Expert Opinion:
Evaluation of the European Commission's study on new genomic techniques

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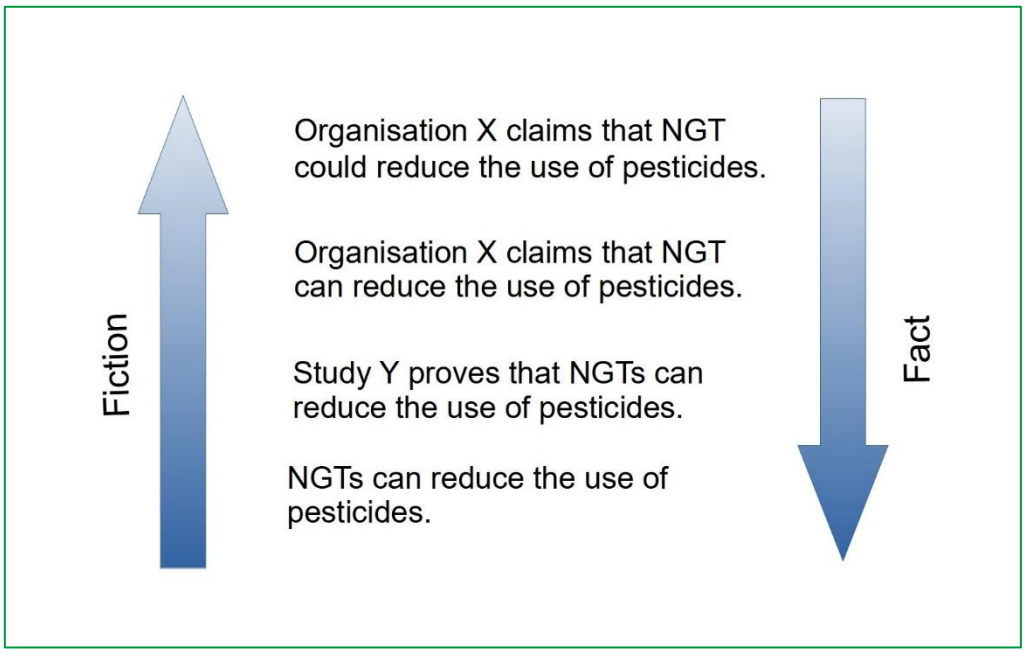

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Cover picture: Rhetorical strategy: Implicitly, some arguments are presented as more real than others. Own illustration, inspired by Latour 1987, p. 44.

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List of Abbreviations

Art.	Article
bng	team of authors (Bietergemeinschaft Neue Gentechniken)
CBD	Convention on Biological Diversity
cf.	compare (confer)
CJEU	Court of Justice of the European Union
COM	European Commission
COM study	European Commission (2021), see References
CRISPR/Cas	Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR associated
DNA	deoxyribonucleic acid
DSB	double-strand break
ECJ	European Court of Justice
EFSA	European Food Safety Authority
e.g.	for example (exempli gratia)
EGD	European Green Deal
EGT	established genomic techniques
ENGL	European Network of GMO Laboratories
ESA	European Seed Association
EURL	EU Reference Laboratories
ERA	environmental risk assessment
EU	European Union
fn.	footnote
JRC	European Commission's Joint Research Centre
GDO	gene drive organism
GMO	genetically modified organism
HT	herbicide tolerance
lit.	character (litera)
NGO	nongovernmental organisation
NGT	new genomic techniques
no.	number
ODM	oligonucleotide directed mutagenesis
p.	page

para.	paragraph
PEG	polyethylene glycol
R&D	research and development
RNA	ribonucleic acid
RTDS	Rapid Trait Development System
SAM HLG	Scientific Advice Mechanism High Level Group of Scientific Advisors
SDGs	sustainable development goals
SDN-1/-2/-3	side directed nuclease(s) 1/2/3
SMEs	small and medium-sized enterprises
TALEN	transcription activator-like effector nuclease
TEU	Treaty on European Union
TFEU	Treaty on the Functioning of the European Union
UN	United Nations
ZFN	zinc finger nuclease

Abstract

In April 2021, the European Commission published the “Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16” (COM study). First, the COM study is based on expert opinions and publications, e.g. two papers from the Joint Research Centre on market applications and technological development of NGT. Second, the COM study relies on two “targeted consultations” of stakeholders and Member States.

The present expert opinion evaluates the COM study and its supplementary material and examines whether the study argues consistently and whether the supplementary material is adequately considered. Based on this, options for action are discussed. The guiding principle of the present expert opinion is a high level of protection for the environment, human health, and consumer choice.

A main conclusion of the present expert opinion is that the COM study is not a study in the proper sense. There are several reasons for this. First of all, there are significant methodological weaknesses. The COM study does not systematically analyse the state of research, does not make transparent the criteria for evaluating the material on which it is based, but merely summarises it. Its conclusions appear arbitrary and not based on a systematic analysis.

The COM study does not comply with some of the Commission’s own standards. E.g. this refers to the selection of stakeholders who participated in the stakeholder survey. The Better Regulations Guidelines stipulate that stakeholders must be carefully selected to ensure that all interested parties have their views represented. However, proponents of NGTs are overrepresented in the COM study. The levels of the study's arguments are not clearly separated: statements and opinions by stakeholders and Member States are placed on equal footing with findings from empirical studies regarding these facts. The COM study does not make sufficiently clear how it deals with deviating views/statements/positions of Member States and stakeholders.

Essential special features of the NGTs are not dealt with, e.g. that NGTs can modify areas of plant genomes that are not accessible to other methods. Unintended effects of the NGT applications are also not sufficiently considered by the COM study – regardless of whether they result from intentional or unintentional changes.

The COM study pays particular attention to the question to which extent NGT crops can contribute to achieving the goals of the European Green Deal and related policies including the EU’s Biodiversity Strategy, the Farm to Fork Strategy and the UN Sustainable Development Goals. Several plant NGT products were identified that could contribute to the Green Deal and related policies, but all this remains at a hypothetical level.

From a regulatory point of view, the Deliberate Release Directive 2001/18/EC and the Food and Feed Regulation 1829/2003/EC are intended to be adapted by an amending regulation. The regulation type is obvious because the Commission wants to prevent different practices in the various Member States, which is best achieved by this legal act because it has direct effect in the Member States.

As a consequence of a possible deregulation, various concrete protected goods come under threat. These include for example the coexistence of GE free goods or certain ecologically

sensitive areas. Also, the polluter pays principle could be violated. Accordingly, the present expert opinion formulates options for action that focus on these protected goods.

Summary

In April 2021, the European Commission published the "Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16" as a Staff Working Document of the Directorate-General SANTE. The present expert opinion evaluates the study and the supplementary material which was published with the study on the Commission's website. The expert opinion examines whether the study argues consistently and whether the supplementary material and additional expert opinions were adequately considered in the study. Based on this, options for action are discussed.

The guiding principle of the present expert opinion in evaluating the COM study is a high level of protection for the environment, human health, and consumer choice.

The COM study is systematically evaluated according to the following subject areas:

- Implementation and enforcement of GMO legislation with regard to new genetic technologies
- Analysis of the current and future technical developments of NGTs
- State of the utilisation of new genomic techniques for agriculture, industry, and pharmacy
- Risk assessment of plants developed with NGTs
- Analysis of the ethical and socio-economic implications of new genetic technique

The details of the methodical procedure of the present expert opinion are laid down in its Chapter 2.

A main conclusion of the present expert opinion is that the COM study is not a study in the proper sense. There are several reasons for this. First of all, the methodological weaknesses are of significant importance for this conclusion. The COM study does not systematically analyse the state of research, does not make transparent the criteria for evaluating the material on which it is based, but merely summarises it. Its conclusions appear arbitrary and not based on a systematic analysis.

A first finding relates to the methodological approach of the COM study (Chapter 3.1 of the present expert opinion). The COM study is based on two different sources. First, it relies on expert opinions and publications (e.g., two papers from the Joint Research Centre, JRC, on market applications and the state of technological development of NGT). These are described and evaluated in the COM study. Second, the study relies mainly on two surveys ("targeted consultations") of stakeholders and Member States.

The present expert opinion criticizes the procedure for evaluating the scientific debate, because the **COM study does not systematically analyse the state of research**. Based on such a literature review, research needs and gaps could then be identified.

Furthermore, the present expert opinion evaluates the implementation of the targeted consultation of the COM study, as part of which questionnaires were completed by Member States and stakeholders on issues around NGT. These completed questionnaires served the COM study to a large extent as the basis for its argumentation. **The targeted consultations have a dual role in the COM study.** On the one hand, targeted consultations are participation processes within the framework of Better Regulation in the EU, which has certain principles that are set out in the Better Regulations Guidelines. On the other hand, as mentioned, they

serve the COM study as a source for its argumentation. Thus, they can also be considered and evaluated from the perspective of social science data collection.

The present expert opinion used both criteria and came to the following conclusions:

- **The COM study expanded its scope** and moved away from a discussion of the implementation of the current GMO regulation respective of the European Court of Justice ruling (Case C-528/16).
- The two questionnaires given to Member States and stakeholders differ slightly, and the COM study does not account for these differences. Unlike in other risk-benefit debates the term "risk" is not used by the COM study. In the wording of the COM study, "opportunities and benefits" are considered on the one hand, and "challenges and concerns" on the other. The term "risk" seems to be replaced by the term "concern". Thus, **scientific questions on potential risks and their evaluation are not directly addressed**.
- **The COM study does not comply with some of the Commission's own standards.** This refers to the selection of stakeholders who participated in the stakeholder survey. The Better Regulations Guidelines valid as that time (European Commission, 2017, p. 69) stipulate for such consultations that stakeholders must be carefully selected to ensure that all interested parties have their views represented. However, proponents of NGTs are overrepresented in the COM study.
- The COM study clearly **lacks the requisite transparency in several respects**, making it a challenge to reconstruct its results:
  - Although the study and the completed questionnaires were published, it is not clear whether all additional documents that were uploaded by the stakeholders and Member States have been made public (see section 3.1.2.2.4 "Lack of transparency" in the present expert opinion). Furthermore, there is no indication on the European Commission website that stakeholders and Member States attached additional documents to their completed questionnaires. Similarly, there is no indication that the Commission evaluated these supporting documents. Also, the additional material has not been cited in the COM study.
  - Across its numerous sections, the COM study does not indicate which questions in the questionnaire refer to which specific analyses. Therefore, the authors of this present expert opinion had to reconstruct which material was summarised by which section of the COM study in order to compensate for this intransparency.
- The COM study only summarises the material on which it is based (completed questionnaires, supplementary material among others). It is essential for scientific studies that the criteria or heuristics used to evaluate documents and questionnaires are made transparent. The COM study gives no, or only very few, references in this respect. The conclusions of the **COM study therefore appear arbitrary and not based on any systematic analysis**.
- The **levels of the study´s arguments are not clearly separated**; this specifically concerns the obligation to "distinguish evidence from opinion" (see European Commission, 2009, p. 20). Statements and opinions by stakeholders and Member States are placed on equal footing with findings from empirical studies regarding these facts. There is a crucial difference between an assertion that can be substantiated and an assertion that is a mere opinion. Justifications of assertions can be made in particular via scientific studies. By largely reflecting the responses of stakeholders and Member States in the targeted consultations,

the COM study is at the level of a public debate. Also, in reproducing the opinions expressed in the targeted consultations, the COM study treats some statements as if they describe reality, while others are treated as if they were only hypotheses or speculations of a few. For example, statements about the benefits of NGTs are presented as if they have already materialised. Concerns, on the other hand, are treated as mere opinions and invalidated by means of counter-arguments.

Regarding **implementation and enforcement of GMO legislation** concerning NGTs the COM study first gives an overview of the regulation of NGTs in 31 non-EU states. According to the study one third of those countries already have adapted their laws and even from the two thirds of countries who still regulate NGTs under general genetic engineering law, half of them discuss a specific legal framework for NGTs. So this overview gives the impression that the majority of countries want specific rules for NGTs. However, the Commission does not explain and makes transparent what the criteria for selecting only just those 31 countries were.

The mutagenesis decision of the European Court of Justice had to clarify whether targeted mutagenesis – as opposed to random mutagenesis – falls under the Deliberate Release Directive. The **court was clear in its finding that targeted mutagenesis does fall under the Directive** and is not exempted like random mutagenesis. The main reason for this was that, as opposed to random mutagenesis, there is so far no history of safe use for targeted mutagenesis. And if this is the case the precautionary principle demands that this technique falls under the Directive.

The present expert opinion examines how far the COM study considered important points of the ECJ's decision. The result was that **the COM study seems to interpret the decision of the European Court of Justice in a very narrow way and therefore not consistent with the central lines of the Court's reasoning**. These central lines of the reasoning were (*inter alia*):

- The precautionary principle is of particular importance and
- Article 3, paragraph 1 of the Deliberate Release Directive must be strictly interpreted.

In its decision in Case C-528/16, the ECJ had stated that directed mutagenesis processes ("new techniques/methods of mutagenesis") cannot be exempted from the obligations of the Deliberate Release Directive. In particular, the second central line of the argumentation of the ECJ – as mentioned above – leads, in the view of the present expert opinion, to the conclusion that **NGTs, which were not directly part of the proceedings before the ECJ, cannot be exempted from the obligations of the Directive either**.

All genetic engineering techniques developed after adoption of the Deliberate Release Directive in the year 2001 which do not show a history of safe use, must fall under the directive. Accordingly, the question arises as to how the COM study, for its part, interprets the wording of the Council of the EU: "a study in light of the ruling of the ECJ". For this purpose, the present expert opinion has also examined the passages in which the COM study refers to the ECJ ruling. Another misleading statement is that the term "mutagenesis" of the directive would need to be clarified. After all it was the ECJ who clarified this term in a way which cannot be clearer.

Regarding the implementation of the European genetic engineering law the **identifiability and traceability are controversial issues**. This point is important because a unique identification of each GMO is prerequisite for the authorisation of its products. The study gives the impression that this identifiability currently is not possible and also will not be possible. On this assumption the study draws the conclusion that as this is not possible the rules regarding

identifiability have to be discarded. However, there are strong signs that in future such an identifiability can be developed. In the meantime, document-based traceability systems can close the gap, as it is common in other regulatory systems. So the conclusion of the COM study that the lacking identifiability demands a waiver of those traceability systems, is not valid.

It is conspicuous that **the COM study does not or only very little deal with aspects which are legally mandatory when amending environmental law**. By far the most important principle when considering a deregulation of GMOs is the **precautionary principle**. It requires precautionary measures like risk assessment when, as it is the case with NGTs, the risks still are uncertain. The study nearly ignores this fundamental principle of European environmental law completely.

Equally relevant is that the **polluter pays principle**, which stipulates that the one who damages the environment has to be held liable for that, is not addressed. This would not be possible any more in case of certain forms of deregulation. The study does not address this important issue with one sentence.

A deregulation of NGTs also challenges **GMO-free agriculture** fundamentally, as this could undermine the European and national provisions to protect GMO-free agriculture and thus puts especially the organic sector at risk. This issue also was addressed only very limited without considering any legal aspects.

Not mentioned at all was the **protection of ecologically sensitive areas** and the exigencies of the Cartagena Protocol, which the European Union in its legislation has to comply with.

The present expert opinion **reveals a contradiction in the aim of the Commission** to secure the precautional principle at the one hand and in fact to lower the standards for certain NGTs, that can pose risks to human health and the environment.

The present expert opinion investigates the **current and future technical developments of NGTs** in the Commission's study. The COM study puts a lot of effort into placing NGTs in line with of other plant development techniques by emphasising similarities at the molecular level. The study states that the changes in the genome caused by NGTs are similar to those that can be achieved, for example, by means of non-directed mutagenesis techniques or cross-breeding. However, since the COM study only provides superficial descriptions of the changes and only makes isolated comparisons, its descriptions are not convincing. This is all the more true as it does not take into account essential special features of the NGTs. For example, **the COM study does not mention that NGTs can modify areas of plant genomes that are not accessible to other methods**.

Off-target changes and effects respectively are not adequately addressed by the COM study. The justification for this follows the assessments of EFSA, but it skips the positions of Member States and stakeholders – who partly favour the consideration of off-targets with respect to risk assessment. The reasoning is also irritating because the COM study does not consider the broad range of NGTs. It seems that due to the selection of specific molecular biological reviews, the COM study obtains a relatively broad evidence base for its argument, that off-targets in NGT plants and products are of the same type as in those obtained by other means. With regard to off-target changes, the COM study draws a comparison of NGTs with other techniques and procedures, for example, non-directed mutagenesis. The present expert opinion criticises this comparison as there are no off-target changes at all in the plants modified with non-directed mutagenesis at that certain time of the process, since all changes are

welcome. In this respect, it is also not as meaningful if NGTs cause fewer off-target effects than undirected mutagenesis as the COM study presents it. Unintended effects of the NGT applications are also not sufficiently considered by the COM study – regardless of whether they result from intentional or unintentional changes.

The COM study does not make it sufficiently clear **how it deals with deviating views/statements/positions of Member States and stakeholders**. This is unfortunate as such and also in terms of content. One stakeholder stated for example: "[A]ll genomic alterations or allelic combinations generated by CRISPR/Cas9 generally are identical to naturally occurring variations is a misleading oversimplification." The present expert opinion supports this argument, while the COM study writes in its conclusions (yet again): "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis" (p. 59).

As mentioned above **detection and identification** of NGT plants and products are a very special issue in the COM study. On the one hand, the COM study is not up to date with the current discussion. On the other hand it takes a **hesitant stance** when it comes to possible solutions. But – and this is to put it in a comparative perspective – when it comes to **the realisation of the potential of NGTs** to develop sustainable plants and products, the COM study is **very optimistic**. The methods to specifically detect and identify specific NGT products do currently not exist. Regarding the question, what possibilities exist to overcome the identified problems, the COM study does not come up with much. It notes that an amount of 5.7 million Euro was spent in five years for detection methods, risk assessment and monitoring distributed all over the EU alltogether. A rather small amount of money for a problem that has been known for years and that practically all Member States and stakeholders consider to be of central importance.

The present expert opinion examined the **representation of the utilisation of NGTs in the agri-food sector** in the COM study. The focus was placed on the agri-food sector because it was noted that the other sectors are not adequately covered by the COM study. Neither the JRC technical review of the use of NGT applications nor the COM study covers the full range of NGT applications, as claimed. Regarding the goals of genome editing in plants, the COM study found that "most traits under development relate to modified composition, biotic and abiotic stress tolerance, and plant yield. Similarly, beyond cereals and oil crops, there is a greater focus on vegetables, fruits and legumes" (COM study, 2021, p. 51).

The present expert opinion has made its own queries to an online dashboard that was made available by the authors of the supplementary material to the COM study (Parisi & Rodríguez-Cerezo, 2020). The results of these queries only partially support the information provided by the COM study. Notably, they do not reflect the relative importance of new traits which are designed to improve tolerance to abiotic stress. Herbicide tolerance, on the contrary, should have been classified by the COM study with a higher relative importance. The COM study pays particular attention to the question **to which extent NGT crops can contribute to achieving the goals of the European Green Deal**. The EU's Biodiversity Strategy, the Farm to Fork Strategy and the UN Sustainable Development Goals are also expected to benefit. The COM study states that Parisi & Rodríguez-Cerezo (2021) had identified several plant NGT products that ***could* contribute** to the Green Deal. In this context, the communication of EU Commissioner Stella Kyriakides is significant: At the day of the presentation of the COM study she already said that the NGT plant products ***can* contribute** to the Green Deal.

The extent to which crops with the above traits can actually contribute to the goals of the European Green Deal or the UN SDGs **cannot be answered blanketly**. Such an answer depends on numerous factors and can therefore only be assessed as part of a comprehensive case-by-case assessment. Unfortunately, the COM study does not provide any insight into concrete projects. A specific crop with a particular new trait is only identifiable as an absolute exception. Because the COM study refers only to the general statements of Parisi & Rodríguez-Cerezo (2021), even the statement that NGT plants could contribute to the goals of the Farm to Fork Strategy, the Biodiversity Strategy, and the UN SDGs has actually little substance. This is not surprising when considering the approach and the sources taken by Parisi & Rodríguez-Cerezo (2021). Over 40 percent of their data set (184 out of 426 plant projects) is from the private sector. Directly asking the developing companies is of course obvious because it seems to provide the greatest possible proximity to the source of the relevant information. However, there remains a relatively high degree of uncertainty, as the companies themselves are players in the debate over NGT regulation, which may lead some of them to make the outlook seem more optimistic in order to ensure a favourable regulatory environment. In addition, companies usually insist that the details must be treated as confidential business information. It would have been reasonable for Parisi & Rodríguez-Cerezo (2021), respectively the COM study, to critically reflect on the sources and their roles in the debate on the future regulation of NGT plants and products.

The COM study does not really take into account what experiences have been made with the commercialisation of GMOs. This applies to transgenic plants which are on the market for some decades as well as to the first commercialised NGT plants and products. The COM study either presents very little or outdated information. There is also nothing in the COM study about projects with NGT plants and products that were started but then cancelled. In the assessment of the present expert opinion, this could have been important information for the presentation of the possible future development of NGT plants and products.

In any case, it is noted that **the COM study only presents possible or potential, i.e. hypothetical contributions of NGT plants and products** to the above-mentioned policies.

Chapter 3.5 of the present expert opinion analyses the COM study with regard to the risk assessment of NGT plants and products. The COM study largely refers to a document prepared by EFSA (Paraskevopoulus & Federici, 2021) and to the responses of Member States and stakeholders to the targeted consultation. The present expert opinion identifies the following as the **central findings of the COM study on risk assessment**:

> "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59).

Certain aspects of this finding have already been criticised by the present expert opinion in the section on technology. These include, for example, the attempts of the COM study to present the molecular changes in the genome – caused by NGTs or arising by other means – as similar (see Chapter 3.3 above). Further on, the above results are not approved, because **the terms risk profile and risk level are used without clarifying what they actually mean. Another point of criticism is that the COM study does not consider environmental risks.** As shown in the present expert opinion, current research illustrates the relationships between intended and unintended changes or effects in the NGT plants and products with – for example –

ecological effects. The release of genetically modified plants into the environment can be associated with negative impacts on other organisms, biodiversity, and ecosystem services. Last not least the argument that risk profiles might be similar to conventional plant, can be questioned by itself, but more importantly does not exclude substantial risks, especially risks to the environment.

It is noteworthy that the only conclusion of the COM study regarding the case-by-case approach is that "[e]mbedding rigid risk-assessment guidance in legislation limits case-by-case assessment and makes it difficult to adapt risk-assessment requirements to scientific progress" (p. 59). This is especially important, since the case-by-case approach is currently used in the EU for the risk assessment of GMOs and has been demanded by Member States and stakeholders for the assessment of the risks of genome-edited plants and products. Thus, it remains unclear for the present expert opinion how the COM study comes to exactly this conclusion. From the substance of the COM study itself and from the relevant legal framework the conclusion cannot be derived in this way.

