Federal Agency for Nature Conservation

For a science-based regulation of plants from new genetic techniques

Deregulation of NGT plants contradicts the precautionary principle.

POLICY BRIEF #02/2024

Key Messages

- The precautionary principle enshrined in primary law of the EU must remain central in the regulation on plants obtained by certain new genetic techniques (NGT). The current legislative proposal does not fulfil this requirement.
- It is impossible to exclude potential risks of NGT plants just from the size and number of changes of the DNA sequence. Even small changes by genetic engineering can have a high-risk potential for the environment and health.
- NGT plants can have potential risks comparable to other genetic engineering techniques and can change plants in ways that go beyond conventional breeding.
- Also, a reference to "naturalness" is misleading, as a higher "resemblance with nature" is not *per se* associated with a lower risk.
- Risk assessment of NGT plants must be carried out case-by-case as part of their authorisation process for deliberate release, cultivation and import in the EU.
- Deregulating NGT wild plant species, including trees and algae, along with crop species poses additional unnecessary risks from a nature conservation point of view.
- Currently, only the genetic engineering law can ensure appropriate environmental risk assessment and risk management of, as well as control and testing standards for NGT plants; other EU regulatory regimes such as plant variety law are unsuitable in this regard.
- The European Commission cannot be authorised to amend essential test criteria by means of a delegated act. This decision is reserved for the legislative act.

Keywords: risk assessment; science-based; precautionary principle; NGT plants; GMO regulation; RNA interference;

Introduction

Technological progress makes genetic engineering a rapidly developing field. In its proposal of July 2023, the European Commission (EC) aims to deregulate a subset of new genetic techniques (NGT).[1] This proposal would exempt certain NGT plants from the current EU regulatory framework for genetically modified organisms (GMOs) based on a considered equivalence with conventionally bred plants. The German Federal Agency for Nature Conservation (BfN) and others[2] argues that this approach of considered equivalence lacks a valid scientific basis and violates the precautionary principle, since plausible risks cannot be excluded. If the proposal is adopted, the majority of current NGT plants (both domesticated and wild species) would receive a so-called category 1 (NGT1) status, allowing their use and environmental release without any risk assessment and any risk management measures which are in place for current GMOs.

In the view of BfN, a science-based regulation in line with the existing EU laws must be the prerequisite for a sustainable and safe use of NGTs.

Importantly, the **EC proposal** concerns not just crops, but **all plants including trees and wild plants** although the underlying study provided hardly any data for the application of NGTs to trees or wild plants and virtually none about environmental impacts. This is incomprehensible as it is known that interference with wild plant species can be associated with an increased risk for biodiversity.

This policy brief on the EC proposal for the regulation of NGT plants is written from a **nature conservation perspective** with a focus on **environmental risk assessment**. Other, equally important subjects are mentioned, but not extensively elaborated here.

1 Why all NGT plants need to be risk assessed

1.1 General scientific considerations

A considered equivalence of NGT plants to conventionally bred plants as in the EC proposal is both irrelevant and incorrect from a scientific point of view: NGTs and their prime technique CRISPR/Cas, as other GM techniques, enable genetic modifications that can go beyond what is imaginable in nature or for conventional breeding. After all, this is why NGTs are seen as superior to conventional breeding methods. In the context of **NGTs** any reference to **"naturalness"** is misleading and not a proxy for reduced risk. Relevant from a risk assessment perspective is only whether potential risks can be associated with the introduced genetic modification. Key to regulation is that NGT plants can pose comparable risks as other GM plants.[3]

Genes and resulting proteins are part of interconnected, interdependent, and highly complex networks often fulfilling multiple roles in parallel and determining the actual phenotype of an organism. Therefore, **small changes of genetic information can have major phenotypic consequences, which might translate into a high-risk potential** for the environment and human and animal health. It is thus impossible to make general assumptions about the risk potential of an organism just from the size and the number of introduced genetic modifications. Still, Annex I of the EC proposal builds on proposed equivalence criteria that consider only changes in the genotype for categorising NGT plants. Phenotypic consequences and associated traits, which are pivotal to risk assessment, are not considered here.

