are allowed in appropriate cases (C.3.1 and C.3.2);
5. facilitate the observation "in a systematic manner" of the release of the GMO in the receiving environment and the interpretation of these observations "with respect to human health or the environment" (C.4).

In 2002, the Council adopted, by way of a Decision, guidance notes "supplementing Annex VII"[12]. The guidance notes "shall be used as a supplement to Annex VII of Directive 2001/18/EC" (Article 1). The guidance notes repeat in the introduction that the purpose of the monitoring plans is to "trace and identify any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOs as or in products after they have been placed on the market".

The guidance notes first repeat the objective and general principle of the monitoring plan of Annex VII to Directive 2001/18 and then add: "In addition, monitoring of potential adverse cumulative long-term effects should be considered as a compulsory part of the monitoring plan"(part B). They clarify what is to be understood by by the terms "direct effects", "indirect effects", "immediate effects" and "delayed effects".

With regard to unforeseen effects, the guidance notes indicate: "it is very difficult if not impossible to predict the appearance of potential, unforeseen or unanticipated effects that were not highlighted in the risk assessment. General surveillance for potential unforeseen or unanticipated effects should, therefore, be considered as a part of the monitoring strategy" (part C). This statement indicates that notifier may not limit his monitoring plan to those risks identified in the environmental risk

[12] Decision 2002/811/EC of 3 October 2002 establishing guidance notes supplementing Annex VII to Directive 2001/18/EC, OJ 2002, L 280 p.27.

assessment which had to be made according to Article 13(2.b) and Annex II section D to Directive 2001/18.

The guidance notes also expressly state that the time-period for monitoring would depend on the circumstances, but could extend to a number of years (part C- 1.5). This is another indication that potential cumulative effects of genetically modified plants hand herbicide residues are to be controlled.

Case-specific monitoring (part C-1.3.1) should focus on “all the potential effects on human health and the environment identified in the risk assessment”. It should begin with determining the case-specific objectives of the monitoring strategy, which “include” the identification of the occurrence and impact of potential adverse effects of the GMO or its use that were made in the environmental risk assessment. The strategy should indicate that these assumptions are to be confirmed by the case-specific monitoring. With regard to potential effects on human health, the guidance notes specify that such effects will depend on the inherent nature of a GMO and its specific genetic modification.

For unforeseen adverse effects that were not predicted in the risk assessment, the guidance notes make provision for a “general surveillance” (part C- 1.3.2) which consists of “routine observation (“look – see”) approach”. Such surveillance should be carried out over a longer period of time and possibly a wider area than the case-specific monitoring, though the type of general surveillance would depend on the type of unforeseen adverse effects. The notes indicate that the general surveillance could make use of established routine surveillance practices “where compatible”; then the established routine surveillance practice should be described in the plan, including any necessary alignment to the general surveillance. “Food surveys“ are expressly mentioned (part C -1.7) as one example of existing systems.

The guidance notes contain a number of other indications, such as the monitoring methodology (part C- 2) and analysis, reporting and review (part C-3) which will not be set out here.

Overall, the main purpose of the monitoring plan is to confirm the assumptions that were made in the environmental risk assessment on (the absence of) potential adverse effects. However, the guidance notes expressly indicate that the monitoring

strategy should also include a strategy with regard to unforeseen events not assessed in the environmental risk assessment.

(b) Particular provisions of Regulation 1829/2003

Regulation 1829/2003 applies to genetically modified food and feed. Articles 3 to 14 apply to genetically modified food, Articles 15 to 23 to genetically modified feed. The placing on the market of genetically modified food or feed requires an authorisation (Article 4 for food, Article 16 for feed).

Article 5(5) of Regulation 1829/2003 provides that an application for GMOs or food containing or consisting of GMOs must be accompanied by, amongst other things, "information and conclusions about the risk assessment carried out in accordance with the principles set out in Annex II to Directive 2001/18/EC or, where the placing on the market of the GMO has been authorised under part C of Directive 2001/18/EC, a copy of the authorisation decision". Furthermore, such an application shall be accompanied by "a monitoring plan for environmental effects conforming with Annex VII to Directive 2001/187EC..." (Article 5(5)(b)).[13]

Article 6(4) provides: "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…"

Under, Articles 5(3)(k) and 17(3)(k) of the GM Regulation an application for marketing authorisation has to contain a proposal for post-marketing monitoring regarding the use of the food for human consumption and feed for animal consumption "where appropriate". Similarly, in giving a positive opinion in relation to an application EFSA has to include such post-marketing monitoring requirements "where applicable" (Articles 6(5)(e) and 18(5)(e) of the GM Regulation.

The authorisation of a genetically modified food is granted by the Commission by way of the so-called comitology procedure (Article 7 and Article 35). The authorisation has to include the particulars referred to in Article 6(5), which includes where appropriate

[13] For such cases, Articles 13 to 24 of Directive 2001/18 are declared inapplicable.

a monitoring plan. In its decision, the Commission is not bound by the opinion of EFSA. Instead, the Commission has to take the EFSA opinion into account, as well as "any relevant provision of Community law and other legitimate factors relevant to the matter under consideration" (Article 7(1)).[14] In other words, the Commission has to determine, whether the monitoring plan has to include the control of potential adverse effects of the genetically modified plant during the use and consumption stage. Even when the EFSA, in any of its opinions, does not comment on the need for such a control, the Commission was obliged to decide on that issue.

The provisions on feed containing or consisting of GMOs mirror the provisions on genetically modified food: A provision corresponding to Article 5(5) of Regulation 1829/2003 is laid down in Article 17(5), a provision corresponding to Article 6(4) is found in Article 18(4). In addition, where appropriate EFSA also has to give the particulars of the relevant monitoring plan (Article 18(5.g)). The Commission, when authorising the genetically modified feed, also has to also refer to the monitoring plan (Article 19(2)).

It follows from these provisions that for genetically modified food or feed, information and conclusions about the risk assessment must be given. This risk assessment must have been carried out in accordance with the principles set out in Annex II to Directive 2001/18 (Article 5(5.a) and Article 17(5.a) see section 2 above). Also a monitoring plan has to be submitted with the application for authorisation (Article 5(5.b) and Article 17 (5.b)). Where EFSA expresses an opinion in favour of the authorisation, it has to address the monitoring plan (Article 6(5.g) and Article 18(5.g)) and indicate "post-market monitoring requirement based on the outcome of the risk assessment" (Article 6(5.e) and Article 18(5.e)).

The European Commission has the responsibility for authorising the placing on the market of genetically modified food or feed. Accordingly, it has an obligation to attach the necessary conditions to the authorisation in order to ensure that the food or feed has no adverse effects on human health, animal health or the environment (Article 4(1)). It has its own responsibility in this regard and may not rely on the – non-binding – opinion of EFSA; in the past, the Commission occasionally did add supplementary conditions on the placing on the market of genetically modified food products[15].

[14] Further, under Article 7(1) the Commission has to provide an explanation for the difference, where its decision is not in accordance with EFSA's opinion.

Under Regulation 1829/2003, genetically modified food or feed placed on the market, must be monitored according to the principles laid down in Directive 2001/18 (see section 2 above). The monitoring plan must attach greater importance to potential adverse effects and to the unforeseen effects of the genetically modified food or feed on human or animal health than in the application of Directive 2001/18 alone, as it is the very purpose of Regulation 1928/2003, expressed in Recitals 2 and 3 and its Articles 1, 4 and 16, to protect human health. Further, the information and conclusions concerning the risk assessment must take into consideration this need to protect human and animal health.

The Court of Justice confirmed this interpretation and stated that[16]:

> "Regulation 1829/2003 applies to the specific field of food and feed. As regards food, its first objective, referred to in article 4(1), is also to avoid adverse effects on human health and the environment. However, Directive.. 2001/18 [was] drafted primarily from the angle of the concept of 'deliberate release' which is defined in article 2(3).. as an intentional introduction of a GMO into the environment, without specific containment measures designed to limit their 'contact' with the 'general population and the environment'. That approach thus appears to be more general, including with regard to the placing on the market of a GMO as a product. In this respect, … recitals 25, 28 and 32 in the preamble to Directive 2001/18 link the need to introduce an assessment and authorisation procedure to the situation in which the placing on the market includes a deliberate release into the environment. Although Regulation 1829/2003 also includes, in particular in Articles 5(5) and 6(4), aspects of environmental risk assessment of food, it is, as regards food, based overwhelmingly on an appraisal emphasizing protection of human health which is linked to the specific fact that that food is, by definition, intended for human consumption. Thus, in accordance with recital 3 in the preamble, in order to protect human health, foods containing, consisting or produced from GMOs must undergo a 'safety' assessment. Regulation 1829/2003 thus introduces an additional level of control. That regulation would be rendered nugatory, if the view were to be taken that an assessment carried out and an authorisation issued pursuant to

[15] See for example Commission decision 2010/135/EU, OJ 2010, L 53 p.11, Recital 18 and Article 4(e), where additional monitoring measures were requested.

[16] Court of Justice, case C-442/09 *Bablok,* Judgment of 6 September 2011, paragraphs 97 – 102.

> Directive … 2001/18 covered all subsequent potential risks to human health and the environment".

The least which one can conclude from these remarks by the European Court of Justice is that the safety assessment – in other words the environmental risk assessment and the post-marketing monitoring evaluation – must be, under Regulation 1829/2003, at least as strict as under Directive 2001/18, if not stricter.

Conclusion

It follows from all these provisions, that under Directive 2001/18, a notifier's documentation must contain a comprehensive environmental risk assessment of the GMO, which includes all potential adverse effects on human and animal health. Unlikely occurrences must also be included in the assessment and evaluated. The monitoring plan must be case specific and also contain a strategy for monitoring events that were not foreseen in the environmental risk assessment.

The purpose of Directive 2001/18 is also to protect human and animal health, and as GMO plants are consumed by humans, the environmental risk assessment and the monitoring plan must, therefore, also contain an assessment of such potential effects (risk assessment) and a strategy to verify whether such adverse effects actually occur. Indeed, the development of allergies or other adverse effects, due to the consumption of genetically modified plants which are herbicide-resistant, and which possibly contain herbicide residues, are not so unlikely that the monitoring of such effects can be omitted.

The competent authority has to give written consent for the placing on the market of a GMO as or in a product (Article 19). The consent has to specify, among other things, the monitoring requirements in accordance with Annex VII to the Directive (Article 19(3.f)). This provision clarifies that the competent authority is not bound, in the monitoring conditions, which it puts on the consent with regard to monitoring, by the monitoring plan of the notifier. Rather, this plan is, legally, a mere proposal. Thus, the competent authority, which gives written consent, has a responsibility of its own to ensure that all direct and indirect, immediate and delayed, cumulative and unforeseen effects of the GMO on human and animal health and the environment are properly monitored.

