Oslo, june 6th 2023

A new political course for gene technology in the food system – recommendations from the majority of the Norwegian Public Committee on Gene Technology (Genteknologiutvalget)

In november 2020, the Norwegian Government appointed a committee to propose changes to the GMO legislation in light of scientific developments. The following are main recommendations for new regulations from the majority of the committee (7 out of 11 members) with relevance for EU regulations. The recommendations concern deliberate release of organisms developed with new breeding techniques (genome editing) and other forms of genetic engineering, particularly intended for food production and also environmental applications. These include differentiated requirements for regulatory approval, labelling, traceability, co-existence, intellectual property rights and positive incentives for innovation.

Recommendations for Norwegian national policy/regulations and a more extensive review of scientific and regulatory background information can be found in the original publication[1].

Preface and summary

In this report, a proposal for new regulation of gene technology is described, marking a clear shift from the current system. The majority of the committee members (Anna Wargelius, Muath Alsheikh, Sigrid Bratlie, Trygve Brautaset, Espen Gamlund, Arne Holst-Jensen and Camilla Tøndel) believe this is right for two main reasons:

1. **Current gene technology regulations and policy hinder innovation and access to safe and useful products:**

- There are few GMO products approved for food or feed in Norway and Europe, especially for cultivation/national bio-production. A strict regulatory framework and policy also stifles innovation because the threshold for market access is high.

- Current regulations and the consumer resistance to GMOs on which it rests are based on an assumption that there is something inherently risky and/or ethically problematic about products made with gene technology. We believe such an assumption is incorrect and refer to decades of accumulated knowledge documented in thousands of research studies and formal risk assessments showing that there have been no significant risks associated with GMOs so far. No technology is 100% risk-free. It is the application that largely influences actual risk. Risks and challenges associated with products made with gene technology, like with products made with conventional technology, are related to the product's traits and not the technology per se. When authorities deem a product safe, we must trust that decision,

[1] https://www.regjeringen.no/no/dokumenter/nou-2023-18/id2982905/

otherwise our regulatory systems do not work. Norway and Europe generally have a very high level of protection in the food chain, and it is unlikely that unsafe products reach the market regardless of how they are produced.

2. **The current gene technology regulations are even less suitable for for products and organisms made with gene editing and other new genetic techniques that enable targeted changes in the organisms DNA, in our proposals referred to as precision-bred products (PB)**

- We believe that current requirements for documentation and the extent of risk assessments and associated burden for both regulatory authorities and developers in the approval process, are disproportionately high for products that are comparable to conventional products. This is the same conclusion reached by expert groups worldwide. In the European Commission's study from 2021[2], it is concluded that "there are strong indications that the legislation is not fit for purpose for some NGTs (new genomic techniques) and their products, and that it needs to be adapted to scientific and technological progress." In the subsequent public consultation[3], which received thousands of responses from organizations and individuals from the public, private, and non-governmental sectors, a staggering 80% believed that the current GMO regulation is not suitable for plants developed using new genetic techniques (gene editing).

- We would like to emphasize that gene technologies are enabling tools for the bioeconomy. We believe that the current high and costly approval requirements hinder innovation and the development of products that can contribute to addressing significant societal challenges, such as climate adaptation and increased food security. This potential is also emphasized by, among others, FAO[4], IPCC[5] and the Chief Advisors to the UN Food systems summit[6]. It is also supported by the aforementioned EU public consultation where around two-thirds of stakeholders argued that the current regulations would have a negative impact on their sector's activities and their ability to achieve the goals of the Green Deal and the Farm-to-Fork Strategy. For Norwegian (and probably many European) plant and animal breeders, the costs associated with approval would be too high to incorporate gene editing into their breeding programmes (elaborated later).

- If Norway and the EU are to have significantly stricter requirements than the rest of the world, it will particularly weaken the competitiveness of companies exporting to the international market. It could also result in international developers, who have better access to the technologies, delivering sustainable and useful innovations to the Norwegian/EU market more efficiently than local developers can. Not least, it hinders innovation outside of capital-intensive businesses and industrialized sectors and contributes to monopolization in key areas. Continuation of the current GMO regulations for new breeding techniques would hinder Norwegian/EU competitiveness both domestically and internationally.

---

[2] https://food.ec.europa.eu/system/files/2021-04/gmo_mod-bio_ngt_eu-study.pdf
[3] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/13119-Legislation-for-plants-produced-by-certain-new-genomic-techniques/public-consultation_en
[4] https://www.fao.org/science-technology-and-innovation/gene-editing-techniques-and-agrifood-systems/en
[5] https://www.ipcc.ch/sr15/
[6] https://sc-fss2021.org/wp-content/uploads/2021/06/FSS_Brief_IAP_Europe.pdf

- The current Norwegian/EU GMO regulations do not differentiate between PB (Precision Breeding) products, which, for all practical purposes, are equivalent to conventional products, and products produced using older genetic modification techniques. Everything is classified as GMOs due to a legal definition that was created before the existence of new breeding techniques such as gene editing. We believe that labeling PB products as GMOs would be misleading for consumers and would itself hinder innovation in the field due to reputational risks for producers. It would undermine the potential of the technology for sustainable transformation. Furthermore, requiring GMO labeling and separate production lines for PB products would entail such significant practical and economic consequences for many producers and companies in the value chain that it would not be feasible in practice. Thus, continuing with the current GMO regulations is, in practice, a rejection of gene editing in Norwegian/EU food production. This is further elaborated on later in the document.

- In the current situation, with the knowledge we have about what this technology can achieve, we believe it is riskier to maintain strict regulations that hinder or unnecessarily delay innovation than to relax regulations. Given the opportunities that genetic technology can create in terms of climate change mitigation, food security and sustainability, it is ethically more defensible to adopt a more enabling regulatory framework.

In line with the above, we therefore recommend significant changes to regulations and governance and policy changes:

We propose a new model for regulating products and organisms developed through genetic technology that provides a faster, more predictable, and risk-proportional path from research and innovation to the market that ensures the safety for health and the environment while also promoting the development of sustainable products. We propose two categories/definitions for different types of genetically altered organisms: Precision Bred (PB) for changes within the species' gene pool and Genetically Modified (GM) for changes outside the species' gene pool. Furthermore, two levels of regulation are established within each category depending on existing knowledge and experience with the trait, resulting in a total of four levels of regulation. Consideration is also given to the precision of the changes and whether unintended changes may have occurred. The higher the level of uncertainty associated with the genetic change or trait, the higher the level of regulation. An intended consequence of this differentiation is that the assessment and approval will be faster, more predictable, and more resource efficient than it is currently. It is also a goal to achieve a greater coherence between the regulation of traditional breeding in the food chain and new, more precise forms of breeding and development.

The most important feature of the model is that organisms and products within the PB category, which only have changes within the species' gene pool (targeted mutations, cisgenes, and intragenes), are largely equated with conventional products in terms of approval requirements and market conditions (labeling, traceability, coexistence, intellectual property rights, public consultation, etc.). We consider this not only scientifically appropriate but also crucial for the adoption of new breeding techniques (gene editing etc) in Norwegian/European breeding and food production in an economically and practically feasible manner for the producers/industry. The principles of differentiation can be applied to both national bioproduction, import of products and experimental releases, with some adjustments for each purpose.

We also propose several measures to stimulate more sustainable and socially beneficial innovation that benefits a wider range of people. For example, we draw inspiration from the field of "orphan drugs" – medications for "unprofitable" patient groups with significant unmet needs – where various measures are used to incentivize developers. We also recommend that patent rights for organisms and products developed through genetic technology are limited according to the principles of differentiated regulation: PB products, which can be compared to conventional products and therefore have a simpler path to market, should not be eligible for IPR other than what applies for conventional products either. We believe that this measure would prevent unfair competition and unreasonable restrictions on product access, which has been part of the criticism against GMOs.

It may be a significant challenge to overturn decades of technology skepticism deeply rooted in various parts of society. However, we still believe it is an important task that must be undertaken to succeed with new policies. It is crucial that decision-makers, stakeholders in the food value chains, consumer organizations and society as a whole contribute to a knowledge-based, nuanced, and constructive dialogue regarding gene technology going forward.

