London, 18 March 2013

IN THE GENERAL COURT OF THE EUROPEAN UNION

(1) TESTBIOTECH

(2) EUROPEAN NETWORK OF SCIENTISTS FOR SOCIAL AND ENVIRONMENTAL RESPONSIBILITY ("ENSSER")

(3) SAMBUCUS

Applicants

Represented by Kassie Smith QC and Julianne Kerr Stevenson, Barristers, Monckton Chambers

against

THE EUROPEAN COMMISSION **Defendant**

APPLICATION FOR A JUDICIAL REVIEW

Case No. [ ]

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I. INTRODUCTION

(a) Summary of the Claim

1. Testbiotech, ENSSER and Sambucus challenge the European Commission's decision, dated 8 January 2012 and received on 9 January 2012, refusing to review its Decision 2012/347 granting a market authorisation under Regulation 1829/2003 on genetically modified food and feed ("GM Regulation") to Monsanto Europe SA for its genetically modified soybean "MON 87701 x MON 89788" ("**the Soybean**"), which will hereinafter be referred to as the **"Commission Decision" [PD/7]**.

2. The Grounds upon which Testbiotech, ENSSER, and Sambucus challenge the Commission Decision are, in summary:

    a. **Ground A:** EFSA's assessment that the Soybean is 'substantially equivalent' to its appropriate comparators is unlawful, is based on a scientific assessment which was not carried out in accordance with its own guidance, and/or is based on a manifest error of assessment;

    b. **Ground B:** EFSA's failure to give adequate or any consideration to the potential synergistic/combinatorial effects between the Soybean and other factors, and/or to require an adequate toxicity assessment to be conducted is contrary to its own guidance, legal obligations and/or it constitutes a manifest error of assessment;

    c. **Ground C:** EFSA's failure to require an adequate immunological assessment to be carried out is contrary to its own guidance, legal obligations and/or constitutes a manifest error of assessment.

    d. **Ground D:** EFSA's determination that no post-market authorisation monitoring of the consumption of the Soybean is manifestly in error and/or is vitiated by the flaws identified by Grounds A to C.

(b) Relief sought

3. Testbiotech, ENSSER and Sambucus request that the Court:

    a. Declare the application admissible and well-founded;
    b. Annul the contested decision;
    c. Order the Commission to pay Testbiotech, ENSSER and Sambucus' costs; and

d. Order any other measure deemed appropriate.

(c) The Applicants' Standing

4. Testbiotech, Institute for Independent Impact Assessment of Biotechnology, is a not-for-profit making association registered in Germany at Frohschammerstr. 14 80807 Munich. It is included in the Register of Associations at the Amtsgericht Muenchen (local court, Munich) VR 202119 (see: Testbiotech's Statute/Articles of Association at **[PD/14]** and Registration Document at **[PD/13]**). Testbiotech was founded in 2008 by a group of experts and registered as a non-profit organisation to promote independent research and public debate on the impacts of biotechnology. Testbiotech is a centre of expertise concerned mainly with the ecological, social and ethical consequences of modern biotechnology. Special emphasis is placed on genetic engineering applications in agriculture.

5. Testbiotech is a non-governmental organisation ("NGO") which meets the criteria set out in Article 11 of Regulation 1367/2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Environmental Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies ("**the Aarhus Regulation**"). This fact was recognised by the Commission on page 1 of the Commission Decision **[PD/7]**.

6. ENSSER is a not-for profit organisation which is registered at Amtsgericht Braunschweig with Registration Number: 200636 **[PD/18]**. The purpose of the association is the advancement of science and research for the protection of the environment, biological diversity and human health against negative impacts of new technologies and their products. Its Date of Registration was 3 December 2009 (see: ENSSER's Statute at **[PD/15]**). Sambucus is a not-for profit environmental organisation which engages in a range of cultural activities (see: Sambucus' Statute **[PD/17]**). Sambucus is registered at: Vereinsregistereintragung Amtsgericht Walsrode, VR 170422Steuer.Nr. Its Registration Number is 40/201/11188 **[PD/19]**. Both of these organisations are NGOs which meet the criteria set out in Article 11 of the Aarhus Regulation. This fact was against recognised by the Commission on page 1 of the Commission Decisions sent to these organisations **[PD/10&12]**.

7. Accordingly, and under Article 12(1) of the Aarhus Regulation, Testbiotech, ENSSER and Sambucus are entitled to institute proceedings before the Court in accordance with the relevant provisions of the Treaty on the Functioning of the European Union ("TFEU"). For ease of reference all three Applicants are hereinafter referred to solely as Testbiotech.

II. APPLICABLE LAW

(a) Legislation regulating the placing of genetically modified food and feed on the European market

8. Regulation 1829/2003 on genetically modified food and feed ("**the GM Regulation**") **[AU/1]** provides that, in order to protect human and animal health, food and feed that consists of, contains, or is produced from genetically modified organisms should undergo a risk and safety assessment before it is placed on the market in the European Union.

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

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

    a. "*have adverse effects on human health, animal health or the environment*": Articles 4(1)(a) and 16(1)(a) GM Regulation; or

    a. *"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"* and/or *"differ from feed which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for animals or humans"*: Articles 4(1)(c) and 16(1)(d) respectively;

    b. Be placed on the market "*unless it is covered by an authorisation granted in accordance with"* the GM Regulation: Articles 4(2) and 16(2) GM Regulation.

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

    a. "*a copy of the studies, including, where available, independent, peer-reviewed studies, which have been carried out and any other material which is available to demonstrate*

[1] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC

that the food complies with the criteria referred to in Article 4(1) [/16(1)]": Articles 5(3)(e) and 17(3)(e) GM Regulation; and

b. "*either an analysis, supported by appropriate information and data, showing that the characteristics of the food are not different from those of its conventional counterpart, having regard to the accepted limits of natural variations for such characteristics and to the criteria specified in Article 13(2)(a), or a proposal for labelling the food...*": Articles 5(3)(f) and 17(3)(f) GM Regulation.

12. Article 5(5) also provides that the application must be accompanied by:

> *"(a) the complete technical dossier supplying the information required by Annexes III and IV to Directive 2001/18/EC and information and conclusions about the risk assessment carried out in accordance with the principles set out in Annex II to Directive 2001/18/EC or, where the placing on the market of the GMO has been authorised under part C of Directive 2001/18/EC, a copy of the authorisation decision;*
>
> *(b) a monitoring plan for environmental effects conforming with Annex VII to Directive 2001/18/EC, including a proposal for the duration of the monitoring plan; this duration may be different from the proposed period for the consent.*

13. The application is then considered by the European Food Safety Authority, which will provide an opinion, among other matters, on whether the food/feed complies with the criteria referred to in Articles 4(1) / 16(1): Articles 6(3)(a) and 18(3)(a) GM Regulation.

14. In preparing its opinion, the Authority must consult the national competent authorities of the Member States: Articles 6(4) and 18(4) GM Regulation.

15. On the basis of the opinion of European Food Safety Authority, any relevant provisions of Union law and other legitimate factors relevant to the application under consideration, the Commission produces a draft decision: Articles 7(1) and 19(1) GM Regulation.

16. The Commission's draft decision is submitted to the Standing Committee on the Food Chain and Animal Health. This Standing Committee assists the Commission in accordance with the procedure outlined in Article 5 of Decision 1999/468 laying down the procedures for the exercise of implementing powers conferred on the Commission: Articles 7(3), 19(3) and 35(2) GM Regulation. This provides for the Standing Committee to issue an opinion on the application. If the opinion is in accordance with the Commission's draft decision the Commission adopts the decision. If it is not, the Commission has to submit a proposal to the Council: Article 5(3) and 5(4) of Decision 1999/468. If the Council neither adopts nor opposes the proposal within the relevant period, the Commission adopts the decision: Article 5(6) of Decision 1999/468.

(b) Risk assessment of applications for authorisations under the GM Regulation

17. The European Food Safety Authority **("EFSA")** was established by Regulation 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (**"the Food Safety Regulation"**) **[AU/3]**.

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

    a. The "General Objective" of "*a high level of protection of human life and health and the protection of consumers' interests*": Article 5 of the Food Safety Regulation (reflected in Recital (3) ;

    b. The principle of "Risk Analysis". According to Article 6 of the Food Safety Regulation (emphasis added):

    > *"(1) In order to achieve the general objective of a high level of protection of human health and life, food law shall be based on risk analysis except where this is not appropriate to the circumstances or the nature of the measure.*
    >
    > *(2) Risk assessment shall be based on the available scientific evidence and undertaken in an independent, objective and transparent manner."*

    c. The "Precautionary Principle". According to Article 7(1) of the Food Safety Regulation:

    > *"In specific circumstances where, following an assessment of available information, the possibility of harmful effects on health is identified but scientific uncertainty persists, provisional risk management measures necessary to ensure the high level of health protection chosen in the [Union] may be adopted, pending further scientific information for a more comprehensive risk assessment."*

19. The case-law of the General Court establishes that a "risk assessment" or "risk analysis" process entails the following (emphasis added):

    > *"...a scientific process which is commonly accepted as consisting, in so far as possible, in the identification and characterisation of a hazard, the assessment of exposure to the hazard and the characterisation of the risk..."*: Case T-475/07 *Dow AgroSciences Ltd v Commission*, judgment of 9 September 2011, at para. 146 **[AU/4]**; Case T-13/99 *Pfizer Animal Health v Council* [2002] ECR II-3305 at para. 145 **[AU/5]**; Case T-70/99 *Alpharma v Council* [2002] ECR II-3495 at para. 162 **[AU/6]**.
    >
    > *"In such a situation, 'risk' thus constitutes the degree of probability that the acceptance of certain measures or practices will adversely affect the interests safeguarded by the legal order.*

..."; Case T-475/07 *Dow AgroSciences Ltd v Commission,* judgment of 9 September 2011, at para. 147 **[AU/4]**; Case T-13/99 *Pfizer Animal Health v Council* [2002] ECR II-3305 at para. 147 **[AU/5]**.

"The responsibility for determining the level of risk which is deemed unacceptable lies, provided that the applicable rules are observed, with the [Union] institutions responsible for the political choice of determining an appropriate level of protection for society. ...": Case T-475/07 *Dow AgroSciences Ltd v Commission*, judgment of 9 September 2011, at para. 148 **[AU/4]**; Case T-13/99 *Pfizer Animal Health v Council* [2002] ECR II-3305 at para. 150-151 **[AU/5]**.

In determining that level of risk, the [Union] institutions are bound by their obligation, under the first subparagraph of [Article 168 TFEU], to ensure a high level of human health protection. ...": Case T-475/07 *Dow AgroSciences Ltd v Commission*, judgment of 9 September 2011, at para. 149 **[AU/4]**.

20. The GM Regulation was adopted with a view to achieving these General Principles. Recitals (2), (3) and (9) make clear (emphasis added) **[AU/1]**:

"(2) A high level of protection of human life and health should be ensured in the pursuit of [Union] policies.

(3) In order to protect human and animal health, food and feed consisting of, containing or produced from genetically modified organisms...should undergo a safety assessment through a [Union] procedure before being placed on the market within the [Union].

(9) The new authorisation procedures for genetically modified food and feed should...make use of the new framework for risk assessment in matters of food safety set up by [the Food Safety Regulation]. Thus, genetically modified food and feed should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard, to be undertaken under the responsibility of the European Food Safety Authority (Authority), of any risks which they present for human and animal health and, as the case may be, for the environment. This scientific evaluation should be followed by a risk management decision by the Community, under a regulatory procedure ensuring close cooperation between the Commission and the Member States."

21. In the context of these General Principles, EFSA is mandated to issue guidance on the manner in which it will assess applications for authorisations under the GM Regulation. In particular (emphasis added):

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

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

22. EFSA has issued two Guidance documents of particular relevance to the present case. These are the *"Guidance Document of the Scientific Panel on Genetically Modified Organisms for the Risk Assessment of Genetically Modified Plants and Derived Food and Feed"*, adopted on 24 September 2004, final edited version of 28 April 2006 (**"the Risk Assessment Guidance"**) **[AU/10]**, and the *"Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants containing stacked transformation events"*, adopted on 16 May 2007 **("the Stacked Event Guidance")** **[AU/11]**. These were the Guidance Documents which were in force at the relevant time as the relevant application was submitted on 27 August 2009 and included in the list of references to EFSA's Opinion on that application: see page 31.

23. EFSA also referred to its Scientific Opinion on the assessment of allergenicity of GM plants and microorganisms and derived food and feed, which was adopted on 30 June 2010 (**"the Allergenicity Opinion"**) **[AU/12]**.

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

(c) The standard of review applied by the General Court to challenges to risk assessments under the GM Regulation

25. The General Court has recently confirmed the standard of review it will apply in cases where the Commission has exercised a discretion whether to grant a market authorisation based on a technical assessment of the risks entailed by the product. In Case T-475/07 *Dow AgroSciences Ltd v Commission*, judgment of 9 September 2011, the General Court noted that the Institutions have a broad discretion in making complex technical assessments (at [150] **[AU/4]**), and that following the judgment of the Court of Justice in Case C-236/01 *Monsanto Agricoltura SpA* [2003] ECR I-8195 at [135] **[AU/7]** a judicial review of such an assessment *"...must be limited to examining whether it is vitiated by a manifest error of assessment or a misuse of powers or whether the legislature has manifestly exceeded the limits of its discretion."* The General Court went on to confirm, however, that (emphasis added):

> *"153. The abovementioned limits to the review by the European Union Courts do not, however, affect their duty to establish whether the evidence relied on is factually accurate, reliable and consistent, whether that evidence contains all the information which must be taken into account in order to assess a complex situation, and whether it is capable of substantiating the conclusions drawn from it (Case C-525/04 P* Spain v Lenzing *[2007] ECR I- 9947,*

paragraph 57, and Case C-405/07 P Netherlands v Commission *[2008] ECR I-8301, paragraph 55).*

154. ...it must be recalled that, where a Community institution has a wide discretion, the review of observance of guarantees conferred by the Community legal order in administrative procedures is of fundamental importance. The Court of Justice has had occasion to specify that those guarantees include, in particular for the competent institution, the obligations to examine carefully and impartially all the relevant elements of the individual case and to give an adequate statement of the reasons for its decision [internal references omitted]."

(d) Guidance of the European Food Safety Authority is capable of giving rise to legitimate expectations

26. It is a principle of EU law that legitimate expectations generated by the precise assurances of Union institutions are to be protected: see *inter alia,* Case T-326/07 *Cheminova v Commission* [2009] ECR II-2685 at para. 179 **[AU/8]** and the case-law cited therein.

27. A *"precise assurance"* for these purposes is (Case T-326/07 *Cheminova v Commission* [2009] ECR II-2685 at para. 179 **[AU/8]**) :

"Regardless of the form in which it is communicated, information that is precise, unconditional and consistent which comes from an authorised and reliable source constitutes such assurance".