The following three examples, which would be categorized as NGT1 according to the EC

[1] Referred to in the proposal as new genomic techniques.

[2] See below, e.g. https://www.anses.fr/fr/system/files/BIOT2023AUTO0189.pdf?download=1

[3] Ruling of the ECJ in case C-528/16.

proposal´s equivalence criteria (Annex I), illustrate the need for a risk assessment:

- Plant genes can be reprogrammed by few small genetic modifications to **produce insecticides based on RNA interference (RNAi)**. The potential risk of such NGT1-RNAi plants for (protected) **non-target organisms** would be comparable to the risk of transgenic RNAi plants, which, in this case, is assessed (Box, Figure 1).[4]
- Tolerance to abiotic stress, i.e. **drought tolerance**, could increase the fitness of NGT plants and subsequently their **invasive potential**, with adverse effects on biodiversity**.**
- Many plant families produce **secondary plant metabolites** to protect themselves against pest organisms. Small genetic modifications could alter their composition and quantity in NGT plants making them **toxic to humans and animals**.

The criteria of Annex I of the EC proposal also allow for off-target sequence changes by the applied technique. However, this is limited to a narrow class of off-target effects, ignoring different possibilities for unintended changes by the genetic modification, e.g. larger rearrangements or other changes unrelated to the original target sequence.

In summary, the proposed approach to exempt certain NGT plants from risk assessment, only based on a molecular comparison, is scientifically not justifiable, because it cannot exclude risks. Our view is shared by a comprehensive analysis of the equivalence criteria by ANSES, the French National Agency for Food, Environmental and Occupational Health and Safety.[5]

RNAi: potential risks by NGT1 plants

RNA interference (RNAi) is already applied for insecticidal purposes in transgenic GMOs and spray applications, which must undergo risk assessment. However, NGT1-RNAi plants would be deregulated, despite sharing principally the same mode of action and thus **similar risk profiles** i.e. potential adverse effects on non-target organisms, **harming important protection goals** (e.g. biodiversity, protected species). Consequently, **risk assessment** should also be **required for NGT1-RNAi plants**. For details see.[4]

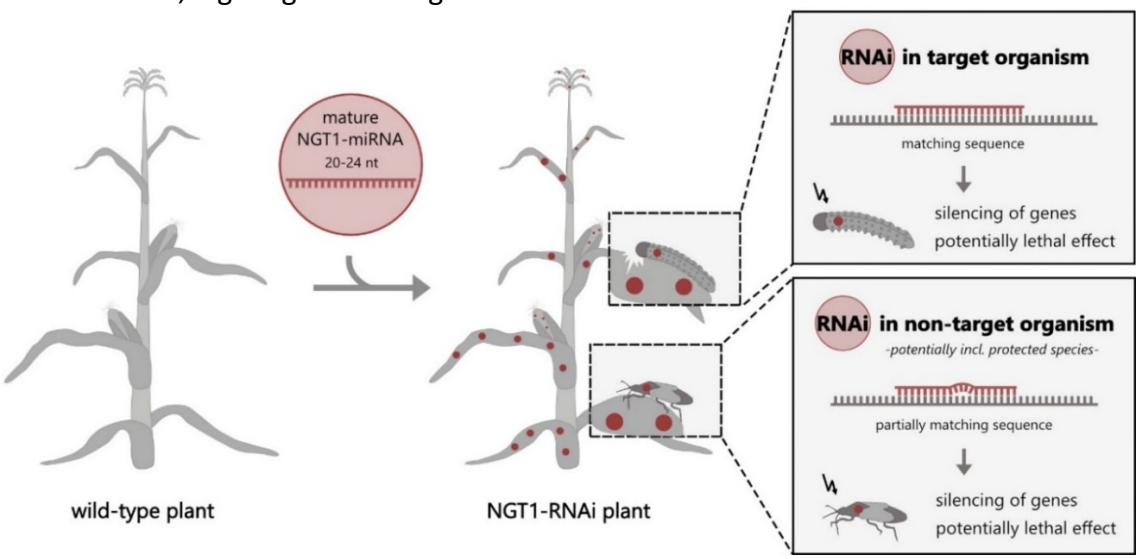

Figure 1. NGT1-RNAi plants can be designed to produce short edited RNA elements (so-called miRNAs) possessing insecticidal effects on target and potential non-target organisms (incl. protected species). These effects are based on the mode of action of RNA interference (RNAi) which causes silencing of genes with (partially) matching sequence and therefore, can have potentially lethal consequences. See also Box above. (nt: nucleotide; red dots: edited miRNA produced by NGT1-RNAi plant)