In the above-mentioned scientific report by Paraskevopoulus & Federici (2021), the authors summarise various reports and scientific opinions from the Member States and EFSA's own work. However, differences that may arise between the positions are not adequately taken into account – an observation made several times throughout the COM study.

The COM study does not raise the question of how much and what information is needed for a risk assessment. At the same time, it states for example that ODM – among other techniques – does not lead to new risks in connection with off-target effects. It also states that less information is available on this technology. An examination by the present expert opinion revealed that just one single scientific paper formed the basis of the assessment by EFSA and the COM study – far too little to be able to comment in a qualified manner.

The present expert opinion also analysed whether the deregulation of certain NGTs is compatible with the exigencies of the European engineering law regarding risk assessment. In doing this the overall approach was a different assessment regarding complete or partial deregulation. As it seems to be the intention of the Commission that certain NGTs should be deregulated by law the starting point was, that this can only be legal if the deregulation itself lives up with the requirements of the European genetic engineering law regarding risk assessment. The result of the analysis was that this for a number of reasons is not the case. For instance, a broad release into the environment only is legal after an examination of the indirect or delayed adverse effects and the cumulative long-term effects. Both is not possible at this stage as there is nearly no experience with cultivation regarding those NGTs. Further a central principle of risk assessment, the case-by-case principle, is infringed by deregulating whole groups of NGTs without looking at each single event. Regarding food and feed toxicological studies are required which also have not been conducted so far.

If all those requirements of the European genetic engineering law regarding risk assessment are not addressed and the marketing of such products without risk assessment is allowed, the precautionary principle at least demands a post-market monitoring of those products as a compensation. But even this is not intended.

Chapter 3.6 of this present expert opinion analyses the **ethical and socio-economic implications of NGTs** in the COM study. These topics are dealt with in the COM study in chapters 4.6 to 4.11, but no statements are made there at the substantive level. The COM study only

reflects the statements of the two targeted consultations – the stakeholder consultation and the consultation of the Member States.

Practical problems were only touched on and not discussed. One focus of the COM study was, for example, the impact of NGT on SMEs. This question could not be answered with the methods used; rather, a need for further research was identified. Secondly, the COM study avoids talking about risks. Instead of using the term "risk" and contrasting it with certain benefits, the **study redefines the positive and negative aspects of a technological application**. On the other hand, it lists "challenges and concerns". It can be shown by the present expert opinion that "challenges" means not only the possible negative consequences for health, the environment and the economy, but also obstacles to the realisation of benefits. For example, in one of its sections (COM study, section 4.7), the COM study mentions negative impacts on biodiversity and ecosystems as an NGT-related concern. Without a transition, obstacles to the realisation of the technology are discussed. This conflates problems of technology users with problems of those affected by a technology application. A final problem is the view of the consumer. In the COM study **citizens are viewed as consumers**. Consultation processes, surveys and citizen dialogues are explicitly seen as procedures to gain acceptance by the consumers and in public debate and not as part of a democratic participation process.

Another important drawback is that the **COM study does not move from the presentation of the arguments to the central problems at the substantive level**. For example, stakeholders express specific problems and challenges in dealing with NGT plants and products in their responses in the targeted consultations. The COM study presents the challenges and problems with NGT plants and products via the stakeholder survey. However, for each of these problem areas, there is also a scientific debate that is not addressed in the COM study. Within the scope of the present expert opinion, neither a systematic evaluation of the completed questionnaires nor a systematic review of the scientific debate was possible. This would have been a task of the COM study.

An examination and evaluation of proposals for a potential new regulation of NGTs only can be made if precise proposals in form of drafts are presented. As this so far is not the case, it first is necessary to sift through the circulating documents of the EU-Commission for clues in which direction the reform could go. In the discussions (COM study, 2021, Chapter 5) and even in the conclusions (COM study, 2021, Chapter 6) of the study itself, there are only a few tangible concrete proposals. Apart from that one finds only generalities such as the formulation: "any future measures (as requested by the Council) should address how they should be interpreted and implemented in synergy" (COM study, 2021, p. 57).

Looking at one of the main causes of the Commission's communication, which is the maintaining of the competitiveness of the European biotech industry (COM study, 2021, p. 51) one cannot escape the impression that the Commission considers the current NGT regulation not fit for the interests of the biotech industry. The same is true for emphasising the alleged benefits of NGTs regarding the European Green Deal, sustainable agriculture and the UN sustainable development goals (COM study, 2021, p. 59). With the latter, the Commission is adopting the biotech industry's promises without any critical appraisal. If this suspicion of being too close to industry were true, it would be a serious violation of the EU Commission's duty of neutrality as a state institution. The reform process would then be burdened with a mortgage from the outset. In two places does the COM study at least hint at the direction it wants to take. For example, it reads "Embedding rigid risk-assessment guidance in legislation limits case-by-case assessment" (COM study, 2021, p. 59). This formulation can only be understood

as meaning that the application of the current rules on risk assessment tends to result in a violation of the case-by-case principle and – taken further – that risk assessment for NGTs must therefore be scaled back. The case-by-case principle is thus used as an argument for the alleged need for less rigid risk assessment regarding NGTs. However, this turns the case-by-case principle of the European genetic engineering law on its head. According to this "an environmental risk assessment should always be carried out in each individual case". If – as the Commission wants – the requirements for risk assessment are to be reduced across the board for certain NGTs, the case-by-case principle is violated, as it requires an assessment of each individual event. This statement in the COM study is therefore inconsistent and telling at the same time. At any rate it cannot be used as a justification for deregulation. Although the Commission will not make a concrete proposal until the second quarter 2023, the broad outlines can already be seen from the above mentioned statements.

From a regulatory point of view, there are many indications that both the Deliberate Release Directive 2001/18/EC and the Food and Feed Regulation 1829/2003/EC are intended to be adapted by an amending regulation. The regulation type is obvious because the Commission wants to prevent different practices in the various Member States (European Commission, 2021b), which is best achieved by this legal act because it has direct effect in the Member States. In the case of an amendment in form of a directive, the Member States could still have legal leeway in implementation. Furthermore, the fact that the Commission uses terms like "mechanisms for rapid adaptation to technical progress" (European Commission, 2021b) speaks much in favour of the Commission envisaging a two-step procedure. This means that it first wants to be empowered for the issuing of implementing acts and then make the actual changes on this basis in the comitology procedure. It could therefore be that the reform proposal announced for the second quarter of 2023, which is very much in the political spotlight, will not itself bring the substantial new rules in terms of content.

In terms of content, everything speaks for deregulation of certain NGTs. How far this will go in detail is not yet clear. Central statements, which run through both the COM study and the Inception Impact Assessment (European Commission 2021b) in numerous places, speak of certain forms of genome editing like SDN-1, SDN-2 and cisgenesis being classified just as safe as plants bred using conventional methods. This suggests complete deregulation.

As a consequence of a possible deregulation, various concrete protected goods come under threat. These include for example the **coexistence of GE free goods or certain ecologically sensitive areas**. Also, the **polluter pays principle** could be violated. The present expert opinion analyses the corresponding challenges on the basis of two possible scenarios: partial and complete deregulation. Generally, for each of those issues the first and foremost cause is to prevent as much as possible complete deregulation. The retaining of the rules on identification and traceability is of utmost importance for the polluter pays principle, securing of coexistence and the protection of ecologically sensitive areas. For the latter compensatory amendments in European and national nature protection law and in the Environmental Liability Directive should be considered. Very important for the GMO-free agriculture is to make sure that any amendment of the European genetic engineering law does not deprive the Member States from protecting GMO-free agriculture, not only against classical GMOs but also against NGTs. From a regulatory point of view the Commission should be prevented from empowering itself to far-reaching implementation measures behind closed doors.

Consequently, the present expert opinion formulates the following options for action:

Overarching aspects

Generally, there should be a three-tier approach: In the first place avoiding complete deregulation. In a second place looking which partly regulation could be tolerable and which not. As fall-back option compensatory amendments in other areas than genetic engineering law should be considered.

Ensuring identifiability and traceability

It has to be stressed in the public debate, that the claim of the COM study, even in future there would be no chance of unique identification of NGTs is wrong and thus does not support an abolishment of identification rules and other deregulation pushes.

Securing the polluter pays principle

Identification and traceability provisions are of utmost importance for the polluter pays principle and therefore have to be maintained. Additionally, the Environmental Liability Directive should be adapted in a way that it covers also NGTs.

Preservation of the coexistence principle

Depending on the extent of the deregulation it should be made sure that the current empowerment of the Member States to protect GMO-free agriculture will not be undermined by the amendment.

Compliance with the Cartagena Protocol

The Cartagena Protocol (CP) does not foresee an exemption for NGTs and thus prescribes a risk assessment not only for classical GMOs but also for NGTs. Therefore, in case of a watering down of risk assessment rules, it should be pondered a legal proceeding before the ECJ to review the compliance of the amendment with the CP.

Protection of ecologically sensitive areas

Depending on the extent of deregulation compensatory protection provisions should be considered to maintain the protection of ecologically sensitive areas. This should be done both on the level of the European Union and on the federal and state level of Germany.

Halting the loss of biodiversity: sustainable agricultural practices and natural restoration

According to the EU Biodiversity Strategy for 2030 the transition to fully sustainable practices in agriculture should be conducted. Therefore, it should be made sure that the planned amendments are designed in such a way that they do not conflict with the goal of halting biodiversity loss through sustainable land management. Beyond that the potential conflict with the Biodiversity Strategy should be placed more in the focus of public debate.

1 Introduction

In the European Union, genetically modified organisms are regulated by the EU Deliberate Release Directive.[1] The techniques used to genetically modify organisms have evolved considerably since this Directive came into force in 2001; they are grouped under the term "New Genomic Techniques/New Genetic Technologies" (NGTs).

On 25 July 2018, the European Court of Justice (ECJ) ruled in case C-528/16 that plants produced using directed mutagenesis which is categorised as an NGT – are covered by the provisions of the EU Release Directive. Through its Decision (EU) 2019/1904 of 8 November 2019,[2] the Council invited the EU Commission to prepare a study on the state of NGT in light of this ECJ ruling, within the framework of Union law[3], and propose a course of action if necessary. This Commission's study was published on 29 April 2021 (European Commission, 2021).

The Commission's study contains statements to a range of issues, namely on the status of implementation and application of GMO legislation, on organisms developed by means of NGTs for agriculture, industry and pharmaceuticals, an overview of the risk assessment of plants developed by means of NGTs, on the current and future developments of NGTs, and on ethical and social aspects of genome editing. The results of a targeted consultation of EU Member States and stakeholders are also part of the study.

The Commission's study has been heavily criticised from various sides. In addition to the accusation of an "industry-biased" selection of the interviewed stakeholders, the EU Commission's study on new genetic engineering methods has been criticised in particular for being "unscientific and influenced too strongly by industry interests".[4] There are clear indications that the study seeks to "set certain political accents beyond balance" (Spranger, 2021).

Against this background, the aim of the present expert opinion is to assess the Commission's study, the documents on which it is based, and the consistency of its arguments. In this evaluation, the COM study's arguments are compared to additional material, put in the context of the current public debate, and weighed against a survey of selected experts. Furthermore, the present expert opinion examines to what extent the maintenance of a high level of protection for the environment, human health, and consumer choice are addressed by the Commission's study. Based on the results of the foregoing analyses, options for action concerning NGTs are then presented.

The impetus for the present expert opinion came from the Federal Agency for Nature Conservation (Germany). We would like to thank the working field of "Assessment of Genetically Modified Organisms/Enforcement of the Genetic Engineering Act", and in particular Dr. Wolfram Reichenbecher for expertise and kind cooperation. We would also like to thank the workshop participants, such as the interview partners for contributing their expertise. Thanks also to Dr. Joshua Rahtz, who supported the team with the English translation in the meantime.

[1] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC, OJ L 106, 17.4.2001, p. 1.

[2] Council of the European Union, 2019.

[3] Directive 2001/18/EC, Regulation (EC) No 1829/2003, Directive 2009/41/EC and Regulation (EC) No 1830/2003.

[4] E.g. Deutscher Naturschutzring (2021).

2 Methodical procedure of the present expert opinion

The present expert opinion evaluates the "Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16". The study was published by the European Commission in April 2021 as a Staff Working Document of the Directorate-General SANTE (European Commission, 2021).[5] The guiding principle for the present expert opinion is a high level of protection for the environment, human health and consumer choice.

Based on this focus the central questions are:

- Is the study consistent?
- Are the supplementary material and additional expert opinions adequately considered in the study?
- What options for activity are there for BfN considering its tasks and current publications on NGTs?

In order to answer these questions, the relevant parts of the COM study are systematically considered and summarised according to the following subject areas and chapters of the present expert opinion:

- Implementation and enforcement of GMO legislation with regard to new genetic technologies (Chapter 3.2)
- Analysis of the current and future technical developments of NGTs (Chapter 3.3)
- State of the utilisation of new genomic techniques for agriculture, industry, and pharmacy (Chapter 3.4)
- Risk assessment of plants developed with NGTs (Chapter 3.5)
- Analysis of the ethical and socio-economic implications of new genomic techniques (Chapter 3.6)

In each subject area (section 3.2 to 3.6), parts of the COM study were analysed. The following questions were central to the analysis from each subject area perspective:

1. What are the new or known outcomes and challenges of the COM study?
2. How well researched and well-founded are the results, analyses and challenges presented in the Commission's study?
3. What are the current issues and challenges in dealing with the ECJ ruling in the fields of society, technology, economy, environment, politics and ethics, and to what extent were these examined and taken into account by the COM study?

The expert opinion was prepared in three work packages (WP):

WP 1: In the first work package, the COM study and the corresponding supplementary material were analysed according to the above-mentioned framework conditions (essentially Chapter 3 of the present expert opinion*)*. In the context of this work package, additional material

[5] European Commission (2021) is cited in what follows as the "COM study". When referring to this document in the text, the present expert opinion also uses the term "Commission's Study".

from the public debate was also consulted and expert interviews were conducted by the authors of the present expert opinion.

WP 2: The second work package analysed the challenges in dealing with NGT and examined proposals for action from the political and public discourse. A key criterion was a high level of protection for the environment and human health, as well as ensuring consumer choice. Due to the lack of concrete reform proposals in the COM study, the present expert opinion has identified challenges and measures (Chapter 4). The results of the study were discussed with experts in a workshop organised as part of the project. The main points from this workshop were integrated into the present expert opinion.

WP 3: Options for action (Chapter 5). Following the evaluation of the Commission's study in WP 2, various options for action were presented to and discussed with the BfN at a working meeting against the background of its tasks, previous activities and current positions on new genetic engineering. This was intended to support the BfN in the discussions in the EU on how to deal with the ECJ ruling.

Various sources were consulted for the preparation of the present expert opinion. The main source of course was the COM study itself. In addition, the following material was considered:

Supplementary material and expert opinions: The expert opinion reviewed the additional material and expert opinions that were mainly referred to in the COM study. An overview of this material, which includes the completed questionnaires[6] of the targeted consultations, is listed in Table 3 and in the COM study.[7]

Statements from the public debate: Furthermore, additional material from the public debate on NGT and the ECJ ruling, such as NGOs, was consulted. For this reason, position papers from research institutions and NGOs were collected and reviewed with regard to their substantive issues. They were evaluated in more detail where it was helpful for an understanding of the issues raised in the COM study. A systematic analysis of the public debate was not the task of the expert opinion.

Expert interviews: Expert interviews were conducted at the end of WP1 as part of the present expert opinion. The expert interviews served to critically examine the results of the expert opinion with regard to their validity. The expert interviews were conducted as problem-centred interviews. This form of interview confronts the interviewee with a specific problem defined by the interviewer and allows the interviewee to discuss this problem in the course of the interview (see Spöhring, 1989, p. 177 ff.). A summary of the results of the analysis, thematically adapted to the interview, was provided as input for the discussions where appropriate.[8] Various experts were interviewed on each of the thematic areas. The selection was made in consultation with BfN. Thematically overarching questions of the expert interviews were: Which sources are used in the Commission's study and which are omitted? Were arguments from the public and scientific debate taken into account or not taken into account by the

[6] Online: https://ec.europa.eu/food/plants/genetically-modified-organisms/new-techniques-biotechnology/ec-study-new-genomic-techniques/stakeholders-consultation_en.

[7] Supplementary material as listed in the COM study (p. 116) and further documents (see Table 3, chapter 3.1.1.2 below).

[8] Partly interviewed experts had also published scientific papers or other documents, that might have been quoted in the course of the present expert opinion.

COM? The interviews were recorded, anonymised and transcribed (for details regarding the interviews see Table 1).

Workshop: An expert workshop was organised to validate the results of WP 1 and WP 2. This one-day workshop, conducted in presence, focussed on central results of the evaluation and the options for action derived from them.

Table 1: List of expert interviews conducted (with video conference tools) in the course of the present expert opinion.

Interview number	Interviewee (working context, field of work)	Date
#1	Scientist; published peer reviewed articles and reviews on NGTs	8 April 2022
#2	NGO staff, EU NGTs	12 April 2022
#3	Competent authority EU Member State	13 April 2022
#4	Scientist; academia	27 April 2022
#5	NGO staff, EU NGTs	28 April 2022
#6	NGO staff, EU NGTs	12 May 2022
#7	Scientist; academia	22 April 2022
#8	Scientist; academia	7 August 2022

All four authors form the team (bng) that jointly prepared and is responsible for the present expert opinion. Each of them is focused on a respective subject area and topic. These were based on their professional background:

- Christof Potthof, biologist: new genomic techniques, European GMO debate, risk assessment.
- Birgit Peuker, sociologist: ethical and social as well as socio-economic dimension, analysis of the methods of targeted consultations.
- Christoph Palme, lawyer: regulatory framework.
- Anke Schumacher, biologist: nature conservation issues.

Lead authors were appointed especially for the chapters regarding the methodological approach of the COM study, the subject areas, WP2 and WP3 of the present expert opinion. The lead authors were supported by the team (bng), see Table 2.

It was also useful to write thematically comprehensive joint chapters to the above questions:

“How well researched and well-founded are the results, analyses and challenges presented in the Commission’s study?” (second question).

This is dealt with in:

- Chapter 3.1 “General evaluation of the COM study’s methodological approach” and

- Chapter 3.8 “Evaluation of the overall structure and argumentation of the COM study”.

“What are the current issues and challenges in dealing with the ECJ ruling in the fields of society, technology, economy, environment, politics and ethics, and to what extent were these examined and taken into account by the COM study?” (third question).

This question is dealt with in for example:

- Chapter 3.7 “Considering of ECJ-Judgement C-528/16” and
- Chapter 3.5.3.1 “Environmental risks”.

Table 2: Lead authors for selected chapters of the present expert opinion.

Chapter	Lead	Support
Chapter 3.1: General evaluation of the COM study’s methodological approach	Peuker	rest of the bng team
Chapter 3.2: Implementation and enforcement of GMO legislation with regard to NGTs	Palme	rest of the bng team
Chapter 3.3: Current and future technical developments of NGTs.	Potthof	rest of the bng team
Chapter 3.4: State of the utilisation of NGTs in the agri-food sector	Potthof	Schumacher, rest of the bng team
Chapter 3.5: Risk assessment of plants developed with NGTs	Potthof/Palme	Schumacher, rest of the bng team
Chapter 3.6: Ethical and socio-economic implications of new genomic techniques	Peuker	rest of the bng team
Chapter 4: Challenges and measures	Potthof/Palme	rest of the bng team
Chapter 5: Options for action	Potthof/Palme	rest of the bng team

The basis for the various chapters of the COM study is very heterogeneous. Thus, the material on which the study is based, such as supplementary material, further documents, published and unpublished research papers of the COM study, was referenced and evaluated section by section. That is, in some chapters the presentation was based on a lot of material, in others on less (see also Table 5 in Chapter 3.1.1.2.1). This has resulted in the present expert opinion treating the respective representations in the subject areas differently. It also means that for each substantive chapter a specific and appropriate approach was chosen.

During the initial research on the analysis of the COM study and its supplementary material, it became clear that the COM study did not fulfil the requirement of a comprehensive treatment of the various organism groups (animals, microorganisms) and health applications respectively. It is also important to note that EFSA has not yet assessed the safety of “targeted mutagenesis and cisgenesis beyond plant applications, nor the safety of other techniques”, i.e. until the COM study is published in April 2021 (European Commission, without date, b). In addition, the EU Commission plans for “animals and microorganisms, or other new genomic techniques” continues to build up “scientific knowledge” (European Commission, without date, b). For these reasons, the present expert opinion has focused to a large extent on NGT plants and products. The other organism groups and the health applications are only considered in exceptional cases (e.g. see Chapters 3.4.1.2 to 3.4.1.4 below).

All completed questionnaires were reviewed during the preparation of the present expert opinion. However, a systematic evaluation could not be carried out here. It also became clear

that the reproduction of statements from the target consultations are important sources for the COM study. These statements are expressed from the perspective of the Member States and stakeholders. It often remains unclear whether they are merely assertions or substantiated statements. The present expert opinion therefore analyses not only the procedure of the target consultations,[9] but also how the COM study dealt with the statements. The procedure was as follows:

- The individual statements were marked (coded).
- For each identified statement, it was determined how often the statement was made in the questionnaires of the stakeholder survey and the survey of the Member States according to what the COM study indicates.
- It was also observed – only in the stakeholder survey – what the COM study indicated from which group the statement was voiced (for example NGOs, academics, GM-free sector).
- Furthermore, it was examined how the statement was then presented in the concluding chapters.

The analyses of how the statements are handled can be found in the respective thematic sections 3.2 to 3.5 under the subheading "Stakeholder and Member State views on [subject area]". For the socio-economic and ethical aspects, the analysis can be found under the subheading "New or known outcomes and challenges" (section 3.6.1). A summary of the analysis of the presentation and evaluation of the targeted consultations in the COM study can be found in Chapter 3.8 "Evaluation of the overall structure and argumentation of the COM study" in this present expert opinion.

[9] See Chapter 3.1 "General criticism of the Commission's study methodological approach" below.

3 Analysis of the Commission's study (Work Package I)

3.1 General evaluation of the COM study's methodological approach

Section 3.1.1 "Design and structure of the COM study" of this chapter discusses the methodological approach of the Commission's study. The discussion is followed by section 3.1.2 "Evaluation of the methodological approach of the COM study" evaluating the approach. Also, this section provides additional information and contextualises the study.

The document has 6 chapters, including an Executive Summary. The document is divided into an introduction ("Background and objectives of the Commission study on new genomic techniques") and a methodology section ("Methodology of the Study"). These sections are followed by the text's principal component, which describes the results of the study in detail ("Status of genomic methods under EU law"). The study closes with two chapters "Discussion" and a short conclusion ("Conclusions"), followed by an annex comprised of several tables (Chapter 7), and a listing of supplementary material accessible via hyperlinks (Chapter 8).

