TESTBIOTECH Background 09 - 11 - 2013

Testbiotech comment on the Scientific Opinion on application EFSA-GMO-NL-2011-93 for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto

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Introduction
Soybean MON 87708 made by Monsanto is genetically engineered to be resistant to the herbicide dicamba. The application for placing MON 87708 on the market is directly related to food and feed, import and processing. The degradation of dicamba leaves residues such as 3,6-dichlorosalicylic acid (DCSA) and formaldehyde in the plants.

1. Molecular characterisation
The molecular characterisation should take the emergence of new double stranded RNA that might be transmitted as a biologically active substance at the consumption level into account.

A request should be made for data on the impactof the newly introduced DNA, its gene products and the new metabolic pathway in the plants own gene regulation.

2. Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)
The outcome of the comparative analysis shows that several of the endpoints measured were significantly and consistently different. Differences were observed, for example, in the levels of carbohydrates, protein, arginine, aspartic acid, glutamic acid, histidine, phenylalanine, proline, palmitic acid, oleic acid, eicosenoic acid and behenic acid. EFSA, however, simply assumes that these differences are not relevant for the food safety of soybean MON87708.

The EU comparative analysis should be regarded as nothing more than a starting point to define further steps in risk assessment. Significant observable differences must be investigated further to find the reason why they are happening, and their impact on relevant plant characteristics. Observable differences in plant components can indicate other changes affecting the level of anti-nutritional, hormonal or immunologically active substances in the plant. It is possible that any such relevant changes in plant characteristics may only be observed under specific environmental conditions. The dossier forwarded to the authorities, however, only contains data from US fields (none from South America) and only for one year (2009). Thus, prior to drawing any conclusions on safety, the observed differences should have triggered a request from EFSA for more studies, for example, under defined environmental stress conditions.

Toxicology
The outcome of the 90 days feeding study showed several changes in two of the four groups fed with genetically engineered plants. More detailed and long-term investigation of the health impact of the MON87708 soybeans should have been requested.

Allergenicity
The digestion test as performed with the newly introduced enzymes does not allow any conclusions on the fate of the protein under realistic conditions in the gut of humans or animals.

The number of blood samples from individuals used for testing is very low. No analysis of risks for individuals with an impaired immune system such as elderly or infants was undertaken.

Others
If MON87708 is authorised, the pattern of exposure to dicamba (and its residues) in the food chain will be changed. Further interactions between the residues from spraying with the plants metabolism and components will become an issue that cannot be left aside in risk assessment of these soybeans.

In parallel to the GMO panel, the pesticide panel of EFSA published a *Reasoned opinion on the modification of the MRL for dicamba in genetically modified soybean* (EFSA Journal 2013;11(10):3440). Taken together the two EFSA opinions show substantial gaps in the overall risk assessment of this product:

- Due to the inserted DMO proteins, the herbicide dicamba is metabolised to 3,6-dichlorosalicylic acid (DCSA) and formaldehyde. The formaldehyde component was not part of the EFSA risk assessment. According to the IARC, formaldehyde I a human carcinogen (IARC 2012[1]), and therefore the additional exposure through residues must be addressed.

- The way how ADI and MRL were established is confusing and shows too many untertainties: The metabolism pattern of the active substance in genetically modified plants was shown to be different and the available data did not allow EFSA to conclude whether dicamba and DCSA act through the same toxicological mode of action. Another metabolite, DCGA, was identified but there was insufficient toxicological data to set a specific ADI. The acceptable daily intake (ADI) proposed for the metabolite DCSA is much lower than the one proposed for dicamba. However the proposed maximum residue level (MRL) for DCSA is higher (0,4 mg/kg in soybean) than for dicamba (0,05 mg/kg in soybean). This seems to be a contradiction. In any case, the load of residues from spraying with dicamba will be increased significantly within the food chain, if MON87708 comes on to the market.

- There was no assessment of interaction between plant components such as immunological or anti-nutritional, hormonal or immunologically active substances with the residues form spraying.

Several other genetically engineered plants with tolerance to various herbicides have pending market authorisations for the EU, making a systematic approach necessary to deal with new patterns of exposure, interactions between the substances and the accumulated impact on human and animal health. Risk assessment of MON87708 should take into account potential interactions and accumulated effects between the residues from spraying with dicamba and residues from spraying

[1] http://monographs.iarc.fr/ENG/Monographs/vol100F/mono100F-29.pdf

with other herbicides. Furthermore, the residues left in other genetically engineered plants from spraying with herbicides and potential interactions and accumulated effects should be taken into account as these plants can be mixed with MON87708 in food and feed.

4. Conclusions and recommendations

Risk assessment by EFSA is failing to deal properly with findings from the comparative analysis. The assessment of toxicological, hormonal and immunological effects is inadequate. Further, risk assessment does not take the many safety issues regarding the usage of the complementary herbicide into account. In conclusion, there are too many uncertainties remaining and the application should be rejected.

A systematic approach has to be developed to deal with interactions and accumulated effects from the usage of these plants in food and feed before any decision is taken on genetically engineered plants that are resistant to herbicides,.

Monitoring

Monitoring taking residues from spraying with herbicides into account must be undertaken at the consumption stage. If authorised, soybean MON 87708 will mainly be used in feed products so the national veterinary networks and services should be involved in the monitoring of effects on animal health.