Request for internal review of the market authorisation for genetically engineered maize MON80934 x MON88017, Monsanto, Genuity VT Triple PRO Corn, under Article 10 of Regulation (EC) No. 1367/2006

Document prepared by Testbiotech e.V. (Germany) and GeneWatch UK

Content

Summary and legal background:

In June 2011 the Commission issued a market authorisation for maize MON80934xMON88017, based on an opinion from EFSA. (COMMISSION DECISION of 17 June 2011 authorising the placing on the market of products containing, consisting of, or produced from genetically modified maize MON 89034 × MON 88017 (MON-89Ø34-3xMON-88Ø1 7-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (notified under document C(2011) 4164), 2011/366/EU.

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

Based on this regulation, Testbiotech (Germany) and GeneWatch UK are requesting reexamination and withdrawal of market authorisation for MON80934xMON88017 for the following reasons:

- insufficient standards for risk assessment
- disregard of relevant scientific publications by EFSA
- missing scientific quality standards in the documents prepared by industry
- lack of risk management concerning legally required monitoring

Issues including the expression rate of the additional proteins, their persistence in the environment, their potential synergies, genetic stability and interactions between plants and the environment are relevant for risk assessment for food and feed and environmental risk assessment. Relevant EU regulations in this context are Regulation 178/2002, Council Decision 2002/811, Directive 2001/18 and Regulation 1829/2003. These regulations require a high standard for the protection of human health and the environment with the precautionary principle being the underlying paradigm.

Some of the relevant EU regulations being violated or disregarded by this authorisation are:

Directive 2001/ 18: Recital 8; Recital 19; Recital 20; Recital 43; Article 4, 1. & 3.; further Annex II (such as principles of the environmental risk assessment), Annex III B (such as genetic and phenotypical stability, interactions with the environment) and Annex VII in combination with Council Decision 2002/811.

Regulation 1829/2003: Recital 9; Article 1 (a); Article 4, 3.; Article 5, 3. (i); and complementary provisions of Chapter III of Regulation 1829/2003.

Regulation 178/2002: Article 5, 1.; Article 14, 4.; Article 18, 1.; Article 22, 3; Article 23.

It is evident from the document as prepared by Testbiotech and GeneWatch that these standards are not met by the risk assessment as performed on MON80934xMON88017. Therefore we are issuing this formal request for internal review of the authorisation under Article 10 of Regulation (EC) No. 1367/2006.

This case is also of general relevance for the setting of the standards for risk assessment by EFSA that currently are under discussion to be adopted as EU regulations. Further discussions are needed to assure the high level of protection for human health and the environment required by the framework of the EU regulations.

1. Introduction:

This document was prepared by taking into account the opinions of EFSA on the parental lines (MON80934 and MON88017) as well as of the one on the final stacked event. Further, the opinions from the experts of Member States were evaluated.

In addition, publications on the selectivity of Bt toxins, on interaction between the plants and the environment and on residues from spraying with the herbicide formulations were taken into account because these issues were not or were only partially assessed by EFSA.

Three separate reports on the two parental lines and the stacked events were prepared, listing the risks, unintended effects, uncertainties and shortcomings of risk assessment for each of them.

After that some crucial issues are discussed more generally by taking into account the outcome of these three reports.

2. Overview of risk assessment of the parental lines

2.1 MON80934

Maize MON89034 was developed by Monsanto, EU market authorisation for food and feed was given in 2009.

General overview:

MON89034 contains a unique combination of insecticidal proteins. In the parts of this plant, a highly synthetic Bt toxin, Cry1A.105 is produced. This toxin is a combination of Cry1Ac/ Cry1Ab and Cry1F. There is no native form of this combined protein, so safety can not be concluded by comparison with native Bt toxins used previously. This synthetic toxin is combined with another toxin from *Bacillus thuringiensis*, Cry2Ab2.

In general, the mode of action of Bt toxins is not fully understood. It is a matter of controversial debate (Pigott & Ellar, 2007). Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009). Thus risks for human health can not be excluded by assumptions or considerations but only by empirical testing before market authorisation.

Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).

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 its toxicity. EFSA omitted evaluation of this specific problem in the case of Cry1A.105 which is a synthetic Bt toxin, derived from a combination of at least two natural occuring Bt toxins. This toxin is a combination of Cry1Ac/ Cry1Ab and Cry1F.

There is no native form of this combined protein, it is evident that safety can not be concluded by comparison with the ones from native Bt toxins used before. There is a general problem in comparing Bt toxins as produced in plants with those that are originally produced by *Bacillus thuringiensis* because these toxins are all technically modified by the process of genetic engineering. But in this case the Bt toxin has to be considered as artificial, being a new combination of parts of toxins existing previously. In the genetically engineered plants, this synthetic toxin is combined with toxins from *Bacillus thuringiensis*, Cry2Ab2.

Synergistic effects can become highly problematic for non target organisms. Interactivity between the toxins or in combination with environmental toxins, bacteria, plant enzymes or pesticides can cause unexpected higher toxicity and lower selectivity (Then, 2010). These effects can impact on human health as well as on ecosystems.

Feeding studies with the maize showed significant findings in rats (especially kidney problems) that were not investigated further. The immunological impact of the toxin was not assessed in detail despite the fact that Cry1Ac is known to be a potent immune active substance. Potential risks for human health are supported by a report by Gallagher (2010) dealing with kidney problems and immune reactions that were observed in feeding studies with genetically engineered eggplant which also expresses a modified Cry1Ac protein.

