EUROPEAN COMMISSION
HEALTH & CONSUMERS DIRECTORATE-GENERAL

Brussels, 18.11.2011
C(2011) 8551 final

Dear Ms Wallace,

Subject: **Request for internal review of the Commission Decision on the authorisation of the genetically modified maize MON 89034 x MON 88017 under Article 10 of Regulation (EC) No. 1367/2006**

Thank you for your letter dated 25 July 2011 whereby you requested, on behalf of your organisations, the Commission to review its Decision 2011/366/EU[1], dated 17 June 2011, authorising the placing on the market of genetically modified maize MON 89034 x MON 88017 under Regulation (EC) No 1829/2003 of the European Parliament and of the Council on genetically modified food and feed[2]. A separate letter has been addressed to TestBiotech because the Commission considers its request inadmissible.

Your request for internal review has been lodged on the basis of Title IV of Regulation (EC) No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies[3].

You argue that this Commission Decision is unlawful because of the following reasons:

(1) insufficient standards for risk assessment;

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[1] OJ L 163, 23.6.2011, p. 55–58

[2] OJ L 268, 18.10.2003, p. 1.
[3] OJ L 264, 25.9.2006, p. 13.

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(2) disregard of relevant scientific publications by EFSA;

(3) missing scientific quality standards in the documents prepared by industry;

(4) shortcomings in risk management.

Against this background, you argue that Commission Decision is unlawful because it infringes Article 4 (1) and (3) of Directive 2001/18/EC of the European Parliament and of the Council[4], Articles 1(a), 4 (3) and 5(3) of Regulation (EC) No 1829/2003 and Articles 5 (1), 14 (4), 18 (1), 22 (3) and 23 of Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 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[5].

The Commission however cannot follow this interpretation of the above mentioned Decision. Please find below the Commission answer to your allegations.

[4] OJ L 106, 17.04.2001, p.1

[5] OJ L 031 , 01/02/2002, p. 24

1. Insufficient standards for risk assessment

The strategy for the risk assessment developed by EFSA in collaboration with the Member States ensures a high level of protection of human health and the environment and is in line with international guidelines such as Codex Alimentarius and OECD.

In December 2008, the Council noted that the EU has a comprehensive framework for the authorisation of GMOs which aims at ensuring a high level of protection of the environment, human and animal health. In this context, the Council also indicated that it was necessary to continue processing applications without undue delays and respecting the relevant EU international obligations[6].

Even in the context of the application of the precautionary principle to which you make reference, the decision to authorise or not a product should be based on a risk assessment, as comprehensive as possible, and should be no more restrictive to trade than required to achieve the high level of protection provided by the Treaties (see for instance Article 7 of Regulation (EC) No 178/2002 on the precautionary principle).

The Commission constantly monitors the legislation for possible improvements. Currently the Commission is working on the development of the environmental risk assessment guidance based on the EFSA guidelines finalized last year or the development of a Regulation providing guidance for the submission of applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003.

1 a. Your allegations with regard to Bt proteins

MON 89034 x MON 88017 contains a unique combination of insecticidal proteins. In parts of this plant, a highly synthetic Bt toxin is produced. You consider that 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. According to you, EFSA omitted to consider this specific problem in the case of Cry1A.105 which is a synthetic Bt toxin, derived from a combination of at least two naturally occuring Bt toxins.

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[6] Conclusions of the Enviromental Council meeting of 4 December 2008. Link to the conclusions: http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressdata/en/envir/104509.pdf

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You suggest that since there is no native form of this combined protein, the safety of such protein can not be concluded by comparison with the ones from native Bt toxins used before.

Moreover, the mode of action of Bt toxins is, according to you, not fully understood, thus risks for human health can not be excluded by assumptions or considerations but only by empirical testing.

The risk of Bt proteins in question for human and animal health was extensively evaluated by the EFSA GMO Panel. Both, maize MON 89034 and MON 88017 were assessed and favourable EFSA scientific opinions were issued[7]. Contrary to your statement, specific toxicity studies were performed on the proteins Cry1A.105, Cry2Ab2 and Cry3Bb1 and the evaluations were therefore not made by comparison with the ones from native Bt toxins.. Neither proteins showed toxicity in acute oral toxicity studies in mice, nor did they show relevant similarities to known toxic or allergenic proteins in bioinformatics-supported comparisons of their amino acid sequences.

