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-605/21

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) 2021/61 ("**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[1] ("**Monsanto**") to market genetically modified maize MON 87427 x MON 87460 x MON 89034 x MIR162 x NK603 and its sub-combinations ("**the Modified Maize**").

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 circumstances in which the plant is likely to be cultivated, namely, in conditions of drought and of repeated sprayings of and/or high volumes of herbicide. 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 Maize 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 included in the Register of Associations at the Amtsgericht München (local court, Munich) VR 202119 (see Statute/ Articles of Association at **[A.22]** and Registration Document at **[A.23]**. Testbiotech was founded in 2008 and registered as a non-profit organisation to

[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".

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.24]** 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.28]**):

    "… 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.25]** 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 and animal life:

> *"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.26]** 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) 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, 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.27]** which provides a comprehensive and detailed set of rules, particularly for stacked events, such as the Modified Maize 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 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…"*

34. 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 are not provided, 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

35. 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.29]**. 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 …"

36. 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. 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 … .

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 Maize

37. The Modified Maize 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 87427 expressing CP4 EPSPS protein for tolerance to glyphosate-containing herbicides;

    b) MON 87460 producing a "cold shock protein" (CSPB) associated with enhanced abiotic stress tolerance in bacteria. It also produces neomycin phosphotransferase II which inactivates a range of important antibiotics, including neomycin and kanamycin;

    c) MON 89034 expressing the insecticidal proteins Cry1A.105 and Cry2Ab2;

    d) MIR162 expressing the insecticidal proteins Vip3Aa20 and phosphomannose isomerase (PMI);

    e) NK603 expressing two variants of CP4 EPSPS protein for tolerance to glyphosate-containing herbicides.

38. **"Glyphosate"** is the active ingredient in some agricultural herbicides (which are often used as "complementary" herbicides in fields with transgenic herbicide-resistant plants). 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.

39. "**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**".

40. "**Vip3Aa20**" is a protein which is also derived from the bacterium *Bacillus thurigiensis*. It can be used as an insecticide.

41. Phosphomannose isomerase, or "**PMI**" is an enzyme which is used as a selectable marker (a gene which allows for the identification of cells which have been transformed during the process of genetic engineering based on the expression of that gene). It plays a role in the metabolism of mannose, which normally inhibits root growth, respiration and germination. Cells which express PMI are capable of using mannose as a carbon source.

42. The Modified Maize thus combines the insecticide traits of MON 89034 and MIR162, the herbicide tolerant traits of MON 87427 and the drought-tolerant traits of MON 87460. Because it combines the modified genes of its Parents, it is called a "**stacked event**".

(b) The Authorisation Application and Internal Review

43. Monsanto filed application EFSA-GMO-NL-2016-134 ("**the Application**") **[A.1]** in the Netherlands seeking authorisation under the GM Regulation for the Modified Maize and its derived products for food and feed uses, import and processing in the European Union, and its scientific analysis in support of the application **[A.2]**. The Application excludes cultivation within the EU.

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

45. EFSA considered the Application in order to determine *inter alia* whether the Modified Maize 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 Maize on the market were to be authorised.

46. EFSA issued an Opinion on the Application on 3 July 2019 ("**the EFSA Opinion**") **[A.3]**. It concluded, in material part (EFSA Opinion, Summary, p.233):

> "*The GMO Panel concludes that the five-event stack Modified Maize and its subcombinations are as safe as its non-GM comparator and the tested non-GM reference varieties with respect to the potential effects on human and animal health and the environment"*

47. 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 (AB2, p. 273, **[A.4]**):

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

48. The Resolution specifically criticised the draft authorisation decision on the basis that herbicide-tolerant GM crops result in a higher use of complementary herbicides, due in large part to the emergence of herbicide-tolerant weeds and that it was to be expected that the Modified Maize would be exposed to both higher and repeated doses of glyphosate, and that therefore a higher quantity of residues may be present in the harvest (K, p. 270, **[A. 4]**), and that the Bt toxin content of the Modified Maize had not been shown to be safe for the immune system and could increase the allergenicity of other proteins (Q - R, p. 271, **[A. 4]**).

49. In spite of these trenchant objections by Parliament, the Modified Soybean was nonetheless authorised by the Commission on 22 January 2021 **[A.5]** and the authorisation was published in the Official Journal of the EU on 26 January 2021.

50. 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.6; A.7]**.

51. The Commission responded on 8 July 2021 with the Decision **[A.8; A.9]**. 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

52. Testbiotech contends that the Commission has committed manifest errors of assessment in having confirmed the authorisation of the Modified Maize 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.