Specific risks and unintended effects:

- Genetic engineering unintentionally changed the structure of the promoter from the cauliflower mosaic virus.
- The content of the additional proteins produced in the plant are highly variable (for example Cry1A105 in leaves 27-850 µg/g dwt). This may indicate genetic instability and result in unexpected reactions to specific environmental conditions. Several investigations show that genetically engineered plants have unexpected reactions under stress conditions (see for example: Matthews et al., 2005). This can also impact on the Bt content in the plants (Then & Lorch, 2008).
- The toxins display a high level of expression compared to other genetically engineered plants.
- The additional proteins are degraded by processing with heat by only a small percentage, thus Bt toxins will mostly survive processing.
- In comparison with its conventional counterparts, 44 significant differences in compositional analysis were observed in field trials in the US. Similar findings could only be found in some historical data unrelated to the actual field trials. Since it is not sufficiently clear under which specific conditions these additional historical data were generated, this kind of comparison inevitably contains major uncertainties.
- In agronomic parameters, several significant differences were identified in comparison to the control plants. For example there was a much higher rate of stalk lodging in the genetically engineered plants after a wind storm. It is possible that the metabolism of the plants is changed beyond the intended additional gene functions.
- A 90 day feeding study with rats showed significant differences compared to the control group. In particular, female animals showed several complications in the kidneys. As the

experts from the Belgian authorities describe: *"The kidneys of the high-dose (33%) test group females showed findings not found or at lower incidence in the control group. One rat was found dead on day 14. There were 5 findings of chronic progressive nephropathy, 3 findings of transitional cell hyperplasia, 2 cases of sub-acute inflammation and hydronephrosis, papillary necrosis and tubular necrosis. Most of these findings were attributable to the two rats which were found to have calculi (see Macroscopic examination). It is worth discussing these items and having a closer look, whether these findings are solely due to chance. In case any doubt remains, further testing is recommended."*

- There are several proteins in maize that can cause allergic reactions. The newly introduced gene construct might for example enhance an immune response to these endogenous plant protein(s).
- Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009).
- 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 its toxicity. All the Bt toxins produced in the plants are technically modified.
- these plants might be eaten as mixtures with other genetically engineered plants. Tests should be performed on potential accumulated effects such as combinatorial or accumulated effects.
- Synergistic effects can become highly problematic for non target organisms: interaction of the toxins with each other or with other compounds can cause higher toxicity and lower selectivity (Then, 2010). These effects may impact on human and animal health as well as on ecosystems.
- Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).

Type of feeding trials conducted:

- An acute toxicity test was performed, feeding single isolated Bt toxins, but not in combination. These proteins were not isolated from the plants but produced by bacteria.
- A 90 day feeding study with rats on subchronic health effects was conducted with maize kernels.
- A 42 day feeding study with poultry on nutritional effects was conducted with maize kernels.

Overview of shortcomings of the opinion of EFSA:

- no investigations were conducted to determine changes in plant gene activity or metabolic profile.
- functional genetic stability under various defined environmental conditions was not shown. Genetic stability was only considered in the context of the heredity of the gene constructs to following generations.
- in comparison with its conventional counterparts, many significant differences in the compositional analysis were found but these were not investigated further. Instead references were made to unspecific and questionable 'historical' data from industry unrelated to the actual field trials, e.g. the ILSI database.
- significant differences in agronomic performances should have been investigated in relation to interactions between the genome and the environment under defined environmental conditions.
- an acute toxicity test with the isolated Cry proteins derived from bacteria was performed. The proteins were not tested in combination. The duration of the tests was qualified as being below the standards as recommended by the EFSA Guidance.
- risks were not investigated in detail despite significant findings from feeding trials indicating potential negative impacts on human and animal health. The applicant was not asked to deliver further studies.
- there have been no feeding studies over the whole lifetime of animals and none including following generations.
- no specific testing was performed for immunological reactions despite the fact that the protein Cry1Ac that has some similarities with Cry1A.105 can trigger immune reactions.
- no endocrinological studies were performed to investigate potential impacts on the reproductive system
- no investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals.
- no investigation conducted for DNA traces in animal tissue after feeding.
- no assessment of combinatorial effects with other genetically engineered plants used in food and feed.
- tests on potential combinatorial effects of the toxins were only performed in insects. No other 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 and pesticides.
- there was no empirical investigation of the actual persistence of the Bt toxins and their potential accumulation in the environment.

Shortcomings in risk management (monitoring):

- The protocols used for conducting the measurements of the Bt toxins have not been fully published or evaluated by independent laboratories. As a result, independent institutions can hardly monitor the actual content of Bt concentration in the plants during cultivation or in food and feed products.

- No plan for surveillance as required by European regulation was made available that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.

Documents and publications:

EFSA (2008a) Scientific Opinion of the Panel on Genetically Modified Organisms on application (Reference EFSA-GMO-NL-2007-37) for the placing on the market of the insect-resistant genetically modified maize MON89034, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal (2008) 909, 1-30

EFSA, 2008 b, Comments and opinions submitted by Member States during the three-month consultation period, Annex to EFSA, 2008a, EFSA (2008a) Scientific Opinion of the Panel on Genetically Modified Organisms on application (Reference EFSA-GMO-NL-2007-37) for the placing on the market of the insect-resistant genetically modified maize MON89034, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal (2008) 909, 1-30, accessed via http://registerofquestions.efsa.europa.eu/roqFrontend/questionsListLoader?panel=GMO

Gallagher, L., 2010, Bt Brinjal Event EE1 The Scope and Adequacy of the GEAC Toxicological Risk Assessment, Review of Oral Toxicity Studies in Rats. http://www.testbiotech.de/node/444

Matthews D, Jones H, Gans P, Coates St & Smith LMJ (2005): Toxic secondary metabolite production in genetically modified potatoes in response to stress. Journal of Agricultural and Food Chemistry, doi: 10.1021/jf050589r.

