Maize MON 94804

Organisation: Accreditation body
Country: Bulgaria
Type: Non Profit Organisation

Comments:

I appreciate the possibility to share my opinion on the approval of a new genetically modified maize MON 94804 for food and feed.

My opinion is that no genetically modified plants should be allowed in Europe.

Let them be used in the USA where this is already a non-reversible approach and even if farmers want to use non-genetically modified seeds the whole system for supply with such seeds is made in a way that makes this next to impossible.

However, in Europe such plants should be banned. All these investments in research of the genetically modified seeds and plants which include also testing on animals, for an end result that a plant with one or two slight advantages to the conventional ones may possibly be used could have been invested in far more useful and beneficial in long term activities which would give far more significant benefits than just "shorter height of a plant".

The research is not convincing because it does not cover long term effects of the plants on the environment and on humans and animals. One thing is a one off eating of food or feed made from these plants and it may indeed be safe, but what about effects from regular consumption?

What would be the effect of this plants on the ecosystem in which they would be grown?

My position as a citizen of the EU is that Europe does not need such seeds and all these investments in research if genetically modified plants are safe or not are not justified by any visible or tangible benefit for the environment and the humans and animals.

I do not agree with approval of this type of genetically modified maize MON 94804 for food and feed.

Maize MON 94804

Organisation: Testbiotech e.V. - Institute for Independent Impact Assessment of Biotechnology
Country: Germany
Type: Non Profit Organisation

Comments:

Introduction

The GMO Panel assessed maize MON94804 (EFSA, 2024a). This maize is genetically engineered to produce an artificial miRNA intended to selectively suppress two genes within a larger gene family involved in the biosynthetic pathway of gibberellic acid (GA).

The development of the artificial GA20ox_SUP miRNA started initially with miR1425 from rice; mature miRNA was replaced with sequences specific to GA20ox3 and GA20ox5 genes from Zea mays. The miRNA is meant to downregulate the expression of these two genes each of which is known to have several copies in the maize genome.

This significantly reduces the growth of the plants. Compared to the original plants, the genetically engineered (GE) plants are expected to have a height reduction of approximately 1/3, without this having a negative impact on the maize grain yield (normal growth of ears and reproductive tissues).

1. Systematic literature review

A systematic review as requested in Regulation (EU) No 503/2013 was not provided by the applicant. Further, it has to be stated that there is a clear lack of independent science, i.e. all available scientific papers regarding event MON94804 and GA20ox_SUP miRNA were written by the applicant.

2. Molecular characterisation

The insertion made use of the Cre-Lox system that allows site specific recombination and the excision of selectable markers. As a result, the plants supposedly only carry one copy of the insert without the additional markers. The main elements of the gene construct are a promoter that is meant to be active primarily in vegetative plant tissue (RTBV) and the DNA sequence to produce the artificial miRNA. The target genes are also intended to be involved in growth, but not in the development of reproductive organs (Paciorek et al., 2022)

The genetic engineering process led to the emergence of several new open reading frames in the genome of the maize. However, EFSA states that proteins that may emerge from these

DNA sequences would not raise safety concerns. According to EFSA, the analyses indicated that the expression of any ORF showing significant similarities to toxins or allergens in maize MON 94804 is unlikely.

The plant genome was analysed for off-target genes which are very similar which may be, therefore, ‘off-target’ sequences, and thus able to interfere with the miRNA. However, no such sequences were reported.

Data on the gene activity of the target genes (mRNA levels of GA20ox3 and GA20ox5) and the levels of the major bioactive gibberellins (GA1 and GA4) in maize MON 94804 were provided for analysis of the impact on the metabolism of the plants. The results indicate that the expression of target genes in several kinds of tissue in the GE plants was reduced, e. g. in the stalk, silk and grain, leaves and forage. EFSA (2024a) does not mention the fact that a paper published by the applicant (Paciorek et al., 2022) found that only one other gibberellin variant produced by members of the same gene family (GA20ox1) was quantified. This gene is not anticipated to be suppressed by GA20ox_SUP and is the closest homologous gene to GA20ox3 and GA20ox5 in the maize genome. In some tissues, expression of GA20ox1 deviated from the control, which was interpreted as a compensatory mechanism of a GA-dependent feedback loop that regulates the expression level of some GA genes.

As Paciorek et al. (2022) state: “It is important to note that both the native expression of the GA20ox genes, as well as the activity of the RTBV promoter driving expression of the miRNA, which suppresses these genes, are dynamic and may have different relative quantities within the different tissues or time points that were sampled in the presented analyses. This could potentially affect the relative stoichiometry between the miRNA and target mRNA and, consequently, impact suppression efficiency in sampled tissues.”

EFSA did not take the data into account showing that the introduction of the artificial miRNA not only interferes with the targeted genes, but also involves other regulatory functions.