[4] Bohle et al. (2023). https://doi.org/10.20944/preprints202311.1897.v1

[5] https://www.anses.fr/fr/system/files/BIOT2023AUTO0189.pdf?download=1

1.2 Legal considerations

The EC proposal to exempt certain NGT plants from risk assessment does follow neither primary law of the EU nor the established case law of the European Court of Justice (ECJ).

The ECJ has ruled that **the correct application of the precautionary principle**, enshrined in Art. 190 para. 2 TFEU[6], "presupposes, first, identification of the potentially negative consequences (…), and, second, a comprehensive assessment of the risk (…) based on the most reliable scientific data available and the most recent results of international research."[7]

Since the comparison between NGT plants and conventional plants

- is not suitable for a comprehensive assessment of the risks of NGTs,
- is not based on the most reliable scientific data and
- does not take into consideration the most recent results of international research,

Annex I of the proposal **does not meet the legal standard to properly apply the precautionary principle**. Also, the ECJ has permanently highlighted the importance of this European primary law principle for the interpretation of European gene technology law, including the case by case analysis of potential risks (Case C-528/16, para 50 ff; Case C-688/21, para. 44 et seq.).[8]

This is all the more alarming, therefore, as **the Commission does not implement any kind of regulatory follow-up** and instead assumes that once equivalence has been certified, this justifies the assumption of "eternal stability" of the genetic modifications made.[8] Buchholz comes to similar conclusions and highlights that risk management measures are completely cancelled for category 1 NGT plants, even if risks are identified in the future.[9]

Furthermore, the Commission wants to introduce the possibility for itself **to amend the equivalence criteria by means of delegated acts** (Art. 5 para 3 of the proposal). This authorisation violates Art. 290 para. 1 subpara. 1 TFEU, which only allows the completion of provisions that are primarily manifested in the detailing and concretisation of the regulations contained in the respective legislative act. As can be seen from the case law of the ECJ, "the parameters for the assessment and authorisation" of food-related products and the "essential safety requirements" are among the key aspects that the legislator itself must regulate (Case C-66/04, para 53 et seq.).

Additionally, a legal opinion shows that various **specialised European laws outside of the genetic engineering law do not provide adequate control** and testing standards for the new techniques.[10]

[6] TFEU: Treaty on the Functioning of the European Union.
[7] Case C-616/17 para 46; see, by analogy, Case C-343/09, para. 60, and Case C-77/09, para 75.
[8] See Spranger (2023) in Further Reading.
[9] https://www.gruene-bundestag.de/fileadmin/media/gruene-bundestag_de/themen_az/gentechnik/pdf/Gruene_im_Bundestag_Gutachten__Vereinbarkeit_des_Kommissionsvorschlags_zu_NGT_mit_dem_Vorsorgeprinzip.pdf
[10] See Spranger (2017) in Further Reading.

2 Further considerations

In addition to the scientific basis for risk assessment and legal considerations, other equally important subjects and challenges can only be briefly touched upon here:

- **Detection methods:** it is possible to develop specific methods for the detection and identification of many NGT plants if the sequence change in the DNA is disclosed, e.g. in an international database.[11] Traceability standards could support this by e.g. establishing a due diligence approach for products that might contain unapproved GMOs.[12]
- **Patenting:** regulating NGT plants in the Biopatent Directive as suggested is ineffective as this Directive is not recognised internationally.
- **Sustainable agriculture:** the deregulation of NGT plants is demanded to combat global challenges, i.e. climate change. However, a contribution of NGT crops to sustainable agriculture cannot be assumed in general, but **would require a proof of benefit for each case**. Such an approach is lacking in the EC proposal and would need to be based on scientific evidence rather than on assumptions. Also, current NGT crops are more likely to combat symptoms rather than causes of environmental damage by agricultural practices.