28. It is established in the Court of Justice's case law that guidance documents issued by the Institutions are capable of meeting this test, and thus of giving rise to legitimate expectations: see Joined Cases C-189/02 P, C-205/02 P, C-208/02 P and 213/02 P *Dansk Rørindustri A/S and Others v Commission* [2005] ECR I-5425 at [209]-[211] **[AU/9]**. The Court held that (emphasis added):

"211. In adopting such rules of conduct and announcing by publishing them that they will henceforth apply to the cases to which they relate the institution in question imposes a limit on the exercise of its discretion and cannot depart from those rules under pain of being found, where appropriate, to be in breach of the general principles of law, such as equal treatment or the protection of legitimate expectations. It cannot therefore be excluded that, on certain conditions and depending on their conduct, such rules of conduct, which are of general application, may produce legal effects."

29. It is also established that where, as in this case, the regulatory context confers roles both on EFSA and on the Commission or Council, then a precise assurance by either body can give rise to a legitimate expectation (Case T-326/07 *Cheminova v Commission* [2009] ECR II-2685 at para. 181 **[AU/8]**; emphasis added):

"In the light of the role thus conferred on EFSA in the procedure for evaluating an active substance, it could be considered that both precise assurances by the Commission and those

made by EFSA in the course of the procedure for evaluating a substance are capable of giving rise to a legitimate expectation..."

30. It thus follows that guidance issued by the European Food Safety Authority is capable of giving rise to a legitimate expectation that that guidance will be followed.

III. OVERVIEW OF THE APPROACH TO RISK ASSESSMENT REQUIRED OF EFSA IN RELATION TO STACKED EVENTS

31. On receipt of an application EFSA must assess whether: (a) the appropriate comparator(s) to which the product has to be compared have been identified; and (b) the design and quantity of the field trials are such that the necessary data has been and/or will be obtained.

32. Second, EFSA's official guidance makes clear that once the appropriate comparator(s) have been identified and the necessary data collected, the risk assessment proceeds in two main steps (Risk Assessment Guidance, Section II(2), at p.12 **[AU/10]**; emphasis added):

> *"... [T]he safety assessment of GMOs consists of two steps, i.e. a comparative analysis to identify differences, followed by an assessment of the environmental and food/feed safety or nutritional impact of the identified differences, including both intended and unintended differences."*

(a) Preliminary Step: The identification of the appropriate comparators and field trial design

33. **Choice of Comparator:** For EFSA to be able to properly carry out the 'first step' of the risk assessment process, the comparative analysis, the appropriate comparator(s) must be identified.

34. As explained in Paragraph 11(b) above, an applicant for an authorisation is required by Articles 5(3)(f) and 17(3)(f) GM Regulation to provide "*an analysis, supported by appropriate information and data*" showing that its product's characteristics "*... are not different from those of its conventional counterpart, having regard to the accepted limits of natural variations for such characteristics...*".

35. A "conventional counterpart" is defined as "*a similar food or feed produced without the help of genetic modification and for which there is a well-established history of safe use.*": Article 2(12) GM Regulation. Under Articles 6(3)(a) and 18(3)(a), one of EFSA's tasks in order to prepare its opinion on whether the food/feed would have adverse effects on human health, animal health or the environment, is to verify that the information provided by an applicant complies with the requirements *inter alia* of Articles 5(3) and 17(3).

36. However, EFSA's official guidance also identifies further comparator(s) which are necessary in different circumstances in order to allow for a proper risk assessment to be carried out. In relation

to Stacked Events, EFSA's guidance makes clear that the comparators used must include the **parent plants or single events** (Stacked Events Guidance, Section 2; at p.2 **[AU/11]**; emphasis added):

> *"In line with the EFSA Guidance Document [the Risk Assessment Guidance], the most appropriate comparator(s) for the GMO plant containing the stacked event should include the GM parental materials as well as appropriate non-transgenic genotype(s)... The applicant should provide detailed information justifying the choice of comparators."*

37. Second, where the product is herbicide tolerant (such as in the case of the Soybean), EFSA's official guidance makes clear that 'step 1' of the safety assessment should include a comparison between the "conventional counterpart" and the modified product both with, and without, the use of herbicide (Risk Assessment Guidance, section 3(D)(7.2), at p.23 **[AU/10]**)

> *"In the case of herbicide tolerant GM plants, it is advisable to include both blocks of genetically modified plants exposed to the intended herbicide and blocks not exposed to the herbicide. This design would allow assessment of whether the expected agricultural condition might influence the expression of the studied parameters."*

38. The 'step 1' comparative analysis can also only be conducted on the basis of properly designed field trials. The product is grown in the field, alongside its "conventional counterpart" and the "appropriate comparator" plants. In designing the field trials, an applicant should ensure that any results generated can be correlated with the conditions in which the trials were conducted (Risk Assessment Guidance, Section 3(D)(7.2), at p.23 **[AU/10]**)

> *"... The field trials should be designed in order that sufficient statistical power is obtained to detect differences. ... The scale and number of experiments should be sufficient to reflect the experiences under field conditions in a range of geographic locations over more than one season. ... The field experiments should be adequately described, giving information on important parameters such as treatment of the field before sowing, date of sowing, climatic and other cultivation conditions during growth and time of harvest, as well as the conditions during storage of the harvested material. ..."*

39. The Stacked Events Guidance also observes that (section 3.4.4., p.5 **[AU/11]**; emphasis added)

> *"Differences in the specific cultivation, management and harvesting techniques between plants containing the stacked events and the parental lines, and any environmental impacts of such differences, should be evaluated and, where appropriate, supported by relevant data."*

(b) 'Step 1' - The Comparative Analysis

40. The plants generated by the fields trials are then tested and assessed (taking into account any differences in the environmental conditions in which they were grown) to determine their similarities/differences. In particular, EFSA must compare the different plants' (Risk Assessment Guidance, Section II(2), at p.13 **[AU/10]**):

a. Molecular characterisation;

b. Chemical composition;

c. Agronomic and morphological characteristics.

41. Section 7.4 of the Risk Assessment Guidance explains that (at p.25, **[AU/10]**; emphasis added)

> *"Compositional analysis represents a key component of the comparative approach for identifying unintended effects during the risk assessment process. However, unintended effects may also manifest themselves through, for example, changes in susceptibility to important pests and diseases, through morphological and developmental changes or through modified responses to agronomic and crop management regimes. Therefore, the comparison between the GM plants and their most appropriate comparators should address also plant biology and agronomic traits, including common breeding parameters (e.g. plant morphology, flowering time, day degrees to maturity, duration of pollen viability, response to plant pathogens and insect pests, sensitivity to abiotic stress).*

42. Section 3.2.2 of the Stacked Events Guidance also states (at p.4 **[AU/11]**):

> *"In addition to possible compositional modifications of stacked events, there may be changes to agronomic and phenotypic characteristics. These may be indicative of unintended effects such as modified susceptibility to biotic and abiotic stresses. Possible differences in phenotypic characteristics and agronomic properties of stacks must be assessed in field trials over at least one season, as indicated above. Again, on a case-by-case basis, additional information on agronomic traits of the stacked events may be required from additional field trials."*

43. Where differences are identified under 'step 1', these will require further investigation – 'step 2' - unless they are consistent with *"the accepted limits of natural variations for such characteristics..."*: Articles 5(3)(f) and 17(3)(f) GM Regulation. If they are consistent, the plant will be found to be **substantially equivalent** to its comparators.

44. EFSA's guidance states that the *"accepted limits of natural variations"* may be determined by two methods (Risk Assessment Guidance, Section 3(D)(7.1), at p.23 **[AU/10]**; emphasis added):

> *"The data for commercial varieties used in the comparison may be generated by the applicant and/or complied from the literature. The databases used for comparison should be specified. When using literature data, however, they have to be adequately assessed for quality (e.g. type of material analyzed, analytical method used). Ranges as well as mean values should be reported and considered..."*

45. If the differences are outside the *"natural variations"* for the plant, then further investigations are conducted into the biological significance of those differences. This is to assess the unidentified differences *"specifically with respect to their safety, nutritional impact and environmental impact"*: Risk Assessment Guidance, section 2, at p.14 **[AU/10]**. This is one part of 'step 2' of the safety assessment.

(c) 'Step 2' - The Safety Assessment

46. As noted above, the safety assessment covers both the unintended and the intended differences between the plant and its comparators. It is important to note that a determination of substantial equivalence is not sufficient to displace the need for a safety assessment, as recognised by Recital (6) of the GM Regulation (emphasis added):

> *"... substantial equivalence is a key step in the procedure for assessment of the safety of genetically modified foods, it is not a safety assessment in itself..."*

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

48. EFSA has indicated that the circumstances in which it will require a toxicological investigation of the whole food/feed are (Risk Assessment Guidance, section 3(D)(7.8.4), at pp.29-30 **[AU/10]**; emphasis added):

> *"If the composition of the GM plant is modified substantially, or if there are any indications for the potential occurrence of unintended effects, based on the preceding molecular, compositional or phenotypic analysis, not only new constituents should be tested. In such a case, the testing programme should include at least a 90-day toxicity study in rodents...*
>
> Or
>
> *In the case of complex genetic modifications involving the transfer of multiple genes, the potential risk(s) of possible interactions between the express proteins new metabolites and original plant constituents should be assessed. The outcome of the molecular analysis and knowledge of the mode of action of the newly expressed proteins may provide indications for possible synergistic interactions, as well as information on the response to combined administration of proteins to target organisms and regarding effects on the activity of target enzymes. Generally, feeding trials with this type of GM foods/feeds is requested in order to assess the impact of consumption on human and animal health. On a case-by-case basis this is also applicable to food and feeds derived from GM plants obtained through traditional breeding of parental GM lines (combined events)."*

49. In the latter case, the Stacked Events Guidance does explain that: *"Where all single events have been assessed, the risk assessment should focus mainly on issues related to ... (c) potential interactions between events"* Stacked Events Guidance section 2 at p.2 **[AU/11]**; see also section 3.1.2 at p.3 **[AU/11]**.

50. However, the Stacked Events Guidance confirms that in relation to "possible interactions", or synergistic effects, between the proteins (Stacked Events Guidance section 3.3.1 at p.4 **[AU/11]**):

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

51. A "synergistic effect" is an effect which shows a higher efficacy (e.g. in toxicity levels) than can be predicted from the efficacy of its single compounds i.e. it is when the working together of two compounds or biological elements produce a result greater than the sum of their individual effects.

52. **Allergenicity assessment:** As noted above, As noted above, at page 4 of section 3.3.1 of the 2007 Stacked Event Guidance it is stated that **([AU/11];** emphasis added):

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

53. Further, EFSA's Scientific Opinion on the assessment of allergenicity of GM plants and microorganisms and derived food and feed (EFSA Journal, 8(7):1700) which was published on 30 June 2010 ("**the Allergenicity Opinion**") recognises the need to assess **adjuvanticity**. In particular, the Allergenicity Opinion states that (Allergenicity Opinion, section 1.10.5 of Annex 1, p.48 **[AU/12]**):

"When a food contains a substance known to functionally or structurally resemble a known strong adjuvant, or to belong to a class of proteins known often to have allergy adjuvant activity (e.g. bacterial toxins) the possibility of adverse immune responses being caused by the adjuvant should be considered."

54. In support of this approach, EFSA cites scientific literature showing that inserted proteins in stacked event plants can have an impact upon the immune system. In particular, in discussing potential methods for screening, it cites animal models that may be used to assess adjuvanticity, relying on a variety of sources in scientific literature which range in date of publication from 1999 to 2009 (section 6.2.4, Annex 6, at pp.155-156 **[AU/12]**).

55. Thus, scientific literature has been available at all relevant times confirming that genetically modified food and feed **can** potentially impact adversely on human health and animal health by stimulating immune responses.

56. Moreover, it is worth noting that EFSA has also recognised the need to consider the potential impact of genetically modified food and feed on the immune systems of humans and animals in its updated Guidance for risk assessment of food and feed from genetically modified plants, adopted on 14 April 2011 (after Monsanto submitted its application but before EFSA adopted its Opinion) ("**the 2011 Guidance**") (2011 Guidance, section 3.1.5.3, at p.28 **[AU/13]** emphasis added):

> "*Adjuvants are substances that, when co-administered with an antigen increase the immune response to the antigen and therefore might increase as well the allergic response. In cases where known functional aspects of the newly expressed protein or structural similarity to known strong adjuvants may indicate possible adjuvant activity, the possible role of these proteins as adjuvants should be considered. As for allergens, interactions with other constituents of the food matrix and/or processing may alter the structure and bioavailability of adjuvant and this modify its biological activity (EFSA, 2010c).*"

57. **Effects of Processing:** Section 7.3 of the 2006 Risk Adjustment Guidance states that: *"Additional analysis of processed products (food/feed, food ingredients, feed materials, food/feed additives or food flavourings), may be required on a case-by-case basis and when justified scientifically (see also Section III, D 7.6). The analyses should preferably be carried out according to appropriate quality standards"* **[AU/10].**

IV. FACTUAL BACKGROUND

58. The genetically modified soybean "MON 87701 x MON 89788", the "**Soybean**", is a hybrid product. It is created by traditional breeding methods, used to combine the genetic material of two parent plants: soybean MON 87701 and soybean MON 89788 ("**the Parents or the Single Events**").

59. Both Parents are themselves genetically modified:

    a. MON 87701 is a soybean which has had its DNA sequence modified through the insertion of the insecticide protein "Cry1Ac". It was authorised by Commission Decision 2012/83 **[PD/8]**.

    b. MON 89788 is a soybean which has had the DNA sequence for glyphosphate herbicide resistance based on the protein "CP4 EPSPS" inserted into its Genome. It was authorised by Commission Decision 2008/933 **[PD/9]**.

60. "Cry" proteins are toxins derived from the bacterium *Bacillus thuringiensis.* This is a gram-positive soil dwelling bacterium. The Cry toxins can be extracted and used as a biological pesticide. These toxins are also commonly referred to as "Bt toxins".

61. Glyphosate is the active ingredient in some agricultural herbicides. Glyphosate kills plants by inhibiting the enzyme EPSPS. This enzyme catalyses a critical step in the shikimic acid pathway for the biosynthesis of aromatic amino acids in plants and microorganisms, and its inhibition leads to reduced protein synthesis and plant growth. The CP4 EPSPS protein has a low affinity for the glyphosate compared to the wild-type EPSA enzyme which allows plants treated with glyphosate-based herbicides to continue to grow i.e. it makes them resistant to herbicides.

62. The Soybean thus combines the insecticide traits of MON 87701, and the herbicide resistant traits of MON 89788. As it combines the modified genes of both Parents, it is called a "**stacked event**".

63. The proteins Cry1Ac and CP4 EPSPS are collectively referred to below as "**the Proteins**".

64. Monsanto Europe SA ("**Monsanto**") filed application EFSA-GMO-NL-2009-73 ("**the Application**") in the Netherlands, seeking authorisation under the GM Regulation for the Soybean and its derived products for food and feed uses, import and processing in the European Union **[PD/1]** and **[SU/1]**. The Application excludes cultivation within the EU.

