



Expert Group “New Genomic Techniques”, Ecological Society of Germany, Austria and Switzerland (GFÖ)

New genomic techniques from an ecological and environmental perspective: science-based contributions to the proposed regulations by the EU Commission

Executive summary

- 1) The proposal of the EU Commission falls short of acknowledging fundamental ecological principles at the level at which NGT will be applied.**
- 2) Deregulating NGT1 for *all plant species* world-wide could become a serious threat for biodiversity conservation and sustainability. NGT1 should not go beyond agricultural applications.**
- 3) The threshold between NGT1 and NGT2 does not consider environmental risks.**

1) Summary

We concede that the proposal of the EU Commission related to NGT modified plants is a solid attempt to address legal uncertainties in NGT applications regarding their equivalence to classical breeding methods. Yet, **the proposal should better consider several fundamental ecological principles**. Due to the 'law of large numbers' and high likelihood of outcrossing, it may be expected that **NGT1 modified plants will have undesirable ecological effects** on wild populations, communities and ecosystems.

A clear distinction must be made between applications replacing classical breeding for food and feed, especially for plants where the genome is known, and wild plant species. Specifically, our **main concern** is the suggested expansion of the regulation to '**all plants**', i.e. approx. 300,000 plant species world-wide. This allows unlimited application of NGT1 in wild populations with unpredictable consequences for biodiversity and nature conservation. We strongly recommend an appropriate risk assessment of all NGTs according to the precautionary principle. This is especially important for applications within natural populations where outcrossing into the wild – a main assessment criterion in classical GMOs - is almost certain. Our appeal does not preclude the use of wild genotypes and species for domestication and agricultural breeding purposes.

We also call for a **clear justification for the proposed threshold** distinguishing between unregulated NGT1 and regulated NGT2, that relies on sound and replicated scientific evidence. The suggested quantitative threshold (20 x 20 genomic alterations) assumes a positive correlation between the number of genetic modifications and potential risks. Environmental risk relates to the novelty of phenotype, which is often unrelated to the number of genomic changes. Also, the manner in which NGT1 is currently defined may allow for potentially unlimited sequential genomic changes, and thus deregulation of all NGT.

On a more general note, the proposal falls short of acknowledging state-of-the art scientific evidence about the causes for the current environmental multi-crises (biodiversity loss, nutrient crisis, toxic substances, climate change) and approaches to mitigate them. These measures, advocated recently by specialist national and EU-wide committees and institutions as very fast, safe, and highly effective, such as **diversification**, should not get out of sight. We thus appeal to the EU commission to **pursue, and support, the rapid implementation of ecological intensification measures** with a higher priority and effort than the implementation of NGT in intensive, solely monoculture-based agriculture.

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2) Background

On July 5th, 2023, the EU Commission has presented a proposal for a new regulation of plants produced via New Genomic Techniques (NGT). Under the current legislation, these plants are regulated in the same manner as hitherto existing 'classical' Genetically Modified Organisms (GMOs). The goal of the proposal by the EU commission was find criteria that can be easily assessed and implemented for regulating NGT depending on their equivalence to classical breeding methods (see proposal history: <https://food.ec.europa.eu/plants/genetically-modified-organisms/new-techniques-biotechnology.en>)

In a nutshell, the main point of the EU Commission's proposal includes the distinction of two categories of NGTs in plants: Category 1 (NGT1 in the following) and Category 2 (NGT2):

NGT1 are considered equivalent to plants produced by conventional breeding. They would be subject to a verification, labeling and cataloguing procedure but otherwise exempt from the requirements of the GMO legislation which includes a case-by-case risk assessment. A recent study by the German BfN (Bohle et al. 2023) showed that 94% of existing NGT applications would fall under this category.

For all other NGT plants (NGT2 plants), the requirements of the current GMO legislation would apply. I.e. they would be subject to risk assessment and authorization before could be put on the market.

The equivalence criteria for NGT 1 are based on the number of mutations introduced by targeted mutagenesis and cis-genetics that may also occur spontaneously. Specifically, a threshold of max. 20 locations in the genome with each max. 20 changes in nucleotides (insertions and deletions), i.e. 400 changed nucleotides, was defined ('20 x 20' in the following), beyond which a plant would be classified as NGT2.

The proposal and associated documents capitalize on cultivated plants, mainly crops, and the potential value for food and feed production in agriculture. Nevertheless, the proposal explicitly includes 'all plant species' and is thus open for releases of modified organisms in a wider range of contexts in wild plant populations. For the time being, the EU Commission proposes to exclude animals and microorganisms for the regulation due to the lack of sufficient knowledge about them. The use of NGTs in organic agriculture will be prohibited with this regulation, to enable consumers to choose non-modified products.