3.1.1 Design and structure of the COM study

3.1.1.1 Objective of the COM study

The European Commission's "Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16" was prepared at the request of the Council of the European Union. In its study, the Commission expands on the subject matter indicated by the Council's request. The Commission's study includes broader policy objectives such as the European Green Deal and the Farm to Fork Strategy, among others (COM study, 2021, p. 6). The COM study justifies its approach by referring to the request of the Council. The Council's request encompassed various areas in the application of NGTs for plants, animals and microorganisms, and did not limit itself only to practical questions:

> "While the CJEU [10] ruling focused on new mutagenesis techniques, the Council's request was broader and referred to new genomic techniques in general. […] In line with the above, the objective of this study is to provide clarity on NGTs, in the form of updated and comprehensive information, on a broad variety of topics and assist in deciding, if appropriate, any further action in this policy area" (COM study, 2021, p. 6).

This approach has been criticized by other stakeholders and is discussed later in the present expert opinion.[11]

3.1.1.2 Methodology of the COM study

The COM study presents its methodological approach in Chapter 3, "Methodology of the study" (see COM study, 2021, p. 7ff.). The study indicates that it relies on two separate sources. It is firstly based on expert opinions and publications, which are described and evaluated; for example, two papers of the Joint Research Center (JRC) on market applications and the state of technology development of NGT. Secondly, main it draws on two surveys ("targeted consultations"). Most of the topic-specific sections of the COM study present the outcomes of the two targeted consultation surveys.

[10] Court of Justice of the European Union (CJEU), "ECJ" (European Court of Justice) in the course of the present expert opinion.

[11] See section 3.1.2.2.1.

3.1.1.2.1 Supplementary material, expert opinions and additional material used by the COM study

The COM study requested supplementary material from EFSA and the European Commission's Joint Research Centre; the material is compiled and listed in section 8 of the COM study ("Supplementary material"). The list also includes stakeholders' and Member States' replies to the targeted consultation.

The COM study also evaluates expert opinions. These are listed on the Commission study's website.[12] Furthermore, the COM study uses other publications not included in the listings of Chapter 8, such as the 2019 Eurobarometer or the evaluation of the EU legislative framework in the field of GM food and feed, compiled by the Food Chain Evaluation Consortium in 2010 (FCEC, 2017). Last but not least, original research was carried out as part of the COM study, e.g. conducted by the Commission's Directorate-General for Research and Innovation (DG RTD).

An overview of the various material used by the COM study is compiled in the following Table 3.

Table 3: Material used by the COM study.

Abbreviation in the COM study	Title	Content	Abbreviation in the present expert opinion
Supplementary material			
	Member States' and stakeholders' replies to the targeted consultation.	Original replies within the questionnaires of the targeted consultation; short presentation of the respective organisation; sectors of activity/fields of interest of the association (stakeholder only).	
JRC/JRC review	Current and future market applications of New Genomic Techniques – JRC Science for Policy Report.	Evaluation of market approvals and pipelines by Parisi & Rodríguez based on own research on the applications of the NGT.	Parisi & Rodriguez-Cerezo, 2021 (JRC market review)
	Current and future market applications of New Genomic Techniques – JRC Science for Policy Report – web dashboard.	Dashboard based on a database of Parisi & Rodríguez-Cerezo; adapted queries possible.	Parisi & Rodríguez-Cerezo, 2020
JRC/JRC review	New Genomic Techniques: State-of-the Art Review. JRC Technical Report.	Systematic literature review using online scientific databases.	Broothaerts et al., 2021; JRC (technical review)
EFSA	Overview of EFSA and national authorities' scientific opinions on the risk assessment of plants developed through New Genomic Techniques.	EFSA provided an overview on the risk assessment of plants developed using NGTs, taking into account its own scientific opinions and those from Member State competent authorities and national institutions, as published since 2012; no critical appraisal of the Member State scientific opinions.	Paraskevopoulos & Federci, 2021
Expert opinions			

[12] European Commission (without date, a).

Abbreviation in the COM study	Title	Content	Abbreviation in the present expert opinion
SAM HLG	New techniques in agricultural biotechnology. High Level Group on Scientific Advisors. Explanatory Note 02/2017.	Explanatory note on NTG in agricultural biotechnology (plants, animals, micro-organisms), comparing NGTs with conventional breeding techniques and established genomic techniques (precision, efficiency, detectability, cost and speed of product development).	SAM HLG, 2017
EURL/ENGL	European Network of GMO Laboratories (ENGL): Detection of food and feed plant products obtained by new mutagenesis techniques.	EU Reference Laboratory (EURL), together with the European Network of GM Laboratories (ENGL) compiled (after request of the European Commission in 2018) "a report on the possibilities and limitations of analytical detection methods, in particular: – whether and under what conditions current analytical possibilities allow detection and quantification of all types of mutagenesis events and other new breeding techniques (NBTs); and – if not, what possibilities exist to overcome any issues identified " (COM study, 2021, p. 25).	ENGL, 2019
EGE	Ethics of Genome Editing.	Discussion of the ethical aspects of NGT with respect to our understanding of humanity, naturalness and diversity in general. Detailed ethical analyses of the most important areas of application such as genome editing in humans, animals and plants as well as gene drives.	EGE, 2021
Additional material			
Eurobarometer 2019		Food Safety in the EU. Survey requested by EFSA.	Eurobarometer, 2019
	Own research of the COM study.	NGT legislation in non-EU countries.	
	Own research of the COM study, conducted by the Commission's Directorate-General for Research and Innovation (DG RTD).	Analysis of EU funding for NGT-related projects.	
	Evaluation on behalf of the COM.	Evaluation of the EU legislative framework in the field of GM food and feed Framework.	FCEC, 2010
	Evaluation on behalf of the COM.	Evaluation of the EU legislative framework in the field of cultivation of GMOs.	EPEC, 2011

3.1.1.2.2 Targeted Consultations

The COM study relies on two surveys (or targeted consultations) for one of its main sources. One survey targeted Member States, while a second focused on stakeholders. These surveys were carried out using questionnaires comprised of open questions. Member States and

stakeholders used text boxes in their responses, each limited by the number of characters. The completed questionnaires are published on the European Commission study website.[13]

Survey of Member States: 27 States were surveyed. Specifically those national authorities competent in questions of genetic engineering were surveyed (see COM study, 2021, p. 7). Except for Malta all other of the 27 Member States completed the questionnaire. On the other hand, Norway, which is part of the European Economic Area (EEA), submitted a completed questionnaire (see COM study, 2021, p. 7, fn. 20).

Stakeholder survey: Stakeholders are defined as interested parties. According to the EU Commission's standards for such consultations as established in the "Better Regulation Guidelines", stakeholders should be carefully selected to ensure that all interested parties have their say and their views are heard (see European Commission, 2017, p. 69).[14] According to the COM study, one criterion for organisations participating in the stakeholder survey is that they be active EU-wide. Those not meeting this standard could cooperate with other eligible groups (see COM Study, 2021, p. 6). The initial selection of stakeholders was based on the members and observers of DG SANTE's Advisory Group on Food Chain and Animal and Plant Health.[15] Additionally, pharmaceutical and cosmetics organisations, as well as environmental groups were invited (COM study, 2021, p. 7f.). Stakeholders could furthermore participate via a "spontaneous expression of interest" (COM study, 2021, p. 8).[16] In total, 107 stakeholders were invited to be part of the survey; 71 confirmed their interest and received the questionnaire, and 58 stakeholders ultimately completed the questionnaire (COM study, 2021, p. 64).

A draft of the questionnaire was discussed with the Member States and stakeholders at workshops ("Ad hoc stakeholder meeting on new genomic techniques"). The questionnaire was then adapted in response to stakeholders' commentary. The Member States meeting took place on the 15th January 2020; that of the stakeholders on the 10th February 2020.

A majority of the stakeholders who ultimately completed the questionnaire attended the workshop on the 10th February 2020.[17] The stakeholder workshop had a total of 40

[13] The completed questionnaires may be downloaded at the following link: https://ec.europa.eu/food/plants/genetically-modified-organisms/new-techniques-biotechnology/ec-study-new-genomic-techniques/stakeholders-consultation_en (last access 13 October 2022)

[14] This document was updated in November 2021 after the publication of the COM study. See European Commission 2021d, 2021e.

[15] According to the website of this group, it is a group of stakeholders who are regularly consulted on EU food legislation issues. The group was established on the basis of a decision 2004/613/EC. For more information about the group and their current members see the following link: https://ec.europa.eu/food/horizontal-topics/expert-groups/advisory-groups-action-platforms/advisory-group-fcaph_en.

[16] The fact that this procedure described in the COM study actually took place in this was doubted by an interview partner who was interviewed by the authors of the present expert opinion. According to this interview partner, it may be doubted that the Advisory Group was the main basis of the selection of stakeholders (Interview 5). A comparison of the list of advisory members and the invited stakeholders indicates the following: The list of members of the advisory group includes members who were not originally invited to the targeted stakeholder consultation. Another notable detail concerns those stakeholders accepted through spontaneous responses. Interview 5 reveals that not all groups expressing an interest in participating were accepted. Interview 5 claims that no criteria for the selection of stakeholders existed.

[17] Analysis of this expert opinion: Comparison of participants in the "Ad hoc stakeholder meeting on new genomic techniques" and Table 6 "EU-level stakeholders invited to the targeted consultation on NGTs" in Annex B of the COM study, p. 54f. Some of the stakeholders who were still at this meeting did not complete the questionnaire.

participants. 18 of stakeholders who completed the questionnaire had not participated the workshop.

The survey period began after the finalisation of the questionnaires at each workshop. We can only find out the end of the survey from the COM study: It concluded on the 30th April 2020 for Member States and on the 15th May 2020 for stakeholders (see the dates mentioned in the questionnaires in Annex B, COM study, 2021, p. 67ff.). The "Better Regulation Guidelines" stipulate as a minimum standard sufficient time for respondents, which usually means 12 weeks (see EU Commission, 2017, p. 79, EU Commission 2021d, p. 15.). This allows us to calculate approximately the start of the survey period: Accordingly, the questionnaires would have to be sent to the respondents by th 6th February or 21th February 2020 at the latest.

The survey was conducted online via the online tool EUsurvey (https://ec.europa.eu/eusurvey/, see COM study, 2021, Annex B, pp. 67-74: "Stakeholders will be invited to reply to the questionnaire via EUsurvey"). Uploading supporting material was also possible. This supporting material has been published along with the questionnaires. Following the completed questionnaires, this supporting material was partly added to a PDF file (which can now be downloaded from the above hyperlink).

The two questionnaires for the Member States and the stakeholders differ slightly. The COM study does not provide an explanation for these differences. A comparison of the two questionnaires, as documented in the annex of the COM study (see COM study, 2021, Annex B, pp. 67ff.) is given in the following Table 4.[18]

Table 4: Comparison of the Member States' and stakeholder' questionnaires.

Topic in the questionnaire	Member States questionnaire	Stakeholder questionnaire
Implementation and enforcement of the GMO legislation with regard to new genomic techniques:		1. Are your members developing, using, or planning to use NGTs/NGT-products?
		2. Have your members taken or planned to take measures to protect themselves from unintentional use of NGT-products?
		3. Are you aware of initiatives in your sector to develop, use, or of plans to use NGTs/NGT-products?
		4. Do you know of any initiatives in your sector to guard against unintentional use of NGT-products?
	1. Have you been consulted by companies/organisations/research institutes for regulatory advice or another issue on products developed or to be developed by NGTs?	5. Are your members taking specific measures to comply with the GMO legislation as regards organisms obtained by NGTs?
	2. Have you taken specific measures (other than inspection) related to the application of the GMO legislation to NGT-products?	6. Has your organisation/your members been adequately supported by national and European authorities to conform to the legislation?

[18] The table quotes the questions from the questionnaires as documented in the COM study. Grammar and spelling have not been adapted to the convention in this expert evaluation.

Topic in the questionnaire	Member States questionnaire	Stakeholder questionnaire
	- If yes or no, have you encountered any challenges or limitations, including administrative burden or costs?	
	3. Have you adapted your inspection practices to cover all NGT-products and to ensure the enforcement of traceability requirements?	
	4. Do you have experience or information on traceability strategies, which could be used for tracing NGT-products?	7. Does your sector have experience or knowledge on traceability strategies, which could be used for tracing NGT-products?
		8. Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?
	5. What other experience can you share on the application of the GMO legislation, including experimental releases (such as field trials and clinical trials), concerning NGT-products in o agri-food sector; o industrial sector; o medicinal sector.	9. Do you have other experience or knowledge that you can share on the application of the GMO legislation, including experimental releases (such as field trials or clinical trials), concerning NGTs/NGT-products?
	6. Have plant varieties obtained by NGTs been registered in national catalogues?	
	7. Do you require specific information in national catalogue when registering plant varieties obtained by NGTs?	
Information on research and innovation (Member States)/Information on research on NGTs/NGT-products (stakeholder):	8. Have you supported with national funding programmes NGT-related research projects/programs (ongoing or finalised in the last 5 years), including on identification or traceability?	
	9. How do you see NGT-related research evolving?	10. Are your members carrying out NGT-related research in your sector?
	10. Have you identified any NGT-related research needs from private or public entities?	11. Are you aware of other NGT-related research in your sector?
		12. Has there been any immediate impact on NGT-related research in your sector following the Court of Justice of the EU ruling on mutagenesis?
	11. Could NGT-related research bring opportunities/benefits to science, to society and to the agri-food, medicinal or industrial sector?	13. Could NGT-related research bring benefits/opportunities to your sector/field of interest?
	12. Could NGT-related research bring challenges/concerns to science, to society and to the agri-food, medicinal or industrial sector?	14. Is NGT- related research facing challenges in your sector/field of interest?
		15. Have you identified any NGT-related research needs/gaps?

Topic in the questionnaire	Member States questionnaire	Stakeholder questionnaire
Information on public dialogues and national surveys:	13. Have you or other institutions/bodies/entities organised national dialogues concerning NGTs?	
	14. Have you or other institutions/bodies/entities organised national surveys, which assessed public opinion on NGTs?	
Information on ethical aspects:	15 Have any national bodies or expert groups discussed or issued opinion on the ethical aspects of NGTs?	*see question 26 on ethics*
Information on potential opportunities and benefits from the use of NGTs and NGT-products:	16. Could the use of NGTs and NGT-products bring opportunities/benefits to the agri-food, medicinal or industrial sector?	16. Could NGTs/NGT-products bring benefits/opportunities to your sector/field of interest?
	17. Could the use of NGTs and NGT-products bring opportunities/benefits to society in general, such as for the environment, human, animal and plant health, consumers, animal welfare as well as social and economic benefits, in the short, medium and long term?	17. Could NGTs/NGT-products bring benefits/opportunities to society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic benefits?
	18. Do you see particular opportunities for SMEs on the market access to NGTs?	18. Do you see particular opportunities for SMEs/small scale operators to access markets with their NGTs/NGT-products?
	19. Do you see benefits/opportunities in patenting or accessing patented NGTs or NGT-products?	19. Do you see benefits/opportunities from patenting or accessing patented NGTs/NGT-products?
Information on potential challenges and concerns of NGT products:	20. Could the use of NGTs and NGT-products raise challenges/concerns for the agri-food, medicinal or industrial sector?	20. Could NGTs/NGT-products raise challenges/concerns for your sector/field of interest?
	21. Could the use of NGTs and NGT-products raise challenges/concerns for society in general, such as for the environment, human, animal and plant health, consumers, animal welfare as well as social and economic challenges, in the short, medium and long term?	21. Could NGTs/NGT-products raise challenges/concerns for society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic challenges?
	22. Do you see particular challenges for SMEs on market access to NGTs?	22. Do you see particular challenges for SMEs/small scale operators to access markets with their NGTs/NGT-products?
	23. Do you see challenges/concerns in patenting or accessing patented NGTs or NGT-products?	23. Do you see challenges/concerns from patenting or accessing patented NGTs/NGT-products?
Safety of NGTs/NGT-products:		24. What is your view on the safety of NGTs/NGT-products? Please substantiate your reply.
		25. Do you have specific safety considerations on NGTs/NGT-products?
Ethical aspects of NGTs/NGT-products:	*see question 15*	26 What is your view on ethical aspects related to NGTs/NGT-products? Please substantiate your reply.

Topic in the questionnaire	Member States questionnaire	Stakeholder questionnaire
		27. Do you have specific ethical considerations on NGTs/NGT-products?
Consumers' right for information/freedom of choice:		28. What is your view on the labelling of NGT-products? Please substantiate your reply.
Final question:	24. Do you have other comments you would like to make?	29. Do you have other comments you would like to make?

The comparison of the two questionnaires illustrates that they are not identical but differ. When considering the following points, it should be kept in mind that the type of question has an influence on the type of response.

- For the first topic, the questionnaires pose several questions concerning the regulation of NGT (questions 1-7 in the questionnaire for Member States, questions 1-9 in the questionnaire for stakeholders). Here, questions are asked about GMO legislation and traceability strategies. The two questionnaires differ in the following respects: those questions asking about the current use of NGTs or NGT-products (posed to stakeholders only); whether products are labelled (stakeholders only); and whether plants produced with NGT are registered (Member States only).
- The next topic of the questionnaire concerns information on research and innovation (question 8-12 questionnaire for Member States) or research on NGT and its products (questions 10-15 in the questionnaire for stakeholders). These questions differ in that only stakeholders are asked whether the decision of the European Court of Justice has had a negative impact on NGT-related research in their sector. The Member States are only asked whether they have supported NGT with national funding programmes. Already at this point in the questionnaire, questions were asked about the opportunities and benefits of NGT on the one hand and the challenges and concerns on the other. These questions are specific to NGT-related research. Further below they are formulated again, in relation to NGT and the products developed from it.
- Questions on information on public dialogues and national surveys on NGT are only included in the questionnaire for Member States.
- Both Member States and stakeholders are asked about the ethical aspects of NGT, although at different points in the respective questionnaires and with different content.
- Questions regarding the benefits and opportunities, as well as challenges and concerns about NGT are identical in both the Member States' and stakeholders' questionnaire. It is worth noting that specific aspects of SMEs and intellectual property rights are also covered at this point in both documents.
- Questions on safety and labelling of NGT are only included in the stakeholder questionnaire. It is remarkable that Member States were only asked about traceability, but not about labelling.
- Both Member States and stakeholders had the opportunity to make general comments on

the questionnaire at its conclusion.

The study notes in its introduction that targeted consultations are instruments of "evidence-based policymaking", which is a common practice in the EU (COM study, 2021, p. 7f.). Targeted consultations and stakeholder consultations are instruments of Better Regulations. The intention to improve legislation is based on an Interinstitutional Agreement on Better Law-Making between the Member States. A new version was signed in 2016 which replaced previous ones dating to 2003 and 2005.[19]

The aim of Better Law-Making is to ensure that EU legislation is efficient, effective, simple, and clear. Overregulation and unnecessary burdens for individuals, public actors, and SMEs is also to be avoided (see European Commission, 2021d, p. 11f.). The document provides guidelines for conducting stakeholder or targeted consultations, to be distinguished from public consultations as another form of consultation process (see European Commission 2017, European Commission 2021d; European Commission, 2021e).[20] The requirements for stakeholder consultations in the "Better Regulation Guidelines" are presented in greater detail later on in this present expert opinion.[21]

3.1.1.3 Presentation of the COM study results

The content structure of the COM study is comparable to that of the questionnaires. In addition to material from the surveys, supplementary material and expert reports were evaluated by individual topic, and the authors of the COM study conducted their own analyses. The following Table 5 illustrates how the questionnaires and supplementary material correspond to the various sections of the study. It must be stressed that the following reconstruction of the resources upon which the COM study relies for its constituent sections has been assembled as part of the present expert opinion. Such information was not indicated by the COM study itself.

Table 5: Reconstruction of the use of sources in the COM study (2021).

Sections of the COM study	Questions in the questionnaires*	Supplementary material
1. Executive Summary		
2. Background and objectives of the Comission study on new genomic techniques		
2.1 Council request for a Commission study		
2.2 Scope and objectives of the study		
3. Methodology of the study		
3.1 General methodology		
3.2 Targeted consultation		
3.3 Overview of NGT legislation in non-EU		

[19] Interinstitutional Agreement between the European Parliament, the Council of the European Union and the European Commission on Better Law-Making. Official Journal of the European Union, OJ L 123, 12.5.2016, Document 32016Q0512(01). Online: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016Q0512(01)&from=EN (accessed 15 January 2023).

[20] In the new version of the guidelines published after the COM study was conducted, there is a note that is missing in the 2017 guidelines. It states that the guidelines are not legally binding. See European Commission 2021d, p. 3: "they cannot be construed as legally binding rules or legal commitments toward outside actors and stakeholders".

[21] See section 3.1.2 "Evaluation of the methodological approach of the COM study" of this expert opinion.

