Maize MON 87419

Organisation: OGM dangers
Country: France
Type: Association

Comments:

Dear Commission,

My experience for the last twenty years is that Commission does not reply to consultations, does not care about the advice of the public. As a consequence, consultations are only the spectacle of a consultation to _look like_ a democracy. But it is a techno-cracy.

I have not the faintest hope that fake food be released in my environment.And the intent of the Commission to stop labels adds to my anger.

If the commission goes on faking labels on food, it will hurt the whole alimentary chain from peasans to retailers (and consumers inbetween).

I did not even propose to the members of OGM dangers to say chat they think since it is useless. When the English government made such a consultation, even though it was overwhelmingly in favor of labeling it said it would un-label. Why cooperate with gvernements that do not do what citizens want ?

Meanwhile, you are also weakening the authority of all politicians. When there will be revolts, you will claim it is irrational. But it is very reasonnable!

Sincerely yours

Maize MON 87419

Organisation: De Gentechvrije Burgers, Europees Consumentenplatform
Country: The Netherlands
Type: Others...

Comments:

Lelystad, 24 februari 2023

Betreft Genetically modified maize MON 87419

We – the GMO-Free Citizens (a European consumer platform based in Lelystad) and the Lelystad Ekopark Foundation – object to EU market authorisation for MON GA21 × T25 genetically modified maize.

Abstract (Quote)

"Genetically modified maize MON 87419 was developed to confer tolerance to dicamba- and glufosinate-based herbicides. These properties were achieved by introducing the dmo and pat expression cassettes. The molecular characterisation data and bioinformatic analyses do not identify issues requiring food/feed safety assessment. None of the identified differences in the agronomic/phenotypic and compositional characteristics tested between maize MON 87419 and its conventional counterpart needed further assessment, except for the levels of arginine and protein in grains which did not raise safety and nutritional concerns. The GMO Panel does not identify safety concerns regarding the toxicity and allergenicity of the dicamba mono-oxygenase (DMO) and phosphinothricin N-acetyltransferase (PAT) proteins as expressed in maize MON 87419. The GMO Panel finds no evidence that the genetic modification impacts the overall safety of maize MON 87419. In the context of this application, the consumption of food and feed from maize MON 87419 does not represent a nutritional concern in humans and animals. The GMO Panel concludes that maize MON 87419 is as safe as the conventional counterpart and non-GM maize varieties tested, and no post-market monitoring of food/feed is considered necessary."

https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2023.7730

Our comment: We have our doubts about this. Many people currently have cancer or allergies – or both. Moreover, MON 87419 maize was banned in the USA in 2016! Why do you still approve it?

We – the European GMO-Free Citizens and the Ekopark Foundation in Lelystad (the Netherlands) – do not wish to eat this genetically modified maize that has been rejected by the USA. We want to eat unsprayed food that has not been genetically manipulated. This is also better for the environment.

Nor do we want genetically modified maize as animal feed. And we do not want you to put it back on the EU market. If you were to approve it (which we would regret), we would want every product and every end product to be labelled as a GMO, even if GMOs can no longer be detected in an end product.

We read:

'GM dicamba-tolerant corn deregulated in US'

Details

Published: 24 March 2016

The US Department of Agriculture (USDA) will no longer regulate a GM corn developed by Monsanto to resist its dicamba herbicide

According to Extoxnet, a pesticide information project of several US universities, “Dicamba is suspected of being a human teratogen” and “Data from laboratory studies are inadequate for EPA to determine if dicamba can increase the risk of cancer in humans”.

—and

“The corn line, known as MON87419, also resists glufosinate herbicide, the USDA said in a statement on its website.”

MEER: https://www.gmwatch.org/en/main-menu/news-menu-title/archive/90-2016/16833-gm-dicamba-tolerant-corn-deregulated-in-us

We – the European GMO-Free Citizens and the Ekopark Foundation in Lelystad (the Netherlands) – do not wish to eat this genetically modified maize. We want to eat unsprayed food that has not been genetically manipulated. This is also better for the environment.