Under Regulation 1829/2003, the competent authority is require to ensure that a proper safety and risk assessment of the GMO is carried out to ensure that it does not have adverse effects on human health, animal health or the environment. This requires that not only is a thorough and scientifically adequate safety assessment is carried out, but also where appropriate that suitable monitoring is carried out.

2. Factual background

The genetically modified maize MON89034 × 1507 × MON88017 × 59122 (SmartStax), the "Maize", is a hybrid product. It is created by using traditional breeding methods, to combine the genetic material of four parent plants: Maize89034 and MON88017, developed by Monsanto, and maize 1507 and maize 59122, developed by Dow AgroSciences and Pioneer/ DuPont ("the Parental Plants").

The Parental Plants are themselves genetically modified:

a. MON89034 is a maize, which has had a DNA sequence for synthetical insecticide proteins "Cry1A105" and "Cry2Ab2" inserted into its genome. It was authorised by Commission Decision 2009/813/EU of 30 October 2009.

b. MON88017 is a maize which has had a DNA sequence for glyphosate herbicide resistant protein "CP4 EPSPS" and insecticide proteins "Cry3Bb1" inserted into its genome. It was authorised by Commission Decision 2009/814/EU of 30 October 2009.

c. 1507 is a maize which had a DNA sequence for glufosinate herbicide resistant protein "PAT" and sequence for insecticide proteins "Cry1F" inserted into its genome. It was authorised by Commission Decisions 2005/772/EC of 3 November 2005, 2006/197/EU of 3 March 2006 and 2011/365/EU of 16 June 2011.

d. 59122 is a maize which had a DNA sequence for glufosinate herbicide resistant protein "PAT" and sequence for insecticide proteins "Cry34Ab1" and "Cry35Ab1" inserted into its genome. It was authorised by Commission Decision 2007/702/EC of 24 October 2007.

"Cry" proteins are toxins derived from the bacterium *Bacillus thuringiensis*. This is a gram-positive soil dwelling bacterium which is also used as a biological pesticide. The Cry toxins – in their natural crystal form - can be used as a pesticide. These toxins are also commonly referred to as "Bt toxins".

EPSPS and PAT proteins (enzymes) can also be derived from soil dwelling bacteria. They confer tolerance to glyphosate- and glufosinate based herbicides.

The Maize thus combines the insecticide traits of four parental plants, and the herbicide tolerance traits of three parental plants. As it combines more than one modified gene, it has “stacked genes” and is called a “gene stacked event” or “stacked event”.

On 24 October 2008, Dow AgroSciences Ltd on behalf of Dow AgroSciences LLC and Monsanto Europe S.A. on behalf of Monsanto Company submitted to the competent authority of the Czech Republic an application, in accordance with Article 5 and Article 17 of Regulation (EC) No 1829/2003, for the placing on the market of foods, food ingredients, and feed containing, consisting of, or produced from MON89034 × 1507 × MON88017 × 59122 maize. The application also covers possible segregating subcombinations of the single GM events constituting MON89034 × 1507 × MON88017 × 59122 maize. The application excludes cultivation within the EU.

The Maize and the derived products, that the companies have applied for to bring into the EU, are genetically modified organisms, or food/feed containing genetically modified organisms, within Article 2 of Directive 2001/18 and Article 2(5) of the GM Regulation. The grains are biological entities capable of replication or of transferring genetic material, and are therefore “organisms” within Article 2(1) of Directive 2001/18. Their genetic material has been altered in a way that does not occur naturally, within Article 2(2) of Directive 2001/18.

The European Food Safety Authority (“EFSA”) considered the Application, in order to determine inter alia whether the Maize would have adverse effects on human health, animal health or the environment, contrary to Articles 4(1)(a) and 16(1)(a) GM Regulation, if its placing on the Union market were to be authorised.

In accordance with Articles 6(4) and 18(4) of the GM Regulation, EFSA consulted the competent national authorities of Member States on the Application.

Following that consultation, EFSA issued an Opinion on the Application on 27 September 2010 (EFSA 2010a, “EFSA Opinion”). It was complemented by a second

opinion on the segregating subcombinations on 29 September 2011 (EFSA 2011). In its opinion from 2010 EFSA concluded (EFSA 2010a):

> "In conclusion, the EFSA GMO Panel considers that the information available for maize MON89034 x 1507 x MON88017 x 59122 addresses the scientific comments raised by the Member States and that the maize MON89034 x 1507 x MON88017 x 59122, as described in this application, is as safe as its conventional counterpart and commercial maize varieties with respect to potential effects on human and animal health and the environment. In addition, the EFSA GMO Panel is of the opinion that crossing of maize events MON89034, 1507, MON88017 and 59122 to produce maize MON89034 x 1507 x MON88017 x 59122 does not result in interactions between the events which would affect the safety of maize MON89034 x 1507 x MON88017 x 59122 with respect to potential effects on human and animal health and on the environment, in the context of its intended uses. Based on the data provided for maize stack MON89034 x 1507 x MON88017 x 59122, the single maize events MON89034, 1507, MON88017, 59122, and for the two double stacks 1507 x 59122 and MON89034 x MON88017, the EFSA GMO Panel is of the opinion that there is no biological reason to expect that any of the other sub-combinations5 of the individual events present in the segregating progeny would raise a safety concern. The EFSA GMO Panel concludes that maize MON89034 x 1507 x MON88017 x 59122 is unlikely to have adverse effects on human and animal health and the environment, in the context of its intended use."

In the absence of a decision by the The Standing Committee on the Food Chain and Animal Health, the appeal committee, and on the basis of the EFSA Opinion, the Commission decided on 6 November 2013 to grant the market authorisation (Commission decision 2013/650/EU, published on 11 of November 2013[17]).

The Commission decided (Article 2 of the decision):

> "The following products are authorised for the purposes of Article 4(2) and Article 16(2) of Regulation (EC) No 1829/2003 in accordance with the conditions set out in this Decision:
>
> (a) foods and food ingredients containing, consisting of, or produced from the GMOs specified by their unique identifiers in Article 1;

[17] http://ec.europa.eu/food/dyna/gm_register/index_en.cfm

(b) feed containing, consisting of, or produced from the GMOs specified by their unique identifiers in Article 1;

(c) the GMOs specified by their unique identifiers in Article 1 in products containing them or consisting of them for any other use than (a) and (b), with the exception of cultivation.”

The Commission agreed with the plan of the applicant on the monitoring plan for environmental risks. Further, the Commission decided upon the monitoring plan for food consumption (point I of the Annex):

“Post-market monitoring requirements for the use of the food for human consumption: Not required.”

3. Grounds for the complaint

Ground A: Failures in EFSA's assumption the Maize is 'substantially equivalent'

Introduction:

Ground A is that EFSA committed a manifest error of assessment in concluding that the Maize is 'substantially equivalent' to its conventional counterpart apart from the insertion of the proteins. EFSA concluded substantial equivalence without sufficient scientific evidence. Data were missing from the Maize and its control groups and there were only a very limited number of field trials. As the experts from Member States (Germany) summarise (EFSA 2010b):

> "Data from the compositional analysis were presented from only one season (USA, 2006; based on production plan 06-01-52-04). Due to contamination of test material with other GMO only four of the five sites could be used for the compositional analyses. Compositional data for GMO without HR-treatment were not presented. The very limited number of sites (and climates) and years do not allow to test for possible effects of environmental variables. Since the compositional analysis presents a key element for the assessment of food/feed further data, including additional sites and years, should be presented."

Although required by EFSA guidance, the authority failed to request further data such as compositional analysis of the Maize not sprayed with complementary herbicides and of the Parental Plants grown at the same site.

In comparison to their conventional counterparts, both the stacked event and the parental plants show a number of significant differences. By referring to unspecific reference material and the ILSI database, which is known to be unreliable, differences in phenotype and in plant composition were interpreted as having no biological relevance.

Thus, the whole risk assessment of EFSA is manifestly flawed since the following steps in risk assessment and the final conclusions are largely based upon the compositional analysis.

Reasoning

A1 Major uncertainties in the assumptions concerning the Parental Plants

The statement of EFSA that the Parental Plants are substantially equivalent to their isogenic comparators is questionable. In the risk assessment of the Parental Plants, the ILSI data base and other historical data were used as a reference to explain differences between the genetically engineered plants and comparators. Since it is not sufficiently clear under which specific conditions these additional historical data were generated, this kind of comparison inevitably leads to major uncertainties and cannot be used as evidence to assume biological relevance of these observed differences. Even the EFSA recognises the unreliability of this database. As Joe Perry, the current Chair of EFSA's GMO Panel stated:

> "I think we're in a situation where we would be unwise at the present time (maybe in the future this will be different), but at the present time we can't trust the ILSI database. There is not sufficient environmental information from where these trials were done and that's why we insist that the commercial reference variety should be planted simultaneously with the GM and the non-GM. Otherwise I think we are in an unsafe situation and I would worry that the limits would be too wide."[18]

Since no new the compositional data from the Parental Plants were derived during field trials with the Maize, the weaknesses in assuming compositional equivalence for the Parental Plants is relevant also for the assessment of the Maize. EFSA failed to ensure that the Maize was compared to its Parents in the same conditions. Instead it relied upon its previous assessment (in different conditions) of the Parents which suffered from its own flaws. Further, the ILSI database was also used in the risk assessment of the Maize to show that it does not differ compositionally from its conventional counterparts.

[18] Observations of Mr. Joseph Perry, Vice-Chair, at EFSA's consultative workshop on its draft guidance for the selection of Genetically Modified (GM) plant comparators, held in Brussels on 31 March 2011, http://www.efsa.europa.eu/en/events/event/gmo110331.htm

Despite having identified a number of statistically significant differences between the Maize and its conventional counterpart, EFSA nevertheless concluded that there was ‘substantial equivalence’ between them on the basis that the differences were small and fell within the range of variation: (i) presented by a number of non-GM maize varieties (“the reference substances”); and/or (ii) reported by historical data (from the ‘ILSI’ database), neither of which had been properly analysed to ensure they were capable of substantiating the conclusion drawn from it. Instead, they operated as scientific ‘noise’ to mask the differences which should have been properly analysed following sufficient clinical trials. Moreover, in scientific terms, a statistically significant difference may be biologically relevant and therefore present a safety concern even if it is ‘small’.

Instead of setting aside the observed significant differences from compositional analysis, EFSA should have explored them in much more detail by subjecting the plants to defined environmental conditions and conducting investigations into gene activity and metabolic profile. In this regard, the uncertainties stemming from the parental plants should have also been taken into account.

As a result, EFSA´s assumption of equivalence for the stacked Maize is founded on a flawed assumption and is not based on sufficient and reliable data.

A2 Missing comparators

Since there were justifiably severe doubts about the substantial equivalence of the parental traits, a detailed investigation of the plant components of the stacked Maize would have been necessary.

