Innspill til EFSA GMO Extranet søknad EFSA/GMO/BE/2010/79
11. september 2010

Soya MON 87701.

General comments
There seems to be a misprinting on page 169 in the Technical Dossier where it is stated: "The mean levels of Cry1Ac protein in harvest seed is 4.9%".According to Table 7 and Table 8 the mean Cry1Ac levels are 4.7 µg/g dw and 5.1 µg/g dw, respectively. The mean Cry1Ac level should therefore be 4.9 µg/g dw, not 4.9%, since 4.9% is 49 mg/g dw.

D.07.08
Toxicology
In the acute toxicity studies in mice, the applicant has used a single dose of Cry1Ac-protein, i.e. 1290 mg/kg body weight. According to the OECD guideline 401 "Acute oral toxicity", a limit test at one dose level of at least 2000 mg/kg bodyweight should be carried out. In the OECD guideline 423 it is recommended to use 3 doses.

"Acute oral toxicity" studies (OECD 401 or 423) is not recommended studies for evaluation of NOAEL since these studies are only performed for 14 days and will not be able to show long term effects of the substance. According to toxicological practice NOAEL is the lowest dose where there is no adverse effect, i.e. at least one higher dose has to give an adverse effect. The Norwegian GMO Panel is of the opinion that the applicant should use neither NOAEL nor MOE (margin of exposure) when assessing potential health risk from dietary exposure of Cry1Ac derived from MON 87701.

D 7.09
Allergenicity:

According to the applicant the epitope test shows that Cry1Ac protein does not share structurally and immunologically relevant amino acid sequence similarities with known allergens, and that the Cry-protein has no similarities to IgE epitopes of allergenetic proteins. However, this Cry-protein has immunogenic potential to elicit strong IgG-response (Vazquez et al.1999) and the induction of IgG antibodies to food antigen and even crosspriming against a bystander antigen may be of biological significance (Brandtzaeg, 2010). Experimental studies both *in vitro* and *in vivo* have demonstrated that IgG antibodies that are not balanced by a mucosal IgA response can enhance the epithelial penetration of bystander proteins (Brandzaeg, 2010).

Due to remaining uncertainty that Cry1Ac may enhance systemic and mucosal immune responses to co-administrated antigens, the Norwegian GMO Panel still sees the need for further clarification on the possible role of Cry proteins as adjuvants.

Brandtzaeg, P. (2010) Food allergy: separating the science from the mythology. Nat. Rev. Gastroenterol. Hepatol. 7, 380–400; doi:10.1038/nrgastro.2010.80

Vazquez RI. Moreno-Fierros L. Neri-Bazan L. De La Riva GA. Lopez-Revilla R., 1999. *Bacillus thuringensis* Cry1Ac protoxin is a potent systemic and mucosal adjuvant. Scand J Immunol., 49: 578-84.