53. Testbiotech's three grounds of challenge are as follows. EFSA 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 exposure to drought conditions and/or failed to require an adequate assessment under drought conditions to be conducted.

    b) **Ground B:** 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 conditions of repeated and/or high application of herbicide.

    c) **Ground C:** failed to give any or any adequate consideration to the potential impact of gene stacking on plant composition and agronomic characteristics in combination with exposure to drought conditions and herbicide applications.

Ground A: EFSA's failure to assess the impact of gene stacking on gene expression in combination with exposure to drought conditions

(i) Testbiotech's position

54. Testbiotech's position on Ground A is set out at section 2.1.3 of its Request for Internal Review (p. 306, **[A.7]**).

55. In summary, Testbiotech's challenge under this ground is that EFSA did not properly evaluate the potential for drought conditions to effect gene expression in the Modified Maize.

56. **Gene expression**, or **protein expression** refers to the activity and concentration of the newly expressed proteins, *i.e.*, the traits which the plant has been genetically engineered to produce rather than the other, "natural" plant components.

57. It is inexplicable that EFSA did not require the Modified Maize to be assessed under drought conditions given that the Modified Maize has been deliberately engineered to have enhanced drought tolerance and this is overwhelmingly likely to be the environmental condition in which the Modified Maize will be grown.

58. Accordingly, no data was made available by Monsanto to assess whether the expected environmental conditions under which the plants are likely to be cultivated will influence gene expression, as required by the section 1.3.2.1(b) of Annex II of the 2013 Regulation. Nor was gene expression data, obtained from field trials related to the conditions in which the crop is grown (*i.e.*, under drought conditions) made available as required by section 1.2.2.3 of Annex II of the 2013 Regulation. Contrary to assertions by EFSA, no such data is available from the parental plants or any sub-combinations.

59. The field trial conditions were entirely inadequate to investigate this for the following reasons, each of which is elaborated on below:

    a) The field trials took place in a very narrow geographical cluster of sites, all of which were in North America, and are unrepresentative of the conditions in which it is to be expected the Modified Maize will be cultivated.

    b) This limits the stressors to which the plants were exposed during the field trials to those which are generally (and were specifically) present in five US states in 2014 over the course of one season.

    c) Specifically, the plants were not exposed to drought conditions, which is critical for assessing the gene expression of the plant under drought conditions given that it is genetically engineered to be drought-tolerant and is overwhelmingly likely to be cultivated in drought conditions.

(ii) EFSA's opinion

60. First, EFSA concluded that the range of receiving environments under which the Modified Maize was produced was adequate to identify possible unintended changes to gene expression introduced with the genetic modifications **(**section 3.4.2.4, p. 244, **[A.3]**).

61. This position is not consonant with the basic facts of the case. The range of environments in which the field trials for gene expression were carried out was extraordinarily narrow.

Only four samples (each for grain and forage) from five closely located field sites (IARL, ILFI, ILMN, ILRD and OHTR (p.167, **[A.2]**)), were used for generating the data on gene expression. The selected field trial sites (Illinois, Iowa, and Ohio (section 3.4.2.1, page 244 **[A.3]**) represent a very limited range of climatic and environmental conditions in major maize growing regions, and, in particular, do not represent the climatic conditions in major exporters of maize to the EU.

62. The narrow range of sites utilized has a direct impact on the circumstances in which the plants were grown. No extreme weather conditions (except frost) were reported during cultivation in 2014 (section 2.4.2.4, p. 244, **[A.3]**). Weather data from 2014 demonstrates that there was more precipitation than normal at the trial sites in Illinois (p. 174, **[A.2]; [A.10]**). Therefore, a relevant stressor, drought which would be expected to influence the gene expression, composition or phenotype of the Modified Maize was not covered by the field trial data.

63. Even more striking is the difference between the climatic conditions in the major maize growing regions of the US and the conditions in maize growing regions in other regions of the world, which may have substantially higher or lower precipitation rates or average temperature. An exemplar of this is Brazil, which is a major producer of genetically engineered maize and is the second largest importer of maize to the EU, with 29% of total imports in 2021-20 (p. 406, **[A.11]**).

64. Accordingly, the range of sites used in field testing was insufficiently broad to provide the necessary evidence of the reaction of the crop to the variety of environments in which it is grown.

65. Second, EFSA contends that because it previously assessed the relevant parent – MON87460 – under "water limited" conditions and there was no indication of an interaction between the events, there was no need to request a field trial under drought conditions in respect of the Modified Maize (fn 14, section 3.4.2.4, p. 244 **[A.3]**).

66. This is flatly incorrect. No data on gene expression is available from MON87460 grown under drought conditions. Limited data on plant composition is available from MON87460 grown under drought conditions. An analysis of plant composition is a separate, and subsequent stage of the analysis of the safety of a stack to the analysis of gene expression.

