

**Testbiotech comment on the assessment of genetically engineered soybean A2704-12 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-009) from company Bayer**

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**Introduction**

Soybean A2704-12 was first authorised for import into the EU 10 years ago. The EFSA GMO panel recently re-assessed this genetically engineered soybean that is resistant to glufosinate for renewal of authorisation (EFSA 2019a). Regrettably, the EFSA re-assessment completely ignores the fact that there has been a considerable increase in the number of problems with herbicide-resistant weeds in the past ten years and that, therefore, the agronomic conditions under which herbicide resistant soybeans are cultivated have also changed. This has inevitably led to higher amounts of pesticides being sprayed onto the crops; and new data are required before any decision on the safety of the GE soybean can be made.

**1. Molecular characterisation**

EFSA should have requested data that took the increasing problems with herbicide-resistant weeds in fields where the soybean is grown into consideration; these weeds very often show multiple resistances that can lead to crops being treated with higher amounts of glufosinate and other pesticide applications. In fact, the USDA data base shows that there has been a strong increase in overall pesticide applications in soybean cultivation within last ten years, with substantial dosages of glufosinate being applied ([https://www.nass.usda.gov/Quick\\_Stats/Lite/result.php?84BEAC98-E84C-3AC0-9EAE-E6885717C3F2](https://www.nass.usda.gov/Quick_Stats/Lite/result.php?84BEAC98-E84C-3AC0-9EAE-E6885717C3F2)). According to USDA, the average applications of glufosinate (a.i.) were 0,66 kg/ (a.i.) ha in 2017, with an application rate of 1,3. Bayer in its own recommendations suggests up to 1,6 kg (a.i.)/ha per season. This is in line with Monsanto, in its patent application WO2008051633, recommends that up to 1,6 kg (a.i.) / ha of glufosinate is used on the soybean crops. It has to be assumed that similar dosages are also applied in regions with high weed pressure. Higher numbers of pesticide applications will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genomic activities in the plants due to interaction with the additionally inserted gene constructs.

This aspect, which is the most relevant in regard to the re-assessment of this event, was completely ignored in the EFSA risk assessment. EFSA should have requested that Bayer submit data from field trials with the highest dosage of the complementary herbicides that can be tolerated by the plants, including repeated spraying. The material derived from those plants should also have been assessed by using omics techniques to investigate changes in the gene activity of the transgene, as well as the natural genome of the plants.

Further, in the original application, several open reading frames were identified, but not assessed in regard to all relevant biological active compounds such as miRNA. Therefore, EFSA should have requested more detailed analysis of the relevant gene products.

## **2. Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)**

In the past ten years, agricultural practice in the cultivation of herbicide-resistant soybeans has changed considerably; there has also been a substantial increase in the number of regions where these soybeans are grown and, therefore, new field trials should have been requested from the applicant for all relevant regions. It has to be assumed that the plants will be exposed to higher dosages and sprayed more frequently with the complementary herbicide in comparison to agronomic practice 10 years ago. A higher number of applications will not only lead to a higher burden of residues in the harvest, but may also influence plant composition and agronomic characteristics. The USDA data base shows a strong increase in overall pesticide applications in soybean cultivation within last ten years, with substantial dosages of glufosinate being applied ([www.nass.usda.gov/Quick\\_Stats/Lite/result.php?84BEAC98-E84C-3AC0-9EAE-E6885717C3F2](http://www.nass.usda.gov/Quick_Stats/Lite/result.php?84BEAC98-E84C-3AC0-9EAE-E6885717C3F2)). According to USDA, the average applications of glufosinate (a.i.) were 0,66 kg/ (a.i.) ha in 2017, with an application rate of 1,3. Bayer in its own recommendations suggests up to 1,6 kg (a.i.)/ha. This in line with Monsanto, in its patent application WO2008051633 recommends up to 1,6 kg (a.i.) / ha of glufosinate to be sprayed in the soybean cultivation. It has to be assumed that similar dosages are also applied in regions with high weed pressure. A higher number of pesticide applications will not only lead to a higher burden of residues in the harvest, but may also influence plant composition and agronomic performance due to the additionally inserted gene constructs.

This aspect, which is the most relevant in regard to this specific event, was completely ignored in the risk assessment. Both the practical conditions in large scale cultivation in specific regions and increasing weed occurrence were left aside.