65. The Soybean, and the derived products, that Monsanto applies to bring into the EU are genetically modified organisms, or are food/feed containing genetically modified organisms, within Article 2 of Directive 2001/18 and Article 2(5) of the GM Regulation. The Soybeans are biological entities capable of replication or of transferring genetic material, and are therefore "organisms" within Article 2(1) of Directive 2001/18. Their genetic material has been altered in a way that does not occur naturally, within Article 2(2) of Directive 2001/18. Accordingly, the plant has been notified to the Commission under Part B of Directive 2001/18.

66. EFSA considered the Application, in order to determine *inter alia* whether the Soybean would have adverse effects on human health, animal health or the environment, contrary to Articles 4(1)(a) and 16(1)(a) GM Regulation, if its placing on the Union market were to be authorised.

67. In accordance with Articles 6(4) and 18(4) of the GM Regulation, EFSA consulted the competent national authorities of Member States on the Application **[PD/2]**.

68. Following that consultation, EFSA issued an Opinion on the Application on 26 January 2012 ("**the EFSA Opinion**") **[PD/3]**. It concluded, in material part:

    a. **Molecular Characterisation (EFSA Opinion, section 3):** The molecular characterisation of the Soybean does not indicate safety concerns, because *"conventional*

breeding methods were used in the production of soybean MON 87701 × MON 89788, no additional genetic modification was involved. Southern analyses demonstrated that the integrity of the inserts in the MON 87701 and MON 89788 events was retained in soybean MON 87701 × MON 89788. The levels of Cry1Ac and CP4 EPSPS proteins in the seeds (and all other tissues examined) of soybean MON 87701 × MON 89788 have been demonstrated to be comparable with those in the single events" (EFSA Opinion section 3.2, p.10 **[PD/3]**)

b. **Comparative Analysis for the purpose of the Compositional Assessment (EFSA Opinion, section 4):**

   i. Choice of Comparator/Field Trial Design: A field trial design with the Soybean that did not include either the Parents or treatment with the target herbicide was accepted without explanation (EFSA Opinion section 4.1.2, p.13 **[PD/3]**).

   ii. Compositional Analysis : The Soybean is compositionally equivalent to its comparator, except for the Proteins, "*in the light of the field trial design, biological variation and level of the studied compounds in commercial non-GM soybean varieties*" (EFSA Opinion section 4.1.3, p.15 **[PD/3]**);

   iii. Agronomic Traits and GM phenotype: The crossing of *"insect-resistant soybean MON 87701 with glyphosate-tolerant soybean MON 89788 to produce the stacked soybean MON 87701 × MON did not result in any consistent changes in phenotypic and agronomic characteristics, as compared with its comparator, with the exception of a small increase in final stand count which is not considered biologically relevant by the EFSA GMO Panel"* (EFSA Opinion section 4.1.4, p.17 **[PD/3]**);

   iv. Accordingly, EFSA found the Soybean to be **substantially equivalent** to its comparator because *"no biologically relevant differences were identified in the composition or agronomic and phenotypic characteristics of soybean MON 87701 × MON 89788, as compared with the comparator soybean A5547, and that the composition of soybean MON 87701 × MON 89788 fell within the range observed in non-GM soybean varieties, except that it expresses the CP4 EPSPS and Cry1Ac proteins."*

c. **Food/Feed Safety Assessment (EFSA Opinion, section 5)**:

i. Effects of Processing: No assessment of the effect of processing on the Soybean was required because *"[t]aking into account the compositional analysis, providing no indication of relevant compositional changes except for the stacked soybean expressing the CP4 EPSPS and Cry1Ac proteins, the Panel has no reason to assume that the characteristics of soybean MON 87701 × MON 89788, and derived processed products, would be any different from those of the corresponding products derived from soybean MON 87701, soybean MON 89788 and conventional soybean varieties"* (EFSA Opinion section 5.1.3, p.18 **[PD/3]**);

ii. Toxicological Assessment: No toxicological assessment of the whole Soybean is necessary, because the *"... molecular characterisation undertaken on soybean MON 87701 × MON 89788 identified no altered stability of the single soybean events (see section 3.1.5) when these were brought together by crossing, and expression analysis of the Cry1Ac and CP4 EPSPS proteins revealed no relevant change in expression levels in soybean MON 87701 × MON 89788 compared with the single soybean events MON 87701 and MON 89788, respectively (see section 3.2)... [N]o biologically relevant differences were identified in the compositional characteristics of soybean MON 87701 × MON 89788 in comparison with non-GM soybean varieties, except that it expresses the CP4 EPSPS and Cry1Ac proteins, and an assessment found no indication for interaction between the single events that could influence the safety of soybean MON 87701 × MON 89788 for humans and animals"* (EFSA Opinion section 5.1.4.3, p.19 **[PD/3]**);

d. Allergenicity: The potentially increased allergenicity of the Soybean, as compared with the Parents, does not require assessment, because EFSA found that the evidence showed that *"bringing together the single soybean events MON 87701 and MON 89788 by conventional crossing to form the stacked soybean MON 87701 × MON 89788 does not result in any observable differences in allergen content between soybeans MON 87701 × MON 89788 and its comparator. The EFSA GMO Panel considers it unlikely that potential interactions will occur in soybean MON 87701 × MON 89788 that might change the allergenicity of the whole crop."* (EFSA Opinion section 5.1.5.2, lines p.20 **[PD/3]**);

e. Post-market monitoring of GM food/feed: Post-market monitoring of the Soybean's use as food or feed was not necessary because *"[t]he risk assessment concluded that no data have emerged to indicate that soybean MON 87701 × MON 89788 is any less safe than*

its comparator A5547. In addition, soybean MON 87701 × MON89788 is as nutritious as conventional soybeans."

69. The draft Commission Implementing Decision authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean MON87701xMON89788 pursuant to Regulation (EC) No 1829/2003 on genetically modified food and feed was presented and submitted to the Standing Committee on the Food Chain and Animal Health for an opinion: **[PD/4]**. The relevant meeting was held on 2 May 2012: **[PD/4]**.

70. The Standing Committee noted a number of reasons which were mentioned by Member States for not supporting the draft Decision [**[PD/4]**. These included:

"- molecular characterization, compositional analysis and toxicological studies are not considered as satisfactory;

- no sufficient study and data for the comparative analysis between the GM soybean and its counterpart;

- labelling and traceability methods not satisfactory due to hybrid character of the GMO;

- the conclusion of the risk assessment is not considered as fully satisfactory;

- lack of harmonisation between the legal framework of the herbicide regulation and GMO regulation..."

71. The Austrian delegation issued a declaration which provided, so far as relevant, that **[PD/4]**:

"Austria objects the placing on the market of genetically modified soybean MON87701xMON89788 (MON-877Ø1-2xMON-89788-1) due to the following reasons:

a. The risk assessment which has been carried out is not suitable to give a scientific proof for the safety of this product:

This concerns in particular

- molecular characterisation (lack of quality to proof genetic stability),

- conclusions of compositional analysis have to be scrutinized

- toxicological assessment of the stacked event for potential interactions between Cry1Ac and CP4 EPSPS is missing

- lacks of environmental monitoring plan are obvious..."

72. The Standing Committee decided to give **no opinion**.

73. The votes of the Committee were as follows: 149 votes in favour, 87 votes against, 109 abstentions. The Chair of the Standing Committee indicated that the Commission would be

invited to submit a proposal to the Appeal Committee in accordance with Regulation (EU) No 182/2011.

74. Testbiotech understands that the Council failed to reach a decision on the Application because the matter was reverted to the Commission. Accordingly, in the absence of a decision by the Council, and on the basis of the EFSA Opinion, the Commission decided on 28 June 2012 to grant the market authorisation **[PD/5]**.

75. Testbiotech sought an internal administrative review of that decision, on 6 August 2012, under Article 10 of the Aarhus Regulation and Article 36 of the GM Regulation ("**Request for Internal Review**") **[PD/6]**. ENSSER and Sambucus submitted identical Requests for Internal Review.[2]

76. The Commission responded on 8 January 2013 ("**the Commission Decision**") **[PD/7]**.[3]

V. GROUNDS OF CHALLENGE

77. Testbiotech contends that the Commission has committed a manifest error of law and/or of assessment in refusing to review its decision to grant the market authorisation. As set out above, Testbiotech's four grounds of challenge are as follows:

78. The Grounds upon which Testbiotech challenges the Commission's decision are, in summary:

    a. **Ground A:** EFSA's assessment that the Soybean is 'substantially equivalent' to its appropriate comparators is unlawful, is based on a scientific assessment which was not carried out in accordance with its own guidance and/or is based on a manifest error of assessment;

    b. **Ground B:** EFSA's failure to give adequate or any consideration to the potential synergistic/combinatorial effects between the Soybean and other factors, and/or to require an adequate toxicity assessment to be conducted is contrary to its own guidance, legal obligations and/or it constitutes a manifest error of assessment;

    c. **Ground C:** EFSA's failure to require an adequate immunological assessment to be carried out is contrary to its own guidance, legal obligations and/or constitutes a manifest error of assessment.

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[2] Sambucus' covering letter is at **[PD/11]** and ENSSER's covering letter is at **[PD/16]** . The Applicants have not provided duplicate copies of the Application as this seemed unnecessary.

[3] ENSSER and Sambucus received identical copies of Commission Decision barring the name of the addressee, see: **[PD/10]** and **[PD/12]**

d. **Ground D:** EFSA's determination that no post-market authorisation monitoring of the consumption of the Soybean is manifestly in error and/or is vitiated by the flaws identified by Grounds A to C.

79. To the extent that the matters set out below establish that EFSA failed to comply with its own guidance, Testbiotech submits that this failure frustrated its legitimate expectation that EFSA would comply with its guidance in order to fulfil its obligations under the GM Regulation.

GROUND A: EFSA's assessment that the Soybean is 'substantially equivalent' to its conventional counterpart

80. Ground A of Testbiotech's challenge can be subdivided into the following five grounds:

a. **A1:** Contrary to the clear requirements stipulated by its guidance, EFSA did not require Monsanto to include the Parents or Single Events in the field trials conducted for the purpose of the Application. Accordingly, no proper compositional comparison (or safety assessment) could be properly carried out as there was lack of comparable date from key comparators;

a. **A2**: Despite having identified a number of statistically significant differences between the Soybean and its conventional counterpart, EFSA nevertheless concluded that there was 'substantial equivalence' between them on the basis that the differences were small and fell within the range of variation: (i) presented by 20 non-GM soybean varieties (**"the reference substances"**); and/or (ii) reported by historical data (from the 'ILSI' database), neither of which had been properly analysed to ensure they were capable of substantiating the conclusion drawn from it. Instead, they operated as scientific 'noise' to mask the differences which should have been properly analysed following sufficient clinical trials. Moreover, in scientific terms, a statistically significant difference may be biologically relevant and therefore present a safety concern even if it is 'small';

b. **A3:** EFSA failed to take into account the fact that there is a substantial amount of scientific literature which documents the fact that spraying genetically modified plants with glyphosate-based herbicides affects the composition of such plants, which are also likely to influence agronomic and phenotypic effects. As a result, EFSA failed to require a proper investigation in the potential compositional effects of these residues which is of material concern;

c. **A4:** EFSA failed to properly assess the data obtained from the field trials conducted by Monsanto in relation to agronomic and phenotypical differences. EFSA manifestly failed

to require the investigation of the numerous statistically significant differences found between the Soybean and its conventional counterpart, and also failed to require Monsanto to carry out proper stress-testing. These failures were then compounded by a clear error of law in that EFSA only assessed a number of differences in order to determine whether the Soybean had the potential to become a weed, not whether these differences raised a potential adverse effect on humans or animals;

d. **A5:** Contrary to EFSA's own guidance, see Paragraphs 41 to 42 above, EFSA failed to require Monsanto to properly investigate the potential effect of specific biotic and abiotic stressors on the Soybean. In particular, there was only limited and inconsistent stressors applied within sites and across sites so there was no data available upon which a proper comparative assessment could be based. This error was then compounded by EFSA's failure to require Monsanto to assess the impact of abiotic and biotic stressors on the Soybean and its conventional counterpart as well as other appropriate comparators.

81. This approach was manifestly in error, unlawful and/or contrary to EFSA own published guidance. The Commission upheld these manifest errors.

Ground A(1)

(i) *EFSA's Opinion*

82. **Ground A1** is that contrary to the clear requirements stipulated by its guidance in relation to 'step 1', EFSA did not require Monsanto to include the Parents or Single Events in the field trials conducted for the purpose of the Application. This obligation is an important one because in particular:

a. It ensures that the environmental conditions in which the parents and the stacked event are grown are the same;

b. This in turn allows a proper comparison to be made between the different sets of data:

i. It allows EFSA to identify all of the statistically significant differences between the stacked event and the Single Events;

ii. Once this has been done, EFSA will be able to carry out a proper assessment of significantly statistical differences in order to determine whether there has been any unintended effects which are biologically relevant, and therefore require further exploration as part of the safety assessment; or

iii. It will allow EFSA to identify any patterns or trends in the results which may require further exploration as part of the safety assessment.

83. EFSA failed entirely to address this point. It made no reference to Monsanto's failure to include the Parents or to justify its acceptance of that failure. As noted above at Paragraph 68(b), Monsanto only used one comparator in its field studies alongside the Relevant Stacked Event, which was soybean A5547. EFSA merely outlined this fact in the Opinion without explanation as to why such a limited comparison would be sufficient.

84. EFSA's complete failure to address this point is entirely inconsistent with EFSA's Stacked Events Guidance. That Guidance is adopted specifically to deal with a scenario in which two genetically modified parent plants are combined into a hybrid plant with a stacked gene event. If it were sufficient to assess only the parent plants against their conventional counterparts then sections 2 and 3 of that Guidance (cited at Paragraphs 36 and 39 above) would be nugatory. In fact the Guidance is explicit that an assessment of the stacked event is required. EFSA has manifestly failed to comply with this guidance.

85. Of particular concern is the fact that a clear compositional difference was identified between one of the Parents, MON 88701, and its conventional counterpart in that it displayed a much higher content of Vitamin E. The Soybean grown in different field trials did not disclose such a high level of this vitamin. However, in the absence of growing the Soybean and its Parents (as well as its conventional counterpart) in parallel in field trials conducted under the same parameters it is impossible to know whether: (a) the deviation between the levels of Vitamin E disclosed are caused by the plants' genetic backgrounds, genetic engineering or environmental factors; or (b) there is a discernible pattern or trend in the levels of Vitamin E disclosed by the different plants which may be a cause for concern or at least requires further investigation.