67. In short, the analysis of gene expression of genetically modified plants is aimed at assessing the activity and the concentration of the newly produced proteins. This forms part of the molecular risk assessment. By contrast, the analysis of plant composition of genetically modified plants is aimed at assessing all of the natural components of the plants and at assessing whether those components have been (unintentionally) changed by the genetic engineering process. Information on the gene expression of either the Modified Maize or the relevant parent plant under drought conditions is completely absent from the application.

68. Further, even in the event that information on gene expression was available from the relevant parent plant grown under drought conditions (which it is not), that information would not be conclusive on the safety of the Modified Maize. In essence, in this response, EFSA seeks to conclude from (1) the fact that it has previously assessed the drought-tolerant parent plant on a standalone basis and (2) the fact that there was no indication of interaction between the various parent plants under non-drought conditions that (3) it would not be expected that, in combination with one another, the stacked events under drought conditions would result in changes in protein expression. But this does not follow. The combination of events in a stacked event, such as the Modified Maize, may have synergistic effects which may not occur when any of the factors are taken in isolation.

69. It is for Monsanto to evidence, and for EFSA to verify, that the specific combination of traits in the Modified Maize is safe when cultivated under the agronomic conditions to which it is likely to be exposed. A consideration of the traits, or of the agronomic conditions in isolation from one another cannot produce the requisite evidence as it ignores the potential for the traits to interact with one another, or with environmental stressors.

70. Environmental stress – including, for example, exposure to drought conditions – can cause unexpected patterns of expression in the newly introduced genes. There is an abundance of evidence in the scientific literature showing that drought or heat can significantly impact the content of Bt in the plant tissue. Further, the EPSPS enzymes are known to show effects on more than one trait, especially if exposed to environmental stress. Fang et al. (2018) demonstrates that stress responses can lead to unintended changes in plant metabolism inheriting additional EPSPS enzymes. In this context, there are strong indications that the EPSPS enzyme, which confers glyphosate tolerance, also interferes with the auxin metabolism in the plants (Fang et al., p. 417, [**A.12]**). This plant hormone plays a key role

in growth, fecundity and adaptation to environmental stressors. Thus, changes in the auxin content can also result in changes in plant composition that can raise safety concerns. Several publications support these findings by showing unintended effects in plants inheriting additional EPSPS genes (Beres, 2019, pp. 544 – 546 [**A.13**]; Beres et al., 2018, pp. 596 – 597, **[A.14]**)

71. The EPSPS enzymes occur in the stacked Modified Maize in higher concentrations compared to the parental plants. Moreover, the Modified Maize is the first plant in which the EPSPS gene has been combined with the CSPB gene, which confers drought resistance and is plainly intended to be exposed to more extreme climate conditions. Consequently, the cultivation of the Modified Maize is the first time that the combination of artificial gene constructs will be deliberately exposed to extreme drought conditions, and it ought to have been tested under these conditions in order to assess impact on gene expression.

72. As it stands, Monsanto has provided no data on the gene expression of the Modified Maize when cultivated under the environmental conditions to which it is overwhelmingly likely to be exposed. As such, no data (and no independent data) is available on (1) the CSPB gene under drought conditions, (2) the gene expression of the CSPB gene in combination with the EPSPS gene under drought conditions, or (3) the Bt toxins in combination with the EPSPS gene under drought conditions. This data is not available because EFSA did not require Monsanto to provide it.

73. These serious deficiencies in the information provided in support of the application ought to have been fatal to Monsanto's application. Based on the information provided, EFSA could not have lawfully determined that the Modified Maize reached the high level of safety required in order to be lawfully marketed in the EU.

(iii) The Commission decision

74. First, the Commission concluded that it was not necessary to request field trials under drought conditions for the Modified Maize for the following reasons:

    a) EFSA considered the meteorological and agronomic conditions sufficiently replicated the range of environmental and agronomic conditions under which the Modified Maize would be cultivated in practice.

b) EFSA had previously assessed the event conferring enhanced drought tolerance, MON87460, and in its opinion, a comparative analysis was specifically conducted for this event under water-limited conditions and other stressful conditions. Combined with the fact that EFSA had also concluded that there was no indication of an interaction between the events as described in section 3.4.1.4 of the EFSA opinion, it was not necessary to request the inclusion of a field trial under drought conditions.

75. This response replicates the errors in the EFSA opinion and is dealt with at [60] – [64] above.

76. Second, in considering the scientific literature relied on by Testbiotech in its Request for Internal Review, the Commission determined that the findings reported by Trtikova et al. (2015) **[A.15]**, had been previously assessed by EFSA and the findings were limited to genetically modified maize MON810, and that EFSA's conclusions on the findings of Trtikova et al. in respect of MON810 were valid and applicable to the Modified Maize (p. 356, **[A.9]**).

