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Risk assessment of NGT plants: Overview of initial findings and recommendations regarding the 'Proposal for a Regulation of the European Parliament and of the Council on plants obtained by certain new genomic techniques and their food and feed'

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Summary

The proposal of the EU Commission should be rejected unless it undergoes major revision and amendments. If the proposal is fundamentally revised and amended, the following points should be implemented:

1. Category 1 of the proposal should be deleted;
2. Category 2 should be amended and applied to all domesticated NGT plants that cannot persist, spread or propagate in the environment;
3. The current GMO regulation should still apply to NGT plants that belong to non-domesticated species or to domesticated species that can persist, spread or propagate in the environment;
4. Make sure that all intended and unintended genetic changes and their potential effects caused by the processes of NGTs, which are unlikely to result from other 'at random' processes, are subjected to molecular risk assessment;
5. Make sure that no unintended insertions of transgenes and their fragments can escape the approval process;
6. Amend the NGT regulation to assess, control and mitigate potential interactions between NGT organisms that share the same environments;
7. Data on the genetic changes introduced into the plants are the main basis for any risk assessment, and the data must be made available to the public and independent experts.

Introduction

This backgrounder has been compiled to provide information on initial findings in regard to the EU Commission proposal for the future EU regulation of NGT plants.[1] Our aim was to identify some of the fundamental elements that need be taken into account in further discussions on the proposal, in particular with regard to risk assessment. This backgrounder is intended to provide supplementary information in addition to our earlier findings on the EU Commission draft proposal for criteria concerning the equivalence of NGT plants to conventional plants (so called Category 1).[2] We recommend that the proposal of the EU Commission is rejected unless it undergoes major revision and amendments.

Why should NGT plants be regulated and subjected to mandatory approval processes?

First of all, let us state that we are not generally opposed to the idea of specific legislation for NGT plants within current GMO regulation. However, from a scientific perspective, we see no possibility of exempting some of these plants from mandatory risk assessment (RA). In short, there are two reasons for this:

(1) NGTs allow new genotypes and traits to be generated in different ways and with different outcomes compared to previously used genetic engineering methods or conventional breeding (including non-targeted mutagenesis). In fact, in most cases, NGTs are used to achieve genomic changes which go beyond what is known from conventional breeding, even without the insertion of additional genes. Detailed analyses and molecular risk assessment are, therefore, in each case, necessary to identify the differences and similarities between NGT plants and conventional breeding first, before any conclusions can be taken.

(2) While it is possible to target a specific site in the genome with gene scissors, it is not possible to sufficiently predict or control the result of these interventions either in the genome, the cells, the plants or the environment. Therefore, RA should not be limited to the intended effects of the final products, but should also include the unintended effects caused by the processes.

Our statements are underpinned by some basic findings on biological mechanisms: In comparison to conventional breeding (including non-targeted mutagenesis) methods, NGTs can overcome the boundaries of natural genome organization and the mechanisms in the cells whose purpose is to maintain gene functions. Relevant factors in this respect include repair mechanisms, gene duplications, genetic linkages and further epigenetic mechanisms. By overcoming these boundaries, NGTs can make the genome much more extensively available for genetic changes. The resulting genotypes (the patterns of genetic changes) can be vastly different compared to those derived from conventional breeding, both in regard to intended and unintended changes.

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1 COM (2023) 411 final 2023/0226 (COD), Proposal for a Regulation of the European Parliament and of the Council on plants obtained by certain new genomic techniques and their food and feed, and amending Regulation (EU) 2017/625, https://food.ec.europa.eu/plants/genetically-modified-organisms/new-techniques-biotechnology_en

2 https://www.testbiotech.org/content/background-eu-commission-draft-proposal-criteria-equivalence-ngt-plants

Why should Category 1 be deleted from the proposed regulation?