86. Moreover, due to EFSA's failure to require Monsanto to use the Parents as comparators in the field trials of the Soybean, no proper comparison was made between the effect of spraying glyphosate on the Soybean and its Parents. This is because: (i) there were differences between the glyphosate treatment administered to the soybeans grown in the context of the field trials of the Parents and that applied in the field trials of the Soybean; and (ii) incomplete data was submitted in relation to Monsanto's application for authorisation of the Parents which meant there was no data available for a proper comparison in relation to the Soybean.

87. *The Soybean Trials*: In particular, the field trials of the Soybean involved the following glyphosate based treatment:

Argentina – Roundup UltraMax, 1.25 kg a.e./ha (Technical Dossier, Table 12, p.64 **[SU/1]**)

US - Roundup WeatherMax, 0,74 – 0,86 kg a.e./ha (Technical Dossier, Table 13, p.64 **[SU/1]**)

(It is worth noting that there is not even internal consistency between the spray used and the volume of application as between the field trials of the Soybean, which is a point returned to below.)

88. *The Trials of the Parents*: For the purpose of acquiring agronomical data or data in relation to the effect of stressors on the Parents, no trials were conducted where the plants were sprayed with glyphosate products.

89. In relation to compositional data:

Argentina – 5 sites were sprayed with RoundupMax and one site was sprayed with Roundup Ultra Max. The spray quantity was 1.5lbs ae/A.

First set of data obtained from US: The glyphosate spray used was not named.
Additional data obtained from trials in the US – 1.68 kg/ha Roundup WeatherMax.

90. This failure to ensure that data was available to allow for a proper comparison of the effect of applying glyphosate to the Soybean and its Parents is of particular concern because there are a number of publications which recognise that the application of glyphosate to genetically modified plants can have an impact on the composition and mineral nutrition of a plant: see below at Paragraphs 120 to 124. This impact can also vary depending upon the dosage of spray applied.

91. Accordingly, it is plain that no proper comparison could be made between the Soybean and its Parents based on field trials conducted at different times and with either varying glyphosate sprays used, varying quantities of spray applied and/or no spray used at all.

(ii) *Commission Decision*

92. As to **Ground A(1)**, Testbiotech's Request for Internal Review specifically addressed this point **[PD/6]**. At page 22 of its Request, Testbiotech explained (by reference to the Stacked Events Guidance) that *"the investigation of the differences between the stacked Soy and its comparators should include the isogenic and the transgenic parental plants (as well as the crossings) in direct comparison of the field trials. However the applicant chose to use only one comparator (A5547) which is qualified as "conventional line that has a similar genetic background to the test substances" (Berman et al., 2008)."* Testbiotech explained that this failure was particularly

glaring in this case because of the criticisms which could be levelled against EFSA's approach to its assessment of the Single Events (Request at pp.21-22).

93. In response, the Commission first of all states in Annex II to the Decision that (pp.1-2; **[PD/7]**):

    a. The Conventional Counterpart used complies with the 2007 Stacked Event Guidance, and in particular it relies upon the fact that the conventional counterpart used was soybean A5547. This was the soybean variety originally transformed to produce MON 87701 (one of the Relevant Stacked Event's parental lines);

    b. Monsanto also included 20 non-GM commercial soybean varieties in order to provide an estimate of the range of natural variation;

    c. EFSA's assessment of the Relevant Stacked Event was built upon the assessment of both Single Events in previous opinions. EFSA found that the combination of the single events in the Relevant Stacked Event is stable and that there were no interactions between stacked events.

94. However, the Commission then goes on to state (emphasis added) (Commission Decision, Annex II, p.2, **[PD/7]**):

> *"[The 2007 Stacked Event Guidance] requires the parental lines in the field and do not require the completion of all the single events (in this case the parental lines). Since, in this case, both parental lines had previously been risk assessed, the inclusion of the conventional counterpart without the parental was considered sufficient. It is fully in line with the spirit of both the 2007 Guidance Document (parental must be risk assessed) and the EFSA Guidance Document (EFSA 2011b) (singles are a pre-requisite).*

95. In short, the Commission admits that EFSA failed to comply with its guidance. Instead of acknowledging the importance of this failure, the Commission relies on the alleged 'spirit' of the guidance, which is apparently inconsistent with its explicit terms, to justify this complete failure on the part of EFSA.

96. The other three points made by the Commission, listed above at Paragraph 93, do not take the Commission's case any further for the following reasons:

    a. Testbiotech does not dispute that soybean A5547 could be used as a conventional counterpart to the Soybean. The dispute is over EFSA's failure to ensure that the Parents were not also included in the field trials as required by its own guidance;

b. As explained below, Monsanto's use of 20 non-GM reference substances is not in principle incorrect. However, reference substances cannot be used as a substitute for the appropriate comparators. They are only relevant once all significantly statistical differences between the stacked event and its comparators have been identified. Even then, as set out below, the use of a large amount of convention reference substances can generate data 'noise' which could mask the biological relevance of unintended differences between the plant and its comparators.

c. The third point simply ignores the terms of EFSA's own guidance. In most cases, the risk assessment of the single events pre-dates the assessment of the stacked event. If prior assessment was sufficient, this would render the guidance requirement that parents or single events be used in the field trials nugatory. In any event, any such reliance on the prior assessment would have to be underpinned by a clear consideration of whether the parameters and environmental conditions in which the trials of the Parents were conducted were comparable to those in which the Soybean was grown. No such analysis or consideration is evident from EFSA's Opinion.

Ground A(2)

(i) *EFSA Opinion*

97. **Ground A(2)** is that having failed to ensure that Monsanto included appropriate comparators in its field trials of the Soybean, EFSA then allowed Monsanto to rely on, the alleged 'smallness' of the statistically significant differences, a wide range of 'reference substances' and the ILSI database to explain away the significant number of statistical differences between the composition of the Soybean and its conventional comparator. This approach was manifestly flawed for the following reasons.

98. *USA Field Trials:* In these field trials, the Soybean was sprayed with glyphosate and A5547 was treated with maintenance pesticides. EFSA acknowledged that when the compositional data for seed samples obtained in these field trials were evaluate across sites (EFSA Opinion, section 4.1.3, p.14 **[PD/3]**; emphasis added):

> *"...statistically significant difference between soybean MON 87701 × MON 89788 and its comparator was found for 20 analytes: the proximate protein; the amino acids alanine, aspartic acid, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, proline, serine, threonine and valine; the fatty acids palmitic acid, stearic acid, linolenic acid and arachidic acid; and lectin, daidzein and genistein."*

99. *Argentina Field Trials:* The statistical evaluation of compositional data of the seed samples obtained from the Argentinian field trials revealed (EFSA Opinion, section 4.1.3, p.14 **[PD/3]**; emphasis added):

> *"...statistically significant differences between glyphosate-sprayed soybean MON 87701 × MON 89788 and its untreated comparator for 11 analytes: the proximate ash; the two amino acids glutamic acid and leucine; the fatty acids stearic acid, linoleic acid and arachidic acid; and vitamin E, stachyose, daidzein and genistein. The evaluation per site illustrated that, among the 11 constituents that were significantly different in soybean MON 87701 × MON 89788 and the comparator in the across-site analysis, four showed a statistically significant difference at one site, three at two sites, two at three sites and one at four of the five sites. Only the level of acid detergent fibre differed significantly between soybean MON 87701 × MON 89788 and its comparator in forage... [and] 16 additional statistically significant differences identified in the per-location statistical analysis of other soybean constituents."*

100. EFSA also acknowledged that across the field trials in the USA and Argentina analysis of the data had led to the identification of (EFSA Opinion, section 4.1.3, p.15; emphasis added) *"20 differences between the genetically modified soybean and its comparator in 2007 and 11 in 2007/2008. Six constituents were altered in both growing seasons. These were glutamic acid (altered in one of the ten field sites), leucine (two sites), stearic acid (eight sites), arachidic acid (five sites), daidzein (five sites) and genistein (four sites)."*

101. EFSA had also requested composition data from the Argentinian field trials in which the Soybean had not been treated with glyphosate (EFSA Opinion, section 4.1.3, p.14 **[PD/3]**; emphasis added). Analysis of this data revealed: *"statistically significant differences between the two soybean materials for 12 analytes: the proximates moisture and ash; the amino acid tryptophan; the fatty acids stearic acid, oleic acid, linoleic acid and arachidic acid; and vitamin E, raffinose, stachyose, daidzein and genistein. The evaluation per site illustrated that among these 12 constituents, four showed statistically significant differences at one site, three at two sites, two at three sites and three at four of the five sites."*

102. EFSA disregarded all of these significant statistical differences on three bases: (1) the differences were often said to be small; (2) a comparison between the Soybean and "reference substances" grown at the same location. These "reference substances" were used to establish a "tolerance interval" for the various characteristics that were to be analysed, and some of the apparently "statistically significant differences" were within this tolerance interval – i.e. within the natural variation shown by the reference substances; (3) a comparison between the Soybean and a range of values derived from the ILSI Crop Composition Database (Technical Dossier, Table 1, p.79 **[SU/1]**).

103. EFSA's adoption of this approach to the large number of statistically significant differences identified was manifestly in error for the following reasons.

104. *Quantity:* The size of the differences between two plants has to be considered in context. The fact that a difference is small does not mean that it is not biologically relevant, in particular where a pattern or trend is identifiable.

105. *Reference Substances*: As the Commission stressed in its Decision, Monsanto included 20 non-GM varieties of soybeans in the field trials. This data was used to establish the range of acceptable natural variations or 'tolerance interval' between different commercial varieties of soybeans.

106. Testbiotech accepts that this approach can be appropriate in principle. However, where EFSA has failed to ensure that appropriate comparators have been used in the field trials, there is a material risk that the reference substances created data 'noise' which masked the true extent of the differences between the Soybean and its conventional comparator, as well as the potential extent of the differences between the Soybean and its Parents.

107. Moreover, the use of 20 varieties of reference substances plainly prevents any meaningful comparison being made because it allows for the generation of statistical noise which may mask significant differences between the Soybean and its conventional counterpart that should be of **material concern**.

108. Statistical/data "noise" is a well-known problem in scientific research. The expression is used to refer to situations in which excessive or unessential data is introduced into an experiment which makes it more difficult to identify its effects. In relation to field trials conducted in relation to GMOs, the range of reference substances used may cover a broad spectrum of variations – a plant can display a wide variety of compositional and other differences depending upon where it is grown and other factors. The variation between 20 different varieties of one plant may be of a higher magnitude than the variation identified between the GM plant and its comparator(s). However, this should not lead to the automatic dismissal of the differences identified in the field trials between the GM plant and its comparator(s). EFSA should take into account the fact that a broadly defined range of natural variations may in fact mask relevant differences between the GM plant and its comparator(s).

109. Furthermore, Monsanto only provided very limited information about the environmental conditions in which the field trials were conducted. No statistical analysis was undertaken to

correlate the deviation between observed in relation to certain environmental stressors, and the data and did not allow for a proper comparison of the differences between the plants grown at difference sites (see Paragraphs 136 to 147 below in relation to EFSA's treatment of abiotic stressors). Moreover, no information was made available in relation to the environmental conditions under which the data were generated and which methods were used to extract or measure the compounds listed within the ILSI database. The problems with the use of the ILSI database are discussed in more detail directly below.

110. *The ILSI Database*: On a number of occasions EFSA relied upon the soybean constituent levels published in the ILSI crop composition database (ILSI 2006) as a basis upon which to disregard the statistically significant differences between the Soybean and A5547.

111. However, Monsanto had failed to provide complete and/or sufficient information in its application or otherwise:

a. to correlate the findings from the field trials with environmental conditions, contrary to the requirement in the Risk Assessment Guidance section 3(D)(7.2), at p.23 **[AU/10]**, cited at Paragraph 38 above, that "*field experiments should be adequately described, giving information on important parameters such as...climatic and other conditions during growth...*" (emphasis added);

b. to correlate the information it had derived from literature with the historical environmental conditions that had pertained in the trials documented in that literature, contrary to the requirement in the Risk Assessment Guidance section 3(D)(7.1), at p.23 **[AU/10]**, cited at Paragraph 44 above, that "*When using literature data, however, they have to be adequately assessed for quality (e.g. type of material analyzed, analytical method used*";

c. to consider whether the results from the field trials were generated in conditions that correspond with those that pertained in the trials considered by the literature that was being relied upon.

112. Thus neither Monsanto, nor EFSA, have conducted any analysis of whether the information relied on to explain the statistically significant differences as 'natural variations' is in fact at all relevant or appropriate.

113. The risks of relying on the ILSI database in this way – without properly analysing the relevance and appropriateness of the literature relied upon to the comparison being made - appear to be acknowledged by EFSA:

a. As noted above, the Risk Assessment Guidance Section 3(D)(7.1), at p.23 **[AU/10]**, (cited at Paragraph 44 above) requires that the "quality" of the literature relied upon should be assessed; and

b. The former Vice-Chair (now Chair) of EFSA's GMO Panel has stated publicly:

> *"I think we're in a situation where we would be unwise at the present time (maybe in the future this will be different), but at the present time we can't trust the ILSI database. There is not sufficient environmental information from where these trials were done and that's why we insist that the commercial reference variety should be planted simultaneously with the GM and the non-GM. Otherwise I think we are in an unsafe situation and I would worry that the limits would be too wide."*
>
> (Observations of Mr. Joseph Perry, Vice-Chair, at EFSA's consultative workshop on its draft guidance for the selection of Genetically Modified (GM) plant comparators, held in Brussels on 31 March 2011[4]).

114. On the basis of the points made directly above, Testbiotech contends that there is no basis upon which EFSA could have concluded that the comparison made was "appropriate" under the terms of Articles 5(3)(f) and 17(3)(f) GM Regulation. Contrary to the requirements of EFSA's Risk Assessment Guidance Sections 3(D)(7.1) and 3(D)(7.2), at p.23 **[AU/10]**, (cited at Paragraphs 38 and 44 above) there has been a manifest failure to provide complete and/or sufficient information on the parameters within which the field trials were conducted and to assess the quality of the literature relied upon.

115. Further, and in consequence, contrary to the requirements of and Articles 6(3)(a) and 18(3)(a) GM Regulation, either EFSA has failed to consider whether Monsanto's analysis was supported by "appropriate information and data", or EFSA has unlawfully and manifestly incorrectly concluded that the information provided by Monsanto was *"appropriate"*.

116. This error is also potentially **highly** material to the conclusion that the Soybean does not present a risk of adverse effects on human and/or animal health, contrary to Articles 4(1) and 16(1) GM Regulation. A properly conducted comparison of the field trial results with properly

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[4] Link from EFSA's website at http://www.efsa.europa.eu/en/events/event/gmo110331.htm given to the video recording of the event at http://www.flyonthewall.com/FlyBroadcast/efsa.europa.eu/StakeholdersMeeting0311/index.php?language=original&stream=wmv

analysed literature **might well have demonstrated that the statistically significant differences observed were biologically relevant**, and therefore required analysis at 'step 2'.