Sections of the COM study	Questions in the questionnaires*	Supplementary material
countries		
3.4 State of the art on NGTs		
3.5 Overview of EU NGT research funding		
3.6 Risk assessment opinions on plants developed using NGTs		
4. Status of new genomic techniques under EU law		
4.1 State of the art on NGT		
4.1.1 SAM explanatory note on new techniques in agricultural biotechnology		SAM HLG
4.1.2 JRC review on scientific and technological developments – key findings		JRC
4.1.3 JRC review on market applications – key findings		JRC
4.2 Legal status of organisms developed through NGTs		
4.2.1 The EU GMO legislation		EU GMO Legislation
4.2.2 Application of the EU GMO legislation to new mutagenesis techniques		EU GMO Legislation
4.2.3 Application of EU GMO legislation to organisms produced through cisgenesis and intragenesis		EU GMO Legislation
4.2.4 Application of EU GMO legislation to organisms in which the genetic material is altered without changes in the nucleic acid sequence		EU GMO Legislation
4.2.5 Past evaluations of the EU GMO legislation as regards NGTs		EU GMO Legislation, two evaluations FCEC, 2010 and EPEC, 2011
4.2.6 Regulation of NGTs in non-EU countries		NGT legislation in non-EU countries
4.3 Implementation and enforcement of EU GMO legislation with regard to NGTs		
4.3.1 EURL/ENGL report on the detection of new mutagenesis products		ENGL (2019)
4.3.2 Member States' and stakeholders' views on implementation and enforcement		
Implementation and enforcement of the GMO legislation as regards NGTs	Q2/MS; Q5/SH	
Challenges for current and alternative traceability systems	Q3, Q4/MS, Q7, Q8/SH	
Information on field and clinical trials and national catalogues of plant varieties	Q6, Q7/MS	
Stakeholders' views on national and EU-level support relating to NGTs	Q1/MS, Q6/SH	
4.4 Safety of new genomic techniques		
4.4.1 EFSA's overview on risk assessment opinions of plants developed through NGTs		EFSA
4.4.2 Member States' and stakeholders' views regarding safety	Q24, Q25 /SH	
4.5 New genomice techniques research and innovation		
4.5.1 EU funding for NGT research		DG RTD analysis of EU funding
4.5.2 Member States' and stakeholders' activities in NGT-related research	Q8/MS, Q10/SH	

Sections of the COM study	Questions in the questionnaires*	Supplementary material
4.5.3 Member States' and stakeholders' views on research and innovation		
Benefits and concerns relating to NGT research	Q11, Q12/MS, Q13, Q14/SH	
Impact of the CJEU ruling and the GMO regulatory framework on NGT research	Q12/SH	
Research needs	Q10/MS, Q15/SH	
4.6 Member States' and stakeholders' views on potential NGT-related opportunities and benefits		
4.6.1 Member States' views	Q16, Q17/MS	
4.6.2 Stakeholders that see benefit in NGTs	Q16, Q17/SH	
4.6.3 Stakeholders that do not see benefits in NGTs	Q16, Q17/SH	
4.7 Member States' and stakeholders' views on potential NGT-related challenges and concerns		
4.7.1 Member States' views	Q20, Q21/MS	
4.7.2 Stakeholders' views	Q20, Q21/SH	
4.8 Views relating to Small-Medium-Enterprises and intellectual property		
4.8.1 SMEs	Q18, Q22/MS, Q18, Q22/SH	
4.8.2 Intellectual property	Q19, Q23/MS, Q19, Q23/SH	
4.9 Stakeholders' views on the labelling of NGT products	Q28/SH	
4.10 Public dialogues and surveys on NGT		
4.10.1 Public dialogues reported by Member States	Q13/MS	
4.10.2 National and EU-wide surveys	Q14/MS	Eurobarometer 2019
4.11 Ethical aspects of NGTs		
4.11.1 Member States' views	Source can not be reconstructed	
4.11.2 Public dialogue initiatives and Member State expert opinions	Q15/MS	
4.11.3 Stakeholders' views	Q26/SH	
4.11.4. Opinion of the European Group on Ethics		EGE
4.12 Other Comments by Member States and stakeholders	Q24/MS, Q29/SH	
5. Discussion		
6. Conclusions		
7. Annexes		
8. Supplementary material		
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

3.1.2 Evaluation of the methodological approach of the COM study

3.1.2.1 Criteria of the evaluation

The following section is a critique of Commission study's methodological approach. Two different criteria form the basis of this critique: Firstly, it follows the EU's own quality criteria for conducting targeted consultations. These criteria are outlined over the course of the following sections. Secondly, the present expert opinion assumes that the designation "study" is only justified if basic scientific standards are met. For this reason, scientific standards can also be used as criteria for the assessment. Both criteria in the assessment of the COM study are presented in the following two sections.

3.1.2.1.1 The EU Commission's own quality criteria

In its Council Decision (EU) 2019/1904 the European Council indicates that the requested study should be in accordance with the Interinstitutional Agreement on Better Law-Making.[22]

The European Treaty also stipulates that the Commission is generally tasked with conducting broad consultations[23] (see European Commission, 2017, p. 69). According to Better Law-Making principles, a stakeholder consultation is a formal process in which the Commission gathers information or perspectives from stakeholders. This explicitly includes environmental considerations. The guidelines for conducting stakeholder surveys were last renewed in November 2021, i.e. after the publication of the COM study. Therefore, the version quoted below is the one which was operative when the COM study was conducted.

It mentions five minimum standards are mentioned (see European Commission, 2017, p. 69f.):[24]

- (1) **Clarity:** "All communication and the consultation document itself should be clear, concise and include all necessary information to facilitate responses" (p. 69).
- (2) **Targeting:** "When defining the target group(s) in a consultation process, the Commission should ensure that all relevant parties have an opportunity to express their opinions" (p. 69).
- (3) **Publication:** Concerns public relations, for example, that the call is published online. To "ensure adequate awareness-raising publicity and adapt its communication channels to meet the needs of all target audiences. Without excluding other communication tools, (open public) consultations should be published on the internet and announced at the 'single access point'" (p. 69f.).
- (4) **Consultation period:** "The Commission should provide sufficient time for planning and

[22] Recital (5) of Council Decision (EU) 2019/1904 particularly, refers to paragraph 10 of th mentioned Interinstitutional Agreement on Better Law-Making. This calls for an impact assessment to accompany the study (Council of the EU, 2019, p. 103, see also Article 3 of the request).

[23] See Art. 11 Treaty on European Union (TEU) The principle is called "Call for evidence". This involves requesting documents, which are then translated into all official EU languages. These are then published in a web portal "Have Your Say". Website in German: https://ec.europa.eu/info/law/better-regulation/have-your-say_de. On this platform, citizens and companies can comment on various EU policies and current legislation. To do so, they need to register or log in with a social media account (see EU Commission, 2021d, p. 13).

[24] In the new version with slightly different wording see EU Commission, 2021d, p 15.

responses to invitations and written contributions" (p. 70).[25]

- (5) **Feedback:** "Receipt of contributions should be acknowledged and contributions published." (p. 70).

With regard to these criteria, the methodological approach of the COM study will be evaluated below. NGOs subsequently criticised the targeting, i.e. the selection of stakeholders who were included in the targeted consultations.[26]

3.1.2.1.2 Standards of social science

Scientific research usually involves the following steps: definition of the research problem and the formulation of the research question; structuring of the object of investigation through theoretical considerations; operationalisation; empirical data collection; analysis of data. In this last step, findings are presented with respect to the research question (see Friedrichs, 1990).

At each of these stages, certain criteria apply in order to substantiate any statements in a social scientific study (see Bauer & Blasius, 2014; Friedrichs, 1990, Giddens, 2006, p. 78ff.).

- **Problem definition and formulation of the research question:** Studies are conducted on the basis of research problems that arise in social reality. One task of any study is the specification of a research question based on the current state of the relevant field (see esp. Giddens, 2006, p. 78f.). In its introduction, the COM study outlines the research problem. However, the COM study's research question is not specified; rather, the question posed by the ECJ ruling is expanded upon. In particular, the COM study lacks a review of the current state of research in the relevant literature.
- **Choice of methods:** Choice of research methods is dependent on the research question. Can the stated question be adequately investigated with the chosen methods? In the COM study, one of the chosen methods is a written questionnaire with open response categories. This may provide insight into the consequences of NGT for stakeholders and Member States from their perspective. Consequences that stakeholders and Member States are not aware of cannot be captured in this way.
- **Sample:** A population is represented by a sample. The selection procedure must also be specified (see Friedrichs, 1990, p. 125). A biased sample leads to a bias in the results. As will be shown below, the COM study, especially in the stakeholder survey, inadequately described the population and insufficiently justified the selection of stakeholders.
- **Data collection procedures:** The selection of variables and the scale quality of the variables must be appropriate (see esp. Friedrichs, 1990, p. 107). In the COM study, a number of questions were included in the questionnaires. The terminology and formulations of the questions are designed to answer the research question. They should therefore not be formulated arbitrarily, but in a well-founded manner. Furthermore, the scales in the COM

[25] This principle is more specified in the new version: For example, one rule is 12 weeks from publication. The period varies depending on the form of participation. To "allow sufficient time for planning and responses to invitations and written contributions. As a rule, 'calls for evidence', which include public consultations, are published for 12 weeks" (EU Commission 2021d, p. 15, the Table 12 on page 16 also specifies shorter times for some other forms of participation).

[26] For more details see section 3.1.2.2 "Critical points of the methodology of the COM study" in this expert opinion.

study, essentially the indication of the frequency of the statements expressed and the division of the stakeholders into stakeholder groups, are important in guiding the interpretation of the results. These scales are however not clearly defined and are used differently in the chapters of the COM study.

- **Data analysis:** The collected data are interpreted with regard to the research question. For example, the answers from the surveys are described and then analysed comparatively. This requires accounting for similarities and differences. The COM study describes answers from the targeted consultation and compares them with each other only in part. However, this analysis is not complete, and yields numerous inconsistencies. Likewise, links back to the central research question are often missing in the interpretation of the data.
- **Presentation of results:** The readership expects a study to present the results objectively and completely. In qualitative research processes, such as the evaluation of target group surveys, one quality criterion is the transparency of the process. Accordingly, each phase should be accompanied by an explanation for why certain decisions were taken over the course of the research process. Transparency is primarily established through traceability (see Flick, 2014, p. 421).

3.1.2.2 Central points of the evaluation of the COM study´s methodology

This section discusses critical points in the methodology of the COM study, and bases itself on the criteria described in the previous section. Four points of criticism are highlighted: the focus of the study, the selection of stakeholders for the targeted consultation, a lack of transparency, and the presentation of the opinions yielded by the targeted consultations. The COM study has been criticised by other organisations, namely NGOs and civil society groups. Criticism from other stakeholders has not been prominently voiced and is not known to the present expert opinion. Such criticism is addressed in the present expert opinion; their publications (flyers, policy papers etc.) are cited where appropriate.

3.1.2.2.1 Focus of the COM study

The COM study was prepared at the request of the Council of the European Union. This request was made on 8 November 2019 (Council of the European Union, 2019, p. 103-104). According to the authors of the COM study, the request was made in response to practical problems arising from the ECJ judgment, yet the study addresses more general points as its main focus.

Article 1 of the request of the Council of the European Union reads:

> "The Council requests the Commission to submit, by 30 April 2021, a study in light of the Court of Justice's judgment in Case C-528/16 regarding the status of novel genomic techniques under Union law." (Council of the European Union, 2019, p. 104)

The Council's statement refers not only to new mutagenesis techniques, but to all new genomic techniques (see section 3.2.5.1.1 "Interpretation in the COM study" in the present expert opinion). Furthermore, the recitals to the articles imply that the request is not a response only to the practical consequences of the ruling, but also concerns further consequences issuing from the application of new genomic techniques generally.

Recital 4 states that:

> "The ruling brought legal clarity as to the status of new mutagenesis techniques, but also raised practical questions which have consequences for the national competent authorities, the

> Union's industry, *in particular in the plant breeding sector, research and beyond*. Those questions concern, *inter alia*, how to ensure compliance with Directive 2001/18/EC when products obtained by means of new mutagenesis techniques cannot be distinguished, using current methods, from products resulting from natural mutation, and how to ensure, in such a situation, the equal treatment between imported products and products produced within the Union." (emphasis by the authors, Council of the European Union, 2019, 14.11.2019, p. 103)

The text highlighted by italics in the above quotation emphasises the broader context. In the wording "in particular in the plant breeding sector, research and beyond", the consideration of the opportunities and concerns which make up a large part of the COM study, is only justified by the addendum "beyond". It enables the COM study to discuss possible socio-economic consequences of new technologies as well as specific legal conditions.

Yet this broad focus of the COM study was criticised by some NGOs, due to the fact that the expanded scope moved away from a discussion of the implementation of the current GMO Regulation respective of the European Court of Justice ruling (ECJ 2018a). For example, a discussion paper by Friends of the Earth Europe notes:

> "Instead of looking for gaps in the implementation of existing GMO safety laws, it instead opens up the scope much more broadly, allowing for the laws to be rewritten and weakened." (FoEE, 2021, p. 5)

The present expert opinion takes up the criticism initiated by the NGOs, and explores whether the general objective of examining the effects of the ECJ ruling was obscured in the substantive chapters.

With regard to the various organism groups addressed in the COM study, it formulates a broad claim: "The scope of the study covers the use of NGTs in plants, animals and microorganisms, in a broad variety of potential applications, including in the agri-food, medicinal and industrial sectors" (COM study, 2021, p. 6). The COM study has not fulfilled this contribution – as the present expert opinion shows. Even if the data collection at least partially compiles comprehensive and also valuable findings, the presentation in the study itself does not meet the claim in any way. All in all, the data are not sufficient as regards applications with animals and microorganisms. And, as shown above, EFSA had not yet carried out its study (see Chapter 2 "Methodical procedure of the present expert opinion").

3.1.2.2.2 Critique of the questionnaire

As mentioned before, the two questionnaires given to Member States and stakeholders differ slightly, and the COM study does not account for these differences. Interview 5, conducted by the authors of the present expert opinion, offers one explanation. When the questionnaire was discussed with stakeholders at the meeting on 10th February, the European Commission took up some questions raised over the course of this discussion: "The Commission has been open" (Interview 5). Some points raised in the questionnaires do not pose anything new, as for example the extent to which companies apply labelling rules: "There is no question at all whether they apply it. Everything else is illegal" (Interview 5). Unlike in other risk-benefit debates the term "risk" is not used by the COM study. In the wording of the COM study, "opportunities and benefits" are considered on the one hand, and "challenges and concerns" on the other. The term "risk" seems to be replaced by the term "concern". This leads to some difficulties in the interpretation of the targeted consultation results, to be discussed later in this

expert opinion.[27] Interview 5 summarises its criticism as follows: "The way the Commission has structured the questionnaire, the language it uses, the questions it asks and the combination of questions it asks, already gives a direction as to what result it wants. And that is highly problematic" (Interview 5).

3.1.2.2.3 Selection of stakeholders

The selection of stakeholders who participated in the stakeholder survey does not meet the EU Commission's standards for such consultations according to the Better Regulations Guidelines valid as that time (European Commission, 2017, p. 69). These guidelines stipulate that stakeholders must be carefully selected to ensure that all interested parties have their views represented. By contrast, as the analysis below documents, proponents of NGT are overrepresented.

The selection of stakeholders in the COM study has been criticized by NGOs for not meeting the Better Regulations quality standards. The group Global 2000 has criticised the study for its "disproportionately large number of industry associations", counter-balanced by only a small number of civil society groups (see Global 2000, 2021, p. 4). A joint position paper by several NGOs reaches a similar conclusion. Only 14 percent of the stakeholders surveyed were civil society groups, while 74 percent of surveyed groups were drawn from the industrial sector (Agroecology in Action et al. 2021, p.7). The NGOs cited here argue that this led to distortions in the COM study's results.[28]

It is also notable that the recommendations set out in the "Better Regulation Guidelines" nevertheless do not specify a method for obtaining balanced selections. A basic strategy is referred to as "map stakeholders": "The basic rule is to consult broadly and transparently among stakeholders who might be concerned by the initiative, seeking the whole spectrum of views in order to avoid bias or skewed conclusions ('capture') promoted by specific constituencies" (see European Commission, 2017, p. 76). According to the Better Regulations Guidelines in use at the time of the targeted consultations, successful stakeholder mapping involves identifying and prioritising categories of stakeholders (see European Commission, 2017, p. 76).

The COM study published a list of the organisations that participated in the stakeholder survey. This list is included in the annex of the COM study (see COM study, 2021, Annex B, Table 6, p. 64f.). However, the COM study did not publish the mapping of stakeholders as recommended by the "Better Regulation Guidelines". For example, the study could have examined which groups along the value chain and which civil society organisations might be affected, e.g. environmental and consumer rights groups. Better Regulations recommends discovery of which stakeholders are affected by a particular policy before targeted consultations are initiated. Because the COM study does not provide such an analysis, the present expert opinion reconstructs here which stakeholder groups were involved.

The present analysis is based firstly on a published list of the organisations which took part in the stakeholder survey. Secondly, the analysis draws on those questionnaires completed by

[27] See section 3.6.2.2 "no risk-benefit debate" in this expert opinion.

[28] Interview 5 conducted by the authors of this expert opinion shows that there is an "unwritten rule" in the consultation processes of the European Commission: "And the basic rule is, if you [have] a very broad definition of civil soci2ety organisation, that usually one third are civil society organisations and two thirds are close to industry" (Interview 5).

stakeholders, which are made available as "supplementary material" on the European Commission's website.[29]

The aim of the analysis is the discovery of which stakeholders, and their specific number in each category, ultimately were involved in the stakeholder survey. All 58 stakeholder questionnaires were used for the analysis. In order to assign the participating organisation to a stakeholder category, answers in the questionnaires referring to information about the organisation were analysed.[30] To this end, an open question preceding the content-related survey was posed. Its text read: "Please mention the sectors of activity/fields of interest of your association".[31] Answers to these open-ended questions were then categorized, that is, organisations with similar answers were assigned to the same category.

Organisations' tendency to favourable or critical positions with respect to genetic engineering was investigated. Assessments on this point were based on initial rough screenings of their positions. Positions which clearly express awareness of greater risks compared to benefits were classified as critical. Some positions evaded clear classification (that is, they could not be categorised as either "yes" or "no" on the point of critical awareness). Those positions which clearly saw more benefits than risks were classified as non-critical.

Table 6: Categorisation of stakeholder groups based on the interests.

Category	Critical?			
	Yes	Yes and No	No	Sum
Science	2		5	7
Seed producer	3		2	5
Industrial Biotechnology			4	4
Agricultural cultivation	2		5	7
Wholesaler			5	5
Food production	2	1	5	8
Ornamental/horticulture			3	3
Retailer		1	1	2
Consumer protection	2	1		3
Environment and nature conservation	6			6
Other	3	1	4	8
Sum	**20**	**4**	**34**	**58**

Categorisation was based on the interests represented by an organisation and not on organisational form. Accordingly, no category specifically named "NGOs" was used. For example, companies in the organic farming and food industry are not civil society groups. For this reason, the approach used in the present analysis was designed first to categorise which interests

[29] See https://ec.europa.eu/food/plants/genetically-modified-organisms/new-techniques-biotechnology/ec-study-new-genomic-techniques/stakeholders-consultation_en.

[30] In some cases, this question was also answered in another field of the questionnaire.

[31] This question is not documented in the COM study, but can be traced from the completed questionnaires, which can be downloaded from the European Commission website: https://ec.europa.eu/food/plants/genetically-modified-organisms/new-techniques-biotechnology/ec-study-new-genomic-techniques/stakeholders-consultation_en (last access 13 October 2022).

each respective associations held, and only then whether they are more critical or supportive of NGT.

The results of the analysis are shown in table 6. The table shows that organisations from the agricultural and food industries make up the majority of those surveyed. Pharmaceutical and cosmetics organisations are included in the category "Other". The table illustrates that opinions supportive of NGT are overrepresented. Opinions prizing consumer protection are underrepresented.[32] Furthermore, no NGT-supportive positions indicate parallel support for environmental protection, nature conservation, and consumer protection.

Sources of error. The above analysis carried out by the authors of the present expert opinion provides only a rough overview of stakeholder participation and the representative balance of viewpoints. The following points should be noted:

- Not every organisation surveyed as a stakeholder represents the same number of members. As the above-mentioned position paper also indicated (Agroecology in Action et al. 2021, p. 7), many of those organisations surveyed are so-called umbrella organisations. Because some organisations – such as certain firms – are active in various umbrella organisations, one firm could in practice have been consulted or considered more than once.
- Some associations conducted a survey among their members before preparing their replies to the questionnaires (e.g. European Flour Millers (EFM), European Potato Trade Association (EUROPATAT), Euroseeds, etc.), while others did not. Answers based on such a survey are more representative of the organisation consulted as stakeholders than others where only one department completed the questionnaire.
- According to the study, the questionnaires were analysed in the manner (see COM study, 2021, p. 8)[33] regardless of whether the organisations were large or small. The questionnaires given to smaller organisations with few members were treated as equivalent to those given to large umbrella organisations with many members, including those which attempted to reflect the differentiated opinions within their member organisations.

Of equal importance as the number of organisations per stakeholder groups is the extent to which statements derived from the completed questionnaires were taken into account in the COM study, specifically in its two final chapters. The present expert opinion analyses the argumentation of the COM study,[34] which was made on the basis of its targeted consultations; it then compares this with the COM study's final chapters.[35] Furthermore, the authors of this evaluation have reasonable doubts that the COM-study even considered the responses of stakeholders and Member States in the targeted consultations (see section 3.6.3.6 "Development policy argumentation " in the present expert opinion).

[32] This is due to the fact that there is only one consumer protection association at EU level. The various consumer protection groups are represented through an umbrella organisation. See interview 5.

[33] This approach is considered in greater detail in section 3.1.2.2.5 in this expert opinion.

[34] For the detailed analysis, see the sections 3.2.7 "Stakeholder and Member States views on GMO legislation", 3.3.4 "Stakeholder and Member States views on NGT-related research", 3.3.4.1 "Stakeholder and Member States views on research and innovation", 3.5.4 "Stakeholder and Member States views on risk assessment", 3.6 "Ethical and socio-economic implications of new genomic techniques" of the present expert opinion.

[35] A concluding interpretation can be found in section 3.8 "Evaluation of the overall structure and argumentation of the COM study" of this present expert opinion.

3.1.2.2.4 Lack of transparency

Transparency is among the most important aspects of the "Better Regulation Guidelines". The "Better Regulation Guidelines", published before the COM study was conducted, state that better regulation is defined primarily by openness and transparency (European Commission, 2017, p. 4):

> "Better regulation is not about regulating or deregulating. It is a way of working to ensure that political decisions are prepared in an *open, transparent manner*, informed by the best available evidence and backed by the comprehensive involvement of stakeholders" (European Commission, 2017, p. 4).[36]

Transparency in the conduct of consultations is also expected of NGOs active in European politics,[37] as well as a criterion of scientific examinations which refer to themselves as a "study".[38] In this context, the COM study clearly lacks the requisite transparency in several respects, making it a challenge to reconstruct its results. Below, the qualities accounting for this lack of transparency are specified, and are followed by suggestions for improvement.

Publications of the results

The Better Regulations Guidelines for stakeholder surveys also covers the presentation of results. In line with the transparency criteria, completed questionnaires are to be provided online. This standard been met by the COM study. Questionnaires are made available on the European Commission's website to be viewed and downloaded.

However, the supporting documents which stakeholders and Member States attached in the course of these surveys as evidence for their views is only available through the questionnaires. Such supporting documents are often comprised of entire studies and expert reports. See, for example, the reponse of "The Committee of Professional Agricultural Organisations of the European Union (COPA)".[39] Following the response in the questionnaire template, the following documents are attached:

- Slides on "Sustainability with Climate Focus" with Hans Berggren, Sveriges Stärkelseproducenter (SSF) as author,
- The Danish Council on Ethics' "Statement on GMO and Ethics in a new era",
- and a paper "Genome editing: Europe needs new genetic engineering legislation" by the German Bioeconomy Council ("Bioökonomierat").

However, it is also not clear whether all uploaded documents were published in this way. If we compare the questionnaire from COPA with the one from Austria, there is the filename in

[36] As already mentioned, the Better Regulation Guidelines and the Better Regulation Toolbox were updated in November 2021 after the finalisation of the COM study. In this document, transparency remains one of the key criteria for the Better Regulation (European Commission, 2021d, p. 9). In the corresponding toolbox it says: "Being transparent to the outside world is important if initiatives are to be understood and credible. Results of evaluations, impact assessments and consultations should be publicly available. The reasons for disagreeing with alternative views should be explained." (European Commission, 2021e, p. 9)

[37] This according to an interview conducted by the authors of this expert opinion. See Interview 5.

[38] See ALLEA, 2017, DFG, 2019.