3) Aim of this statement

The legislative initiative is a bottom-up approach, seeking solutions on the plant breeding (molecular) level with the hope to find solutions for problems observed at higher biological organisational (population to ecosystem) level. Namely, NGT has been advocated as a main, low-risk (NGT1) measure for supporting sustainability and the EU Green Deal. While we acknowledge the goal to utilize NGT for the adaption of crop species to, for example, climate change, the proposal falls short in considering benefits and risks at such a higher organizational level. In our opinion, ecological aspects of NGT have been largely underrepresented in the public and scientific discourse, as well as in national statements about NGTs (e.g., by the German Research Foundation DFG, and the Leopoldina).

The main goal of this statement is to fill that gap.

4) Environmental risks from an ecological perspective

A) Environmental effects of introducing NGT1 plants into the wild without prior risk assessment

It should be noted that the **careful application of NGT for breeding purposes in food plants**, where a long history of mostly safe applications is available, may have its merits, such as speeding up the introduction into the market. Also, the proposal is based on legitimate arguments related to comparative risk assessment in agriculture. Yet, possible ecological effects as well as potential differences of NGT to conventional breeding from an ecological perspective need to be discussed.

Since we currently lack ecological studies about the potential environmental benefits and risks of the deregulation of NGT-plants, we must draw from scientific knowledge in related topics. Here, the insight of myriads of studies of neobiota, i.e. newly introduced species or genotypes, may be used as an analogy for newly introduced NGT-modified plants.

The main environmental risk of introducing new organisms into the wild is outcrossing and subsequent spread of novel organisms and/or genes into natural populations and communities (e.g., Ellstrand et al. 2013) with unpredictable consequences for entire ecosystems (Snow et al. 2005). Due to the unpredictability of such effects, ecologists have advocated the **precautionary principle**: introduction should not be allowed until risks have been excluded after scientific scrutiny (Snow et al 2005). This calls for a **careful reassessment of environmental risks** associated with introducing NGT plants into the wild, explicitly considering the consequences of abandoning the precautionary principle.

Scientific evidence from invasion ecology points to the realistic, but unpredictable, risk for single introductions of neobiota with severe environmental consequences (an estimated 1%, Simberloff 2005), despite the fact that newly introduced species have evolved under very different environmental conditions. This is not the case for NGT plants, because they are usually produced in order to thrive under current environmental conditions. Thus, it is unlikely that NGT plants would experience similar genetic bottlenecks as newly introduced species, i.e. a 1% likelihood of new genotypes causing environmental problems is likely a conservative estimate. Furthermore, **the 'law of large numbers'** in invasion research (Lockwood et al. 2009), tells us that the more individuals or species are introduced, the more likely is their establishment and spread in the wild. This is the key to understand the global spread of invasive species, and subsequent legislation related to transport of new species or genotypes. **NGT-modified plants are unique** compared to breeding methods or GMOs, because the expected ease and appeal of the method, new cultivars and new genotypes of wild plants have been – and will be- potentially developed in **very large numbers**. This, will, as opposed to classically-bred plants, largely increase the likelihood for spread into the environment, thus **counteracting existing attempts** to limit the global spread of novel organisms (e.g., EU 2014).

The establishment and spread of an organism is also promoted by the fitness relevance of the trait. (e.g. Vacher et al. 2004: *Brassica* sp., Fuchs et al. 2004: squash). An example is pathogen resistance (Bartsch et al. 1996) which is beneficial for plants and has thus a large potential to disrupt ecological interactions. Several proposed NGT modifications aim at modifying fitness-related traits, further **increasing the likelihood of unpredictable effects after outcrossing**.

B) Expansion of the new regulation to all plant species

A **main concern** from an ecological point of view, and where likelihood of introgression is relevant, is the fact that the proposed new regulation states up front that it applies to **all plant species**, i.e. an estimated 300,000 species (Mora et al. 2011). From a conservation biological point of view, **this expansion to all plants**, compared to the approx. 15 major crop species, is highly problematic

against the background of rapid species extinction - the most pressing environmental crisis (Rockström et al. 2009). Tampering with genetic constitution in non-crop plants can have severe consequences for natural adaptation processes, such as maladaptation for confounded factors in targeted selection. Such introductions could prevent us in the future to follow unbiased evolutionary responses (e.g. to climate change), i.e. responses that are not anthropogenically manipulated.

For these reasons, national (e.g. §40 Abs. 2 Satz 3 BNatSchG) and international (e.g. Convention of Biodiversity - CBD) laws and regulations concerned with biodiversity conservation have ruled out any measure jeopardizing the genetic integrity of wild populations, e.g. by introducing new genotypes. For example, the BNatSchG prohibits the introduction of plants and animals into a specific place if a risk for natural populations and communities cannot be ruled out.