Therefore, in view of the EFSA analysis, the Commission can not accept your claims.

1.b. Your allegation on potential synergies that can enhance toxicity

You state that only interaction between the Bt toxins was investigated. Potential synergies with EPSPS proteins or with residues from herbicide spraying were left aside while according to you 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. These effects can also impact on human health before market authorisation.

Contrary to your statement, interactions between the Bt toxins and EPSPS proteins were investigated. In the framework of the assessment of maize MON 89034 x MON 88017, the EFSA GMO Panel concluded that, based on the known function and mode of action of the newly expressed proteins Cry1A.105, Cry2Ab2, Cry3Bb1 and CP4 EPSPS, the occurrence of interactions among these proteins are unlikely[8]. Neither the structure integrity of the insert in maize MON 89034 x MON 88017 nor the protein expression levels were found to be changed in comparison to the single events MON 89034 and MON 88017.

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[7] Scientific Opinion of the Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-CZ-2005-27) for the placing on the market of the insect-resistant and herbicide-tolerant genetically modified maize MON 88017, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. *The EFSA Journal* (2009) 1075, 1-28.
http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2005-280

Scientific Opinion of the Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-NL-2007-37) for the placing on the market of the insect-resistant and herbicide-tolerant genetically modified maize MON 89034, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. *The EFSA Journal* (2008) 909, 1-30.
http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2007-042

[8] Scientific Opinion of the Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-CZ-2007-39) for the placing on the mamrket of the insect-resistant and herbicide-tolerant genetically modified maize MON 89034 x MON 88017 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2010; 8(3); 1564.
http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2007-056

It has to be stressed that the EFSA GMO Panel has considered in its evaluation of the environmental risk assessment the potential interaction of the GM plant with non-target organisms. In the opinion on MON 89034 x MON 88017, it is stated that "Considering the scope of application (that excludes cultivation) and the intended uses of maize MON 89034 x MON 88017, the EFSA GMO Panel concluded that the exposure of the potentially sensitive non-target organisms to the Cry1A.105, Cry2Ab2 and Cry3Bb1 proteins is likely to be very low and of no ecological relevance." It added that "The EFSA GMO Panel evaluated whether the Cry1A.105, Cry2Ab2 and Cry3Bb1 proteins might potentially affect non-target organisms by entering the environment through manure and faeces from gastrointestinal tracts of animals fed maize MON 89034 x MON 88017."[9]

Therefore even where scientific publications cited by you could be considered in the context of the cultivation of maize MON 89034 x MON 88017, because the application by Monsanto did not consider cultivation in its original application, they are not relevant for the present application.

In light of the above, your allegations should therefore be rejected.

1.c. Interaction between the plant and the environment

You explain that it is necessary to explore the life cycle of the Bt proteins and the range of the possible variations and the impact factors on the rate of expression which was not done in this case, despite the fact that Bt content in the plants showed huge variations.

Moreover, according to you, 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).

According to you, 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. You suggest a system to investigate the genetic and metabolic reactions of the plants to changing environmental conditions – before release into the environment.

Allegedly, 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.

Contrary to your statement, the range of possible variations of protein expression was assessed. The expression levels of Cry1A.105, Cry2Ab2, Cry3Bb1 and CP4 EPSPS proteins in the grains of maize MON 89034 x MON 88017 have been demonstrated to be comparable with those of the single events. Tissue samples for analysis of the levels of newly expressed proteins were collected from five field trials conducted in USA during 2005. The trials were located within the major maize-growing regions of the USA and provided a variety of environmental conditions.

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[9] Page 21-22 of the Scientific Opinion of the Panel on Genetically Modified Organisms on MON 89034 x MON 88017

The range of variation of protein expression was thus duly assessed and EFSA did not identify the need to request further experiments in this aspect.

According to the GMO Panel the Southern analysis of maize MON 89034 and MON 88017 and maintenance of the phenotype indicated genetic and phenotypic stability of the events over multiple generations. As conventional breeding methods were used in the production of maize MON 89034 x MON 88017, no additional genetic modification was involved. The integrity of the structures of the single events in the stack was demonstrated by Southern analyses.

In addition a series of field trials with maize MON 89034 x MON 88017 were conducted across 5 USA locations in 2004. These field trials data did not show changes in plant characteristics that indicate altered fitness and invasiveness of maize MON 89034 x MON 88017. It should be stressed that in total 10 trials have been conducted in these two years (2004-2005).