[39] File name "gmo_mod-bio_stake-cons_stake-reply-11_copa".

the reply to the questionnaire from Austria that something has been uploaded, but this file is not included as an attachment from the questionnaire.[40]

Furthermore, there is no indication on the European Commission's website that such additional documents are attached to the questionnaires. A list of supporting documents with attendant links should have been given. Whether the supporting documents were ever evaluated over the course of the COM study remains ambiguous. In the view of the present expert opinion, the COM study did not succeed in making clear in what way the positions, assessments and evaluations of Member States and stakeholders were incorporated into the results, conclusions and recommendations for action of the study. There is no indication in the COM study that these documents have been evaluated. The material in question has not been cited.

Furthermore, we have the suspicion that even the questionnaires themselves were not systematically evaluated. One example is the developmental argument that appears in several questionnaires, but only as a single statement expressed by a single stakeholder in the annex of the study (see section 3.6.3.6 "Development policy argumentation" in the present expert opinion).

Presentation of the results of the targeted consultations

Across its numerous sections, the COM study does not indicate which questions in the questionnaire refer to which specific analyses. The authors of this present expert opinion reconstructed which material was summarised by which section of the COM study (see Table 5). The reconstruction was based on a thematic comparison of the content sections of the COM study, and the questions in the questionnaire. Although the questionnaires are given as a source, the COM study itself contains no stated correspondence between its analysis and the questionnaires used as sources. The appendix to the COM study should have documented not only the questionnaire (see COM study, 2021, Annex B, p. 67ff.), but also which points in the analysis in the COM study relate to the relevant questions, or sources. The COM study appears to proceed systematically in this regard. It should have made this procedure transparent.

Lack of consistency

The COM study only summarises the material on which it is based. For scientific studies of documents and questionnaires, it is essential that the criteria or heuristics used to evaluate the material are made transparent. Criteria are properties according to which a state of affairs or an object is considered. They can likewise be associated with indicators that specify when a characteristic is more and when it is less expressed. The COM study does not appear to have such criteria, and if it does, they are not stated. It is therefore not clear how the COM study arrives at the results and conclusions it highlights in the concluding chapters.

The COM study claims to be a study, but it does not make transparent on what basis the authors chose the selected methods: The study gives no, or only very few, references to sources in which the chosen methods have already been described. For example, a classification system for plant development with four stages is used (see Chapter 3.4.2.2 below). The decision for the industry data as a main source for the JRC market review is another example for an important method. This has significant consequences for the outcome of the review. As the present expert opinion shows in Chapter 3.4.2.4 "Sources of the data" below, the decision

[40] See file "gmo_mod-bio_stake-cons_ms-reply-aut", p. 19.

leads to a very limited ability to publish the results of the review. It is a good scientific practice, to make transparent, why a certain method or procedure had been chosen. This approach provides the opportunity to link the own research to past or ongoing (academic) discussions. Linking can also be done through differentiation, e.g. by explaining why a method that has been common or used in the past is not appropriate in a certain context. Thus, the COM study's conclusions appear to be arbitrary and not based on any systematic analysis.

3.1.2.2.5 Evidence is not distinguished from opinion

As indicated above, the selection of stakeholders is biased toward organisations who favoured NGT in their completed questionnaires. In the following those statements put forward in the COM study are examined in greater detail. Firstly, it should be stated that the levels of the study's arguments – specifically concerning the obligation to "distinguish evidence from opinion" (see European Commission, 2009, p. 20) – are not clearly separated. Statements and opinions by stakeholders and Member States are placed on equal footing with findings from empirical studies regarding these facts. This approach is made explicit in the methods section of the COM study:

> "*All views collected from the consultation have been analysed in this study on their own merit*; no conclusions are drawn on the basis of the number of respondents in support of a given view. In several cases, the views reported in this study, especially those relating to benefits or concerns for a sector or for society in general, rest on reasoning and assumptions, sometimes extrapolated from past experience with GMOs from EGTs" (emphasis by the authors, COM study, 2021, p. 8).

There is a crucial difference between an assertion that can be substantiated and an assertion that is a mere opinion. Justifications of assertions can be made in particular via scientific studies. By largely reflecting the responses of stakeholders and Member States in the targeted consultations, the COM study is at the level of public debate. Opinions can also be scientifically studied. The repertoire of social science methods provides many controlled methods for making well-founded statements about the public debate.

Also, in reproducing the opinions expressed in the targeted consultations, the COM study treats some statements as if they describe reality, while others are treated as if they were only hypotheses or speculations of a few. For example, statements about the benefits of NGTs are presented as if they have already materialised. Concerns, on the other hand, are treated as mere opinions and invalidated by means of counter-arguments.[41]

3.1.2.3 Conclusion: Levels of perceived reality

The results of the two targeted consultations take up a large part of the topic-specific sections of the COM study. The research question of the study, which addresses the consequences of NGTs for the economy, society and ecosystem, for example, however cannot be answered by this approach. By simply reproducing the answers of the two questionnaires, the study does not answer the scientific question of what the consequences might be. To the contrary, it presents only opinions regarding such consequences.

Figure 1 shows which realities exist in relation to NGT. The lowest level in the figure illustrates reality as we perceive it with our senses and by means of scientific methods. However, there is a second reality above this: the reality of how this reality is spoken about in society. It is the

[41] See for a more detailed analysis section 3.8.1 "Presentation of the arguments" in this expert opinion.

opinions about this reality, which are not scientifically validated, but can very well be investigated by the social sciences through the application of social science methods. The next level is when this level of social discourse is perceived and reproduced from the perspective of a social actor. Furthermore, how this discourse is reproduced from an actor's point of view may be investigated further. At each point, the inquiry moves further away from a reality in which problems with NGT are solved practically.

Although the COM study systematically summarises the material, it lacks a systematic analysis. And although the document claims to be a "study", it is no more than a summary of arbitrarily selected material combined with a non-transparent stakeholder survey.

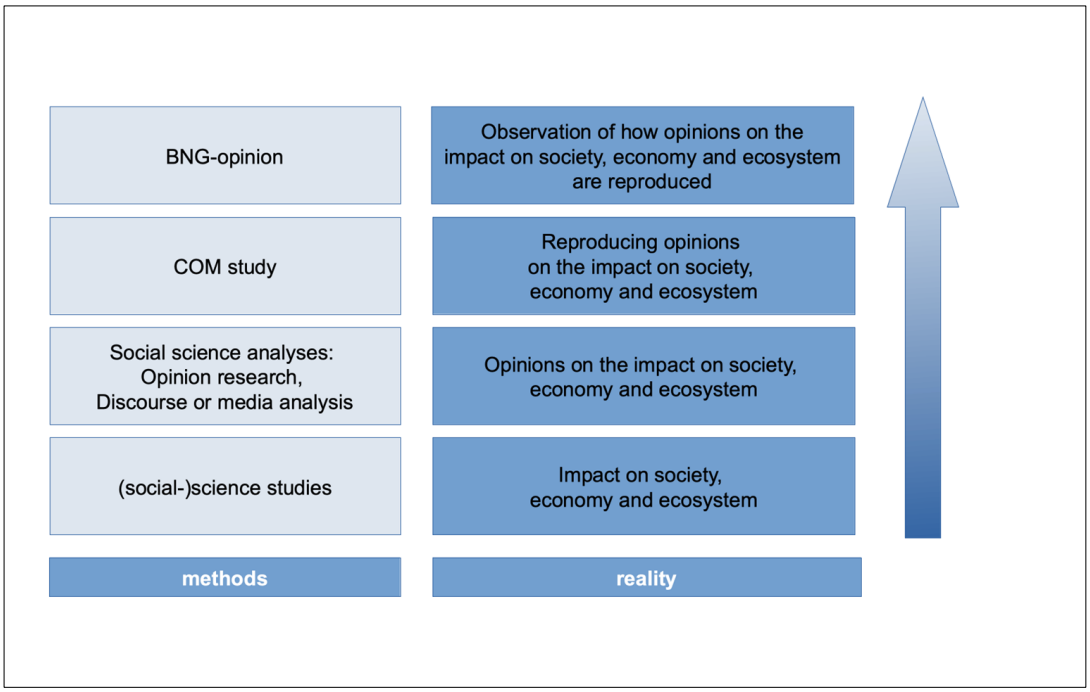

Figure 1: Levels of perceived reality – Impact of NGTs.

3.2 Implementation and enforcement of GMO legislation with regard to NGTs

3.2.1 Regulation of NGTs in non-EU countries

Before turning to the situation in the EU the Commission examines the NGT regulations in 31 non-EU states (COM study, 2021, p. 23) and groups those states into the following categories.

3.2.1.1 Adaptation of law

One third of the non-EU countries examined have already adapted their law to NGTs, introducing either product-based or process-based exemptions from the scope of GMO regulation. Some countries combine product- and process-based exemptions in such a manner that only those NGTs obtained by certain techniques, where there are only minor deletions or substitutions in the final product, are exempted. The aim of this approach is to deregulate all those processes and products with modifications which – at least according to the Commission – also occur in nature or in conventional breeding (COM study, 2021, p. 23).

3.2.1.2 Application of overarching rules

Two-thirds of the examined non-EU countries currently regulate NGTs under general genetic engineering law, with half of those discussing a specific legal framework for NGTs. Interestingly China also is under those countries, although it is not shown, whether they discuss a specific legal framework.

Even more overarching is the approach of Canada, which does not have any specific regulation for GMOs whatsoever but looks solely at whether the end product has properties which were not present in comparable unmodified organisms (so-called novel traits) – regardless of whether those novel traits were created by classical breeding, classical genetic engineering, or by NGTs (COM study, 2021, p. 23).

3.2.1.3 Procedural issues

Regardless of the type of regulation, many states offer a pre-test to companies developing NGT products, so as to clarify the regulatory status of the product in question or to shorten the approval process for NGT products (COM study, 2021, p. 24).

3.2.1.4 Methodological procedure of the COM study

However, the methodological approach used by the COM study to arrive at these results remains obscure. The selection of the non-EU states analysed is incomprehensible. There are currently 193 states in the world. However, the study only looks at 31 of them and does not specify any criteria according to which these states were selected. And as it also is not revealed which were the sources for this information, the methodical approach of getting those informations cannot be checked. This approach makes it possible to pick out exactly those states that come closest to the Commission's reform ideas and leave out the others. There is no systematic examination of all jurisdictions. Therefore, these results cannot claim to be representative, if the Commission intended this.

3.2.2 Legal Status of GMOs in the EU

In order to assess whether and how the EU GMO legislation has been implemented and enforced with respect to NGTs, an overview of the EU GMO regulation framework is first required.

3.2.2.1 Deliberate Release Directive

In the EU, GMOs are regulated by several instruments. Basic instrument is the Deliberate Release Directive 2001/18/EC. Its central concept is the precautionary principle, meaning that "all appropriate measures have to be taken to avoid adverse effects on human health and the environment".[42] This principle is implemented in order to assure that for every GMO released into the environment, a risk assessment and a mandatory authorisation by the relevant surveillance authority have been undertaken.[43] One leading guideline is the case-by-case principle,[44] which prohibits the authorisation of groups of GMOs *en masse*;[45] rather it requires that each individual GMO product must to be considered separately. Even after having obtained an authorisation to bring a product to market, the operator is obliged to monitor the

[42] Art. 4 para. 1 Dir. 2001/18/EC.
[43] Art. 4 para. 2 Dir. 2001/18/EC.
[44] See recitals 18 and 19 of the Deliberate Release Directive.
[45] Art. 4 para. 3 Dir. 2001/18/EC.

product.[46] The product must also be labelled as a GMO-product.[47] Finally, the Cartagena Protocol on biosafety must be observed.[48] This directive is mentioned and outlined in the COM study (COM study, 2021, p. 19 and Annex E).

3.2.2.2 Food and Feed Regulation

Building on the Deliberate Release Directive, special rules are set up by the food and feed Regulation 1829/2003/EC, which aims to secure a high "level of protection of human life and health, animal health and welfare, environment and consumer interests."[49] The Directive mandates *especially* that "the product must not have adverse effects on human health, animal health or the environment, mislead the consumer or differ from the food which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for the consumer."[50] To ensure this, authorisation is also required[51], all transformation events are to be indicated,[52] and methods for detection and sampling must also be provided.[53] If need be, information required by Annex II of the Cartagena Protocol must to be submitted.[54] Finally – as opposed to most other products on the market – such products must also be monitored even after being placed on the market,[55] and they must be labelled as GMOs.[56] These aspects are also outlined in the COM study (COM study, 2021, p. 19 and Annex E).

3.2.2.3 Traceability Regulation

Finally, Regulation 1830/2003/EC contains rules for safeguarding the traceability of GMO food and feed products. This traceability is designed to facilitate both the withdrawal of products where unforeseen adverse effects on human or animal health and the environment occur, as well as the targeted monitoring of potential effects on ecosystems specifically.[57] In order to ensure this traceability, anyone receiving GMO product must be informed of this fact by way of labelling and unique identifiers. Additionally, all persons involved are to preserve relevant documentation for five years.[58] This applies to all operators beginning from the date on which the product is placed on the market. Special rules are set up in reg. 1829/2003/EC for the information of the end-consumer. These aspects also are outlined in the COM study (COM study, 2021, p. 19 and Annex E).

3.2.2.4 Mutagenesis I decision of the ECJ

The development of NGTs after the adoption of the Deliberate Release Directive in 2001 led in recent years to discussions about whether those NGTs also fall under its purview, and those regulations extending it, even where no transgenic DNA is detected in the final product. In 2018, the European Court of Justice (ECJ) was compelled to decide on this point in the case of

[46] Art. 20 Dir. 2001/18/EC.
[47] Art. 21 Dir. 2001/18/EC.
[48] Art. 32 Dir. 2001/18/EC.
[49] Art. 1 para. 1 lit. a) Reg. 1829/2003/EC.
[50] Art. 4 para. 1 Reg. 1829/2003/EC.
[51] Art. 4 para. 2 Reg. 1829/2003/EC.
[52] Art. 5 para. 3 lit. b) Reg. 1829/2003/EC.
[53] Art. 5 para. 3 lit. i) Reg. 1829/2003/EC.
[54] Art. 5 para. 3 lit. c) Reg. 1829/2003/EC.
[55] Art. 5 para. 5 lit. b) Reg. 1829/2003/EC.
[56] Art. 12 ff. Reg. 1829/2003/EC.
[57] Recital 3 Reg. 1830/2003/EC.
[58] Art. 4, 5 Reg. 1830/2003/EC.

targeted mutagenesis.[59] It first found that according to Art. 2 No. 2 of Directive 2001/18/EC, a product qualifies as a GMO within the meaning of this directive whenever it is an organism other than a human being "whose genetic material been altered in a way that does not occur naturally by mating[60] and/or natural recombination". GMOs that have been created with the help of NGTs are thus in principle covered by the Directive. Since the specific case on which the ECJ decided concerned a particular type of NGTs, namely mutagenesis, for which the Directive provides an exemption in Art. 3 para 1 in conjunction with Annex IB, the court was compelled to consider whether the method of targeted mutagenesis using genetic engineering techniques also falls under this exemption. The ECJ answered in the negative, and clarified that the exemption only applies to GMOs obtained by methods that were traditionally used in a number of applications at the time of the adoption of the Directive in 2001 and had long been considered safe.[61] The exemption thus only covers conventional *in vivo* mutagenesis methods that had been classified as safe for many years, and not the method of targeted mutagenesis using genetic engineering techniques, which emerged only much later. In sum, NGT processes are covered by the Deliberate Release Directive 2001/18/EC except conventional mutagenesis. Since Regulation 1829/2003/EC and Regulation 1830/2003/EC refer to this definition of GMO in the Deliberate Release Directive, the findings of the ECJ also apply to the scope of those regulations, i.e. in particular to food and feed traceability.

3.2.3 Implementation of EU genetic engineering legislation

3.2.3.1 Identifiability of NGT products

A prerequisite for the approval of any type of GMO is its unambiguous identifiability,[62] which, according to the European reference laboratories, is possible in the case of genome-edited plants if the modified genome sequence is known. However, at least according to the Commission, certain ambiguity is present in this standard because conventional breeding may produce the same mutations as genome editing (COM study, 2021, p. 25). By the same token, NGT products could not be approved in the EU at present, and NGT products imported without being authorised in the EU cannot be legally monitored for safety (COM study, 2021, p. 25). As an initial step to resolve this impasse, some Member States have adapted their monitoring systems, by for example developing new questions and checklists related to NGTs in their application forms (Questionnaire Germany No. 2, p. 4). They have also considered increasing the probability of detection using bioinformatics, statistics (Questionnaire Estonia, No. 4.), (patent) database,[63] UPOV,[64] identification protocols (Questionnaire France, No. 4, p. 8.), anti-counterfeiting methods (Questionnaire France, No. 4, p. 8.), and requirements of NGT-free certificates at the EU's external borders (Questionnaire Denmark, No. 3). Some Member

[59] Decision of 25 July 2018 – C-528/16.
[60] E.g. by cross breeding.
[61] The ECJ underpinned this finding by invoking recital 17 of the Directive 2001/18/EC.
[62] See Art. 5 Abs. 3 lt. b, i Reg. 1829/2003/EC.
[63] Some Member States here see restrictions due to the invocation of business secrets.
[64] UPOV is an abbreviation of the international Union for the Protection of New Varieties of Plants.

States plead for keeping a permanently updated list of NGT-products circulating outside the EU[65], or for border control of suspected products (Questionnaire Lithuania, No. 3).

3.2.3.2 Traceability of NGT products

GMO products must be traceable at any time pursuant to contemporary legislation,[66] but Member States contend that this is currently impossible given of the lack of available analytical methods (COM study, 2021, p. 27). Some Member States instead are now considering or have already introduced alternative document-based traceability systems,[67] such as those that have long been used in organic farming, especially in combination with sampling and matching with international NGT databases (Questionnaire Austria, No. 4). The use of mass balance systems or even the use of block chain, secured by random sampling and comparison with international NGT databases has also been discussed (COM study, 2021, p. 27). Some Member States see this approach as a problem for the competitiveness of European companies because of the high level of effort necessary for compliance (COM study, 2021, p. 27). Finally, some states have endorsed a proposal to forego the positive labelling of NGT products, and to label only NGT-free products – that is, negatively (COM study, 2021, p. 27).

3.2.3.3 Plant variety protection law

There are currently no NGT varieties in any of the national variety catalogues. However, this fact carries little meaning, as an indication of the GMO/NGT status has never been required under this variety law. Nevertheless, some Member States have now altered this standard, and have introduced an obligation to indicate whether NGT products are applied for registration in the variety catalogue (Questionnaire Croatia, No. 3,7 and questionnaire Denmark, No. 2). In the COM study itself there is no discussion regarding the identification of NGT status in the plant varieties already listed in these catalogues. Yet, given the fact that a third of the Member States do not actually inquire into the technique used to develop plant varieties during the registration process (COM study, 2021, p. 28), such identification appears impossible for a large number of cases.

3.2.3.4 Other aspects

In many countries, the same rules apply to the risk assessment of NGTs as for classical GMOs. But even after the ECJ decision, Finland (Questionnaire Finland, Annex 1, B, p 3,4) still holds that not all NGTs are covered by the Deliberate Release Directive if the deletion mutants obtained with new mutagenesis techniques have no foreign genetic material present in the final organism. Finland also refuses to apply the ECJ ruling on the Systems Directive (Questionnaire Finland, Annex 1, B, p 3,4) whilst Germany applies the ruling on this Directive (Questionnaire Germany, No. 1). France has expressed doubts as to whether epigenetic techniques of RNA-directed DNA methylation (RdDM) are covered by the Directive (Questionnaire France, No. 2).

[65] This does not necessarily require that in the non-EU states the respective NGT products fall under GMO regulation, as there are some non-EU states that perform a preliminary assessment of whether the respective NGT product falls under GMO regulation. The information submitted for this purpose could also be used for analysis in the EU, France, No.3 at the end.

[66] Reg. 1829/2003/EC

[67] Such systems also have to be used in classic (transgene) GE regarding highly refined products like e.g. vegetable oils.

3.2.4 What issues and challenges were not investigated?

One of the most important legal principles of the European environmental law[68] and specifically of the European genetic engineering law[69] is the precautionary principle. It requires precautionary measures when scientific evidence about an environmental or human health hazard is uncertain and the stakes are high. The COM study mentions this principle,[70] but only infrequently and superficially. It is mentioned six times total across the complete study, which is quite seldom considering its significance. In comparison to that the term "traceability" occurs 46 times und the term "labelling" even 60 times. And what is more the study does not address the all-important question of whether it is a violation of the precautionary principle to completely deregulate entire classes of NGTs and release them into the environment without a risk assessment.

Another important principle of European environmental law is the "polluter pays" principle.[71] This stipulates that polluters bear the costs of their pollution, including the costs of those measures taken to prevent, control, and remedy pollution, and those costs imposed on society. This principle would be inverted by the deregulation of NGTs, as the lack of identifiability and traceability of potential damage to human and animal health and biodiversity would interfere with holding polluters liable.[72] Yet this crucial principle is not addressed at all in the COM study.

The question of coexistence is addressed only very superficially. The study includes no analysis of the impact of deregulation of NGTs on the ability of the Member States to ensure GMO-free agriculture.[73] As the national laws securing coexistence build on the identification of GMOs, a deregulation would undermine the national coexistence laws and result in an unavoidable contamination of conventional und organic food by NGTs, thereby putting an end to consumer choice.[74]

Likewise remaining unaddressed is the question of whether deregulation of entire classes of GMOs can be compatible with the Cartagena Protocol on Biosafety.[75] The European Union is party to this protocol, and thus must abide by the rules that were established regarding protocols for risk assessment.[76]

Finally, at no point does the study mention the deregulation's consequences for the protection of ecologically sensitive areas, such as the areas of the European Natura 2000 network or areas protected under national law. The biodiversity of such nature reserves is especially vulnerable to NGTs, and their protection might very well be undermined by deregulation.[77].

[68] Enshrined in Art. 191 para 2 sentence 2 TFEU.
[69] Art. 1 Dir. 2001/18/EC.
[70] In comparison to that the term "traceability" occurs 46 times und the term "labelling" even 60 times.
[71] Enshrined also in Art. 191 para 2 sentence 2 TFEU.
[72] Cf. Chapter 4.1.1.3.2.3.
[73] Enshrined in Art. 26a Dir. 2001/18/EC.
[74] Cf. Chapter 4.1.1.3.2.5.
[75] https://bch.cbd.int/protocol/
[76] Cf. Chapter 4.1.1.3.2.6.
[77] Cf. Chapter 4.1.1.3.2.7.

3.2.5 Expositions on identifiability unbalanced

In its conclusions (COM study, 2021, p. 59f.), the Commission states in general terms that the currently applicable GMO regulation would no longer be "fit for purpose" with respect to NGTs, and therefore would need to be adapted to the technical progress yielded by them. Thus, the Commission ultimately asserts that the current GMO regulation cannot be applied to NGTs. Yet this claim ignores key statements in the Commission's own study and disregards additional relevant material, which is an indication of bias.