Further data are definitely needed before any conclusions can be drawn on safety of the maize: it is known that miRNAs are a part of complex regulatory mechanisms. The premature RNA undergoes further processing in the plant, and thereby interacts with specific plant enzymes. Its effects in many cases are not restricted to the target gene, but often involve metabolic cascades of several hundred other gene functions.

However, no data are available on interactions between the articificial miRNA (except the feedback loop with another GA as mentioned), the products (intermediate) emerging from further processes in the cells, the persistence of these molecules in the cells and their inference in other regulatory networks.

Furthermore, gene expression and its impact on GA production and metabolic impact was only investigated in field conditions with no particular stress factors. This is surprising since gibberellic acid is known to be involved in many biotic and abiotic stress responses (Castro-Camba et al., 2022a). According to current scientific knowledge, GA interferes with the activity of many other plant hormones and signalling pathways, such as abscisic acid, ACC synthase, auxin, brassinosteroids, cytokinins, jasmonates, other miRNAs (miRNA160), strigolactones and others.

As the experts from member states have affirmed (EFSA, 2024b), gibberellins are major regulators of various physiological processes in plants. Apart from plant stature, they also regulate germination and flowering. They also play a role in the regulation of stress tolerance and are part of complex regulatory crosstalk with other plant hormones in various signalling pathways, e. g. physiological processes affecting plant composition. In addition, they are involved in the immune response of plants to pathogens; the reduction in gibberellins is known to be associated with increased drought resistance in plants.

Therefore, the respective data which have been provided are insufficient to allow conclusions on potential changes on a molecular level occurring in reaction to stress response. Consequently, the assessment of maize MON94804 should be improved by, e. g. a focused assessment of stress response to specifically exerted stressors. Furthermore, Omics should be applied to assess the metabolic changes on several levels in the plants, and data should be provided on potential changes in the composition of precursor molecules within the biosynthetic pathway of the gibberellins.

Consequently, the GE maize plants tested in field trials do not sufficiently represent the products intended for import. The data presented by the applicant are insufficient to conclude on safety as requested in EU GMO regulation.

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

Field trials to assess plant composition as well as agronomic and phenotypic characteristics of the GE maize were conducted in the US for the duration of one year (2020) at eight (compositional analysis) sites. There were no reports of extreme weather conditions from some of the fields.

No experiments were conducted under specific stress conditions. Therefore, the data as provided are insufficient to conclude on safety.

EFSA did not take into account that Paciorek et al. (2022) showed that the introduction of the artificial miRNA not only interferes with the targeted genes, but also involves other regulatory functions. Furthermore, Paciorek et al. (2022) report some differences in ear components that were interpreted as representing environmentally driven variations.

Further data are definitely needed before any conclusions can be drawn on safety of the maize: gibberellic acid is known to be involved in many biotic and abiotic stress responses (Castro-Camba et al., 2022a). GA interferes with the activity of many other plant hormones and signalling pathways, such as abscisic acid, ACC synthase, auxin, brassinosteroids, cytokinins, jasmonates, other miRNAs (miRNA160), strigolactones and others. It was also shown that gibberellins impact plant composition (Castro-Camba et al., 2022b).

As the experts from member states affirm (EFSA, 2024b), gibberellins are major regulators of various physiological processes in plants, which beside plant stature also regulate germination and flowering. They also play a role in the regulation of stress tolerance and are part of complex regulatory crosstalk with other plant hormones in various signalling pathways, e. g. for physiological processes affecting the composition of plants. In addition, they are involved in the immune response of plants to pathogens. A reduction in gibberellins is known to be associated with increased drought resistance in plants.

Therefore, the data which are provided insufficient to allow conclusions on potential changes in plant composition and agronomic performance in reaction to stress response. Consequently, the assessment of maize MON94804 should be improved by, e. g. a targeted assessment of stress response to specifically exerted stressors. Furthermore, Omics should be applied to make a more detailed assessment of the metabolic changes on different levels in the plants.

Consequently, the GE maize plants tested in field trials do not sufficiently represent the products intended for import. The data presented by the applicant are insufficient to conclude on safety as requested in EU GMO regulation.

Overall, the applicant failed to demonstrate food and feed safety. No conclusions can be drawn from the EFSA risk assessment. The application for market authorisation of MON94804 has to be rejected.

4. Toxicity

Risk assessment of GA20ox_SUP miRNA is not based on any experimental data, such as investigation of the gene products in isolation, or that produced in bacterial systems. No data are provided on potential uptakes from the intestine or on potential cross-species activity.

Instead, EFSA refers to Davalos et al. (2019) and simply assumes that the artificial miRNA would be rapidly degraded. However, this study only partially supports the opinion of EFSA. Indeed, Davalos et al. (2019) report that, supported by specific menchanisms, miRNA can be taken up from the gut. Furthermore, cross-species activity of plant miRNA is also reported in studies that Davalos et al. (2019) did not take into account, such as Wang et al. (2018) and Rabuma et al. (2022).