The Commission therefore considers that EFSA assessed all the above mentioned elements and does not share your allegations.

1.d. Field trials

You further claim that the plants were not sprayed with the herbicide formulations during the field trials and that the stacked events were not compared with the parental lines during the field trials.

EFSA has addressed the issue of non sprayed plants in its opinion. The EFSA GMO Panel previously concluded that the maize events MON 89034 and MON 88017 (the latter treated and untreated with the respective target herbicide) were compositionally and agronomically equivalent to their respective conventional counterparts, except for the newly introduced traits. The EFSA GMO Panel noted the fact that treatment of the single maize event MON 88017 with the target herbicide to which it is tolerant did not affect its agronomic and compositional characteristics compared to untreated maize MON 88017 plants. The single maize event MON 89034 is not a herbicide tolerant event and thus the spraying treatment has no application in this case. Given that the single events were compared with their respective conventional counterpart and were found to be equivalent with their counterpart, EFSA did not consider it necessary to compare the stack events with the parental lines.

The EFSA GMO Panel, therefore, accepted the design of field trials with maize MON 89034 x MON 88017 without inclusion of the single events and treatment with the target herbicide.

It therefore appears that EFSA has taken into consideration the necessary elements for its assessement in accordance with its obligations under the relevant provisions of EU Law and that your allegations should, hence, be refuted.

1.e. Maximum residue levels

You claim that no assessment was made of risks stemming from residues from spraying with the pesticide formulations and their metabolites and that the recent overviews of scientific literature show the toxicity of glyphosate, its metabolites and its additives need to be re-evaluated.

The scope of the application by Monsanto is limited to food and feed uses, import and processing and excludes cultivation. The risk assessment with the purpose of setting

maximum residue levels in imported commodities falls within the scope of Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and is independent of the risk assessment conducted under the provisions and requirements of Regulation (EC) No 1829/2003 and Directive 2001/18/EC of the European Parliament and of the Council[10]. However, before authorising a new GM food and feed under Regulation (EC) 1829/2003, the Commission always ensures that an MRL has been fixed for the herbicide residue in question and its metobolites on the concerned products. For more details, please see: http://ec.europa.eu/sanco_pesticides/public/index.cfm#

Your allegation is in this respect not pertinent to the evaluation of GMOs and should therefore be refuted.

1.f. Feeding studies

You suggest that as the analysis of the EFSA opinion and of the data from industry allegedly shows, the relevant risks were, according to you, 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 MON 89034 x MON 88017, you consider that 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. You further remark that rats fed with MON 89034 have allegedly showed signs that their kidney function might be impacted. You also say that 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 and no endocrinological studies performed to investigate potential impacts on the reproductive system.

Sub-chronic 90-day feeding studies with maize MON 89034 and MON 88017 were provided in previous applications. Concerning MON 89034, the EFSA GMO Panel considered the urinary bladder calculi as well as the associated kidney alterations as incidental findings which were not related to administration of maize MON 89034. The same applies to the nephroblastomas, a very rare tumour of the kidney, which were observed in two female animals of the control group. Therefore the GMO Panel concluded that maize MON 89034 and derived products are unlikely to have any adverse effects on human and animal health in the context of its intended uses.

As far as maize MON 88017 is concerned, the GMO Panel concluded that the 90-day feeding study in rats gave no indication of any adverse effects. Therefore MON 88017 and derived products are unlikely to have any adverse effects on human and animal health in the context of its intended uses.

A 90-day feeding study on MON 89034 x MON 88017 was not requested by EFSA since the GMO Panel considered the outcomes of 90-day rat feeding studies with grains of the singleevents and other relevant factors. No adverse effects were observed in these studies. No new genes in addition to those present in the parental maize varieties have been introduced in maize MON 89034 x MON 88017. Neither the structural integrity of the insert in maize MON 89034 x MON 88017 maize nor the protein expression levels have been found to be changed in comparison to the single events MON 89034 and MON 88017. Moreover, the composition

[10] OJ L 106, 17.04.2001, p.1

of maize MON 89034 x MON 88107 has been found to be equivalent to its conventional counterpart and commercial non-GM maize varieties. The EFSA GMO Panel considered all the data available for maize MON 89034 x MON 88017, and the newly expressed proteins Cry1A.105, Cry2Ab2, Cry3Bb1 and CP4 EPSPS, and is of the opinion that interactions between the single maize events that might impact on the food and feed safety of maize MON 89034 x MON 88017 are unlikely.

