Cotton T304-40 × GHB119 × COT102

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Type: Non Profit Organisation

Comments:

Introduction

The GMO Panel assessed cotton T304-40 ×GHB119 × COT102 (EFSA, 2025a). The parental plants combined in the stacked are

• T304-40 expressing Cry1Ab and PAT/bar conferring insecticidal effects and resistance to glufosinate-ammonium based herbicides,

• GHB119 expressing PAT/bar and Cry2Ae conferring resistance to glufosinate-ammonium based herbicides and insecticidal effects,

• COT102 expressing APH4 and Vip3Aa19 conferring resistance to antibiotic hygromycin B and insecticidal effects.

All data as provided by the applicant are obtained from the species Gossypium hirsutum, however EFSA expanded the results of its assessment to Gossypium barbadense without having empirical evidence.

1. Systematic literature review

A systematic review as requested in Regulation (EU) No 503/2013 was not provided by the applicant. Despite the fact that there are many publications on the parental plants, EFSA agreed that it would not be necessary to deliver a systematic review. This practise of EFSA undermines the legally required standards according the Implementing Regulation 503/2013.

2. Molecular characterisation

The current practice of EFSA fails to fulfill the legally requested standards as requested by EU Regulation 1829/2003. According to the Regulation, it is requested that 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 Regulation 1829/2003). As requested in Recital 10 of the Regulation: “Thus, genetically modified food and feed should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard, to be undertaken under the

responsibility of the European Food Safety Authority (Authority), of any risks which they present for human and animal health and, as the case may be, for the environment."

In the case of the present application

• only few data were assessed in regard to biologically active molecules that may emerge from open reading frames caused by the insertion of transgenes (taking into account only proteins);

• limited and outdated data (from the years 2015-2017) on gene expression were assessed that stem from a low number of field trials not representing the climatic and regional conditions under which these plants will be grown;

• data from only one genetically engineered variety were expanded to all varieties in which these constructs may be integrated;

• data from one species (Gossypium hirsutum) were expanded to another species (Gossypium barbadense).

Data from only four sites in Argentina and Brazil from the years 2015-2017 and a very limited number of samples are insufficient to represent the conditions under which these plants will be grown. For example, current climate and agricultural practices (due to increase of herbicide resistant weeds) are likely to be different from those in 2015-2017. Since climate change is ongoing in regions where the plants are cultivated, the data from the applicant should allow to extrapolate for a period of 10 years (the duration of the aimed market approval). Therefore, the data provided are invalid and do not allow any conclusion in regard to risk assessment.

Data from the present application should have been compared to the application on cotton GHB614 x T304-40 ×GHB119 × COT102: In the case of this other application (four-stacked event including resistance to glyphosate), data from trials in the USA from the year 2013 were provided. These data on gene expression show clear differences compared to those of the three-stack of the present application:

• Protein levels of the Cry1Ab are generally higher in the four-stack.

• Protein levels of Cry2Ae in the four-stack are much lower in kernels, but much higher in pollen.

• Protein levels of Vip3Aa19 are generally higher in the four-stack, there are huge differences between the two applications in regard to the kernels.

• Also the protein levels on Pat/bar are significantly different between the two applications.

In result the data provided in the case of these applications are inconclusive.

To fulfill the requirements of the EU GMO regulation, EFSA should have requested additional data on

• all biological active molecules that may emerge from new open reading frames;

• field trials that are up to-date with current agricultural practise and climatic conditions;

• targeted experiments to assess the effects of a broader range of environmental stressors;

• targeted experiments to assess the effects of higher-dosage spraying with the complementary herbicides;

• application of 'Omics' to investigate changes in the gene activity of the transgenes, as well as changes in the plants' own genes;

• the impact of the genetic backgrounds of different varieties and the species of Gossypium barbadense.

Furthermore, in awareness of the absence of independent data on the GE cotton, the production of the data should have been conducted under control of independent experts.

In conclusion, the data provided on the GE cotton do not sufficiently represent the products intended for import. The data provided by the applicant and accepted by EFSA are insufficient to conclude on the impact of environmental conditions, stressors, herbicide applications and genetic backgrounds on gene expression and plant metabolism.

3. Comparative assessment of plant composition, and agronomic and phenotypic characteristics

The current practice of EFSA fails to fulfill the legally requested standards as requested by EU Regulation 1829/2003. According to the Regulation, it is requested that 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 Regulation 1829/2003). As requested in Recital 10 of the Regulation "Thus, genetically modified food and feed should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard, to be undertaken under the responsibility of the European Food Safety Authority (Authority), of any risks which they present for human and animal health and, as the case may be, for the environment."

In the present application, the data provided by the applicant underline the need for further investigations: Data from only four sites trials Argentina and Brazil between the years 2015-2017 are insufficient to represent the conditions under which these plants will be grown. For example, current climatic conditions and agricultural practices (due to increase of herbicide resistant weeds) are likely to be different from those in 2015-2017. Since climate change is ongoing in regions where the plants are cultivated, the data from the applicant should allow to extrapolate for a period of 10 years (the duration of the intended market approval). Therefore, the data provided are invalid and do not allow to conclude the risk assessment.

