Vår ref:2015/H_121
Deres ref: 2015/1816

Miljødirektoratet
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Dato: 31.03.15

Vedlagt er innspill fra GenØk – Senter for Biosikkerhet på høringen av søknad **EFSA/GMO/NL/2014/121** fra Monsanto Company som gjelder mat, fòr, import og prosessering av genmodifisert soya **MON 87751**.

Vennligst ta kontakt hvis det er noen spørsmål.

Med vennlig hilsen,

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Assessment of the summary of the technical dossier submitted under EFSA/GMO/NL/2014/121 for approval of MON 87751 soy

Sent to

Norwegian Environment Agency

by

GenØk- Centre for Biosafety
April 2015

ASSESSMENT OF THE SUMMARY OF THE TECHNICAL DOSSIER RELATED TO EFSA/GMO/NL/2014/121 FOR APPROVAL OF MON 87751 SOY

As a designated National Competence Center for Biosafety, our mission at GenØk in advice giving is to provide independent, holistic and useful analysis of technical and scientific information/reasoning in order to assist authorities in the safety evaluation of biotechnologies proposed for use in the public sphere.

The following information is respectfully submitted for consideration in the evaluation of product safety and corresponding impact assessment of event **MON 87751 soy**, setting out the risk of adverse effects on the environment and health, including other consequences of proposed release under the pertinent Norwegian regulations.

Recommendation

From our analysis, we find that the deficiencies in the summary of the dossier do not support claims of safe use, social utility and contribution to sustainable development of MON 87751 soy**. Critically, the Applicant has not included any of the required information to assess social utility and sustainability as required in Appendix 4 of the Norwegian Gene Technology Act, which would be necessary for consideration of approval in Norway.** A new application or reapplication should only be reconsidered with the delivery of the information requests recommended here, including any additional information deemed significant by the Norwegian authorities.

Therefore, in our assessment of **MON 87751 soy**, we conclude that based on the available data, the Applicant has not provided the required information under Norwegian law to warrant approval in Norway at this time.

ASSESSMENT OF THE SUMMARY OF THE TECHNICAL DOSSIER RELATED TO EFSA/GMO/NL/2014/121

About the event

MON87751 soy was developed through *Agrobacterium*-mediated transformation of two T-DNAs: One to confer insect tolerance through the expression of *Bt* insecticidal proteins *Cry1A.105* and *Cry2Ab2*. Cry1A.105 consists of elements from Cry1Ab, Cry1F and Cry1Ac. The proteins provide protection from feeding damage caused by certain lepidopteran pests.
The second T-DNA containing, *splA* and *aad* expression cassettes, used for early event selection.

This application is for food, feed, processing and import. This application has not been authorized in a third country yet, however regulatory submissions have been made in the US, in Canada and Argentina and will be made to countries that import significant quantities of soybean or food and feed products.

MON87751 has been field tested in the US and Argentina since 2010, in Chile in 2012 and Brazil 2013

Assessment findings

Safety of Cry genes

MON 87751 soy combines different classes of Bt proteins named Cry toxins. These toxins are claimed and believed to be safe, however lately the potential of non-target effects of Bt toxins concerning mode of action have been addressed (Gilliand et al 2002, Crickmore 2005, Hilbeck and Schmidt 2006, Mesange et al, 2012).

In relation to non-target and environmental effects, in two meta-analyses of published studies on non-target effects of Bt-proteins in insects, (Lövei and Arpaia 2005) documented that 30% of studies on predators and 57% of studies on parasitoids display negative effects to Cry1Ab transgenic insecticidal proteins. A review by (Hilbeck and Schmidt 2006) on all Bt-plants found 50% of studies documenting negative effects on tested invertebrates.

Additionally, a recent review by van Frankenhuyzen (2013) indicated that several Cry proteins exhibit activity outside of their target orders. This study also found that many Cry proteins had only been tested with a very limited number of organisms: thus, activity outside of the target organisms of many Cry proteins may be undocumented simply because testing has not included sensitive organisms up to now (van Frankenhuyzen, 2013). Allowing for the fact that for practical reasons, not every potentially sensitive species can be tested for sensitivity to Bt toxins, it still cannot be excluded that sensitive species have been overlooked in testing until now. The issue is complicated further by the number of variables which can affect toxicity testing, which may include toxin preparation and purification, life stage of the specimens, differences in toxin expression hosts, as well as solubilization (or lack thereof) of the toxin, among other factors (van Frankenhuyzen 2009).