This approach is in line with the Report of the EFSA GMO Panel Working Group on Animal Feeding Trials which states " In the situation where molecular, compositional, phenotypic, agronomic and other analyses have demonstrated equivalence between the GM plant derived food and feed and their near isogenic counterpart, except for the inserted trait(s), and do not indicate the occurrence of unintended effects, experiences with GM plants modified for agronomic input traits have demonstrated that the performance of 90-day feeding trials with rodents or feeding trials with target animal species have provided little if anything to the overall safety assessment (except for added confirmation of safety).[11]

Concerning the other studies it has to be noted that they are requested on a case-by-case basis, in line with the requirements set by the EU legislation for the risk assessment, and were not considered as being necessary for these GMOs. This approach is in line with the EFSA report which states that " In cases where structural alerts or other information are available about the possibly altered occurrence of food components in the GM food and feed compared to its counterpart, the performance of specific toxicological testing, e.g. chronic, reproductive, etc., should be considered case-by-case, but preferentially only for the single substance of concern."

Given the above-mentioned, the Commission remarks that EFSA was perfectly in line with the requirements of Regulation (EC) No 1829/2003 as regards feeding studies. In this regard, please note that there is no requirement in the EU legislation for EFSA to request to conduct a 90-day feeding study on the hybrid. As explained above, they are requested on a case-by-case basis and especially with regard to the present case, such study has been conducted for the single events. Furthermore, contrary to your allegations, no adverse effects were observed in these studies. Therefore, the Commission refutes your allegations on this issue and considers there were no errors in EFSA's assessments, given the above analysis.

1.g. Your claims on allergenicity

In the area of allergenic risks, you claim that 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.

You also consider that 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

With regard to your concerns on alleged uncertainties of the methods for investigation of allergenic risks as described in the Codex Alimentarius, light should be cast to the fact that the

[11] http://www.efsa.europa.eu/en/efsajournal/doc/1057.pdf

Codex is funded by the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO) and has 180 member governments, including the European Union as a member organisation and all Member States.

First of all, the Commission considers that the allergenicity of maize MON 89034 x MON 88017 was duly assessed by EFSA which concluded that it is unlikely that potential interactions occur that might change the allergenicity of the newly expressed proteins. The impact of the proteins like Cry1Ac on the immune system mentioned by you is not supported by any scientific argumentation.Your studies have been sent for consultation to EFSA which was of the opinion that adjuvanticity might be an example of some immunological reactions triggered by Cry proteins. Nevertheless, the EFSA GMO Panel considers that the issue on adjuvanticity does not represent a safety concern for consumers of Cry proteins maize derived foods from maize MON 89034 x MON 88017. An adjuvant effect of Cry proteins has indeed been demonstrated in animals; however, the studies were performed using relatively high doses and routes of administration that are different from those occurring during intake of maize containing Cry proteins by human consumers. In addition, the adjuvant effect observed enhanced the immune response to co-administered proteins but it was not shown to induce an allergic reaction or an IgE response. Therefore, the GMO panel does not consider that there is a safety concern for the health of humans or animals that consume food/feed derived from maize MON 89034 x MON 88017 containing Cry proteins.

Again, given the above-mentioned, the Commission fails to see any objective basis for your claims and has therefore to reject them.

1.h. Other remarks on the risk assessment

According to you, 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.

Contrary to your statement, it should be highlighted that the EFSA GMO Panel considered the nature and magnitude of the observed compositional differences between maize MON 89034 x MON 88017 and its conventional counterpart in the light of the field trial design, biological variation and level of the studied compounds in commercial non-GM maize varieties, and provided a scientific rationale for concluding that maize MON 89034 x MON 88017 is compositionally equivalent to its conventional counterpart and commercial non-GM maize varieties except for the introduced traits. Therefore, you failed to establish that EFSA's assessment was flawed in this regard.

1. i. You further claim that no investigation was conducted for DNA traces in animal tissue after feeding.

It has to be noted that no assessment of DNA traces in animal tissue after feeding is requested by the EFSA guidance on the risk assessement of GM plants because such an assessment is not pertinent for the evaluation of safety under Regulation (EC) No 1829/2003.