One argument for why the implementation of the current GMO regulation could not work for NGTs is their lack of identifiability. It is true that identifiability is much more difficult for certain NGTs than for classical genetic engineering. However, by concluding that "[t]here are strong indications that it [the EU genetic engineering law[78]] is not fit for purpose for some NGTs and their products" (COM study, 2021, p. 59) and the ample expositions questioning the identifiability (see COM study, 2021, p. 25) the Commission insinuates that the law must be adapted given the lack of capacity for identification. In doing so, the Commission contradicts its own statements (COM study, 2021, p. 25) wherein it quotes from a report undertaken by the EU Reference Laboratory which designates only as *questionable* whether such test methods can be developed in a short period of time *for all genome edited plants*. Whether something is *questionable* for all genome edited plants is entirely a different matter than whether such testing is essentially impossible.

A further step along this line is by dismissing the improvement of test methods as a moot point, given the supposed impossibility. By this assertion, the Commission's conclusions reveal themselves as biased: the COM study itself claims at one point that such technical limitations on identification may possibly be overcome:

> "Possible solutions mentioned by stakeholders to overcome the analytical limitations include expanding analytical tests to -omics techniques, the use of whole genome sequencing and the establishment of a global database containing all necessary information on NGTs and related patents" (COM study, 2021, p. 27).

In its conclusion, the Commission not only subverts statements appearing in the main text of its own study, but it also disregards those proposals made by certain Member States regarding the mitigation of the identification problem. Only by this imbalance is the Commission able to claim that the identification of NGTs is entirely impossible and allows to conclude that the current regulation of genetic engineering can no longer be applied to NGTs generally.

3.2.5.1 Scope of the ECJ ruling Mutagenesis I

3.2.5.1.1 Interpretation in the COM study

The COM study attempts to define the scope of the ECJ Mutagenesis I judgment, i.e. Case C-528/16, narrowly (ECJ 2018). Thus, the Executive Summary of the study (COM study, 2021, p. 5) states that:

> "The Court judgement only concerns mutagenesis techniques and does not concern other NGT namely cisgenesis/intragenesis, RNA-dependent DNA methylation, reverse reading and agroinfiltration".

[78] Meant is the EU genetic engineering law.

A more detailed justification for this view can be found in Chapter 4 (Status of new genomic techniques under EU law). There, the Commission recapitulates its explanation that the ECJ ruling applies in to directed mutagenesis only (COM study, Chapter 4.2.2), even though mutagenesis is a phenomenon which may also occur in nature (COM study, Chapter 4.2.3). Additionally, the technologies of cisgenesis and intragenesis are also covered by the Directive, since they are not covered by the scope exception in Annex I.B in the first place (COM study, Chapter 4.2.3).

The COM study nevertheless recommends against application of the ECJ ruling to organisms in which the genetic material is altered without changes in the nucleic acid sequence, provided that the changes can also occur naturally by mating and/or natural recombination (COM study, Chapter 4.2.4).

3.2.5.1.2 Evaluation of this interpretation

The most salient feature of this aspect of the Commission's study is its atypical presentation. Instead of clearly stating its aims, namely a restriction of the scope of application of the ECJ ruling, the language is formulated as a description of all organisms to which European genetic engineering law in the view of the study is still applicable:

> "In view of the above, organisms in which the genetic material has been altered without change of the nucleic acid sequence, in a way that does not occur naturally by mating and/or natural recombination, are GMOs subject to the provisions of the GMO legislation".

The statement that the ECJ ruling is not considered applicable to organisms in which the genetic material is altered without changes in the nucleic acid sequence – provided that the changes can also occur naturally by mating and/or natural recombination – thereby only emerges by close reading of the study's conclusion. This awkward presentation of a conclusion at odds with important substantive points of the study at least is remarkable.

Finally, the study's rationalisation of these discrepancies is itself contradictory and borders on incoherence (see COM study 4.2.4). The study holds that the interpretation of the term "altered" with respect to the definition of GMOs found in Art. 2 No. 2 of Directive 2001/18/EC is to be interpreted restrictively. By this, the study means that the term is not meant to cover organisms in which the genetic material is altered without changes in the nucleic acid sequence, provided that such changes may also occur naturally by mating and/or natural recombination.

Here, the COM study contradicts itself quite openly. On the very same page in which it advances the above argument, it also states that there are no indications for a restrictive interpretation in the directive itself (COM study, 2021, p. 21); yet it then proposes a restrictive interpretation two paragraphs later (COM study, 2021, p. 22). As justification, the study claims in the abstract that this reasoning follows from the ECJ judgment, although the ECJ judgment at no point deals with organisms in which the genetic material is altered without changes in the nucleic acid sequence where such changes also occur naturally by mating and/or natural recombination.

Ultimately, the COM study disregards completely the basic reasoning of this ECJ ruling, namely the argumentation with recital 17, according to which only those organisms are to be exempted from the directive which are obtained by techniques for genetic modification, which have been traditionally used in a number of applications and thus have a history of safe use. Even for organisms in which the genetic material is altered without changes in the nucleic acid

sequence, a history of safe use does not yet exist. This also is true for organisms, where such the changes also can occur naturally by mating and/or natural recombination acid sequence.

3.2.6 Additional material from the public debate

3.2.6.1 Identification of NGTs

The claim that the identification of NGTs would not be possible might also be refuted based on an extensive study commissioned by the Austrian Environmental Agency. According to this study, the identification of genome-edited plants is not possible with conventional quantitative real-time PCR (qPCR), especially when single nucleotide variants (SNVs) are involved. However, the study claims that it could nevertheless one day be possible to develop PCR tests. By way of example, an LNA-based detection system for SNVs has recently been developed that can detect genome-edited canola. Other possibilities include the use of RNaseH-dependent real-time PCR and digital droplet PCR (ddPCR). Such methods would need to be validated, but this is in any case possible. With proper training and technical upgrades, surveillance authorities should be able to identify genome-edited plants using reference material submitted in an application process. Monitoring of NGT products from other regions of the world would also be possible if databases such as EUginius also contain data on products from countries where NGTs are not regulated (Ribarits et al., 2021).[79]

3.2.6.2 Contradiction between official announcement and actual doing

Already the COM study itself but especially the Inception Impact Assessment on "Legislation for plants produced by certain new genomic techniques" as of 24 September 2021 (European Commission 2021a) shows a deep contradiction between official announcements and factual doing of the Commission. This has been analysed by the independent think tank Testbiotech with the following words:

> „While officially calling for adequate regulation and high safety standards, the EU Commission seems in reality to be following a different strategy: the document appears to indicate an intention and plans for far reaching deregulation of plants derived from new genetic engineering (New GE). Risks associated with the processes of New GE are either not given sufficient weight or are completely disregarded. Neither is the complexity of New GE applications sufficiently represented.
>
> The Commission is further ignoring the huge technical potential of tools, such as CRISPR/Cas gene scissors, to cause new and specific risks. Both the intended alterations and the unintended effects can differ extensively from those resulting from non-targeted mutagenesis and conventional crossing. Therefore, no conclusions on the general safety of plants derived from the processes of New GE can be drawn without carrying out detailed risk assessment or a 'product-based risk assessment'. Neither is it sufficient to simply consider the intended traits.
>
> Consequently, the published document is likely to misinform and misdirect the further discussions. The Commission is in danger of proposing new EU regulation which is not sufficiently based on science, but driven by the interests of industry and other stakeholders with an interest in the application and marketing of these technologies and products" (Testbiotech 2021, p. 1).

[79] For further details see Chapter 3.3.3.7.

Very important is also the following exposition: "The Commission document ignores the successes, the flexibility and the advantages of current EU regulation" (Testbiotech, 2021, p. 2). This finding is endorsed by the results of the present expert opinion.

3.2.7 Stakeholder and Member States views on GMO legislation

Section 4.3.2 of the Commission's study entitled "Member States' and stakeholders' views on implementation and enforcement" analyses the views of Member States and stakeholders regarding the application of GMO legislation as collected in its two surveys ("targeted consultation") (see COM study, 2021, p. 26ff.). The section in the COM study is divided into four unnumbered subsections. Questions from the questionnaire of the targeted consultations can be assigned to these subsections retrospectively. The following Table 7 provides an overview.

The responses evaluated in the subsection "**Implementation and enforcement of the GMO legislation as regards NGTs"** are intended to provide information on the adaptation of the legal framework to NGTs in the Member States and among stakeholders (see COM study, 2021, 26f.). "Most"[80] Member States had not adapted their "GMO enforcement system" as a result of the ECJ ruling or to the NGT. The Member States provided various reasons for this. First, certain reasons regarding the detection method were given: there was no reliable detection methods ("most" Member States); no prospect of success in developing detection methods ("some" Member States); and detection methods might not be acceptable as evidence in court ("some" Member States).

Other reasons given by Member States were as follows: there is no definition of NGT at national level and therefore no need for adaptation ("some" Member States); or similarly, the European Court of Justice has ruled that NGT are covered by GM legislation and therefore the existing legal framework is sufficient ("other" Member States). Some Member States indicated a preference for waiting on a harmonised EU approach before adapting the legal framework. Only "few" Member States have adapted their legal framework. The measures mentioned by these Member States were an extension of the scope of controls or the provision of additional information ("providing the supervision bodies and GM laboratories with extra information", COM study, 2021, p. 26).

Responses of the stakeholders are presented after those of the Member States. The COM study reports both similarities and differences between the responses from the Member States. "Almost all" stakeholders from the group of food business operators and academics ("food business operators or researchers/academics")[81] stated that there are analytical limits resulting in an impossibility of enforcing GMO laws with respect to NGT products. Some stakeholders felt that the development of detection methods was too resource intensive and lacked any prospect of success. Stakeholders from the group of "NGOs", on the other hand, referred to the ECJ ruling and contended that there is a legal obligation to develop detection methods.

[80] Although it is unsystematic, the COM study indicates the quantity of organisations and Member States which have cited each respective argument. For the purpose of analysis, this analytical category is also cited here to give the reader a sense of the use of these quantifiers.

[81] In the presentation of the stakeholder responses, the COM study points out, albeit unsystematically, the group of stakeholders from which the respective argument originates. For the purpose of analysis, this analytical category is also cited here to give the reader a sense of the use of these categories. See also section 3.8.1 "Presentation of the arguments" in this expert opinion.

Table 7: Questions in the targeted consultations on GMO legislation. Presumably evaluated in section 4.3.2 "Member States' and stakeholders' views on implementation and enforcement" in the COM study, 2021.

Unnumbered subsections	Number of question/Questionnaire*	Wording of the question
Implementation and enforcement of the GMO legislation as regards NGTs	Q2/MS	Have you taken specific measures (other than inspection) related to the application of the GMO legislation to NGT-products?
	Q5/SH	Are your members taking specific measures to comply with the GMO legislation as regards organisms obtained by NGTs?
Challenges for current and alternative traceability systems	Q3/MS	Have you adapted your inspection practices to cover all NGT-products and to ensure the enforcement of traceability requirements?
	Q4/MS	Do you have experience or information on traceability strategies, which could be used for tracing NGT-products?
	Q7/SH	Does your sector have experience or knowledge on traceability strategies, which could be used for tracing NGT-products?
	Q8/SH	Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?
Information on field and clinical trials and national catalogues of plant varieties	Q6/MS	Have plant varieties obtained by NGTs been registered in national catalogues?
	Q7/MS	Do you require specific information in national catalogue when registering plant varieties obtained by NGTs?
Stakeholders' views on national and EU-level support relating to NGTs	Q1/MS	Have you been consulted by companies/organisations/research institutes for regulatory advice or another issue on products developed or to be developed by NGTs?
	Q6/SH	Has your organisation/your members been adequately supported by national and European authorities to conform to the legislation?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

Some stakeholders in the survey also suggested possible solutions for overcoming the analytical limitations in the development of detection methods. They mention the following solutions: "expansion of analytical testing to -omics techniques [82], whole genome sequencing and the establishment of a global database containing all necessary information on NGTs and

[82] The term "-omics techniques" is used to refer to those techniques in molecular biology that end in "-omics": Gen*omics* (techniques of genome research), Prote*omics* (concerning protein metabolism), Epigen*omics* (concerning the epigenome) and others.

related patents" (see COM study, 2021, p. 27).[83] The COM study only lists these proposed solutions and does not explain them or examine their practicability.

This section of the COM study makes clear that there are different positions presented. There is an indication of who presents which arguments, and articulation of their distinct positions. In some cases, the number of the stakeholders or Member States making each statement is quantified (using the quantity designations "some", "most" and "several").

Under the second sub-heading "**Challenges for current and alternative traceability systems"**, both traceability and labelling are discussed. Only stakeholders were asked explicitly about labelling.[84] The COM study first presents the Member States' answers to questions of traceability. All Member States ("all") contended that no valid analysis strategy exists, and that therefore the enforcement of relevant laws is impossible.

"A number of" Member States see "contained use", "some" alternative control strategies and "a few" alternative traceability techniques as a solution to this problem. One suggested example of alternative traceability techniques is a document-based system. The COM study objects, on the grounds that such alternative traceability techniques would distort competition and disadvantage producers in the EU. It remains unclear whether this response derives from the opinions of the respondents themselves or from views of the COM study's authors.

The proposal for GMO-free certificates reported by the COM study is of unclear provenance (Member State survey or stakeholder survey). Again, after mentioning this proposal, the study raises an objection, namely that such certificates would involve considerable financial and human resources. It is also unclear who raised this objection. If it originates from the COM study itself, then it is unsubstantiated. Other suggestions for solutions to the problem of traceability mentioned in the COM study are as follows: "end-to-end transparency", "mass balance", "identity preservation schemes" (see COM study, 2021, p. 27).

These proposals are also criticised in the COM study, which rehearses the opinion of "some" stakeholders that these solutions are only applicable for small quantities and require the trust of suppliers. One solution proposed in the COM study, as stated in the consultation, is to exempt NGT from traceability requirements and apply it only in certain market segments, such as the organic sector. This proposal is also criticised – though the source of the criticism remains obscure – on the basis that organic labels are the wrong instrument for the traceability of NGT. Assumptions follow about who would have to bear the costs for traceability schemes: the main producers or the sector that develops and uses the technology. Some ("other") stakeholders would emphasise the view that the costs would in any case be disproportionate to the benefits. The various proposals for traceability and labelling are apparently not only reproduced by the study, but also discussed in terms of their practicability. However, the arguments put forward are not substantiated. In other sections, there is even less examination of practicability.

[83] The COM study devotes one sentence to the question of whether there are products on the market within or outside of the EU. The connection to the foregoing material is not clear, and is not discussed by the COM study.

[84] Similarly, only stakeholders were asked a question about their views on labelling (question 28 of the stakeholder questionnaire: "What is your view on the labelling of NGT-products? Please substantiate your reply". However, this question is analysed in another part of the COM study (see section 4.9 in the COM study, 2021, p. 43f.; see also section 3.6.3.3 "Labelling" in this expert opinion).

Under the subheading **"Information on field and clinical trials and national catalogues of plant varieties"**, informative answers from the consultation of the Member States are evaluated (COM study, 2021, p. 29f.). "All" Member States stated that no plant produced by NGT was registered in the national catalogues. "A number of" Member States had authorised field experiments even after the ECJ ruling.

Some Member States had expressed concerns about the current legislation in this context. In their opinion, the current legislation would hinder technological development and force breeders to use less efficient methods. As a result, some field experiments had been withdrawn. "One" Member State would have banned field experiments until 2023. The COM study does not specify which Member State this was. It would have been helpful to know which Member States made each respective statement. The COM should have included references to the relevant questionnaires.

The analyses under the fourth subheading **"Stakeholders' view on national and EU-level support relating to NGTs"** evaluates – contrary to its title – material drawn from consultation with the Member States in addition to that derived from stakeholders. "Most" Member States reported that they had been consulted for regulatory advice. They had also organised information events on topics related to NGT. "Most" stakeholders from the "agri-food operators and academics/researchers" sector complained about a lack of support from the EU, especially regarding reliable detection methods and legal certainty.

The COM study indicates the range of different experiences: "Some" stakeholders felt that the dialogue with EU institutions was very difficult or non-existent, while "others" found the cooperation very useful. It would have been helpful at this point if the COM study had indicated which stakeholder groups were being referred to in each case. This would have answered the question of which stakeholders felt more or less involved. In this way, the EU could have reflected on its own dialogue structures and improved them in order to involve neglected stakeholders more and to reduce imbalances. As it stands, however, the information given by the COM study remains incomplete.

3.2.8 Interim summary of implementation and inforcement

Regarding implementation and enforcement of GMO legislation concerning NGTs the study first gives an overview of 31 non-EU states. According to the study one third of those countries already have adapted their laws and even from the two thirds of countries who still regulate NGTs under general genetic engineering law, half of them discuss a specific legal framework for NGTs. So this overview gives the impression that the majority of countries want specific rules for NGTs. However, the Commission does not explain and makes transparent what the criteria for selecting only just those 31 countries were.

The legal status of GMOs in the EU is governed by the Deliberate Release Directive prescribing among others a strict application of the precautionary principle, risk assessment, an authorisation process prior to marketing as well as labelling and monitoring obligations.

Regarding food and feed those rules are accompanied by the food and feed regulation where among others toxicological tests are required. Furthermore, products may not be misleading or differ from conventional food and feed in a nutritionally disadvantageous way.

The Traceability Regulation contains rules to safeguard traceability of GMO food and feed products in order to detect any adverse effects and to be able to withdraw products with

unforeseen adverse effects on human and animal health or the environment. Furthermore there are special rules for the information of the end-consumer.

The mutagenesis decision of the European Court of Justice had to clarify whether targeted mutagenesis – as opposed to random mutagenesis – falls under the Deliberate Release Directive. The clear finding of the court was that targeted mutagenesis does fall under the Directive and is not exempted like random mutagenesis. The main reason for this was that, as opposed to random mutagenesis, there is so far no history of safe use for targeted mutagenesis. And if this is the case the precautionary principle demands that this technique falls under the Directive.

The present expert opinion examines how far the COM study considered important points of the ECJ's decision. The result was that the COM study seems to interpret the decision of the European Court of Justice in a very narrow way and therefore not consistent with the central lines of the Court's reasoning. These central lines of the reasoning were (inter alia):

- The precautionary principle is of particular importance and
- Article 3, paragraph 1 of the Deliberate Release Directive must be strictly interpreted.

In its decision in Case C-528/16, the ECJ had stated that directed mutagenesis processes ("new techniques/methods of mutagenesis") cannot be exempted from the obligations of the Deliberate Release Directive. In particular, the second central line of the argumentation of the ECJ – as mentioned above – leads, in the view of the present expert opinion, to the conclusion that NGTs, which were not directly part of the proceedings before the ECJ, cannot be exempted from the obligations of the Directive either.

Regarding the implementation of the European genetic engineering law the identifiability and traceability is a controversial issue. This point is important because a unique identification of each GMO is prerequisite for the authorisation of the products. The study gives the impression that this identifiability currently is not possible and also will not be possible. On this assumption the study draws the conclusion that as this is not possible the rules regarding identifiability have to be discarded. However, there are strong signs that in future such an identifiability can be developed. In the meantime, document-based traceability systems can close the gap, as it is common in other regulatory systems. So the claim that the lacking identifiability demands a waiver of those traceability systems, is not valid.

It is conspicuous that the COM study does not or only very little deal with aspects which are legally mandatory when amending environmental law. By far the most important principle when considering a deregulation of GMOs is the precautionary principle. It requires precautionary measures like risk assessment when, as it is the case with NGTs, the risks still are uncertain. The study largely disregards this fundamental principle of European environmental law.

Equally relevant is that the polluter pays principle, which stipulates that the one who damages the environment has to be held liable for that, is not addressed. This would not be possible any more in case of certain forms of deregulation. The study does not address this important issue with one sentence.

A deregulation of NGTs also threatens GMO-free agriculture, as this could undermine the European and national provisions to protect GMO-free agriculture and thus puts especially the organic sector at risk. This issue also was addressed only superficially without considering any legal aspects.

Not mentioned at all was the protection of ecologically sensitive areas and the exigencies of the Cartagena Protocol, which the European Union in its legislation has to comply with.

The present expert opinion reveals a contradiction in the aim of the Commission to secure the precautional principle at the one hand and in fact to lower the standards for certain NGTs, that can pose risks to human health and the environment.

3.3 Current and future technical developments of NGTs

This section refers to the development of those techniques summarised in the context of the COM study and characterised as "new genomic techniques". Technical aspects of the outcomes of the Commission's study will also be discussed here.

Chapter 3.4 "State of the utilisation of genomic techniques for agriculture, industry, and pharmacy" of the present expert opinion deals with applications of the new genomic techniques in "real life" plants (including products such as food, feed, seed and fibre).

With respect to the analysis of the current and future technical developments, the European Commission's Joint Research Centre (JRC) had undertaken a detailed technical review (Broothaerts et al., 2021). The technical review has served as the most important source for the COM study's chapter on the "State of the art on NGTs" (COM study, 2021, Chapter 4.1) together with the Member States' and the stakeholders replies to the Commission's study as part of the targeted consultation (for details see Chapter 3.1.1.2). Additionally, the authors of the aforementioned COM study chapter highlight and use parts of an (older) explanatory note written by the Group of Chief Scientific Advisors (SAM HLG, 2017).[85] The methodology of the COM study is outlined in Chapter 3.4 State of the art on NGTs, and the key findings of the Broothaerts et al. (2021) view can be found in Section 4.1.2 of the Commission's study (COM study, 2021, p. 9).

Technical developments of NGTs as such, and specifically the technical developments of a certain NGT product, its regulation and risk assessment are closely connected. The risk assessment is based on the technical developments, and it should keep pace. The European Food Safety Authority (EFSA) had been asked by the Commission to conduct a review, titled "Overview of EFSA and European national authorities' scientific opinions on the risk assessment of plants developed through New Genomic Techniques" (Paraskevopoulos & Federici, 2021). Consequently, some references to EFSA publications can be found in this chapter of the present expert opinion as well.

Last but not least, certain outstanding questions remain concerning detection and identification of NGT plants and products. Those aspects can be found in this chapter as well. The European Network of GMO Laboratories (ENGL) together with the EU Reference Laboratories (EURL) published the report "Detection of food and feed plant products obtained by new mutagenesis techniques" by March 2019 (ENGL, 2019), see Chapter 3.3.3.7 below. Although it was not written at the request of the European Commission in the context of the COM study, the ENGL report was taken into account by the COM study.