Another quantitative review by (Marvier et al 2007) suggested a reduction in non-target biodiversity in some classes of invertebrates for GM (Bt) cotton fields vs. non-pesticide controls, yet found little reductions in biodiversity in others. More recent research on aquatic environments has sparked intense interest in the impact of Bt-crops on aquatic invertebrates *Daphnia magna* (Bøhn et al 2008), and caddisflies (Rosi-Marshall et al 2007). These publications warrant future study, given the potential load of novel target proteins (in combination with herbicides) that may end up in agricultural runoff and end up in aquatic environments. Further, (Douville et al. 2007) present evidence of the persistence of the *cry1Ab* transgene in aquatic environments: more than 21 days in surface water and 40 days in sediment. A follow-up on this study in 2009 indicated possible horizontal gene transfer of transgenic DNA fragments to aquatic bacteria (Douville et al 2009).

Impacts on soil microflora and fauna, including earthworms (Zwahlen et al. 2003), mychorizzal fungi (Castaldini et al. 2005) and microarthropods in response to Cry endotoxins have also been reported (Wandeler et al 2002, Griffiths et al 2006, Cortet et al 2007). The significance of tri-trophic effects of accumulation, particularly of insecticidal Cry toxins (Harwood et al. 2006, Obrist et al. 2006) is, however, yet to be firmly established. It has been demonstrated that sub-chronic dosages of Cry proteins may affect both foraging behavior and learning ability in non-target bees (Ramirez-Romero et al 2008), and may have indirect effects on recipient populations, and, given the key-stone role of bees as pollinators, on both primary production and on entire food-webs.

The use of multiple, related transgenes in a single (stacked) event may accelerate resistance development to both transgene products. This was the experience of Zhao et al (2005), who tested the effect of using broccoli plants containing Cry1Ac, Cry1C or both, on resistance development in a population of diamondback moths (*Plutella xylostella*). They found that the stacked use of similar Cry proteins in close proximity to single gene events led to accelerated resistance development to both traits (Zhao et al 2005). Bravo and Soberón (2008) commented on this effect, acknowledging that gene stacking is not a universal solution to resistance development to Cry proteins. Studies such as these beg the question as to whether the stacked use of related Cry proteins, such as Cry1Ab and eCry3.1Ab, in the same event is advisable.

In relation to health impacts, a publication by (Dona and Arvanitoyannis 2009) reviews the potential health implications of GM foods for humans and animals, including incidences and effects of increased immunogenicity, amounts of anti-nutrients, possible pleiotropic and epigenetic effects, including possible reproductive and developmental toxicity. They conclude that while there is strong evidence for health concerns on many fronts, exposure duration many have not been long enough to uncover important effects. Studies should also include subjects with immunodeficiency or exposed to other stress agents.

Indications of harm to non-target organisms in the environment, and possible impacts to human and animal health prompted the Austrian Authorities to invoke a safeguard clause to ban the use of Cry1Ab-containing maize even MON810 (Umweltbundesamt, 2007). We refer to this report as a detailed analysis of potential adverse effects from a Cry1Ab-producing GMO.

Recommendation:

- The regulator is encouraged to ask the applicant address the potential of non-target effects of Bt toxins, especially in the context of their combined use in a stacked event.
- The regulator is encouraged to ask the Applicant to consider the possibility of cross resistance development to multiple Cry proteins due to the use of stacked events.

Social utility and sustainability aspects

In addition to the EU regulatory framework for GMO assessment, an impact assessment in Norway follows the Norwegian Gene Technology Act (NGTA). In accordance with the aim of the Norwegian Gene Technology Act, production and use of the GMO shall take place in an ethically and socially justifiable way, under the principle of sustainable development. This is further elaborated in section 10 of the Act (approval), where it is stated that: "*significant emphasis shall also be placed on whether the deliberate release represent a benefit to the community and a contribution to sustainable development"*. These issues are further detailed in the regulation on consequence assessment section 17 and its annex 4.

The NGTA, with its clauses on societal utility and sustainable development, comes into play with a view also to health, environmental and socio-economic effects in other countries, such as where GMOs are grown. The application does only concern import, food and feed use and processing of **MON 87751 soy**. Hence, it is not intended for cultivation in Europe or Norway.

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