8 October 2021

IN THE GENERAL COURT OF THE EUROPEAN UNION

TESTBIOTECH e.V

with a registered address at Frohschammerstraße 14, 80807 München, Germany,

represented by Kassie Smith BL of Monckton Chambers, 1 & 2 Raymond Buildings, Gray's Inn, London, WC1R 5NR, United Kingdom, member of the Bar of Ireland

Applicant

against

THE EUROPEAN COMMISSION

Defendant

APPLICATION FOR JUDICIAL REVIEW

Case No. T-606/21

Testbiotech e.V, Frohschammerstraße 14, 80807 München, Germany

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I. INTRODUCTION

(a) Summary of the Claim

1. Testbiotech seeks judicial review of the European Commission's decision, dated 8 July 2021 ("**the Decision**") refusing to revoke or amend Commission Implementing Decision (EU) 2021/66 ("**the Commission Implementing Decision**"). The Commission

Implementing Decision granted an authorisation under Regulation (EC) no 1829/2003 on genetically modified food and feed ("**the GM Regulation**") permitting Monsanto Europe SA ("**Monsanto**")[1] to market genetically modified soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 and its sub-combinations ("**the Modified Soybean**").

2. The essence of Testbiotech's complaint is that, in both the Decision and the antecedent Commission Implementing Decision, the Commission committed manifest errors of assessment in determining that the application complied with the requirements of the GM Regulation and of Implementing Regulation 2013/503 ("**the 2013 Regulation**") in failing to require Monsanto to conduct field trials in the agronomic circumstances in which the plant is likely to be cultivated and in failing to require animal feeding trials to be conducted in order to assess the allergenicity and/or toxicity of the Modified Soybean. As a result, the data generated in the field trials conducted do not comply with the requirements of the 2013 Regulation or of the GM Regulation. In the circumstances the Commission could not lawfully conclude that the Modified Soybean met the requisite high level of safety required under the GM Regulation.

(b) Relief sought

3. Testbiotech therefore requests that the Court:

    a) Declare the application admissible and well-founded;

    b) Annul the Decision;

    c) Order the Commission to pay Testbiotech's costs; and

    d) Order any other measure deemed appropriate.

(c) The Applicant's standing

4. Testbiotech, the Institute for Independent Impact Assessment of Biotechnology, is a not-for-profit association registered in Germany at Frohschammerstr. 14, 80807 Munich. It is

[1] During the course of the application which is the subject of this challenge, Monsanto informed the Commission that it had converted its legal form and had changed its name to Bayer Agriculture BCBA, Belgium. For consistency with the documents underpinning this application, it is referred to throughout this Application as "Monsanto".

included in the Register of Associations at the Amtsgericht München (local court, Munich) VR 202119 (see Articles of Association (p. 596, **[A.20])** and Registration Document (p. 605, **[A.21])**. Testbiotech was founded in 2008 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. Testbiotech is included on the EU transparency register, identification number 151554816791-61.

5. Testbiotech is a non-governmental organisation which meets the criteria set out in Article 11 of Regulation (EC) no 1367/2006 ("**the Aarhus Regulation**"). This is recognised by the Commission on page 2 of the Decision.

II. APPLICABLE LAW

(a) The Aarhus Regulation

6. The Aarhus Regulation **[A.22]** is intended to implement the Aarhus Convention. The cornerstone of the Aarhus Convention is the principle that environmental NGOs are deemed to have a legal interest of their own to bring certain judicial proceedings "on behalf of" the environment. This principle is enshrined in Article 2(5) read with Article 9 of the Convention. The preamble to the Aarhus Convention provides as follows:

> "*… Recognizing that adequate protection of the environment is essential to human well-being and the enjoyment of basic human rights, including the right to life itself,*
>
> *Recognizing also that every person has the right to live in an environment adequate to his or her health and well-being, and the duty, both individually and in association with others, to protect and improve the environment for the benefit of present and future generations,*
>
> *Considering that, to be able to assert this right and observe this duty, citizens must have access to information, be entitled to participate in decision-making and have access to justice in environmental matters, and acknowledging in this regard that citizens may need assistance in order to exercise their rights…*
>
> *Recognizing further the importance of the respective roles that individual citizens, non-governmental organizations and the private sector can play in environmental protection…"* (emphasis added).

7. Articles 10 and 12 of the Aarhus Regulation are designed to fulfil the Aarhus Convention's goal of allowing access to justice in environmental matters. These Articles thus establish administrative and judicial review procedures which enable NGOs meeting the requirements of Article 11 of the Regulation to challenge the acts and omissions of the Community institutions which contravene provisions of European environmental law.

8. Article 10(1) of the Aarhus Regulation states that any non-governmental organisation which meets the criteria set out in Article 11 is entitled to make a request for internal review to the EU institution or body that has adopted an administrative act under environmental law.

9. Under Article 2(1)(g), 'administrative act' means any measure of individual scope under environmental law, taken by an EU institution or body, and having legally binding and external effects.

10. Under Article 2(1)(f), 'environmental law' means EU legislation which, irrespective of its legal basis, contributes to the pursuit of the objectives of EU policy on the environment as set out in the Treaty: preserving, protecting and improving the quality of the environment, protecting human health, the prudent and rational utilisation of natural resources, and promoting measures at international level to deal with regional or worldwide environmental problems.

11. Environmental law, within the meaning of the Aarhus Regulation, covers (Case T-33/16 *TestBiotech eV v Commission* ECLI:EU:T:2018:135 at [69], **[A.26]**):

> *"… any provision of EU legislation, concerning the regulation of genetically modified organisms, that has the objective of dealing with a risk, to human or animal health, that originates in those genetically modified organisms or in environmental factors that may have effects on those organisms when they are cultivated or bred in the natural environment. That finding is no less applicable in situations where the genetically modified organisms have not been cultivated within the European Union."*

12. Article 12(1) provides that a non-governmental organisation which made a request for internal review pursuant to Article 10 may institute proceedings before the Court of Justice in accordance with the relevant provisions of the Treaty.

(b) The GM Regulation

13. The GM Regulation **[A.23]** 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. As the Recitals (2), (3) and (9) make clear, it reflects the core Union objective of ensuring a high level of protection of human life and health:

> *"A high level of protection of human life and health should be ensured in the pursuit of [Union] policies…*
>
> *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]…*
>
> *…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 [EFSA], of any risks which they present for human and animal health and, as the case may be, for the environment…"* (emphasis added).

14. "**Genetically modified organism**" is defined in Article 2(2) of Directive 2001/18 **[A.25**] 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*".

15. "**Organism**" is further defined in Article 2(1) of Directive 2001/18 as *"any biological entity capable of replication or of transferring genetic material"*.

16. Food or feed derived from genetically modified organisms ("**GMOs**") must not have adverse effects on human health, animal health or the environment (Article 4(1)(a) and 16(1)(a) of the GM Regulation).

17. This is ensured, *inter alia*, by a strict licensing regime: pursuant to Article 4(2) of the GM Regulation, GMOs may not be placed on the market for food use unless an authorisation has been granted in accordance with the requirements set out in the remainder of the Regulation.