Nor do we want genetically modified maize as animal feed. And we do not want you to put it back on the EU market. If you were to approve it (which we would regret), we would want every product and every end product to be labelled as a GMO, even if GMOs can no longer be detected in an end product.

https://nj.gov/health/eoh/rtkweb/documents/fs/0634.pdf

More on the herbicides used;
https://www.testbiotech.org/sites/default/files/Tox_Evaluation_Glyphosate_Dicamba_Isoxaflutole.pdf

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Maize MON 87419

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

Comments:

1. Systematic literature review

A systematic review as referred to in Regulation (EU) No 503/2013 was not provided by the applicant.

The applicant should have applied a broad range of research and also taken other dicamba and/or glufosinate-resistant transgenic plants into account. Furthermore, at least in regard to environmental risks, it is also necessary to review literature which might indicate indirect, delayed and cumulative long-term risks, or interactions with other genetically engineered plants which might occur from spillage and further crossings. Therefore, the literature research should have taken into account potential persistence, spread and crossings with other transgenic plants which enter the environment via spillage along transport routes etc. In this context, the biological characteristics of potential offspring are also relevant for the application. Any literature research should include all relevant publications concerning the crop species and its relatives. The environmental risk assessment should, moreover, take indirect, unintended, delayed and long-term cumulative effects of animal excretions into account. Therefore, literature research should include all genetically engineered plants which may be mixed into the diet and thus cause environmental hazards.

In addition, in regard to food and feed safety, interactions with other genetically engineered plants which might be mixed with the event in diets also need to be considered. Implementing Regulation 503/2013 (point 3.2.3) requests that "the applicant shall evaluate the data generated to estimate possible short-term and long-term risks to human or animal health associated with the consumption of genetically modified food or feed with respect to the expression of new proteins/metabolites, as well as significantly altered levels of original plant proteins/metabolites." Apparently, this legal request is not limited to the specific event. It comprises risk assessment of mixed diets in equivalence to risk assessment of stacked events, since the risks are also equivalent. A much more comprehensive literature review is, therefore, needed in order to consider potential interactions with other regulated GMOs.

2. Molecular characterisation

Junction sequence analysis and next generation sequencing (NGS) were performed in order to determine insert copy number and to confirm the absence of plasmid backbone and T-DNA II sequences; NGS sequencing on PCR amplified fragments was to determine size and organisation of the inserted sequences.

In order to assess the sequences encoding the newly expressed proteins or any other open reading frames (ORFs) present within the insert and spanning the junction sites, it was assumed that the proteins that might emerge from these DNA sequences would raise no safety issues; and, therefore, no detailed investigations were carried out in this regard. Furthermore, other gene products, such as unintentionally produced ncRNA (non-coding RNA) from additional open reading frames, were not assessed. Thus, uncertainties remain about other biologically active substances arising from the method of genetic engineering and the newly introduced gene constructs.

Gene expression under environmental stress conditions

Environmental stress can cause unexpected patterns of expression in the newly introduced DNA (see, for example, Trtikova et al., 2015). However, the expression of the additional enzymes was only measured under field conditions in the US for one year (2013). The plants should have been subjected to a much broader range of defined environmental conditions and stressors to gather reliable data on gene expression and functional genetic stability.

Data on herbicide application rates and their impact on gene expression

Due to increased weed pressure, it has to be expected that these plants can and will be exposed to high and also repeated dosages of complementary herbicides. Higher applications of herbicides will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. This aspect was ignored in risk assessment.

Protein levels of DMO (consisting of DMO + 7 and DMO + 12), and PAT were analysed in material harvested from field trials across five locations in the US during the 2013 growing season. However, from the data available to the public, there is no information on herbicide dosages. This means that data essential for an independent assessment is missing. From the available information, it appears that the complementary herbicides were not applied in combination and only sprayed once.

