GMWatch response to consultation on applications for nine genetically modified organisms for food and feed uses (FSA, 30 Nov 2021–25 Jan 2022)

January 2022

General points

GMWatch opposes the applications for the nine GMO maize products/events for food and feed uses. It notes that all the risk assessments are based on those of EFSA, which are inadequate to establish safety. On the basis of the information provided and omitted by the GMO developers, these applications should be refused.

Contrary to current law (EU 2001/18), no post-market monitoring programmes are described in the applications to detect adverse effects on health and the environment.

In addition, technology has moved on in recent years and there are now analytical methods (-omics: specifically, transcriptomics, metabolomics and proteomics) that could easily be used to identify unintended changes in the gene activity, metabolism, and protein profile of these GMOs. Such unintended changes, in single-event GMOs compared with the parent lines, and in stacked events compared with single events, have been identified in –omics studies on GMOs[1] [2] [3] and could lead to unexpected toxicity and/or allergenicity.

One study found that stacking herbicide and insecticide transgenes in a stacked trait variety induces synergistic effects in the protein profile of the stacked trait GM plant. Also, metabolic pathways that might affect the safety of this stacked GM maize event were changed in the stacked trait crop when compared to the single-trait parent crops.[4]

---

[1] Mesnage R et al (2016). An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process. Sci Reports 6: 37855. http://www.nature.com/srep/2016/161219/srep37855/full/srep37855.html

[2] Agapito-Tenfen SZ et al (2013). Comparative proteomic analysis of genetically modified maize grown under different agroecosystems conditions in Brazil. Proteome Science 11(1):46. http://www.proteomesci.com/content/11/1/46/abstract

[3] Agapito-Tenfen SZ et al (2014). Effect of stacking insecticidal cry and herbicide tolerance epsps transgenes on transgenic maize proteome. BMC Plant Biology 14(1):346. http://www.biomedcentral.com/1471-2229/14/346/abstract

[4] Agapito-Tenfen SZ et al (2014). Effect of stacking insecticidal cry and herbicide tolerance epsps transgenes on transgenic maize proteome. BMC Plant Biology 14(1):346. http://www.biomedcentral.com/1471-2229/14/346/abstract

Another study criticized EFSA's dismissal of evidence of the combinatorial effects of stacked-trait GM plants. The data showed how two Cry toxins acted in combination (added toxicity) and that the same Cry toxins showed combinatorial effects on the model organism Daphnia magna when the organisms were exposed to both Cry toxins together with Roundup. However, EFSA dismissed these peer-reviewed results.[5]

For all the stacked events, data must be required on the combinatorial effects of the multiple GM traits in the stack – for example, Bt toxin and herbicide-tolerance traits. GM herbicide-tolerant plants as grown by farmers contain residues of herbicides. As recommended by the RAGES research project, the interactions of these residues with Bt toxins, as well as of combinations of Bt toxins, must be assessed for potential impacts on the health of consumers and the environment, as required by Regulation 1829/2003, which demands that "any risks which they present for human and animal health and, as the case may be, for the environment" must be subjected to "a scientific evaluation of the highest possible standard".[6]

The FSA should require that the developer carry out investigations on combinatorial effects and submit the data as part of the application. These data must then be carefully evaluated by the FSA.

Annex B: RP476 – MIR604 maize (renewal)

1. Do you have any concerns on the safety of the products/events which have not been considered below with respect to the intended consumers, stakeholders or impacts?

Yes. Testbiotech has published a detailed and fully referenced critique on these and other flaws in the application,[7] which neither EFSA nor the FSA have addressed. We support Testbiotech's critique and request the FSA to satisfactorily address all the points made in it before approval is given to this GMO event.

In addition, MIR604 is a stacked event expressing the cry3A gene and the phosphomannose isomerase (PMI) gene from the bacterium E. coli.

---

[5] Bohn T (2018). Criticism of EFSA's scientific opinion on combinatorial effects of 'stacked' GM plants. Food and Chemical Toxicology 111(2018):268-274. https://www.sciencedirect.com/science/article/abs/pii/S0278691517306907?via%3Dihub

[6] Then C et al (2020). Assessment of health risks associated with the consumption of products derived from genetically engineered plants with a combination of traits.

[7] Testbiotech (2019). Background 8-12-2019. Testbiotech comment on EFSA's assessment of genetically engineered maize MIR604 for renewal authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-013) from Syngenta. https://www.testbiotech.org/node/2456

Implementing Regulation 503/2003, which is still in force in the UK, states that stacked events can only be assessed and authorised if the parental plants were previously assessed and authorised. However, there seem to be no data on the parental plants with regard to PMI and mCry3A in isolation.

The FSA should address research showing that Bt toxins have several modes of action, which are not well understood, are not specific only to the targeted insect pest(s),[8] and have altered and enhanced toxicity compared with naturally occurring Bt toxins.[9]

A subchronic feeding study in rats performed with MIR604 for the original risk assessment showed significant differences in the GM-fed animals, as mentioned in the comments from Member States: “Noticeable is the partly significant lower food consumption of the male rats in both GMO maize-fed-groups during the whole test, which leads to a significant lower increase in body weights in the group of 10% GMO maize-fed male rats. Together with other results, especially the significant changes in the haemogram of male rats in the group which was fed with 10% GMO maize thus can give a hint to possible adverse effects of MIR604 maize on the health of the test animals. As a consequence a subsequent feeding study should be requested to address the above uncertainties. The study should cover a longer exposure preferably over two generations to test for chronic effects.”[10]

However, EFSA failed to request further studies and instead dismissed the findings as “not toxicologically relevant” on spurious grounds, including discounting statistically significant differences compared with the concurrent control group in favour of invoking comparisons with unvalidated “historical control data”, which is bad scientific practice. As Keenan et al (2009) pointed out, “The concurrent control group is the most relevant comparator for determining treatment-related effects in a study."[11] The FSA should re-evaluate the rat feeding study using sound scientific practice.

The Bt proteins tested and assessed in the original risk assessment are not expressed in the GM Bt plants in question and thus have a different structure and

---

[8] Hilbeck A, Otto M (2015). Specificity and combinatorial effects of Bacillus thuringiensis cry toxins in the context of GMO environmental risk assessment. Front Environ Sci 3: 71. doi: 10.3389/fenvs.2015.00071

[9] Latham JR et al (2019). The distinct properties of natural and GM cry insecticidal proteins. Biotechnology and Genetic Engineering Reviews 33(1):62-96. https://doi.org/10.1080/02648725.2017.1357295

[10] The Member State comments appear to have been removed from the EFSA website but are quoted in: Testbiotech (2019). Background 8-12-2019. Testbiotech comment on EFSA’s assessment of genetically engineered maize MIR604 for renewal authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-013) from Syngenta. https://www.testbiotech.org/node/2456

[11] Keenan C et al (2009). Best practices for use of historical control data of proliferative rodent lesions. Toxicologic Pathology. May 19. https://journals.sagepub.com/doi/full/10.1177/0192623309336154

biological activity. Data should be provided on the Bt proteins as expressed in the GM plants.