Conclusion

NGTs such as CRISPR/Cas and other genome editing methods can be used to modify the genomes of plants in a far-reaching and targeted manner, constituting a source of risk. The various specialized European regulations outside of genetic engineering law are **no alternative areas of law** as they do not provide adequate control and testing standards for the NGTs. However, only an appropriate **regulation can ensure safe products for humans and the environment.**

Therefore, appropriate regulation is an opportunity to utilize the potential of NGTs over the long term in a sustainable manner. If politics and society equally address this complex issue and organise regulation and research policy responsibly, the future can be shaped sustainably, as the current biodiversity crisis leaves no room for weakening the legally enshrined precautionary principle.

Further Reading

The following publications are (co-)authored by BfN and/or result from research projects commissioned by BfN.

Bohle, F.; Schneider, R.; Mundorf, J.; Zühl, L.; Simon, S.; Engelhard, M. (2023): Where Does the EU-Path on NGTs Lead Us? Preprints 2023, 2023111897. https://doi.org/10.20944/preprints202311.1897.v1

This analysis shows that 94% of NGT applications affected by the EC proposal would be classified as NGT1 and could enter the market without any risk assessment, although according to a screening of the intended traits they could pose similar environmental risks as current GMOs.

Dolezel, M.; Eckerstorfer, M.; Miklau, M.; Heissenberger, A.; Engelhard, M.; Simon, S. (2022): Synthetic Biology. Scan the horizon for impacts on biodiversity. BfN, Bonn.

[11] https://doi.org/10.3390/foods10020430

[12] https://doi.org/10.3390/foods13030369

https://attachments.cbd.int/567962e74dc1af45194e3f51e4acc1ae/SyntheticBiology.pdf

This brochure addresses synthetic biology with a focus on new genetic engineering technologies such as synthetic gene drives and applications with potential impacts on biodiversity. It specifically provides background information for negotiations on the level of the Convention on Biological Diversity (CBD).

Eckerstorfer, M.F.; Grabowski, M.; Lener, M.; Engelhard, M.; Simon, S.; Dolezel, M.; Heissenberger, A.; Lüthi, C. (2021): Biosafety of Genome Editing Applications in Plant Breeding: Considerations for a Focused Case-Specific Risk Assessment in the EU. BioTech 10(3), 10. https://doi.org/10.3390/biotech10030010

This publication argues for a case-specific risk assessment for plants obtained from new genetic techniques, including genome editing, since there is no common denominator for risks of such plants. The guidance for the environmental risk assessment and monitoring of genome-edited plants should be further developed to facilitate a focused approach that integrates considerations related to the traits as well as to the methods applied.

Eckerstorfer, M.F.; Dolezel, M.; Engelhard, M.; Giovannelli, V.; Grabowski, M.; Heissenberger, A.; Lener, M.; Reichenbecher, W.; Simon, S.; Staiano, G.; et al. (2023): Recommendations for the Assessment of Potential Environmental Effects of Genome-Editing Applications in Plants in the EU. Plants 12(9), 1764. https://doi.org/10.3390/plants12091764

This review recommends that plants obtained from genome editing should be assessed case-by-case and argues that the guidance for their environmental risk assessment needs to be developed further. It also discusses that the comparison of genome-edited plants with plants developed by conventional breeding should be conducted on a scientific case-by-case basis rather than at a general, technology-based level.

Federal Agency for Nature Conservation (Bundesamt für Naturschutz, BfN) (2021): New developments and regulatory issues in plant genetic engineering. BfN Viewpoint paper. BfN, Bonn https://www.bfn.de/sites/default/files/2021-10/Viewpoint-plant-genetic-engeneering_1.pdf

This viewpoint paper takes a stand on the European process for the revision of the regulation of new genetic engineering techniques (NGTs). It emphasises that the precautionary principle should be upheld and that proof should be provided when sustainability benefits are claimed for genetically modified crops.