77. This response is reductive. The findings of Trtikova et al. cannot be considered solely in relation to the specific event in question in that case (MON810) or to plants expressing the Cry1Ab protein. Instead, Trtikova et al. must be considered as part of a broad and robust body of research which indicates that gene expression in general, as well as Bt and Vip3Aa20 content in particular, are influenced by environmental or varietal backgrounds (pp. 609 – 610, **[A.15]**). It is wholly insufficient in the circumstances for EFSA to point to previous consideration of findings in the context of a single event and to conclude that its risk assessment and management practice recommendations remained applicable. This body of research required fresh consideration by EFSA in relation to the specific circumstance of the Modified Maize, in particular given (i) the significantly more complex stacked genes it comprises, and (ii) the agronomic conditions under which the Modified Maize is likely to be cultivated.

78. Third, regarding the other publications referred to by Testbiotech concerning the impact of climate conditions on protein expression levels, EFSA recognised that there is evidence in the peer-reviewed scientific literature suggesting that stressful conditions could influence protein expression levels. However, the Commission concluded that the possible

consequences for protein expression levels are unpredictable and may result in either higher or reduced protein expression levels (section 1.2.1. page 357, **[A. 9]**).

79. This, again, is no response to the point raised by Testbiotech. In light of the precautionary principle, the fact that the possible consequences for gene expression of stressful conditions is ***unpredictable*** gives greater weight to the need for a careful assessment of gene expression under appropriate field conditions. It is not, as the Commission appears to conclude, a reason to dismiss the potential impact of environmental factors on gene expression of the Modified Maize. Plainly, investigation was necessary to examine whether and to what extent the expression of the additional proteins is impacted by environmental stressors such as drought. Monsanto wholly failed to undertake these investigations, and EFSA ought to have required them.

80. Fourth, the Commission appears to discount the scientific analysis presented in the findings of Wang et al. (2014), Yang et al. (2017), Fang et al. (2018), Beres et al. (2018) and Beres (2019), on the basis that these effects were observed in rice, *Arabidopsis* and *Conyza canadensis* and not in maize (section 1.2.1, p. 356, **[A. 9]**).

81. The fact that the findings were observed in non-maize plants is no basis on which to discount the relevant scientific findings. *Arabidopsis* is a well-known model plant which has been described as "*the standard reference plant for all of biology"* (Koornneef & Meinke (2010), p. 613, [**A.16**]). *Arabidopsis* is used in many cases to detect genetic effects before they are examined in other species. If pleiotropic effects (*i.e.,* unanticipated effects on genes which were not the intended target of the intervention) of the EPSPS enzymes occur in *Arabidopsis*, these findings are clearly relevant for crops with the additional EPSPS genes inserted, unless further investigation demonstrates that in the specific case of those further events (in this case, in the Modified Maize) the effects are proven by Monsanto to not occur.

82. This conclusion is reflected in the literature. For example, Beres (2019) and Beres et al. (2018) state that these effects are not unlikely to also occur in other plant species (Beres (2019), p. 534, **[A.13]**; Beres et al (2018), p. 597, **[A.14]**). Indeed, the analysis in Beres et al (2018) started from observations made in over 10 weedy species, where researchers discovered that, under exposure to high amounts of glyphosate, the plants independently acquired glyphosate-resistance by overproducing the EPSPS gene, making as many as 100 additional copies of the EPSPS gene in response to high levels of glyphosate (Table 1, p.

591, **[A.14]**). These concerning conclusions in relation to these weedy species were then built upon in the later examination of *Arabidopsis*.

83. Accordingly, the suggestion that the findings are relevant only for *Arabidopsis* is contradicted by the underlying scientific investigation, which was significantly broader than merely holding in the case of rice. Pleiotropic effects have already been demonstrated in species belonging to both groups of flowering plants: monocotyledons (such as rice and maize) and dicotyledons (such as *Arabidopsis*). As it stands, the findings in relation to *Arabidopsis* is compelling evidence that gene expression may be affected in plants which have been genetically modified with the EPSPS gene. Neither Monsanto, EFSA nor the Commission present any evidence that these effects are not also present in maize.

84. Therefore, given the existing evidence, it was clearly for Monsanto to deliver data to validate or invalidate the pleiotropic and fitness related effects of the EPSPS enzymes. Given that it did not do so, it could not have been lawfully concluded that the Modified Maize was safe for import into the EU.

85. Fifth, the Commission concluded that it was unfeasible, in practice, to assess GM events "*under all possible receiving environments*". Therefore, applicants must select sufficiently different locations to capture the environmental variability within the set of possible receiving environments in which the GM stack Modified Maize may be cultivated. (section 1.2.1, p. 356, **[A.9]**).