(ii) Commission Decision

117. Testbiotech drew the points made under **Ground A(2)** to the Commission's attention at pages 23 to 24 of its Request for Internal Review **[PD/6]**. It emphasised the fact that EFSA had failed to ensure that Monsanto used appropriate comparators, and instead had allowed a large number of reference substances and data held in the ILSI database to explain away statistically significant differences without proper investigation.

118. At page 2 of the Decision, the Commission merely asserts that: (a) the appropriate comparator was used; (b) the use of non-GM commercial reference substances is a *"fundamental part"* of EFSA's comparative approach; and (c) the statistically significant differences identified fell within the range disclosed by the reference substances and the ILSI database **[PD/7]**.

119. The first point is flawed for the reasons given above under **Ground A(1)**. The second and third points fail to engage with the criticisms advanced by Testbiotech. As noted above, Testbiotech accepts that EFSA's guidance anticipates the use of reference substances and literature being used as part of the comparative analysis. However, reliance on such substances and literature must be subject to sufficient scrutiny and control in order to prevent the creation of data 'noise' which masks the true extent of the differences between the Soybean and its conventional counterpart. The Commission singularly failed to address the Testbiotech's specific criticisms of EFSA's reliance on the data obtained from a large number of varying reference substances and the ILSI database in this case.

Ground A(3)

(i) EFSA Opinion

120. **Ground A(3)** is that EFSA failed to take into account the fact that there is a **substantial** amount of scientific literature which documents the fact that spraying genetically modified plants with glyphosate-based herbicides affects the composition of such plants which is also likely to influence agronomic and phenotypic effects.

121. At page 15 of its Opinion, EFSA concluded that (section 4.1.3 **[PD/3]**): the only statistically significant differences across locations between soybean MON 87701 × MON 89788 and its comparator that were consistently observed in both the USA and Argentina across the seasons

were changes in the level of some fatty acids and increased levels of daidzein and genistein. These differences were small and not considered biologically relevant. However, scientific literature has recorded that increased levels of daidzein and genistein can be of relevance as these substances are known to exhibit hormonal activity and are considered to be the major phytoestrogens in soy. In particular, Duke et al., (2003) **[SU/2]** found higher levels of daidzein in the seeds of genetically engineered soybean 40-3-2, which is another glyphosate (roundup) resistant soybean. This supports the conclusion that there can be a specific pattern of change in components of a genetically engineered plant when it rendered glyphosate-resistant. Accordingly, EFSA should have required Monsanto to conduct further studies under different environmental conditions to determine the potential impact of these differences.

122. Table A in Appendix I to this Application (which was provided to the Commission in Testbiotech's Request for Internal Review **[PD/6]**; copies of which are provided in Appendix III as referenced) documents the numerous other publications which show that spraying genetically modified plants with glyphosate can cause significant compositional changes when compared with their conventional counterparts or other appropriate comparators.

123. Moreover, a recent study into the effect of glyphosate-based sprays on glyphosate tolerant soybeans established that particular formulations of glyphosate can cause different levels of damage to nutrient accumulation and dry matter production (Cavalieri et al, 2012).[5] The study looked at a number of the variety of Roundup products: Roundup Original, Roundup Ready, Roundup Transorb, Roundup WG, Roundup Ultra and Zapp Qi. Roundup Transorb, Roundup WG, Roundup Ultra caused the greatest damage.

124. However, despite numerous statistically significant differences being identified between the glyphosate-treated Soybean and its non-treated conventional counterpart, EFSA failed to require any further investigation of the potential impact of spraying glyphosate on the Soybean. This constituted a manifest error of assessment because it meant that EFSA relied upon an incomplete evidence base to reach its determination that the Soybean is substantially equivalent to its conventional counterpart.

(ii) *Commission Decision*

125. In relation to **Ground A(3)**, Testbiotech outlined its concerns at pages 29 to 33 **[PD/6]**. In the Decision, the Commission dismisses Testbiotech's concerns on the basis that (Commission Decision, Annex II, pp. 4-5 **[PD/7]**):

[5] Only the summary of this study is provided as the remainder of the publication is only available in Spanish.

a. The differences in the levels of daidzein and genistein identified between the Soybean and its conventional counterpart fell within the range displayed by the reference substances. Accordingly, the Commission relied upon a manifest failure in EFSA's approach to the comparative analysis to justify its failure to investigate differences that could indicate unintended effects caused by the stacking of the Proteins;

b. Next, the Commission suggests that the large amount of scientific research compiled by Testbiotech, and set out in Appendix I to this Application, was *"not applicable"* because no differences in composition had been identified between the Soybean, its comparator and the reference substances treated with glyphosate. This simply ignores the critical point: not only were differences identified, the scientific literature relied upon Tesbiotech is highly material because it suggests that a proper investigation of the effect of spraying could lead to the identification of **additional and significant differences.**

Ground A(4)

(i) *EFSA Opinion*

126. Under Ground **A(4)**, Testbiotech contends that EFSA failed to properly assess the data obtained from the field trials conducted by Monsanto in relation to agronomic and phenotypical differences.

127. At page 16 of the Opinion, EFSA explains that for the purpose of this assessment it considered two sets of results **[PD/3]**. The first set of results was generated through the field trials at 8 sites in Argentina in the season 2007/2008. These field trials included four reference substances at each site and Glyphosate-based herbicides were not used. EFSA explained that (**[PD/3]**; emphasis added):

> *"...In the phenotypic comparison [based on the first set of results] around half of the parameters studied differed between soybean MON 87701 × MON 89788 and A5547. Early stand count (140.6 vs 105.9 plants in defined rows), final stand count (130.0 vs 97.1 plants in defined row), test weight (171.8 vs 169.2 g/250 ml) and yield (2.8 vs 2.5 t/ha) were increased, whereas lodging (2.4 vs 3.3 scale points), grain moisture content (10.9 % vs 11.6 % fresh weight) and 100-seed weight (15.3 vs 16.0 g) were decreased. Of these differences early and final stand count were significantly higher at seven out of the eight field trial sites studied. Test weight was increased at six of eight sites and yield at three of eight sites. A reduction in seed moisture content was observed at seven of eight sites, a lower 100-seed weight at four of eight sites, and reduced lodging at five of eight sites."*

128. Accordingly, EFSA recorded that there was a substantial number of statistically significant differences between the Soybean and its conventional counterpart. With respect to early and final

stand count in particular, EFSA expressly stated that the differences were 'significant'. These differences should have been properly investigated under 'step 2' because they indicate that there could have been biologically relevant unintended effects caused by the stacking of the Parents. It is also important to note that these differences could have been affected by different climate conditions.

129. In the Supporting Documents section of Appendix III to this Application, Testbiotech has provided publications showing the types of investigation or stress-testing techniques which can be used: see, for example Matthews et al, (2005) **[SU/5]** and Zolla et al, (2008) **[SU/6]**. In Matthews et al., the researchers exposed the plant to defined stressors in a measured and consistent way. The stressors included blight, viruses and slugs. In Zolla et al, the researchers used adjacent but separate growth chambers in order to ensure the plants were exposed to the same environmental effects, for example, the same humidity and the same amount of light. There is also a substantial amount of scientific evidence that different environmental conditions can impact on Bt-producing plants (Then & Lorch, (2008) **[SU/7]**).

130. Instead of requiring the proper investigation of the statistically significant differences identified, EFSA stated (EFSA Opinion, section 4.1.4, p.16 **[PD/3]**; emphasis added):

> *"As the measured endpoint for all parameters showing a statistically significant difference between soybean MON 87701 × MON 89788 and its comparator was within the range in levels of these constituents in soybean reference varieties in the combined site analysis, the applicant argued that no biologically relevant difference in terms of increased potential for the soybean to become a weed between soybean MON 87701 × MON 89788 and its comparator was identified, except the expected difference in tolerance to glyphosate. No developmental differences in categorical parameters (flower colour, plant pubescence and plant growth stage) were observed between soybean MON 87701 × MON 89788 and its comparator."*

131. This reasoning is fundamentally flawed. EFSA again allows Monsanto to explain away the differences identified on the basis of the *"range in levels of [the biological constituents] in [the] soybean reference varieties in the combined site analysis"*. However, the combined site analysis takes together the results obtained at a number of different field trials sites and in respect of numerous varieties of commercial soybean varieties. As set out above, data obtained from reference substances cannot be used as a substitute for a proper comparative analysis and investigation of differences identified. EFSA should also prevent data obtained from the growth of a large number of reference substances being used to create data 'noise' which masks potentially material differences between the Soybean and its conventional counterpart.

132. Moreover, the highlighted text in the passage quoted above discloses a clear error of law. When carrying out a risk assessment under the GM Regulation, EFSA is not required to determine

whether or not the statistically significant differences identified through the comparative analysis suggest that the stacked event has an **increased potential to become a weed.** EFSA is charged with determining whether or not the stacked event may have adverse effects on **human health, animal health or the environment** (Articles 4(1)(1) and 16(1)(1) of the GM Regulation). The framework of analysis and/or the endpoint of that analysis were wrong and, accordingly, the analysis of the data obtained was inadequate. Moreover, these flaws in EFSA's approach meant that EFSA failed to require Monsanto to produce further data which would have allowed a proper analysis of the differences identified.

133. At pages 16 to 17 of the Opinion, EFSA then explained that (section 4.1.4 **[PD/3]**; emphasis added; internal references omitted):

> *"On request from the EFSA GMO Panel for additional agronomic and phenotypic data, the applicant supplied data from field trials in the USA in 2009 in which soybean MON 87701 × MON 89788 sprayed with glyphosate and maintenance pesticides19, or sprayed with maintenance pesticides only, was compared with the comparator A5547 sprayed with maintenance pesticides. Of the five field trials initiated in the soybean-growing regions of the USA, one site (Arkansas) was dropped from the study owing to poor germination and emergence as a result of excessive rain. Differences were observed in two agronomic characteristics between the glyphosate-sprayed soybean MON 87701 × MON 89788 and the comparator, namely seedling vigour and final stand count. The differences, however, were not large, and measured values fell within the range found in commercial non-GM soybean varieties grown in the same field trials.*
>
> *When plants were not treated with glyphosate, one statistically significant difference was observed between soybean MON 87701 × MON 89788 and its comparator – and that was a higher stand count. The increased mean values in stand count were within the range observed in commercial non-GM soybean varieties grown in the same field trials.*

134. From the highlighted text it is clear that in both the first and second sets of data provided by Monsanto a statistically significant difference was identified between the stand count of the Soybean and its conventional counterpart (as well as other differences). However, on each occasion EFSA simply accepted Monsanto's explanation that the differences were within the range of natural variation displayed across the reference substances. For the reasons given above, EFSA was manifestly in error in doing so.

(ii) Commission Decision

135. The Commission's response to **Ground A(4)** was merely to state that EFSA's analysis of the agronomic and phenotypical data was right for the reasons it gave (Commission Decision, Annex II, p.3 **[PD/7]**). The Commission merely summarised EFSA's approach to the interpretation of

this data and failed entirely to deal with the specific criticisms advanced by Testbiotech at pages 24 to 25 of its Request for Internal Review **[PD/6]**.

Ground A(5)

(i) *EFSA Opinion*

136. **Ground A(5)** is that contrary to EFSA's own guidance, see Paragraphs 41 and 42 above, EFSA failed to require Monsanto to properly investigate the potential effect of specific biotic and abiotic stressors on the Soybean.

137. As section 3.2.2 of the Stacked Events Guidance recognises, see Paragraph 42 above, stacked events should be subjected to specific biotic stressors under various environmental conditions in order to carry out an adequate comparative analysis and identify all unintended differences between the stacked event and its comparators.

138. The EFSA Opinion only makes limited reference to certain biotic stressors – such as arthropod damage, mosaic virus and pest insects hat (EFSA Opinion, section 4.1.4 at p.16 **[PD/3]**). The dossiers submitted by Monsanto to EFSA contained some reference to the impact of biotic stressors on the plants. However, the scope of the information provided was wholly inadequate because: (a) the biotic stressors which were referred to were stressors that 'happened' to be present in the field. No specific stress testing (controlled exposure to stressors) was conducted on a consistent basis across the field trials in order to allow a proper comparison; and in any event (b) no statistical analysis was undertaken of the data obtained.

139. This substantive failure is particularly worrying when several scientific research publications have shown that genetically engineered plants can exhibit unexpected reactions under stress conditions, which can impact food safety. For example, such unexpected reactions have been identified where a higher concentration of fungal toxins are present in plants (Zeller et al, (2010) **[SU/8]**). The publication Matthews et al, (2005) **[SU/5]** shows that genetically engineered plants react in different ways to biotic and abiotic stressors than plants grown through conventional breeding techniques.

140. With respect to abiotic stressors, as section 7.4 of the Risk Assessment Guidance **[AU/10]** indicates (see Paragraph 41 above), a proper risk assessment should include an assessment of the impact of specific abiotic stress factors that have been explored under defined environmental conditions. Only once this has been achieved, can the data collected can be subject to appropriate

scrutiny in order to identify any potential adverse effects on human health, animal health and the environment.

141. However, the Technical Dossier provides the following summary of how Monsanto purported to take into account the potential effect of abiotic stressors on the Soybean during the field trials (p.46 **[SU/1]**; emphasis added).

> *"Three abiotic stressors and three diseases were evaluated using a continuous 0 – 9 rating scale of increasing symptomology at all sites at four intervals during the growing season. The field coordinator at each site chose abiotic stressors and diseases that were either actively causing plant injury in the study/production area or were likely to occur in soybean during a given observation period. Therefore, abiotic stressors and diseases assessed often varied between observations at a site and between sites. MON 87701 × MON 89788 and the control were considered different in susceptibility or tolerance to an abiotic stressor or disease on a particular observation date at a site if the range of injury severity to MON 87701 × MON 89788 did not overlap with the range of injury severity to the control across all replications. These data were not subjected to statistical analysis...."*

142. This approach to the potential impact of abiotic stressors is **manifestly inadequate**. In order to understand and/or properly analyse these results, Monsanto should have been required to provide more detailed information about how the data was generated and how it was evaluated. More worryingly, as the dossier notes, no statistical analysis was performed. No specific stress testing was conducted on a consistent basis across the field trials in order to allow a proper comparison. Accordingly, this information manifestly does not provide the basis upon which EFSA could reach a conclusion on the potential impact of abiotic stressors on the Soybean.