Nearly half of the data assessed showed significant differences to the plants used as comparator. Data from the present application should have been compared to the application on cotton GHB614 × T304-40 ×GHB119 × COT102: In the case of this other application (four-stacked event including resistance to glyphosate), data from trials in the USA from the year 2013 were provided. These data show changes in a similar group of plant constituents including gossypol. Since gossypol is known as being toxic to mammals, these findings should have been investigated in more detail.

To fulfill the requirements of the EU GMO regulation, EFSA should have requested additional data on

• field trials that are up-to-date with current agricultural practise and climatic conditions;

• the field trials conducted in all relevant regions where the GE cotton will be cultivated;

• targeted experiments to assess the effects of a broader range of environmental stressors;

• targeted experiments to assess the effects of higher-dosage spraying with the complementary herbicides;

• application of 'Omics' techniques to investigate changes in the plant composition;

• the impact of the genetic backgrounds of different varieties and Gossypium barbadense on plant composition, and agronomic and phenotypic characteristics.

Furthermore, in awareness of the absence of independent data on the GE cotton, the production of the data should have been conducted under control of independent experts.

In conclusion, the data provided on the GE cotton do not sufficiently represent the products intended for import. The data provided by the applicant and accepted by EFSA are insufficient to conclude on the impact of environmental conditions, stressors, herbicide applications and genetic backgrounds on plant composition and agronomic and phenotypic characteristics.

4. Toxicity

The current practice of EFSA fails to fulfill the legally requested standards as requested by EU Regulation 1829/2003. According to the Regulation, it is requested that 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 Regulation 1829/2003). As requested in Recital 10 of the Regulation: "Thus, genetically modified food and feed should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard, to be undertaken under the responsibility of the European Food Safety Authority (Authority), of any risks which they present for human and animal health and, as the case may be, for the environment."

In the present case, EFSA failed to take into account that the insecticidal proteins (IP) as produced in transgenic plants are known to show effects that go beyond the specific mode of action as intended:

a) Combinatorial or cumulative effects in interaction with other toxic substances.

Several studies show that the toxicity of the IPs can be largely increased if it is combined with exposure to other toxic substances. Under these circumstances, also the specificity of the IPs can be altered and therefore increase the range of potentially affected non-target organisms. This is especially relevant for transgenic plants since IP traits are often combined with herbicide resistance in stacked evens, are grown together in the fields or mixed in the food chain.

b) Interactions between the IPs and plant constituents.

In the case of IPs, it is known that proteinase inhibitors, being present in species such as soybeans, maize and cotton can hamper the degradation of the toxins. Therefore their toxicity can be drastically enhanced after ingestion. In general, the degradability of the IPs in the gut, but also in the environment, is a crucial factor for their health and environmental safety.

c) Interactions or cumulative effects caused by several IPs being expressed in the same plant or mixed in diets

It is known that IPs occurring in Bacillus thuringiensis can interact and synergise with each other. Currently, about 30 IPs that can be expressed and combined in transgenic plants in the fields and in the food chain were already assessed by EFSA or can be found in pending applications. Therefore, the question of interactions, combinatorial or accumulated effects is very relevant for environmental risk assessment as well as food and feed safety.

d) Effects on the microbiome

IPs can impact the composition of the gut microbiomes. These effects are independent from their specific mode of action in target insects. Potential effects transmitted by the change in microbiomes may include health risks related to the immune system or the gut organs.

e) Effects of IPs on the immune system

In the case of IPs, for some of the Cry toxins it is known that they can be used as adjuvants to boost the effects of vaccines. In some cases, also potential allergenicity is discussed. Effects on the immune system may also be triggered by other adjuvantic or immune boosting molecules or a mixture of several Cry proteins that, for example, may be present in the same diet. Effects on the immune system can also be triggered by changes in the intestinal microbiome.

These findings cause the rise of hazards and well argued risk hypotheses that need to be explored to fulfill the requirements of EU GMO regulation (see also EFSA, 2025b).

Therefore, to fulfill the requirements of EU regulation, EFSA should have request additional data on

• interactions with co-factors (such as plant constituents hampering the degradation of the IPs and other toxins) or accumulated effects, that are likely to enhance toxicity and increase the range of possibly affected organisms;

• effects going beyond the intended mode of action of IPs in certain Lepidoptera and that can be relevant for adverse health effects such as for immunotoxicty and negative effects caused by changes in the gut microbiomes.

However, in the case of the present application, EFSA failed to do so. No empirical data were requested to examine potential combinatorial or cumulative effects of the IPs, with the residues from spraying with the complementary herbicides or with plants constituents such as proteinase inhibitors.