Proposal for differentiated regulation of organisms produced by gene technology (targeted mutagenesis, cis-/intragensis, transgenesis ++)

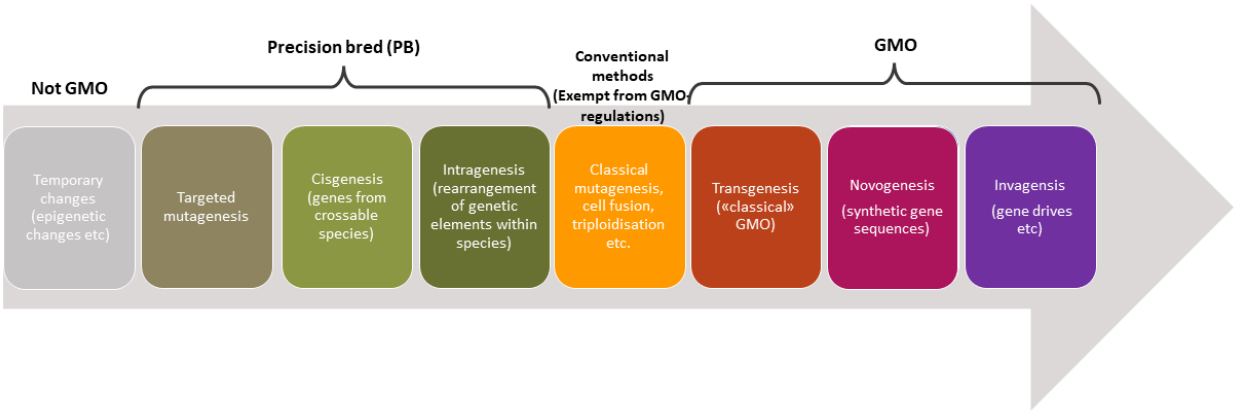
We believe it is essential to establish a regulatory system that facilitates sustainable innovation with gene technology across the entire food system and other relevant fields (medicine, industry, nature conservation, etc.). We argue that it is possible to establish sound regulatory principles that can apply across species and accommodate future technological development. Therefore, new regulations should apply to all types of organisms, both plants, animals, and microorganisms. Considerations related to animal welfare and varying levels of knowledge for different organism groups are taken into account through the principles of the model. If there is genuine uncertainty about risk or ethical/sustainability aspects, the requirements are adjusted accordingly.

Differentiated regulation based on type of genetic change and knowledge about trait

Like the EU Commission, we draw a clear distinction between genetic changes that do not cross species boundaries and that could have been achieved with conventional methods on the one hand (targeted mutagenesis, cis-/intra-genesis), and those that cross species boundaries and cannot be achieved with conventional methods (transgenes etc.) on the other. A similar distinction has been made in other countries or regions that have differentiated regulation of organisms made with new genomic techniques from regulation GMOs, including the UK and many other countries in the world. Such a distinction – changes within the species gene pool versus changes outside the species gene pool – constitutes a main element in our proposed model. By the species' gene pool, we mean all genetic material and gene variants that would have been available by modifying the specific organism using conventional/non-regulated breeding technologies. We place great emphasis on the fact that the risk associated with genetic changes made with genome editing or other gene technologies does not differ from the risk associated with equivalent changes that are made with conventional methods (classical mutagenesis, crossbreeding). In fact, the risk will often be lower for products produced with targeted genome editing technologies (like CRISPR) than with conventional

methods, because the occurrence of so-called unintended changes is lower with targeted technologies than with other conventional methods[7] [8]. Because targeted mutagenesis and cis-/intragenesis only alter specific genes instead of having to change many genes to achieve one specific trait (as in crossing or random mutagenesis), the degree of genetic change is lower than for conventional methods. Therefore, we introduce the concept/classification 'precision breeding' (PB) – similar to the new UK precision breeding bill[9]. The scientific rationale for this distinction as a function of the 'degree of genetic change' and relative risk is illustrated in figure 1.

Figure 1: Distinction between Precision Breeding and GMO as a function of the 'degree of genetic change' and relative risk compared to conventional breeding



However, since the risk of a product is not primarily linked to the type of genetic change but to the traits of the product, we also place significant emphasis on the history of safe use (HoSU), familiarity with the environmental effects of the modified traits and knowledge about the function of the altered gene. This is in line with the EU Commission roadmap. Such a model is also comparable to the system for approval of "bioequivalent" drugs - where data from previously approved drugs with the same mechanism of action are taken into account in the risk assessment because they are sufficiently comparable. We apply the same principle here: Where knowledge is largely transferable between organisms and products, such knowledge should be used to a greater extent to simplify the assessment process. In cases where there is a high degree of predictability that the risk is low and that the product does not negatively affect sustainability or ethical aspects, a highly simplified approval process may be sufficient.

In line with EFSAs statement on 'Criteria for risk assessment of plants produced by targetedmutagenesis, cisgenesis and intragenesis' (2022)[10], we argue that risk is largely determined by three main parameters: whether the genetic change is within or outside the species' gene pool, whether the genetic change is made precisely and without unintended effects, and whether existing and transferable knowledge about the altered trait exists. We propose a model in which the requirements for approval is determined by a decision tree based on EFSA's proposed criteria for risk

[7] https://data.europa.eu/doi/10.2777/574498
[8] https://www.fao.org/3/cc3579en/cc3579en.pdf
[9] https://bills.parliament.uk/bills/3167
[10] Criteria for risk assessment of plants produced by targeted mutagenesis, cisgenesis and intragenesis - - 2022 - EFSA Journal - Wiley Online Library

assessment of plants altered with targeted mutagenesis and cis-/intra-genesis, but with adjustments and adaptations to also apply to animals and microorganisms as well as all types of genetic changes, including transgenes, invagenes, and novogenes. The higher the degree of uncertainty about possible risk, the more extensive the approval requirements.

Our model can therefore be seen as a regulatory operationalization of EFSA's proposed criteria for risk assessments. Four different regulatory levels are proposed based on the combination of outcomes of the main parameters. Table 1 indicates which regulatory level a product will be placed on based on the outcome of the criteria. Conceptually, the model is intended to be used for the approval of organisms and products for all purposes; experimental release, national bio-production (cultivation of plants, livestock production, etc.) and import. However, the contents of the assessments will vary in each case to take into account practical and technical aspects as well as international law and trade agreements (discussed later).

As shown in table 1, the applicant must demonstrate that the intended changes occurred as planned and that no significant unintended changes have occurred (B). If this cannot be demonstrated, further documentation and assessments will be required, which can affect the final regulatory level placement and likelihood of approval. The same applies if there is significant uncertainty about risk or ethical/sustainability aspects related to the altered trait, or if the documentation provided is incomplete. Such cases where basic criteria are not met are marked in red in the main model (the decision tree) in figure 2 further down. The main focus hereafter is a description of the path to market/release for products that meet the criteria and documentation requirements at the indicated level.

Table 1: Conceptual distribution of organisms and products in accordance with three main parameters related to risk

A) Are genetic changes within the species gene pool? *(Targeted mutagenesis, cis-/intragenesis)*	Yes ✓	Yes ✓	No ✗	No ✗
B) Are the intended genetic changes as planned, and are there no unintended changes that give cause for concern?	Yes ✓	Yes ✓	Yes ✓	Yes ✓
C) Can we be reasonably sure that the product is safe and has no other significant negative impacts based on existing, transferrable knowledge? *(History of safe use / familiarity and/or known structure and function)*	Yes ✓	No ✗	Yes ✓	No ✗
Assessed at level:	**1** No risk assessment	**2** Simplified assessment tailored to PB	**3** Simplified assessment tailored to GMO	**4** Standard assessment

Approval should also include an assessment of ethical defensibility (based on four main criteria; benefit, sustainability, fair distribution and transparency – elaborated later). The model is intended to cover experimental release, national bio-production, and the import products that can be used for

food, feed or other purposes. Conditions for market access such as labeling, traceability, patents, etc. are differentiated according to the core principles in the model, where plants, animals, and microorganisms with genetic changes within the species gene pool are largely equated with conventional products.

An intended consequence of such a risk-proportional and differentiated regulation is that the assessment and approval process is faster, more predictable and resource efficient than today, and lowers the innovation and commercialization threshold. It is also our aim to ensure a greater degree of consistency between the regulation of traditional breeding and newer, more precise forms of breeding in the food chain.

