

Comments from The Norwegian Scientific Committee for Food Safety (VKM) GMO Panel on the application for maize MON 87427 x MON 89034 x MIR162 x NK603 (EFSA-GMO-NL-2016-131)

Comparative assessments

- A) The applicant should explain in detail why the processing steps involving low temperatures, such as production of high-protein maize gluten meal, does not increase the relative concentration of the transgenic proteins rather than reduce the concentrations. This may be of particular importance for the stacked event since a higher pre-processing concentration of transgenic proteins is expected than for the single events. Knowledge of protein concentrations is of importance when considering possible effects of combinations of transgenic proteins.
- B) The VKM GMO Panel does not find that the following claim made by the applicant is substantiated:

"CP4 EPSPS, Cry1A.105, Cry2Ab2, Vip3Aa20 and PMI proteins have no synergistic or antagonistic effects to each other. Their modes of action and sites of biological activity are different and there is no known or conceivable mechanism of interaction between CP4 EPSPS, Cry1.A105, Cry2Ab2, Vip3Aa20 and PMI which could lead to adverse health effects in animals or humans."

This statement should be justified by evidence-based data or followed up by appropriate studies in accordance with the EFSA guidelines (2011). The applicant has not provided data that exclude possible combined effects of the newly expressed proteins in the stacked event. Different modes of action do not necessarily prevent interaction.

Food and feed safety assessment

Most immunologic adjuvant experiments on Cry –proteins have been performed on Cry1Ac, and some of these studies have indicated adjuvant properties (VKM, 2012). To our knowledge the Vip3Aa20, Cry1A.105 and Cry2Ab2 proteins have not been studied experimentally for potential adjuvant properties. Although these proteins do not show sequence resemblance to known adjuvants like cholera toxin and *E. coli* heat-labile enterotoxin (as referred to by the applicant in Brunner *et al.*, 2010 and Reed *et al.*, 2008), The VKM GMO Panel therefore highlight the need for further clarification on the potential role of these proteins as adjuvants as part of the risk assessment. This may be of particular

importance for high-protein fractions, e.g. maize gluten meal, produced under low temperatures, since levels of the transgenic proteins could be up-concentrated in these fractions.

The VKM GMO Panel considers that the referred experimental data from the single events alone do not sufficiently answer uncertainties related to the combined exposure of the transgenic proteins, e.g. from protein isolates from the stacked event, and requests that the applicant provide experimental data to exclude adjuvant properties.