Instead, EFSA tried to dilute uncertainties and reasoned concerns by invalid reasoning such as:

• only mentioning the intended mode of action of IPs, but neglecting multiple effects that go beyond;

• claiming there would be no evidence for adjuvanticity in the GMOs assessed by the Panel, leaving aside the fact that relevant experiments were not conducted and therefore the relevant data are missing;

• assuming quick degradation of the toxins, despite empirical data are evidencing the opposite.

In addition, a large body of evidence is neglected by EFSA showing that

• plants constituents such as proteinase inhibitors that are known to enhance toxicity of the insecticidal proteins;

• combinations with other toxins (such as residues from spraying with complementary herbicides) or stressors can render accumulative or synergistic effects enhancing toxicity of IPs;

• adverse effects caused by Bt toxins on non-target species as well as on mammalian cells and organisms.

There may be several reasons for EFSA's invalid assessments. No matter why, EFSA never managed to establish any method to reliable assess combinatorial or accumulated effects caused by insecticidal toxins. With an ever increasing list of IPs and other new proteins (NEPs) being produced in transgenic plants and entering the food chain and the environment, this pertained scientific incompetence is not only a sign of mismanagement (supported by the EU Commission), but can become a matter of negligent endangerment.

In consequence, even after decades of imports of IP producing plants, EFSA never assessed their real toxicity, which can not be reliably determined without taking into account plant constituents such as proteinase inhibitors. Further known gaps in the practice of EFSA are the assessment of changes in the microbiomes and the evaluation of omics data. Instead of reducing the gaps in current practice, EFSA seems to be mostly interested in constructing and defending a world of transgenic plants without risks and uncertainty.

In conclusion, EFSA assessment of the toxicity of the stacked cotton is unacceptable.

5. Environmental risk assessment

Although the present application does not request approval for cultivation, environmental risk assessment is necessary and requested by EU Regulation 1829/2003 by referring to the standards of EU Directive 2001/18. Relevant issues are potential spread after spillage and environmental exposure via animal faeces or leftovers from food and feed processing.

• In regard to spread after spillage of viable seeds, it is known that in Southern Europe, in some regions locally naturalised cotton plants emerged in in the same area where cotton is

grown. No data were requested on the factual persistence and effects of spontaneous further crossing of the stacked cotton, therefore the assessment of EFSA is inconclusive. Consequently, no import of viable seeds into regions that could enable persistence or reproduction of volunteers can be allowed.

• In regard to exposure to the environment via animal faeces it would be necessary to request data on the factual degradation of the toxins and potential mixtures of toxic residues in the dung as well as their potential accumulation in the soil or aquatic ecosystems. Similarly, such data would be needed to assess the impacts from potential leftovers from food and feed production.

Without these data, the environmental risk assessment remains inconclusive (see also EFSA, 2025b).

6. Others

Monitoring

For monitoring and methods to identify the specific event, Implementing Regulation 503/2013 requests:

The method(s) shall be specific to the transformation event (hereafter referred to as 'event-specific') and thus shall only be functional with the genetically modified organism or genetically modified based product considered and shall not be functional if applied to other transformation events already authorised; otherwise the method cannot be applied for unequivocal detection/identification/quantification. This shall be demonstrated with a selection of non-target transgenic authorised transformation events and conventional counterparts. This testing shall include closely related transformation events.

If approval for import is given, the applicant has to ensure that post-market monitoring (PMM) is developed to collect reliable information on the detection of indications showing whether any (adverse) effects on health may be related to GM food or feed consumption. Thus, the monitoring report should at very least contain detailed information on: i) actual volumes of the GE products imported into the EU, ii) the ports and silos where shipments of the GE products were unloaded, iii) the processing plants where the GE products was transferred to, iv) the amount of the GE products used on farms for feed, and v) transport routes of the GE products. Environmental monitoring should be run in regions where viable material of the GE products such as kernels are transported, stored, packaged, processed or used for food/feed. In case of losses and spread of viable material (such as kernels) all receiving environments need to be monitored. Furthermore, environmental exposure through organic waste material, by-products, sewage or faeces containing GE products during or after the production process, and during or after human or animal consumption should be part of the monitoring procedure.

Conflicts of interest

Testbiotech published a report on the current EFSA GMO Panel (Testbiotech, 2024). According to the investigation, members of the GMO panel with interests in developing genetically engineered plants have gained considerable influence within the authority. Testbiotech is therefore demanding corrections in the composition of the GMO Panel. Unless

balance is restored, any assessment by the Panel in its current composition has to be regarded as biased.

References

EFSA (2025a) Assessment of genetically modified cotton T304-40 × GHB119 × COT102 (application EFSA-GMO-BE-2018-155). EFSA J, 23(12): e9753. https://doi.org/10.2903/j.efsa.2025.9753

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Testbiotech (2024) NGT plant developers take over the EFSA GMO Panel, https://www.testbiotech.org/publikation/ngt-plant-developers-take-over-the-efsa-gmo-panel/