Criteria for Risk Assessments

Requirements for documentation and the criteria/contents of a risk assessment should be predictable. We suggest basing this on EFSA's six criteria for risk assessment of plants produced with targeted mutagenesis and cis-/intragenes[11]. These should also be adapted and used for animals and microorganisms.

The first four criteria are based on molecular characterization. We suggest using all these criteria including off-target analyses. Furthermore, we argue that the same criteria can in principle also be used for GMOs, with some adjustments in the assessments.

The following criteria have been proposed by EFSA:

- Criterion 1 – Is any exogenous DNA sequence(s) present?
- Criterion 2 - Is the DNA sequence(s) from the breeders' gene pool??
- Criterion 3 - what is the type of integration? (criterion only applies to organisms with cis- or intragenic changes)?
- Criterion 4 - Is there an unintended interruption of an endogenous gene?
- Criterion 5 - History of safe use/familiarity? (Are the effects of the altered allele on health and environment known)
- Criterion 6 – Is the function and structure associated to the new allele known?

This can be summarized and translated into three general main parameters (as shown in table 1):

A) Whether the genetic change is within or outside the species' gene pool (criterion 1 and 2)
B) Whether the genetic change has been made precisely and without unintended effects (criterion 3 and 4)
C) Whether there is existing and transferable knowledge about the trait and gene function (criterion 5 and 6)

[11] Criteria for risk assessment of plants produced by targeted mutagenesis, cisgenesis and intragenesis - - 2022 - EFSA Journal - Wiley Online Library

Proposal for Decision Tree Based on Risk Proportionality and Predictability

Figure 2 shows a decision tree (adapted and extended from the EFSA decision tree) for a tiered approval system with four levels. The final level placement depends on whether the organism/product meets the relevant criteria and whether the applicant meets the requirements for documentation. It is an adapted version of EFSAs decision tree For products that do not meet the criteria, or in cases where the documentation is insufficient, the authorities can at any time request further documentation or move the product to another level as they find appropriate. Such a procedure is not described in detail here. The following is a description of the path to market for products that fulfil the criteria.

The first step (A) in the decision tree will be to classify **what type of genetic change(s) has been introduced with gene technology in the relevant product (criteria 1 and 2)**. This is relevant in deciding what documentation and analyses are needed to assess risk. Products are sorted according to whether the change is within or outside the species' gene pool, i.e., precision bred (PB) or genetically modified (GMO). PB includes two subgroups depending on whether there are targeted mutations or if DNA sequences have been added/reorganised in the genome (cis-/intragenes). Within GMO there are also different subgroups called transgenes (genes from another species), novogenes (designed gene sequences), and invagenes (including gene drivers). The last two categories are still early in development and likely not relevant for release on a large scale in the short term. Given the limited knowledge base about the risk profile of these types of organisms, requirements for assessment and regulation should be further developed. Here, the GMO branch of the decision tree focuses on transgenic organisms.

Once a product is classified as either PB or GMO at this stage, it is not possible to change this classification and the associated path through the decision tree later. However, if a product is 'mis-classified' by the applicant, the authorities will move the product to the correct classification.

In the second step (B) of the decision tree, it should be determined **whether the intended genetic change (the new allele/gene) has the correct sequence (criterion 3) and whether unintended changes have occurred in the organism's genome that may have unintended effects (criterion 4)**. This should be documented using appropriate DNA analyses. Which analyses should be required depends on technical aspects such as the type of genetic change and which methods are best suited at any given point - something that can change with technological development (presumably addressed by existing and future EFSA guidelines). The answer to these two questions (criterion 3 and 4) determines the entry point to the next step in the decision tree. If the answer is "no" to one or both of these criteria, the authorities should make an assessment of whether unintended changes in either the new allele/gene or the genome in general may pose a risk. If a possible risk is identified, an additional assessment is made before the product can proceed. What is required in terms of documentation in this additional assessment depends on the nature of the risk and the degree of uncertainty. The outcome of this assessment can influence the final placement on the level and likelihood of approval.

The third step (C) in the decision tree aims to clarify **whether there is sufficient existing knowledge about or experience with the altered trait to determine that the product does not pose an unacceptable risk or other negative effects**. In scientific terms, the question can be posed as whether the allele/gene and the resulting trait has a history of safe use for health and the environment (HoSU and familiarity) (criterion 5). If criterion 5 cannot be met, knowledge about the allele/gene's structure and function should be described and can be given weight when determining the level of risk assessment (criterion 6). All products that have progressed after assessment in step B

will be assessed according to these criteria. These criteria and the understanding of them are further described in EFSA's proposal for criteria for risk assessments.

The basis for comparison to assess whether the product meets these two criteria is existing products/characteristics that are already in use for the same purpose. If the authorities in their assessment conclude that there is sufficient knowledge to predict low risk and sufficient ethical defensibility, requirements for documentation are significantly reduced. Products/organisms that are comparable to conventional products with known traits can be approved without risk assessment. This will initially apply to PB products made with targeted mutagenesis or cisgenes where the new gene/allele has an established acceptable risk profile from comparable products (criterion 5), or because the knowledge of the gene's function is sufficient (criterion 6). A GMO that meets both criterion 5 and 6 will still undergo risk assessment, but in a simplified form.

For PB products where the applicant does not have sufficient documentation for criterion 5 and/or 6, a simplified assessment at level 2 will be necessary. In addition to PB products with targeted mutations or cisgenes without HoSU/familiarity or well known structure and function, this will apply to all intragenic products because they will not be comparable with existing products. If a simplified assessment reveals a likely risk and/or other negative effects, the product may be subjected to a more comprehensive risk and ethical defensibility assessment. Step C is intended to make better use of existing, transferrable knowledge. The principle is comparable to the system for approval of "biosimilar" drugs - where data from previously approved drugs with the same mechanism of action is used as a basis in an assessment because the drugs are sufficiently comparable.

The outcome of criterion 5 and 6, combined with the outcomes of the previous four criteria, determines which regulatory level a product is ultimately placed on and whether it is then approved or declined.

Figure 2 illustrates the decision tree and the four regulation levels. The figure also includes differentiated requirements for detection and public consultations (before approval) and differentiated terms for market access after approval (labelling, traceability, monitoring, IP) where PB is sidelined with conventional products. These aspects are further elaborated on later in this document.

