



GenØk - Centre for Biosafety

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**Assessment of the technical dossier submitted under
EFSA/GMO/NL/2011/97 for approval of transgenic cotton, T304-
40 from Bayer CropScience AG**

Submitted to

Direktoratet for Naturforvaltning

by

**Centre for Biosafety – GenØk
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SUMMARY OF THE ASSESSMENT OF THE TECHNICAL DOSSIER RELATED TO EFSA/GMO/NL/2011/97

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 T304-40, setting out the risk of adverse effects on the environment and health, including other consequences of proposed release under the pertinent Norwegian regulations.

This submission is structured to address specific provisions for an impact assessment required under the Norwegian Gene Technology Act of April 1993, focusing on the requirements in Appendix 2 - Principles for environmental risk assessment pursuant to sections 13-16 of the regulations, and Appendix 4 - Evaluation of ethical considerations, sustainability and benefit to society, cf section 17 of the “Regulations relating to impact assessment pursuant to the Gene Technology Act” of December 2005, pursuant to section 11 cf section 8. The information presented here may be applicable to more than one provision in different appendices.

We have targeted our critique to address the information needs under the relevant provisions that relate to our particular area of competence in biotechnology assessment as comprehensively as possible. Lack of commentary on our part towards any information under consideration should not be interpreted as specific endorsement of that information.

This submission was built in large part using the **Biosafety Assessment Tool** (<https://bat.genok.org/bat/>) produced by the University of Canterbury and GenØk – Centre for Biosafety. This is a free-to-the-public resource for hazard identification and risk assessment of genetically modified organisms.

All page numbers following quoted text that is not directly referenced refers to the technical dossier “Insect resistant and glufosinate tolerant cotton event T304-40 for food and feed uses, and for import and processing in accordance with articles 5 and 17 of Regulation 1829/2003 GM Food and GM Feed”, submitted by the Applicant.

Lastly, Codex Alimentarius guidelines allow Norway to ask for specific data of the type we identify and recommend obtaining. Norway therefore may request such information without concern of a challenge from the World Trade Organisation.

Specific recommendations

Based on our findings, we propose a few specific recommendations, summarized here and detailed in the critique below.

The Direktoratet for naturforvaltning is encouraged to request the following:

1. The regulator is encouraged to conduct a review of the environmental and health-related adverse effects to determine whether CryIAb meets satisfactory criteria for safety within the Norwegian regulatory context.
2. The Applicant should submit required information on the social utility of T304-40 and its contribution to sustainable development, in accordance with the Norwegian Gene Technology Act.

Overall recommendation

Based on our assessment, we find that the deficiencies in the dossier do not support claims of safe use, social utility and contribution to sustainable development of T304-40. **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.** Hence at minimum, the dossier is deficient in information required under Norwegian law. 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 T304-40, we conclude that based on the available data, including the safety data supplied by the Applicant, the Applicant has not substantiated claims of safety satisfactorily or provide the required information under Norwegian law to warrant approval in Norway at this time.

ASSESSMENT OF THE TECHNICAL DOSSIER RELATED TO EFSA/GMO/NL/2011/97

About the event

The transgenic T304-40, developed by Bayer CropScience AG, was developed via *Agrobacterium*-mediated transformation to confer insect tolerance through the expression of the Cry1Ab lepidopteran insecticidal toxin derived from the soil bacterium, *Bacillus thuringiensis subsp. berliner* (B.t. berliner). T304-40 also contains the bar coding sequence encoding the specific enzyme phosphinothricin acetyl-transferase (PAT), that acetylates the herbicide glufosinate ammonium and thereby detoxifies the herbicide.

Assessment findings

1. Analysis of the safety of the Cry1Ab protein for the environment and human health

The applicant states that “*Bacillus thuringiensis* (B.t.) insecticidal crystal proteins are ubiquitous in nature and almost a century of studies dedicated by many expert groups to these insecticidal proteins has brought a detailed understanding of their structure and function. B.t. strains are generally classified as non-pathogenic bacteria in several national classifications for micro-organisms.” (p.9). Yet the Applicant fail to address the relevant literature on the environmental and health implications of the Cry I class of proteins, and Cry1Ab in particular.

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.

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 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 transgenic insecticidal protein Cry1Ab in aquatic environments and suggest that that sustained release of this potentially bioactive compound from Bt maize production could result in negative impact on aquatic biodiversity. 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.

In relation to health impacts, a recent 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.

<p>Recommendation: The regulator is encouraged to conduct a review of the potential environmental and health-related adverse effects to determine whether CryIAb meets satisfactory risk assessment criteria within the Norwegian regulatory context.</p>
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2. 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. 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 Applicant has not provided relevant information that allows an evaluation of the issues laid down in the aim of the Act, regarding ethical values, social justification of the GMO within a sustainable development. Given this lack of necessary information for such an evaluation, the Applicant has not demonstrated a benefit to the community and a contribution to sustainable development from the use of T304-40. The Applicant should thereby provide the necessary data in order to conduct a thorough assessment on these issues, or the application should be refused.