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Pigott, C.R. & Ellar, D.J., 2007, Role of Receptors in Bacillus thuringiensis Crystal Toxin Activity: Microbiol Mol Biol Rev 71 (2): 255–281

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Soberón, A., Gill, S.S., Bravo A., 2009, Signaling versus punching hole: How do Bacillus thuringiensis toxins kill insect midgut cells? Cell. Mol. Life Sci. 66 (2009) 1337 – 1349

Then C., 2010, Risk assessment of toxins derived from Bacillus thuringiensis – synergism, efficacy, and selectivity, Environmental Science and Pollution Research, http://dx.doi.org/10.1007/s11356-009-0208-3

Then C. & Lorch A., 2008, A simple question in a complex environment: How much Bt toxin do

genetically engineered MON810 maize plants actually produce?: in Breckling B, Reuter H, Verhoeven R (eds) (2008) Implications of GM-Crop Cultivation at Large Spatial Scales., Theorie in der Ökologie 14. Frankfurt, Peter Lang, http://www.gmls.eu/index.php?contact=ja

van Frankenhuyzen, K., 2009, Insecticidal activity of Bacillus thuringiensis crystal proteins, Journal of Invertebrate Pathology 101 (2009) 1–16

2.2 MON88017

Maize MON88017 was developed by Monsanto, EU market authorisation for food and feed was given in 2009.

General overview:

This maize is another variation of plants that produce insecticidal proteins against the larvae of corn rootworms (*Diabrotica spp.*). Very similar properties are inherited in MON863, a maize that showed several significant effects in animal feeding trials that were classified as signs of toxicity (Seralini et al., 2007).

In general, the mode of action of Bt toxins is not fully understood. It is a matter of controversial debate (Pigott & Ellar, 2007). Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009). Thus risks for human health can not be excluded by assumptions or considerations but only by empirical testing before market authorisation.

Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).

Synergistic effects can become highly problematic for non target organisms. Interactivity between the toxins or in combination with environmental toxins, bacteria, plant enzymes or pesticides can cause unexpected higher toxicity and lower selectivity (Then, 2010). These effects can impact on human health as well as on ecosystems.

In this case, resistance against glyphosate (brand name such as Roundup) is combined with the insecticide, which leads to a combination of potential hazardous residues from spraying (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009; Then 2011) on the plants.

Specific risks and unintended effects:

- By inserting the DNA, a part of genomic DNA of the maize was deleted and an additional fragment was inserted unintentionally into the genome.
- In comparison with its conventional counterparts, many significant differences in

compositional analysis were observed. Similar findings could only be found in some historical data unrelated to the actual field trials. Since it is not sufficiently clear under which specific conditions these additional historical data were generated, this kind of comparison inevitably contains major uncertainties.

- In agronomic parameters, several significant differences were identified in comparison to the control plants. The differences were not consistent over all field trials. The reason for this might be that these differences only emerge under particular environmental conditions. Several investigations show that genetically engineered plants can exhibit unexpected reactions under stress conditions (see for example: Matthews et al., 2005). This can also impact the Bt content in the plants (Then & Lorch, 2008).
- There are several proteins in maize that can cause allergic reactions. The newly introduced gene construct might for example enhance an immune response to these endogenous plant protein(s).
- Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species (Soberon et al., 2009).
- Synergistic effects can become highly problematic for non target organisms. Interaction of the toxins with each other or with other compounds can cause higher toxicity and lower selectivity (Then, 2010). These effects may impact on human and animal health as well as on ecosystems.
- Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).
- The plants might be eaten mixed with other genetically engineered plants. Tests should be performed on potential accumulated effects such as combinatorial or accumulated effects.
- The plants are made tolerant to glyphosate preparations by introducing a gene construct for the EPSPS enzyme. As recent overviews of the scientific literature show (PAN AP, 2009, Antoniou et al, 2010), the toxicity of glyphosate, its metabolites and its additive like POEA (polyoxyethylene alkylamine) need to be re-evaluated.

Type of feeding trials conducted:

- An acute toxicity study with mice was performed, feeding isolated Bt toxin Cry3Bb1 and the enzyme EPSPS that enables tolerance to glyphosate (but not in combination). These proteins were not isolated from the plants but produced by bacteria.
- A 90 day feeding study with rats on subchronic health effects was conducted with maize kernels
- A 42 day feeding study with poultry on nutritional effects was conducted with maize kernels

Overview of some shortcomings of the EFSA opinion:

- no investigations were conducted to determine changes in plant gene activity or metabolic profile.
- functional genetic stability under various defined environmental conditions was not shown.

Genetic stability was only considered in the context of the heredity of the gene constructs to following generations.

- in comparison with its conventional counterparts, many significant differences in the compositional analysis were found but these were not investigated further. Instead references were made to unspecific and questionable 'historical' data from industry unrelated to the actual field trials.
- significant differences in agronomic performances should have been investigated in relation to interactions between the genome and the environment under defined environmental conditions.
- there have been no feeding studies over the whole lifetime of animals and none including following generations.
- no empirical investigations were performed concerning allergies or other impacts on the immune system.
- no endocrinological studies were performed to investigate potential impacts on the reproductive system.
- no investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals.
- no investigation for DNA traces in animal tissue after feeding was conducted.
- no assessment was made of risks stemming from residues from spraying with the pesticide formulations and their metabolites.
- no assessment was made of combinatorial effects with other genetically engineered plants used in food and feed.
- 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 and pesticides.
- no empirical investigation was made of the actual persistence of the Bt toxins and their potential accumulation in the environment.

Shortcomings in risk management (monitoring):

- The protocols used for conducting the measurements of the Bt toxins have not been fully published or evaluated by independent laboratories. As a result, it is difficult or impossible for independent institutions to monitor the actual content of Bt concentration in the plants during cultivation or in food and feed products.
- No plan for surveillance as required by European regulation was made available that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.
- Monitoring of health effects should include the risks associated with the spraying of glyhosate formulations and their residues on the plants.