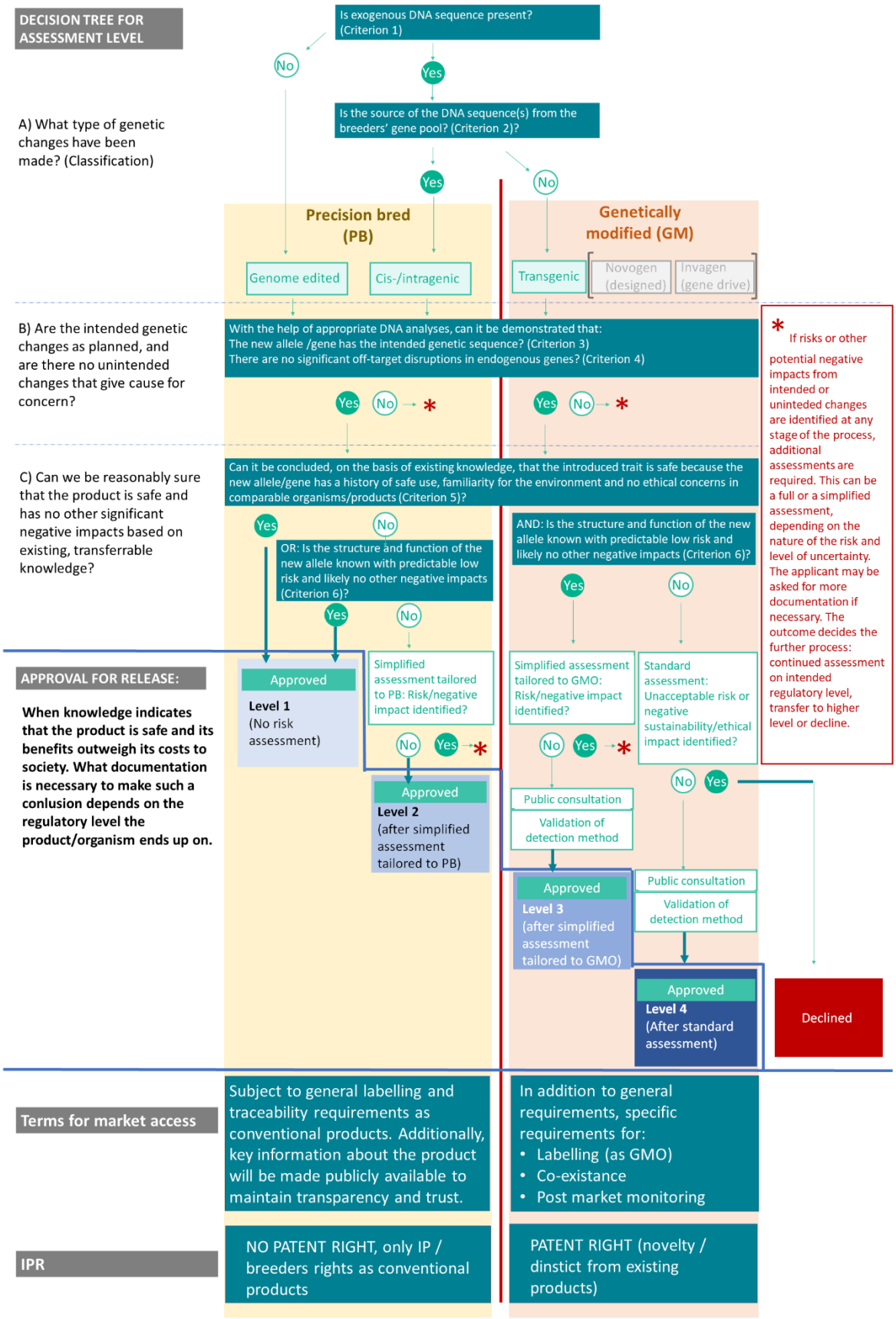


Figure 2: Proposed decision tree for assessment and terms for market access for PB and GMO organisms and products based on the principles of risk proportionality, predictability and non-discrimination.

Further description of the different assessment/approval levels

Level 1: PB products/organisms with known traits and predictable risk profile (HoSU/familiarity or alleles with well known structure and function)
Intended for PB products (with no added DNA that is not found within the species' gene pool according to criteria 1 and 2) that get a "yes" on criteria 3, 4, and either 5 or 6. Thus, these products have the intended gene sequence and no worrying unintended changes, and alleles/traits that are known from comparable products that have a history of safe use for health and environment and are ethically justifiable. PB products made with targeted mutagenesis and/or cisgenesis could have been produced by conventional breeding or arisen naturally and are therefore generally comparable to conventional products. Therefore, it might be sufficient for such products to have either HoSU/familiarity (criterion 5) or knowledge of the allele's function (criterion 6), for them to qualify for level 1.

Such products can, with a high degree of predictability, be determined to be as safe as (or safer than) their conventional equivalents, and a further risk assessment would therefore not be necessary. A similar approach is described in EFSA's statement from 2022: "[...] the new allele obtained through genome editing and the associated trait characterizing the final product are already present in a consumed and/or cultivated variety of the same species. In this case, the risk assessment may focus on the knowledge of that variety (the history of safe use) and specific data on the edited gene and its product may not be needed."

The products are also at least as sustainable/ethically defensible as conventional products since they undergo an evaluation of ethical defensibility (to prevent unethical or unsustainable products from reaching the market) that conventional products do not.

Although not expected to present risks or other negative consequences different from conventional products, we recommend to keep this product group within the regulatory framework, rather than excluding them. This can build trust in a technology that has faced significant skepticism from consumers. Making information available in a public registry, for instance, can also promote transparency. Furthermore, it will maintain regulatory oversight allow the use of targeted positive incentives (further described later).

At this level, a highly simplified approval or notification (without risk assessment) is sufficient as long as the applicant can document the type of genetic change and existing knowledge from comparable organisms/products that demonstrate negligible/low risk and sufficient ethical defensibility (sustainability, animal welfare etc).

Data from experimental releases/field trials will not be necessary, as we don't anticipate that these will provide any new information isn't already addressed by existing knowledge from comparable conventional products. Similarly, there shouldn’t be a requirement for public consultation for PB products/organisms as the impacts placing them on the market aren’t expected to differ from conventional products. Moreover, a detection method will not be required since these organisms/products are indistinguishable from conventional products.

This highly simplified approval process takes into account the known characteristics of the product, makes better use of existing knowledge and ensures that the products carry the same low health and environmental risks as comparable conventional products. The range of products that qualify for level 1 assessment is likely to be limited initially, but is expected to increase over time as more

experience is gained with the safe and sustainable use of a growing number of products. This is in line with the intention of the precautionary principle, where the level of knowledge is key.

If plausible risk or other negative effects are detected during the assessment, the application is moved to a higher level or the applicant will be asked for additional documentation.

Examples of Organisms/Products appropriate for Level 1

Current regulation of genome edited animals in the United States is a practical example of a regulation that resembles Level 1 in our model. In 2022, the FDA (the authority responsible for gene-edited animals) decided - based on a preliminary assessment - to forgo a risk assessment of gene-edited cattle with a mutation/gene variant that results in short fur (slick coat) and better heat tolerance[12]. This gene variant and the resulting trait naturally occurs in other cattle breeds used in food production and has a long history of safe use for health and the environment. The gene-edited animals showed no deviation from the expected phenotype and were in good health upon inspection. The developer submitted sequence data (whole genome sequencing) that documented both intended and unintended genetic changes. Unintended mutations were not expected to pose any risk. The product is therefore cleared for the U.S. market without the need for approval or specific labelling requirements etc.

In our proposal, an applicable and comparable case would be if Geno – a Norwegian cattle breeding company – uses genome editing to increase the frequency of existing gene variants for hornlessness (polled) and beneficial milk protein variants in their breeding population. These are known gene variants and traits that - given that the genetic changes are made accurately, and one can reasonably ascertain that there are no unintended changes - are not expected to entail any risk or ethical downsides different from conventionally bred animals.

A relevant example from plants is if the Norwegian plant breeding company Graminor wishes to introduce a mutation causing dwarf straws in different lines of wheat, making them less prone to breaking in wind and rain. Such mutations are well known from other conventionally bred wheat lines and other crop species, and produce a predictable effect/phenotype. A comparable case is the introduction of a short-straw gene variant in teff (*Eragrostis tef)* - a grain type that is gluten-free and high in beneficial nutrients. Teff is an important food crop in Ethiopia and other developing countries, and is also grown in the U.S. This gene-edited variant with short straws, developed in collaboration between American and Ethiopian researchers, was cleared for the U.S. market in April 2023 without the need for approval[13]. The authority (USDA/Aphis) cites familiarity with the trait and the allele as the reasoning. The trait could reduce teff wastage by around 25%.

In some cases, knowledge might be transferable between species, and a PB product may be approved at Level 1 even if the allele doesn't exist in the species beforehand. For instance, MLO mutations that provide mildew resistance are well known and have a long history of safe use in various plant species, including barley. Such experience and knowledge are likely to be largely transferable to gene-edited mildew-resistant (MLO-mutated) wheat[14] in terms of risk profile. While MLO mutations can usually be obtained through conventional methods, practical barriers make this unfeasible in wheat. Therefore, MLO-wheat might be eligible for Level 1 approval even though the allele is new in the species. This would likely be in line with EFSA's description of what is considered

[12] https://www.fda.gov/media/155706/download
[13] https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa_by_date/sa-2023/aphis-rsr-ddct-msls
[14] https://www.nature.com/articles/s41586-022-04395-9

to have HoSU/familiarity: "[...]the gene/allele and the associated trait has a history of consumption as food and feed and/or familiarity for the environment".

A third example could be cisgenic organisms where a gene is transferred from a crossable relative and it's a variant of a gene that already exists in the organism (a homologous gene). This could, for example, be maize with a gene originating from its relative teosinte to reintroduce beneficial traits that have been lost through breeding, in this case increased protein content and nitrogen efficiency[15]. The same would apply, for example, to transferring late blight resistance genes from one potato variety to another.

A fourth example is gene edited sterile salmon with a targeted mutation in the *dnd* gene[16]. Since this is a targeted mutation where the structure and function of the allele is well known (criterion 6), the environmental impact can largely be deduced (sterile fish with no ability to spread), and there is data on fish health and welfare available, it could be eligible for Level 1.