Kawall, K. (2019): New Possibilities on the Horizon: Genome Editing Makes the Whole Genome Accessible for Changes. Frontiers in Plant Science 10, 525. https://doi.org/10.3389/fpls.2019.00525

The focus of this review is on possibilities of genome editing as a method of new genetic engineering. It argues that compared to breeding, genome editing enables more extensive changes in the genome, particularly also in places that were previously difficult to access due to natural protection mechanisms.

Kawall, K. (2021): Genome-edited *Camelina sativa* with a unique fatty acid content and its potential impact on ecosystems. Environmental Sciences Europe 33, 38. https://doi.org/10.1186/s12302-021-00482-2

This publication looks at the case study of a genome-edited plant and its potential impact on biodiversity, demonstrating that the change in plant constituents can have an impact on the interaction of plants with insects.

Koller, F.; Cieslak, M. (2023): A perspective from the EU: unintended genetic changes in plants caused by NGT—their relevance for a comprehensive molecular characterisation and risk assessment. Frontiers in Bioengineering and Biotechnology 11,1276226. https://doi.org/10.3389/fbioe.2023.1276226

This review focuses on unintended genetic changes that can be caused by the application of new genetic techniques, in particular CRISPR/Cas, and identifies differences in comparison to non-targeted mutagenesis methods used in conventional breeding. The paper argues that the assessment of both intended and unintended genetic changes should be part of a mandatory comprehensive molecular characterisation and risk assessment of plants obtained by new genetic techniques.

Koller, F., Schulz, M., Juhas, M. et al. (2023): The need for assessment of risks arising from interactions between NGT organisms from an EU perspective. Environmental Sciences Europe 35, 27. https://doi.org/10.1186/s12302-023-00734-3

According to this publication, it is particularly important for organisms developed with new genetic techniques to not only assess impacts of individual

events, but also additive impacts of potential large-scale release into a shared environment of modified organisms involving a range of different traits. The paper argues that cumulative effects and effects from interactions could exceed the sum of the risks of the individual events.

Koller, F.; Cieslak, M.; Bauer-Panskus, A. (2024): Environmental Risk Assessment Scenarios of Specific NGT Applications in Brassicaceae Oilseed Plants. Preprints 2024, 2024020255. https://doi.org/10.20944/preprints202402.0255.v1

The publication gives an overview of current market-oriented applications of new genetic techniques in relevant Brassicaceae oilseed crops: changes in oil quality, yield, growth and resistance to abiotic and abiotic stress are goals in oilseed rape (*Brassica napus*) and camelina (*Camelina sativa*). The publication develops environmental risk assessment scenarios for these crops and shows that for a comprehensive risk assessment, the technological potential of the new genetic techniques employed, the plants´ biology and the scale of releases have to be considered in combination.

Potthof, C.; Peuker, B., Palme, C. Schumacher, A. (2023): Expert Opinion: Evaluation of the European Commission's study on new genomic techniques. BfN, Bonn. https://www.bfn.de/sites/default/files/2023-03/bng_finalreport_COM-study_Feb2023.pdf

This expert opinion evaluates the European Commission's 2021 study on new genomic techniques and its supplementary material, which is the basis for the European Commission's 2023 proposal for a new regulation on plants produced by certain new genetic techniques (NGTs). The guiding principle of the evaluation is a high level of protection for the environment, human health, and consumer choice. The expert opinion concludes that the European Commission's study is not a study in the proper sense for a couple of reasons. It also stresses that in case of a deregulation, various protected goods would come under threat.

Ribarits, A.; Eckerstorfer, M.; Simon, S.; Stepanek, W. (2021): Genome-Edited Plants: Opportunities and Challenges for an Anticipatory Detection and Identification Framework. Foods 10, 430. https://doi.org/10.3390/foods10020430

This publication proposes a forward-looking framework for the provision of information for the detection and identification of genetically modified organisms, with a focus on genome-edited plants. The possibilities and challenges for detection are discussed and recommendations are derived.