86. The response of the Commission does not respond to the point raised by Testbiotech. It is, of course, not feasible to test in *"all possible environments"*. The question is whether the range was sufficiently diverse to capture the range of meteorological and agronomic conditions to which the crop is likely to be exposed. For the reasons set out above, this was plainly not the case in the design of the field trials in respect of the Modified Maize.

(iv) Conclusion on Ground A:

87. The experimental design and the tested materials for the Modified Maize were wholly inadequate to identify possible unintended changes introduced with the genetic modifications; and the meteorological and agronomic variability at the sites selected for the protein expression data were insufficient to ensure a range of environmental and agronomic conditions reflecting those under which the Modified Maize will be cultivated in practice,

in breach of the requirements in subsection 1.3.2.1(b) of Annex II of the 2013 Regulation. Accordingly, in breach of the requirement at section 1.2.2.3 of Annex II of the 2013 Regulation, protein expression data, obtained from field trials related to the conditions in which the crop is grown, was not made available in support of the application.

88. 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.

89. 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 Maize met the high level of safety required to be lawfully authorised in the EU.

Ground B: the impact of gene stacking on gene expression in combination with herbicide applications

(i) Testbiotech's position

90. Testbiotech's position on Ground B is set out in section 2.1.3.2 of its Request for Internal Review (p. 310, **[A.7]**).

91. As set out above at [37], the Modified Maize expresses genes conferring herbicide resistance. Due to increased weed pressure from weeds which are resistant to glyphosate (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 Maize's tolerance of herbicide, it ought to have been field-tested under real-world conditions of high and repeated doses of herbicide.

92. Only four samples (each for grain and forage) from five closely located field sites (p.167, **[A.2]**), were used for generating the data on gene expression. While some of the data includes samples with and without spraying of the complementary herbicide, some only includes data from crops treated with glyphosate. In order to conduct a proper assessment, Monsanto ought to have been required to compare data from unsprayed parental plants and unsprayed Modified Maize with data from sprayed parental plants and sprayed Modified

Maize. Having not done so, the data generated does not allow for any safe comparison or conclusion on the impact of the complementary herbicide on gene expression. The comparison carried out is entirely uninstructive as to the safety of the stack.

93. Monsanto reasoned that "*there is no known mechanism by which glyphosate application to MON 87427 × MON 87460 × MON 89034 × MIR162 × NK603 could affect protein expression levels in this product, and therefore no impact of this treatment is anticipated*." (section 1.2.2.3, p. 32, **[A.2]**) However, this assumption is entirely divorced from the scientific literature which demonstrates that stress responses can lead to unexpected changes in plant metabolism inheriting additional EPSPS enzymes (Fang et al., p. 417, **[A.12]**; Yang et al. (2017), pp. 628 – 634, **[A.17]**).

94. The failure to test the plants under real-world conditions of high and/or repeated applications of glyphosate to which it will likely be subject in the course of ordinary cultivation has fatal consequences for the safety of the conclusions reached during the field testing. When the Modified Maize is exposed to higher rates of glyphosate application, the plants may experience stress conditions, impacting gene expression and plant composition as well as the biological characteristics of the Modified Maize. Miyazaki et al. (2019) demonstrates that the amount and timing of spraying glyphosate as a complementary herbicide on herbicide-tolerant genetically engineered plants can impact their composition (Miyazaki et al., "*GMO risk assessment",* p. 648, **[A.18])**. These changes in plant composition can arise from, or be influenced by, the expression of the additionally inserted genes. Therefore, the assessment of gene expression, compositional analysis and assessment of phenotypical characteristics of herbicide-tolerant genetically engineered plants should take dosage, the number of sprayings and the timing of herbicide application into account. It is evident that these factors can influence plant and product safety.

95. Despite the fact that it ought to have been assumed that the plants would be subject to higher dosages of herbicide, herbicide applications in the field trials did not represent current agricultural practices. The glyphosate treatment was only sprayed at an early stage of vegetation and at comparably low dosages of 0.87 kg a.e./ha (p.157, **[A.2]**). This is despite the fact that current industry recommendations suggest dosages of up to approx. 3.5 kg a.i./ha glyphosate post-emergence, 7 kg per season, and that even higher rates can be sprayed on herbicide–resistant maize (Miyazaki et al., p. 644 **[A.18]**).

96. The failure to field test the Modified Maize under real-world conditions of high and/or repeated applications of glyphosate 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. It is wholly insufficient for Monsanto to have (i) failed to present meaningful comparisons of the cultivated crop with and without the application of glyphosate, and (ii) to have cultivated the Modified Maize in conditions applying significantly lower dosages of herbicide than industry practice would dictate is utilised.

(ii) The EFSA opinion

97. The EFSA opinion deals very lightly with the topic of herbicide. It noted that "*[a]ll materials were treated with conventional herbicide management regimes"* (section 3.4.2.2, p. 243, **[A. 3]**). Overall, EFSA concluded that the tested materials and "*most of*" the management practices in the Modified Maize application were typical of receiving environments where the Modified Maize could be grown [section 3.4.2.4, p. 243 **[A. 3]**).