18. Article 5 sets out the process to be followed in an application for authorisation for food use. Article 5(3)(f) requires that the application be accompanied by:

"… 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…"

19. This is substantially replicated in Article 17(3)(f) in respect of an application for feed use.

20. Article 6(3)(a) provides that in preparing its opinion, the European Food Safety Authority ("**EFSA**"):

> "*…shall verify that the particulars and documents submitted by the applicant are in accordance with Article 5 and examine whether the food complies with the criteria referred to in Article 4(1)"*

21. This is, again, substantially replicated in Article 18(3)(a) in respect of an application for feed use.

22. Once the application is received, it is then transferred to EFSA for an Opinion. EFSA then evaluates the application, consults competent authorities in Member States and produces an Opinion on whether the GMO should be authorised (Articles 6 and 18). On the basis of this Opinion, any relevant provisions of EU law and any other legitimate factors relevant to the application, the Commission produces a draft decision, which is submitted to the Standing Committee on the Food Chain and Animal Health and becomes final in accordance with the comitology procedure (Articles 7(1), 19(3) and 35(2)).

(c) The 2013 Regulation

23. While the GM Regulation provides the overarching framework for the assessment of marketing authorisation applications, applications must also comply with the detailed legislative rules specified in the appropriate Implementing Regulation in force. The current Implementing Regulation in force is the 2013 Regulation **[A.24]** which provides a comprehensive and detailed set of rules, particularly for stacked events, such as the Modified Soybean in the present case.

24. The scope of the 2013 Regulation is set out in Article 1 thereof:

> *"This Regulation shall apply to applications submitted under Article 5, 11, 17 and 23 of Regulation (EC) No 1829/2003 for the authorisation of:*
>
> *(a) genetically modified plants for food or feed uses;*
>
> *(b) food or feed containing or consisting of genetically modified plants;*

(c) food produced from or containing ingredients produced from genetically modified plants or feed produced from such plants."

25. Chapter II sets out 'General Requirements' for the applications. Under Article 3(1):

> *"The application submitted under Article 5(1) and 17(1) of Regulation (EC) No 1829/2003 shall:*
>
> *(a) be submitted in accordance with the requirements for the preparation and presentation of applications set out in Annex I;*
>
> *(b) contain all the information required by Annex I, in accordance with the specific requirements of Articles 4, 5 and 6."*

26. Annex I sets out extensive requirements for the scientific and other information that must be contained in an application.

27. Under Article 5(1) of the 2013 Regulation:

> *"Information, including studies, required to accompany the application as referred to in Article 5(3)(a) to (f) and (h) and in Article 17(3)(a) to (f) and (h) of Regulation (EC) No 1829/2003 shall be provided in accordance with the scientific requirements for the risk assessment of genetically modified food and feed set out in Annex II to this Regulation"*

28. Annex II sets out a detailed list of the scientific requirements on information to be provided for the purposes of the risk assessments conducted by EFSA and the Commission prior to authorisation being granted.

29. Under Annex II, the following is required (in relevant part):

> *"I. INTRODUCTION*
>
> *…*
>
> *2.2. The risk assessment of genetically modified food and feed containing stacked transformation events shall also include an assessment of the following aspects:*
>
> *(a) stability of the transformation events;*
>
> *(b) expression of the transformation events;*
>
> *(c) potential synergistic or antagonistic effects resulting from the combination of the transformation events shall be subject to an assessment in accordance with Sections 1.4 (Toxicology), 1.5 (Allergenicity) and 1.6 (Nutritional assessment).*
>
> *For genetically modified food and feed containing, consisting of or produced from genetically modified plants, whose cultivation is associated with the production of*

genetically modified material containing various subcombinations of transformation events (segregating crops), the application shall include all subcombinations independently of their origin which have not yet been authorised. In such a case, the applicant shall provide a scientific rationale justifying that there is no need to provide experimental data for the concerned subcombinations or, in the absence of such scientific rationale, provide the experimental data…"

30. Section II of Annex II requires the following in respect of gene expression of genetically modified organisms (in relevant part):

"II. SCIENTIFIC REQUIREMENTS:

…

1.2.2.3. Information on the expression of the insert(s)

The applicant shall provide information:

- *to demonstrate whether the inserted/modified sequence results in intended changes at the protein, RNA and/or metabolite levels;*
- *to characterise the potential unintended expression of new ORFs identified under point 1.2.2.2(f) as raising a safety concern.*

For those purposes, the applicant shall provide the following information:

...(e) Protein expression data, including the raw data, obtained from field trials and related to the conditions in which the crop is grown…

(f) With regard to the stacking of transformation events by conventional crossing, expression data shall be provided to assess the potential interactions between the events which may raise any additional safety concerns over protein and trait expression compared with the single transformation events. The comparison shall be carried out with data obtained from plants grown in the same field trials. On a case-by-case basis, and where concerns arise, additional information may be necessary."

(emphasis added)

31. Subsection 1.3.1 details the considerations which must be taken into account in the choice of comparator in field trials:

"1.3.1. Choice of the conventional counterpart and additional comparators

In the case of herbicide tolerant genetically modified plants and in order to assess whether the expected agricultural practices influence the expression of the studied endpoints, three test materials shall be compared: the genetically modified plant exposed to the intended herbicide; the conventional counterpart treated with conventional herbicide management regimes; and the genetically modified plant

treated with the same conventional herbicide management regimes." (emphasis added).

32. Subsection 1.3.2.1(b) details the protocols to be followed in the design of field trials:

> ***"1.3.2.1(b) Specific protocols for experimental design***
>
> *The different sites selected for the field trials shall reflect the different meteorological and agronomic conditions under which the crop is to be grown; the choice shall be explicitly justified. …"* (emphasis added).

33. Section 1.4 details the obligation on the applicant to assess the toxicological impact of changes to the genetically modified organism from genetic modification. Toxicological assessment must (in relevant part):

> "*(a) demonstrate that the intended effect(s) of the genetic modification has no adverse effects on human and animal health;*
>
> *…*
>
> *(d) identify potential adverse effects on the whole genetically modified food/feed or address remaining uncertainties through the performance of 90-day feeding studies."*

34. Subsection 1.4.1 details the testing requirements for newly expressed proteins, and, in particular, requires an analysis of the potential interaction between those new proteins and existing plant constituents:

> **"*Testing of newly expressed proteins***
>
> …
>
> *To demonstrate the safety of newly expressed proteins, the applicant shall provide:*
>
> *(a) A molecular and biochemical characterisation of the newly expressed protein, including determination of the primary structure, molecular weight (for example using mass spectrometry), studies on post-translational modifications and a description of its function. In the case of newly expressed enzymes, information on the enzyme activities including the temperature and pH range for optimum activity, substrate specificity, and possible reaction products shall also be provided. The potential interaction with other plant constituents shall also be evaluated."* (emphasis added).

35. Animal feeding studies are required in the case of stacked events where (subsection 1.4.4.1):

> "*…indications of potential adverse effects are identified during the assessment of: (i) the stability of the inserts; (ii) the expression of the inserts; and (iii) the potential*

synergistic or antagonistic effects resulting from the combination of the transformation events".

36. Section 1.5 of Annex II deals with "allergenicity". The assessment of allergenicity is complicated by the fact that "*allergenicity is not an intrinsic, fully predictable property of a given protein but is a biological activity requiring an interaction with individuals with a pre-disposed genetic background".* Accordingly, "*given this lack of complete predictability, it is necessary to consider several aspects in the assessment of allergenicity to obtain a cumulative body of evidence which minimises any uncertainty with regard to the protein(s) in question"* (subsection 1.5.1).