Chapter 3.3.1 of the present expert opinion outlines the technical outcomes and challenges of the COM study. Technical outcomes in this context, are results that the COM study identifies about the state of the art of NGTs. Some findings are expressed explicitly. In part,

[85] By then, the "Scientific Advice Mechanism (SAM) High Level Group of Scientific Advisors".

however, implicit findings may also be established by the COM study.[86] In Chapter 3.3.2, specific methodological points of criticism are presented for this topic area. While Chapter 3.3.3 asks how well the COM study has researched this area, Chapter 3.3.4 shows the presentation of the positions of Member States and stakeholders. Chapter 3.3.5 shows topics that, according to the assessment of the present expert opinion, were not addressed by the COM study.

3.3.1 New or known technical outcomes and challenges of the COM study

3.3.1.1 Similar products – similar levels of risk

The most important outcome of the COM study in the context of technical aspects and developments is exemplified by the following passage:

> "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59).

This conclusion evidently combines technical and risk-assessment aspects. The question arises as to how the similarity of the products mentioned is to be constituted. Various approaches may be employed in analysing such similarities. The COM study focuses on new genomic techniques. In this respect, it is appropriate for the present expert opinion to focus on the question what are the technical contributions of the new genomic techniques to the making of NGT plants and products. This approach leads to the quality of the changes of their DNA, and the parameters for the investigation and comparison. Therefore, the present expert opinion firstly shows what can be found in the COM study about molecular changes in NGT products. Later, information on the molecular changes of the other techniques and methods for plant breeding and development will be presented if they are addressed in the COM study.[87] This part of the present expert opinion deals with the following question:

What are in detail the parameters for the investigation and comparison of molecular changes of the genome?

The question is of great importance, since the COM study repeatedly compares – or rather, it claims to compare – the plants and products, obtained by NGTs, by cis- or intragenesis, by techniques of random mutagenesis, or by conventional breeding. As can be seen in the passage exemplified above, the effects of the different techniques and methods are also partially put on an equal footing in the COM study.[88] The changes induced by these different genomic techniques and breeding methods are also part of these comparisons:

> "EFSA concluded, on the basis of recent experimental evidence, that the off-target mutations potentially induced by SDNs are of the same type as, and fewer than, those in conventional breeding, including spontaneous mutations and those produced by physical and chemical mutagenesis" (COM study, 2021, p. 53).[89]

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[86] If, for example, the COM study states that the NGT plants and products cannot be found or identified, then this is a statement about the problems with the corresponding methods. Implicitly, however, the COM study assumes certain technical conditions. This is what the present expert opinion calls an implicit statement or an implicit technical finding. For the details of the example given, see Chapter 3.3.1.3 below.

[87] See Chapter 3.3.1.4 below.

[88] In this example, the effects are the "similar products" with "similar risk profiles".

[89] For details regarding the recent experimental evidence see Chapter 3.3.3.3.

This gives the impression that a detailed examination – a comparative investigation of the techniques, the methods and the changes – has taken place.

Molecular changes obtained by NGT

On-target changes result from the use of a genome editing tool at a known location in the genome with a distinct DNA sequence. The locations, i.e. targets, were previously identified and chosen by researchers and plant developers before on the basis of sequence information and knowledge of the respective gene functions. In the words of the COM study: "[N]ew technological developments mean that changes can be directed to a selected genomic location, thus enabling more precise editing of the genome" (COM study, 2021, p. 12). Characterisations of the changes in the COM study are rare. The most important section in this respect is in Chapter 4.1.2 of the COM study ("Characteristics of NGT genetic modifications"; COM study, 2021, p. 13). In Chapter 4.1.2 it reads for example:

- "Sequence variations to the genome may be entirely novel or may occur already in other individuals of the species. NGTs may also introduce into an organism new sequences derived from other species" (COM study, 2021, p. 12).
- "A NGT may generate different genome alterations depending on how it is used. Moreover, similar alterations, e.g. a single nucleotide substitution, can often be generated by different NGTs [...] NGT-targeted alterations are increasingly precise, in terms both of being localised to a specific target site and of the specific DNA alteration that is intended. The alterations are generally more subtle than with established genomic techniques, although insertions of long sequences may be achieved by some NGTs when used in combination with a suitable donor template. Consequently, products obtained by NGTs or hybridisation techniques, or occurring naturally are becoming indistinguishable from each other." (COM study, 2021, p. 13).
- "As the changes are often small and instructed by similar changes identified in other organisms" (COM study, 2021, p. 13).

Later[90] the COM study notes:

> "EFSA observed that the potential for random changes to the genome caused by the insertion event is not limited to cisgenesis, intragenesis and transgenesis; in fact, it is independent of the breeding methodology. Mutational processes, such as insertions, deletions or rearrangements of endogenous genes and regulatory sequences, are also known to occur in conventional breeding" (COM study, 2021, p. 30).

These examples show that the descriptions of the NGT changes in the COM study remain rather general. Details are scant, molecular details are practically not shown at all. The COM study presents the basic principles of SDN techniques, for example. In these, a double-strand break (DSB) of the DNA is only initiated at a selected site of the genome. The actual genome editing is then a result of the repair of this DSB by one of several – but not further explicated – cellular repair systems, which occasionally creates mutations. These techniques could be used with or without a donor sequence, which may serve as a template in the repair process. Other techniques use, the COM study continues, "either catalytically impaired SDNs that generate only a single-strand break in the DNA or SDNs with completely abolished cleavage activity that only recognise and bind a target sequence, or involve oligonucleotides for DNA

[90] In the context of Chapter 4.4 "Safety of new genomic techniques".

editing" (COM study, 2021, p. 12). The CRISPR-Cas SDN technology is presented by the COM study over the course of six lines. It is characterised as a platform "for many of the other NGTs" to which various functionalities can be added, and, following the COM study, it is easy to implement; furthermore, it is "useable for simultaneous editing at multiple sites" (COM study, 2021, p. 12f.).

The molecular delivery systems of the NGTs are also discussed – albeit in a cursory and superficial manner. The systems are used to transport the NGT components into the cells. These are the systems of transgenesis: gene gun, bacterial and viral systems.[91] Some lead to transient expression of genes. Others may initially insert fixed gene sequences into the genomes of modified plants, which are later removed. Overall, the COM study emphasises that the need for different systems reflects the diversity of NGTs (see COM study, 2021, p. 13).

The COM study rely on Broothaerts et al. (2021) as their main source for technical descriptions of new genomic techniques. Accordingly it is also their main source, for discussion of the molecular changes which can be inserted into plant cells using NGTs or other techniques and methods. Besides this, the SAM HLG, the central scientific advisory body of the EU Commission, plays an important role. In 2017, the SAM HLG had published a report on genome editing and NGT (SAM HLG, 2017). The COM study places what may be seen as a summary of results and assessments of the SAM HLG report prominently at the beginning of its own chapter on the state of the art on NGTs (COM study, 2021, p. 11f.). This presentation undoubtedly emphasises the contents of the SAM HLG report. But statements about NGTs remain largely general. As the SAM HLG noted:

> "[G]enome editing makes it possible to target insertions, resulting in comparatively fewer unintended effects on the expression of other genes or their disruption. It also enables small, precise and specific changes, such as point mutations, which can also be observed in nature" (COM study, 2021, p. 11, Chapter 4.1.1).

Broothaerts et al. (2021) describe different "types of nucleic acid alterations induced by NGTs" with more details (Broothaerts et al., 2021, Table 1, p. 15f.; see Table 8). At the same time they relativise that the "table does not specify all the functionalities of each NGT as many of them may be used in different versions and under different conditions, which cannot be all displayed in a single table" (Broothaerts et al., 2021, p. 14).

Broothaerts et al. then come to a number of conclusions, the most important being: "Some NGTs may have a very narrow application, e.g. linked to a specific base, while others could affect several types of changes depending on how they are used" (Broothaerts et al., 2021, p. 17). Broothaerts et al.'s conclusion suggests that it is quite possible to characterise the changes and modifications introduced by NGTs at a level of detail beyond what the COM study attempts. Moreover, Broothaerts et al., make clear that differences emerge when a technique is used or implemented differently. This constitutes quite a different conclusion when compared to the COM study's "same type of" or "similar alterations" language.

[91] Biochemical techniques like PEG (polyethylene glycol) are not mentioned in the COM study, although presented in Broothaerts et al. (2021).

Table 8: The types of nucleic acid alterations that may be induced by distinct NGTs in different organisms (selection) Intended sequence alteration, type of NGT, modifications on the molecular level, obtained by NGTs (description quoted according to Broothaert et al., 2021, p. 15f.

Intended sequence alteration	NGT	Modification
Substitution of one or a few bases	Base editing	Mostly C <> T or A <> G, with some exceptions
	Site-directed nuclease (SDN)	All base substitutions possible
	Oligonucleotite-directed mutagenesis (+SDN)	One or few base substitutions, defined by donor template
	Prime editing	One or few base substitutions, defined by RNA donor template
	Site-specific recombination	Replacement of short target sequence
Substitution of contiguous sequence	Site-specific recombination	Replacement of donor sequence
	Site-specific recombination	Replacement of donor sequence
	Site-directed nuclease (SDN)	Replacement of donor sequence
Sequence disruption	Site-specific transposition	Insertion of donor sequence
	Site-directed nuclease (SDN)	Deletion or insertion of random basepairs
	Site-directed nuclease (SDN)	Sequence replacement by donor sequence
Sequence deletion	Two site-directed nucleases or two sgRNAs	Sequence deletion
	Prime editing	Sequence deletion defined by RNA donor template
	Site-specific recombination	Sequence deletion defined by RNA donor template
Sequence insertion	Site-specific recombination	Sequence insertion, defined by donor template
	Prime editing	Sequence insertion, defined by RNA donor template
Gene regulation	DNA Methylation	Removal of methyl groupsfrom gene promoter region
	Histone H3K27	Enrichment of acetylated H3K27 at target site
	Transcription activation (CRISPRa)	H3K27 acetylation, H4K4 trimethylation
	DNA Methylation	De novo addition of methyl groups to gene promoter region
	Histone H3K27 deacetylation	Removal of methyl groups from H3K27
	Histone H3K4 demethylation	Removal of methyl groups from H3K4
	CRISPR interference (CRISPRI9	H3K9 & H3K27 trimethylation
	RNA base editing	Deamination of adenosine or cytosine in RNA
RNA sequence correction	RNA base editing	Deamination of adenosine or cytosine in RNA
	RNA splice isoform manipulation	Exon in- or exclusion from mature RNA
RNA knockout	RNA interference	Cleavage of RNA

The COM study does mention that an NGT may produce different changes in a genome depending on how the technique is used, but its presentation is not convincing. The study does not provide any further information to contextualise such claims. Instead, it moves on to a new topic: "Moreover, similar alterations, e.g. a single nucleotide substitution, can often be generated by different NGTs" (COM study, 2021, p. 13). Here, too, an adequate explanation is missing. The same problem also occurs in the study's contention that a possible change cannot always be associated with the use of a specific technology. The causal link to the previous sentence remains unclear:

> "Not every desired alteration can be readily achieved at any sequence, because some NGTs may be restricted as to the recognition and binding of their targets. *Therefore*, the technique itself *cannot always* be directly linked with the type of alteration that could be obtained" (COM study, 2021, p. 13, emphasis by authors).

Also noteworthy is the phrase "cannot always". It suggests that it is entirely possible, i.e. mostly and not just in exceptions, to associate certain changes with certain NGTs. This possibility, however, is not pursued by the COM study, although it is at least partially laid down in its supplementary material or in the opinions of the Member States and/or stakeholders.[92]

Subsequently, the COM study turns to off-target alterations. The study begins its analysis with an evaluation criterion according to which the "efficiency of creating a desired genomic alteration has to be weighed against the probability of generating unintended effects at off-target sites" (COM study, 2021, p. 13). This is followed by a sentence stating that off-target changes have been described in the literature. The COM study pursue the details of the changes themselves any further. Rather, it turns to the optimisation strategies, leaving it partly unclear whether these are already working or whether their development can be expected from the perspective of the COM study. It is also shown that off-target changes can in some cases be predicted on the basis of bioinformatics methods. But the reader cannot know what "some cases" means and it is unclear how it relates to the remaining cases (see COM study, 2021, p. 13). The quantitative ratio of the text passages is important to note: while the COM study deals with the fact that off-target changes were described in less than one line, the optimisation strategies are described over six lines.[93]

Paraskevopoulus & Frederici (2021) mention some details of changes with respect to SDN techniques. It reads as follows:

> "According to opinion 3 (p. 25), data sets describing the type of mutations generated by SDN-1 *are reported mainly for Arabidopsis*, rice and soybean. The most frequently detected mutations are *insertions of a single adenosine or thymidine nucleotide, followed by small deletions of predominantly one nucleotide and deletions of < 10 nucleotides*. Other detected mutations are *nucleotide replacements and insertion of > 1 nucleotides*, but to a lesser extent. There is the indication that dependent on the gRNA, the targeted locus or the experimental setting, *the mutation spectrum may differ* (Opinion 3, p. 25f.)" [Paraskevopoulus & Frederici, 2021, p. 17; emphasis by authors; for opinion 3 see Hilscher et al., 2017).

[92] See for example Chapter 3.3.3.7 below.
[93] See Chapter 3.3.2.5 below.

For example, if mutagenesis with EMS[94] in *Arabidopsis* plants triggers a base exchange from C to T in most cases. Can this be considered to be the same (to be "same type of") as if, for example, the use of a certain zinc finger nuclease results in an arbitrary base exchange (from C to T)?[95] Or would it be already "of the same type", if a base exchange would happen after the use of zinc finger nucleases, no matter what kind of?

As for the description of the molecular level of the changes caused by NGTs, the COM study itself remains on the surface at best. The presentation of the similarity of changes, as described vaguely by the COM study, is thus neither be concretised nor confirmed. The 'offers' from the supplementary material remain unused. Nor does it add anything to the claim of a substantial comparison of different approaches to modifying the genome.

3.3.1.2 Intended changes, obtained by NGTs

The COM study notes that with NGTs often traits are being integrated in plants that are already known from other crops. But of course, attempts are also being made to insert new traits into the plants, i.e. traits for which previously used techniques or conventional breeding had not yet succeeded.[96] In this context, an important development can be observed: The developers of NGT plants and products are focusing less on making the new genetic technologies work as cleanly as possible. This means that the exact functioning of the NGTs is apparently not the focus of interest. Rather, it is more on the results. Whether this is due to an error in the technology or to the planned function is apparently regarded as secondary (Interview 1).[97] This development is also reflected in the COM study: "The efficiency of creating a desired genomic alteration has to be weighed against the probability of generating unintended effects at off-target sites" (COM study, 2021, p. 13). However, this has not yet had any effect on the narrative accompanying the development of NGT plants and products. The narrative continues to be characterised by precision. The COM study lists the current changes to be generated with NGTs. The intended changes are not presented specifically, but only summarised in categories, e.g. "[r]esistance to biotic stressors such as nematodes, fungi, bacteria, viruses and other pests, pathogens or parasites" or "[m]odified colour or flavour" (COM study, 2021, p. 16[98]). The COM study highlights that NGTs can be applied in elite lines, shortening the development time for organisms with desired phenotypes. Since the changes are small and often modelled on other plants, the phenotypes of NGT plants are more predictable. Less time is also needed for subsequent tests (see COM study, 2021, p. 13). One of the special features within the intended changes of NGTs is multiplexing. It is mentioned only once in the COM study, in the appendix. Apparently, it was brought forward by a stakeholder: "The unintended effects of multiplexing techniques, possible with NGTs, are a concern" (COM study, 2021, Annex D, "Table 12: Further challenges and concerns reported by stakeholders"). Broothaerts et al. (2021) show that multiplexing enables the simultaneous modification of the genome at

[94] For details of the mutagenesis with EMS see for example: Unan, Deligoz, Al-Khatib & Mennan (2022): Protocol for ethyl methanesulphonate (EMS) mutagenesis application in rice. Online: https://open-research-europe.ec.europa.eu/articles/1-19 (accessed 3 November 2022).

[95] See EFSA, 2012, p. 16; with reference to Ossowski et al. (2010).

[96] See COM study, 2021, p. 15.

[97] The Cibus rapeseed can be seen as an example; see Chapter 3.4.3.1 "Commercialised plants obtained with NGT" below.

[98] For details see Chapter 3.4 below.

different sites. It is possible in conjunction with different NGTs e.g. the CRISPR-Cas based techniques (p. 23; for details see Chapter 3.3.3.5 below).

The outlook of this part of the COM study is correspondingly optimistic – albeit very general:

> "[T]he technology will be increasingly deployed across the various biological kingdoms; further improvements to current and next-generation NGTs in the coming years in various organisms will probably expand the opportunities for agricultural breeding, industrial biotechnology and human gene therapies and vaccines" (COM study, 2021, p. 14).

3.3.1.3 Detection and identification – technical issues

The Commission's study took account of the ENGL report "Detection of food and feed plant products obtained by new mutagenesis techniques" (ENGL, 2019) as the main source of information on this issue. It should be noted that Subchapter "4.3.1 ENGL report on the detection of new mutagenesis products" of the COM study is part of Chapter "4.3 Implementation and enforcement of EU GMO legislation with regard to NGTs". Accordingly, the COM study does not classify the topic of detection primarily in a technical, but rather in a regulatory context. However, there are a number of technical details that need to be taken note of.[99] The ENGL report had been requested by the European Commission in October 2018. Following the Commission's study, the report aims to show the possibilities and limitations of analytical detection and identification methods, in particular:

- "[W]hether and under what conditions current analytical possibilities allow detection and quantification of all types of mutagenesis events and other new breeding techniques (NBTs); and
- if not, what possibilities exist to overcome any issues identified" (COM study, 2021, p. 25).

The ENGL report states, that the term "detection" encompasses the following aspects:

- (1) "[T]he 'finding' of a target sequence, i.e. detection *sensu stricto*, without necessarily being specific for the genome-edited event"
- (2) "[I]dentification of the detected sequence as a specific genome-edited event"
- (3) "[Q]uantification of the genome-edited event" (ENGL, 2019, p. 6).

Firstly, the COM study stresses – with respect to the ENGL report mentioned above – that it would be very unlikely to detect unauthorised genome-edited plant products in food or feed, if information on the altered DNA would not be available prior to an investigation. This is important regarding market control analysis and would be due to the technology currently used, the PCR method, which is designed to find current GMOs. The PCR technique could not be adapted for the search for genome-edited plant products, as there are no typical DNA constructs in the products discussed here.[100] If an analysis method were chosen in which sequencing was carried out first, a change could indeed be found. However, the COM study goes on to write about the assessments of the ENGL report, it would not automatically be possible to confirm the presence of a genome-edited plant product. This is the case since the change found may have arisen by means of another approach than genome editing. This could be

[99] For the regulatory aspects of detection see Chapter 3.2.3 above.
[100] Besides SDN-3 plants and products.

conventional breeding or random mutagenesis, and the resulting organisms would be exempted from GMO legislation.

Following ENGL, the COM study secondly states that it is questionable whether event-specific – and quantitatively reliable – methods can be developed to find all genome-edited plant products. However, such a method would be a necessary prerequisite for the authorisation of a GMO according to the current state of regulation. If a plant-based product would contain a non-unique DNA alteration, a detection method might not be specific enough to identify the genome-edited plant (see COM study, 2021, p. 25). The COM study indicates the conclusion of the ENGL report as follows: The "validation of an event-specific detection method and its implementation for market control will be feasible only for genome-edited plant products carrying a known DNA alteration that has been shown to be unique" (COM study, 2021, p. 26). Finding unknown genome-edited plant products would be impossible and there were several topics that need to be further investigated.

The COM study also uses the report of the SAM HLG (2017) in the context of the question about detection and identification of NGT: With respect to the final question, whether detection and identification of NGT would be possible, the Commission's study describes the position of the SAM HLG as follows: "Nevertheless, it is *generally not possible* to determine whether the changes are the result of natural causes or the use of any breeding technique." (COM study, 2021, p. 11; emphasis by authors) The whole paragraph of the COM study reads:

> "The SAM HLG observed that prior information on an NGT product enables detection with a variety of analytical techniques. Detection is more challenging in the absence of information on the changes introduced, but a significant attempt can be made through the application of whole genome sequencing in combination with bio-informatics; in such cases, detection depends on the availability of a suitable reference genome. Nevertheless, it is *generally not possible* to determine whether the changes are the result of natural causes or the use of any breeding technique" (COM study, 2021, p. 11; emphasis by authors).

The COM study summarises the JRC technical report of Broothaerts et al. (2021) in a similar manner:

> "NGT-targeted alterations are increasingly precise, in terms both of being localised to a specific target site and of the specific DNA alteration that is intended. The alterations are generally more subtle than with established genomic techniques, although insertions of long sequences may be achieved by some NGTs when used in combination with a suitable donor template. *Consequently, products obtained by NGTs or hybridisation techniques, or occurring naturally are becoming indistinguishable from each other*" (COM study, 2021, p. 13; emphasis by authors).

The quote is taken from the COM study's Subchapter "4.1.2 JRC review on scientific and technological developments – key findings". However, in the JRC technical report itself the wording is slightly different. It reads: "Consequently, the products obtained by NGTs, by hybridisation techniques or occurring naturally are *becoming more and more indistinguishable* from each other" (Broothaerts et al., 2021, p. 67; emphasis by authors).

The complete paragraph from Broothaerts et al. states the following:

> "NGT-targeted alterations are more and more precise, both in terms of being localised to a specific target site and in terms of the specific, intended DNA alteration. Compared to EGTs [established genomic techniques] the alterations are generally more subtle, although insertions of long sequences may be achieved by some of the NGTs when used in combination

> with a suitable donor template. Consequently, the products obtained by NGTs, by hybridisation techniques or occurring naturally are *becoming more and more indistinguishable* from each other" (Broothaerts et al., 2021, p. 67; emphasis by authors).

The COM study indicates the fact that only a part of the NGT plants and products is concerned, for which the detection, identification and quantification may not be possible or not be possible immediately with the following formulation: "*it is questionable whether such methods can be developed readily for all genome-edited plant products".* The COM study substantiates this by referring to the possible lack of specificity of methods to detect plant products that do not contain a unique alteration. Furthermore, accurate quantification could be challenging if only a few base pairs are altered (see COM study, 2021, p. 25, emphasis by author). In addition, the COM study states that requirements are high: "Finally, all methods have to comply with performance criteria and be fit for testing complex matrices and processed products, which is the routine situation in enforcement" (COM study, 2021, p. 55).

Presenting "[p]ast evaluations of the EU GMO legislation as regards NGTs" the Commission's study claim, that the evaluators back in 2010[101] noted that

> "while modifications introducing new DNA sequences can be easily detected, the problem with targeted mutagenesis is that there is not the same degree of 'molecular novelty' and the end product might not differ from those obtained via traditional breeding or random mutagenesis. Also, even if it were possible to detect the modification, it would be impossible *in certain cases* to determine whether it was based on 'old' or 'new' techniques" (quoted following COM study, 2021, p. 22; emphasis by authors)

In this context, it remains unclear to what extent the identification of this technical challenges at that time (2010) is still relevant today. For example, CRISPR did not exist in 2010. Secondly, on the factual level, the wording "in certain cases" remains the most important. These "certain cases" are, however, not characterised – better: not systematically and clearly characterised – neither in the evaluation from 2010, nor in the COM study.