Documents and publications:

Antoniou, M., Brack, P., Carrasco, A., Fagan, J., Habib, M., Kageyama, P., Leifert, C., Nodari, R. O., Pengue W., 2010, GM Soy: Sustainable? Responsible?, GLS Bank & ARGE gentechnikfrei. http://www.gmwatch.eu/?option=com_content&view=article&id=12479

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Paganelli, A., Gnazzo, V., Acosta, H., López, S. L., Carrasco, A. E. (2010) Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signalling. Chem. Res. Toxicol., August 9. pubs.acs.org/doi/abs/10.1021/tx1001749

PAN AP, Pesticide Action Network Asian Pacific (2009) Monograph on Glyphosate, www.panap.net/en/p/post/pesticides-info-database/115

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

Shulmina AI, Dronova LA, Shubin VV, et al. (1985) Determination of the chymotrypsin inhibitors, secondary structure of the chymotrypsin inhibitor from corn by the circular-dichroism method. BIOCHEMISTRY-MOSCOW 50, 7: 980-982

Soberón, A., Gill, S.S., Bravo A., 2009, Signaling versus punching hole: How do Bacillus thuringiensis toxins kill insect midgut cells? Cell. Mol. Life Sci. 66 (2009) 1337 – 1349

Then, C., 2011, Vorsicht „Giftmischer“: Gentechnisch veränderte Pflanzen in Futter-und Lebensmitteln, ein Testbiotech-Report, http://www.testbiotech.de/sites/default/files/Testbiotech_Giftmischer_April_2011.pdf

Then C. & Lorch A., 2008, A simple question in a complex environment: How much Bt toxin do genetically engineered MON810 maize plants actually produce?: in Breckling B, Reuter H,

Verhoeven R (eds) (2008) Implications of GM-Crop Cultivation at Large Spatial Scales., Theorie in der Ökologie 14. Frankfurt, Peter Lang, http://www.gmls.eu/index.php?contact=ja

van Frankenhuyzen, K., 2009, Insecticidal activity of Bacillus thuringiensis crystal proteins, Journal of Invertebrate Pathology 101 (2009) 1–16

3. Overview of risk assessment of the stacked events MON80934xMON88017

Maize MON80934xMON88017 was produced by the company Monsanto by crossing the parental lines. Market authorisation was issued in June 2011.

General overview:

This maize produces several insecticidal toxins (Cry1A.105, Cry2Ab2, Cry3Bb1) derived from various strains of Bacillus thuringiensis. Further it was made resistant to glyphosate. It is produced and sold by Monsanto company under its brand name Genuity VT Triple PRO Corn. The maize is made resistant against pest insects above ground (larvae from *Lepidotera* species) and in the soil (larvae from *Coleoptera* species).

MON89034 x MON88017 contains a unique combination of insecticidal proteins. In parts of this plant, a highly synthetic Bt toxin is produced. This toxin is a combination of Cry1Ac/ Cry1Ab and Cry1F. There is no native form of this combined protein, so safety can not be concluded by comparison with native Bt toxins used previously. This synthetic toxin is combined with another toxin from Bacillus thuringiensis, Cry2Ab2 and with Cry3Bb1. Cry3Bb1 is also produced in another genetically modified maize called MON863, which studies suggest may cause negative health impacts (Seralini et al., 2007).

Diagram: Combination of various Bt toxin and components from Bt toxins in VT Triple Pro Corn

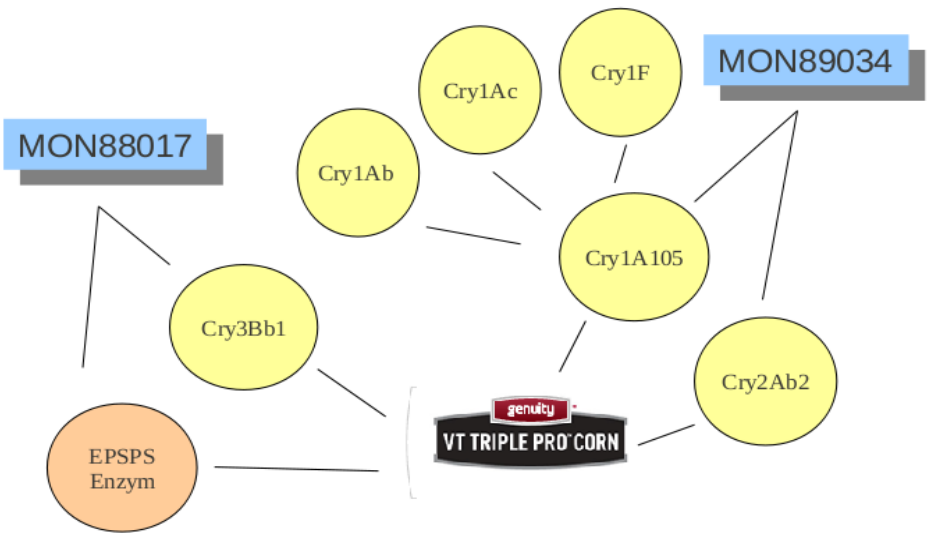

Table: origin of the proteins used in VT Triple Pro Corn

New protein produced in MON 89034 × MON 88017	Origin of the gene sequence
Cry1Ab (Cry1A.105)	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry1Ac (Cry1A.105)	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry1F (Cry1A.105)	*Bacillus thuringiensis*, subspecies *aizawai*
Cry2Ab2	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry3Bb1	*Bacillus thuringiensis*, subspecies *kumamotoensis*
EPSPS enzyme	*Agrobacterium* sp. strain CP4

In general, the mode of action of Bt toxins is not fully understood. It is a matter of controversial debate (Pigott & Ellar, 2007). Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009). Thus risks for human health can not be excluded by assumptions or considerations but only by empirical testing.

Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).

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 its toxicity. EFSA omitted evaluation of this specific problem in the case of Cry1A.105 which is a synthetic Bt toxin, derived from a combination of at least two natural occuring Bt toxins. This toxin is a combination of Cry1Ac/ Cry1Ab and Cry1F. There is no native form of this combined protein, it is evident that safety can not be concluded by comparison with the ones from native Bt toxins used before. There is a general problem in comparing Bt toxins as produced in plants with those that are originally produced by *Bacillus thuringiensis* because these toxins are all technically modified by the process of genetic engineering. But in this case the Bt toxin has be considered as artificial, being a new combination of parts of toxins existing previously. In the genetically engineered plants, this synthetic toxin is combined with toxins from *Bacillus thuringiensis*, Cry2Ab2.