37. Section 3.3 details the obligation on the applicant to ensure that the final risk characterisation demonstrates no adverse effects on human and animal health:

> ***"3.3. The result of risk characterisation***
>
> *In accordance with the requirements of Articles 4 and 16 of Regulation (EC) No 1829/2003, the applicant shall ensure that the final risk characterisation clearly demonstrates that:*
>
> > *(a) the genetically modified food and feed has no adverse effects on human and animal health…"*

38. The 2013 Regulation thus sets detailed standards for the information to be provided by the applicant, and for the methods and assessment processes to be employed by EFSA and the Commission when considering whether to grant a market authorisation. If the information required by the Annexes to the 2013 Regulation is not provided by an applicant, it cannot be properly concluded that a product derived from a genetically engineered plant has been demonstrated to be safe.

(d) The standard of review applied by the General Court to challenges to market authorisation

39. The standard of review applicable to challenges to a Commission refusal to reconsider a marketing authorisation decision was discussed by the General Court in Case T-177/13 *TestBiotech eV v Commission*, judgment of 15 December 2016 [**A.27**]. While acknowledging that the Commission should enjoy a considerable margin of discretion in granting marketing authorisations and examining requests for internal reviews, the Court stressed that this discretion is not unlimited and that the precautionary principle still applies:

"76. …it should be observed at the outset that the objective of the Aarhus Convention to give the public broad access to justice requires that the EU Courts do not conduct a more limited or less strict examination of a decision rejecting a request for internal review made pursuant to Article 10 of Regulation No 1367/2006 as unfounded than what it would do in a case in which a natural or legal person seeks annulment of an authorisation decision under Regulation No 1829/2003. Moreover, when a case has been brought before it concerning such a decision, the General Court is also bound by the precautionary principle…

…

80. Moreover, where the EU institutions have a broad discretion, respect for the rights guaranteed by the EU legal order in administrative procedures is of even more fundamental importance. Those guarantees include, in particular, the duty of the competent institution to examine carefully and impartially all the relevant aspects of the individual case, the right of the person concerned to make his views known and also his right to have an adequately reasoned decision ..."

40. An applicant for judicial review is not required to prove that the GMO in question is unsafe; rather (contrary to the Commission's submissions in that case), it is only required to provide material raising serious doubts as to the lawfulness of the authorisation decision. The Court explained that this reflected the information asymmetry faced by applicants in comparison to the Commission, and the general precautionary principle under EU environmental law:

"84. However, it should be noted that, under Regulation No 1829/2003, in the area of marketing authorisations for genetically modified food and feed, non-governmental organisations' access to relevant information is usually restricted to information that is publicly available and to which the Commission also had access at the time of its in-depth assessment of the risks in terms of the conditions laid down in Article 4(1) and Article 16(1) of that regulation.

85. Where the Commission concludes that the evidence adduced by a party requesting an internal review is substantial and liable to raise serious doubts as to the lawfulness or well-foundedness of the grant of that authorisation, it is required to examine all relevant information of its own motion, since its role in an internal review under Article 10 of Regulation No 1367/2006 is not that of an arbitrator, whose remit is limited to making an award solely on the basis of the information and the evidence provided by the party requesting the review... .

86. <u>That remit also follows from the fact that the Commission is bound by the precautionary principle, which is a general principle of European Union law. That principle, as interpreted in the Court's case-law, means that where there is uncertainty as to the existence or extent of risks to human health, protective measures may be taken without having to wait until the reality and seriousness of those risks become fully apparent</u> … .

87. It should also be borne in mind that Article 168(1) TFEU requires that a high level of human health protection be ensured in the definition and implementation of all EU policies and activities. The protection of human health takes precedence over economic considerations, with the result that it may justify adverse economic consequences, even those which are substantial, for certain traders … .

88. Therefore, and contrary to the Commission's assertions in the first contested decision, the first applicant cannot be required '[to] prove that the [authorisation] decision is in breach of Regulation (EC) No 1829/2003'; rather, it must provide a set of material raising serious doubts as to the lawfulness of the authorisation decision." (emphasis added).

III. FACTUAL BACKGROUND

(a) The Modified Soybean

41. The Modified Soybean is a hybrid product. It is created by combining the genetic material of parent plants (which were themselves genetically modified) with the following expressed proteins:

    a) MON 89788 expressing CP4 EPSPS protein for tolerance to glyphosate-containing herbicides;

    b) MON 87708 expressing the DMO protein for tolerance to dicamba-containing herbicides;

    c) MON 87751 expressing the insecticidal proteins Cry1A.105 and Cry2Ab2;

    d) MON 87701 expressing the insecticidal protein Cry1Ac.

42. **"Glyphosate"** is the active ingredient in some agricultural herbicides (which are often used as "complementary" 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 micro-organisms. Inhibiting this enzyme leads to reduced protein synthesis and plant growth. Crops expressing the CP4 EPSPS protein have a low affinity for glyphosate compared to plants without the protein (*e.g.*, the target weeds). This allows crops treated with glyphosate-based herbicides to continue to grow when treated with glyphosate-based herbicides, while the non-tolerant weeds die.

43. **"Dicamba"** is the active ingredient in some agricultural herbicides. Dicamba kills plants by mimicking natural plant hormones known as auxins, which regulate many plant processes including cell growth and protein synthesis. Dicamba can induce rapid cell

growth and limit transpiration and photosynthesis in the plant. This leads to irregular plant growth, leaf drop and starvation. Plants expressing the DMO protein are capable of degrading dicamba and so are tolerant of it.

44. "**Cry**" proteins are toxins derived from the bacterium *Bacillus thurigiensis*, a soil-dwelling bacterium. The Cry toxins can be extracted and used as a biological pesticide. These toxins are commonly referred to as "**Bt toxins**".

45. The Modified Soybean thus combines the insecticidal traits of MON 87751 and MON 87701, with the herbicide tolerant traits of MON 89788 and MON 87708. Because it combines the modified genes of its Parents, it is called a "**stacked event**".

(b) The Authorisation Application and Internal Review

46. Monsanto filed application EFSA-GMO-NL-2016-128 ("**the Application**") **[A.1]** in the Netherlands seeking authorisation under the GM Regulation for the Modified Soybean and its derived products for food and feed uses, import and processing in the European Union, which was supported by its application dossier **[A.2]**. The Application excludes cultivation within the EU.

47. The Modified Soybean is a genetically modified organism, or is food/feed containing genetically modified organisms, within Article 2(5) of the GM Regulation.