EFSA should have requested that Bayer submit data from field trials with the highest dosage of the complementary herbicides that can be tolerated by the plants, also including repeated spraying. The material derived from those plants should have been assessed by using omics techniques to investigate changes in plant composition and agronomic characteristics.

Further, data representing more regions and more extreme environmental conditions, such as those caused by climate change, would have been necessary.

New field trials should have also been requested because the EU has introduced new standards for conducting trials and assessment of the data. (see Regulation 503/2013).

## **3. Toxicology**

Both the EU pesticide regulation and the GMO regulation 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 to be a prerequisite for granting authorisation. There is very little data available on which degradation products in which concentrations can to be expected from the application of glufosinate on herbicide-resistant soybeans. Since glufosinate is classified as showing reproductive toxicity (<http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN>) EFSA should have requested data on the levels of residues from spraying within last ten years. Even if this is not within the remit of the GMO panel, the risk assessor and the risk manager have to make sure that these data are provided before any decision is made on the renewal of the authorisation.

Further, while the GMO panel considers the assessment of the toxicity of the residues from spraying to be outside its remit, it is nevertheless the duty of the GMO panel to consider and assess the specific metabolism in the plants, and the specific metabolites that might occur in the plants after application of the complementary herbicides. These residues might show a specific pattern or accumulation that only occurs in this specific event. The pesticide panel can only assess the toxicity

of these metabolites, if the GMO panel request specific data on metabolism and metabolites, also considering the various formulas, mixtures and combination of the complementary herbicides. So even if it is the case that the pesticide panel only needs to assess the toxicity of these metabolites, it is the duty of the GMO panel to request these specific data that are needed to conclude on the safety of the plants. Therefore, EFSA should request the notifier to present data regarding the residue levels of glufosinate and its respective metabolites (such as NAG) in the soybean A2704-12.

According to JMPR (Joint Meeting on Pesticide Residues administered by FAO and WHO) data, field trials in the US with glufosinate-resistant soybeans led to residue levels close to the currently applied MRL of 2 mg/kg (JMPR, 2012). This shows that careful monitoring of the residues in the imported soybeans is urgently needed.

In addition, as mentioned, a higher number of applications of the complementary herbicide 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 is due to interaction with the additionally inserted gene constructs. These changes can have a serious impact on health since soybeans are known to produce many bioactive compounds, such as allergens and estrogens.

There are further relevant issues: for example, the potential impact on the intestinal microbiome also needs to be considered. Such effects might be caused by the residues from spraying with glufosinate because glufosinate interferes with bacterial growth and in certain circumstances acts as an antimicrobial agent; this can lead to shifts in bacterial community structures (Ahmad and Malloch 1995; Hsiao et al. 2007; Pampulha et al. 2007; Kopcáková et al. 2015; see also EFSA, 2019 b). 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. Further, Bremmer and Leist (1997) examined the possible conversion of NAG to glufosinate in rats. Up to 10% deacetylation occurred at a low dose of 3 mg/kg bw as shown by the occurrence of glufosinate in the faeces. The authors concluded that most of the conversion was caused by bacteria in the colon and rectum, although toxicity findings indicate partial bioavailability (Bremmer & Leist, 1997).

Despite all these open questions regarding potential impacts on health, we are not aware of a single sub-chronic or chronic feeding study carried out with whole food and feed derived from the soybeans.

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

#### **4. Allergenicity**

No data were presented to show that plant composition is unchanged in regard to allergenic potential.

As mentioned, a higher number of applications of the complementary herbicide 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. These changes can have serious impacts on health since soybeans are known to produce many allergens.

Consequently, the assessment in regard to allergenicity cannot be regarded as conclusive.

#### **5. Others**

According to Regulation (EU) No 503/2013, 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 soybean imported into the EU,
- ii) the ports and silos where shipments of the GE soybean were unloaded,
- iii) the processing plants where the GE soybean was transferred to,
- iv) the amount of the GE soybean used on farms for feed, and
- v) transport routes of the GE soybean.

Environmental monitoring should be run in regions where viable kernels of the GE soybean are transported, stored, packaged, processed or used for food/feed. In case of losses and spread of the GE soybean, all receiving environments need to be monitored.

Furthermore, environmental exposure through organic waste material, by-products, sewage or faeces containing the GE soybean during or after the production process, and during or after human or animal consumption should be part of the monitoring procedure.

## **6. Conclusions and recommendations**

The EFSA risk assessment cannot be accepted.

## **References**

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