98. Given the significant discrepancy between the rates of herbicide applied in the field testing and standard industry practice (where field testing rates were approximately 25% of what is used in industry practice, leaving aside the fact that *even higher* rates may be applied to herbicide resistant maize) EFSA's conclusion on this point is inexplicable and entirely untenable.

(iii) The Commission decision

99. The Commission agreed with EFSA's assessment.

100. First, the Commission agreed with EFSA's conclusion that the timing and rate of the applied intended herbicides were in line with the recommendations of the manufacturers (section 1.2.2, p. 358, **[A. 9]**).

101. This is 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 an unparticularised manufacturer's regimen.

102. Second, the Commission contended 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 (section 1.2.2, p. 358, **[A. 9]**).

103. This is, equally, 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 agricultural practices in the countries of cultivation. 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 generically engineering plants to be herbicide tolerant: it allows cultivators to use higher amounts of herbicide to control weed pressure without damaging the crop.

(iv) Conclusion on Ground B

104. The experimental design for the testing of the Modified Maize was wholly inadequate to identify possible unintended changes introduced with the genetic modifications in combination with the management practices under which the Modified Maize 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 analysed on that basis. 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 at section 1.2.2.3 of Annex II of the 2013 Regulation.

105. 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.

106. 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 Maize met the high level of safety required to be lawfully authorised in the EU.

GROUND C: The impact of gene stacking on plant composition and agronomic characteristics in combination with exposure to drought conditions and herbicide applications

(i) Testbiotech's position

107. Testbiotech's position on Ground C is set out at section 2.2 of its Request for Internal Review (p. 314, **[A.7]**).

108. Testbiotech's concern is that environmental stress conditions (such as those triggered by drought and by repeated sprayings of high volumes of herbicide) may cause unexpected and unintended effects in plant composition as well as the phenotypic and agronomic characteristics of the Modified Maize. Accordingly, the Modified Maize ought to have been tested under conditions of both drought and high/repeated sprayings of herbicide on the basis that exposure to these stressors in tandem with one another may have combinatorial or synergistic effects on the plant composition of the Modified Maize. Robust data should have been presented to assess whether these changes raised food and feed safety concerns.

109. The stacked Modified Maize, due to the expression of the CSPB protein, inherits a trait which enables cultivation of the plants under drought conditions. The trait is combined with gene constructs (the EPSPS enzyme and the production of Bt toxins) which are likely to cause major changes in plant composition exposed to environmental stressors (such as drought). In addition, three other proteins are expressed in the stacked Modified Maize which are absent in conventional Modified Maize: NPTII which confers antibiotic resistance, PMI which was used in the selecting process during plant production, and Vip3Aa20, which confers insecticidal toxicity.

110. These traits and genetic elements can synergise and interact with each other. These effects may impact plant composition, especially if the Modified Maize is exposed to environmental stress conditions, as it is likely to be under real-world cultivation.

111. As explained at [55] – [89] and [90] – [106], above, the sites selected for field trials were clustered in a narrow set of state within the US, and the field trials were deficient as they were not conducted under drought conditions or under real world conditions of high and/or repeated sprays of herbicide, which seriously undermines the safety of the data collected under those conditions when relied on to conclude on the safety of the Modified Maize.

112. As discussed above at [70], the scientific literature establishes that stress responses can lead to unintended changes in plant metabolism inheriting additional EPSPS enzymes, and that there are strong indications that the EPSPS enzyme, which confers glyphosate tolerance, also interferes with the auxin metabolism in the plants. Auxin plays a key role in growth, fecundity (*i.e.,* the capacity to produce offspring) and adaptation to environmental stressors. Thus, changes in the auxin content can result in major changes in overall plant composition which impact the safety of the stack.

113. The unintended effects of the EPSPS enzymes may interfere with the activity of the other gene constructs, for example, via the auxin hormone. These enzymes are produced in the Modified Maize at higher concentrations compared to the parental plants. Therefore, the likelihood of interaction between the gene constructs and gene expression, plant composition as well as agronomic and phenotypic characteristics is exacerbated in the stacked Modified Maize compared to the parental plants.

114. Previous research also indicates that expression of Cry1A.105, Cry2Ab2 and EPSPS proteins in genetically engineered maize can induce changes in the overall proteins expressed by maize with impacts on the plant's natural metabolic pathways (Agapito-Tenfen et al. (2013), "*Conclusion*" p. 673, **[A.19]**; Bevenuto et al. (2017), section 4, p. 695 **[A.20]**); and changes in the genome and transcriptome of the plant (Ben Ali et al. (2020), p. 704; 720, **[A.21]**). These studies concerned NK603, one of the parent plants involved in the creation of the Modified Maize and the findings are clearly highly relevant and concerning for the safety of the stack.