143. In the Opinion, EFSA stated (section 4.1.4 of the EFSA Opinion, at p.16, **[PD/3]**; emphasis added):

> *"In the field trials conducted in Argentina in the season 2007/2008, plant response to abiotic stressors and the effects of disease damage were measured four times during the growing season at all eight field trial sites, whereas arthropod damage and abundance were evaluated 15 and nine times, respectively, during the growing season at three of the eight sites. The stressors were defined by experts at each field trial site and varied between sites. A difference between soybean MON 87701 × MON 89788 and its comparator was noted in one of the 192 comparisons made for abiotic stress and plant disease damage. This was caused by soybean mosaic virus at one of the field trial sites during observation 2 (MON 87701 × MON 89788 none vs A5547 slight). This disease damage category was within the range of damage observed among the reference soybean varieties."*

144. The underlining added to the above passage is intended to highlight the minimal and manifestly flawed investigation which EFSA erroneously accepted as meeting the requirements of its own guidance. The Stacked Event's response to abiotic stressors was only measured four times across the field trials in Argentina. There was no proper scope for comparison between this

limited set of data because the stressors were defined in the field and varied between sites. Such a limited and variable investigation could not produce the basis for a proper risk assessment of the impact of abiotic stressors on the Stacked Event.

145. Moreover, as noted above, several scientific research publications have established that genetically engineered plants can exhibit unexpected reactions under stress conditions. These include, for example:

a. Zeller et al, (2010) **[SU/8]** discussed above at Paragraph 133;

b. In the research resulting in the publication Matthews et al, (2005) **[SU/5]** the genetically engineered potatoes were subjected to several biotic (such as infections) and abiotic stress factors. They found several differences between the potatoes in the formation of their defending compounds. The authors concluded that:

> *"Transgenic and nontransgenic potato lines were exposed to a range of biotic and abiotic stresses and a range of environmental conditions in the field and during storage. After the stress had taken effect, a comparison was made between the two groups of the potato glycoalkaloid and sesquiterpene levels. Significant differences were observed in the levels of both in the transgenic and control material and in infected and non-infected material."*

c. Then & Lorch, (2008) **[SU/7]** which summarises a range of scientific evidence showing the impact of environmental conditions on plants which have had a Cry protein/Bt toxin inserted into it.

146. This failure is further compounded by EFSA's manifestly flawed approach to the assessment of the impact of abiotic and biotic stressors. EFSA entirely failed to require Monsanto to assess the impact of abiotic and biotic stressors on the Soybean and its conventional counterpart as well as other appropriate comparators, which had been treated with glyphosate-based and other herbicides (see Paragraphs 80 to 85 above). The EFSA Opinion specifically notes that the plants grown in the field trials in Argentina in season 2007/2008, which were the source of the limited data for the impact of abiotic stressors, were not sprayed with glyphosate-based or other herbicides (EFSA Opinion, section 4.1.4, p.16 **[PD/3]**).

147. Accordingly, EFSA's approach to the assessment of the impact of abiotic and biotic stressors on the Soybean was manifestly in error, and contrary to EFSA's own published guidance.

(ii) *The Commission Decision*

148. The Commission's response to **Ground A(5)** merely summarises the data relied upon and findings made by EFSA (Commission Decision, Annex II, pp.3-4, **[PD/7]**. It fails to engage with the specific points made by Testbiotech, other than to suggest that the scientific literature drawn to its attention is *"not relevant"* because they refer to other crops. This response is clearly in error. Scientific research suggesting that spraying can have unintended effects on plants cannot simply be discounted on the basis that it relates to different crops from soybeans. Findings made in relation to other crops provide scientifically relevant material in the context of an analysis of the Soybean. As a matter of routine scientists extrapolate from other findings. In any event, such reliance would not be necessary if EFSA had ensured that appropriate research was done in the case of the Soybean, which for the reasons given above it failed entirely to do.

149. With respect to the Commission's response to Testbiotech's contention that EFSA failed to require Monsanto to assess the impact of abiotic and biotic stressors on the Soybean which had been treated with glyphosate-based and other herbicides, see Paragraph 125 above in relation to its response to **Ground A(3).**

Conclusion on Ground A

150. In light of the above, Testbiotech maintains that the entire Decision was flawed, and cannot stand. The Commission should have reviewed its authorisation, and requested that EFSA consider the Application in greater detail. By failing to do so, the Commission has:

a. Maintained an authorisation, under the GM Regulation, without ensuring that:

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

ii. Monsanto had provided to it, and to EFSA, "appropriate" information and data to support the comparative analysis submitted with the application under Articles 5(3)(f) / 17(3)(f) GM Regulation;

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

b. Maintained an authorisation, under the GM Regulation, without ensuring that to do so is fully in accordance with its duties:

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

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

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

c. Unlawfully defeated a legitimate expectation that EFSA would act in accordance with its own guidance in advising the Commission on applications for authorisation under the GM Regulation, and that the Commission would ensure such compliance by EFSA before reaching its authorisation decisions.

GROUND B: Failure to consider synergistic/combinatorial effects and/or to require an adequate toxicity assessment

151. Ground B is that even if EFSA's determination that the Soybean was substantially equivalent to its comparator was lawful, which for the reasons given under Ground A is denied, EFSA failed to require Monsanto to carry out sufficient research into the potential synergistic and combinatorial effects of the stacking of the Proteins and/or an adequate toxicity assessment because:

a. **Ground B(2):** EFSA erred by relying upon its flawed finding of substantial equivalence (see **Ground A**). In any event, as a matter of principle even if that finding is not manifestly in error, which is denied, a finding of substantial equivalence does not displace EFSA's duty to carry out a proper safety assessment;

b. **Ground B(2):** EFSA's finding that interactions between the Proteins in the Stacked event, with other plant constituents and/or other factors is wholly flawed for the following reasons:

i. **First,** the selectivity of the newly expressed Cry proteins has not been sufficiently investigated to date and, accordingly, their potential toxicity is not known. Moreover, there has been an insufficient assessment of the interactivity between the Cry proteins/Bt toxins with other plant constituents, including co-

stressors such as cadmium and nematodes, protease inhibitors, bacteria and plant enzymes;

ii. **Second,** there has been insufficient assessment of the expression of the Bt toxins generally, in different climatic conditions and the *"emerging gemonic effects"* evident from the higher content of the newly expressed proteins in the Relevant Stacked Event in comparison with the Parents;

iii. **Third,** there are a number of external factors which may have **combinatorial or synergistic** effects with Bt toxins/Cry proteins, in particular environmental conditions and residues from spraying the genetically-modified plant with glyphosate-based treatments. However, EFSA has failed to require the further investigation necessary to establish if any such effects occurred in relation to the Soybean;

iv. **Fourth,** EFSA's failure to require a sufficient investigation into the effects of different levels of processing on the Soybean means that there has been no proper analysis of the degradation of protease inhibitors and any potential synergies;

v. **Fifth,** EFSA failed to require Monsanto to investigate the emerging genomic effects between the Parents and the Soybean even though such effects suggest that it is not possible to predict the properties of the Soybean on the basis of those displayed by its Parents;

c. **Ground B(3):** It failed to require Monsanto to carry out an adequate toxicity assessment because:

i. **First,** despite scientific evidence showing that the application of glyphosate-based sprays to genetically modified food increases their toxicity, EFSA failed to require Monsanto to carry out a proper assessment of the potential toxicity of the Soybean through, for example, *in vitro* toxicity tests;

ii. **Second,** EFSA failed to require the potential effect of the Soybean on the reproductive system and the transfer of biologically active compounds from the Soybean to animal tissue or humans through consumption. Again, EFSA failed to do this despite a body of scientific evidence showing these potential effects;

iii. **Third,** EFSA failed to take into account the fact there is evidence showing that Bt toxins potentially have detrimental health effects in animals.

152. EFSA's toxicity assessment is manifestly in error, unlawful and/or contrary to its own published guidance. However, in its Decision the Commission erroneously maintained the authorisation of the Soybean.

EFSA's Opinion

153. EFSA concluded in section 5.1.4.3 **[PD/3]** that there was no need to carry out any further animal safety studies of the whole GM food/feed, for three reasons:

a. No adverse effects had been observed in the 90-day rat feeding studies involving the Parents;

b. The Soybean had been found to be substantially equivalent to its conventional counterpart; and

c. *"... [A]n assessment [had] found no indication for interaction between the single events that could influence the safety of soybean MON 87701 × MON 89788 for humans and animals..."* This 'assessment' was based on EFSA's statement that it had (EFSA Opinion, section 5.1.4.1, p.19 **[PD/3]**; emphasis added):

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

154. This reasoning was manifestly flawed for the following reasons:

Ground B(1)

155. **Ground B(1)** is that EFSA's reliance upon its finding of substantial equivalence, Paragraph 153(b), as one of the main reasons why no further toxicology assessment of the whole Soybean was required is wrong both in principle and as a matter of substance.

156. As to the issue of substance, reliance upon EFSA's finding of substantial equivalence is flawed, for reasons given in **Ground A** above.

157. Moreover, as a matter of principle, relying upon a finding of substantial [compositional] equivalence as a reason not to carry out a full and proper toxicological assessment is wrong. As Recital (6) of the GM Regulation observes, *"[w]hilst substantial equivalence is a key step in the procedure for assessment of the safety of genetically modified foods, it is not a safety assessment in itself"* **[AU/1].** Rather, as noted above, the Stacked Events Guidance (which sets out how EFSA intends to meets its obligations under the GM Regulation) requires (**[AU/11]**; emphasis added):

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

Commission Decision

158. Testbiotech raised its concerns with EFSA's reliance upon its finding of substantial equivalence to justify not requiring a toxicological assessment of the Soybean at page 37 of its Request for Internal Review **[PD/6].**

159. In response, the Commission simply asserts that EFSA properly applied the comparative approach (Commission Decision at p.6 **[PD/7]**). In doing so, the Commission acknowledges that the application of the principle of substantial equivalence is a (emphasis added) *"key step"* in the safety assessment. However, the Commission failed to engage with Testbiotech's key concern: whilst the assessment of substantial equivalence is a key part of the procedure of conducting a safety assessment, it is not a safety assessment in of itself. The fact that such a finding has been made, even if it is correctly reached (which is denied in this case), cannot be relied upon as a justification for not conducting a proper safety assessment.

Ground B(2)

160. Under **Ground B(2),** Testbiotech contends that the third reason outlined at Pararaph 153(c) is wholly flawed for the following **five** reasons.

161. **First,** the selectivity of the newly expressed Cry proteins has not been sufficiently investigated to date and, accordingly, their potential toxicity is not known. Moreover, the mode of action of Bt toxins is a matter that is **not presently scientifically understood**. For example, Zhang et al, (2006) **[SU/9]**, Soberon, et al (2009) **[SU/10]**, Broderick et al, (2006) **[SU/11]**, Broderick et al, (2009) **[SU/77]**, Johnston & Crickmore (2009) **[SU/12]**, Mason et al, (2011) **[SU/13]**, Jiminez-Juares (2007) **[SU/14]** all reach different conclusions as to the mode of action in

target organisms. If the mode of action of the individual proteins alone is not understood with any degree of certainty, EFSA has no sound basis for assuming that they will not interact or show synergistic effects.

162. **Second,** Bt toxins have also been found to have **synergistic effects** with each other. For example, Lee et al. (1996) **[SU/15]** and Sharma et al, (2010) **[SU/16]**. Thus there is reason to believe that the Proteins **would** interact.

163. Moreover, scientific evidence confirms that a range of other constituent parts of the plant such as chemicals and enzymes may have **combinatorial effects** with Bt toxins. Table B in Annex II to this Application provides a summary of scientific literature indicating the numerous plant constituents which can affect the toxicity of Cry1A toxins. For example, bacteria, protease inhibitors and other chemicals.

164. Other examples include the powerful effect that some plant enzymes that diminish the digestion of proteins (protease inhibitors) can have on the toxicity of Bt toxins, where toxicity has been found to increase up to 20 times even in the presence of very low levels of protease inhibitors: Pardo Lopéz et al, (2009) 589-595 at section 2.1 at p.590 **[SU/17]**. The interactivity of protease inhibitors with Cry proteins is highly relevant in the context of the Soybean because all soybeans have high levels of such inhibitors. Thus there is reason to believe that the Proteins would interact with other elements;

165. **Third**, there are a number of external factors which may have **combinatorial or synergistic** effects with Bt toxins/Cry proteins.

166. Environmental conditions are particularly material in this regard. It is simply not known how the Soybean or plants containing Bt toxins/Cry proteins will react and/or the expression rate of the newly introduced proteins will be affected by in different climatic conditions. In particular, in the context of climate change, it is important to understand how the Proteins and the plant will be affected by increasingly extreme weather conditions such as droughts, flooding or environmental conditions such as soil and fertiliser. Scientific evidence shows that genetically engineered plants can exhibit unexpected reactions under stress conditions, which can also impact the Bt toxin content/expression rate in the plant (A number of publications are summarised in: Then & Lorch (2008) **[SU/7]**; see also Kamath et al (2010) **[SU/18]**).

167. Monsanto only presented data obtained in field trials in two countries and each took place over one year/harvesting season. Further investigation was therefore manifestly necessary in order

to determine the potential impact of different environmental conditions on the Soybean (EFSA Opinion, Section 4.1.2, p.13 **[PD/3]**).

168. In addition, as set out above, the CP4 EPSPS protein was specifically inserted into the Soybean in order to allow it to be tolerant of glyphosate-based sprays. This tolerance means that it will contain residues from spraying with such sprays (and will not stop growing like a natural variation of soybean). The potential toxicity concerns associated with the application of glyphosate spray to the Soybean is discussed in more detail below at Paragraphs 181 to 187.

169. **Fourth**, the degradation of protease inhibitors is entirely dependent on the method of heat processing. Even the presence of very low levels of protease inhibitors can multiply the insecticidal activity of Cry toxins. Although EFSA considered the following processes: solvent extraction, hard pressing, extrusion and heating (at 190 °C) (EFSA Opinion, section 5.1.3, at p.18 **[PD/3]**), soybeans are subject to a number of different methods of heat processing to make different products such as sprouts, soybean meal and soymilk. These different levels of processing should have been assessed in to order to identify all potential synergies.

170. **Fifth,** it is critical to note that the Soybean had a substantially higher content of the newly expressed Proteins in its tissues than the Parents (Technical Dossier, p.40, Table 6, **[SU/1]**) which shows that it is displaying emerging genomic effects. EFSA failed to undertake a proper assessment of these emerging effects.

171. 'Genomic effects' are effects which cannot be predicted by the properties of the parental plants. These can be caused by conventional breeding and/or through the interaction of the stacked event and the effects of conventional breeding. The changes identified in one generation may or may be identified in subsequent generations. Relevant effects can include a change in the level of the newly expressed proteins in different generations of the plants. This is one of reasons why, for example, De Schrijver et al, (2006) **[SU/19]** emphasise the need for stacked events and their parents to be grown in parallel during field trials of the former event in order to assess whether there are any genomic effects.

172. Of particular concern in relation to the Soybean was that not only was its Protein contents substantially higher than its Parents, the content was sometimes found to be above factor 2 (which means that the content is doubled). This higher protein content clearly shows that the Soybean is displaying genomic effects which cannot be predicted from the study of the Parents and this should have been investigated.