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

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

50. This consultation resulted in the submission of a slew of critical comments to EFSA during the three-month consultation period by the competent authorities of Member States, including criticisms that **[A.3]:**

a) no analysis had been done regarding glyphosate residues or glyphosate metabolites on the stacked GM soybean;[2]

b) no testing of the possible synergistic or antagonistic effects of the Bt toxins with the herbicide residues had been undertaken;[3]

c) questions on the safety of the stacked GM soybean and derived food and feed remained unanswered;[4]

d) the potential long-term reproductive or developmental effects of the food or feed had not been assessed;[5]

e) due to missing information, the safety of the stacked GM soybean could not be fully assessed;[6] and

f) that the toxicological assessment and the environmental risk assessment were unacceptable and that the risk assessment did not fulfil requirements for assessing risks to the immune system.[7]

51. In spite of these criticisms, following the consultation, EFSA issued an Opinion on the Application on 3 July 2019 ("**the EFSA Opinion**") ("*Summary",* p. 282, **[A.4]**). It concluded, in material part:

> "*…the GMO Panel concludes that MON 87751 x MON 87701 x MON 87708 x MON 89788, as described in this application, is as safe as and nutritionally equivalent to the non-GM comparator and the commercial non-GM soybean reference varieties… tested"*

52. Following the publication of the EFSA Opinion, on 17 December 2020 the European Parliament adopted a resolution objecting to the authorisation of the Modified Soybean and calling on the Commission to withdraw its draft implementing decision ("**the Resolution**") on the basis that (AF2, p. 319, **[A.5])**:

> *"… the draft Commission implementing decision is not consistent with Union law, in that it is not compatible with the aim of Regulation (EC) No 1829/2003, which is, in accordance with the general principles laid down in Regulation (EC) No 178/2002 of the European Parliament and of the Council, to provide the basis for ensuring a high level of protection of human life and health, animal health and welfare, and*

[2] Austria AUT comment_08; Austria AUT Comment_11; Germany BfN Comment 4; Hungary HU4.
[3] Austria AUT Comment_08; Austria Comment AUT_10; Austria AUT Comment_12; Germany BfN Comment 4; Hungary HU3; Hungary HU8; Hungary HU11.
[4] Hungary, HU10.
[5] Austria AUT Comment_05; Austria AUT Comment_08; Hungary HU21.
[6] Austria, AUT Comment_10; Germany BfN Comment 1; Germany BfN Comment 9; Germany BVL Comment 2.
[7] Austria AUT Comment_11; Austria AUT Comment_12; Belgium, Comment from Belgium; Hungary HU13; Germany BfN Comment 5.

environmental and consumer interests, in relation to GM food and feed, while ensuring the effective functioning of the internal market".

53. The Resolution specifically criticised the draft authorisation decision on the basis that it was to be expected that the Modified Soybean would be subject to higher and repeated doses of herbicide, leading to a higher quantity of residue in the harvest (G – N, p. 315, **[A.5]**), and that a number of scientific studies demonstrated an impact on the immune system of exposure to Bt toxins and that current toxicological studies were insufficient to conclude that consumption of the Modified Soybean was safe for human and animal health (Q – S, p. 316 **[A.5]**).

54. In spite of these trenchant objections by both the Parliament and the Member States, the Modified Soybean was nonetheless authorised by the Commission on 22 January 2021 and the authorisation was published in the Official Journal of the EU on 26 January 2021 **[A.6]**.

55. Testbiotech sought an internal administrative review of that decision on 8 March 2021 under Article 10 of the Aarhus Regulation and Article 36 of the GM Regulation (the "**Request for Internal Review**") (**[A.7]; [A.8]).**

56. The Commission responded on 8 July 2021 with the decision letter rejecting Testbiotech's request for internal review, and with the Decision (**[A.9]; [A.10]**). The Commission determined that the request was unfounded and that the Commission Implementing Decision was in accordance with the applicable EU legislation.

IV. GROUNDS OF CHALLENGE

57. Testbiotech contends that the Commission has committed manifest errors of assessment in having confirmed the authorisation of the Modified Soybean without ensuring that an appropriate risk assessment of the 'highest possible standard' had been carried out and that Monsanto had provided 'appropriate' data under Article 5(3)(f), Article 6(3)(a), Article 17(3)(f) and Article 18(3)(a) of the GM Regulation and of Article 5 of the 2013 Regulation; and in refusing to review its decision to grant the marketing authorisation.

58. Testbiotech's two grounds of challenge are as follows. The Commission (and EFSA in the antecedent opinion) has committed manifest errors of assessment in that it has:

    a) **Ground A:** failed to give any or any adequate consideration to the potential impact of gene stacking on gene expression in combination with herbicide

applications and/or failed to require an adequate assessment under real-world conditions of repeated and/or high application of the two herbicides to which the Modified Soybean expresses tolerance.

b) **Ground B:** failed to give any adequate consideration to the potential for toxicity and/or allergenicity in the Modified Soybean as a result of synergistic effects between the proteins it is genetically modified to express, naturally occurring protease inhibitors in soybeans, exposure to herbicide and/or herbicide residue in the harvest and/or failed to require animal feeding trials of the stack to be conducted.

GROUND A: the impact of gene stacking on gene expression in combination with herbicide applications

(i) Testbiotech's position

59. Testbiotech's position on Ground A is set out in section 2.1.2.2 of its Request for Internal Review (p. 353, **[A.8])**.

60. As set out above at [41], above, the Modified Soybean expresses multiple genes conferring herbicide resistance. Due to increased weed pressure (itself partially a result of the cultivation of plants which are genetically engineered to be herbicide resistant, and so, the high application of herbicide in normal cultivation leading to an increase in weeds which are resistant to that herbicide) and the Modified Soybean's tolerance of herbicide, it ought to have been assumed in the design of the field tests that these plants will be exposed to high and repeated dosages of glyphosate alone and in combination with dicamba when cultivated in practice.

61. Higher rates of herbicide application leads to a higher burden of herbicide residues in the harvest and can also influence the expression of the transgenes or other genome activities in the plants. This is demonstrated in academic data ((Miyazaki et al., 2019, "*Pesticide Risk assessment",* p. 413, **[A.11]**) and was also recognised by experts of the Member States (see [50], above).

62. Despite the clear potential for changes to gene expression from exposure to high application of herbicide, the application of the herbicide in field trials was substantially lower than

would be expected under real-world conditions. Glyphosate was applied at a rate of 0.87 kg a.e./ha only **[A. 2]**. This is despite the fact that the expected application rate in the US would be an average overall rate of 6 to 7 kg/ha (USDA, 2019; Miyazaki et al., 2019, p. 410 **[A.11]**). This is significant as over 70% of the soybeans imported into the EU in 2018-19 (the latest year for which statistics are available) originated in the US (p. 428, **[A.12]**).

63. Even higher rates of application can be expected in South America (see, for example, Miyazaki et al., 2019, p. 410 **[A.11],** Avila-Vazquez et al., (2018), p. 459 **[A.14]**). This is also significant as over 20% of the soybeans imported into the EU originated in Brazil and Paraguay (p. 428, **[A.12]**).

64. Leaving aside the practice of cultivators in the real world, an application rate of 0.87 kg a.e./ha also differs substantially from the recommendations of manufacturers. On its own "Roundup Ready Soybean" product label (p. 448, **[A.13]**), Monsanto recommends spraying a combined total maximum application rate of 5.3 quarts per acre, which is equivalent to c. 8.2kg a.i/ha. The total in-crop recommended application maximum is 64 fl oz per acre per year, which is equivalent to c. 3.1kg a.i/ha.

65. Moreover, under real-world conditions, it will frequently be the case that only one of the two herbicides to which the crop expresses tolerance will be used. This is likely for a number of reasons, including the fact that different regions will suffer from different weed problems (for which different herbicides are optimised), will maintain different agricultural management practices, and will have access to herbicides at different prices. For example, in a region with higher proportions of weed grasses (which are not affected by dicamba), or where a cultivator is spraying herbicide in an area adjacent to a field in which non-resistant plants are grown (as dicamba may drift with the wind to nearby plots), a cultivator may spray only glyphosate-based herbicides on the crop. In Argentina, Brazil and the US, there will be different prices, different herbicide formulations and varying regimes of herbicide applications in soybean cultivation. None of these specific agronomic practices were considered in the design of the field trials or in EFSA risk assessment.

