

**BILATERAL TECHNICAL MEETING BETWEEN MEMBERS OF THE EFSA PANEL ON GENETICALLY
MODIFIED ORGANISMS AND THE VKM NORWEGIAN DELEGATION**

According to Article 30.2 of the Regulation (EC) No 178/2002

ADJUVANTICITY OF CRY PROTEINS

Agreed meeting report of the meeting of 13 January 2009

The below report does reflect the common understanding of EFSA and the VKM Norwegian delegation of the meeting. This report is not, and cannot be regarded as, representing the position, the views or the policy of the EFSA or of any national or EU Institution, agency or body.

Participants

	Martinus Løvik	Norwegian Institute of Public Health
Norwegian delegation:	Audun Nerland	Faculty of Odontology and Medicine, University of Bergen.
	Arne Mikalsen	VKM Panel on GMO
EFSA GMO Panel:	Anderson Christer, Willem Seinen, Ilona Kryspin Sørensen, Gijs Kleter, Harry Kuiper, Jean-Michel Wal	
EFSA GMO Unit:	Antonio Fernandez Dumont, Ellen van Haver, Elisabeth Waigmann	

The Chair of the EFSA GMO Panel welcomed the Norwegian delegation. The purpose of the meeting was to have an exchange of scientific views on the topic of adjuvanticity of Cry proteins. Notes will be taken by EFSA staff and an EFSA meeting report will be sent to the Norwegian Scientific Committee for Food Safety (VKM).

Arne Mikalsen from the Norwegian delegation presented the organization of the Norwegian Scientific Committee for Food Safety (VKM) and the Norwegian Food Safety Authority (NFSA).

Arne Mikalsen and Audun H. Nerland explained the concerns of the VKM regarding safety issues of Bt proteins and particularly, their potential adjuvant effects. A comprehensive review of the literature was presented, analyzed and discussed including clinical observations in farm workers exposed to spores from *Bacillus thuringiensis*, *in vivo* experiments on animal models as well as *in vitro* studies. The VKM delegates explained that although questions regarding the biological relevance of those observations and their possible impact on the safety of the corresponding GM crops have been posed to the applicants of insect resistant Bt maize, satisfactory responses have not been received. Moreover, the VKM delegates mentioned that comments to EFSA opinions on GM crops

expressing Bt proteins (e.g. Cry1Ac and other similar proteins such as Cry1Ab since they have demonstrated to have amino acid sequence homology and therefore are likely to have similar biological properties) are regularly sent to EFSA. The VKM delegates considered that EFSA responses need further clarifications. In particular, the VKM delegates emphasized their concern on the adjuvant effect of Bt proteins as demonstrated in animal experiments and expressed that it might be based on a similar mechanism as the adjuvant effect of cholera toxin.

During the discussion, the members of the EFSA GMO Panel confirmed that they are aware of the literature cited and of the issues raised by the Norwegian Competent Authority. The EFSA GMO Panel considers that this issue does not represent a safety concern for consumers of Bt maize derived foods. With regards to clinical observations on farm workers, the GMO Panel noted that it was an occupational exposure to raw material, i.e. spores of *Bacillus Thurengiensis* and not to the purified newly expressed Cry proteins as expressed in Bt maize. They also noted that the observation of binding of Cry proteins to mammalian epithelial intestinal cells was shown to be not specific and did not induce damage. It was agreed that an adjuvant effect of Cry proteins has indeed been demonstrated in animals; however, the studies were performed using relatively high doses and routes of administration that are different from those occurring during intake of Bt maize by human consumers. Moreover, the adjuvant effect of Cry1Ac enhanced the immune response to co-administered proteins but was not shown to induce an allergic reaction or an IgE response. A recent publication by Guimaraes *et al.* (2008)¹ was presented in which it is shown that the mechanisms involved in the adjuvanticity of Cry proteins and cholera toxin are different. Therefore, the GMO panel does not consider that there is a safety concern for the health of humans or animals that consume food/feed derived from Bt maize.

As a general consideration, it was expressed that the assessment of allergenicity of GM foods/feeds as currently performed according to Codex Alimentarius and EFSA Guidance Document (EFSA, 2006), is essentially focussed on IgE mediated hypersensitivity, and so far the issue of adjuvanticity is not explicitly addressed. It was mentioned that the EFSA self-tasking working group on the allergenicity assessment of GM foods is however preparing an updated Guidance Document that will take into account the issue of adjuvanticity.

It was also noted that when the recipient of the genetic modification is known to be allergenic, the EFSA GMO Panel does not only assess the allergenicity of the newly expressed proteins, e.g. Cry protein, but also the allergenicity of the whole genetically modified plant by comparison with that of the non-GM comparator.

In conclusion, EFSA thanked all participants for attending the meeting and for the fruitful discussions. It was pointed out that it is important and useful to hold these technical meetings between experts of the EFSA GMO Panel and national experts in order to facilitate scientific exchange and to clarify Member States comments. With regards to the specific issue raised on the assessment of adjuvanticity of newly expressed proteins and the impact on food/feed safety of GM foods, EFSA will take into consideration the comments of the Norwegian Competent Authority in the updated Guidance Document on assessment of allergenicity of GMOs which will be made available for public consultation by the end of 2009.

¹ Guimaraes V.D. , Drumare M.F., Ah-Leung S., Lereclus D., Bernard H., Cre´minon C., Wal J.M. and Adel-Patient K. (2008) Comparative study of the adjuvanticity of *Bacillus thuringiensis* Cry1Ab protein and cholera toxin on allergic sensitisation and elicitation to peanut. *Food and Agricultural Immunology* **19**, 325-337.