173. Moreover, it is critical to observe that the assessment of the Parents did not address the issues outlined above. The **individualised assessment** of the Parents or Single Events plainly cannot have investigated the potential interactions either:

a. Between the Single Events; or
b. Between the Stacked Event and other constituent part of the plants;
c. Between the Stacked Event and external factors.

174. The investigation of the three issues outlined directly above is precisely what the Stacked Events Guidance envisages.

Commission Decision

175. Testbiotech drew all of the flaws in EFSA's approach outlined above under **Ground B(2)** to the Commission's attention in its Request for Internal Review (pp. 36-47 **[PD/6]**).

176. The Commission's response to the **first** and **second** flaws outlined above at paragraph 161 to 164 is to dismiss Testbiotech's concerns because (Decision, Annex II, at pp.6-7 **[PD/7]**):

a. Testbiotech has apparently *"failed to provide any new scientific information that might change EFSA's conclusions on the toxicity assessment"* of the Soybean (**first** flaw);

b. The vast amount of scientific evidence provided by Testbiotech was *"taken out of context and do[es] not provide new information that might change the conclusions on the toxicity assessment"* of the Soybean (**second** flaw)

177. The first point simply ignores the vast amount of literature advanced by Testbiotech and set out at Paragraphs 161 to 164 above and in Table B in Appendix II to this Application. The second point is not explained and is rejected. In light of EFSA's failure to require a toxicity assessment to be carried out in relation to the Soybean, there is obviously a lack of direct evidence in relation to it. However, it is perfectly acceptable to draw upon studies that have been carried out in relation to the effects of Cry toxins as indicators of the potential effects which **could** be discovered if a proper assessment was carried out (see, for example, Then, (2009) **[SU/83]**).

178. With respect to the part of the **third** and **fifth** flaws identified above at Paragraphs 165 to 168 and 170 to 174, the Commission merely summarises the field trials undertaken by Monsanto and states that due to the *"non-toxic nature of the newly expressed proteins to humans and animals, the data provided is considered adequate. Differences between the levels of expression of [the Soybean] and its parental lines were either not consistent throughout the growing season or very*

small, and in no way show emerging genomic effects in the stack" (Decision, Annex II, p.7 **[PD/7]**). It is the potential toxicity of the Stacked Event which EFSA was supposed to determine. The mere assertion that the Proteins are 'non-toxic' without investigation is unsustainable. Moreover, the Commission fails to deal with the specific criticisms levelled against EFSA's failure both to ensure that proper field trials were carried out and to recognise genomic effects and differences which were in fact found in the inadequate field trials.

179. The Commission's response to the **fourth** (failure to properly investigate the potential synergies caused by heat processing) flaw outlined above at Paragraph 169 entirely misses the point. The Commission merely refers to the manifestly flawed finding of substantial equivalence and points to the fact that Monsanto provided data in relation to the effects of subjecting the Soybean to baking treatment. However, as set out above, baking soybeans is only one of the ways in which they are processed. EFSA took no account of the fact that the Soybean could be used as sprouts or for producing soymilk. These omissions mean that, contrary to EFSA's guidance, no analysis was done of the potential implications of processing the Soybean for such use.

Ground B(3)

180. **Ground B(3)** is that EFSA manifestly failed to require Monsanto to carry out an adequate toxicity assessment. In light of the points made at Paragraph 153 above, EFSA determined that it did not need to require Monsanto to carry out a toxicity assessment of the whole Soybean. Not only was this decision based on manifestly flawed reasoning, as outlined above, it was also wholly unsustainable because there was clear evidence that a number of potential toxicity issues required further investigation.

181. **First,** despite scientific evidence showing that the application of glyphosate-based sprays to genetically modified food increases their toxicity, EFSA failed to require Monsanto to carry out a proper assessment of the potential toxicity of the Soybean.

182. As explained above, the protein MON 89788 was inserted into the Soybean in order to increase its tolerance to being treated with glyphosate spray. This is designed to enable to be grown on a large scale and it is likely that the Soybean will be sprayed several times with glyphosate spray during its period of growth. As a result, it is to be expected that the Soybean will carry a greater amount of glyphosate residues.

183. A number of scientific experts warn that a higher toxicity can be expected for glyphosate than had previously been thought (Benachour et al, (2009) **[SU/20]**; Paganelli et al (2010) **[SU/21]**; PANAP (2009) **[SU/49]**). Scientific evidence also shows that there is several health risks

associated with genetically modified soybeans which are tolerant to glyphosate formulations in combination with residues from the spraying of complementary herbicides.

184. For example, Malatesta, et al, (2002) **[SU/22]**, Malatesta, et al, 2005 **[SU/23]**, Malatesta, et al, 2008 **[SU/24]**; Cisterna et al, (2008) **[SU/25]**, Magana-Gomez et al, (2008) **[SU/48]** recorded a number of effects of feeding genetically modified soybeans to mice, especially in the liver and pancreas, which indicated negative health effects.

185. Moreover, the consumption of glyphosate residues can influence bacteria in the gut (see: Shehata et al, (2012) **[SU/26]** and (2013) **[SU/27]**. Constant exposure to herbicide residues, such as glyphosate, can also have indirect health impacts, for example, it can cause changes to the intestinal flora of humans, which can increase the risk of developing illnesses. It is already known that application of glyphosate can cause changes to the composition of the soil microbial flora. Glyphosate is also effective against certain bacteria, such as E. coli (Forlani et al (1997) **[SU/28]**; Carlisle & Trevors, (1988) **[SU/29]**), and can, in high concentrations, damage the intestinal flora of cattle (Reuter et al, (2007) **[SU/30]**). Even low doses impact the microbial flora of poultry and there is a reduction in the number of beneficial microbes (Shehata et al (2012) **[SU/26]**). Similar effects have also been recorded in relation to cattle (Shehata et al (2013) **[SU/27]**). It is therefore entirely possible that the permanent application of glyphosate could cause changes to human intestinal flora.

186. The need to take into account the fact of residues from spraying in assessing genetically modified food is underlined by the fact that a significant proportion of consumers seem to have a substantial load of pesticide residues in their blood. In 2011, EFSA wrote to the European Commission (DG Sanco) in response to the latter's request for an opinion on the publication by Aris & LeBlanc (2011) (**"the DG Sanco Letter", [SU/31]**). EFSA stated (emphasis added):

> *"From the consumer health perspective, the observations described by the authors on the presence of glyphosate and glufosinate in non-pregnant women blood (5% and 18% of the subjects, respectively) and of 3-MPPA in non-pregnant women, pregnant women and the fetal cord blood are not unexpected. It is known that pesticides are generally well absorbed by the gastrointestinal tract and that an exposure to the two herbicides investigated through the consumption of food commodities is plausible."*

187. Accordingly, an assessment of the possible interaction between Bt toxins and glyphosate spray residues are **highly material** to an assessment of the safety of the Soybean. This should have involved targeted feeding studies and in vitro toxicity tests in order to allow for the proper assessment of any potential risk of toxicity.

188. **Second**, EFSA failed to require the potential effect of the Soybean on the reproductive system and the transfer of biologically active compounds from the Soybean to animal tissue or humans through consumption.

189. It is common scientific knowledge that soybeans produce several hormonally active substances which can, for example, act as estrogens. The insertion of Proteins may have had an unintentional effect on these substances. In particular, as noted above at Paragraphs 98 to 101 and 121, the Soybean displayed heightened levels of daidzein and genistein when compared to its Parents, which are substances that are known to exhibit hormonal activity (De Lemos, (2001) **[SU/3]**). Moreover, scientific evidence shows that the application of glyphosate can act as an endocrine disruptor (see, for example, Gasniera et al (2009) **[SU/32]**). EFSA should, therefore, have required Monsanto to conduct targeted endocrinological studies in order to investigate the impact on the reproductive system.

190. It is also known that DNA and RNA are transferred from genetically engineered soybeans to animal tissue (see, for example, Ran et al, (2009) **[SU/33]** and Tudisco et al (2010) **[SU/34]** and Zhang et al (2011) **[SU/35]**). This should have also been taken into account and investigated by EFSA.

191. **Third,** EFSA failed to take into account the fact there is evidence showing that Bt toxins potentially have detrimental health effects in animals (mammals), Ito et al (2004) **[SU/36]**, Huffmann et al (2004) **[SU/37]**, Thomas & Ellar (1983) **[SU/38]**, Gallagher (2010) **[SU/39]** and Mesnage et al (2012) **[SU/40]** show that toxins that belong to Cry-classification (such as Cry1Ac) may cause adverse effects.

192. Testbiotech does not know whether the Proteins will in fact interact with each other, or with other elements, in a manner which enhances their individual toxicity. But it does contend that in the light of the above there was **no sound basis upon which EFSA could conclude that it was possible to exclude entirely the possibility** of synergistic or combinatorial effects. The evidence relied upon by the Commission is not capable of substantiating the conclusions drawn from it (Case T-475/07 *Dow AgroSciences Ltd v Commission*, judgment of 9 September 2011, at para. 153 **[AU/4]**).

193. Accordingly, contrary to its own guidance (see Paragraphs 47 to 51 above), EFSA failed to require Monsanto to carry out a proper toxicological assessment of the Soybean to establish whether or not there was potential for increased toxicity.

194. Moreover, it appears that Testbiotech's concerns in this regard are shared by a number of Member States:

a. At page 10 of the Member States Comments **[PD/2]**, the French Ministère de L'Economie (Consommation) observed that (translation):

"No experimental 90-day oral toxicity study in rats is provided. With a study of this kind it is possible to evaluate the safety of all the components of the seed of genetically modified soya carrying either transformation event MON87701 or the two events MON 87701 and MON 89788.

A study of this kind was submitted in the dossier pertaining to the request for marketing authorization of the genetically modified soya MON 89788. This study, which lacked raw data, did not enable the Afssa [French Food Safety Agency] to draw a conclusion regarding the safety of soya carrying event MON89788.

The data were, however, supplied to the EFSA, which, in its opinion of 2 July 2008, deemed that this study permitted the conclusion that MON89788 soya was as safe as the reference variety A 3244 (EFSA J., 2008, 758, 1-23)..."

b. At page 92 of the Member States Comments **[PD/2]**, the Spanish Ministry of the Environment, and Rural and Marine Affairs observes that: *"[Monsanto] it is not necessary to carry out a 90-day subchronic toxicity study with MON 87701 x MON 89788 in rats, however there are not any other repeated dose toxicity study with proteins together, or other studies that allow to know the security of continuous consumption of two events when they are consumed together. Therefore, in our opinion would be necessary to have results on the study mentioned above..."*

c. In addition, the Austrian Federal Ministry of Health stated at pages 47 to 48 of the Member States Comments **[PD/2]** that:

"In addition, as this stacked event constitutes a soybean variety with a completely new combination of transproteins, we criticise in particular that an assessment of any potential for increased toxicity to humans and animals due to the stacked event GM soybean MON87701xMON89788 - which may arise from additive, synergistic or antagonistic effects of the gene products - has not been provided (EFSA 2007). Anyhow, as a 90-day rat feeding study with single event MON89788 (Kirkpatrick 2007) was performed for evaluating potential health effects, it is not clear why analogue tests for the stacked system (GM soybean MON87701xMON89788) as well as for the single event MON87701 are not regarded necessary.

In summary, there is no evidence of safe use of the stacked event containing both plant-produced transproteins in the long run. Therefore, [Monsanto] is requested to conduct a repeated dose 90-day oral toxicity study in rodents with the GM soybean MON87701xMON89788, that can provide an estimate of a no-observed-adverse-effect level of exposure (see also comment on Chapter D.7.7 - margin of exposure) which can be used for establishing safety criteria for human exposure (OECD 1998)...."

The Commission's Decision

195. Testbiotech drew all of the flaws in EFSA's approach outlined above under **Ground B(3)** to the Commission's attention in its Request for Internal Review (pp. 36-47 **[PD/6]**).

196. As to the point made as part of the **first** flaw identified above about EFSA's failure to require the investigation of the potential combinatorial and synergistic effects of spraying the Soybean with glyphosate and maintenance pesticides, the Commission states (Decision, Annex II at p.8 **[PD/7]**; emphasis added):

> *"The compositional analyses provided by the applicant included data from GM plants sprayed with glyphosate and maintenance pesticides. Thus, unintended effects on the composition of [the Soybean] resulting from any hypothetical interactivity of the newly expressed proteins with these herbicides have been considered."*

197. This passage betrays the same failure as exhibited by EFSA in relying upon its finding of substantial equivalence to justify its refusal to carry out 'step 2' of the analysis required by its own guidance. A finding of substantial compositional equivalence, even if correct or legally sustainable (which is denied in this case) is not sufficient to displace the need for a proper safety assessment. Accordingly, the data provided for the purpose of the compositional analysis is not sufficient to displace the need for toxicological studies or in vitro testing.

198. A different argument is advanced by the Commission at pages 3 to 4 of the Decision as being the reason why EFSA failed to assess the potential effects of spray residues in combination with the Proteins inserted into the Soybean. This argument is that the *"assessment of the effects on human health of plant protection products, is not regulated by the GMO legislation"* but by other specific regulations. The Commission states that the applicable legislation in this case is Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EC (**"the Pesticide Regulation"**).

199. The Pesticide Regulation establishes a Community regime for setting and controlling Maximum Residue Levels ("MRLs") in food and feeding stuffs. Annex 1 to the Pesticides Regulation lists the food or feed to which the Regulation applies. Soya beans are included on that list. Annex II to the Pesticide Regulation then specifies a MRL which applies to soya beans. The Pesticide Regulation establishes a standardised MRL by product.

200. This standardised MRL can be adjusted to take into account the fact it is being applied to herbicide tolerant crops. In a letter from EFSA to the Commission dated 2011 it was stated that (**"the Maize Letter"** at page 7 **[SU/41]**)):

> *"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. Residue trials would need to be performed according to the agricultural practice relevant to the herbicide tolerant crops and an evaluation of the consumer safety is a prerequisite for the setting of any higher maximum residue level necessitated by that use."*

201. In addition, Kleter et al, (2011) (it is important to note that Mr Kleter is a member of the GMO panel) stated that **[SU/42]**

> *"No general trend of an increase or decrease in the levels of herbicide residues in GM herbicide-resistant crops has been observed in supervised field trials performed within the framework of herbicide registration. It is therefore not possible to infer generalisations on the impact of these GM crops on the MRLs that are to be set for the residues of the herbicide active ingredients, but this has to be considered on a case-by-case basis. This is also reflected in the changes in MRLs following the registration of herbicides for use on GM herbicide-resistant crops. Increases in the MRLs were recommended by JMPR in a few cases, for example for glufosinate in soybean and for glyphosate in cottonseed, while in many other cases this was not recommended."*

202. No trials have been conducted and no adjustment has been made to the MRL set for Soybean to take into account glyphosate or herbicide tolerant soybeans. In the absence of this amendment, EFSA cannot simply ignore the potential effect of the residues on the basis of the application of a MRL that does not take into account the insertion of the Proteins.