EFSA Guidance (2007) also requests:

> “In line with the EFSA Guidance Document [2006], the most appropriate comparator(s) for the GMO plant containing the stacked event should include the GM parental materials as well as appropriate non-transgenic genotype(s).”

Further EFSA Guidance, 2006, requests:

> "in case of herbicide-tolerant GM-plants it is advisable to include both blocks of genetically modified plants exposed to the intended herbicide and blocks not

exposed to the herbicide. This design would allow assessment of whether the expected agricultural condition might influence the expression of the studied parameters"

Accordingly, the investigation of the differences between the stacked Maize and its comparators should include the isogenic and the non-transgenic Parental Plants (as well as the crossings) in direct comparison of the field trials, with and without spraying. As the experts from Member States (Germany) requested (EFSA 2010b):

> “In accordance with the EFSA Guidance Document (EFSA, 2006) we would like to stress that in the case of herbicide tolerant GM plants both blocks of genetically modified plants exposed to the intended herbicide(s) and blocks not exposed to the herbicide(s) should be included with regard to the production of material for comparative assessment. This design would allow assessment of whether the expected agricultural condition might influence the expression of the studied parameters within the compositional analysis as well as the analysis of agronomic traits. Therefore, the applicant should be requested to demonstrate that forage and grain from maize MON 89043 x 1507 x MON88017 x 59122 are compositionally equivalent to and as nutritious as forage and grain from conventional maize regardless of herbicide treatment. This applies analogously to the comparative assessment of the phenotypic, agronomic, and ecological characteristics of maize MON 89043 x 1507 x MON88017 x 59122.”

However, the Applicants chose not to file any data on the Parental Plants (except expression data for the transgene) or on the Maize not sprayed with complementary herbicides. In the light of uncertainties on compositional changes in the Parental Plants, this is not only a violation of EFSA´s Guidance, but also creates great uncertainty regarding the equivalence of the plants with conventional plants which is a starting point for subsequent steps in risk assessment as performed by EFSA (“comparative approach”).

As a result, EFSA´s assumption of equivalence of the stacked Maize is founded on a flawed assumption of substantial equivalence of the Parental Plants and is, furthermore, not based on sufficient and reliable data from the appropriate comparators.

A3 Wrong interpretation and lack of phenotypic data

EFSA also failed to properly assess the data from field trials examining agronomic data and phenotypic differences. EFSA (2010) only very roughly describes the outcome of field trials on phenotypic and agronomic data:

> "In the present application, the analyses of agronomic and phenotypic characteristics of maize MON89034 x 1507 x MON88017 x 59122, its conventional counterpart and twelve commercial maize varieties included a range of parameters related to plant morphology, physiology, appearance and performance, including stressors and plant health. A number of parameters showed statistically significant differences in the per-location statistical analysis of the comparison between maize containing stack MON89034 x 1507 x MON88017 x 59122 and its conventional counterpart but this was not consistently observed in each location."

Concerns of experts from Member States (Austria) were raised that more data would be needed to draw any conclusions (EFSA 2010b):

> "We are, therefore, of the opinion that the notifier should submit further data on ecologically relevant parameters (e.g. duration of pollen viability, flowering time or susceptibility towards pest and disease (investigated under pest or disease pressure). Moreover, the experimental design did not include plots which were not treated with the non-selective herbicides (glyphosate and glufosinate-ammonium), and thus, did not allow for a comparison between treated and untreated plots."

These concerns were answered by EFSA very generally (EFSA 2010b):

> "In an environmental risk assessment, agronomic/phenotypic data give an indication on whether the fitness, persistence and invasiveness of the GM plant differ from that of its non-GM counterpart."

This answer suffers from the same deficiencies as, for instance, the investigation carried out by Rosenbaum (2008), which did not consider the risks of food and feed but only higher fitness ("pest potential") as the endpoint to assess the data (see also Then, C. 2011a). However, this is not in line with the EFSA Guidance (2006):

> "Compositional analysis represents a key component of the comparative approach for identifying unintended effects during the risk assessment process. However, unintended effects may also manifest themselves through, for

example, changes in susceptibility to important pests and diseases, through morphological and developmental changes or through modified responses to agronomic and crop management regimes. Therefore, the comparison between the GM plants and their most appropriate comparators should address also plant biology and agronomic traits, including common breeding parameters (e.g. plant morphology, flowering time, day degrees to maturity, duration of pollen viability, response to plant pathogens and insect pests, sensitivity to abiotic stress)."

Consequently, much more data are relevant for food and feed risk assessment than those provided by the Applicants and assessed by EFSA. Thus, any difference in the phenotype of the plants (in reaction to various environmental conditions) can be relevant for risk assessment for food and feed. Viewed from this aspect, EFSA failed to request data on a relevant parameter and used a wrong endpoint for assessing the data. Further (as mentioned above) EFSA completely failed to request data from the Maize not treated with the complementary herbicides and from the Parental Plants growing under the same conditions. Finally, EFSA failed to request data from a broad range of relevant stress conditions that can impact both the phenotype of the plants and the plants´ composition.

A4 Missing data on the impact of relevant geo-climatic regions

EFSA's 2007 Guidance Document states in section 3.2.1 that in relation to the compositional assessment of stacked events,

> "at least one year of field trial data is required, with trials performed together with appropriate controls in geographical localities representative of the climatic conditions under which such crops will be cultivated."

Further,

> "possible differences in phenotypic characteristics and agronomic properties of stacks must be assessed in field trials over at least one season, as indicated [in relation to the compositional assessment). Again, on a case-by-case basis, additional information on agronomic traits of the stacked events may be required from additional field trials."

However, in relation to the Maize, the number of field trials and the data from the relevant geo-climatic regions is too low to draw any final conclusions about

equivalence. Currently, it appears that the Maize is being grown in the US but there are at least two other major countries, which export maize into the EU, both of which also grow genetically engineered plants: Argentina and Brazil. The market authorisation granted in the EU is not restricted to certain regions so that data from all relevant maize exporting countries should have been requested.

A5 Missing data on the impact of biotic and abiotic stressors

Several investigations show that genetically engineered plants can exhibit unexpected reactions under stress conditions (see for example: Matthews et al., 2005, Zeller et al., 2010, Li et al., 2013).

Agapito-Tenfen et al (2013) show protein differences between genetically engineered maize and conventional field-grown maize. While these differences do not represent a safety issue per se, they are an important factor when considering unintended effects in the plants to be assessed. These unexpected reactions can impact the composition of the plants and give rise to unintended biologically active substances. The functional stability of the transgene under various defined environmental conditions, therefore, has to be investigated to assess safety for food and feed.

Section 7.4 of the 2006 Guidance recognises this by stating that (emphasis added)

> "the comparison between the GM plants and their most appropriate comparators should address also plant biology and agronomic traits, including common breeding parameters (e.g. plant morphology, flowering time, day degrees to maturity, duration of pollen viability, **response to plant pathogens and insect pests, sensitivity to abiotic stress**)."

As noted above, the 2007 Guidance also refers to the possibility of the unintended effects of the stacked event including modified susceptibility to biotic and abiotic stresses.

The impact of specific stress factors should have been explored under defined environmental conditions in order to perform proper risk assessment, followed by appropriate statistical evaluation and use of more recent scientific methods such as metabolic profiling. The data presented by Rosenbaum (2008) are not sufficient to

conclude on these issues. As the experts from Member States (Austria) summarise (EFSA 2010b):

> "Pest pressure and infestation in general seemed to be negligible, as no or only little stressor symptoms were found only. Similarly, no abiotic stress through compaction, drought or frost was observed. As a consequence, statistical evaluation did not provide any differences between the test, the control and the reference substances. However, the reverse argumentation that actually there are no differences is not allowed."

No conclusion can be drawn from these more or less arbitrary data if and under which environmental conditions the Maize might be more or less sensitive to biotic or abiotic stressors than its comparators. In general, the reaction of the transgenic plant to specific biotic and abiotic stressors has to be investigated in much more detail and under defined environmental conditions before any conclusion can be drawn on food safety. For example, it is also necessary to examine how the Maize reacts to extreme weather conditions as they occur under ongoing climate change.

A6 Missing scientific standards

The investigations into interaction with the environment, phenotypic characteristics, as well as some investigations examining the plants´ composition do not meet basic standards of GLP (Good Laboratory Practice). This is explicitly stated in several of the Applicant dossiers dealing with the stacked Maize such as those drawn up by Rosenbaum (2008); McRae (2008); Levine et al. (2008a and b). Similar deficiencies can also be found in data on the Parental Plants.

The dossier drawn up by Rosenbaum (2008) dealing with phenotypic reactions to environmental conditions is particularly concerning when it comes to scientific standards.

The investigations were commissioned and paid for by Monsanto. They were conducted in Monsanto Laboratories. Regarding quality control no independent laboratories were involved, most data were not published in peer-reviewed magazines, and the wording of the report even indicates manipulation of the data.

The investigations were only performed for one season and on relatively small plots. Rosenbaum (2008) only considered the question of whether the plants showed a higher degree of fitness or invasiveness and whether their agronomic properties could be compared to other maize plants.

No food and feed related risks were explored. Neither were there any investigations into metabolic changes within the plants or gene activity, nor were there any detailed analyses of compositional changes throughout the season. Risks related to food and feed cannot be concluded from the data that was presented.

Relevant agronomic criteria were not taken into account (e.g. the date of flowering or viability of pollen). Some significant findings that indicate interactions with the environment or an overall change in gene activity and plant metabolism were dismissed without any further investigations. For example, a higher incidence of plant disease was found in one site. Further, six criteria were found to be significantly different (e.g. pollen shed, ear height, plant height and grain moisture) in comparison with the findings for the control plants at the individual sites. None of these findings were investigated further.

Apparently, several individuals were involved in data collection and data evaluation:

> “During the process of data summarization and analysis, experienced scientists familiar with each experimental design and evaluation criteria were involved in all steps. This oversight ensured that the data were consistent with expectations based on experience with the crop.”

There is no explanation as to who these experts were or how the data were made consistent with expectations. This wording indicates a possible manipulation of the data. Only one Monsanto member of staff is mentioned under acknowledgements for

> “assistance with the statistical analysis of the data.”

The EU Commission does acknowledge the lack of sufficient scientific standards in the presented dossiers. In its recent implementing regulation on applications for the authorisation of genetically modified food and feed (EU Commission, 2013b), the Commission requires quality assurance for studies such as Good Laboratory Practice (GLP). But, of course, sufficient scientific standards have to be requested for each and every risk assessment of genetically engineered plants. According to existing EU

Regulation, all products placed on the market have to be investigated in accordance with “the highest possible standard” (Regulation 1829/2003, recital 9).