Nevertheless, EFSA is of the opinion that the design of the field trials is in accordance with the expected agricultural practices. To justify this opinion, EFSA should have presented more detailed reasoning.

Current EFSA practices are such that it is not possible to access the original data submitted by the companies within the period of consultation. Therefore, the opinion has to provide all the data necessary to allow other experts to conclude on whether the provisions of GMO regulation are fulfilled.

In light of the information available, we assume that the application and the data provided do not sufficiently represent customary agricultural practices, which could include the use of single herbicide applications, high dosages and repeated spraying.

Impact of genetic backgrounds on gene expression

It is known that the genomic background of the varieties can influence both the expression of the inserted genes and plant metabolism (see, for example, Lohn et al., 2020; Trtikova et al., 2015, Linares et al., 2023). However, it seems that the data on gene expression were confined to a single variety. Therefore, EFSA should have also requested additional data from transgenic maize varieties, e. g. those cultivated in South America.

EFSA did not taken these issues into consideration. 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, therefore, insufficient to conclude on the impact that genetic backgrounds have on gene expression, as requested in EU Regulation 503/2013.

Summary of molecular analysis

EFSA should have requested that the applicant submit data from trials conducted under a broad range of defined environmental stress conditions, with the highest dosage of the complementary herbicides that can be tolerated by the plants, including repeated spraying and the application of each of the relevant herbicides alone and in combination. The material derived from those plants should have been assessed by using 'Omics' techniques to investigate changes in the gene activity of the transgene and in the natural genome of the plants.

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

Implementing Regulation 503/2013 requests:

"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."

"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. The choice of non-genetically modified reference varieties shall be appropriate for the chosen sites and shall be justified explicitly."

The data presented by Monsanto do not meet the requirements of Implementing Regulation 503/2013: (1) the field trials were not conducted in all relevant regions where the GE maize will be cultivated, and no extreme weather conditions were taken into account (such as drought); (2) the field trials did not take all relevant agricultural management practices into account; (3) not all relevant genetic backgrounds were taken into account.

Data on environmental factors and stress conditions - and their impact on plant composition and phenotype

Field trials to assess plant composition as well as agronomic and phenotypic characteristics of the GE maize were conducted in the US for one year (composition) and three years (agronomic and phenotypic characteristics) respectively. Testbiotech welcomes this step of multi-annual field trials. However, no extreme weather conditions were reported from the field trials ("No exceptional weather conditions were reported at any of the selected sites..."), so no conclusions can be drawn on how gene expression will be affected by more severe climate stress due to drought, irrigation or high temperatures.

In order to assess changes in gene expression, the plants should have been grown in various environmental conditions and exposed to well-defined environmental stress conditions, including taking into account other maize growing regions than the US.

Nevertheless, EFSA is of the opinion that the design of the field trials is in accordance with the expected agricultural practices. To justify this opinion, EFSA should have provided a much more detailed reasoning. Due to current EFSA practices, it is not possible to access the original data from 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 of GMO regulation are fulfilled. In light of the information available, we assume that the application and the data provided do not sufficiently represent the agricultural practices and bio-regional conditions under which these plants are likely to be grown.

No experiments were requested to show to which extent specific environmental conditions influence plant composition and agronomic characteristics. Hence, no data were made available as requested in Implementing regulation 503/2013 to assess whether the expected environmental conditions under which the plants are likely to be cultivated will influence the expression of the studied endpoints.

Data on herbicide application rates and their impact on plant composition as well as agronomic and phenotypic characteristics

Due to the mode of action of the active ingredients in the complementary herbicides, it is plausible that complementary herbicide applications will cause stress responses in the plants, and thus impact gene expression and plant composition. These effects may vary with the amount of herbicide sprayed onto the crop and the various active ingredients which can be used.

From the information available, it appears that the complementary herbicides were only applied once (post-emergent, during the growth stage of the plants) and not in combination.