While we agree that the overall number of mutations can be lower in NGT plants in comparison to non-targeted mutagenesis, we also emphasize that such comparisons need to be put into context: the technical characteristics of NGTs mean that the specific sites of the mutations, their frequency (in regard to specific sites) and the (intended or unintended) gene combinations resulting from the NGTs may, nevertheless, be highly unlikely to occur with conventional methods.

The analysis of NGT plants (such as camelina with a change in oil composition and tomatoes with enhanced content in GABA[3]) being considered for release and marketing illustrate the premise of our arguments: It is based on pure speculation that the genotypes and phenotypes as those resulting from these NGT applications may also occur in nature or could be derived from conventional breeding. As yet, these traits have never been seen or achieved in conventional breeding, and this is not something that is very likely to happen in near future. Consequently, it is not sufficient to assume that some of these genotypes and phenotypes may theoretically also occur in nature (see Recital 14 of the EC proposal).

If genotypes (including unintended genetic changes) that are unlikely to result from natural processes or traditional breeding techniques are generated, this means that their biological effects (phenotype) may also differ.

However, if applied, the criteria of Category 1 would lead to New GE plants that are substantially different from those achieved with conventional breeding being legally classified as equivalent and could be marketed and released without specific controls.

We deeply regret that the Commission and EFSA were not able to provide reasoned and comprehensive opinions regarding these crucial issues. For example, in regard to unintended genetic changes, EFSA only considered the number and the type (insertion, deletion, etc.) of modifications or mutations, but never delivered criteria comprising the biological effects associated with (small) genetic changes at specific sites.[4] However, despite lacking the necessary scientific justification, it appears that this incomplete EFSA assessment is the basis for Category 1 in Annex I.

How to apply the precautionary principle for NGTs?

Current GMO regulation is also intended to provide the future framework for GMO regulation. The precautionary principle is the fundamental basis of GMO regulation and should, therefore, not be disregarded in this context. The basic principles and elements of RA embedded in current regulation should certainly not be abandoned.

As a general principle, the EU requires each individual genetically engineered organism (‘event’) to undergo risk assessment on a case-by-case basis prior to environmental release or being brought to market. The risk assessment requirements are set out in Annex II of Directive 2001/18/EC which was amended by Commission Directive (EU) 2018/350. It foresees the risk assessment of each event, taking into account its intended and unintended effects, as “intended and unintended changes can have either direct or indirect, and either immediate or delayed effects on human health and on the environment.” (Annex, C1). Therefore, as set out in Annex (C1) of the Commission Directive

[3] See our analysis of the criteria of Category 1 of the EC proposal: https://www.testbiotech.org/content/background-eu-commission-draft-proposal-criteria-equivalence-ngt-plants

[4] https://www.testbiotech.org/en/news/did-eu-commission-interfere-scientific-independence-efsa

(EU) 2018/350 [2], the risk assessment “shall identify the intended and unintended changes resulting from the genetic modification and shall evaluate their potential to cause adverse effects on human health and on the environment.” Furthermore, Annex II of Directive 2001/18/EC in its “Principles for the environmental risk assessment” gives weight to cumulative long-term effects: “A general principle for environmental risk assessment is also that an analysis of the cumulative long-term effects relevant to the release and the placing on the market is to be carried out. ‘Cumulative long-term effects’ refers to the accumulated effects of consents on human health and the environment (…).” Furthermore, similarly to Commission Directive (EU) 2018/350, Commission Implementing Regulation (EU) No 503/2013 also requires the assessment of stacked events in regard to their “potential additive, synergistic or antagonistic effects resulting from the combination of the transformation events.”

Based on the above statements, mandatory risk assessment of intended and unintended genetic changes, including their potential effects, also needs to be a requirement in future NGT regulation. Consequently, this would make it essential to identify any intended and unintended genetic changes which are unlikely to result from conventional breeding (for example, in regard to the site, the frequency and its potential gene products). The methodology should comprise whole genome sequencing (WGS), including long-read sequencing.

