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Head of Cabinet to Commissioner Tonio Borg
Joanna Darmanin
Health & Consumers Directorate-General
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Munich, 31 October 2013

Dear Joanna Darmanin

Authorisation of SmartStax – summary of some arguments

We are writing to you today as you might very soon be making a decision on the market authorisation of SmartStax (and Power Core). We would therefore like to summarise why the arguments such as brought forward in your letter of 2 October 2013 (Ref. Ares(2013)3175373 – 02/10/2013) remain unconvincing and why you should not allow SmartStax (and PowerCore) to be marketed in the EU in food and feed:

1. There has been no investigation into the adjuvant (immunogenic) properties of Bt toxins. It is known that Bt toxins can invoke and boost immune reactions (Esquivel-Pérez and Moreno-Fierros, 2005; Moreno-Fierros et al., 2003; Vásquez et al., 1999; Vásquez-Padrón et al., 1999; Vásquez et al., 2000; Verdin-Terán al. 2009). Signs of immune reactions have been found in several feeding studies (Sagstad et al., 2007, Frøystad-Saugen, 2008, Walsh et al., 2011, Finamore et al., 2008, Kroghsbo et al., 2008, Adel-Patient et al., 2011). These effects are likely to be dependent on the dosage of Bt toxins. SmartStax has a much higher concentration of Bt toxins than other plants such as the parental plants which were tested in feeding studies. Further, the concentration of Bt toxins in the plants varies substantially (see Then, 2011). It is evident, that Bt toxins can survive digestion to a much higher degree than has been assumed so far (Chowdhury et al., 2003; Walsh et al. 2011). Consequently, there is substantiated concern that the plants can have adverse effects on health.
2. The exact mode of action of Bt toxins is decisive for the assessment of health risks (as well as for environmental risks).

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There are several contradictions and differences in the theories explaining the mode of action of Bt toxins (see for example Pigeott & Ellar, 2007) but EFSA has never looked into these differences or the impact they may have. Faced with all these uncertainties, it appears that an adverse impact of Bt toxins in mammals cannot be excluded. There are several publications showing effects in mammalian cells or showing that such effects are likely to happen (Thomas and Ellar, 1983; Shimada et al., 2003; Huffmann et al. 2004; Ito et al. 2004; Mesnage et al., 2012; Bondzio et al., 2013). Synergies between the Bt toxins might be crucial for potential adverse effects (see Then, 2010). These uncertainties are especially relevant for the risk assessment of synthetic or modified toxins such as those produced by SmartStax. Recently the GRACE project discussed the mode of action of Bt toxins and identified it as a relevant and controversial issue that needs further investigation (GRACE 2013). Since the exact mode of action is not known, the number of uncertainties is too high to allow the usage of plants that produce up to six Bt toxins in food and feed.

3. There has been no investigation into the possible interaction between the insecticidal toxins and the residues from pesticides. We had an opportunity to see an unpublished paper from the EU Commission (EU Commission, 2013) which discusses potential chemical reactions of residues from spraying with several herbicides. This paper appears to reflect the way the Commission is currently dealing with these questions. However, as far as SmartStax (and PowerCore) are concerned it is not a chemical reaction between the insecticidal proteins and the residues from spraying which is most relevant. It is the impact of cells and organisms being exposed to several stressors in parallel that is of much greater relevance. As, for example, Kramarz (2007) shows this can be relevant for the impact that Bt toxins can have on organisms that are normally not susceptible to Bt toxins. EFSA has never addressed this question surrounding the potential effects on health from SmartStax (and PowerCore).
4. We also have to point out that new questions have arisen on the transfer of biologically active substances from genetically engineered plants to humans. As Zhang et al (2011) found, RNA from food plants can enter the bloodstream after ingestion and interfere with cell regulation in mammals. The amount and quality of artificial RNA in SmartStax has never been determined. A further recent study raises substantial doubts on the suitability of animal feeding trials to assess the transfer of DNA from food plants to humans. Spisak et al. (2013) presented some unexpected findings showing there is some likelihood that functional DNA enters the human bloodstream via ingestion. Their investigation revealed that the

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rate of transfer was dependent on the state of health of the individual. We are not aware of any study that has investigated the risk of DNA from genetically engineered plants entering the bloodstream in humans. Since there seems to be no reliable knowledge of the transfer rate of artificial DNA from genetically engineered plants to the human bloodstream, there needs to be some investigation carried out in this respect before any new authorisations can be issued.

5. On studying the dossiers provided by industry on the risk assessment of SmartStax and its parental plants, we were concerned to find two worrying patterns in the quality of the data provided and its assessment by EFSA: (i) In several studies, industry does not comply with basic scientific standards such as the good laboratory practice. (ii) EFSA accepted dossiers that do not comply with the standards set by its own Guidance. This problem concerns field trials in particular. We have not yet finalised our analysis, but we believe these deficiencies in complying with the relevant standards are likely to be a violation of the EU Food & Feed regulation (Regulation 1829/2003) and can be regarded as a legal barrier to the authorisation of SmartStax.

There are some further issues that should be discussed and investigated, before a decision is made on SmartStax (and PowerCore). For example, without a system to track them it is not possible to monitor effects on health from these products once they are on the market. It is a false interpretation of the facts if the EU Commission pretends that there will be practical methods of detecting these plants in food and feed. To the best of our knowledge identifying and differentiating these plants from their parental plants or from their sub-combinations is not possible without concerted scientific effort. This is not a suitable method under practical conditions.

To conclude we strongly recommend rejecting the market applications for SmartStax and PowerCore, and not opening the market for products where there can be no certainty that they will not impact on health.

With kind regards

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