“Dicamba-containing herbicide was applied at the V2–V4 growth stage and the glufosinate ammonium-containing herbicide at V4–V7 growth stage.” (EFSA, 2023a)

EFSA is of the opinion that the design of the field trials is in accordance with the expected agricultural practices. To justify this opinion, EFSA should have provided a much more detailed reasoning. Due to current EFSA practices, it is not possible to access the original data from the companies within the period of consultation. Therefore, the opinion has to provide all necessary data to allow other experts to conclude on whether the provisions of GMO regulation are fulfilled. In light of the information available, we assume that the application and the data provided do not sufficiently represent agricultural practices, such as higher dosages and repeated spraying.

EFSA should have requested the applicant to submit data from field trials on all the relevant active ingredients used in agricultural practice, including all dosages and combinations of the complementary herbicides which might be used in agricultural practice in GE maize producing countries. Without these data, no reliable conclusions can be drawn as requested in Implementing Regulation 503/2013 (in particular for herbicide tolerant GE plants) to assess whether anticipated agricultural practices influence the expression of the studied endpoints (see also Miyazaki et al., 2019).

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 the impact of the herbicide applications on gene expression, plant composition or the biological characteristics of the plants as requested in EU Regulation 503/2013.

Agronomic and phenotypic characteristics

According to EFSA, statistical analysis of the 3-year data was applied to 11 endpoints:

• For maize MON 87419 (not treated with the intended herbicides), a statistically significant difference compared with the conventional counterpart was identified for the endpoint final stand count, which fell under equivalence category I.

• For maize MON 87419 (treated with the intended herbicides), a statistically significant difference compared with the conventional counterpart was identified for the endpoint plant height, which fell under equivalence category I.

Unfortunately, no information regarding herbicide dosages is given. Comments from member states experts (EFSA, 2023b) however indicate that no high-dosages were used.

It is known that the genomic background of the varieties can influence both the expression of the inserted genes and plant metabolism. However, it appears that the data on gene expression were confined to a single variety. Therefore, EFSA should also have requested additional data from transgenic maize varieties that are, for example, cultivated in South America.

EFSA did not take these issues into consideration. 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, therefore, insufficient to conclude on the impact of the genetic backgrounds on gene expression, as requested in EU Regulation 503/2013.

Data from compositional analysis show the need for further investigations

Data for the compositional analysis were taken from field trials conducted in the US for one year. 78 constituents were subjected to statistical analysis (9 in forage and 69 in grain).

• For maize MON 87419 not treated with the intended herbicides, statistically significant differences with the conventional counterpart were identified for 18 endpoints (16 in grain and 2 in forage). All these endpoints fell under equivalence category I or II except for protein levels in grain, which fell under equivalence category III.

• For maize MON 87419 treated with the intended herbicides, statistically significant differences with the conventional counterpart were identified for 18 endpoints (15 in grain and 3 in forage). All these endpoints fell under equivalence category I or II except for arginine expressed as % AA in grain, which fell under equivalence category IV.

Given the above reasoning on the impact of environmental factors, the herbicide applications and genetic backgrounds, as well as a number of significant findings, EFSA should have requested more data: data on agronomic and phenotypic endpoints should be generated from a wider range of clearly defined stress factors, including all relevant agricultural practices and genetic backgrounds.

Findings by Christ et al. (2017) showing that the PAT/BAR enzyme may also acetylate endogenous amino acids should have been another starting point for further investigations.

A more detailed analysis would have been necessary to investigate changes in plant composition and phenotype, and also to investigate potential unintended changes in metabolic pathways and the emergence of unintended biologically active gene products.

The material derived from the plants should have been assessed by using 'Omics' techniques to investigate changes in the gene activity of the transgene and the plant genome, and also to investigate changes in metabolic pathways and the emergence of unintended biologically active gene products (see Benevenuto et al., 2022). Such in-depth investigations should not depend on findings indicating potential adverse effects, they should always be necessary in order to draw sufficiently robust conclusions to inform the next steps in risk assessment.

In addition, in awareness of the absence of any independent data on this maize, we strongly recommend establishing a system with independent controls to repeat the trials and double check the data on plant composition and agronomic characteristics.