For microorganisms intended for release, the knowledge base is more limited and thus the level of uncertainty higher than for many plant and animal species. Therefore, few products will in be suitable for Level 1 in the short term. However, there are some examples of microorganisms that could qualify. Lactic acid bacteria (Lactobacillus) are an extremely diverse group with a lot of genetic variation that are generally considered safe (GRAS) and have been used safely in food production for over a hundred years. Gene editing of such species to transfer gene variants/traits between strains could meet the requirements for approval at Level 1.

The range of products/organisms that qualify for Level 1 will increase in line with an increasing knowledge base.

Level 2: PB products/organisms with new traits (no HoSU/familiarity or sufficiently understood allele structure and function)

For PB-products that do not meet the requirements for HoSU/familiarity and where adequate knowledge of the allele's structure and function and their significance for the risk profile is lacking, we argue that a simplified health and environmental risk assessment should be conducted. This is justified by the fact that the risk scope associated with products at this level does not differ from the risk scope for conventional products with similar genetic changes. However, since risk is largely associated with the trait and not the type of genetic change, it may be reasonable to require some documentation to ensure that the product is safe and sustainable/ethically justifiable. Products/organisms approved at this level can therefore be said to be better documented safe and beneficial than conventional products with new traits which are not risk assessed in the same way.

To be placed on this level, the application should include documentation related to on-target and off-target effects, and no risk should have been identified on the basis of this. However, at this level, the applicant cannot adequately address criteria 5 and 6, i.e., it cannot be demonstrated based on existing knowledge that the gene variant and the trait it provides have a low risk. Thus, EFSA should conduct a simplified health and environmental risk assessment adapted to a PB profile.

An assessment of ethical defensibility is also made before approval. This includes an assessment of animal welfare. This assessment should preferably by performed by a competent ethics committee. Products at this level have new traits and are therefore could involve as yet unknown

[15] https://www.nature.com/articles/d41586-022-03336-w
[16] https://www.nature.com/articles/srep21284

ethical/sustainability challenges. A significant positive contribution to sustainability or other societal benefits could indicate a fast-track procedure or other positive measures.

The documentation at level 2, in addition to that required at level 1, should focus on a simple characterization of the new trait. This can be from a small field trial (which in itself should be approved by notification, se later description of experimental releases), animal life cycle analyses, analyses from simulated ecosystems for microorganisms, or similar.

If plausible risk or other negative effects are detected during the assessment, the application is moved to a higher level or the applicant will be asked for additional documentation.

As for level 1, there shouldn't be a requirement for public consultation for PB products/organisms at level 2 as the impacts placing them on the market aren't expected to differ from conventional products. Moreover, a detection method will not be required since these organisms/products are indistinguishable from conventional products.

Examples of Products/Organisms appropriate at Level 2

An example that may be suitable for level 2 is gene-edited pigs with a targeted mutation providing resistance against PRRS disease. The gene variant/trait is not previously known from any species and should therefore be examined in a simplified assessment to exclude negative effects, particularly related to animal welfare.

Another example could be the introduction of homologous genes from Pacific salmon (*Oncorhynchus spp.)* into Atlantic salmon (*Salmo salar*) to increase resistance to sea lice[17]. Although these are classified as different species, they are closely related and share many of the same genes. Therefore, a simplified assessment at level 2 might be appropriate.

A crop example could be gene-edited sterile garden plants, which are being developed by the Norwegian company Eliteplanter in collaboration with NIBIO[18]. Although such a genetic change would presumably make the plants safer for use than conventional varieties because it reduces the risk of spreading, it might still be appropriate to assess them at level 2 with a simplified risk assessment because the trait is not well-known from other plants used for the same purpose and because the plant species themselves are foreign species in Norway.

For microorganisms, a relevant example for level 2 could be gene-edited soil bacteria that fix nitrogen for various crops such as corn and wheat[19]. Both the genetics and the trait are known from other soil bacteria that naturally fix nitrogen for legumes, and the gene-edited product is already in relatively widespread use in the US. However, knowledge about microorganisms and their interaction with the environment is generally more uncertain than for common crops and livestock, so it may be appropriate to assess them at level 2 rather than level 1 for the time being, until the knowledge base is better.

Furthermore, it might be appropriate to place all organisms/products with so-called intragenes at level 2, which are genes composed of various genetic elements found within the species, but not in that specific combination. This could typically be a gene with a new promoter ("volume knob")

[17] https://nofima.com/projects/crispresist/
[18] https://eliteplanter.no/kan-nobelprisvinnende-teknologi-crispr-benyttes-for-a-utvikle-hageplanter-med-lavere-spredningspotensial/
[19] https://www.pivotbio.com/

leading to a higher gene expression than normal. EFSA has previously concluded that new risk factors can arise with intragenes compared to conventional organisms.

Level 3: GMOs with known traits and somewhat predictable risk profile (HoSU/familiarity and well known gene structure and function)

Transgenic GMOs or products derived from GMOs can also have a degree of history of safe use and predictable impact on the environment. Some GMOs have been in use for several decades, without demonstrated negative effects. Such knowledge can be taken into account in a risk assessment if it is transferrable to new GMOs. However, because there is generally a higher level of uncertainty about GMOs than conventional products (and thus PB), we argue that there should be a risk assessment, but simplified compared to a standard assessment. Operationalization of this level requires a clear definition of what HoSU/familiarity means in a GMO context (for example, how long a GMO should have been in use).

Ethical defensibility is also assessed, preferably by a competent ethics committee. Although the traits of the product may be known from previously approved GMOs, we argue that since GMOs are significantly different from conventional products, they should be subject to such an assessment. A significant positive contribution to sustainability or other societal benefits could indicate a fast-track procedure or other positive measures.

A public consultation is also required before approval is granted. Also, a detection method (where appropriate, i.e. DNA-containing organisms/products) is required.

If plausible risk or other negative effects are detected during the assessment, the application is moved to a higher level or the applicant will be asked for additional documentation.

Examples of organisms/products appropriate for level 3

An example could be a so-called stack - a transgenic organism with a combination of several genes that have previously been approved individually in the same species. There is already a lot of transferrable information from previous risk assessments of the individual genes/products. However, it may be appropriate to carry out a simplified assessment of the genes in combination to rule out any unexpected synergies. Such a simplified assessment is already practiced for stacked events that are hybrids between already risk-assessed and approved GMOs.

Another example could be products made from GMOs, but where no residues remain from the genetic modification. This could, for example, be omega-3 enriched canola oil for use in fish feed[20], where the oil does not contain either DNA or proteins. Such non-living, DNA-free products have a predictably low environmental risk and will have HoSU if all the components have been safely consumed over time.

At this level, GMOs where the transgenic trait itself has HoSU and familiarity within the intended area of use can potentially also be appropriate. This could, for example, be a gene from one common food crop transferred to another common food crop, such as a health-promoting antioxidant gene

[20] https://aquaterraomega3.com/

from blueberries inserted into tomatoes (recently applied for and expected to be approved shortly in the US)[21].

Level 4 - GMOs with new traits (insufficient HoSU/familiarity)

We are of the opinion that, in principle, several decades of experience with risk assessments of GMOs have not uncovered plausible significant risks. Therefore, we would ideally suggest that the requirements for approval / risk assessment should also be reduced at level 4. However, there is currently little political leeway for this, particularly in light of ongoing EU processes that only concern organisms/products made with new breeding techniques/genome editing (targeted mutagenesis and cisgenes). Therefore, our proposal for level 4 largely resembles current requirements for approval of GMOs. One important recommendation we make regardless, for animal ethical reasons, is to reduce the use of experimental animal feeding studies to a minimum, and only where there is a plausible and specific health risk from consumption of the GMO. Apart from this, a full health and environmental risk assessment is proposed at level 4.

Ethical defensibility is also assessed, preferably by a competent ethics committee. Although the traits of the product may be known from previously approved GMOs, we argue that since GMOs are significantly different from conventional products, they should be subject to such an assessment. A significant positive contribution to sustainability or other societal benefits could indicate a fast-track procedure or other positive measures.

A public consultation is also required before approval is granted. Furthermore, a detection method (where appropriate, i.e. DNA-containing organisms/products) is required.

