GenØk - Centre for Biosafety

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Assessment of the technical dossier submitted under EFSA/GMO/UK/2010/83 for approval of transgenic maize event MIR604 by Syngenta Seeds S.A.S

Submitted to

Direktoratet for Naturforvaltning

by
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Konklusjon på norsk

Basert på våre funn foreslår vi en rekke konkrete anbefalinger som vi adresserer i vårt høringssvar, og som vi har oppsummert her

Direktoratet for Naturforvaltning bes vurdere følgende

1. Direktoratet for Naturforvaltning bør kritisk etterspørre verdien og bruken av ressurser av å vurdere en søknad om godkjenning hvor søker selv sier at de ikke planlegger å markedsføre denne spesifikke GMOen, men faktisk en GMO som bruker dette genet (Cry3A) som en del av en større transgen DNA-sekvens (såkalt "stacked event"). Denne "stacked" GMOen må uansett gjennomgå en full riskovurdering når det søkes om godkjenning av denne.

2. Vi anbefaler DN å følge opp de uløste spørsmålene stilt av medlemslandene i vurderingen av EFSA-GMO-UK-2005-11. Søker må fremskaffe en mer detaljert overvåkningsplan i henhold til Annex VII, Direktiv 2001/18/EC.

3. Søker må fremskaffe den nødvendige informasjon om samfunnsnytten av MR604 samt bidraget til bærekraftig utvikling (inklusive data om sprøtemiddelbruk og utbredelsen av skadedyrinsekter som er i målgruppen for denne GMOen).

Hovedkonklusjon og anbefalinger

Vi har i vår gjennomgang funnet flere svakheter av begrepsmessig art, mangel på informasjon, feilaktige konklusjoner og mangelfulle empiriske data som hver for seg og til sammen ikke støtter søkers påstand om sikker bruk av MIR604 mais. Søker har ikke fremskaffet noe av den informasjonen som er nødvendig for å kunne vurdere samfunnsnytte og bærekraftighet, noe som er påkrevd i den norske genteknologiloven for godkjenning i Norge. Disse manglene gjør at vi mener at denne søknaden er ufullstendig i sin nåværende form. Vi anbefaler derfor å avslå søknaden samt at en ny søknad bare bør vurderes om søker har adressert de mangler vi har belyst.

Summary of the assessment of the technical dossier related to EFSA/GMO/UK/2010/83

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 MIR604, 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 focused 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 not directly referenced refer to the document Part 1 of the technical dossier "Application for authorization of Event MIR604 maize cultivation in the European Union under Regulation (EC) No 1829/2003 " submitted by the Applicant.

Key findings

After a detailed analysis of many of the portions of the dossier on MIR604 submitted by the Applicant, we outline a number of informational, methodological and conceptual weaknesses that do not justify the Applicant conclusion of safety, based on the given data. Our input focuses on a critique of the Applicant's dossier and covers three broad issues:

1. Faulty assumptions, reasoning, or interpretations by the applicant

2. Missing, incomplete or inadequate information to support scientifically sound claims of safety

3. Missing information in relation to requirements under the Norwegian Gene Technology Act

Within we suggest appropriate action to address the specific deficiencies where possible, and conclude our assessment with a summary recommendation.

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

Recommendations

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

The Direktoratet for naturforvaltning is encouraged to request:

1. The Directorate for Nature Management should question the value and use of resources in evaluating an application for approval where the Applicant states it does not intend to actually market this event, but rather a similar event with which the target gene is included as part of a "stacked" event.

2. The Norwegian Authorities are encouraged to follow up with the outstanding issues raised by member countries in the evaluation of EFSA-GMO-UK-2005-11. Specifically, the Applicant should submit a more detailed plan for post-release monitoring compliant with Annex VII of Directive 2001/18/EC.

3. The Applicant should submit required information on the social utility of MIR604 and its contribution to sustainable development (including data on pesticide usage and potential benefits of the transgenic trait based on target pest distributions in Norway), in accordance with the Norwegian Gene Technology Act.

Overall recommendation

The informational, empirical and deductive deficiencies identified in the dossier do not support claims of safe use, social utility and contribution to sustainable development of MIR604. **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 MIR604, 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/2011/83

About the intended event to be produced and cultivated

The Applicant states that:

"Please note that for Syngenta, the intended product for commercial cultivation in the EU is the Bt11xMIR604xGA21 maize stack. MIR604 approval is needed in order to allow the production of Bt11xMIR604xGA21 maize seed in Europe. The other elements of this stack: Bt11 and GA21 maize have already been submitted and are in different stages of the EU approval process." (p. 7)

About the event

MIR604 maize is genetically engineered to expresses a modified Cry3A (mCry3A) protein for the intended purpose to control the coleopteran pest *Diabrotica virgifera virgifera (Western corn rootworm),* and a phosphomannose isomerase (MIR604 PMI) protein, a selectable marker allowing the transformants to utilize mannose as a primary carbon source.

Scope of the application

As Syngenta Seeds S.A.S. is applying in this case only for approval for cultivation, we will focus our assessment on the informational needs to satisfy such authorizations in Norway.

Assessment

After a detailed analysis of many of the portions of the dossier on MIR604 submitted by the Applicant, we outline a number of informational, methodological and conceptual weaknesses that do not justify the Applicant conclusion of safety, based on the given data.