66. The failure to test the plants under the conditions of real-world applications of glyphosate and dicamba, separately and in tandem with one another has real consequences for the safety of the conclusions reached during the field testing. When the Modified Soybean is exposed to higher rates of herbicide application, the plants can experience stress conditions, impacting gene expression and plant composition as well as the biological characteristics

of the Modified Soybean. These changes in plant composition can arise from, or be influenced by, the expression of the additionally inserted genes. Treating plants in field trials with non-representative amounts of herbicide can conceal changes in plant composition and the interactions between the biologically active compounds in the plants.

67. The conditions under which the field trials were conducted were accordingly divorced from both the real-world conditions under which the crop will be cultivated and from the management regimen recommended by Monsanto on its product label. The field tests accordingly did not meet the requirements of subsection 1.3.2.1(b) of Annex II of the 2013 Regulation which requires field testing to be carried out in the agronomic conditions reflecting those under which the GMO will be cultivated in practice.

68. The data presented by Monsanto is flawed for a further, inexplicable reason. The expression data from the Modified Soybean was generated from crops treated with the complementary herbicide. This was then compared to data from the parental plants which were not treated with the complementary herbicide **[A.2]**. This is in clear breach of the requirements of the subsection 1.3.1 of Annex II of the 2013 Regulation, which requires that comparisons be carried out between the genetically modified plant exposed to the intended herbicide, the conventional counterpart treated with conventional herbicide management regimes, and the genetically modified plant treated with the same conventional management regimes. It is impossible to assess whether anticipated agricultural practices influenced the expression of the studied endpoints based on the data supplied by Monsanto. This is a straightforward breach of the requirement in subjection 1.3.1 of Annex II of the 2013 Regulation which requires that herbicide resistant crops are exposed to the "*intended herbicide*" and compared on the basis of that exposure.

(ii) The EFSA opinion

69. The EFSA opinion concluded that the management practices involved in the field testing, including the application of herbicides used in the testing, were in line with the recommendation of manufacturers and good agricultural practices (EFSA opinion, 3.5.4.3, p. 291 **[A.4]**).

70. Given the significant discrepancy between the rates of herbicide applied in the field testing and standard industry practice (where field testing rates were at the lowest end of

the range recommended by the manufacturer, leaving aside the fact that *even higher* rates may be applied to herbicide resistant soybean) EFSA's conclusion on this point is untenable.

(iii) The Commission decision

71. The Commission agreed with EFSA's assessment.

72. First, the Commission took the position that in the field trials for comparative analysis of herbicide tolerant GM plants, the intended herbicides are to be kept at a similar application rate across sites, to ensure comparability between locations, while the combinations of conventional herbicides applied at the selected sites are to reflect different weed management practices, chosen to maintain the weed pressure under control (p. 392, [**A.10**]).

73. This is no response to Testbiotech's criticism and indeed demonstrates that the field testing undertaken does not fulfil the requirements of the 2013 Regulation. If the application of the complementary herbicide on the fields of the genetically engineered plants is kept at similar rate as in the fields with non-genetically engineered plants, the conditions under which field testing was conducted in no way represents the agronomic conditions to which the plants will be exposed. Under real agricultural practices, significantly higher rates of the complementary herbicides are sprayed on herbicide tolerant genetically engineered plants in comparison to the non-genetically engineered plant which are not made tolerant to these herbicides. This is the benefit of genetically engineering plants to be herbicide tolerant: it allows cultivators to use higher amounts of herbicide to control weed pressure without damaging the crop.

74. Second, the Commission agreed with EFSA's contention that the timing and rate of the applied herbicides are in line with the recommendations of the manufacturers (p. 393, **[A.10]**).

75. This is, equally, no answer to Testbiotech's complaint. The 2013 Regulation requires that the field trials be conducted in light of real-world agricultural practice, not simply in line with the recommendations of a manufacturer's regimen, and, in any event, the doses applied to the Modified Soybean in field trials was at the lowest end of the industry-recommended range.

76. Third, the Commission conceded that the scientific literature cited by Testbiotech (Zanatta et al. (2020), p. 393, **[A.15]**) was relevant to the question of whether gene expression would be affected by high doses of herbicides but nonetheless concluded that the gene expression data generated in the field testing was adequate.

77. No reasoning is advanced for this conclusion in the Commission Decision. It instead cross-refers to section 3.5.6 of the EFSA Opinion, which is where EFSA sets out the compositional data generated in the flawed field testing. It is no justification for the failure to adequately assess the impact of the higher rates of herbicide to which the crop ought to have been exposed in order to generate data from which safe conclusions on gene expression could have been drawn.

78. Fourth, the Commission concluded that publications cited by Testbiotech in its Request for Internal Review were not relevant on the basis that they were generated using material produced in a glyphosate-free environment, or using material not produced from a specific event, or were generated from materials not produced from seeds/grain (p. 393, **[A.10]**).

79. In simple terms, the publications cited by Testbiotech establish (1) that herbicide application affects plant composition and metabolism in herbicide-resistant plants and (2) that there is a clear correlation between the application of different doses (including higher doses) of glyphosate and plant agronomic performance and composition. Neither EFSA nor the Commission is in a position to rule out such effects in the Modified Soybean because it did not require the conduct of tests which would have assessed whether these conclusions did hold true in the case of the Modified Soybean. In that context, it was for Monsanto to establish (and for EFSA and the Commission to verify) that those effects either did not occur, or that they did not pose a safety risk.

80. This response demonstrates the unduly narrow approach taken by both EFSA and the Commission to information considered "relevant" in its conduct of an assessment aimed at ensuring the highest level of safety for food entering the EU. None of the spurious grounds relied on by either EFSA or the Commission to nominally distinguish the subjects of the scientific publications cited by Testbiotech are safe bases on which to discount the conclusions in those papers. As a result, it could not have been concluded in the circumstances that the Modified Soybean was safe and so suitable for authorisation.

(iv) Conclusion on Ground A

81. The experimental design for the testing of the Modified Soybean was wholly inadequate to identify possible unintended changes introduced with the genetic modifications in combination with the management practices under which the Modified Soybean will be cultivated in practice, in breach of the requirement in subsections 1.3.1 and 1.3.2.1(b) of Annex II of the 2013 Regulation which requires that the crops be exposed to the "*intended herbicide"* and "*agronomic conditions under which the crop is to be grown*" and analysed on that basis.

82. Accordingly, protein expression data obtained from field trials "*related to the conditions in which the crop is grown*" was not made available, in breach of the requirement in subsection 1.2.2.3 of Annex II of the 2013 Regulation. Monsanto was in further breach of subsection 1.3.1 of Annex II which requires the comparison of the Modified Soybean to comparator non-GM plants in the same field trials.

83. As a result, the data supplied in support of the application did not fulfil the conditions specified in Articles 5(3)(a) and 17(3)(f) of the GM Regulation. EFSA ought to have rejected it under Articles 6(3)(a) and 18(3)(a) of the GM Regulation.

84. The Commission's determination that the field testing met the requirements of the 2013 Regulation and of the GM Regulation accordingly constitutes a manifest error of assessment. It could not be concluded from the data obtained from field testing that the Modified Soybean met the high level of safety required to be lawfully authorised in the EU.