In this regard, the EFSA statement on the fate of recombinant DNA or proteins in meat, milk and eggs from animals fed with GM feed states that biologically active genes and proteins are common constituents of foods and feed in varying amounts. After ingestion, a rapid degradation into short DNA or peptide fragments is observed in the gastrointestinal tract of animals and humans. To date, a large number of experimental studies with livestock have

shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals like broilers, cattle, pigs or quails.[12] It should also be noted that there is no such requirement in any international guidance either.

Given this rapid degradation of these traces is observed, there is again no basis to accept your allegations that EFSA's assessment was flawed.

1.j. You complain that no investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals.

The impact of a permanent ingestion of this GM maize on the intestinal microbial composition in human and animals has not been assessed as it is not requested by the EFSA guidance on the risk assessment of GM plants. A comparative analysis showed the equivalence of maize MON 89034 x MON 88017 to its conventional counterpart and commercial non-GM maize varieties and EFSA concluded on the basis of the studies provided in the application, that this maize and its derived products are unlikely to have any adverse effects on human and animal health in the context of its intended uses.

Again, as it is the case for your claims under 1.i. there is no basis to accept your allegations that EFSA's assessment was flawed, for the same reasons.

1.k. Additionally, you esteem that no assessment was made of combinatorial effects with other genetically engineered plants used in food and feed

In line with the EFSA guidance on the risk assessment of GM plants and draft EC guidelines, the risk assessment of GM plants and derived food and feed follows, as you already know, a comparative approach, i.e. the derived food and feed are compared with their non-GM near isogenic counterparts in order to identify differences which subsequently are assessed with respect to their potential impact on the environment, safety for humans and animals, and nutritional quality (Concept of Comparative Safety Assessment).

The EFSA Panel concluded that the product in question is as safe as its conventional counterpart and did not consider it necessary to request additional experimental data related to combinatorial effects. The Commission considers that EFSA has conducted its assessment accordingly and that you do not confer any elements to prove that such additional experimental data would be required.

2. Alleged disregard of relevant scientific publications by EFSA

Regarding all publications mentioned in your request the Commission considers following also consultation of EFSA, that they are of no scientific relevance for this specific product and its uses.

Please find attached to this letter a list with the publications and reports not cited in the previous letter sent by Testbiotech of 28 March 2011 on application MON 89034 x MON 88017 with EFSA comments for each of these publications.

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[12] http://www.efsa.europa.eu/en/efsajournal/doc/744.pdf

3. Missing scientific quality standards in the documents prepared by industry

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

According to you, this maize would need to be tested much more carefully for potential health risks. The market application of MON 89034 x MON 88017 is based on series of insufficient studies. You thus consider that EFSA should have rejected these dossiers as inadequate and flawed as they were allegedly never subjected to the scrutiny of independent quality controls.

During the risk assessment process, EFSA which is an independent institution, requests additional information from the applicant, on a case-by-case basis, if data provided in the application are not in accordance with the EFSA guidance or insufficient to assess the safety of a GMO. There is no legal obligation for the studies to be peer reviewed or published. Studies are available for the public upon request in accordance with EU legislation on public access requests[13]. It should also be highlighted that notwithstanding EFSA's role in informing the public mean and its purpose being to provide objective, reliable and easily understandable information, there is no legal obligation for EFSA to fully publish protocols used for conducting the measurements of the Bt toxins.

Usually before EFSA adopts the opinion, several requests of additional information are sent to the company. When the data provided are insufficient to assess the safety of a GMO, EFSA requests additional information and clarification from the petitioner including repetition of some studies.

EFSA presented its opinion on the maize MON 89034 x MON 88017 at the Standing Committee for Food Chain and Animal Health. Member States' and comments of the public were discussed and duly taken into account in the authorisation process.

The Commission considers that you do not confer any elements to prove that testing was not done in a reliable manner and as regards your allegations linked to lack of transparency, they could not be substantiated given that there is appropriate EU legislation (mentioned above) which ensures transparency for the citizens and which the Commission as well as all EU bodies comply with.

4. Shortcomings in risk management.

You claim that there is no plan for surveillance as required by European regulation that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.

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[13] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents (OJ L 145 , 31/05/2001 P. 0043 – 0048)

Article 5 (3) k of Regulation (EC) No 1829/2003 on GM Food and Feed explicitely provides that an applicant shall provide a proposal for post-market monitoring regarding use of the food for human consumption only when appropriate.