1. Faulty assumptions, reasoning, or interpretations by the applicant

1.1 Approval for MIR604 sought when intended event for production and cultivation is Bt11xMIR604xGA21

As previously stated, the Applicant is seeking approval for MIR604 on the assumption that its successful authorization will lead to the acceptance of the same trait, along with others in

combination and also under regulatory consideration independently in the EU, towards the approval of a new "stacked event", in a separate submission, EFSA/GMO/UK/2008/56. The Applicant indicates its intention is not for the commercial use of MIR604, but rather Bt11xMIR604xGA21 maize stack. We do not agree with the basic premise that approval of MIR604 is preliminary to the full consideration of Bt11xMIR604xGA21, as both will require a separate event specific assessment in any case. That is, whenever a new event is applied for release, even if it is the product of other events which are also under application for approval, a full risk appraisal of the intended "stacked" event should be conducted, as differences is genetic background ecological context etc, may influence or limit the value of indirect comparative assessments.

Therefore, if the Applicant has no intent to market MIR604, the assessment here is likely not to produce any value above what would be required for Bt11xMIR604xGA21. Hence the economy of this exercise, in terms of time and financial resources, in our mind, should be seriously questioned. However, we will base our information solely on the event in question, MIR604 rather than the intended event for environmental release Bt11xMIR604xGA21.

Recommendation: The Directorate for Nature Management should question the value an use of resources in evaluating an application for approval where the Applicant states it does not intend to market this event, but rather an event with the target gene as part of a "stacked" event, given the necessity of a full risk appraisal of the intended "stacked" event.

2. Missing, incomplete or inadequate information to support scientifically sound claims of safety

As the event MIR604 is currently being evaluated for food, feed and processing in the EU under Application EFSA-GMO-UK-2005-11, and given that the Applicant relies heavily on the information submitted in this application, we wish to direct attention to the critiques submitted by Member States concerning the informational deficiencies and critiques in EFSA-GMO-UK-2005-11, and includes input from Norway (report available through EFSAs limited-access database).

In summary, a number of member countries found reason to comment on deficiencies in the application, specifically related to the molecular characterization, use of "surrogate" proteins in the experimental studies, the design of the 90 day rat feeding studies, the interpretive inference from the comparative tests, the potential allergenic effects, among others. Based on member state input, we also find reason to question the veracity of the information submitted under Application EFSA-GMO-UK-2005-11, and encourage the competent authorities in Norway to follow up on their previous queries contained therein.

Specifically, based on our reading of the dossier, we could find no documentation of a more elaborated post-release monitoring plan than what was provided in Application EFSA-GMO-UK-2005-11, where cultivation was not applied for. Despite the Applicant claim that

"the presence of MIR604 maize in food and feed will not result in any nutritional changes, therefore post-market monitoring is not considered necessary." (p.66),

we find that the application for cultivation should follow with a more detailed monitoring plan that complies with Annex VII of Directive 2001/18/EC.

Recommendation: The Norwegian Authorities are encouraged to follow up with the outstanding issues raised by member countries in the evaluation of EFSA-GMO-UK-2005-11. Specifically, the Applicant should submit a more detailed plan for post-release monitoring compliant with Annex VII of Directive 2001/18/EC.

3. Missing information in relation to requirements under the Norwegian Gene Technology Act

3.1. 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 (including regions where the GMO is grown). 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 MIR604. The Applicant should thereby provide the necessary data in order to conduct a thorough assessment on these issues, or the application should be considered incomplete.

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.

The Applicant, however, as not included information relevant information on how the event affects agricultural practices, particularly pesticide usage or necessary additional management practices (e.g. resistance management strategies) needed in conjunction with the target transgenic trait, in the countries where it is being grown. The Applicant has stated where the maize is currently permitted for cultivation yet fails to include information related to possible environmental effects and any resistance-development rates expected in the target pest that may occur in these regions, and more information would be required to verify that a reduced usage in pesticide was leading to a environmental benefit when the event in question is cultivated.

Approval of a GMO in Norway is dependent on that the GMO under consideration for approval has been thoroughly tested in the environments in which the GMO can be released (section 15, regulation on Consequence assessment under the Gene Technology Act). In other words, because of the differences in agroecosystems noted above, the MIR604 maize in question has to be thoroughly tested under Norwegian conditions before an application can be approved. The Applicant has not provided such information.

With respect to social utility of the event is highly questionable whether the intended target pest of the insecticidal maize MIR604 is intended to affect, *Diabrotica virgifera virgifera,* represents is a concern for Norwegian agriculture, and hence a benefit (or not) for Norwegian farmers or Norwegian society. The applicant should address the issue of pest distribution in Norwegian Agriculture and analyze the benefit to society coming from MIR604 from its use.

Lastly, it is also important to evaluate whether alternative options exist (e.g. the parental non-GM version of this MIR604) that can achieve the same intended outcome in a safer and more sustainable fashion.

Recommendation: The Applicant should submit required information on the social utility of MIR604 and its contribution to sustainable development (including data on pesticide usage and potential benefits of the transgenic trait based on target pest distributions in Norway), in accordance with the Norwegian Gene Technology Act.

Overall recommendation

Above we highlight a number of conceptual, empirical and informational deficiencies in the dossier that do not justify a conclusion of safe use, social utility and contribution to sustainable development of MIR604. 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 MIR604, 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.