GROUND B: Assessment of allergenicity and toxicity of the Modified Soybean

(i) Testbiotech's position

85. Testbiotech's position on Ground B is set out in section 2.3 of its Request for Internal Review (p. 362, **[A.8]**).

86. In summary, the testing undertaken on the Modified Soybean was wholly inadequate to assess potential immunogenic and toxic impacts of the plant components on humans in the course of normal consumption. The toxicity and immunogenicity assessments undertaken in respect of the Modified Soybean adopted a siloed approach to the different

plant components with potential impacts on human health and did not assess effects caused by the interactions of these components, and further, did not assess these potential impacts in light of the high likelihood that the Modified Soybean will be exposed to high amounts of herbicide in the course of normal cultivation. This is in breach of the requirements in 1.4.1 of Annex II of the 2013 Regulation and is fatal to the safety of the conclusions reached in respect of the immunogenicity and toxicity of the stack. Animal feeding trials were required in order to assess potential synergistic effects of the plant components under subsection 1.4.4.1 of Annex II of the 2013 Regulation

87. Two particular factors ought to have signalled the risk of toxicity and allergenicity in the Modified Soybean.

88. The first factor is that certain enzymes, known as **protease inhibitors** which are naturally produced in soybean plants can prolong exposure to toxins in the gut after ingestion (including the two toxins the Modified Soybean has been genetically engineered to express: Bt toxins Cry1Ac and Cry1A.105). There is a very substantial amount of scientific literature indicating that immune responses (including adjuvanticity in mammals) are triggered by Bt toxins (see, *e.g.*, a review of the literature in Rubio-Infante et al. (2016), section headed "*Immune responses triggered by Bt derivates"* p. 500, **[A.16]**).

89. **Proteases** are enzymes which break down the peptide bonds in proteins. They allow the body to break proteins down into individual amino acids, including, for example, during digestion, blood coagulation and cell renewal. Protease inhibitors are molecules that block the activity of proteases.

90. There is an obvious potential for synergistic effects between protease inhibitors naturally occurring in the Modified Soybean, and the Bt toxins it has been genetically modified to express. The combination of the two is likely to lead to a delay in the degradation of the Bt toxins in the gut after consumption. This delay in degradation extends the exposure of the intestinal immune system to Bt toxins. This extension of exposure may trigger or enhance the toxic effects of the Bt toxins and may trigger or enhance chronic inflammation or other immune responses. The result is that Bt toxins can survive the digestive process to a significantly greater degree than has been assumed by EFSA in its risk assessment.

91. EFSA relied on studies which considered the potential toxic effects of Bt toxins in humans in the absence of protease inhibitors and concluded from its assessment of these studies that the Modified Soybean did not raise safety concerns in humans. These publications are valueless in this context give the risk in this case is synergistic, *i.e.*, it arises as a result of the interrelation between the Bt toxin and the natural plant constituents.

92. The second factor is that residues from herbicide sprayings have potential impacts on the microbiome, which may impact the way in which Bt toxins are digested. Glyphosate is known to show antibiotic activity and to impact the composition of the microbiome. Therefore, antibiotic effects caused by chronic exposure to food and feed derived from glyphosate-resistant genetically engineered plants may trigger significant changes in intestinal bacteria. These changes can also impact the immunogenicity of the Bt toxins.

93. In both cases, the potential impact on the safety of the stack is due to combinatorial and/or synergistic effects of the different components of the Modified Soybean together with effects on the microbiome. Accordingly, in order to falsify these hypotheses or either of them, animal feeding studies in respect of the new stacked event ought to have been required by EFSA.

94. In response to criticism from the competent authorities of Member States EFSA admitted that only "*limited experimental evidence"* was available to it in concluding on the safety of exposure to Bt toxins in the context of immune system responses, and stated that (response to HU13, p. 271, **[A.3]**):

> "… *the testing of adjuvant and allergenic potential of proteins requires stronger and fit-for-purpose standardised study design, and that future studies should consider limitations of current models, using relevant routes and methods of administration, doses, appropriate control proteins, and realistic exposure regimes."* (emphasis added).

95. In spite of this functional acknowledgement that current testing – including the testing undertaken by Monsanto in respect of the Modified Soybean – is not "*fit-for-purpose*", EFSA went on to approve the Modified Soybean for marketing in the EU. This is entirely inconsistent with the purpose of the GM scheme which is to ensure that products authorised for marketing in the EU meet the high levels of safety required by the GM Regulation.

96. Having failed to investigate the potential for synergistic effects between the newly expressed proteins in the Modified Soybeans, the protease inhibitors naturally occurring in it and the substantial likelihood that the Modified Soybean will be exposed to high dosages of herbicide, including glyphosate and its attendant impacts on the microbiome, Monsanto has not satisfied the requirements of the 2013 Regulation in respect of the Application, and EFSA ought to have rejected the flawed data relied on to evidence the purported safety of the stack.

(ii) The EFSA Opinion

97. EFSA concluded that, because none of the newly expressed proteins in the assessed GM plants showed potential for allergenicity, considering current knowledge, no reasons for concerns are expected regarding the simultaneous presence of these newly expressed proteins in the Modified Soybean. Accordingly, no animal feeding studies were necessary to conclude on the safety of the Modified Soybean (section 3.6.3.2, p. 294, **[A.4]**).

98. This response reveals two flaws in EFSA's approach to the safety of the Modified Soybean, both of which pervade the approach taken by EFSA and Commission to the safety of the stack.

99. The first is that it is clear that EFSA reached its conclusions on the allergenicity of the Modified Soybean by considering each of the newly expressed proteins alone, as opposed to considering whether, in tandem with one another, the plant as a whole represented an risk to the immune system upon consumption. This is an entirely insufficient approach to the safety of the Modified Soybean as a whole.

100. The second flaw is that, regardless of whether it is true that the newly expressed proteins are not understood to be allergenic, what is required by the 2013 Regulation is a holistic assessment of whether the newly expressed proteins in tandem with other plant components in the Modified Soybean represent a specific risk (whether allergenic or adjuvantic) or non-specific risk (e.g., chronic inflammation) to the immune system. In this case, it is well-known that protease inhibitors present in soybean plants may enhance toxic or immunogenic effects. Accordingly, assessing the immunogenicity of any of the individual proteins alone is plainly insufficient to conclude on the safety of the stack. It

is also insufficient to meet the requirements of section 1.4.1 of the 2013 Regulation, which requires an assessment of "*the potential interaction with other plant components*", and not simply an analysis of the newly expressed proteins in isolation.

101. It is unsurprising that, having given no adequate consideration to the question of whether synergistic or combinatorial effects would occur in the Modified Soybean, that both EFSA and the Commission wrongly concluded that evidence of synergistic effects were not present and so did not require animal feeding studies in order to investigate these potential impacts on human and animal health. The potential for synergistic effects are obvious in respect of the Modified Soybeans, and animal feeding tests were required in order to conclude on the safety of the stack.

(iii) The Commission decision

102. The Commission supported EFSA's conclusion.

103. First, the Commission concluded that no hypothesis had been identified which required a feeding study to be carried out in relation to the Modified Soybean (p. 397, **[A.10]**).

104. As detailed above at [87] – [95], Testbiotech has more than established the requisite hypotheses with regard to the potential synergistic effects resulting from the combination of events in the stack together with the naturally occurring protease inhibitors and the exposure to high amounts of herbicide. It is EFSA's failure to require any probing investigation of the safety of the Modified Soybean which allows it to claim that the requisite concerns had not been raised in respect of the stack.