The GMO Panel concluded that no data have emerged to indicate that maize MON 89034 x MON 88017 is any less safe than its conventional counterpart. In addition, maize MON 89034 x MON 88017 is, from a nutritional point of view, substantially equivalent to commercial non-GM maize. Therefore, and in line with the EFSA guidance on the risk assessment of GM plants (2006), the EFSA GMO Panel concluded that post-market monitoring of the GM food/feed was not necessary. Based on EFSA's evaluation the Commission has decided not to request such monitoring.

4.a. According to you, no specific detection method for the stacked event was made available, and therefore it would be difficult to distinguish it from the parental lines for monitoring purposes.

In accordance with Commission Regulation 641/2004[14] Art. 3(e) the applicant should provide a description of a method(s) of detection, sampling and event-specific identification of the transformation event, as provided for in Articles 5(3)(i) and 17(3)(i) of Regulation (EC) 1829/2003[15] in accordance with Annex I to this Regulation.

For GMOs with stacked events, the Joint Research Centre, as European Union Reference Laboratory (EURL) for GM food and feed, carries out a verification study to assess the performance of the event-specific methods, previously validated on parental lines, to detect and quantify the transformation event(s) on DNA from the GMO containing two or more transgenic events. The results of JRC verification are available at: http://gmo-crl.jrc.ec.europa.eu/. Authorisation decisions for GMOs with stacked events always include the detection methods for the events present in the GMO at stake, the conditions in which validation of the methods is taking place and the reference material used - as it is the case for the present stack event. The detection methods are always tested on material produced from a GMO with the stacked events as part of validation process. For the single events and the stacks mentioned, the validation methods are available on the above mentioned website.

In addition, it should be emphasized that whereas Regulation (EC) 1830/2003[16] on traceability and labelling of GMOs ensures availability of the appropriate information throughout the entire EU food and feed chain by a compulsory system of transmission and holding the information, for a period of five years, all of which has to be applied by all operators, EU legislation does not define the stages of the production chain at which genetic material has to be detectable.[17]

4.b. You further suggest that monitoring of health effects should include the risks associated with the spraying of glyphosate formulations and their residues in the plants.

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[14] OJ L 102, 06.04.2004

[15] OJ L 268, 18.10.2003

[16] OJ L 268,18.10.2003

[17] This explanation was already provided by the Commission to the Written Question P-2852/10EN

As already mentioned earlier, the risk assessment with the purpose of setting maximum residue levels (or import tolerances) in imported commodities falls within the scope of Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin exactly because it is not linked to the assessment of the genetic modification as such.

Conclusion

In light of the above-mentioned, the Commission can accept none of your allegations on the basis of which you wish to substantiate that the Commission in granting the authorisation in question was in breach of the Articles you mention and especially of Article 4(3) of Regulation (EC) No 1829/2003 and of Articles 5 (1) and 14 of Regulation (EC) No 178/2002 in the sense that it has not been demonstrated that the products in question have any adverse effects on human and animal health or the environment. Given the above mentioned analysis on the scientific aspects of the risk assessment, the Commission considers that you failed to confer any elements to prove that EFSA's assessment had any flaws or that any of the requirements as regards the risk assessment were breached.

With regard to you allegations of breach of Article 14 of Regulation (EC) No 178/2002 which provides as requirements that :

(a) the probable immediate and/or short-term and/or long-term effects of that food on the health of a person consuming it, but also on subsequent generations;

(b) the probable cumulative toxic effects;

(c) the particular health sensitivities of a specific category of consumers where the food is intended for that category of consumers."

and of Article 4 (1) and (3) of Regulation (EC) No 1829/2003, namely:

(a) that the food shall not have adverse effects on human health, animal health or the environment;

(b) it shall not mislead the consumer;

(c) differ from the food which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for the consumer."

The Commission considers that they were respected.

In this regard, the following elements extracted from the detailed answers to your specific questions on the risk assessment, should be highlighted:

- Neither proteins showed toxicity in acute oral toxicity studies in mice, nor did they show relevant similarities to known toxic or allergenic proteins in bioinformatics-supported comparisons of their amino acid sequences. MON 89034 and MON 88017 are equivalent to their conventional counterparts and commercial non-GM maize varieties included in the study

- The EFSA GMO Panel considered all the data available from maize MON 89034 x MON 88017, and the newly expressed proteins Cry1A.105, Cry2Ab2, Cry3Bb1 and CP4 EPSPS, and is of the opinion that interactions between the single maize events

that might impact on the food and feed safety of maize MON 89034 x MON 88017 are unlikely.