Regulatory level 4 is primarily intended for GMOs with new traits. This category typically includes transgenic organisms. Invagenes and novogenes (like gene drives and synthetic/designed gene sequences) are assessed either at this level or at an even higher level. We have not during the preparation of this report had the time/scope to go sufficiently into these categories and recommend that specific criteria are addressed and developed at a later stage.

Products to be assessed at level 4 include all GMO products that do not qualify for approval at lower levels, including products that are initially assessed on level 3 but moved to level 4 due to insufficient documentation.

In the final step of the assessment at level 4, a total evaluation is made where any risk and/or ethical disadvantages are compared against benefits. If the overall benefit is expected to be greater than the risk and other disadvantages, the product is approved. The greater the benefit, the more risk or uncertainty about risk can be accepted. This is comparable to the approval of covid-19 vaccines, which through a rolling review were permitted early in the pandemic despite a non-negligible risk of side effects and a lack of knowledge about long-term effects, because the societal benefit far outweighed the disadvantages. The greater the benefits a product has for society, the heavier they should weigh in an evaluation. This should particularly apply to questions of sustainability, which is also highlighted as an important consideration in the EU Commission's work on new regulations for gene-edited plants and other policy actions.

If the risk or other disadvantages exceed the benefit, the application is declined.

[21] https://www.newscientist.com/article/2309346-purple-superfood-tomato-could-finally-go-on-sale-in-the-us/

General features on all four levels:

It should be the competent authority, based on available documentation, that determines which regulatory level a product belongs, not the applicant. In cases where the level placement is unclear, the developer should be able to consult the authorities for a preliminary classification based on a description of relevant parameters. The authorities should also make available a list of which gene variants/traits/product types qualify for approval at regulatory level 1 as they gain experience with them. Such an overview provides more predictability for developers.

The model will also work for organisms with multiple genetic changes (multiplex/stacking). If all changes/traits qualify for level 1, no risk assessment is required. If one or more of the genetic changes are at a higher level, the application is assessed at the level these changes imply, regardless of whether some genetic changes qualify for level 1.

We generally recommend adapting guidelines and requirements continuously as the number and diversity increase, to ensure a regulatory framework that is as accurate as possible and neither over- nor under-regulates various product groups.

Over time it's possible to envision that some GMOs could also be regulated similar to level 1 in our proposed model. This is contingent on a clear understanding and agreement about what constitutes a sufficient history of safe use for a gene/trait/product type. A useful rule of thumb would be whether the competent authority considers that a risk assessment (either simplified or full) would reveal any new information that isn't already addressed by the existing knowledge base. If it's improbable that a risk assessment would yield such new information, and current knowledge indicates the product is safe (for instance, if similar GMOs have been approved in the past), then the product should be eligible for approval without a risk assessment.

To be considered for either level 1 or 2 regulation, the organism itself should have a history of safe use for its intended purpose, such as a crop intended for food and feed. If the organism/species itself is novel for the intended purpose, a more exhaustive risk assessment should be carried out regardless of the type of genetic change.

Ethical justifiability should be assessed on the basis of four criteria: benefit, sustainability, fair distribution and transparency. This is further elaborated on in the Norwegian report. The intention is to have push-pull mechanisms to steer technology development in a sustainable and ethical direction. Thus, such an assessment can be used to set a minimum threshold for approval to ensure that no clearly unethical or unsustainable products reach the market. Also it can be used to identify particularly beneficial products that are eligible for positive incentives (described in more detail later). We place particular weight on animal welfare. We also recommend to align the ethical assessment with the EU sustainable food systems policy action that is expected later this year. Furthermore, any ban based on ethical grounds for imported products must be in accordance with international trade regulations (WTO).

Experimental release

We recommend to simplify the application process for experimental release even further. For regulatory level 1, a simple notification should suffice. At other levels differentiated, risk-proportional approval requirements based on data from studies under confined use should apply. Furthermore, experimental releases should be exempted from the ethical assessment since the necessary data for such an assessment may not have been generated as this stage. For example,

estimating the benefit of a product/organism will depend on data from the experimental release. For animal experiments, other animal welfare regulations apply.

Anticipated effects of the proposed model for developers / national bio-production

One of the biggest consequences of choice of regulatory system will be the costs for developers of new products. There will be implications both for the development itself and the approval process. Here we describe potential scenarios for the development of new crop varieties for the Norwegian market which is primarily undertaken by the partly state-owned plant breeding company Graminor. The costs are challenging to calculate precisely and will change over time, but the following description reflects an estimated cost level in 2023 at the time of publication of this report.

Access to gene-editing techniques will streamline the breeding/development process. Although it's hard to estimate precisely what it normally costs to develop a conventional crop variety (which will vary between varieties and depends on the number of varieties developed in a given year), Graminor estimates that it costs around 2-5 million Norwegian kroner (up to half a million EUR). With CRISPR, costs could be halved or more, because the development time is significantly reduced. Typically, it takes 10-20 years or more to develop a new variety with conventional crossbreeding. For instance, it took over 45 years to develop late blight-resistant potato varieties with conventional crossbreeding (Bionica and Toluca, introgression of one resistance gene Rpi)[22] [23].

With gene editing, a similar introgression of a resistance gene could take about 2-3 years if the genetic target sequences have been identified. If multiple resistance genes from different potato varieties or targeted mutations are introduced simultaneously, which can provide more lasting resistance, the relative difference in development time will increase even further.

Costs related to field trials of the varieties will also differ between the two regulatory scenarios. If a PB variety is classified as a GMO, as it is currently, the field trials must be conducted under special requirements (safety measures, etc.) that entail significantly increased costs. One case described in this report is the possibility of transferring a gene variant for short straws and increased straw strength into the wheat variety Mirakel. The gene variant is known from other wheat varieties. Field trials with gene-edited Mirakel varieties classified as GMOs will cost significantly more than field trials with conventional varieties, even though the gene variant and its trait/effect are the same. It is challenging to quantify costs precisely, as there has only been one field trial with GMOs in Norway for several decades, and experiences are limited. If PB varieties in experimental releases/field trials are exempted from GMO requirements, as they are in our proposal, the costs will be in line with the costs for conventional varieties, i.e. a few tens of thousands of kroners (a few thousand EUR) for a trial that runs over 2-3 seasons.

Regarding market approval, Graminor has estimated that the data package required at level 1 in our proposed model – PB variety with a history of safe use / familiarity – will cost a few hundred thousand kroner (a few tens of thousands of EUR), where the majority of the cost is for sequencing to map intended and unintended genetic changes. This cost will likely decrease over time as sequencing becomes cheaper. At level 2 – PB varieties with new traits that could have been obtained with conventional methods – there will be additional costs for field trials amounting to a few tens of

[22] https://link.springer.com/chapter/10.1007/978-3-030-28683-5_5
[23] doi: 10.1080/21645698.2021.1993688 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9208627/#cit0027

thousands of kroner. Therefore, at levels 1 and 2, the total approval costs could be expected to be under half a million kroner (up to around 50.000 EUR).

In contrast, the costs for a comparable market approval under today's regulations or any similar regulation would be in the order of at least tens of millions of kroner, probably more than 100 million kroner (more than ten million EUR). This is based on published analyses and reports: A study has estimated that the regulation of gene-edited crops as GMOs will require 9 additional years and 14 million dollars surplus before the product reaches the market, compared to if the crop was regulated as conventional[24]. Agrifood organisations have estimated that approval for GMO products for import into the EU costs between 11-16.7 million euros and that the processing time averages 6 years[25]. The costs for cultivation is likely even higher but there are very limited data on this in the EU.

Graminor has stated to us that if gene-edited/PB varieties are to be classified as GMOs, it will not be economically viable for them to use gene editing to develop products for the market, which would be the outcome if the current regulation prevails. Graminor would then have to rely on conventional techniques in the development of new varieties, for instance, late blight-resistant potatoes, when new strains of late blight emerge. With our proposal, PB is largely equated with conventional products, and it would be possible for Graminor to use gene-editing technology.

Differentiated requirements for market access after approval

Based on the principle of non-discrimination, we argue that PB products/organisms should be equated with conventional products when they reach the market. This involves no specific requirements for labelling, monitoring, traceability or co-existance measures, and intellectual property rights as conventional products. GMOs represent something novel compared to conventional products and should therefore, at least for the time being, be subject to GMO-specific requirements. These aspects are detailed in the following chapters.