105. Second, the Commission concluded that toxicity and immunogenicity of the Bt toxins were correctly assessed by EFSA. It considered that the publications cited by Testbiotech did not to invalidate its assessment of the safety of Bt toxins (alone or in combination) in food and feed from the Modified Soybean. EFSA did not find indications that Bt proteins in the Modified Soybean might act as adjuvants with the potential to enhance a specific immune response and to favour the development of an allergic reaction, and it considered that none of the newly expressed proteins in the Modified Soybean showed potential for allergenicity (p. 399, **[A.10]**).

106. These conclusions are fundamentally unsafe because they consider the safety of Bt toxins in isolation from the effect of protease inhibitors. Further, they do not take into account non-specific immune reactions such as chronic inflammation, which are involved in many health problems and therefore require high level of attention. Neither the Commission nor EFSA consider the potential for chronic inflammation in any detail.. Since Bt proteins are present in higher concentrations in the stacked Soybean compared to the parental plants, these risks need to be much more carefully assessed for their impact on the immune system compared to genetically engineered plants producing just one Bt toxin.

107. As explained, protease inhibitors are likely to play a crucial role in the delayed degradation of the Bt toxin when the Modified Soybean is ingested. The effects that are described indicate, for example, a 20-fold higher toxicity of Bt toxins in the presence of protease inhibitors. Given that these effects are synergistic, it is meaningless to conclude on the safety of the Modified Soybean by considering the components in isolation from one another, as EFSA and the Commission did in this case. By definition, synergistic effects cannot be predicted on the basis of the dosages of the single compounds which are involved. Only experiments which capture the interaction between the Bt toxins and protease inhibitors can demonstrate if and to what extent human health may be impacted by consumption of the Modified Soybean. This necessitates animal feeding trials.

108. The only data available to assess the acute toxicity of the Bt toxins are those from feeding studies with the isolated toxins in mice. This data is what is relied on by EFSA to conclude on limits of safety for the uptake of food and feed derived from the Modified Soybean. Plainly, this data is insufficient to assess acute or long-term toxicity or immunogenicity in the Modified Soybeans because it does not account for synergistic effects in the stack in general, or in particular, the impact of Bt toxins in combination with the protease inhibitors naturally present in the Modified Soybeans on human health. Accordingly, no safe conclusions about the Modified Soybean may be drawn from these experiments.

109. Moreover, the Commission response does not address the potential for the interaction between traits in the Modified Soybean to trigger chronic inflammatory processes at all. The potential for this significant risk to human health to materialize as a result of

consumption of the Modified Soybean is simply entirely absent in the Commission's response.

110. These gaps in the data relied on by Monsanto are exacerbated by the fact that co-factors which enhance the toxicity of the Bt toxins (such as the presence of protease inhibitors or other stressors) can also lower the selectivity of the toxins (Then (2010), section 3, p. 509 **[A.17]**). "**Selectivity**" in this context refers to the capacity of the Bt toxins to only act on a specific and narrow range of organisms (here, insects). However, if selectivity is lowered, the Bt toxins may impact organisms which are not normally susceptible to the Bt toxin in isolation (including, for example, mammals). This has clear consequences for the conclusions reached on the safety of the Modified Soybean, as the toxins it has been deliberately engineered to express may begin to impact organisms which are not its intended target.

111. Third, the Commission concluded that EFSA correctly assessed the "*individual proteins*" newly expressed in the Modified Soybean and included in its consideration updated bioinformatic searches for their homology to toxic proteins, updated literature searches and a conservative exposure assessment in both humans and animals.

112. This is, again, no answer to Testbiotech's complaint because, as this response states on face, it relies on assessments of the individual proteins expressed in the Modified Maize without accounting for synergistic effects within the stack.

113. Fourth, the Commission disputes that its consideration of the Santos-Vigil et al. (2018) (**[A.18])** publication was flawed (p. 402, **[A.10]**). This publication demonstrated the allergenic effects of Bt toxins when ingested. In arriving at this conclusion, the Commission relied on an external report on immunogenicity commissioned by EFSA, Parenti et al. (2019). Parenti et al conclude that (p. 402, **[A.10**]:

> "*[t]he adjuvanticity and immunogenicity of Cry proteins in certain experimental conditions seems plausible but due to low dosage, oral route of administration, food and feed processing and digestion, it is unlikely to emerge as a safety issue in food and feed. This assessment is consistent with the assessment by the EFSA GMO panel whereby they concluded that there is not a safety concern for the health of humans or animals that consume food/feed derived from GM plants containing Cry proteins. [...]*"

114. Significantly, even this selective quotation supports the hypothesis that immune reactions may be triggered by Bt toxins. Accordingly, the question for EFSA was whether the

consumption of the Modified Soybean meets the specific conditions to trigger these effects.

115. A cursory consideration of two relevant factors reveals the serious deficiencies in EFSA's application of the analysis in Parenti et al to the Modified Soybean. These are, taken in turn, (1) the importance of the dosage of the Bt toxins considered in that study, and (2) the role of the microbiome in the digestion of the Bt toxins considered in that study:

    a) Dosage of Bt toxins: Parenti et al (2019) concludes that the dosage of the Bt toxins expressed in food plants are too low to trigger these allergenic effects in humans when consumed (bullet (vi), p. 530, **[A.19])**. However, the effects of the Bt toxins may react synergistically with protease inhibitor proteins naturally present in the Modified Soybean. Parenti et al does not consider the potential enhancing effects of protease inhibitors on the Bt toxins. Its analysis is entirely silent on such effects.

    b) Role of the microbiome: Parenti et al (2019) emphasises that the microbiome may influence the immunogenicity of the Bt toxins after ingestion (section 3.1.3.7, p. 549, **[A.19]**). As explained, glyphosate is known to show antibiotic activity and to impact the composition of the microbiome. Therefore, antibiotic effects caused by chronic exposure to food and feed derived from glyphosate-resistant genetically engineered plants may trigger significant changes in intestinal bacteria. These changes can also impact the immunogenicity of the Bt toxins. Data on dosage, processing and digestion taken in isolation from one another are insufficient to assess these effects in the context of consumption of the Modified Soybean where each of these effects may be present and interact with one another.

116. Reliance on the Parenti report does not cure, and indeed, reveals the fundamental deficiencies in EFSA's consideration of the potential for immunogenicity in the Modified Soybean. The only appropriate way to assess the effect of the toxins, taken together with the impact of the PI proteins and any impact on the microbiome of glyphosate exposure is to simulate ingestion of the entire stacked event, *i.e.*, through animal feeding trials, and EFSA ought to have required Monsanto to conduct such a trial.

117. Fifth, the Commission suggests that EFSA did assess allergenicity of the whole Modified Soybean, and not simply the components involved in isolation from one another, and that, having considered all the information available, EFSA considered that there was no evidence that the genetic modification might substantially change the overall allergenicity of the GM stack soybean assessed when compared to their non-GM comparators and non-GM reference varieties tested (p. 400, [**A.10]**).

118. This is entirely assertive. As set out above, neither the Commission nor EFSA placed themselves in a position to properly conclude on the safety of the newly expressed proteins in tandem with one another, or with the other components of the Modified Soybean, including the protease inhibitors. It is due to EFSA's failure to properly assess the potential for synergistic effects between these components that it did not have any evidence of overall allergenicity such that it could assess the safety of the Modified Soybean compared to its non-GM comparator.