- With regard to its safety to human and animal health, a comprehensive toxicological assessment has been carried out by the EFSA GMO Panel who had initially assessed the single events MON 89034 and MON 88017 and subsequently, issued a scientific opinion on MON 89034 x MON 88017.

- The EFSA GMO Panel considered the nature and magnitude of the observed compositional differences between maize MON 89034 x MON 88017 and its conventional counterpart in the light of the field trial design, biological variation and level of the studied compounds in commercial non-GM maize varieties, and provided a scientific rationale for concluding that maize MON 89034 x MON 88017 is compositionally equivalent to its conventional counterpart and commercial non-GM maize varieties except for the introduced traits.

- The allergenicity of maize MON 89034 x MON 88017 was duly assessed by EFSA who concluded that it is unlikely that potential interactions occur that might change the allergenicity of the newly expressed proteins.

In the same line and in terms of the environmental assessment conducted for the purposes of the authorisation of this product, the Commission considers that the requirements provided for in Article 4 (1) and (3) of Directive 2001/18/EC were respected given that the EFSA GMO Panel concluded that the likelihood of unintended environmental effects as a consequence of spread of genes from its maize in Europe will not differ from that of the single maize events MON 88017 and MON 89034, or of other conventional maize varieties and considered that maize MON 89034xMON 88017 in the context of the intended uses. Additionally, the EFSA GMO Panel considered that given the scope of the application (that excludes cultivation) and the intended uses of maize MON 89034 x MON 88017, the exposure of the potentially sensitive non-target organisms to the Cry1A.105, Cry2Ab2 and Cry3Bb1 proteins is likely to be very low and of no ecological relevance.

Against this backround, the Commission considers that EFSA has duly performed its task as risk assessor in the sense of Articles 22 (3) and 23 of Regulation (EC) No 178/2002.

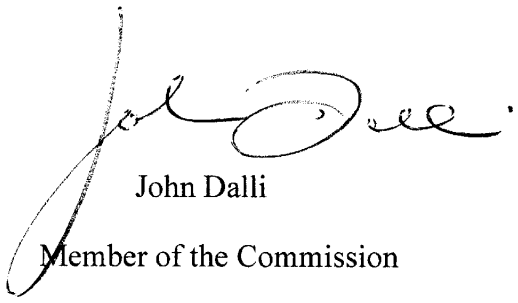
As regards the risk management, none of the elements that you have brought forward and especially in light of Article 5 (3) (k) and (i) of Regulation (EC) No. 1829/2003 and Article 18 of Regulation (EC) No 178/2002, can establish a breach of the risk management requirements and procedures in line with Regulations (EC) No 1829/2003 and Regulation (EC) No 178/2002 as the Commission has explained in detail above.

Therefore, the Commission does not share your analysis that there is a violation of the Laws you mention in your request as the risk assessment and risk management for the application of Monsanto were conducted accordingly.

As a consequence, the Commission considers that the Decision authorising the placing on the market of genetically modified maize MON 89034 x MON 88017 is in line with provisions of law regarding the environment and human and animal health and does not need to be amended by the Commission.

Should you not agree with the present reply, you may bring the matter before the Ombudsman or before the Court of First Instance if you have a complaint which falls within the conditions laid down in Articles 228 and 263 respectively of the Treaty on the Functioning of the European Union.

Yours sincerely,



John Dalli

Member of the Commission

Annex: "List with the publications and reports not cited in the previous letter sent by Testbiotech of 28 March 2011 on application MON 89034 x MON 88017 with EFSA comments for each of these publications".

Annex

Publications and reports not cited in the previous letter sent by Testbiotech on 28/3/2011 on application MON 89034 x MON 88017:

Benachour, N., Siphatur, H., Moslemi, S., Gasnier, C., Travert, C., Seralini, G. E. (2007) Time- and dose - dependent effects of Roundup on human embryonic and placental sells, Arch Environ Contam Toxicol 53:126-33

EFSA comment: Reference for the Pesticides not for GMOs.

Bruns, H. A., Abel, C. A., 2007, Effects of nitrogen fertility on Bt endotoxin levels in maize. Journal of Entomological Science, 42: 35-43.