Labelling

There are strict requirements that the labelling of food, feed, seeds, and other products should be accurate, provide sufficient information, and not mislead consumers. In this way, consumers are empowered to make informed choices, and a generally high level of consumer protection is ensured.

PB products/organisms should not be labelled as GMO, but equated with conventional products. We argue that this is important to avoid misleading the consumer when products are essentially the same. For instance, if genome editing has been used to increase the frequency of desirable gene variants / alleles in a breeding line, products that result from such organisms will be identical to those from non-edited individuals. Similarly, if a trait could have been achieved through crossing but has been introgressed faster by the use of cisgenetics, the resulting organisms/products should not be considered differently.

For GMOs, labelling will still be required. However, in order to ensure that the label is not misunderstood as a warning (GMOs are some of the most thoroughly risk assessed products available), and to ensure that consumers can make informed choices, we recommend some

[24] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6592640/
[25] https://www.embopress.org/doi/full/10.15252/embr.202154529

adjustments to the current labelling requirements for GMOs. Firstly, information such as expiration/best before date, nutritional content, and batch number should at least be as visible (color, size, location, etc.) as labelling related to country of origin, production method (organic, conventional, genetically modified, etc.) and other information not related to food safety, etc. Secondly, the labelling of a product as a GMO should include information about the purpose and method used in the genetic modification (mandatory, information linked to product approval), and that the product is approved for sale in the EU after a comprehensive assessment documenting the absence of health and environmental risks and sustainability/ethical defensibility. Other labelling that may be relevant to highlight specific characteristics must follow ordinary labelling requirements.

As a general reflection, GMO-labelling is in itself a barrier to innovation and adoption of the technology. This is due to a polarized debate that lacks nuance and is unfortunately based on lack of knowledge. This is further elaborated in the chapter on responsible communication and trust building further down.

Traceability

We argue that PB products should be subject to the current general, but strict, traceability requirements that apply to conventional products. This is justified by the intention to treat PB and conventional products equally, and also because requirements for analytical traceability through a validated and specific detection method cannot be met for all PB products. If the genetic change in a PB organism/product could have occurred naturally or developed through conventional methods, it will be technically very difficult or impossible to prove that it is made with genetic engineering. Two reports from the EU's reference laboratory for GM food and feed (JRC) and the European Network of GMO Laboratories (ENGL; the network of national GMO reference laboratories in Europe) point out that several countries outside the EU have chosen to define certain groups of products produced with genome editing techniques as non-GMO and exempt them from regulation. Such products will therefore not be labeled, and when imported into the EU/EEA area, there will be no information or definitive analysis method for detection. Therefore, neither importers nor national authorities will have realistic measures to determine if the product was produced with genetic engineering.

GMOs will still be subject to special traceability requirements according to current EU regulations. GMOs have one or more introduced sequence motifs that can be detected with a high degree of certainty.

Co-existence and production lines

The term "coexistence" is usually used in reference to regulations for cultivation of crops to ensure that those who grow conventional or organic plant crops do not suffer economic losses or experience other disadvantages due to contamination by GMOs in crops grown nearby. The same issue applies to all products that have specific requirements, e.g. meat and dairy from GMO livestock. Businesses must ensure that the entire production line, from raw materials and ingredients to the finished product for sale, is kept separate from conventional lines so that the specific requirements can be documented retrospectively.

We recommend that coexistence regulations should not apply to PB-products/varieties for the same reasons as described above: PB-varieties are comparable to conventional varieties in terms of traits that can be achieved through breeding, and in many cases, they probably cannot be detected and distinguished from equivalent conventional products. Furthermore, separate production lines that

would be required for GMO-labelling would result in significant economic and practical consequences for the entire value chain, as described in the following.

As described previously, a relevant case for Norwegian breeding is to use genome editing to increase the frequency of beneficial gene variants already present in existing breeding populations, to accelerate breeding progress and prevent inbreeding. In the Norwegian Red cattle, this includes genes for polledness (hornlessness) and two different beneficial milk protein variants. The combination of all three variants exists in very few animals and is therefore not easy to breed for. Using gene editing to increase the frequency results in animals that are identical to conventionally bred animals. However, if the current regulatory requirements persist, the gene-edited animals and the conventional animals must be kept completely separate. Meat and milk from the former must be labelled as GMOs, while the latter need not be labelled. This is particularly complicated for milk production, as milk from different animals/farms is usually mixed. If a part of the milk has to be labelled GMO while the rest does not, there must be completely separate production lines from farm to supermarket shelf. And one milk carton must be labelled GMO while another is not labelled, even though the contents is the same. The same applies to all other dairy products. Furthermore, gene-edited animals cannot be crossed with the conventional animals in further breeding if a completely "GMO-free" line is required. This means slower breeding progress in the conventional animals because the genetic variation/different allele combination frequencies will be much more limited. This difference will increase over time as knowledge of genetics/traits evolves and can be more quickly implemented in breeding programs with gene editing than conventional methods.

Another similar example from plant breeding is the potential gene-edited blight-resistant potato currently being developed by Graminor. Introduction of such potatoes into the supply chains while also maintaining "GMO-free" alternatives will require completely separate production lines, where one product variant is labelled as GMO and another is not. Graminor has also described to us how they may want to use gene editing to more quickly transfer beneficial traits from one crop variety to another much faster than by crossing. For example, the wheat variety Mirakel has good baking properties, but currently needs to be supplied with chemical straw shortener in the growth season to prevent straws from breaking. Other conventional wheat varieties have a mutation that gives short straws and therefore better straw strength, but it would be very laborious to cross this variant into Mirakel. With the help of gene editing, this mutation could be transferred to Mirakel more easily and efficiently than by traditional crossing. Even though the genetic change/mutation will then be identical in gene-edited Mirakel as in other conventional wheat varieties with short straws, the former - under current rules - must be labelled GMO while the others need not be labelled. If one wants to maintain a non-gene-edited line of Mirakel (with long straw), this must be kept completely separate from gene-edited Miracle (with short straw) in the entire production line. Grain or processed products from these two variants cannot at any time be mixed because one must be GMO-labelled and the other not.

Producers at various stages of the value chain tell us that it will not be economically and practically feasible to have such separate production lines. It is difficult to quantify exactly what costs and practical adjustments are needed, but all those asked say it will be very extensive and they find it hard to imagine that they can afford to have two production lines.

The Norwegian cattle breeding company Geno has communicated to us that if GMO requirements apply to gene edited animals, it would be practically and economically impossible for them to adopt gene editing technology. They have further stated in the media that if they cannot utilize gene editing, it could potentially weaken their competitiveness on the international market to such an extent that they would be unable to continue breeding work on the Norwegian Red Cattle. The pig

breeding company Norsvin and crop breeding company Graminor have also expressed their desire to access gene editing in order to maintain their competitiveness.

Given this situation, the reality is that very few products requiring GMO labeling and separate production lines will be feasible in Norwegian food production due to practical and economic considerations.

In our proposal approved PB products/organisms can be incorporated into the regular conventional production lines at no additional cost and without requiring special labeling.

We also argue that equating PB products with conventional products could make them suitable for organic food production, which currently prohibits the use of GMOs. We point out that many traits being developed through PB (gene editing), such as improved plant and animal health to reduce pesticide and antibiotic use, could be particularly beneficial for the organic sector.

Fast-track procedure for products/organisms fulfilling large, unmet needs

We propose that products that meet particularly large unmet needs, especially related to sustainable development, can be granted conditional approval based on less documentation than usual. This would apply to products on regulatory levels 2, 3 or 4 (level 1 products are comparable to existing conventional products and therefore not significantly more beneficial). Criteria for determining whether a product qualifies for such a fast-track procedure must be developed. Alternatively, or additionally, authority to make such classifications may be granted to a specific regulatory body. Criteria must be as predictable as possible. One option could be to link this assessment to the EU's sustainability criteria (pull mechanism).

We consider that assessment and approval of the covid vaccines are a good example of such a system in practice. The European Medicines Agency (EMA) conducted a "rolling review" of these applications, meaning they allowed the applicant to submit data and documentation during the application process, as all relevant documentation was not available at the time of submission of the applications. In addition, the vaccines were approved with a conditional marketing authorization. Conditional marketing authorization means that a medicinal product can be sold on the market as soon as sufficient but incomplete data is available that demonstrate that the benefits outweigh the risks.