Outcrossing into the wild is fostered by the relatedness of plants (Ellstrand 2003a, b; Ellstrand et al. 2013, Ellstrand 2018). Consequently, outcrossing among conspecific flowering individuals within a wild population is a certainty, and gene flow from NGT-modified individuals to wild genetically compatible heterospecific plants in the vicinity is likely (e.g. within the Brassicaceae, cereals such as *Hordeum*, *Triticum*, and related genera), and has been shown with classical GMOs (e.g., Chapman & Burke 2006, Ford et al. 2006, Ellstrand et al. 2013). Therefore, with application of NGT1 to wild plants and the expected large number of modified crop plants released into the wild, likelihood of outcrossing and the subsequent **risk of a spread of new alleles is very high**.

A common misconception in that context is that release of modified plants is not risky per se, since alleles with no or detrimental fitness effects will disappear from the gene pool. However, ample scientific evidence suggests that this is not generally the case. A spread of alleles can be both associated with rapid propagation of species or genotypes (e.g. Ward et al. 2008, Ellstrand et al. 2013), but also with spread of detrimental alleles (**outbreeding depression**, e.g. Montalvo & Ellstrand 2001). Yet, outbreeding depression has been missing from the debate, and was apparently not considered when expanding the proposed regulations to all plant species.

It should be noted that the aim of finding a measure for 'equivalence' between NGTs and conventionally bred plants makes clear that the sole target for the new regulations is in plant breeding for cultivation, i.e. food and feed. Thus, the expansion of the NGT1 regulation to 'all plants' **is not even necessary** for the goals of the EU proposal. We therefore suggest that legal measures must be taken to prevent such effects, such as adequate a-priori risk assessment of NGT1. This does not preclude new domestications or the use of natural genetic resources in agriculture.

C) Application of NGT1 in natural populations for non-breeding purposes is very likely

The scenario for many new genotypes of wild plant species being introduced into natural populations should NGT1 be deregulated for all species, **is not hypothetical**. For example, there are many advocates of using classical GMOs in ecological and evolutionary field experiments (e.g. Kessler et al. 2008), and NGTs are now highly accessible for disciplines that have traditionally worked mostly on an organismic, population or an ecosystem level (i.e. beyond breeding). Many appealing questions related, e.g. to local adaptation or differential plant performance in the field are foreseeable.

Additionally, apparently beneficial applications in nature conservation have been proposed (Breed et al. 2019, Phelps et al. 2020), such as 'de-extinction/resurrection' (e.g. Popkin 2018), combatting invasive plants, or amending assisted migration (Chen et al. 2011), which underrates the above risks of introgression. Thus, a scientific discourse about such measures is urgently needed.

D) NGT1 deregulations is at odds with regulations regarding the introduction of new genotypes

The scientific insights outlined are in line with current practice and the above national (e.g., §40 Abs. 2 Satz 3 BNatSchG) and international (e.g., Convention of Biodiversity - CBD) regulations concerned with the genetic integrity of wild populations.

Importantly, these regulations have been formulated for the introduction of naturally evolved genotypes in a practical context such as assisted migration in a climate change context, or reseeded for conservation practices. Both measures have long been controversially discussed in the ecological literature (e.g. MacLachlan et al. 2007, Hewitt et al. 2011) due to the possible adverse effects of outbreeding depression or import of pests (e.g. Hamilton 2001, Ricciardi & Simberloff 2009). Also, observations of introduced 'warm-adapted' ecotypes having none of the intended effects (e.g. Bucharová et al. 2016), or of hybridization actually accelerating extinction under climate warming (Gomez et al. 2015) have questioned the efficiency of such measures. For reseeded practice in conservation, the use of local seed provenances has been strongly advocated by evolutionary biologists as well as conservation biologists (e.g. Breed et al. 2013). Thus, there is a **scientific and legal consensus for a case-by-case risk assessment** when planning such measures (e.g. Hoegh-Guldberg et al. 2008). This is at odds with the proposed general deregulation of NGT1.

E) Knowledge about all plant species is insufficient for justifying deregulation of all NGT1

The proposal states that the new regulations should not apply to animals and microorganisms because of our insufficient knowledge about them, indirectly implying that this knowledge exists for all living plant species on earth. We strongly disagree with this assumption. While genomic data is available for the few main crop species, knowledge about most known wild species is clearly insufficient to make an informed judgement about species-specific and NGT-specific risks from introducing modified plants into the wild. Also, the proposed threshold distinguishing NGT1 from NGT2 will likely have diverging consequences among species, the quality of the changes, and environmental context. Therefore, **deregulating all plants** fulfilling NGT1 criteria as if there was no environmental risk, **is not supported by scientific evidence**.

