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Testbiotech comment on EFSA Scientific Opinion 2011 on the application for placing on the market the genetically modified herbicide tolerant maize GA21 from Syngenta Seeds, for food and feed uses, import, processing and cultivation under Regulation (EC) No 1829/2003

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Molecular data

Multiple copies of the transgene can be found in the plants: four intact and two truncated fragments of the introduced cassette were counted. Six putative open reading frames were identified that can give rise to unintended gene products in the plants.

There is a lack of metabolomic data as well as data showing to which extent the gene activity of plant genes is affected by the introduction of the gene constructs and potential unintended gene products.

These data would be highly relevant, since there are, for example, significant findings indicating that these plants cannot be regarded as substantially equivalent because of an altered content of carotinoids. Carotenoids serve as precursors of physiologically important compounds called apocarotenoids, synthesized through oxidative cleavage. These compounds are involved in phytohormone metabolism, plant communication and other vital plant functions (for an overview see, for example, Ilg et al., 2010). Since the agronomical data also show significant differences in yield, growth and plant height, it seems likely that plant metabolism is unintentionally altered and that changes in the content of phytohormones could be a plausible cause.

Therefore, further molecular and metabolic data should be required.

Comparative assessment

The comparative assessment is flawed due to biased interpretation of the existing data. There were significant differences in plant components (such as carotinoids and others) that indicate unintended and unexpected changes in plant metabolism and plant composition in comparison to the isogenic lines. Given these findings, a detailed study of changes in gene activity and plant metabolism should be performed under various and defined environmental stress factors to examine the genetic stability of the plants, and to investigate to which extent unintended compounds can emerge in the plant tissue. This is also relevant for the expression data of the newly introduced gene constructs.

The EFSA opinion stating that the changes in plant composition are within the range of historical data is not sufficient indication of crop safety (Hilbeck et al 2011). Instead, in order to avoid major uncertainties, there must be more investigation into *why* there are significant differences in plant composition in comparison to the isogenic lines. Only after further detailed examination can these

data be interpreted regarding potential risks.

Toxicology
The 90 days feeding study was based on a small number of animals. There were many significant findings which should have been investigated further. No investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals. There have been no feeding studies over the whole lifetime of the animals, and none including following generations. No endocrinological studies were performed to investigate potential impacts on the reproductive system. No specific testing was performed to find out if these plants can trigger immune reactions. There was no assessment of the combinatorial effects with other genetically engineered plants used in food and feed.

A basic prerequisite for risk assessment in this context are reliable data on residue loads from spraying with glyphosate formulations. The amount of these residues depends on the specific agronomic management used in the cultivation of the herbicide resistant plants. However, reliable data covering the actual range of residue load in the plants are not available (Kleter et al., 2011, EFSA 2011b, Then 2011).

Further, new data indicate that the toxicity of glyphosate and its additives have to be carefully reassessed: Several experts are warning of a higher than expected toxicity (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009;). In this context, the additive POEA also has to be taken into account, as it is even more toxic than glyphosate in these plants. In 2011, German authorities prohibited the usage of certain glyphosate formulations with a high content of POEA for the production of animal feed in order to avoid a risk of toxins being passed through the food chain. In conclusion, the necessary interplay between pesticide regulation and toxicology assessment of these genetically engineered plants has not been established.

Allergenicity
There are several proteins in maize that can cause allergic reactions. The newly introduced gene construct might, for example, enhance an immune response to endogenous plant protein(s).Targeted studies on potential impact on the immune system are necessary to exclude risks for animals, farmers and consumers.

Nutritional
The outcome of the study as presented by industry showed significant differences that should have been explored further.

Others
No plan for surveillance as required by European regulation was made available to allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.

The complementary herbicides used in this case must be regarded as part of the overall product quality. The residues do not occur just occasionally or from time to time. On the contrary, they have to be regarded as inherited technical qualities of these crops that lead to permanent exposure of the food and feed chain. Therefore, risk assessment of these genetically engineered plants cannot just set this specific issue aside. Further, also the monitoring of health and environmental effects has to include the risks associated with the spraying of glyphosate formulations and their residues in the

plants.

Environmental risk assessment
The conclusion of EFSA that maize GA21 has "*no altered agronomic and phenotypic characteristics, except for the herbicide tolerance*", is not sufficiently based on scientific findings, thus more investigations concerning environmental risks are required. Unintended changes in plants components such as changes in the endogenous pathway of carotinoid metabolism can lead to a wide range of unexpected ecological behaviour under specific environmental conditions. EFSA did not consider these scenarios.

EFSA admits that adverse environmental effects can be caused by application of glyphosate: *"These potential adverse environmental effects comprise (1) a reduction in farmland biodiversity, (2) changes in botanical diversity due to weed shifts, with the selection of weed communities mostly composed of tolerant species, and (3) the selection of glyphosate resistant weeds. The potential harmful effects could occur at the level of arable weeds, farmland biodiversity, food webs and the ecological functions they provide."*

However, EFSA does not place sufficient emphasis on the effects on soil microbial communities. While their risk assessment of NK603 for cultivation (EFSA 2009), which is also tolerant to glyphosate, EFSA concludes, that *"potential adverse environmental effects comprise (...) effects on soil microbial communities"*, the same conclusion is not drawn for GA21. EFSA (2011a) states: "*The EFSA GMO Panel considers that the use of glyphosate-based herbicides at recommended field application rates of glyphosate on maize GA21 is unlikely to cause adverse effects to soil microbial communities or beneficial functions mediated by them.*"

Taking into account a broad range of publications showing effects on soil organisms, this EFSA opinion on GA21 is not conclusive.

Taking into account the observations on large-scale cultivation of herbicide tolerant crops in countries such as Argentina and USA, the cultivation of these crops cannot be regarded as sustainable. The expectation that the negative impact of large scale cultivation can be reduced by risk mitigation measures is a matter of theoretical expectation rather than one of practical experience.

Cultivation of these herbicide resistant plants poses risks to biodiversity, plant health, soil fertility and enables the emergence of herbicide resistant weeds (see also Benbrook, 2009). The massive usage of glyphosate in herbicide resistant crops endangers the health of rural communities, aquatic systems as well as impacting biodiversity and soil fertility (see also PAN AP, 2009). Contrary to EFSA´s opinion, there is substantial indication that plant diseases, e.g. increased infestation with fungal diseases (Johal & Huber, 2009), are caused by the large-scale cultivation of glyphosate tolerant crops. The negative impact on plant growth and plant health can even be transmitted to other plants cultivated in the same field in the following year (Bott et al., 2011, Bott et al., 2007).

The risk manager should give a clear signal that agriculture in the EU is giving sufficient weight to sustainability in agricultural production and, therefore, the cultivation of herbicide-tolerant crops such as GA21 should not be regarded as an option.

Conclusion and recommendations
The opinion of EFSA should be rejected.

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