In conclusion, the data from industry as mentioned should have been rejected by EFSA because they are not in accordance with internationally adopted scientific standards and therefore cannot be regarded as of “the highest possible standard” (Regulation 1829/2003, recital 9). Consequently, the market authorisation for the Maize should be withdrawn.

Conclusions on Ground A:

- It follows that there is no basis upon which EFSA could have concluded that the comparison made was “appropriate” under the terms of Articles 5(3)(f) and 17(3)(f) GM Regulation. It should also be noted that in a number of respects EFSA failed to follow and/or comply with the terms of its own Guidance Documents.

- Further, and in consequence, contrary to the requirements of and Articles 6(3)(a) and 18(3)(a) GM Regulation, either EFSA has failed to consider whether the applicants´ analysis was supported by “appropriate information and data”, or EFSA has unlawfully and manifestly incorrectly concluded that the information provided by the applicants was “appropriate”.

- This error is also potentially highly material to the conclusion that the Maize does not present a risk of adverse effects on humans and/or animal health, contrary to Articles 4(1) and 16(1) GM Regulation.

- EFSA’s conclusion that the Maize is safe depends on the assumption that the Maize is substantially equivalent to its conventional counterpart. As such, it is fatally flawed. In particular, on the basis of its conclusion that the Maize and its conventional counterpart are substantially equivalent EFSA concluded that it was not necessary to conduct a toxicological assessment of the whole food/feed. A properly conducted comparison of the field trial results with properly analysed literature might well have demonstrated that the statistically significant differences observed were biologically relevant, and required much more detailed analysis at the following steps.

- As such, EFSA’s conclusion that there would not be an adverse effect on human health and/or animal health from the Maize, under Articles 4(1)(a) and 16(1)(a) GM Regulation, is not reliable.

- Since these flaws in risk assessment as performed on the Maize also can be observed in the Parental Plants, the conclusion that the Maize is safe includes a whole series of substantial flaws and uncertainties. As a result, EFSA´s risk assessment of the stacked Maize is based on pyramiding flaws and uncertainties caused by its previous opinions on the Parental Plants.

Accordingly, the Commission should not have granted the authorisation of the Maize in this case. In particular, it has failed to comply with its obligations under: (a) Articles 4(1)(a) and 16(1)(a) to ensure that that food and feed that would have an adverse effect on human health, animal health, or the environment “must not” be placed on the Union market; (b) Articles 7(1) and 19(1) GM Regulation to take into account not only the EFSA Opinion but also “any relevant provisions of [Union] law”, including the provisions of Union law that require Union institutions to comply with their own guidance and (c) Article 168 TFEU and reflected in Recital (2) GM Regulation to ensure a high level of protection for human health.

Furthermore, so far as relevant, the Commission has unlawfully defeated a legitimate expectation that EFSA would act in accordance with its own guidance in advising the Commission on applications for authorisation under the GM Regulation, and that the Commission would ensure such compliance by EFSA before reaching its authorisation decisions.

Ground B: Failure to investigate real toxicity

Introduction

The potentially toxic effects of a particular genetically modified food/feed are one of the primary matters requiring investigation by EFSA in determining whether it will have adverse effects on human health, animal health or the environment, contrary to Articles 4(1)(a) and 16(1)(a) GM Regulation.

In the case of the Maize, EFSA did not present a risk assessment as legally required and sufficiently based on scientific findings: No feeding studies for investigating health effects were conducted with the stacked Maize, no acute, subchronic, long term and multigenerational study was requested. The only feeding study that was performed with the Maize was a feeding study with broiler to gain nutritional data – this is unsuitable for the detailed investigation of potential health effects (for flaws of the nutritional study see also Bauer-Panskus & Then, 2011).

No tests were performed to determine potential combinatorial or accumulated effects of the toxins, nor of any other factors such as other toxic compounds, bacteria, plant enzymes (trypsin inhibitors) and especially the residues from the complementary herbicide. No investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals.

All in all, EFSA´s risk assessment of the Maize does not fulfil the legal requirements of current EU regulations.

Detailed reasoning

B1: False conclusion stemming from the comparative approach

EFSA concluded that there was no need to carry out any further animal safety studies of the whole GM food/feed, for three reasons:

- According to the previous opinions of EFSA, no adverse effects had been observed in the 90-day rat feeding studies involving the Parental Plants;
- The Maize had been found to be substantially equivalent to its conventional counterpart; and

- EFSA considers it unlikely that interactions between these proteins would occur that would raise any safety concern.

The first reason is a matter of further controversial debate. There are scientific publications on maize 1507 (Dona & Arvanitoyannis, 2009) and several statements on the results of the feeding studies from Parental Plants by the experts of Member States that show there is still a substantial level of uncertainty: Rats fed with maize 59122 showed some significant differences in blood parameters compared to their control groups. Rats fed with MON89034 showed signs that their kidney function might be impaired .

The second of these reasons is flawed, for reasons given in Ground A above: On the basis of existing data, substantial equivalence cannot be concluded for the Maize. As already shown in the complaint, EFSA was wrong even according to its own Guidance not to request further investigations with the whole food and feed.

Additionally, the third reason of EFSA´s is substantially flawed, as the following paragraphs show.

B2: Inadequate method to assess the expression of the Bt Toxin

One of the prerequisites of risk assessment is sufficient data on the expression of the newly expressed proteins. The protocol used for measuring the Bt toxins is known to be highly influential on the outcome. Slight differences in the method/ protocol used in measuring can lead to enormous differences in the results. There are, however, no standardised protocols to measure the content of Bt toxins reliably so that the results can be compared to results from different laboratories (Székács et al., 2011). In the case of Bt toxins there are also no standardised protocols to measure the content of Bt toxins in a way that the results can be reproduced by other laboratories. (Székács et al., 2011). No reliably validated and reproducible method has been made available to independent laboratories, with the result that major uncertainties remain about the exact content of Bt toxin in the Maize.

Stilwell & Silvanovich (2007) measured the expression rate of Cry1A.105, Cry2Ab2, Cry3Bb1 and EPSPS at the Monsanto laboratories (MSL0021070). Phillips (2008)

investigated the expression rate of Cry1F, Cry34Ab1, Cry35Ab1 and PAT at the Dow AgroSciences laboratories (Sub-Report ID: 61026.05).

The teams both worked with ELISA, but appear to have used different protocols. The protocols used by Dow AgroSciences have not been published, the company refers to its own unpublished reports. Some of the protocols used by Dow AgroSciences are even characterised as “under development” (Phillips, 2008, page 22). Monsanto published more details about their methods but they did not involve any external laboratory to evaluate their methods. There was no attempt to compare the results of one laboratory with another, none of the samples were analysed in the laboratories. Thus, it is not possible to decide if the protocols used by the different companies render similar results when applied to the same material. The results were even expressed on a different basis: The Monsanto labs provided data on dry tissue weight (dwt) and on fresh tissue weight (fwt). Dow AgrowSciences only provided data on a dry tissue weight basis. Samples were taken from leaves (over season leaf, OSL), roots (over season root, OSR), whole plants (over season whole plant, OSWP), from pollen and grain.

Since the outcome of measuring Bt content in genetically engineered plants is highly dependent on the protocols used for measuring (Székács et al., 2011), no sufficiently reliable conclusions can be drawn from the data as presented by the Applicants. This means that all further assumptions on exposure of the food & feed chain are suffering from basic flaws.

B3: Insufficient data to assess true range of variations

The data presented by the companies showed significant differences between the stacked events and the parental lines (for example in Cry1Ab.105) that EFSA considered “comparable” although there was no definition of what this meant. Especially the PAT enzyme showed a higher expression rate in SmartStax. This finding was explained away with the doubling of the gene construct in the stacked events.

By mixing the raw data of the particular Bt proteins from single events with those from stacked events (see Then, 2011b) a much broader range of variation (within the different parts of the plants) emerges than is summarized by EFSA and the applicants (see table 1 and figure 2). In several cases, the maximum Bt content exceeds the

minimum Bt content by more than tenfold, but there were also results found where the data showed a twenty fold or an even higher range of variation. Adding up the Bt content of the different parts of the plant shows that the overall Bt content in the stacked events is much higher and should not be considered just as “comparable” with the Bt content in the single events.

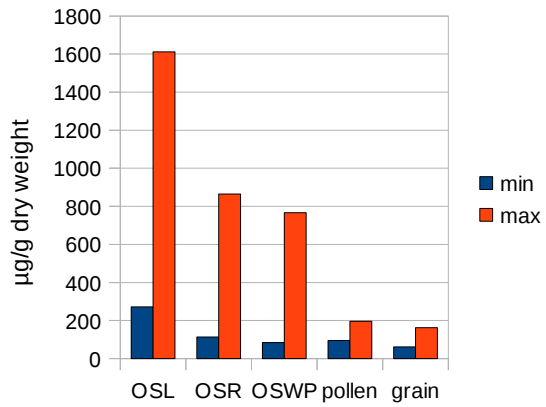
No data is given concerning the life cycle of the Bt protein such as degradation in soil and water, persistence during the passage through the gut of the animals, and to which extent the environment is exposed to Bt proteins through manure.

Table 1 Overview: Ranges of the Bt toxin content in different parts of the plant, using the data from parental lines as well as from SmartStax (µg/g dry weight tissue)

	OSL	OSR	OSWP	Pollen	Grain
Cry1A.105	39 - 210	11 – 240	3,8 – 86	5,1 – 21	1,7 – 4,9
Cry1F	9,84 – 34,3	3,19 – 14,7	2,71 – 15,8	14,3 - 32,2	2,12 – 7,43
Cry2Ab2	60 - 350	4 – 120	3,6 – 130	0,18 – 2,3	2,7 – 7,5
Cry3Bb1	53 – 580	23 – 260	6,9 – 220	7,5 – 24	10 – 38
Cry34Ab1	71,5 – 279	65 – 150	64,1 – 233	68 – 117	43,6 – 102
Cry35Ab2	38,5 – 158	13,8 – 80,5	2,54 – 82,3	–	1,24 – 2,65
Overall content	271,84 – 1611,30	113,61- 865,20	83,65 - 767,1	95,08 – 196,50	61,36 – 162,48

OSL: over season leaf, OSR: over season root, OSWP: over season whole plant

Fig. 2: Overview of ranges of the Bt toxin content in different parts of the plant, using data from parental lines as well as from SmartStax (µg/g dry weight tissue)



OSL: over season leaf, OSR: over season root, OSWP: over season whole plant

Further, it is not clear how these plants and the expression rate of the newly introduced proteins will be influenced by more extreme weather conditions relevant in times of climate change such as drought. The data provided by industry are known to be unreliable on the true range of variation of Bt toxins in the plants, as for example shown by Nguyen and Jehle (2007). Several investigations show that genetically engineered plants can exhibit unexpected reactions under stress conditions. This can also impact the Bt content in the plants (Then & Lorch, 2008). Huge variations in Bt content have, for instance, been found in genetically engineered cotton plants (Adamczyk et al., 2008). But there has been no systematic investigation to determine the Bt content in the Maize under varying environmental conditions. As a result, the true range of variation of Bt content in the plants is unknown.