In addition, the applicant is required to provide further data from ongoing or new studies within predefined deadlines to confirm that the benefits continue to outweigh the risks. A conditional marketing authorization has a duration of one year, with the possibility of renewal, and the product can be withdrawn from the market if any negative effects are documented. Some of the vaccines were also classified as GMOs, and clinical trials of GMO vaccines were in principle required to be approved under GMO regulations. However, because the benefits to society was so large, the vaccines were exempted to ensure a faster path to market.

We argue that the application process for GMO or PB products/organisms that meet large societal needs can follow a similar course as the conditional marketing authorizations described above.

Intellectual Property Rights and Patents

Intellectual property rights are of great importance for both innovation and access to innovations. On the one hand, they stimulate innovation by providing developers with possibilities to profit financially

from their inventions. On the other hand, however, they can lead to an increased degree of monopoly in the market, raise the prices of products, and limit access for other developers and society at large.

If a patent is to be claimed, the innovation must significantly differ from other products on the market. It must also be possible to prove such differences in order to enforce patent rights. Because our model equates PB with conventional breeding methods, PB products should not be eligible for intellectual property rights beyond what generally applies to conventional products. If a product gets an easier path to market on the basis of equality/non-discrimination with conventional products, the developer must also forgo potential benefits that come with rights based on novelty.

GMO products differ from conventional products and should therefore be considered as novel. This justifies a more extensive risk assessment, because there is more uncertainty about consequences than for conventional products. The novelty is also what justifies a patent. The ability to distinguish the product from other products, in the case of GMO by analytical detection methods, is also a prerequisite for the enforcement of patent rights. Such detection is not feasible for PB as previously described.

In conclusion, we argue that intellectual property rights should be differentiated between PB products/organisms and GMOs, where the former should only be granted IPR in line with conventional products whereas GMOs might justify a patent.

However, IPR frameworks are closely tied to international agreements and regulations and must therefore be harmonized with applicable rules at any given time. We recommend that differentiated intellectual property rights, according to the principles of our model, should be discussed in relevant international/EU fora.

Positive incentives to stimulate more sustainable and beneficial innovation and use of gene technology

Incentive Schemes

As previously described, we recommend that products expected to make a significant positive contribution to society may receive a so-called fast-track application process and possibly conditional approval with reduced requirements for documentation in an initial phase. There are also numerous other positive measures that can be used to stimulate beneficial innovation. This can be similar to the field of ‘orphan drugs’ – medicinal products for ‘unprofitable’ patient groups with a large unmet need – where a range of measures are used to incentivize developers. These incentives could, for instance, include extended scientific guidance for academic developers and small and medium-sized businesses. Another step could be to waive application fees, both for field trials and commercial purposes. Moreover, public procurement schemes can be used to prioritize particularly useful products, and dedicated funding schemes can be established for particularly useful projects.

The incentive schemes should, in addition to stimulating Norwegian/European research and innovation, be specifically targeted at developers from low-income countries. This could, for example, be gene-edited disease-resistant bananas from Uganda, gene-edited drought-resistant rice from India, or other products that can enhance food security and the economy of local farmers. In

2018, Canada[26] approved the import of Golden Rice - rice enriched with Vitamin A. The product was not commercially grown at the time, but Canada gave such a permit to pave the way for export to the international market. As of 2023, the rice is approved for cultivation in the Philippines. In similar ways, EU/Norway can help to pave the way for export from less privileged countries to develop their agriculture and strengthen their economy. A relevant case in the near future is gene-edited teff (*Eragrostis tef*) with short straws, which is being developed in a collaboration between American and Ethiopian researchers[27]. Teff is an important crop in Ethiopia and introducing gene variants for short straws can reduce waste by around 25% and thus strengthen food security. Teff and products made from the grain are sold in Norway/EU as an alternative to wheat because it is gluten-free and rich in fiber and other beneficial nutrients. If Norway/EU open their markets for products from this gene-edited variant, we can help to establish an export market for countries that cultivate it.

Responsible Communication and Trust Building

"Genetically modified organisms (GMOs) have become the target of a very intensive and, at times, emotionally charged debate," writes the United Nations Food and Agriculture Organization (FAO)[28].

We share this view and believe that this situation is largely due to the fact that the GMO debate is strongly marked by mistrust. We consider it a public responsibility to contribute to a knowledge-based debate and to build trust in science. Surveys show that knowledge about breeding in general, or gene technology more specifically, is low among the population. For example, 40 per cent of the respondents in a Norwegian population survey (2019)[29] on gene-edited food believed that it is more true than false that genetically modified tomatoes have genes, while ordinary tomatoes do not. Furthermore, 35 per cent believed it was more true than false that traditional breeding has nothing to do with genes. Only half had heard of gene editing at all. Such lack of knowledge is a significant challenge when discussing gene technology in society. An even bigger challenge is mistrust in science, which characterizes many areas of science. The climate debate has for years been marked by some groups not trusting scientific findings and this has delayed necessary political action. The same applies, for example, to the vaccine debate. Unfortunately, GMOs are also subject to significant mistrust. A study conducted by the PEW Research Center in the USA (2015)[30] shows that 88 per cent of scientists affiliated with the American Association for the Advancement of Science (AAAS) considered GMOs safe to eat, a view that was shared by only 37 percent of the general population. In 2020, exemptions from GMO regulations were for Covid vaccines classified as GMO, in order to ensure rapid access during the pandemic. The public consultation in Norway[31] generated more than 1800 responses, almost exclusively from vaccine-skeptical and GMO-skeptical individuals and organizations claiming that these vaccines were experimental and dangerous, especially because they were made with gene technology. The EU Commission public consultation on policy action for

[26] https://www.acsh.org/news/2018/03/17/another-win-golden-rice-canadian-government-approves-12714
[27] https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa_by_date/sa-2023/aphis-rsr-ddct-msls
[28] https://www.fao.org/3/i0110e/i0110e00.pdf
[29] https://www.bioteknologiradet.no/filarkiv/2020/04/Report-consumer-attitudes-to-gene-editing-agri-and-aqua-FINAL.pdf
[30] https://www.pewresearch.org/science/2015/01/29/public-and-scientists-views-on-science-and-society/
[31] https://www.regjeringen.no/no/dokumenter/horing-forslag-til-endringer-i-forskrift-om-nasjonalt-vaksinasjonsprogram-vaksinasjon-mot-covid-19/id2791196/?expand=horingssvar&lastvisited=undefined

plants produced with new breeding techniques (targeted mutagenesis and cisgenesis) similarly generated thousands of critical responses from large anti-GMO campaigns[32].

We are optimistic that a new and more knowledge-based and nuanced debate is dawning. In a series of public surveys from several countries in recent years, including Norway[33], Sweden[34], the United Kingdom[35] [36], and Switzerland[37], the results clearly show that most people are positive towards gene technology in food production, especially new techniques such as gene editing, if the purpose of its use is good.

The same nuances are needed in the political discourse. So far, Norway/EU has maintained a highly restrictive policy on gene technology. This in itself contributes to creating general skepticism and mistrust of genetic technology in the population, because it suggests that there must be something inherently problematic or risky about the technology, even though the scientific evidence indicates otherwise. We recommend that European and Norwegian policymakers change their narrative to better reflect our overarching goal: to ensure that gene technology is used for the maximum benefit of society and the environment.

[32] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12963-Revision-of-the-EU-general-pharmaceuticals-legislation_enec policy
[33] https://www.bioteknologiradet.no/filarkiv/2020/04/Report-consumer-attitudes-to-gene-editing-agri-and-aqua-FINAL.pdf
[34] https://www.genteknik.se/wp-content/uploads/2022/02/Svenskars-installning-till-genomredigering_2022.pdf
[35] https://royalsociety.org/~/media/policy/projects/gene-tech/genetic-technologies-public-dialogue-hvm-full-report.pdf
[36] https://www.food.gov.uk/sites/default/files/media/document/consumer-perceptions-of-genome-edited-food.pdf
[37] https://swiss-food.ch/files/213057_Genom-Editierung_gfsbern_Publ.pdf