Spranger, T. M. (2017): In-depth analysis of various European directives and regulations with regard to their potential to regulate environmental effects of New Technologies besides Genetic Engineering Law. BfN, Bonn. https://www.bfn.de/sites/default/files/2021-10/NT_Auffangrechte_RGutachten_Spranger_en.pdf

The report clearly concludes that there is no adequate control of new genetic engineering techniques outside of genetic engineering law and that other regulatory regimes in the EU, such as seed law, food and feed law, plant protection product law and plant variety protection law, are not suitable for controlling potential environmental risks of organisms obtained from new genetic techniques.

Spranger, T. M. (2023): Expert Opinion on the proposal for a regulation on plants obtained by certain new genomic techniques and their food and feed, and amending Regulation (EU) 2017/625.BfN, Bonn. https://www.bfn.de/sites/default/files/2023-11/spranger-expert-opinion-on-the-proposal-regulation-NGT-VO-E-2017-625-PAC2021_0.pdf

In this expert opinion, the European Commission's proposal is comprehensively assessed from a legal point of view. The report demonstrates that the underlying assumption, that plants derived from certain new genetic techniques generally pose a lower risk than those derived from other genetic engineering techniques is contrary to the case law of the European Court of Justice and to the precautionary principle.

Spranger, T. M. (2023): Brief expert opinion on the criterion of "equivalence" in the proposal for a regulation on plants obtained by certain new genomic techniques and their food and feed, and amending Regulation (EU) 2017/625. BfN, Bonn. https://www.bfn.de/sites/default/files/2023-11/spranger-2023-criteria-of-equivalence-PAC2021.pdf

The expert opinion analyses the criterion of „equivalence" which allows "category 1 NGT" plants to be exempted from risk assessment in the European Commission's proposal. It notes that the criterion of equivalence has no robust scientific basis, is not suitable to decide on the requirement of a risk assessment, and is incompatible with the findings of the European Court of Justice, in particular in Case C-688/21. Further, the proposed

possibility to amend the equivalence criteria by means of delegated acts violates Art. 290 para. 1 subpara. 1 of the Treaty on the Functioning of the European Union (TFEU).

Spranger, M. (2023): Ad hoc expert opinion on the judgment of the European Court of Justice in Case C-688/21. BfN, Bonn. https://www.bfn.de/sites/default/files/2023-07/NII500306-23e_ad-hoc_Urteil_C_688_21_pac.pdf

Following on from its judgement in Case C-528/16, in Case C-688/21, the European Court of Justice establishes settled case law on the interpretation of Article 3(1) of the EU Deliberate Release Directive 2001/18 on the requirements for a procedure or method of mutagenesis that has already been established for a sufficiently long time and is considered safe. This settled case law forms the basis for the further development of European genetic engineering law. The interlinking of the secondary law requirements of Directive 2001/18/EC, in particular with the primary law precautionary principle, means that there are absolute limits to any amendment of the ordinary law on genetic engineering in the event of a possible amendment of Directive 2001/18/EC.

Teufel, J.; López Hernández, V.; Greiter, A.; Kampffmeyer, N.; Hilbert, I.; Eckerstorfer, M.; Narendja, F.; Heissenberger, A.; Simon, S. (2024): Strategies for Traceability to Prevent Unauthorised GMOs (Including NGTs) in the EU: State of the Art and Possible Alternative Approaches. Foods 13, 369.
https://doi.org/10.3390/foods13030369

This article argues that traceability of products that might contain GMOs could be complemented by due diligence regulation in order to minimise the risk of GMO contamination (including GMOs obtained with new genetic techniques such as genome editing) in supply chains. The exemplary transfer of due diligence to a company in the food industry illustrates the potential benefits of mandatory due diligence, particularly for stakeholders actively managing non-GMO supply chains.

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Editor:

Federal Republic of Germany, represented by the Federal Agency for Nature Conservation,
Konstantinstr. 110
D-53179 Bonn

Phone: +49 228 8491-0
E-mail: info@bfn.de
Internet: www.bfn.de

Authors:
Wolfram Reichenbecher, Samson Simon, Luise Zühl, Robin Schneider, Juliane Mundorf, Kristin Hagen, Margret Engelhard (Division I 2.6 Synthetic Biology Assessment, Enforcement of Genetic Engineering Act)

Karl Stracke, Oliver Hendrischke (Division I 2.1 Environmental and Planning Law)

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