It is also important to evaluate whether alternative options, (e.g. the parental non-GM version of T304-40) has achieved the same outcomes in a safer and ethically justified way.

Further, the Norwegian Gene Technology Act, with its clauses on societal utility and sustainable development, comes into play with a view also to health and environmental effects in other countries, such as where GMOs are grown. For instance, it is difficult to extrapolate on hazards or risks taken from data generated under different ecological, biological, and genetic contexts as regional growing environments, scales of farm fields, crop management practices, genetic background, interactions between cultivated crops, and surrounding biodiversity are all likely to affect the outcomes. Hence it cannot be expected that the same effects will apply between different environments and across continents.

Recommendation: The Applicant should submit required information on the social utility of T304-40 and its contribution to sustainable development, in accordance with the Norwegian Gene Technology Act.

3. Ethical considerations in the use of the herbicide glufosinate as a co-product with T304-40 cotton

The intended co-product with this event is the herbicide glufosinate ammonium. Glufosinat ammonium is not legal for use in Norway and in EU (except a limited use on apples) due to both acute and chronic effects on mammals including humans. Glufosinat ammonium is harmful by inhalation, swallowing and by skin contact. Serious health risks may result from exposure over time. Effects on humans and mammals include potential damage to brain, reproduction including effects on embryos, and negative effects on biodiversity in environments where glufosinat ammonium is used (Hung 2007; Matsumura et al. 2001; Schulte-Hermann et al. 2006; Watanabe and Sano 1998). According to EFSA, the use of glufosinate ammonium will lead to exposures that exceed acceptable exposure levels during application.

The evaluation of co-products, that is, secondary products that are specifically designed and intended for use in conjunction with the GMO, is considered important in the risk assessment of a GMO (Dolezel et al, 2009). Therefore, considerations of the co-products also warrant an evaluation of safe use, particularly when there is precedence in policy concerning its used independently.

While it is understood that the Applicant has not applied for deliberate release of T304-40 in Norway, the acceptance of a product in which the intended use includes the use of a product banned in Norway would violate basic ethical and social utility criteria, as laid out in the Act. That is, we find that it would be ethically incongruous to support a double standard of safety for Norway on one hand, and safety for countries from which Norway may import its food on the other. This line of reasoning is consistent with the provisions under the Act to assess ethical, social utility and sustainable development criteria not only for Norway, but also for countries from which Norway imports food.

Therefore, we find it difficult to arrive at justified use of these events without engaging in such an ethical double standard. Specifically, this issue is relevant particularly in revised regulations of 2005 Section 17 “Other consequences of the production and use of genetically modified organisms” points 2 and 3 “ethical considerations that may arise in connection with the use of the genetically modified organism(s), and “any favourable or unfavourable social consequences that may arise from the use of the genetically modified organism(s)”, respectively.

T304-40 as a stand-alone product may prove to be perfectly as safe as its conventional counterpart, yet with consideration of co-product usage this cannot be concluded on the basis of the information presented in this application.

Conclusion

Available information for risk assessment evaluation

This evaluation is based on the Applicant’s own submitted information, along with our own expertise in related fields. The relevant scientific literature is very limited in some cases, yet we have tried to extract information from the peer-reviewed literature that may inform the scientific validity of the information under consideration. In situations where lack of knowledge, complexity and uncertainty are high, particularly in relation to unknown adverse effects that may arise as a result of approval for release of a living modified organism into the environment or food supply, the available information may not be sufficient to warrant approval. Further information may address some of these issues, however an accurate description of uncertainties provided by the applicant would provide a more useful basis for assessing the level of risk that may come with regulatory approval of the LMO, taken on a case-by-case basis.

In all cases, product-related safety testing should have an independent and unbiased character. This goes both for the production of data for risk assessment, and for the evaluation of the data.

The lack of compelling or complete scientific information to support the claims of the Applicant documented here highlights the need for independent evaluation of the dossier as performed here, including the raw data produced by the Applicant. We therefore support better transparency and independent review of information to ensure high standards within the regulatory process. This would include any information provided by the Applicant used to justify confidentiality claims on any scientific data. We encourage the authorities to insist on this level of transparency and accessibility to all scientific data (including raw data) to ensure the scientific validity of the information presented.

Overall recommendation

Above we highlight a number of issues in relation to the questionable safe use of T304-40 that do not justify a conclusion of safe use, social utility and contribution to sustainable

development. 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. Taken together, these deficiencies fail to address the necessary safety regulations under Norwegian Law, and thus the application is incomplete and should not be approved. 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 T304-40 we conclude that based on the available data, including the safety data supplied, the Applicant has not substantiated claims of safety satisfactorily to warrant approval in Norway at this time.

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