115. Data from the (deficient) compositional analysis submitted by Monsanto itself raised concerns which plainly necessitated further investigation. Of a total of 63 points of comparisons raised only data from a low number of agronomic parameters (12 total) were subjected to statistical analysis in accordance with EFSA guidance; of these, 6 (no

spraying) and 8 (only sprayed with the complementary herbicide) were found to be statistically and significantly different.

116. A compositional analysis of 63 points of comparison in the Modified Maize revealed many (and partly major) statistically significant differences. 46 points of comparison were statistically significantly different in plants spayed with the complementary herbicides, and 47 endpoints were statistically significantly different in plants not sprayed with glyphosate, but which were sprayed with other conventional herbicides.

117. When considered holistically, the overall number of significant effects (*i.e.*, statistically significant differences) demonstrates substantial grounds for concern as regards the safety of the stack.

118. Therefore, in light of the precautionary principle, changes in the plant composition and phenotype caused by the stacking ought to have been investigated, including investigation into potential unintended changes in metabolic pathways and the emergence of unintended biologically active gene products in the Modified Maize.

119. However, the data provided by Monsanto and accepted by EFSA is entirely insufficient to conclude that the impact on plant composition of (i) the combination of traits and gene constructs, (ii) environmental factors, (iii) herbicide applications and (iv) the genetic background on gene expression, plant composition as well as on the agronomic and phenotypic characteristics, is safe in the Modified Maize.

(ii) The EFSA opinion

120. EFSA concluded that the field trial sites selected for the protein expression data, and the compositional and agronomic/phenotypic characterisation of the application, ensured a sufficient range of environmental and agronomic conditions (section 3.4.2.4 p. 244, **[A.3]**). This was held to have included environmental stress factors given that, in EFSA's view, plants grown under typical environmental conditions are exposed to a range of abiotic and biotic stressors that occur naturally during cultivation.

121. This response is wholly insufficient, for two reasons. In essence, EFSA seeks to rely on arbitrary environmental factors in order to conclude on the safety of the Modified Maize. This is entirely unscientific. It relies on the exigencies of the weather in a small cluster

of sites to spontaneously simulate the conditions under which the Modified Maize will be grown. The field trials ought to have been deliberately designed with a reduced watering protocol in order to definitively conclude on the safety of the stack under drought conditions.

122. In any event, the analysis of the field trials reveals that the Modified Maize was not exposed to "naturally occurring" drought conditions. Indeed, in one case (at the KSLA site) the plants were deliberately irrigated when drought conditions materialised in order to ensure the crops were not exposed to drought conditions ("*KSLA",* Table 3, p. 175, **[A2]**).

123. Accordingly, the field trials conducted were entirely insufficient to conclude on the safety of the stack when cultivated under the conditions to which the Modified Maize is overwhelmingly likely to be exposed, and the data generated in those field trials is entirely insufficient to discharge EFSA's obligation to ensure that the Modified Maize demonstrates the high level of safety necessary to be marketed in the EU. Key data on how the Modified Maize behaves under real-world cultivation is simply completely missing from the application.

(iii) The Commission decision

124. The Commission upheld the EFSA conclusion that the tested materials in the Modified Maize application were in line with the requirements of the 2013 Regulation as well as with the EFSA Guidance on the agronomic and phenotypic characterisation of genetically modified plants.

125. The Commission contends that Monsanto selected field trial sites located in major Modified Maize producing areas of the United States, and each of these sites reflects different meteorological and agronomic conditions under which the crop is to be grown.. EFSA considered that the meteorological and agronomic variability at the sites selected were sufficient to ensure a range of environmental and agronomic conditions reflecting those under which the GM stack Modified Maize might be cultivated in practice (section 1.2.1, p. 357, **[A.9]**).

126. This response is identical to the response to Grounds A and B and is dealt with above at [60] – [89] and [97] – [106], above.

(iv) Conclusion on Ground C

127. The stacked Modified Maize carries a combination of a traits and gene constructs likely to show or to cause major changes in gene expression if exposed to environmental stress, such as drought or high applications of herbicide. EFSA ought to have required field testing with repeated herbicide applications using higher dosages and with exposure to a much wider range of environmental conditions, including drought conditions in order to assess whether changes in plant composition occurred in the Modified Maize, and whether those changes raised safety concerns.

128. This was required in order to satisfy the condition in subsection 1.3.2.1(b) of Annex II that the crop be tested in the environmental and agronomic conditions reflecting those under which it will be cultivated in practice. Having not tested the crop in the real-world conditions to which it will be exposed, the data supplied on the plant composition of the crop and potential interactions between events was necessarily deficient.