Conclusion on the comparative assessment of plant composition as well as on phenotypic and agronomic characteristics

The data provided by the applicant and accepted by EFSA are insufficient to conclude on the impact of environmental factors, herbicide applications and genetic backgrounds on gene expression, plant metabolism, plant composition, or on agronomic and phenotypic characteristics.

To gather reliable data on compositional analysis and agronomic characteristics, the plants should have been subjected to a much broader range of defined environmental conditions and stressors. Furthermore, EFSA should have requested the applicant to submit data from field trials which reflect current agricultural practices, including all relevant complementary herbicides and all relevant genetic backgrounds.

However, only samples from field sites located in the US were used to generate the data, and the impact of environmental factors and agricultural practices were not assessed in detail. Herbicide applications in the field trials did not represent all the relevant agricultural practices. Only one transgenic variety was grown in the field trials.

Consequently, the data presented by the applicant and accepted by EFSA are insufficient to conclude on the impact of environmental factors, herbicide applications or different genetic backgrounds on plant composition and agronomic characteristics.

Based on the available data, no final conclusions can be drawn on the safety of the plants. Therefore, the data neither fulfill the requirements of Implementing Regulation 503/2013 nor Regulation 1829/2003. This is also underlined by several statements made by experts from Member States (EFSA, 2023b).

In summary, the GE maize plants tested in the field trials do not sufficiently represent the products intended for import.

4. Toxicity

Implementing Regulation 503/2013 requests:

"Toxicological assessment shall be performed in order to:

(a) demonstrate that the intended effect(s) of the genetic modification has no adverse effects on human and animal health;

(b) demonstrate that unintended effect(s) of the genetic modification(s) identified or assumed to have occurred based on the preceding comparative molecular, compositional or phenotypic analyses, have no adverse effects on human and animal health;"

"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;"

Findings from the molecular characterisation and comparative approach

As explained above, many significant changes in plant composition were identified. Even if the changes taken as isolated data might not directly raise safety concerns, the overall number of effects should have been considered as a starting point for a much more detailed investigation into their potential health impacts.

However, the data presented by the applicant did not take into account cultivation of the maize under more extreme drought conditions, i. e. neither under realistic agricultural conditions nor considering all relevant countries of cultivation. The range of differences and their significance are likely to be substantially increased in these conditions. Thus, without more data, the true range of unintended effects cannot be determined and safety cannot be demonstrated, as requested by EU regulation.

Findings from a 28-day study

The applicant performed a 28-day toxicity study with rats. However, this study was rejected by EFSA for quality reasons. Instead of providing a proper 28-day study with a DMO MON 87419 protein, the applicant referred to the 28-day study with the DMO MON 87429 protein previously assessed by the GMO Panel. As there are differences in the DMO proteins, they are not equivalent and EFSA should not have accepted the applicants move.

Findings from a 90-day feeding study

Sprague Dawley rats (16 per sex per group; 2 rats per cage) were allocated to three groups using a randomised complete block design with 8 replications per sex. Groups were fed diets containing maize MON 87419 grains from plants treated with the intended herbicides (dicamba and glufosinate) at 33% and 11% of inclusion level (the latter supplemented with 22% of the conventional counterpart) or the conventional counterpart ground grains (meal) at 33% of inclusion level.

According to EFSA (2023a), "no treatment related adverse effects were observed in rats after feeding diets containing maize MON 87419 grains at 33% or 11% for 90 days."

However, experts from Member States voiced several concerns about the study (EFSA, 2023b), related to the results as such as well the applicant's reporting. Regarding the study outcomes, experts commented:

• "The observed differences between control and verum groups in the 90-day-study should be further investigated and interpreted, in particular possible effects on the hormonal system."