The need for further investigations can be shown by expression data from field trials in the U.S. (Gao 2006) and from greenhouse trials in India (Monsanto 2008) that were submitted to the Indian authorities and concern the toxin expression of Cry1a.105 (see Then, 2013). By comparison, the data from India and from the U.S. show huge differences. For example in the U.S. the mean value for Cry1A.105 in leaf is given as 72-520 µg/g (dry weight), the data from India indicates 22-164 µg/g (dry weight).

A comparison with the data from field trials in Argentina (Hartman et al., 2006) shows further substantial differences compared to the data of the U.S. and India. Data from the U.S. and Argentina also show substantial differences for Bt content in grain: For example the range of data on Cry1A.105 from the U.S. (4,7-7,0 µg/g, dry weight) and Argentina (1,9-3,2 µg/g, dry weight) do not even overlap.

Table 2: Comparison of Cry1A.105 and Cry2Ab2 expression data from MON89034 in overseason leaf (OSL) form trials in the US and Argentina and in whorl leaf from trials in India dry weight, µg/g. Source: Data from Monsanto (Gao, 2006; Hartmann et al., 2006; Monsanto 2008).

	U.S.A 2005		Argentina 2004		India 2008	
	Cry1A.105	Cry2Ab2	Cry1A.105	Cry2Ab2	Cry1A.105	Cry2Ab2
Range	27-850	48-270	60-350	64-470	?	?
Mean	72-520	130-180	160-260	120-270	22-164	51-360
Max Bt content per varieties tested	1120		820		??	

An overall comparison of the data made available in India on Cry1A.105 and in the EU show further variabilities and / or inconsistencies of the expression data. Taken together, there is a substantive level of uncertainty of the true range of expression levels of the Bt proteins in the plants. Several more investigations are needed to get sufficient data concerning the expression levels in different varieties and under various environmental conditions since this is known to impact the Bt content in the plants (Then & Lorch, 2008), further fully evaluated and truly reliable methods for measuring have to be established (see (Székács et al., 2011). Without such data, the true level of exposure on the level of consumption cannot be assessed.

Viewed from this perspective, much more detailed investigations would be necessary. Only investigations under defined environmental conditions can reveal which impact factors are mostly relevant for the content of toxins within the plant´s tissue. Functional genetic stability has to be shown under defined stress conditions and not just in reactions to occasional environmental conditions from only one year as presented by Monsanto (Rosenbaum, 2008).

Furthermore, in comparison to the parental plants the stacked Maize has a substantially higher content of Cry1A.105 in the grains. This effect indicates emerging genomic effects in the stacked Maize that cannot be predicted from the parental plants. Thus, these effects would have needed further investigation. These investigations were also requested by the experts of the Member States.

As a result, the exposure of Bt toxins within the food & feed chain cannot be determined. The assumptions presented by the applicants concerning exposure of livestock and humans are not based on data that are derived from sufficiently reliable methods. Further, the data presented do not show the true range of variations of the Bt toxins in the plants grown under various environmental conditions.

B4: Insufficient investigation of selectivity of the newly expressed toxins

The mode of action of Bt toxins is not fully understood. It is even a matter of controversial scientific debate (Pigott & Ellar, 2007). For example, Zhang et al (2006), Soberon et al (2009), Broderick et al (2009), Johnston & Crickmore (2009), Mason et

al., (2011) reach different conclusions as to the mode of action in target organisms. In addition, Frankenhuyzen (2009), shows that selectivity of Cry proteins is also a matter of huge uncertainty.

Instead of investigating these uncertainties and limits of knowledge, EFSA was happy to follow a simplistic approach to explain the mode of action suggested by the Applicants (Monsanto & Dow AgroSciences (2009) which does not represent the actual level of knowledge:

> "A review of the research characterizing the mechanism of action for Bt crystal proteins has been published by Schnepf et al. (1998) and De Maagd et al. (2001). Based on the accumulated knowledge of Bt Cry proteins, a generalized mode of action has been proposed and includes the following steps: ingestion of crystals by the insect, solubilization of the crystals in the insect midgut, proteolytic processing of the released Cry protein by digestive enzymes to activate the toxin, binding of the toxin to receptors on the surface of midgut epithelial cells of target organisms, formation of membrane ion channels or pores, and consequent disruption of cellular homeostasis (English, 1992). Electrolyte imbalance and pH changes render the gut paralyzed, which causes the insect to stop eating and die (Sacchi et al., 1986). These high affinity Cry-specific receptors have not been detected in intestinal tissues of mammalian species, such as mouse, rat, monkey, or human (Hofmann et al., 1988a; Hofmann et al., 1988b). This explains, in part, observations that mammals are not adversely affected by Cry proteins even when administered at oral doses millions of times higher than target insects would ever encounter (Betz et al., 2000)."

EFSA should have considered the true complexity and real range of uncertainties when it came to trying to understand the mode of action of Bt toxins. For example, there are several other publications calling into question the role of specific receptors in general (Crickmore, 2005; Zhang et al., 2006; see also Pigeott & Ellar, 2007). The gaps in the current understanding of the mode of action of Bt toxins are very relevant for the risk assessment of non-target organisms as pointed out by Lövei et al. (2009):

> "Both the Cry1Ab and Cry1Ac toxins are members of the large family of three-domain Cry toxins, meaning that they share homologous aminoacid sequences in three regions, which are implicated in receptor-specific binding and toxin specificity. Four distinct classes of receptors have been identified: cadherin-like

> proteins, aminopeptidases, alkaline phosphatases and certain glycolipids, and it is clear that the understanding of receptor and toxin specificity is far from complete. Even well-studied Cry toxins have an incompletely determined range of toxicity. Although it is clear that Cry1Ab and Cry1Ac are toxic mainly to Lepidopteran species, it is not yet possible to infer toxin specificity from toxin structure, and thus toxin specificity of a Cry toxin is a scientific hypothesis, not a scientific fact. Moreover, truncation and mutagenesis of synthetic toxins might alter their range of toxicity compared with the native toxins.“

These uncertainties in the understanding of the toxicity of Bt toxins create major uncertainties in regard to risks for human health. As far as potential effects on health are concerned, Thomas and Ellar (1983), Shimada et al. (2003) Huffmann et al. (2004), Ito et al. (2004), Mesnage et al. (2012) and Bondzio et al. (2013) show that toxins belonging to the Cry-classification might have effects on the health of mammals. Some Cry toxins are also known to bind to epithelial cells in the intestine of mice (Vázquez-Padrón et al., 1999, Vásquez-Padrón et al., 2000). Recently the GRACE project discussed the mode of action of Bt toxins and identified it as a relevant and controversial issue that needs further investigation (GRACE, 2013). Since the exact mode of action is not known, the number of uncertainties is too high to allow the use of plants that produce up to six Bt toxins in food and feed.

Since these questions were not investigated during the risk assessment of the Parental Plants, EFSA should not have set aside these questions for the risk assessment of the stacked Maize.

This is especially relevant for the synthetic toxin Cry1A.105. As Pardo Lopez et al. (2009) and Pigott et al. (2008) show, synthetically derived and modified Bt toxins can show much higher toxicity than native proteins. Even small changes in the structure of the proteins can cause huge changes in toxicity. In the case of Cry1A.105, there is indeed evidence that toxicity is enhanced and selectivity is decreased. As a result, the toxicity of Cry1A.105 can affect a wider range of non-target organisms than expected. This finding is also relevant for assessing the risks to human health. As described in Monsanto´s US patent application Patent 6,326,169, Polynucleotide compositions encoding Cry1Ac/Cry1F chimeric O-endotoxins, the toxicity is changed and enhanced in an unexpected way:

> “Another aspect of the invention further demonstrates the unexpected result that certain chimeric Cry1Ab/Cry1F proteins maintain not only the insecticidal characteristics of the parent delta -endotoxins, but also exhibit insecticidal activity which is not displayed by either the native Cry1Ab or Cry1F endotoxins.”

These findings on unexpected changes in the toxicity of the Bt protein, which were not forwarded to EFSA, underline the need for much more detailed investigation into the potential effects of Bt toxins not only on insects, but also on human health.

B5: Not assessing the interactivity of the Bt toxins

Not only is the mode of action of the Cry proteins not fully understood, EFSA also has no basis for assuming that there will be no relevant synergistic or accumulated effects. On the contrary, there are several publications that show that Bt proteins are highly likely to show synergies and interactions with other stressors and plant enzymes (for overview see Then, 2010).

For example, it is known that co-stressors such as cadmium and nematodes can cause toxicity of Cry toxins in slugs (Kramarz et al., 2007; Kramarz et al., 2009), which can be seen as important model organisms. Other combinatorial effects are known to enhance the toxicity of Bt toxins from investigations with pyrethroids (Khalique & Ahmed, 2005; Saleem et al., 1995), Azadirachtin, (Singh et al. 2007), Avidin (Zhu et al., 2005), Bacteria (Mason et al., 2011), Nosema (Reardon et al. 2004) and other Bt toxins (Sharma et al., 2010).

Since the Maize will contain residues from spraying with glyphosate formulations, the possible interaction between Bt toxins and co-stressors such as pesticides are highly relevant to the risk assessment of this product.

Other examples include the powerful effect that some plant enzymes that diminish the digestion of proteins (protease inhibitors) can have on the toxicity of Bt toxins, where toxicity has been found to increase up to 20 times even in the presence of very low levels of protease inhibitors (Zhang et al., 2000, Pardo Lopez et al., 2009). Maize plants have low level of these inhibitors (Shulmina et al, 1985; Monsanto & Dow AgroSciences, 2009) and their degradation depends on the method of heat processing.

Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of Cry toxins.

Even EFSA´s own Guidance (EFSA, 2007) requires these tests (see section 3.3.1):

> "An assessment of any potential for increased toxicity and/or allergenicity to humans and animals or for modified nutritional value due to the stacked events should be provided. These potential effects may arise from additive, synergistic or antagonistic effects of the gene products or by these produced metabolites and may be particularly relevant where the combined expression of the newly introduced genes has unexpected effects on biochemical pathways. This assessment will clearly require a case-by-case approach".

The only tests performed were on the combinatorial effects of the Bt toxins in pest insects (Levine et al., 2008a and b; McRae, 2008).