Consequently, the science does not sufficiently support the EFSA assumptions. Without experimental data on potential cross-species activity, e. g. microbiomes in the gut and the soil, insects or mammalian cells, no conclusions can be drawn on the safety of the maize which produces artificial miRNA in its tissues. This view is also supported by the statements made by the experts from member states.

In regard to whole food and feed risk assessment, it is unclear whether the material used for the feeding study is representative of the food and feed that may derived from the maize. Before any conclusions can be drawn on the outcome of the whole food and feed risk assessment, more data are needed in regard to molecular characterisation, plant composition and the toxicology of the artificially produced miRNA.

5. Environmental risk assessment

The appearance of teosinte in Spain and France (see Testbiotech, 2016; Trtikova et al., 2017) has to be considered in more detail. Maize volunteers are found in the EU on a regular basis, as reported by Palaudelmàs et al. (2009) in Spain or Pascher (2016) in Austria.

Testbiotech is aware of an EFSA (2022) opinion regarding the teosinte situation in France and Spain. Here, EFSA comes to the conclusion that:

“The new evidence retrieved confirms that where maize and EU teosinte plants co-occur and flower synchronously, maize alleles (transgenic or not), can move into teosinte populations at rates that depend on different factors. Hence, the possible introgression of transgenes from maize MON810, Bt11, 1507 and GA21 into EU teosinte may only provide a selective advantage to GM teosinte hybrid progeny under high infestation of target pests and/or when glufosinate-ammonium- and/or glyphosate-based herbicides are applied. However, this fitness advantage will not allow GM teosinte hybrid progeny to overcome other biological and abiotic factors limiting their persistence and invasiveness. Therefore, EFSA considers that the growth habits of EU teosinte plants and teosinte hybrid progeny are such that the acquisition of insect resistance and/or herbicide tolerance is unlikely to change their relative persistence and invasive characteristics under EU conditions."

The science does not sufficiently support this opinion: the characteristics of potential hybrids and next generations need to be investigated and cannot simply be predicted from the data of the original event. It is widely known that there can be next generation effects and interference from the genetic background, none of which can be predicted from the assessment of the original event (Bauer-Panskus et al., 2020). This issue is relevant for gene flow from maize to teosinte, and vice versa.

A recently published paper on hybrids between maize and teosinte found in Spain provides new scientific evidence and challenges previous EFSA assumptions. Arias-Martín et al. (2024) state in this paper that maize/teosinte hybrids found in fields form viable seeds, resulting in plants that may be more vigorous than the parent plants. The time it took these hybrids to reach the reproductive stage was shortened, thus facilitating crossing with maize by favouring synchrony in flowering.

The potential for hybridisation between GE maize and teosinte is mentioned in the EFSA opinion. However, the potential selective advantage of such hybrids due to the introgression of transgenic sequences transferred by maize MON94804 was not investigated. A reduction in gibberellins is known to be associated with increased drought resistance in plants (see EFSA, 2024b). Thus, this trait may potentially affect the survivability of the plants in the open environment, as well as affect their composition. It is therefore relevant in environmental risk assessment (ERA).

Therefore, essential information necessary to conclude on the ERA is missing. Consequently, no final conclusion can be drawn from the environmental risk assessment carried out by EFSA.

EFSA should have requested data from the applicant to show that no adverse effects can occur due to gene flow from the maize to teosinte and / or from teosinte to the maize volunteers. In the absence of such data, the risk assessment cannot be regarded as valid.

Without detailed consideration of the hazards associated with the potential gene flow from maize to teosinte and vice versa, no conclusions can be drawn on the environmental risks of maize spillage.

Consequently, the EFSA environmental risk assessment is not acceptable.

6. Others

As far as monitoring and methods to identify the specific event are concerned, Implementing Regulation 503/2013 requests that:

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 for the collection of reliable information on the detection of indications showing whether any (adverse) health effects may be related to GE food or feed consumption. The monitoring report should, therefore, 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 are transferred to; iv) the amount of the GE products used on farms for feed and v) transport routes used for 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 from 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.

In addition, this maize variety highlights some general problems. These are:

(1) Current EFSA practice makes it impossible to access the original data provided by the companies within the period of consultation. Therefore, the opinion has to provide all the necessary data to allow other experts to conclude on whether the provisions in GMO regulation (esp. 503/2013) are adhered to. We are making this comment after our recent experiences in requesting access to documents which, in many instances, took months to achieve. The Commission should advise EFSA to improve transparency.

(2) A Testbiotech report published in 2021 (Testbiotech, 2021), shows how the European Food Safety Authority (EFSA), which is responsible for risk assessment of GE plants, intentionally sets crucial issues aside. This careless approach exemplifies the overall decrease in general food safety standards that has been ongoing since the introduction of GE plants. The number of events authorised for import has, at the same time, steadily increased. In light of these findings, the Commission should try to avoid 'rubber stamping' all applications for import of GE plants, and thus reduce the overall number of products entering the market, while ensuring that these products undergo much more thorough risk assessment.

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