Overall, **we strongly recommend to limit the proposed deregulations**, and apply NGT1 to a limited number of *explicitly listed* agricultural plant species, **for which knowledge from whole-genome sequencing** allows for testing equivalence of genome editing to classical breeding methods.

F) Defining risk based on a quantitative threshold of genetic modifications

We fully acknowledge the wish for a new regulation that can be easily implemented on the ground. To that end, the draft proposal of the EU commission suggests a threshold (i.e. 20x20 genetic modifications) for distinguishing NGT1 and NGT2. Yet, small changes in the genome are not always associated with small phenotypic changes and *vice-versa*, as also known from breeding. Also, the regulation opens up the possibility for a larger number of modifications because crossings amongst NGT1 plants would be considered NGT1, and NGT1 allow for **potentially unlimited modifications**, because also subsequent modifications of existing NGT1 are deregulated. Therefore, the number of genetic changes in a plant is **meaningless** for future legislation related to NGT. Overall, and as original genetic lines show mutations, too, the proposed threshold is a classification **against a moving baseline**.

From an ecological point of view, the risk of introducing a new genotype into a natural population is mediated by the phenotype, which is determined by the specific *location* of a genetic difference, but not by the *number* of genetic differences between a local and an introduced genotype.

Also, a recent extensive study by the German Federal Agency for Nature Conservation (BfN) has indicated that 94% of current plants produced with NGT would fall into the NGT1 category (Bohle et al. 2023). The same study has also provided scientific evidence for environmental risks, such as non-target effects on organisms interacting with plants, albeit not based on comparative risk assessment. Thus, the proposed regulation is very **likely to result in an almost complete deregulation of NGT**.

Thus, a major challenge in deregulation remains, i.e. obtaining scientifically sound evidence for the equivalence of a plant altered through NGT1 compared to classically bred plants. A meaningful number of experiments that compare the (context-dependent) phenotype of plants produced with alternative breeding methods prior to deregulating NGT1 would be very helpful. We thus recommend that the EU commission **provides a substantial justification**, and possibly adjusts their categorization, based on sound scientific evidence. **Until that point in time, we advocate a case-by-case risk assessment of NGT modifications instead of a general threshold, especially when introducing non-agricultural NGT into wild populations.**

5) Environmental benefits from an ecological perspective - a general note

Several main arguments for deregulating NGTs are based on claims related to ecological sciences. For example, it is assumed that classically bred plants and plants produced with NGT (1) are equivalent, and we have commented to this above. Secondly, the claim is that NGTs could contribute to realizing the Green Deal, and contribute to climate adaptation and biodiversity conservation.

We agree with the view that NGTs could contribute to increasing agricultural yield, at least in the current agricultural system, and if sustainability goals are the sole target for NGT (Purnhagen et al. 2023). Yet, when assessing risks and benefits of a new technology, knowledge about the currently best solution is crucial. Based on ample scientific evidence from (agro-) ecological studies, **the currently most effective, fastest, most productive, and safest approach to transforming the agricultural system towards social and environmental sustainability is 'ecological intensification'**, i.e. the application of ecological knowledge and rules to agro-ecosystems. The best example is to use knowledge from a myriad of experiments indicating that **biologically diverse systems** increases many functional attributes (e.g., Tilman et al. 2014, Dainese et al. 2019). These include productivity/yield and nutrient-use efficiency, resistance and resilience to extreme (climate) events, pathogen resistance, resistance to invasion by unwanted species (see summaries for policymakers by WBGU 2021 and EEA 2022 for many more examples, or Leopoldina 2020). A particularly relevant effect is the well-known reduction in pathogen load by simply mixing more than a single crop genotype (Garrett & Mundt 1999). The increase in yield of, e.g. pathogen insensitive rice varieties, can be enormous (approx. 90%) and up to a point where fungicides do not need to be applied (Zhu et al. 2000), without bearing the risk of rapid evolution of pathogen resistance, as is commonly observed in monocultures (Bourke et al. 2021).

Thus, while environmental benefits of NGTs still need to be assessed, there is ample scientific evidence for ecology-based solutions that are fast, efficient and bear no environmental risk.

We feel that with the intensive debate about NGTs, such solutions have moved out of sight, depriving us from realizing a highly efficient measure for agricultural sustainability which can be implemented immediately. We advocate that the scientifically attested approaches towards a sustainable agriculture based on ecological evidence are pursued with at least as much vigour as the application of NGT.

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