(iv) Conclusion on Ground B

119. The data presented by Monsanto is wholly insufficient to reach any robust conclusions on the immunogenicity and/or toxicity of the Modified Soybean. Instead of assessing the potential for synergistic effects of the newly expressed proteins in tandem with the protease inhibitors naturally present in soybeans and the potential impact of high rates of herbicide and/or herbicide residue in the harvest on the human microbiome, Monsanto (and so, EFSA) merely assessed the potential for specific and unspecific immune reactions and toxicity of the newly expressed proteins in isolation from one another and from other plant components and from the real-world conditions under which the plant will be grown for evidence of potential harm.

120. This approach turns what ought to be a detailed, holistic analysis of how the Modified Soybean will react to real-world conditions into a trivial assessment of single factors in isolation. It is not an appropriate assessment of the safety of the stack when ingested, and it is not compliant with subsection 1.4.1 of Annex II of the 2013 Regulation.

121. Animal feeding trials were required in order to assess potential synergistic effects of the plant components under subsection 1.4.4.1 of Annex II of the 2013 Regulation and having failed to require Monsanto to conduct such a trial, the data presented by Monsanto

in support of the application is clearly insufficient to demonstrate the safety of the crop to the high level required by EU law.

122. Subsection 1.4.1 of Annex II of the 2013 Regulation also requires that "*the potential interaction with other plant constituents shall also be evaluated*". Given the ability of protease inhibitors to delay the degradation of the Bt toxins, the exposure of the gut to these toxins is likely to be prolonged when the Modified Soybean is consumed, which typically can enhance toxicity. Plainly, the effects of the presence of the protease inhibitors is relevant for toxicity assessment of Bt.

123. Further, subsection 1.4 of Annex II of the 2013 Regulation requires an applicant to "*identify potential adverse effects of new constituents and determine their highest dose level that does not result in adverse effects*". The "*highest dose level*" cannot be determined by testing the Bt proteins in isolation from the other constituents of the Modified Soybean. Any risk assessment of the Modified Soybean which does not take into account the combination of plant material with the Bt toxin is not reliable and is likely to dramatically underestimate the risks involved in the consumption of the Modified Soybean.

124. The 90 days feeding studies as performed with parental plants are insufficiently targeted to test the toxicity or immunogenicity hypotheses advanced by Testbiotech and which ought to have been considered in the testing of the Modified Soybean. To test this hypothesis, a significantly more targeted approach would have been necessary, taking into account chronic processes that, e.g., can be caused or accompany inflammation and are likely to escape sub-chronic feeding studies performed with the single parental plants (as was the case here). Further, as set out above, any feeding study conducted on a single parental plant would not capture combinatorial, synergistic or accumulated effects caused by the stacking of traits in the Modified Soybeans.

125. As a result, the data supplied in support of the application did not fulfil the conditions specified in Articles 5(3)(a) and 17(3)(f) of the GM Regulation. Accordingly, EFSA ought to have rejected it under Articles 6(3)(a) and 18(3)(a) of the GM Regulation.

126. The Commission's determination that the immunogenicity and toxicity assessment of the Modified Soybean met the requirements of the 2013 Regulation and of the GM Regulation accordingly constitutes a manifest error of assessment. It could not be

concluded from the data presented that the Modified Soybean met the high level of safety required to be lawfully authorised in the EU.

V. CONCLUSION

127. The concerns raised by Testbiotech in this application are weighty, well-founded, and more than satisfy the requirement expressed in Case T-177/13 *TestBiotech eV v Commission* at [88] of raising "*serious doubts as to the lawfulness of the authorisation decision*".

128. For the reasons given above, Testbiotech invites the Court to grant the relief sought in paragraph [3] above.

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19 September 2021

SCHEDULE OF ANNEXES

A. <u>ANNEXES</u>

1. Monsanto application letter, 17 December 2015, pp. 1 - 6 (para 46 / p. 13)
2. Application for authorisation, Part II "Scientific Information" EFSA-GMO-NL-2016-128, pp. 7 - 202 (para 46 / p. 13)
3. Comments and opinions submitted by Member States ("**Annex G"**), pp. 203 - 277 (para 50 / p. 13)
4. EFSA GMO Panel Scientific Opinion, 3 July 2019 ("**the EFSA Opinion**"), pp. 278 - 309 (para 51 / p. 14)
5. European Parliament Resolution of 17 December 2020, pp. 310 - 321 (para 52 / p.14)
6. Commission Implementing Decision, 22 January 2021 granting Monsanto market authorisation for the Modified Maize ("**the Commission Implementing Decision**") pp. 322 – 328 (para 54 / p. 15)
7. Testbiotech's Request for Internal Review, 8 March 2021, pp. 329 – 330 (para 55 / p. 15)
8. Testbiotech's technical background for its Request for Internal Review, 8 March 2021, pp. 331 – 382 (para 55 / p. 15)
9. Decision Letter rejecting Testbiotech's Request for Internal Review, 8 July 2021, pp. 383 - 386 (para 56 / p. 15)
10. Commission assessment of Testbiotech's request for internal review, 8 July 2021, pp 387 – 404 (para 56 / p. 15)
11. Miyazaki et al. (2019), pp. 405 – 426 (para 61 / p. 16)

12. USDA, National Agricultural Statistics Service (NASS) Agricultural Chemical Use program, pp. 427 – 430 (para 62 / p. 17)
13. Monsanto product label "RoundUp" pp. 431 – 453 (para 64, p. 17)
14. Avila-Vazquez et al. (2018), pp. 454 – 467 (para 63 / p. 17)
15. Zanatta et al. (2020), pp. 468 – 485 (para 76 / p. 20)
16. Rubio-Infante et al. (2016), pp. 486 – 505 (para 88 / p. 22)
17. Then (2010), pp. 506 – 513 (para 110 / p. 27)
18. Santos-Vigil et al. (2018) pp. 514 – 526 (para 113 / p. 27)
19. Parenti et al (2019), pp. 527 – 595 (para 115 / p. 28)
20. Testbiotech's Articles of Association, 23 March 2012, pp. 596 – 604 (para 4 / p. 3)
21. Testbiotech's Registration Document, 16 October 2012, pp. 605 – 607 (para 4 / p. 3)
22. Regulation 1367/2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies ("**the Aarhus Regulation**"), pp. 608 – 615 (para 6 / p. 3)
23. Regulation 1829/2003 on genetically modified food and feed ("**the GM Regulation**"), pp. 616 – 639 (para 13 / p. 5)
24. Regulation 503/2013 on application for authorisation of genetically modified food and feed ("**the 2013 Regulation**") pp. 640 – 688 (para 23 / p. 6)
25. Directive 2001/18 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC, pp. 689 – 727 (para 14 / p. 5)
26. Case T-33/16 *TestBiotech eV v Commission* ECLI:EU:T:2018:135, pp. 728 – 745 (para 11 / p. 4)

27. Case T-177/13 *TestBiotech eV v Commission* ECLI:EU:T:2016:736 pp. 746 – 750 (para 39 / p. 10)

(All Annexes are paginated consecutively. Paragraph references and page numbers in brackets indicate the place in the application where the item is first mentioned and its relevance described).