Synergistic effects can become highly problematic for non target organisms. Interactivity between the toxins or in combination with environmental toxins, bacteria, plant enzymes or pesticides can cause unexpected higher toxicity and lower selectivity (Then, 2010). These effects also can impact on human health before market authorisation.

The recently published study of Sharma et al. (2010) found synergistic effects of Cry1Ab and Cry1Ac in target pest insects. Further synergistic effects between Cry1Ac and other Bt toxins such as Cry2Ab2 and Cry1F are discussed in and Lee et al. (1996), Chakrabarti et al (1998) and Kashdan et al (2007). Synergistic interactivity between Cry2Ab2 and Cry1Ab and between Cry2Ab2 and Cry1Ac has also been discussed in Mattila et al. (2005) and Stewart et al. (2001). Synergistic effects

can become highly problematic for non target organisms. Interactivity between the toxins can cause unexpected higher toxicity and lower selectivity (Then, 2010). These effects can impact on human health as well as on ecosystems.

Despite the fact that kidney problems were discussed in animal feeding studies with MON89034, EFSA did not even request any feeding studies for health risks at the level of combining MON 89034 × MON88017 in a stacked event. In conclusion there is a high level of uncertainty regarding human health risks. The presence of these risks is supported by a report by Gallagher (2010) dealing with kidney problems that were observed in feeding studies with genetically engineered eggplant which also express a modified Cry1Ac protein.

In this case, resistance against glyphosate (brand name such as Roundup) is combined with the insecticide, which leads to a combination of potential hazardous residues from spraying (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009; Then 2011) on the plants.

Specific risks and unintended effects:

- In comparison with its conventional counterparts, many significant differences in compositional analysis were observed. Similar findings could only be found in some historical data unrelated to the actual field trials. Since it is not sufficiently clear under which specific conditions these additional historical data were generated, this kind of comparison inevitably contains major uncertainties.
- In agronomic parameters, several significant differences were identified in comparison to the control plants. The differences were not consistent over all field trials. The reason for this might be that these differences only emerge under particular environmental conditions. Several investigations show that genetically engineered plants can exhibit unexpected reactions under stress conditions (see for example: Matthews et al., 2005). This can also impact on the Bt content in the plants (Then & Lorch, 2008).
- A 90 day feeding study with rats showed with parental MON89034 significant differences compared to the control group. Especially female animals showed several complications in the kidneys.
- There are several proteins in maize that can cause allergic reactions. The newly introduced gene construct might for example enhance an immune response to these endogenous plant protein(s).
- Strict selectivity of the Bt toxins is not shown by empirical evidence but deduced from its mode of action as described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009).
- 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 its toxicity. All the Bt toxins produced in the plants are technically modified.
- A recently published study by Sharma et al. (2010) found synergistic effects of Cry1Ab and Cry1Ac in target pest insects. Further synergistic effects between Cry1Ac an other Bt toxins such as Cry2Ab2 and Cry1F are discussed in and Lee et al. (1996), Chakrabarti et al (1998) and Kashdan et al (2007). Synergistic interactivity between Cry2Ab2 and Cry1Ab and

between Cry2Ab2 and Cry1Ac has also been discussed in Mattila et al. (2005) and Stewart et al. (2001).

- Synergistic effects can become highly problematic for non target organisms. Interaction of the toxins with each other or with other compounds can cause higher toxicity and lower selectivity (Then, 2010). These effects may impact on human and animal health as well as on ecosystems.
- Some plant enzymes that diminish the digestion of proteins (protease inhibitors) can strongly enhance the toxicity of Bt toxins (Pardo Lopez et al., 2009). Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of some Cry toxins. It is known that maize produces such inhibitors (Shulmina et al., 1985).
- These plants will be fed and might be eaten by mixing them with other genetically engineered plants. Tests have to be performed on potential accumulated effects such as combinatorial or accumulated effects.
- The plants are made tolerant to of glyphosate preparations by introducing a gene construct for the EPSPS enzyme. As recent overviews of scientific literature show (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009; Then 2011), the toxicity of glyphosate, its metabolites and its additives, such as POEA (polyoxyethylene alkylamine), need to be re-evaluated.

Type of feeding trial conducted:

- Only a 42 day feeding study with poultry on nutritional effects was conducted

Overview of some shortcomings of the EFSA opinion:

- no investigations were conducted to determine changes in plant gene activity or metabolic profile.
- no investigation under various defined environmental conditions was conducted to determine interactions between the genome and the environment.
- functional genetic stability under various defined environmental conditions was not shown. Genetic stability was only considered in the context of the heredity of the gene constructs to following generations.
- in comparison with its conventional counterparts, many significant differences in the compositional analysis were found but these were not investigated further. Instead references were made to unspecific and questionable 'historical' data from industry unrelated to the actual field trials.
- consistent findings in several field trials indicating interactions between the genome and the environment were not investigated.
- the plants were not sprayed with the herbicide formulations during the field trials.
- the stacked events were not compared with the parental lines during the field trials.
- no further feeding studies with stacked events were conducted despite significant findings in feeding trials with parental lines indicating potential negative impacts on human and animal health.
- there have been no feeding studies with the parental lines or the stacked events over the whole lifetime of animals and none including following generations.

- no specific testing was performed for immunological reactions despite the fact that the protein Cry1Ac that has some similarities with Cry1A.105 can trigger immune reactions.
- no endocrinological studies were performed to investigate potential impacts on the reproductive system
- no investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals.
- no investigation was conducted for DNA traces in animal tissue after feeding.
- no assessment was made of combinatorial effects with other genetically engineered plants used in food and feed.
- no tests were performed to determine potential combinatorial or accumulated effects of the toxins nor of any other factors as other toxic compounds, bacteria, plant enzymes and pesticides in mammals.
- no empirical investigation was made of the actual persistence of the Bt toxins and their potential accumulation in the environment.
- no assessment was made of risks stemming from residues from spraying with the pesticide formulations and their metabolites.