203. In any event, even if the MRL had been adjusted, EFSA still has an obligation under the GM Regulation to consider the potential for interactions and synergies which may occur in relation to the particular genetically modified plant in question.

204. The Commission repeats many of the errors outlined above in its response to the **second** flaw (failure to investigate effects on reproduction and transfer of biologically active compounds). It merely re-states the conclusions reached by EFSA in relation to the Soybean's composition, safety and nutritional value (Decision, Annex II at pp.8-**[PD/7]**). It fails to engage with the reasoning advanced by Testbiotech except to highlight that one particular study relied upon by Testbiotech has been the subject of a mandate posed to EFSA. That study was Zhang et al, (2011) **[SU/35]**. As the Commission acknowledges that EFSA considered that this study raised interesting issues which required further investigation. This point does not refute Testbiotech's argument. It supports it.

205. The Commission's response does not address the **third** flaw in relation to the evidence of Bt toxins potentially have detrimental health effects in animals (mammals) **at all.**

Conclusion on Ground B

206. For the reasons given above, Testbiotech contends that the Commission's Decision was flawed. Although it is true that the need for feeding trials to determine toxicity is assessed on a case-by-case basis, in this case it is clear that EFSA had no sound basis for concluding that no such trial was required. In consequence, the Commission:

a. Fell into manifest error in maintaining the authorisation, and failing to require a proper risk assessment that was of the "*highest possible standard*" by including an adequate toxicity test; and/or

b. Maintained an authorisation, under the GM Regulation, in breach of its duties:

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

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

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

c. Unlawfully defeated a legitimate expectation that EFSA would act in accordance with its own guidance in advising the Commission on applications for authorisation under the GM Regulation, and that the Commission would ensure such compliance by EFSA before reaching its authorisation decisions.

GROUND C: Failure to conduct a comprehensive immunological assessment

207. **Ground C** is that EFSA failed to require Monsanto to carry out a proper and complete immunological assessment. This Ground can be subdivided into the following three sub-grounds:

a. **C(1):** A clear flaw in EFSA's immunological assessment is that, contrary to its own guidance, it did not consider, **at all**, possible adjuvant effects. This failure is particularly striking given that soy is one of the most potent allergenic foods;

b. **C(2):** A manifest flaw in EFSA's assessment of the allergenicity of the Soybean is that contrary to its own guidance it failed to conduct any assessment of the specific allergenic risk posed by the Soybean to infants and other vulnerable subpopulations. Accordingly, it failed to require any investigation into this issue by Monsanto;

c. **C(3):** EFSA failed to require further investigation into the allergenicity of the Soybean despite a number of factors, including the increased content of the Cry1Ac in the Soybean, all indicated that such further investigation was necessary.

208. Despite the fact that EFSA's allergenicity assessment is manifestly in error, unlawful and/or contrary to its own published guidance, the Commission erroneously maintained the authorisation of the Soybean.

Ground C(1)

(i) *EFSA's Opinion*

209. As set out above, EFSA's own guidance provides that (Allergenicity Opinion **[AU/12]**; see also the 2011 Guidance **[AU/13]**; emphasis added):

> "*When a food contains a substance known to functionally or structurally resemble a known strong adjuvant, or to belong to a class of proteins known often to have allergy adjuvant activity (e.g. bacterial toxins) the possibility of adverse immune responses being caused by the adjuvant should be considered.*"

210. **Ground C(1)** is that a clear flaw in EFSA's immunological assessment is that, contrary to its own guidance, it did not consider, **at all**, possible adjuvant effects. Adjuvants are substances which in combination with an antigen trigger a stronger immune response and therefore a greater allergic response than would otherwise be the case. The question is not whether the Proteins cause allergenic effects. It is whether the Proteins act as adjuvants in combination with other antigens which prompts a strong immune response in a person or animal.

211. The failure to assess the adjuvant effects of the Proteins is particularly striking when it was a concern which had been raised by the Member State in relation to both MON 87701 and more importantly in relation to the Soybean as follows (emphasis added):

a. **Mon 87701** (2011 comments; Norway; **[PD/2]**): "*According to the applicant the epitope test shows that Cry1Ac protein does not share structurally and immunologically relevant amino acid sequence similarities with known allergens, and that the Cry-protein has no similarities to IgE epitopes of allergenetic proteins. However, this Cry-protein has*

immunogenic potential to elicit strong IgG-response (Vazquez et al.1999) and the induction of IgG antibodies to food antigen and even crosspriming against a bystander antigen may be of biological significance (Brandtzaeg, 2010). Experimental studies both in vitro and in vivo have demonstrated that IgG antibodies that are not balanced by a mucosal IgA response can enhance the epithelial penetration of bystander proteins (Brandzaeg, 2010). Due to remaining uncertainty that Cry1Ac may enhance systemic and mucosal immune responses to co-administrated antigens, the Norwegian GMO Panel still sees the need for further clarification on the possible role of Cry proteins as adjuvants."

b. **The Soybean** (2012 comments; Belgium; **[PD/2]**): *"If Cry1Ac is not likely to be an allergen itself, it should be emphasized that Cry1Ac has been proposed as an adjuvant for vaccines (Esquivel-Perez and Moreno-Fierros, 2005; Moreno-Fierros et al., 2003; Vasquez et al., 1999; Vasquez-Padron et al., 1999; Verdin-Teran al. 2009), which means that this protein is able to enhance the immune responses against antigens that are coadministered. This is not uncommon for a bacterial protein. The consequence of the presence of such immuno-stimulant in a plant destined to human consumption is not known. Particularly the adjuvant effect via intestinal route is poorly documented. It is not known whether the presence of Cry1Ac might elicit sensitization against the other plant proteins upon ingestion. It might be relevant to study in mice the immune responses against soya proteins when the animals are fed Soybean MON87701 x MON8978."*

212. In this context, EFSA should also have considered the fact that soy is one of the most potent allergenic foods.

(ii) Commission Decision

213. Despite the fact that Testbiotech raised the issue of EFSA's failure to investigate the Soybean's adjuvanticity at pages 48 to 49 of its Request for Internal Review **[PD/6]**, the Commission simply fails to grapple with **Ground C(1)**.

Ground C(2)

(i) EFSA Opinion

214. **Ground C(2)** is that an obvious and worrying flaw in EFSA's approach to the allergenicity of the Soybean is that contrary to its own guidance, EFSA failed entirely to assess and require the

investigation of the specific allergenic risk posed by the Soybean to infants and other vulnerable subpopulations.

215. In section 5.1.5.2 of the Opinion, EFSA states that (p.20 **[PD/3]**):

> *"Soybeans are common allergenic foods. Therefore, new genetically modified soybeans are assessed in order to assure that the allergenicity of the whole GM plant has not been increased by the genetic modification. Such assessments have already been performed for soybeans MON 89788 and MON 87701 (EFSA 2008, 2011a), and it was concluded that the overall allergenicity of the whole soybeans MON 89788 and MON 87701 is unlikely to be different from that of their corresponding conventional counterparts and commercial soybean varieties. On request from the EFSA GMO Panel, the applicant supplied additional data to demonstrate that the overall allergenicity of soybean MON 89788 × MON 89788 was not altered when compared with the overall allergenicity of its comparator A554725. The applicant separated proteins from extracts of soybeans MON 87701 × MON 89788 and A5547 by one- or two-dimensional gel electrophoresis and identified bands of major allergenic proteins and spots of less abundant allergens by tandem mass spectrometry. On visual inspection of the intensities of the bands of the abundant α', α, and β subunits of glycinin beta-conglycinin, the acidic and basic chains of glycinin and trypsin inhibitor on the one-dimensional gel and the less abundant spots Gly m Bd30k (P34), Gly m Bd28k and Gly m 4(SAM22) on the two-dimensional gel in soybeans MON 87701 × MON 89788 and A5547 no differences were observed. Thus, the requested study confirmed that bringing together the single soybean events MON 87701 and MON 89788 by conventional crossing to form the stacked soybean MON 87701 × MON 89788 does not result in any observable differences in allergen content between soybeans MON 87701 × MON 89788 and its comparator.*[6]
>
> *The EFSA GMO Panel considers it unlikely that potential interactions will occur in soybean MON 87701 × MON 89788 that might change the allergenicity of the whole crop."*

216. As is clear from the passages above, no reference is made to these vulnerable subgroups. This is a startling omission when the Allergenicity Opinion specifically raises this point in the following terms (Allergenicity Opinion **[AU/12]**):

> *"The specific risk of allergenicity of GM foods in infants as well as in individuals with impaired digestive functions should be considered and therefore, the differences in the digestive physiology in these subpopulations should be taken into account. Primary sensitisation in the gut of young infants might be favoured by the immaturity of the local immunity and incomplete barrier function of the intestinal gut mucosa as well as incomplete protein degradation by pepsin in the stomach due to a gastric pH above values seen in adults".*

217. Examples showing that Cry toxins can trigger the immune system include fish (Sagstad et al, 2007), pigs (Walsh et al, (2011) **[SU/44]**), mice (Finamore et al, (2008) **[SU/45]**), and rats (Kroghsbo et al, (2008) **[SU/46]**, Gallagher, (2010) **[SU/39]**). This scientific evidence shows that Cry toxins can cause reactions in the intestinal cells and in the blood composition, which are indicative of an immune response of the animals studied to specific plant ingredients. Finamore et

[6] It is critical to note that the study relied upon by EFSA, and highlighted in the passage quoted above, does not concern or address potential adjuvantic effects i.e. **Ground C(1).**

al, (2008) **[SU/45]** points out in particular that these findings are relevant to the consumption of Cry toxins by younger and elderly individuals who have a more susceptible immune system (which is what is specifically recognised by EFSA in its Guidance as quoted above). Despite these findings, EFSA did not request immunological studies to assess this health risks in detail.

(ii) *Commission Decision*

218. Testbiotech drew the Commission's attention to this stark failure at page 51 of its Request for Internal Review **[PD/6]**.

219. The Commission's response to **Ground C(2)** is to simply argue that EFSA complied with international guidance, the Codex Alimentarius (2009) (Commission Decision, Annex II, at p.10 **[PD/7]**). This ignores the point made by Testbiotech. The extent to which EFSA has complied with international guidance is not determinative of the question as to whether or not EFSA has complied with its own guidance if EFSA has chosen, as it is entirely free to do, to impose higher standards upon those applying for the authorisation of genetically modified products under the GM Regulation. As set out above, EFSA's own guidance requires an investigation of the potential impact of such products on vulnerable groups.

Ground C(3)

(i) *EFSA Opinion*

220. **Ground C(3)** is that EFSA failed to require further investigation into the potential allergenicity of the Soybean when the following factors **all** indicated such further investigation was necessary:

a. There remained a large amount of uncertainty in relation to the potential allergenicity of the Parents because the era analysis and the Pepsin test did not provide sufficient evidence for the assessment (a point which was noted by the Member States in relation to the assessment of the Parents). In any event, EFSA did not carry out a sera analysis and/or a pepsin test in order to properly investigate the allergenicity of the Soybean;

b. As noted above, the Soybean's Cry1Ac content is much higher than that expressed in its Parents. Accordingly, it could not be safely assumed that the Parents and the Soybean present the same potential allergenic effects;

c. Combinatorial effects of stacking the Proteins in the Soybean can cause unpredictable reactions in the immune system, which have simply not been explored.

221. As set out above, EFSA's own guidance provides that: "*An assessment of <u>any</u> potential for increased ... allergenicity to humans and animals" must be provided"* (Stacked Events Guidance **[AU/11]**).

222. The Member States also appear to share Testbiotech's concerns **[PD/2]**. For example, the Austrian Federal Ministry of Health stated that (Member States comments and opinions, p.50 **[PD/2]**) :

> *"The notifier does not regard an assessment of the allergenicity of the whole GM soybean MON87701 x MON89788 necessary, because "there are no reasons to believe that the allergenicity potential will be different in MON87701 x MON89788 since no changes in endogenous allergenicity of MON87701 x MON89788 are expected during the traditional breeding process that has been widely adopted and used in the development of new varieties across all crops in agricultural production systems". This argumentation misses the fact that an increased potential for allergenicity to humans and animals caused by additive, synergistic or antagonistic effects of the gene products or by these produced metabolites cannot be ruled out a priori (EFSA 2007)."*

223. The studies summarised above at Paragraph 217 above are equally relevant to this point.

(ii) <u>*Commission Decision*</u>

224. Testbiotech raised the points set out under **Ground C(3)** above in its Request for Internal Review at pages 49 to 51 **[PD/6]**.

225. The Commission's response this Ground is similar to its response under **Ground C(2)** in that it again relies upon EFSA's alleged compliance with the weight-of evidence approach applied under the Codex Alimentarius. This is simply not an answer to Testbiotech's legitimate expectation that EFSA will comply with its own guidance. Beyond this reliance upon the Codex, the Commission merely asserts that the scientific publications raised by Testbiotech do not contain any new information which might have changed EFSA's conclusions. However, the studies relied upon by Testbiotech, set out above at Paragraph 217, all show that Bt toxins or Cry proteins can trigger immunological effects. The Commission does not explain why this is not relevant.

Conclusion on Ground C

226. Accordingly, Testbiotech contends that the Commission's Decision was flawed. For the reasons given above it is plain that the potential adjuvanticity and allergenicity required further investigation based upon research of the highest possible standard. In consequence, the Commission:

a. Fell into manifest error in maintaining the authorisation, and failing to require a proper risk assessment that was of the "*highest possible standard*" by including a comprehensive allergenicity test; and/or

b. Maintained an authorisation, under the GM Regulation, in breach of its duties:

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

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

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

c. Unlawfully defeated a legitimate expectation that EFSA would act in accordance with its own guidance in advising the Commission on applications for authorisation under the GM Regulation, and that the Commission would ensure such compliance by EFSA before reaching its authorisation decisions.

GROUND D: Failure to require post-marketing authorisation monitoring of consumption

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

228. Ground D is that:

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

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

229. Of particular concern is that, as explained above at Paragraphs 181 to 187 (**Ground B(3)**), the Soybean is intended to be tolerant to glyphosate-based spray treatments and as a consequence it is likely to carry residues of such treatments. The effect on humans of consuming genetically modified plants and glyphosate spray residues has not been sufficiently investigated. Accordingly, it was entirely appropriate to ensure that such post-market monitoring was carried out.

230. In the Decision, the Commission disputed the legal basis upon which Testbiotech had advanced this argument (Commission Decision, Annex I **[PD/7]**). However, it failed to address the substance of Testbiotech's argument (Decision, Annex II, p.11 **[PD/7]**. Accordingly, Testbiotech contends that the Commission:

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

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

VI. CONCLUSION

231. For the reasons given above, Testbiotech invites the Court to grant the relief sought in Paragraph 3 above.

Kassie Smith QC
Julianne Kerr Stevenson
Monckton Chambers
18 March 2013

Signed: Julianne K. Stevenson

Name: Julianne Kerr Stevenson
Date: 18.03.13