129. Having failed to do so, the data presented by Monsanto is wholly insufficient to reach any robust conclusions on the impact of environmental factors and stress conditions on gene expression, plant composition as well as the phenotypic and agronomic characteristics of the Modified Maize. Instead of assessing in more detail the overall pattern of changes in plant components, their causes and possible impacts, Monsanto (and so, EFSA) merely assessed the observed changes in isolation from one another for evidence of potential harm. This approach turns what ought to be a holistic analysis of how the Modified Maize will react to real-world conditions into a trivial assessment of single factors in isolation, and does not constitute an appropriate assessment of the safety of the stack when cultivated in the conditions under which it is overwhelmingly likely to be cultivated, *i.e.*, in drought conditions and with real-world conditions of repeated / high dosage applications of herbicide.

130. 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.

131. 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 Maize met the high level of safety required to be lawfully authorised in the EU.

V. CONCLUSION

132. 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*".

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

KASSIE SMITH

Barrister-at-law, Ireland

c/o Testbiotech e.V,
Frohschammerstraße 14,
80807 München,
Germany
19 September 2021

SCHEDULE OF ANNEXES TO THE APPLICATION

A. ANNEXES

1. Monsanto application letter, 28 October 2016, pp. 1 – 6 (para 43 / p. 12)
2. Monsanto application for authorisation EFSA-GMO-NL-2016-134, Part II "Scientific Information" and Amended Report MSL0027532, pp. 7 – 228 (para 43 / p. 12)
3. EFSA GMO Panel Scientific Opinion, 3 July 2019 ("**the EFSA Opinion**"), pp. 229 – 265 (para 46 / p. 12)
4. Resolution of the European Parliament dated 11 November 2020, pp. 266 – 275 (para 47 / p. 13)
5. Commission Implementing Decision, 22 January 2021 granting Monsanto market authorisation for the Modified Maize ("**the Commission Implementing Decision**") pp. 276 – 283 (para 49 / p. 13)
6. Testbiotech's Request for Internal Review, 8 March 2021, pp. 284 – 285 (para 50 / p. 13)
7. Testbiotech's technical background for its Request for Internal Review, 8 March 2021, pp. 286 – 345 (para 50 / p. 13)
8. Decision Letter rejecting Testbiotech's Request for Internal Review, 8 July 2021, pp. 346 – 349 (para 51 / p. 13)
9. Commission assessment of Testbiotech's request for internal review, 8 July 2021, pp. 350 – 371 (para 51 / p. 13).
10. USDA Corn Explorer USA 2020-21 Corn Production, pp. 372 – 383 (para 62 / p. 16)
11. Commission Committee for the Common Organisation of Agricultural Markets, EU Cereals Trade 2020/21 presentation, 26 August 2021, pp. 384 – 415 (para 63 / p. 16)
12. Fang et al. (2018), pp. 416 – 427 (para 70 / p. 17)

13. Beres (2019), pp. 428 – 588 (para 70 / p. 18)
14. Beres et al. (2018), pp. 589 – 601 (para 70 / p. 18)
15. Trikova et al. (2015), pp. 602 – 611 (para 76 / p. 19)
16. Koornneef and Meinke (2010), pp. 612 – 625 (para 81 / p. 20)
17. Yang et al. (2017), pp. 626 – 638 (para 93 / p. 23)
18. Miyazaki et al. (2019), pp. 639 – 660 (para 94 / p. 23)
19. Agapito-Tenfen et al. (2013), pp. 661 – 676 (para 114 / p. 27)
20. Bevenuto et al. (2017), pp. 677 – 700 (para 114 / p. 27)
21. Ben Ali et al. (2020), pp. 701 – 724 (para 114 / p. 27)
22. Testbiotech's Articles of Association, 23 March 2012, pp. 725 – 733 (para 4 / p. 2)
23. Testbiotech's Registration Document, 16 October 2012, pp. 734 – 736 (para 4 / p. 2)
24. 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. 737 – 744 (para 6 / p. 3)
25. Regulation 1829/2003 on genetically modified food and feed ("**the GM Regulation**"), pp. 745 – 768 (para 13 / p. 4)
26. Directive 2001/18 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC, pp. 769 – 807 (para 14 / p. 5)
27. Regulation 503/2013 on application for authorisation of genetically modified food and feed ("**the 2013 Regulation**") pp. 808 – 856 (para 23 / p. 6)
28. Case T-33/16 *TestBiotech eV v Commission* ECLI:EU:T:2018:135, pp. 857 – 874 (para 11 / p. 4)

29. Case T-177/13 *TestBiotech eV v Commission* ECLI:EU:T:2016:736, pp. 875 – 918 (para 35 / p. 9)

(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).