Shortcomings in risk management (monitoring):

- The protocols used for conducting the measurements of the Bt toxins have not been fully published or evaluated by independent laboratories. As a result, it may be difficult or impossible for independent institutions to monitor the actual content of Bt concentration in the plants during cultivation or in food and feed products.
- No plan for surveillance as required by European regulation was made available that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.
- Since no specific detection method for the stacked event was made available, it will be difficult to distinguish it from the parental lines for monitoring purposes.
- Monitoring of health effects should include the risks associated with the spraying of glyhosate formulations and their residues in the plants.

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Further Links:

TESTBIOTECH Background 14-3-2011: EU about to approve genetically engineered maize with potential health risk, http://www.testbiotech.de/sites/default/files/TBT_Background_14_3_2011.pdf

4. Discussion

Issues such as the expression rate of the additional proteins, the potential synergies between the proteins, the interaction with the environment and the need for animal feeding studies are highlighted in the following paragraphs. After that the general standards for risk assessment of EFSA are discussed briefly.

Expression rate of the insecticidal proteins

It is important to know the rate of expression of the additional proteins in the plant in order to assess their genetic stability as well as environmental and food chain exposure. The various gene constructs are not under control by the plant's normal gene regulation. They are, in fact, designed to evade biological mechanisms such as silencing and down regulation by the plant's overall gene regulation (see for example Diehn et al., 1996). The expression rate in single events and stacked events can be influenced by various factors and interactions with external factors and plant metabolism.

It is known that the content of Bt toxins in genetically engineered plants is influenced by environmental factors and can show a wide range of variation (Ngyuen & Jehle, 2007, Then & Lorch, 2008). Furthermore, genetically engineered plants can show unexpected reactions to environmental conditions and stress factors (see for example Zeller et al, 2010), that can also impact on the content of its foreign proteins.

Therefore, it is necessary to explore the actual range of variation, especially of the Bt toxins. Their expression rate does not only impact on their efficacy on pest insects, but also influences the exposure of the food chain and the environment to insecticidal proteins.

In general, the range of concentration of the foreign proteins is relevant to the exploration of genetic stability in genetically engineered plants. It is also relevant to the assessment of potential health impacts such as toxicological and immunological hazards as well as combinatorial effects. Further, it is relevant for the assessment of environmental impacts such as risks for non-target organisms, pest resistance and exposure of soils and other areas of the environment to Bt toxins.

Methods and protocols for measurements and their quality control are decisive in acquiring reliable data and carrying out risk assessment. As for the application of pesticides, fully publishing technical protocols and evaluation by independent institutions are indispensable prerequisites for determining exposure rates. In the case of Bt toxins, so-called ELISA systems are used to determine the content, but their outcome is highly dependent on details of the protocol (see for example Then & Lorch, 2008).

Further, it is necessary to determine environmental impact factors that can influence the rate of gene expression. It is known that the environment can impact Bt content in genetically engineered plants (Then & Lorch, 2008). To determine the most relevant impact factors and the true range of possible variations it is necessary to expose the plants to defined environmental conditions.

The measurements on gene expression were conducted by Monsanto´s laboratories. No independent institutions were involved to prove that testing was done in a reliable manner. Findings were not peer reviewed and published. Not even the protocols used by the labs have been evaluated by independent laboratories, therefore the investigations cannot be repeated by independent institutions and results cannot be checked.

Regarding the data, a lot more investigation is necessary. There is no information concerning environmental impacts on the plants that might have influenced the expression rate (such as climate, soil, fertiliser, overall use of pesticides). Data was only collected during one period of vegetation. The range of the possible variations and the impact factors on the rate of expression were not determined, despite the fact that Bt content in the plants showed huge variations.

The life cycle of the Bt proteins was not explored. No information was given concerning the rate of degradation or potential accumulation in the soil, not even in the case of the synthetic protein Cry1A.105, whose biological properties cannot be derived from comparison with naturally occurring Bt toxins.

In conclusion, the data as presented by industry are insufficient and the risk assessment performed by EFSA is not acceptable. The data are not produced in a reliable way, the protocols for determining the Bt content have not been published, the results have not been peer reviewed. Substantial data are missing and the industry has failed to determine the true range of expression and the relevant impact factors.

It is absolutely necessary in this context, to define the protocol for measuring the toxins, since different methods for measuring can result in highly varying results. The technical protocols should be fully published and evaluated by independent laboratories to allow other institutions to conduct further measurements to control the exact level of toxins.

Potential synergies that can enhance toxicity

The stacked maize produces three different Bt toxins. This combination of toxins does not occur in nature:

- The Bt toxins are derived from different subspecies of *Bacillus thuringiensis.*
- The Bt toxins produced in the plants display modified DNA and changes in the structure of their proteins. They are, therefore, fundamentally different from naturally occurring toxins.
- The Bt toxins in the plants are produced in an activated form. They are not produced in their natural inactive and crystallized form.
- One of the Bt toxins in maize MON8034 x MON 88017 (Cry1A.105) is a synthetic protein that did not previously exist in nature.

Furthermore, the maize contains a gene construct that confers herbicide tolerance to glyphosate (brand names such as Roundup).

It is very well known that synergistic, antagonistic and additive effects occur both between the Bt toxins and between the Bt toxins and other compounds. These effects are used intentionally to enhance toxicity in pest insects (overview: Prado Lopez et al., 2009). However, it is also known that toxicity in non- target organisms can be enhanced (for overview see Then, 2010). In general, synergistic effects can be characterised by emerging effects that exceed those that can be predicted from additive linear dosage-response effect, while additive effects follow a predictable dose-response relationship. Both effects are relevant for assessing the toxicity of Bt plants. Efficacy and selectivity in target and non-target organisms can be impacted by interactivity amongst the toxins or between the toxins and other external factors such as enzymes, pesticides or bacteria (for overview see Then, 2010).