Some of the most apparent deficiencies of the investigations are:

- The studies were only conducted with target organisms. No specific tests related to risks for food and feed e.g. on mammalian cell systems were performed. Therefore, risk assessment of the impact on food and feed cannot be conducted based on these existing studies.
- Only the interaction between the Bt toxins was investigated. Potential synergies with EPSPS and PAT Proteins or with residues from herbicide spraying were left aside. Further, other relevant compounds that can trigger synergistic effects such as components from food or feed (such as proteinase inhibitors, see above) stressors, bacteria and pharmaceutical compositions (such as antibiotics) were completely ignored (for a list of some relevant factors see Then, 2010).

The tests were not performed in independent research facilities under the supervision of independent experts and institutions. There was no independent institution involved in quality control. The results were not published in peer- reviewed articles.

In addition, the findings from investigations carried out by Applicants raise severe doubts, since Tabashnik et al. (2013) showed synergistic effects in pest insects between synthetic forms of Cry1Ac (such as Cry1A.105) and Cry2Ab. Such effects in pest insects were excluded by the Applicants. Consequently, many more empirical

investigations are needed to investigate risks due to combinatorial effects of the proteins as expressed by the Maize. This issue is also relevant in the context of food and feed safety. Because investigations on synergistic health effects in humans and mammals are mostly missing, we can only extrapolate from the findings on insects.

B6: EFSA failed to assure pesticide assessment of the Bt Proteins inserted into the Maize

The Bt toxins produced in the plants were never assessed under the provisions of the pesticide authorisation 91/414 EEC. There are several important differences between the Cry toxin as produced in the plants and its use in traditional mixtures (for a general overview of these issues see Hilbeck & Schmid, 2006; Szecaks & Darvas, 2012). So far, the Bt toxin has only been used in traditional mixtures and in crystallized (inactivated) form. However, the Cry toxins in the plants are already solubilised (activated). Further, the Bt toxins are produced by the plants throughout the whole period of vegetation, while the traditional sprays are used in a targeted way. To be effective, it is likely the Bt toxins also have to be exposed in higher concentration in the plants than it is the case in the traditional mixtures: In the mixtures, additive and synergistic effects require only a low level of the single compound. In addition, the structure of the DNA sequences was changed during the process of transferring the DNA into the plants´ genome. This is not only relevant for the Cry1A.105 toxin (see above).

Without full authorisation of the Cry toxin (as produced in the plants) under pesticide Regulation, placing the Maize on the market clearly establishes double standards for the safety of pesticides within the EU. A much lower standard is applied under GMO regulation than under pesticide regulation.

Since these questions were not investigated during the risk assessment of the Parental Plants, EFSA should not have set aside these questions when it came to the risk assessment of the stacked Maize.

It should also be noted that in the Council Conclusions on Genetically Modified Organisms (GMOs) of the Council meeting of 4 December 2008, Member States demanded a revision of current EU regulations to close the loopholes between the pesticide regulation and the regulation of genetically engineered plants. This demand

is in no way confined to the use of the genetically engineered plants in agriculture but includes all relevant products, which might be authorised on the market[19]:

> "(...) the mandate includes examination of the criteria and requirements for assessing all GMPs, including GMPs that produce active substances covered by directive 91/414/EEC and herbicide-tolerant GMPs with a view to reviewing them if necessary; (…) RECALLS that the use of plant protection products implies authorisations at national level and EMPHASISES THE NEED for competent authorities involved with the implementation of Directive 2001/18/EC and of Council Directive 91/414/EEC concerning the placing of plant protection products on the market, within the Commission and at national level, to co-ordinate their action as far as possible;"

B7: Failure to assess risks from residues of spraying

Since the residues from complementary herbicides are inevitable constituents of plant composition leading to a specific pattern of exposure of the food chain, they cannot be ignored during the risk assessment of genetically engineered plants. The risks of these residues have not been fully investigated under pesticide regulation because specific patterns of exposure, specific metabolites and combinatorial effects relevant for genetically engineered plants are not taken into account under pesticide regulation:

- Commercial large-scale cultivation of these plants means there is strong selective pressure on weeds to develop resistance to these herbicides, this increases the amount of sprayed herbicides and the load of residues. The complementary herbicides are likely to be sprayed several times during crop growth, thus the pattern of usage and the level of residues can be significantly higher compared to non-resistant crop plants.
- Herbicide tolerant plants are meant to survive the application of the complementary herbicide while most other plants will be killed after short time. Thus, residues of glyphosate/glufosinsate, its metabolites and the additives will accumulate and interact in the plants that survive due to their additional genetic information.
- In stacked events, a combination of specific plant constituents is fixed in the genetically engineered plants. The combination of the residues from spraying and of insecticidal proteins (as is the case with the Maize) causes a unique and

[19] http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressdata/en/envir/104509.pdf

unavoidable exposure of the feed and food chain to very specific residues. Possible interactions have to be investigated in detail.

The impacts on health from permanent exposure to specific herbicides due to consumption of plants that are engineered to be resistant to herbicides can be assumed to be different to those from case to case applications in the fields. Permanent exposure to residues from spraying with these herbicides can, even in small concentrations, affect hormone metabolism as discussed for glyphosate (see for example Gasnier et al., 2009; Thongprakaisang et al., 2013). Constant exposure to herbicide residues, such as glyphosate, can also have an indirect impact on health, for example, it might cause changes in the intestinal flora of humans, thereby increasing the risk of developing illnesses. Glyphosate is effective against certain bacteria, such as E. coli (Forlani et al., 1997; Carlisle & Trevors, 1986), and can in high concentrations damage the intestinal flora of cattle (Reuter et al., 2007). Even low doses impact the microbial flora of poultry and there is a reduction in the number of beneficial microbes (Shebata et al., 2012). Furthermore, there are substantial concerns about health associated with the use of the herbicide glufosinate. Glufosinate will be removed from the EU market by 2017[20] . Therefore allowing the import of products such as the Maize that are regularly sprayed with glufosinate as the complementary herbicide is highly questionable.

In conclusion, the residues and their combinations are inevitable constituents of the plant composition leading to a specific pattern of exposure of the food chain. A recent legal dossier, commissioned by Testbiotech (Krämer, 2012[21]) also shows that from a legal point of view, the residues from spraying with complementary herbicides have to be taken into account in the risk assessment of genetically engineered plants. A basic prerequisite for risk assessment in this context is reliable data on residue loads from spraying with glyphosate and glufosinate formulations. The amount of these residues depends on the specific agronomic management used in the cultivation of the herbicide resistant plants. However, reliable data covering the actual range of residue load in the plants are not available (Kleter et al., 2011). Without such data, there can be no sound risk assessment of this product.

[20] Regulation of the European Parliament and of the Council on the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC http://www.europarl.europa.eu/oeil/file.jsp?id=5372312

[21] Attached

It should also be acknowledged that in the Council Conclusions on Genetically Modified Organisms (GMOs) of the Council meeting of 4 December 2008, the Member States demanded a revision of current EU regulations to close the loopholes between the pesticide regulation and the regulation on genetically engineered plants. This demand is in no way confined to the use of genetically engineered plants in agriculture, but includes all relevant products, which might be authorised on the market[22].

B8: Not assessing interactivity with residues from spraying

Seen from the perspective of this technical background, it is evident that glyphosate / glufosinate and the residues from spraying glyphosate / glufosinate on the Maize have to be considered as a potent co-stressor. Its combinatorial impact needs to be assessed during risk assessment. The impact on cells and organisms exposed to several stressors in parallel is of great importance. As, for example, Kramarz (2007) shows, this can be relevant for the impact that Bt toxins can have on organisms that are normally not susceptible to Bt toxins. EFSA has never addressed this question surrounding the potential effects on health from the Maize.

The fact that no such investigations were requested has to be considered as a substantial and crucial failure of EFSA´s risk assessment, which affects the reliability of the opinion in general.

B9: Wrong approach to assess toxicity

The Applicants provided only acute toxicity studies with single toxins that showed no toxicity in mammals. The Applicants concluded their findings (Monsanto & Dow AgroSciences, 2009) by stating:

> “This lack of toxicity was expected based on the absence of a toxic mechanism in mammals, the history of exposure and the rapid degradation of each protein in simulated human gastric fluids.”

This reasoning is manifestly wrong. (1) As shown in this complaint, the lack of specific receptors is not reason enough to assume that Bt toxins do not have a negative impact on health. (2) A history of exposure cannot be assumed since at least one of

[22] http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressdata/en/envir/104509.pdf

the toxins is derived synthetically, and (3) the rapid degradation has not been observed under realistic conditions (see below, point C). However, this is not the only criticism that should have been raised by EFSA (but was not). There is a further very fundamental objection to the reasoning of the Applicants. While they provided a high dosage acute toxicity study with Cry proteins, investigations should have considered long-term exposure in food and feed with the whole plant, containing the Bt toxins, residues from spraying and compounds such as trypsin inhibitors which can increase the toxicity of Bt toxins substantially (Zhang et al., 2000, Pardo Lopez et al., 2009). This pattern of exposure (with a much higher content of Bt toxins than in the Parental Plants) which is unique for the Maize is the one which is relevant if it is introduced in the food and feed chain and therefore needs to be assessed. There was no such investigation.

The only data made available to assess exposure are some estimates of daily intake of the Bt toxins (Monsanto & Dow AgroSciences, 2009). These estimates are not sufficient since the rate of Bt expression was not determined in a reliable way (see above). Even if the estimates were correct, this would not mean that empirical investigations into the long-term combinatorial impact are not needed. As EFSA Guidance (2006) requires:

> "In the case of complex genetic modifications involving the transfer of multiple genes, the potential risk(s) of possible interactions between the express proteins new metabolites and original plant constituents should be assessed. The outcome of the molecular analysis and knowledge of the mode of action of the newly expressed proteins may provide indications for possible synergistic interactions, as well as information on the response to combined administration of proteins to target organisms and regarding effects on the activity of target enzymes. Generally, feeding trials with this type of GM foods/feeds is requested in order to assess the impact of consumption on human and animal health. On a case-by-case basis this is also applicable to food and feeds derived from GM plants obtained through traditional breeding of parental GM lines (combined events)."

B10: Further relevant issues: transfer of biologically active compounds

Zhang et al (2011) found that RNA from food plants can enter the bloodstream after ingestion and interfere with cell regulation in mammals. The amount and quality of artificial RNA in the Maize has never been determined. A further recent study raises substantial doubts about the suitability of animal feeding trials to assess the transfer of DNA from food plants to humans. Spisak et al. (2013) presented some unexpected findings showing there is some likelihood that functional DNA enters the human bloodstream via ingestion. Their investigation revealed that the rate of transfer was dependent on the state of health of the individual. We are not aware of any study that has investigated the risk of DNA from genetically engineered plants entering the bloodstream in humans. Since there seems to be no reliable knowledge of the transfer rate of artificial DNA from genetically engineered plants to the human bloodstream, there needs to be some investigation carried out with the Maize.