If relevant genetic changes are identified, further investigation of their potential effects must be required. The methods applied in this respect should comprise ‘Omics’ (such as transcriptomics and metabolomics) as well as analysis of changes in plant composition and phenotypical characteristics.

Further steps in risk assessment (now Category 2)

We agree that not all applications may require the same amount of data. However, decisions on the amount of data needed can only be made after a full molecular risk assessment (see above).

In this regard, we would be very cautious about the EFSA approach citing ‘flexibility in data requirements for RA’ as referred to in Recital 26 of the EC proposal. This is because EFSA criteria mostly only consider intended effects, whereas unintended effects should also be taken into account if they cannot be excluded for specific events.

We also have concerns about the proposed Article 22 (3). As far as this is concerned, it has to be ensured that potential risk scenarios include all relevant risks, and is not limited to elements that would only allow for incomplete safety checks.

Specific regulations to define further steps in risk assessment in more detail should require the full participation of the EU parliament and member states in the decision-making process. We would, therefore, not support leaving this solely to EFSA and the Commission as proposed in Article 27.

In general, the provisions of existing regulation should be fully applied to NGT plants, but with the possibility of reducing the amount of necessary data if it can be justified in specific cases. However, a decision on the extent to which the amount of data can be reduced, can only be taken after full molecular risk assessment has been carried out.

Therefore, molecular risk assessment should remain mandatory for all NGT plants, as should measures to track, trace and identify these at each stage of potential release and the production process.

Consequently, Category 2 should be amended and applied to all domesticated NGT plants that cannot persist, spread or propagate in the environment. Current GMO regulation has to be applied to all other NGT plants.

Further observations

Below are further observations and reservations in regard to the proposed regulation:

- The crucial verification procedure if a plant belongs to the NGT sector is based on the absence of any transgenic DNA sequences. Therefore, the methodology used for this process has to make sure that no unintended insertions of transgenes and their fragments can escape the approval process.
- If any reference is made to the breeders' gene pool, this reference should apply to a specific date (e.g. prior to the release of the first transgenic plants) to make sure that the gene pool is defined as the gene pool used by conventional breeders, unchanged by introgression of material from genetically engineered plants.
- Since there is no existing experience with genetically engineered non-domesticated plants that can persist and propagate in complex ecosystems, the proposed regulation should be restricted to domesticated plants, leaving all other species within the existing GMO regulation. The same principle has to be applied to domesticated species that can persist, spread or propagate in the environment.
- No specific measures are foreseen to risk assess cumulative effects and interactions with other genetically engineered plants. However, as there may be a scenario in which many NGT organisms with different traits across many species are released into a shared environment at the same time, there will be a need for detailed regulation on how to assess, control and mitigate their potential interactions.
- When deciding on applications, member states and also the public should, as in current practice, be given sufficient time to review, assess and comment.
- Since data on the genetic changes introduced into the plants are the main basis for any risk assessment, the data have to be made available to the public and independent experts.
- The regulatory incentives as proposed in Recital 33-35 and Article 22 and Annex III should be based on a technology assessment (TA) that uses reliable and transparent criteria. It has to be ensured that incentives are not issued on the basis of false expectations and empty promises. We assume that additional regulation regarding TA will be necessary to avoid market distraction.
- The regulation of NGT plants should be seen in combination with developments in patent law. It has to be ensured through the correct interpretation of the existing patent law that conventional plant breeders retain unhampered access to biological diversity, e. g. conventionally-bred varieties, random mutations and naturally occurring gene variants.

Conclusions

To secure livelihood for future generations, we all should agree that the introduction of NGT plants cannot be justified if it could cause:

- ecosystems to collapse,
- health risks to accumulate unnoticed in food,
- breeding to be disrupted by patents,
- the end of choice for consumers.

The EU Commission proposal cannot, therefore, be accepted without major revision.