For example, a recently published study carried out by Sharma et al. (2010) found synergistic effects of Cry1Ab and Cry1Ac in target pest insects. Further synergistic effects between Cry1Ac and other Bt toxins such as Cry2Ab2 and Cry1F are discussed in Lee et al. (1996), Chakrabarti et al (1998), Stewart et al. (2001) and Kashdan et al (2007). Synergistic effects can become highly problematic for non-target organisms. Interaction between the toxins can cause unexpectedly higher toxicity. Even a lower selectivity can be observed, thus the range of possibly affected organisms might be widened (Then, 2010). In this case, the effects might also affect human or animal health.

Furthermore, synergistic effects with the plant's own components (such as trypsin inhibitors that can enhance toxicity of Bt proteins) and other abiotic factors (such as residues from spraying, cadmium) have to be taken into account. For example, it is known that protease inhibitors (such as trypsin inhibitors) can strongly enhance the toxicity of Bt toxins. Even the presence of extremely low levels of protease inhibitors enhances the insecticidal activity of some Cry toxins up to 20-fold (Pardo-Lopez et al., 2009). It is further known that maize produces such inhibitors (Shulmina et al., 1985) and that interaction with cadmium can cause toxicity in non-target organisms (Kramarz et al, 2007).

Moreover, 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 their toxicity. This is especially relevant in the case of Cry1A.105: its toxicity cannot be assessed by comparison with naturally occurring Bt toxins.

Some of the most apparent deficiencies of the risk assessment are:

- Studies on potential synergies 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 on the basis of these existing studies.
- Only interaction between the Bt toxins was investigated. Potential synergies with EPSPS 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) stressors, bacteria and pharmaceutical compositions (like antibiotics) were completely ignored (for a list of some relevant factors see Then, 2010).
- Most relevant are studies that raise new questions concerning the mode of action and the selectivity of Bt toxins (such as Pigott & Ellar, 2007, van Frankenhuyzen, 2009, Soberon et al. 2009). These were not taken into account by EFSA.

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

Interaction between the plants and the environment

Genetically engineered plants inherit technically derived features that are not controlled by the plant‘s gene regulation. Technical failures such as genetic instabilities and/or occurrence of undesired components can be triggered by specific environmental conditions. Relevant effects have already been observed in various genetically engineered plants. In general, it is known that genetically engineered plants can show unexpected effects in reaction to environmental conditions

such as climate, soil quality and various stressors. Interaction with the environment can impact the plant genome, plant metabolism, cause changes in phenotype and affect different biological properties of the plant (e.g. higher invasiveness and fitness).

As Zeller et al. (2010) show, the ecological behaviour of plants can cause effects that are highly relevant for the risk assessment of genetically engineered plants. Genetically engineered wheat showed a complex reaction of reduced fitness, higher incidence of fungal disease and higher burden of toxic residues from the fungal disease. These effects only occurred under environmental conditions, not in the greenhouse. Zeller et al. (2010) also point out that so far there has been hardly any investigation of these interactions:

> *"(...) a careful search in the literature for replicated and randomized studies about the ecological behaviour of GM and control plants in glasshouse versus field environments did not return any published references."*

Interactions with the environment can impact genome regulation, plant metabolism, the phenotype as well as different biological plant behaviour (higher fitness and invasiveness). In general, it is known that genetically engineered plants react to environmental conditions such as climate (Chen et al., 2005), soil (Bruns, 2007) and abiotic and biotic stress (Matthews et al., 2005).

Genetically engineered plants inherit technically derived features that are not controlled by the plant‘s gene regulation. Technical failures such as genetic instabilities and the emergence of undesired components can be triggered by specific environmental conditions. Thus, attention must be paid to effects that might occur under certain environmental conditions such as in particular climates (drought, heat, moist conditions). Technical failures and genetic instabilities might give rise to undesirable components in the plants or diminish valuable components.

The reactions of genetically engineered plants should be studied under controlled conditions, e.g. in laboratories or greenhouses, to enable identification of relevant impact factors. That is why Then & Potthof (2009) propose a system they call a 'crash test' (or 'stress test'), to systematically investigate the genetic and metabolic reactions of the plants to changing environmental conditions - before release into the environment. Once the plants are released into the environment, they are exposed to a much more complex situation that can make it difficult to determine the impact of particular factors. EFSA (2010), for example, states:

> *"Laboratory testing provides the best way to control and manipulate experimental conditions (environmental factors, set-up) and to limit complexity and variability. In contrast, field tests allow the evaluation of trait x environment interactions, but they exhibit the highest experimental complexity and provide the lowest ability to control experimental conditions due to large natural variability. "*

Interactions between the genome and the environment are relevant for environmental risk assessment, as are food and feed related risks, since the composition of the plants might be impacted or plant diseases might trigger toxic residues e.g. from fungal disease.

The risk assessment of MON89034 x MON88017 must be rejected because the data are inadequate. They show the urgent need for clear standards, problem formulation and endpoints for the risk assessment of ecological interactions of genetically engineered plants. They further show the need for rigid quality control and independent investigations.

Feeding studies

The genetically engineered plants inherit a unique combination of insecticidal toxins that are technically modified and even artificially synthesised. These proteins are not sufficiently characterised with regard to their toxicity, selectivity, efficacy and their interactivity. Some of them are known to show immunological activity: the toxin Cry1Ac that is one of the Bt proteins used for the production of the synthetic toxin Cry1A.105, is known to be a potent immune stimulator.

To assess their actual risks, the plant's components and other compounds in food and feed products should be taken into consideration because they might display synergistic effects with insecticidal toxins such as protease inhibitors.

There should also be some discussion on the residues of the herbicide glyphosate and its additives which may have a negative impact on health at very low dosages (e.g. hormone disruption). Because of potential health risks, farmers in Germany are advised not to use certain mixtures of glyphosate for the production of food and feed[1]. A significant level of residues from these herbicides can be expected in the plants because they were created to be tolerant to these chemicals and the plants will be sprayed as part of agricultural practice for herbicide-tolerant genetically engineered plants.