In the Maize there is not only synthetic DNA for the production of Bt toxins but also a several copies of technically derived DNA such as the 35 S CMV promotor which was used in the Parental Plants and now sums up to several copies in each plant cell. As shown by Kitagima et al. (2013), a high number of copies of this promotor DNA might be able to initiate transcription in fish cells. It is a matter for further investigation to find out whether these DNA sequences can be taken up from the human gut in a way that makes them biologically relevant.

As the experts from Member States (Austria) explain, the pyramiding effect of similar DNA sequences might also render genetic instability in the plants (EFSA 2010b):

> Since the inserts introduced into GM maize MON88017 x MON89034 x 1507 x 59122 from different parental events contain a number of similar genetic elements (among others sequences from the 35S-promoter in all inserts, and sequences from the ubiquitin promoter, the rac intron, the nos-terminator, the 35S-terminator and the pat gene in two inserts each) homologous recombination events between the inserts cannot be ruled out. The notifier, thus, is requested to assess the stability of the inserts and the probability that the structure of the inserts is retained

But EFSA did not investigate the impact of these accumulations of specific DNA sequences in regard to genetic instability nor in regard to transfer of biologically active substances at the stage of consumption.

Some conclusions on Ground B:

The Commission's decision and the opinion of EFSA are flawed. The Commission erred manifestly by failing to require a proper risk assessment that was of the "highest possible standard" and, in addition, failed to include toxicity tests as provided for by the EFSA Guidance.

Further, the Commission failed to require proper risk assessment in terms of long-term impact and combinatorial effects. Therefore, the Commission has in this case granted market authorisation without ensuring that:

- the authorisation was issued on the basis of a risk assessment of the "highest possible standard": Recital (9) GM Regulation.

- EFSA had complied with its duties, under Articles 6(3)(a) /18(3)(a) GM Regulation, to ensure that the Applicants had provided to it, and to EFSA, "appropriate" information and data to support the comparative analysis submitted with the application under Articles 5(3)(f) / 17(3)(f) GM Regulation.

- since these flaws in the Commission's decision and the opinion of EFSA have also been observed in the Parental Plants, the conclusion that the Maize is safe conflates a whole series of substantial flaws and uncertainties. Therefore, the Commission's decision and the opinion of EFSA are based on pyramiding flaws and uncertainties from previous opinions and decisions on the Parental Plants.

The Commission has also failed to act in accordance with its duties:

- under Articles 4(1)(a) and 16(1)(a) GM Regulation to ensure that food and feed that would have an adverse effect on human health, animal health, or the environment "must not" be placed on the Union market;

- under Articles 7(1) and 19(1) GM Regulation to take into account not only the EFSA Opinion but also "any relevant provisions of [Union] law", including the provisions of Union law that require Union institutions to comply with their own guidance;

- under Article 168 TFEU and reflected in Recital (2) GM Regulation to ensure a high level of protection for human health.

Furthermore, so far as relevant, the Commission has unlawfully defeated a legitimate expectation that EFSA would act in accordance with its own guidance in advising the Commission on applications for authorisation under the GM Regulation, and that the Commission would ensure such compliance by EFSA before reaching its authorisation decisions.

Ground C: Insufficient assessment of immunological risks

Introduction

The insecticidal proteins as produced in the Maize are known not only to be toxic, but also to cause immune reactions in humans. Bt toxins such as Cry1Ac (which is similar to Cry1A.105) can invoke and boost immune reactions (Esquivel-Pérez and Moreno-Fierros, 2005; Moreno-Fierros et al., 2003; Vásquez et al., 1999; Vásquez-Padrón et al., 1999; Vásquez et al., 2000; Verdin-Terán al. 2009).

Experts from Member States raised concerns during the risk assessment of adjuvant effects, which means that, for example, the immune reaction to allergens is boosted (EFSA 2010b). Experts from Belgium wrote that:

> "It must be emphasized that Cry1A.105 displays high aminoacid sequence identity with Cry1Ac and that Cry1Ac has been proposed as an adjuvant for vaccines (Vasquez et al, 1999, Vasquez-Padron et al. 1999, Moreno-Fieros et al. 2003, Esquivel-Perez et al. 2005), which means that this protein is able to enhance the immune responses against antigens that are co-administered, which is not uncommon for a bacterial protein. Other proteins of the Cry family are also suspected of showing adjuvant properties (Calderon et al. 2007). Therefore, doubt may arise about Cry2Ab2, Cry1F, Cry3Bb1 and Cry34/35 Ab1. The consequence of the presence of such immuno-stimulant in a plant destined to human consumption is not known. Particularly the adjuvant effect via intestinal route is poorly documented. The single concentration of Cry1A.105 in maize grains is compatible with the possibility of an adjuvant effect in the context of normal maize grain consumption (but the concentration after processing of the maize or after cooking is not known). If all Cry proteins also have such adjuvant capacity, the adjuvant effect may be multiplied in MON89034x1507xMON88017x59122 maize. It is not known whether the presence of these Cry proteins in maize may elicit sensitization against the other maize proteins upon ingestion (and which type of sensitization?)."

Belgium also is concerned about allergens being present in the maize that were not taken into account by EFSA (EFSA 2010b):

> "Indeed, some maize allergens have been described in the literature (Pasini et al. 2002, Pastorello et al. 2003, Weichel et al. 2006, Fasoli et al. 2009) and,

recently, patients showed maize-induced anaphylaxis in double-blind placebo-controlled food challenge, with reactions to as little as 100 mg of maize (Scibilia et al. 2008).”

Experts from Norway raised similar concerns (EFSA 2010b):

> “As the different Cry proteins are closely related, and in view of the experimental studies in mice, the GMO Panel finds that the likelihood of an increase in allergenic activity due to Cry1A.105, Cry1F, Cry2Ab2, Cry3Bb1, Cry34Ab1 and Cry35Ab1 proteins in food and feed from maize MON89034 x 1507 x MON88017 x 59122 cannot be excluded. Thus, the Panel's view is that as the adjuvant effect of Cry1A.105, Cry1F, Cry2Ab2, Cry3Bb1, Cry34Ab1 and Cry35Ab1 with reasonable certainty cannot be excluded, the applicant in relation to a possible adjuvant effect of Cry1A.105, Cry1F, Cry2Ab2, Cry3Bb1, Cry34Ab1 and Cry35Ab1 must comment upon the mouse studies showing humoral antibody response of Cry1A proteins. Further, although Cry1A.105, Cry1F, Cry2Ab2, Cry3Bb1, Cry34Ab1 and Cry35Ab1 proteins is rapidly degraded in gastric fluid after oral uptake, there is also the possibility that the protein can enter the respiratory tract after exposure to e.g. mill dust. Finally, rapid degradation is no absolute guarantee against allergenicity or adjuvanticity.”

EFSA (2010b) rejected these concerns by following reasoning:

> “The EFSA GMO Panel is of the opinion that the adjuvant effect of Cry proteins, observed after high dosage intragastric or intranasal administration will not raise any concerns regarding allergenicity caused by maize consumption or contact. Furthermore, maize is not a common allergenic food, and only a rare cause of occupational allergy may occur. (…)
>
> The EFSA GMO Panel has considered the “weight of evidence” regarding potential allergenicity of MON89034 x 1507 x MON88017 x 59122 and its transgenic proteins (…). This weight of evidence also includes, besides the outcomes of the updated bioinformatics-supported comparisons and the issues previously considered in the evaluations of the single parental events (MON89034, 1507, MON88017, 59122), including the history of allergenicity, if any, of the sources of the transgenic proteins and the in vitro resistance of the transgenic proteins towards proteolytic enzymes. Also the potential unintended

change in intrinsic allergenicity of the host maize has been considered in these opinions.

The EFSA GMO Panel is of the opinion that discussion on this issue should be closed. Cry proteins have been already assessed by the GMO Panel. In previous opinions, the EFSA GMO Panel assessed the allergenicity of Cry proteins and the allergenicity of the whole GM plant (i.e. 59122 maize), and took into consideration the potential adjuvanticity of Cry proteins that is mentioned in the comment.

The EFSA GMO Panel confirms its previous opinion and still considers that since maize is not a common allergenic food, even if the presence of a newly expressed Cry protein might enhance an immune response to endogenous maize protein(s), it is very unlikely that this would modify the allergenicity of the whole GM crop."

This reasoning is flawed for several reasons:

- EFSA overlooked several publications that show immune reaction to Bt-expressing plants.
- EFSA overlooked that digestion tests used to test the allergenicity were not reliable.
- EFSA did not take into account permanent intake of adjuvant proteins via food plants and its combinatorial effects to other food components such as allergens from soybeans.
- EFSA did not take into account risks for individuals with impaired immune-response.

C1 EFSA overlooked crucial publications

EFSA overlooked that there are already several publications showing that Bt toxins as produced in the plants can indeed trigger immune system reactions which can be interpreted as adjuvant effect or more generally as non-IgE-mediated immune adverse reactions. The investigations examined fish (for example Sagstad et al., 2007), pigs (Walsh et al., 2011, Carman et al., 2013), mice (Finamore et al., 2008, Adel-Patient et al., 2011), and rats (Kroghsbo et al., 2008, Gallagher 2010). Despite these findings,

EFSA did not request immunological studies to assess the risks for the immune system in detail, but instead simply proposed to close down the debate.

These observed effects are likely to be dependent on the dosage of Bt toxins. The Maize has a much higher concentration of Bt toxins than other plants such as the Parental Plants which were tested in feeding studies. Further, the concentration of Bt toxins in the plants varies substantially. It is evident, that Bt toxins can survive digestion to a much higher degree than has been assumed so far (see below). Consequently, there is substantiated concern that the plants can have adverse effects on health.

Meanwhile it appears that EFSA has reconsidered its previous suggestion of closing down the debate. In December 2013, a report from University of Manchester was published which was commissioned by EFSA (Mills et al., 2013a). This report is on an investigation into the risks to health from “non-IgE-mediated immune adverse reactions to foods” which are relevant for adjuvant effects as discussed. It shows that these risks are relevant but have so far not been considered by EFSA. These findings alone should be encouragement enough for the Commission to withdraw its decision.

C2 False assumption on the digestibility of Cry proteins

As mentioned, potential allergenicity in the Parental Plants was assessed by applying an in vitro digestion assay. As a result, the Cry protein is thought to be degraded quickly in the gastrointestinal tract. However, Chowdhury et al. (2003) as well as Walsh et al. (2011) have found that Cry1A proteins can frequently and successfully be found in the colon of pigs. Thus, the Cry1A proteins can show much higher stability in monogastric species than predicted by current in vitro digestion experiments. These findings should have triggered much more detailed risk assessment by EFSA when assessing the Parental Plants. This issue is even more relevant for the Maize because it contains a much higher content of the Cry protein than the Parental Plants.