• "…. the safety assessment of the DMO protein is not sufficiently documented. With regard to the 90-day subchronic toxicity study, the applicant must specify whether the maize MON87419 used in this study was treated with herbicides to which it is tolerant and provide a power analysis to justify the number of rats used per group and per gender. Finally, the applicant should have outlined in more detail the reasons for its conclusion that the allergenicity of maize MON87419 is likely to be comparable to that of conventional maize. In these circumstances, the Biotechnology Working Group is unable to deliver a conclusion as to the health risks of maize MON87419."

Regarding the reporting, one competent authority wrote:

• "Considering the quality of test procedures, it was rather surprising that the single and the overall conclusions did not meet this standard but dwelled on somewhat stereotypical verbiage such as "there were no statistically significant differences when the control and test groups were compared", and if some differences could not be ignored "the observed differences were not attributed to test diet administration and were considered biological variation." Or, "the observed changes were considered non-adverse and not related to test substance treatment", and, as ultima ratio, "the mean values (for the verum group) were within the historical control ranges." In contrast to that, there were several statistically significant differences or at least trends which should have been commented on ….."

EFSA's response to the concerns remains unsatisfactory. For example, the Agency simply states that: "The GMO Panel was able to conclude that the 90-day feeding study is in line with the requirements of Regulation (EU) No 503/2013 and that no treatment related adverse effects were observed in rats". However, a critical assessment of the experts' questions is missing in most cases.

Effects of residues from spraying with complementary herbicide specific to GE plants and their mixed toxicity

The residues from spraying were considered to be outside the remit of the GMO Panel. However, without detailed assessment of these residues, no conclusion can be drawn on the safety of the imported products: due to specific agricultural management practices in the cultivation of the herbicide-resistant plants, there are, for example, specific patterns of spraying, exposure, occurrence of specific metabolites and emergence of combinatorial effects that require special attention.

EU pesticide regulation and GMO regulation both require a high level of protection for health and the environment. Thus, in regard to herbicide-resistant plants, specific assessment of residues from spraying with complementary herbicides must be considered a prerequisite for granting authorisation.

EU legal provisions, such as Regulation 1829/2003 (and Implementing Regulation 503/2013), state that "any risks which they present for human and animal health and, as the case may be, for the environment" have to be avoided. Therefore, potential adverse effects resulting from combinatorial exposure of various potential stressors need to be tested for mixed toxicity (EFSA, 2019b).

Glufosinate has been shown to impact or disturb the microbiome (Dong et al., 2020), which can have a substantial impact on the long-term toxicity (mixed toxicity) of whole food and

feed derived from the maize. In addition, glufosinate is classified as showing reproductive toxicity (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN) and there are indications of additive or synergistic effects of the residues from spraying (Reuter, 2015).

In general, the microbiome can be seen as a common network of life, encompassing and closely interacting with plants, animals and humans. Microbial networks are thought to have co-evolved with their hosts and have developed a mutualistic relationship that benefits both the host and microorganisms. They act at the interphase and communicate between the organisms and their wider environment while at the same time being part of an organism's closer environment. Microbiomes are considered to be vital for the health of higher organisms, i. e. humans, animals and plants.

Therefore, potential adverse effects resulting from exposure to whole food and feed need to be tested for mixed toxicity (EFSA, 2019). This should also be considered in regard to changes in the intestinal microbiome. For example, Liao et al. (2021) describe effects of dicamba on soil organisms, causing a prevalence of antibiotic resistance genes (ARGs) and mobile genetic elements (MGEs) in soil microbiomes. Similar or different effects may also be relevant for the intestinal microbiome at the stage of consumption and should, therefore, be taken into account for dicamba- resistant GE plants. The described effects are not considered under pesticide regulation, they have to be assessed within GMO risk assessment. The reason: these effects are highly dependent on the specific dosages applied onto the GE plants as well as on their metabolism and the resulting pattern of exposure in food and feed. In addition, cumulative effects (mixtures of GE plants in one diet) may play a decisive role. Under Directive 2001/18/EC, such effects could be considered to be indirect effects which may be immediate, delayed or cumulative. Implementing Regulation 503/2013 (point 1.4.2) requires "testing of new constituents other than proteins". In our opinion, this requirement also includes the assessment of residues from the complementary herbicides, which necessarily become constituents of all genetically engineered plants resistant to them.