EFSA comment: Reference of no safety concern. It is agreed that levels of expression can be influenced by various factors e.g. environmental factors

Chen, D., Ye, G., Yang, C., Chen, Y., Wu, Y., 2005, The effect of high temperature on the insecticidal properties of Bt Cotton. Environmental and Experimental Botany 53: 333–342

EFSA comment: Reference of no safety concern. It is agreed that levels of expression can be influenced by various factors e.g. environmental factors.

Diehn, S.H., De Rocher, E.J., Green, P.J., 1996, Problems that can limit the expression of foreign genes in plants: Lessons to be learned from B.t. toxin genes. Genetic Engineering, Principles and Methods 18: 83-99

EFSA comment: Reference of no safety concern. It is agreed that levels of expression can be influenced by various factors e.g. environmental factors.

Kramarz, P.E., de Vaufleurey, A., Zygmunt, P.M.S. & Verdun, C., 2007, Increased response to cadmium and Bt maize toxicity in the snail Helix aspersa infected by the nematode

Phasmarhabditis hermaphrodita. Environmental Toxicology and Chemistry 26: 73–79

EFSA comment: Might be relevant for a cultivation dossier but not for application 39

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.

EFSA comment: Unintended effected were not observed for Application 39. This publication is not related to maize but potato.

Nguyen, H. T., Jehle, J. A., 2007, Quantitative analysis of the seasonal and tissue-specific expression of Cry1Ab in transgenic maize Mon810. Journal of Plant Diseases and Protection 114:82

EFSA comment: Reference of no safety concern. It is agreed that levels of expression can be influenced by various factors e.g. environmental factors

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

EFSA comment: "Paganelli": Reference for the Pesticides unit.

Séralini, G.E., Mesnage, R., Clair, E., Gress, S., de Vendômois J.S., Cellier, D., 2011, Genetically modified crops safety assessments: present limits and possible improvements, Environmental Sciences Europe 2011, 23:10, doi:10.1186/2190-4715-23-10,

http://www.enveurope.com/content/23/1/10

EFSA comment: The report does not contain new scientific elements that could lead the EFSA GMO Panel to reconsider the outcome of Application 39.

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

EFSA comment: Reference of no safety concern

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

EFSA comment: Soberon et al., 2009, Testbiotech mentions that recent research shows that there are mechanisms for which bt toxins might cause toxicity in other species and even in mammals. In this publication, Soberon et al refer to mammalian cell lines which were transfected with cadherin receptors from lepidopteran insects M. sexta and B. mori. Cadherins are a superfamily of cell surface glycoproteins which are well known Cry-binding insect proteins. In both cases, the expression of these lepidopteran cadherin proteins in mammalian cell lines induced the susceptibility of these cell lines to Cry1Ab toxin, as expected. In the original publication by Tsuda et al 2003,which was cited in the Soberon et al study, it was shown that untransfected mammalian cells were not susceptible to Cry proteins.

Insect receptors to Cry proteins (cadherins) are not naturally present in mammalian cells.

Yoko TSUDA, Fumiki NAKATANI, Keiko HASHIMOTO, Satoshi IKAWA, Chikako MATSUURA, Takashi FUKADA, Kenji SUGIMOTO and Michio HIMENO. Cytotoxic activity of Bacillus thuringiensis Cry proteins on mammalian cells transfected with cadherin-like Cry receptor gene of Bombyx mori (silkworm). Biochem. J. (2003) 369: 697-703.

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

EFSA comment: Might be relevant for a cultivation dossier but not for AP39

Zeller S.L., Kalininal, O., Brunner, S., Keller B., Schmid B., 2010, Transgene x Environment Interactions in Genetically Modified Wheat,

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0011405

EFSA comment: Might be relevant for a cultivation dossier but not for AP39

Reports

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

EFSA comment: The report does not contain new scientific elements that could lead the EFSA GMO Panel to reconsider the outcome of AP39.

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

ESFA comment: The report does not contain new scientific elements that could lead the EFSA GMO Panel to reconsider the outcome of AP39

Then, C. & Potthof, C., 2009, Risk Reloaded – risk analysis of genetically engineered plants within the European Union, Testbiotech report,

http://www.testbiotech.de/sites/default/files/riskreloaded_engl_sc_0_0.pdf

ESFA comment: The report does not contain new scientific elements that could lead the EFSA GMO Panel to reconsider the outcome of Application 39.