Since Bt toxins are not degraded quickly in the gut and can persist in large amounts during digestion, there is enough time during digestion for interaction between various food compounds. If, for example, the stacked Maize is mixed with other components in food and feed, the Bt proteins could trigger immune reactions to other compounds such as allergens from soybeans.

The fact that Bt proteins can survive much longer in the gut than expected is also relevant for assessing its toxicity which might be enhanced further by low dosages of trypsin inhibitors (Zhang et al., 2000, Pardo Lopez et al., 2009). As shown by some publications, Bt toxins can bind to epithelial cells in the intestine of mice (Vázquez-Padrón et al., 1999; Vásquez-Padrón et al., 2000).

Meanwhile EFSA has published a report from University of Manchester confirming that in the vitro test used to date is not likely to provide reliable results (Mills et al 2013b). These findings should be further grounds for the Commission to withdraw its decision.

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C3 Insufficient testing of allergic reactions

As noted above, EFSA Guidance (2007) states that:

> "An assessment of any potential for increased toxicity and/or allergenicity to humans and animals or for modified nutritional value due to the stacked events should be provided. These potential effects may arise from additive, synergistic or antagonistic effects of the gene products or by these produced metabolites and may be particularly relevant where the combined expression of the newly introduced genes has unexpected effects on biochemical pathways."

In consequence, EFSA should have at least requested further testing for the stacked Maize. This should have been done not least for the following reasons:

- uncertainties remain from risk assessment of the Parental Plants
- the content of Bt toxins is much higher in the stacked Maize
- combinatorial effects in the stacked Maize can also cause unpredictable reactions of the immune system.

These points are also supported by statements made by experts from Member States as quoted in the introduction of Point C.

C4 Missing investigations on the impact on infants and the elderly

EFSA is also aware that specific investigations are needed to exclude risks for children and elderly people. EFSA (2010) expresses the need for more detailed investigations in section 1.10.1:

> "The specific risk of potential allergenicity of GM products in infants as well as individuals with impaired digestive functions (e.g. elderlies, or individuals on antacid medications) should be considered, taking into account the different digestive physiology and sensitivity towards allergens in this subpopulation." (page 46)

However, these specific risks for infants and other relevant groups were left aside during EFSA risk assessment, also disregarding relevant publications that show specific immune reactions in infant mice to Bt plants (Finamore et al., 2008).

Some conclusions on Ground 4

The assessment of risks for the immune system as performed by EFSA does not give sufficient weight to the precautionary principle. It does not adhere to the necessary scientific standards as requested by its own Guidance. For example specific risk assessment for allergenic risk to infants was left aside completely.

Since these flaws in the opinion of EFSA can also be observed in the Parental Plants, the conclusion that the Maize is safe conflates a whole series of substantial flaws and uncertainties. As a result, the opinion of EFSA is based on pyramiding flaws and uncertainties from previous opinions on the Parental Plants.

In conclusion, the Commission has failed to perform its duties and obligations under GM Regulation and/or the general principles of EU law as set out above in relation to Ground B.

Since there are new publications available showing the need to carry out much more thorough testing for risks to the immune system (Mills et al., 2013 a and b) and because EFSA has not assessed relevant publications showing immune reactions to Bt plants in animal feeding studies, the Commission should be encouraged to withdraw its decision.

Ground D: Flaws in the substance of the EU Commission decision

D1: Failure to request appropriate case specific monitoring of health effects

In its decision to give market authorisation to the Maize, the Commission made a negative decision on the monitoring plan for food consumption (Annex at (i):

> "Post-market monitoring requirements for the use of the food for human consumption: Not required."

However, as a recent legal dossier compiled by Professor Ludwig Krämer and commissioned by Testbiotech shows, the decision not to monitor any health effects violates the requirements of EU regulations. As concluded in the dossier (attached), by taking into account Directive 2001/18 as well as Regulation 1829/2003:

1. The present practice does not monitor the potential adverse effects on human health from genetically modified plants at the use and consumption stage and therefore does not comply with existing EU legislation.
2. Directive 2001/18 and Regulation 1829/2003 require both that potential adverse effects on human health of genetically modified plants are controlled during the use and consumption stage, including in those cases where such effects are unlikely to occur.
3. The objective of both Directive 2001/18 and Regulation 1829/2003 is to avoid any adverse effect on human health from genetically modified plants. Therefore, the risk assessment must make sure, in both cases, that the cumulative effect of herbicide residues on genetically modified plants during the use and consumption stage is controlled.
4. Wherever the monitoring plan for genetically modified plants does not include the monitoring of the cumulative effect of herbicide residues and genetically modified plants on human health during the use and consumption stage, the authorisation should be amended in order to provide for such monitoring.

Thus, the decision of the EU Commission must be withdrawn or supplemented by a monitoring plan that is organised in a way that allows the discovery of all potential adverse effects of the plant on human or animal health. It also has to include the examination of effects that are unlikely to occur and unforeseen effects. Such effects might occur by the consumption of the genetically modified plants alone or in combination with residues of herbicides, or other residues found in the genetically

modified plants themselves or which exist in other food or feed. Therefore, the effects from residues of the complementary herbicides must also be included.

So far, systematic data are not available on the impact on human and animal health from any of the genetically engineered plants that are authorised for commercialisation within the EU. Consequently, we have the same situation within the EU that the Commission described in a dossier compiled for the WTO in 2005 (European Communities, 2005):

> "As regards food safety, even if some GM products have been found to be safe and approved on a large scale..., the lack of general surveillance and consequently of any exposure data and assessment, means that there is no data whatsoever available on the consumption of these products – who has eaten what and when. Consequently, one can accept with a high degree of confidence that there is no acute toxicological risk posed by the relevant products, as this would probably not have gone undetected – even if one cannot rule out completely acute anaphylactic exceptional episodes. However, in the absence of exposure data in respect of chronic conditions that are common, such as allergy and cancer, there simply is no way of ascertaining whether the introduction of GM products has had any other effect on human health."

There is no doubt that the situation as described by the Commission (European Communities, 2005) is in contradiction with the requirements of current EU regulations.

Since the use of the Maize in food and feed is associated with specific health risks and many uncertainties, case specific monitoring has to be performed if the Maize is allowed on the market.

Additionally, under Articles 5(3)(k) and 17(3)(k) of the GM Regulation an application for marketing authorisation has to contain a proposal for post-marketing monitoring regarding the use of the food for human consumption and feed for animal consumption *"where appropriate".* Similarly, in giving a positive opinion in relation to an application EFSA has to include such post-marketing monitoring requirements *"where applicable"* (Articles 6(5)(e) and 18(5)(e) of the GM Regulation.

Accordingly:

α. Even on the basis of EFSA's flawed comparative and safety assessment of the Maize, it should have required Monsanto to carry out a post-marketing monitoring plan of the consumption of the Maize by humans and animals in light of the statistically significant differences identified between the Maize and its conventional counterpart; and/or

β. In light of the substantial flaws both as a matter of assessment and of law outlined above mean that EFSA's determination that no such monitoring is equally flawed.

Testbiotech therefore submits that the Commission has:

a. Failed to ensure that Monsanto was require to conduct appropriate post-market monitoring of consumption of the Maize, contrary to Article 5(3) of the GM Regulation; and/or

b. For the reasons given above in Grounds A to C, the Commission's Implementing Decision was manifestly flawed. The Commission's granting of the flawed authorisation means that no proper assessment of the need for post-market monitoring of human consumption has been completed.

D2 Lack of traceability disables general surveillance

Even if the monitoring plan as suggested by the Applicants in form of a general surveillance were accepted, the decision of the Commission would still be in conflict with EU regulations. As the experts from Member States (Austria) point out (EFSA 2010b):

> "Providing of four event specific detection methods for each parental line and an maize-specific reference PCR system is not satisfactory in this respect. Generally, a validated event specific detection method for the stacked event should be presented before deciding about the placing on the market of this product. Such an event specific detection method would be, for instance, a validated multiplex PCR where in a single assay all four targets are detected simultaneously. Furthermore, as long as no official (guidance) document on the interpretation of detection results, i.e. how to distinguish between a stacked

event and its respective single events, of the described method for stacked events is available, no approval for placing on the market of this product should be given. Even the notifier gives clear indication of this problem, "Given that MON89034×1507×MON88017×59122 would be indistinguishable from a combination of MON89034, 1507, MON88017 and 59122 in mixed consignments of maize products, certified reference materials of the parental products are considered appropriate for MON89034x1507×MON88017×59122" (see Part V).”

From these findings, it has to be assumed that the monitoring plan as suggested by the Applicants cannot be implemented (Monsanto & Dow AgroSciences, 2009:

> “Where information indicates the possibility of an unanticipated adverse effect, the authorisation holder will immediately investigate to determine and confirm whether a significant correlation between the effect and MON89034 × 1507 × MON88017 × 59122 can be established. If the investigation establishes that MON89034 × 1507 × MON88017 × 59122 was present when the adverse effect was identified, and confirms that MON89034 × 1507 × MON88017 × 59122 is the cause of the adverse effect, the authorisation holder will immediately inform the European Commission, as described.”

Currently the amount of maize import into the EU is subjected to huge variations from year to year, but in general it is increasing importance. But the basis of current knowledge and existing methods to detect the Maize it would not be possible to trace or identify the Maize under practical conditions in a mixture of other maize plants with the single events. Thus, it is not possible to determine and confirm whether there is a correlation between potentially observed effects and human health.

This is in conflict with EU regulations, which requires case specific monitoring through traceability and identification. In 2002, the Council adopted guidance notes “supplementing Annex VII”[23] requiring to

> “trace and identify any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOs as or in products after they have been placed on the market”.

[23] Decision 2002/811/EC of 3 October 2002 establishing guidance notes supplementing Annex VII to Directive 2001/18/EC, OJ 2002, L 280 p.27.

Conclusion

Since the failures and deficiencies in EFSA risk analysis and the decision making of the EU Commission have to be regarded as severe, we request the withdrawal of the decision of the EU Commission.

Art 10 of EU Regulation 1367/2006 allows NGOs active in the field of environmental protection to request re-examination of decisions of the EU Commission.

Based on this regulation, we request the re-examination of the risk analysis by EFSA and the EU Commission and until this re-examination has been completed, market authorisation for the Maize MON89034 × 1507 × MON88017 × 59122 (SmartStax). must be withdrawn.

The requested measure is necessary to reinstall the high level of protection for consumers and the environment as required by current EU regulations, and to prevent the erosion of EU standards safeguarding the implementation of the precautionary principle.

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Attachments:

- (A1) Legal dossier prepared by Professor Dr. Ludwig Krämer
- (A2) - (A6) Testbiotech report about the Maize and the opinion of EFSA published in 2011
- (A7) - (A10) Dossiers about the Parental Plants taken from Database of Testbiotech.