In regard to food and feed safety, EFSA (2020) considers microbiomes to be highly relevant to the health status of their hosts. Therefore, it is desirable to understand the importance of their role in risk assessment. EFSA expects that gut microbiome research (not only in the case of GE plants) will play a relevant role in regulatory science with potential implications for future risk assessments and predictive risk models. As EFSA states: "considering that the gut microbiome is a biological component directly and indirectly involved in the metabolism of food/feed components and chemicals and in the protection of the host against adverse environmental exposure, it would be useful to establish criteria on how to evaluate the potential adverse impacts of perturbators on this defensive barrier, and consequently, on human/animal health."

A 2019 study commissioned by EFSA on adjuvanticity / immunogenicity assessment of proteins included the role of the microbiome. Parenti et al. (2019) state that "one of the most important drivers of immune response is the gut microbiota and other microbial constituent of the human body which are able to regulate host-pathogen balance and to produce systemic pro-inflammatory stimuli. The lifelong antigenic load represented by foods and bacteria/bacterial products leads to a profound remodeling of the gut microbiota and these changes are emerging as a driving force of the functional homeostasis of the immune system. As a matter of fact, a perturbation of the gut microbiota homeostasis due to irregular

lifestyles, stress and age may lead to gut microbiota dysbiosis. This condition may predispose the host to metabolic disorders and inflammation."

These findings are highly relevant to the risk assessment of the GE maize, which inherits combinations of herbicide resistance to dicamba and glufosinate. These residues may cause gut microbiome perturbation, depending on exposure and combinatorial effects. It has to be considered a plausible hypothesis that the effects on the microbiome can trigger effects on the immune system, food uptake and body weight. This hypothesis and mixed toxicity need to be tested before any conclusion can be drawn on the health safety of food and feed. Since no such data can be derived from pesticide risk assessment, experimental data on mixed toxicity of the maize have to be requested from the applicant.

In general, antibiotic effects and other adverse health effects might occur from exposure to a diet containing these plants that were not assessed under pesticide regulation. These adverse effects on health might be triggered by the residues from spraying with the complementary herbicide. Further attention should be paid to the specific toxicity of the metabolites of the pesticide active ingredients.

However, no attempts have been made to integrate the microbiome into the risk assessment of food and feed derived from the GE maize. This is in direct contradiction to Regulation 1829/2003 which requests "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." (Recital 9).

EU legal provisions such as Regulation 1829/2003 (as well as Implementing Regulation 503/2013) state that "any risks which they present for human and animal health and, as the case may be, for the environment" have to be avoided.

As a result, the toxicological assessment carried out by EFSA is not acceptable.

Allergenicity

The assessment of allergenic risks was based on outdated EFSA guidance This contradicts Regulation 1829/2003 which requests that the highest and most recent standards have to be applied.

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 can be found in the EU on a regular basis as has been reported by Palaudelmàs et al. (2009) in Spain or by Pascher (2016) in Austria.

Furthermore, the EFSA (2022a) opinion is wrong for several reasons:

• Without more data on the teosinte species growing in the EU, the likelihood of gene flow from the maize to teosinte cannot be assessed (Trtikova et al., 2017). The same is true for gene flow from teosinte to genetically engineered plants.

• Furthermore, the characteristics of potential hybrids and next generations have to be investigated and cannot be predicted simply from the data from the original event. It is well known that there can be next generation effects as well as interference from the genetic background, which cannot 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 as well as vice versa.

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

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

Consequently, environmental risk assessment carried out by EFSA is not acceptable.

6. Others

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.

In addition, the example of maize 87419 highlights some general problems. These are:

(1) Due to current EFSA practices it is not possible to access the original data from 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 of GMO regulation (esp. 503/2013) are fulfilled. 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 puts 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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