Recent studies (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009; Then 2011) show the need for a comprehensive reassessment of health risks posed by the pesticide glyphosate and its additives such as POEA. It is a matter of deep concern that the current process to reassess glyphosate under pesticide regulation is severely delayed, but meanwhile further market authorisations are being granted for genetically engineered crops that might contain high levels of residues from spraying with glyphosate and its additives.

The continuous ingestion of the combined Bt toxins and the residues from spraying can lead to a change in the composition of the intestinal flora, and thereby indirectly cause severe health hazards in humans and animals. Further, the gene constructs as introduced into the plants and their parts, such as promoters from viral sources, have to be taken into account because these elements might still be biologically active after ingestion. Finally, undesirable components in the plants might emerge because of genetic engineering methods.

As the analysis of the EFSA opinion and of the data from industry shows, the relevant risks were not investigated or only explored very poorly. Therefore, feeding studies to investigate effects on health would be of major importance before any usage in the food chain and feed could be considered. In the case of MON89034 x MON88017, the parental lines used to produce the stacked event were tested in animal feeding studies and showed some signs of toxicity that need further investigation. Rats fed with MON89034 showed signs that their kidney function might be impacted. Furthermore, other genetically engineered crops (MON863) with similar proteins also showed signs of toxicity that need further investigations (Seralini et al., 2007, see also Seralini et al., 2011)

Nutritional studies have almost no relevance to possible health risk assessment. In the case of

[1] www.bvl.bund.de/DE/04_Pflanzenschutzmittel/05_Fachmeldungen/2010/psm_anwendungsbestimmungen_tallowamin-Mittel.html

MON89034 x MON88017, only one nutritional feeding study was performed by industry, there was no feeding study to investigate the effects on human and animal health.

As comments made by experts from many Member States show, this maize needs to be tested much more carefully for potential health risks. The market application of of MON89034 x MON88017 is based on series of insufficient studies. It is a matter of great concern that EFSA did not reject these inadequate and flawed dossiers that were never subjected to the scrutiny of independent quality controls. Instead, EFSA's way of dealing with substantial demands from the Member States was to give more or less rhetorical answers.

General discussion about the standards of EFSA

Recent debate is ongoing within the European Union about standards of risk assessment for genetically engineered plants for food and feed as well as for cultivation. EFSA has published new guidance for food and feed as well as for environmental risk assessment. Further specific documents were released by EFSA dealing with animal feeding studies, stacked events and allergies. So far none of the guidance documents or opinions have been formally adopted by the risk manager. Instead several member states and the European Commission have asked for higher standards for risk assessment. A process has been started to discuss the Guidance of EFSA on the political level that aims to adopt some standards as part of the European regulation.[2]

The case of MON80934 x MON88017 shows that current standards are not sufficient to assure the high level of protection of human health and the environment as required by European regulations (such as Regulation 178/2002, Directive 2001/18 and Regulation 1829/2003). The guidelines of the OECD and the Codex Alimentarius can give some guidance concerning necessary minimum standards being applied for risk assessment, however they are not sufficient per se to comply with the need for consumer confidence, health and environment protection as foreseen in the European regulations.

For example, in the area of allergenic risks, the methods for investigation of allergenic risks as described in the Codex Alimentarius suffer from a substantial level of uncertainties. Thus, from perspective of precaution, the use of proteins that are known to impact the immune system such as Cry1Ac (and their synthetic derivates) should be avoided. Further there are, for example, no sufficiently defined standards for investigating interaction between the plants and the environment, to measure changes in gene activity or metabolic profile or to assess synergistic effects between the additional proteins and other factors. A recent Canadian study has also suggested that Cry1Ab toxin and pesticide residues associated with genetically modified foods can pass from pregant mothers to their fetuses (Aris & LeBlanc, 2001).

Many questions as discussed herein are relevant also for other market applications and authorisations. It should be taken into consideration that EFSA so far only uses the so called comparative approach and not a comprehensive risk assessment per se[3]. Coming from the background of the case of MON80934 x MON88017, it looks like some change in the paradigm of risk assessment is needed.

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5. Conclusions

There are several severe deficiencies in the risk assessment of MON89034 x MON88017: there have been no feeding studies or other in-depth investigations to explore potential health hazards in human and animals. Possible synergies of the toxins in this stacked event were only performed on pest insects. Feeding trials were conducted to test nutritional quality but not to examine health impacts.

During cultivation, the plants showed a high range of variation in the expression of the foreign proteins. This might indicate genetic instability triggered by certain environmental conditions that also might affect other compounds in the plants. No reliable protocols to enable independent control of the toxin load in the plants were provided, nor were there any investigations into the life cycle of the proteins or environmental exposure.

In general, the dossiers of industry show major deficiencies in study design and completely lack independent quality controls.

The European Food Safety Authority EFSA did not deal with these issues in detail. Further they rejected the concerns of experts from various Member States, very often giving formalistic reasons (using their own guidelines as justification) and not answering in substance.

Major deficiencies in risk assessment also render it impossible to carry out effective post-market monitoring of the genetically engineered plants as required by European regulations such as Regulation 178/2002, Directive 2001/18 and Regulation 1829/2003.

Review of market authorisation for MON80934 x MON88017 is of major relevance for protection of human and animal health and the environment. The deficiencies of the risk assessment of this product are various: EFSA overlooked very relevant literature, did not request detailed investigations and accepted documents from industry that lack independent quality controls.

Beyond this specific product the issues as discussed also concernin the general the standards for risk assessment for food and feed and the environmental risk assessment.

Testbiotech and GeneWatch UK urge the European Commission to withdraw market authorisation for MON89034 x MON88017 and to reconsider and amend the current standards of EFSA to assure

a sufficiently high level of the protection of human and animal health and the environment. This is a formal request for internal review of the authorisation under Article 10 of Regulation (EC) No. 1367/2006.