3.3.1.4 Details of some NGTs

Due to the abundance of material, an exhaustive analysis of individual NGTs is not possible within the scope of the present exert opinion. For this reason, some details are only presented as examples. A detail is particularly shown in the present expert opinion if it helps to illustrate a development or a challenge.

The COM study does not go into the details of the different new genomic techniques. Following the concept and workflow of the Commission's study, this kind of information can be found in the supplementary material obtained by Broothaerts et al. (2021). In a brief summary of the SAM HLG report, few details about the NGTs are presented in the COM study. The COM study is more concerned with general statements about NGT, as for example: "A NGT may generate different genome alterations depending on how it is used" (COM study, 2021, p. 13). Usually, the COM study uses technical or molecular information on NGT implicitly, i.e. as technical assumptions that can be derived from other statements or that necessarily follow from them (see Chapter 3.3 above).

[101] See Chapter "Evaluation of the EU legislative framework in the field of GM food and feed", 2010; COM study, 2021, p. 22, fn. 48.

For their part, Member States and stakeholders bring facts and ideas about the new genetic technologies into the process. To what extent these have been taken into account by the COM study remains open.[102]

3.3.1.4.1 Broothaerts et al. sort NGTs in four groups

The COM study and Broothaerts et al. (2021) organise NGTs into four groups:

1. NGTs creating a double-strang break (DSB) in the DNA;
2. NGTs achieving genome editing without breaking the DNA double helix or generating only a single-strang DNA break;
3. NGTs inducing epigenomic changes; and
4. NGTs acting specifically on ribonucleic acid (RNA) (see COM study, 2021, p. 12).

But this system is not used by the COM study, with one exception: The presentation of the results of the market review by Parisi & Rodríguez-Cerezo (2021) mentions these groups. Apart from that, the COM study sorts the NGTs with SDN-1, SDN-2 and SDN-3, not least when it maps the EFSA findings, for example (e.g. p. 29 of the COM study).

In this context, it is of great importance to recognise that naming NGTs as side-directed nucleases (SDNs) is not the only way to take advantage of the NGTs' special mode of operation already in their name. Rather, NGTs are in the opinion of the present expert opinion even more precisely referred to as sequence-specific nucleases (SSN) (Zischewski et al., 2017).

3.3.1.4.2 CRISPR

The Commission's study understands the CRISPR technology in terms of a platform that can be used in a wide variety of ways (see COM study, 2021, p. 12f.). With the term platform, the COM study attempts to render the immense diversity with which CRISPR variants are modified, further developed and combined with one another or with other techniques. In this context, the COM study repeatedly emphasises the enormous potential of NGTs, especially CRISPR. Symptomatic is the use of the term "game-changer" (see COM study, 2021, p. 51) or comments such as "CRISPR is opening the doors to several new possibilities in terms of target organisms and traits" (COM study, 2021, p. 18). Concretisations of this potential are only made to a limited extent. Molecular details of the different endonucleases of CRISPR (Cas9, Cas12a[103] and others) are not mentioned in the COM study. Broothaerts et al. (2021) highlight a special feature of CRISPR-Cas: "[I]ts easy adaptability to multiplex editing, based on the delivery of multiple sgRNAs to the cells" (Broothaerts et al., 2021, p. 33). With respect to the available new genome techniques, Parisi & Rodrígez-Cerezo (2021) have found that the greatest number of plants in their research had been developed via CRISPR (68.5 percent).

Cas9

The term "Cas9" is mentioned only in the appendix of the COM study; with one exception.[104] One reference is of particular interest here: "[A]ll genomic alterations or allelic combinations generated by CRISPR/Cas9 generally are identical to naturally occurring variations is a

[102] See Chapter 3.1.2.2 above and Subchapter on Cas9 below.
[103] Formerly called Cpf1.
[104] The exception refers to a brief mention in connection with a non-browning mushroom produced using CRISPR/Cas9.

misleading oversimplification." [COM study, 2021, p. 82, appendix, Table 12 "Further challenges and concerns reported by stakeholders (supplementary to Section 4.7.2)"] The COM study does not comment on this argument. It is not clear from the table in the appendix from where it comes and in which context it was put forward – apparently by a stakeholder. This example is significant because it illustrates a procedure of the COM study according to which it remains open in various parts of the COM study whether or to what extent the positions of Member States or stakeholders are taken into account (as explained in Chapter 3.1.2.2.4 above).

The lack of clarity about the COM study's consideration of this critique is unfortunate as such and also in terms of content. The present expert opinion generally shares the mentioned argument of a misleading oversimplification.[105]

Cas12a

The COM study cites EFSA on the experimental evidence for the nature of off-target mutations.[106] This evidence is based on three scientific publications, some of which also examined Cas12a. Beneath others, Broothaerts et al (2021) highlight that "[i]t has also been reported to be less cytotoxic at high expression levels compared to Cas9" (p. 33).[107]

Gene drive

The idea of artificial, man-made – as opposed to natural – gene drive organisms (GDOs) has been around for a long time. Until CRISPR was described as a genetic engineering tool, the realisation of this idea was a long way in the future. Theoretically, realisation by other means would also be possible. In this respect, the COM study remains open to NGT gene drives ("NGT-based gene drive applications"; COM study, p. 16). In the present expert opinion, the sorting is done according to the usual method (like Broothaerts et al., 2021, p. 34). GDOs contain genetic elements that are more likely to be passed on to the succeeding generations than would be expected according to Mendelian rules.

Gene drive mediated pest control is one of the discussed utilisations. It refers – beneath others – to the planed spread of wild populations (e.g. mosquitos being malaria vectors) that would be completely genome edited. Using genetic engineering – and genome editing – with wild species is extremely controversial. The gene drive issue had been raised by Member States and stakeholders. The COM study does not go into details. Since gene drives have so far been discussed almost exclusively in connection with animals, they are not a topic for the present expert opinion for this reason either.

3.3.1.4.3 TALENs

TALEN technology plays a special role in the current discussions because it is one of the few commercially used NGTs; high-oleic soy variety plants were produced with TALEN (transcription activator-like effector nuclease). The technology is also mentioned in the COM study in this context. Details of the technique are illustrated in the JRC technical report by Broothaerts et al. (2021). It becomes clear that different concepts for the (further) development of the technology are being pursued. The changes produced with TALENs vary. Deletions of different

[105] See for example Chapter 3.3.3.1 with respect to the molecular characterisation of changes.

[106] See Chapter 3.3.3.3 "Recent experimental evidence for the types of off-target changes" below. Cas12 called Cpf1 in that context.

[107] Unfortunately Broothaerts et al. does not report about cytotoxicity of the Cas9-endonuclease.

sizes are predominant, insertions are rare. With the use of donor templates, "gene correction, replacement or insertion have been reported" (Broothaerts et al., 2021, p. 29). Also shown is that TALEN can be used to modify multiple genes simultaneously: "Shan et al. (2013) successfully targeted seven genes in *Brachypodium* and four in rice by specific TALEN pairs" (Broothaerts et al., 2021, p. 29).

> "In plants, stable insertion of the TALEN construct is often required (e.g. with *Agrobacterium* or ballistic bombardment), and the transgenes are subsequently segregated away in subsequent generations to obtain transgene-free plants (Haun et al., 2014; Wang et al., 2014; Li et al., 2012 & 2016b). In potato TALEN-induced genome modifications were obtained by transient expression of plasmids in protoplasts (Clasen et al., 2016)" (Broothaerts et al., 2021, p. 29).

TALENs are of considerable importance for the development of NGT plants and products and the associated debate for one reason in particular: the company Calyxt has extensive rights to this technology and – until a change in strategy in 2020 (see Chapter 3.4.3.1 below) – systematically expanded its own TALENs-based plant portfolio accordingly.

3.3.1.4.4 ZFNs

ZFNs (zincfinger nucleases) were prominent at the beginning of the debate (around 2000 to 2010) on the targeted modification of genes and genomes. However, they hardly play a role today. This is notable because EFSA and others repeatedly refer to an EFSA publication from 2012 ("Scientific opinion addressing the safety assessment of plants developed using Zinc Finger Nuclease 3 and other Site-Directed Nucleases with similar function"). At that time, ZFNs were important and CRISPR unknown. The development of zinc finger nucleases was accompanied by technical difficulties, so that their loss of importance – at the latest since the discovery of CRISPR tools – is hardly surprising.

3.3.1.4.5 ODM

Oligonucleotide directed mutagenesis (ODM) was one of the first molecular tools for genome editing. Nevertheless, the function of ODM is still not completely clear, as Broothaerts et al. (2021, p.47) report. An ODM variant is known by the abbreviation RTDS™ (Rapid Trait Development System). The US company Cibus has developed canola varieties whose new properties have – at least in part ostensibly – been incorporated with RTDS™ technology.[108]

3.3.1.4.6 Somaclonal variation

Somaclonal variations are consequences of e.g. tissue culture phases of genome editing and other techniques. As the following example shows partly the variations are used by the plant developers: "The ability to generate multiple mutant lines is particularly valuable for potato trait development, as somaclonal variation commonly occurs in plants derived from tissue culture leading to abnormal phenotypes" (Clasen et al., 2016). Another example is mentioned below with respect to the canola variety development of the US company (see Chapter "3.4.3.1 Commercialised plants obtained with NGT"). "The agency now writes that 'the mutation [leading to the herbicide tolerance] has been created as a result of a spontaneous somaclonal variation'" (Meunier, 2020).

[108] For details see Chapter 3.4.3.1 "Commercialised plants obtained with NGT" and 3.5.1.1.4 "How much information is needed for a risk assessment?" below.

3.3.1.5 Speed of development

Various stakeholders cite as a major advantage of NGTs that they enable faster development of new plant varieties compared to other techniques. This is true for example for "[m]any Member States and stakeholders" or SAM HLG (see COM study, 2021, p. 2, p. 11 or p. 51). SAM HLG (2017) made in this context "only qualitative statements as to the relative cost and speed of product development, as publicly available data were scarce." Moreover, the way it is dealt with there does not allow for more comprehensive conclusions to be drawn about the data that was available to the SAM HLG. So assessments of SAM HLG derive from theoretical considerations about the techniques and less so from empirical data. The authors in the original text also point out: "In terms of maturity, the Note [109] makes a qualitative assessment from a purely technical point of view, on how close products of NBT are to field trials and beyond. Detailed publicly available information on such products is however scarce" (SAM HLG, 2017, p. 20).

The importance of the speed of development of genetically modified varieties for the risk associated with them was also emphasised by the ECJ in its judgment of 25 July 2018 (Case C-528/16). For details see Chapter 3.7 "ECJ ruling represented and discussed in the COM study" of the present expert opinion.

3.3.2 Methodological critique of the chapters on the current and future technical developments

The present expert opinion has already pointed out various more general problematic procedures of the COM study (which apply to the entire study) in Chapter 3.1 above. Here we criticise specific aspects of the subject area current and future technical developments of NGTs.

As described above (3.3.1.4.1), the COM study uses the terms SDN-1, SDN-2 and SDN-3 to group the NGTs together. In the process, it is lost that the written meaning – side directed nucleases – is misleading. In fact, it is not the locations as such but their sequences that direct the nucleases. In this respect, it is more precise and also appropriate to speak of sequence-specific nucleases in order to make this point clear (c.f. Zischewski et al, 2017). This goes hand in hand with the fact that the nucleases also cut at non-intended sites (off-targets) and (can) lead to non-intended effects.

3.3.2.1 Conceptual remarks to intended and unintended alterations

Intentional changes result at the phenotypical level. Scientists and plant developers are interested in the (possibly switched off) functions of genes, not – or only secondarily – in the base sequences in the genomes of the newly developed plants. The wording "intended" (sometimes also "desired") is to be understood accordingly, as it is also used in the COM study. The meaning of "unintended" follows accordingly.[110] For the plants and products produced using NGT, this is no different – at least in part – than for those processed using the genetic techniques with *Agrobacterium* or the gene gun, undirected mutagenesis or conventional breeding methods.

[109] The publication of SAM HLG (2017) is called an "explanatory note" in its subtitle.

[110] See for example COM study's Chapter 4.1.1 based on the report of the SAM HLG, 2017, or 4.1.2 on the basis of the Broothaerts et al., 2021.

However, there is a subtle difference. For mutation techniques (non-directed mutagenesis, e.g. with EMS or radiation) and conventional breeding[111] non-targeted modifications are an explicit and logical part of the procedure. This is not in the sense of "they are accepted willy-nilly", but because they are an original part of the techniques and methods. To put it more clearly: In the techniques of non-directed mutagenesis and in conventional breeding, there are no off-target changes at all. In the first phases of processing plants in conventional breeding and mutation techniques, one step is taken where, in principle, any change is welcome. Each of these changes potentially holds an interesting innovation. The point of these techniques and methods is precisely this: first and foremost, to broaden the genetic base at the beginning of breeding. Not all the changes achieved also end up having advantages that are to be retained in a new variety. Accordingly, the undesirable changes – with negative impacts – must be eliminated again. The neutral ones could be ignored. All the other changes undergo a *de facto* status change – from unintended to intended. This change is preceded by an evaluation – itself intentional – by the developer of the variety.

NGTs are completely different. Kawall writes: "As genome editing is a targeted biotechnology, it is misleading to conclude that it enhances genetic variation" (Kawall, 2019, p. 2). It is fundamentally different from undirected mutagenesis or conventional breeding methods. For this reason, non-intentional changes (for example, off-target changes) are only discussed in the context of NGTs from one point of view: At best, they should not arise in the first place.[112]

EFSA and others have put forward the comparison of different approaches to the development of new crop varieties as the silver bullet of risk assessment (see Paraskevopoulos & Federici, 2021; SAM HLG, 2017). However, the concept is flawed at a very crucial point. Precisely because of the systematic differences described above, the question arises as to whether quantitative comparison of off-target changes is the appropriate form for describing risk and safety.

Against this background, what can the statement "the off-target mutations potentially induced by SDNs are of the same type as, and fewer than, those in conventional breeding, including spontaneous mutations and those produced by physical and chemical mutagenesis" (COM study, 2021, p. 53) contribute to the analysis of the different approaches? It still does not say anything about the safety of NGT plants and products even if it is put forward by EFSA, JRC and SAM HLG in this or a similar way.

3.3.2.2 How the COM study considers unintended effects?

At the beginning of this part two quotes from the JRC technical review illustrate very well the starting point of the COM study considering the unintentional effects caused by NGT: (1) "Information on possible unintended (usually called 'off-target') modifications and limitations in our current understanding complement the technical descriptions for each NGT" (Broothaerts et al., 2021, p. 3). (2) "This makes their outcome more predictable, although unintended modifications elsewhere in the genome (so-called 'off-target effects'[6]) remain possible"

[111]The present expert opinion is generally following the idea to differentiate between conventional breeding methods on the one hand and the use of undirected mutagenesis as a technique on the other.

[112] See Chapter 3.3.2.5 for details regarding off-target changes and effects respectively.

(Broothaerts et al., 2021, p. 13[113]). Both examples are left in the context of unintended changes and do not ask questions about any resulting unintended effects.

The COM study addresses unintended changes and their effects caused by NGT in different chapters. This occurs in three different ways: (1) the issue is tabled by one or more Member States, (2) one or more stakeholders raise the issue, or (3) the COM study mentions the issue to show that it is not an issue (see COM study, 2021, p. 13, p. 31, p. 37). Member States and stakeholders emphasise the need for risk assessment. A distinction is made between unintended effects in the form of off-target effects[114] and those resulting from intentional changes (COM study, 2021, p. 31). Examples for the latter category are the ecological effects resulting from the modification of *Camelina*.[115] Among other things, the risk of producing new toxins or allergens are mentioned. Unfortunately the COM study does not show, who exactly put forward this arguments (for more details see Chapter "3.5.4 Stakeholder and Member States views on risk assessment" below).

Of particular importance is a reply by the EFSA corresponding to a recent public consultation.[116] The document had been published in 2022, EFSA stated: "Moreover, the GMO Panel was not mandated to provide a comprehensive literature review on the SDN-based technology and its unintended effects" (EFSA, 2022, p. 25). However, Testbiotech comes to a different explanation. The non-governmental organisation shows in a background paper that EFSA has apparently "overlooked" essential publications. Testbiotech refers to another occasion when EFSA – likewise – pointed out that it had no mandate to investigate unintended effects of SDN-based technology in detail.

> "In a document, recently published, EFSA has created the impression that there is, in most cases, no need to take the unintended genetic changes caused by NGT processes into account. EFSA appears to assume that the unintended genetic changes and the associated risks could not be distinguished from those resulting from conventional breeding. Consequently, the approach as suggested by EFSA would mean a substantial reduction in current standards of risk assessment.
>
> It looks like the EFSA assumptions largely originate from inadequate data: in the context of its previous opinions, the authority has stated several times that it did not have a mandate to comprehensively assess all relevant scientific publications. On the contrary, it seems that EFSA has, in fact, simply 'overlooked' most of the relevant publications" (Testbiotech, 2022).

Even though the missing mandate for the investigation of unintended effects of SDN-based technology was voiced in different contexts, the present expert opinion assumes that this was valid for EFSA's contribution to the COM study. If so, EFSA should have been aware of this knowledge gap about SDN-based technology and its unintended effects. Accordingly, EFSA, and the COM study respectively, should have indicated this shortcoming, instead of rejecting any possible unintended effects put forward by third parties.

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[113] Footnote 6 from Broothaerts et al. (2021): "NGTs introduce alterations at priorly defined target sequences in the genome; any changes at other locations in the genome are called off-target alterations. Some of these could be predicted through bioinformatics analysis of the whole genome sequence of the organism based on their similarity to the target site except for one or more mismatches".

[114] For off-target changes, see Chapter 3.3.3.3 below.

[115] See Chapter 3.5.3.1 "Environmental risks" below.

[116] In 2022 the EFSA carried out a public consultation regarding a draft of the updated scientific opinion on plants developed through cisgenesis and intragenesis.

3.3.2.3 Detection and identification – methodological issues with respect to current and future technical developments of NGTs

The present expert opinion concludes that there may have been a misallocation of the subject of detection and identification due to the COM study's misinterpretation of the issue. The COM study deals with detection and identification primarily from the regulatory point of view. At first glance, this may seem obvious, since, for example, in the course of the targeted consultation, Member States argued that implementation of the European Gene Technology Law is not possible if the detection, identification and quantification of NGT is not certain. The current lack of detection methods is first of all a technical problem. This problem must be analysed in detail and reliably. This is of crucial importance for the European legislator. The fact that molecular detection of NGT plants and products is not always possible (so far) is one of the essential arguments for a weakened regulation of certain NGT (see for example SAM HLG). This error has serious consequences, as it leads to an evaluation of the subject that – as far as assessable within the scope of the present expert opinion – does not correspond to the latest state of the art. The COM study itself lays the path for this error with the questions of the targeted consultation. In the presentation of the COM study, this leads – quasi inevitably and without alternative – to the conclusion that regulation of certain NGT in the manner practiced to date is neither sensible nor feasible.

It should also be noted here that the argument – high improbability of finding proper detection methods – is prominently placed at the beginning of the COM study's Chapter "4.3 Implementation and enforcement of EU GMO legislation with regard to NGTs", thereby increasing its significance. The reader cannot help but perceive the argument as quite central. In addressing this issue, it is striking that the COM study is much more optimistic, for example about the expected positive effects of NGT than about the possibility that detection methods will be developed.

At other points in the COM study, the attitude of its authors also plays a special role. According to the COM study, ENGL have been asked beneath others to report on what is needed to overcome the existing problems in the context of detection and quantification of mutagenesis events and other "new breeding techniques" (COM study, 2021, p. 25). The answer to this question is not explored in the COM study. If the COM study had been interested in the answer, its authors would have noticed that this question has not been dealt with by the EURL and ENGL experts. The experts simply state that detection, identification and quantification of NGT plants and products are not possible under certain conditions. The issues would "lack any experimental evidence. Therefore, they will require further consideration" (ENGL, 2019, p. 1). This is by far not enough as an answer to the question of what is needed to make detection possible.

3.3.2.4 Future solutions instead of present questions

The following description of the NGT can be seen as an example of a particular – very regularly applied – approach in the COM study, where special attention is paid to possible future technical solutions. For example, instead of problematising the use of the current genetic techniques (as a "delivery system" for the active components of an NGT[117]), the COM study here writes that

[117] See Chapter 3.3.1.1 above and Chapter 3.5.5.4 "Unintended effects of established genomic techniques" below.

> "stable integration of the transgenes into the host genome is not a pre-requisite and alternative approaches to DNA delivery (i.e. RNA and/or protein) may be equally effective for inducing genome alterations. Some other NGTs require the administration of only a short (DNA or RNA) oligonucleotide to the targeted cells to obtain a short genome edit. The need for different types of active component and delivery approaches reflects the diversity of NGTs" (COM study, 2021, p. 13).

Of course, this is not wrong *per se*. It is just that in many cases – including here – it has not been proven whether these solutions can be realised or to what extent. Broothaerts et al. (2021, p. 67) write: "alternative approaches to DNA delivery (i.e. RNA and/or protein) *may be equally effective* for inducing genome alterations" (emphasis by authors). The basis on which the COM study arrives at the mentioned statement cannot be reconstructed.

Generally, the practice to pay special attention to possible future technical solutions can also be found regularly in the JRC paper by Broothaerts et al. (2021).

3.3.2.5 Off-target changes – general remarks

Related to the previous is the way the COM study and Broothaerts et al. (2021) deal with the representation of off-target effects and possible counter-strategies.

The descriptions are mostly dominated by information on what is done by scientists and developers of the new genomic techniques to avoid off-target effects. The first two columns in Table 9 show examples of respective descriptions from the COM study and Broothaerts et al. (2021) to illustrate this.

Instead of focussing on counter-strategies, however, it would be important to address the off-target changes and the consequences. But to recognise this as appropriate, the COM study (as well as EFSA and others) would have to acknowledge that off-target effects have or can have undesirable consequences. Counter-strategies might be an approach for the future. For the developments of today, other strategies would be at least as important.

Table 9: Quantitative comparison of the description of off-target effects with possible counter-strategies to illustrate the quantitative balance. All paragraphs quoted from the mentioned sources. In breckets "[]" the number of the respective amount of characters (where appropriate the third column presents context and/or additional information).

DESCRIPTION OF		Context, additional information etc.
off-target effects	**possible counter-strategies against off-target effects**	
Example 1: COM study, 2021, p. 13		
"Off-target alterations following the use of NGTs have been reported in the literature." [86 characters]]	"Diverse optimisation strategies are employed for enhancing the specificity of the technique and for minimising off-target effects. Because the targeted sequence is known, the probability of off-target effects can be predicted in some cases via bioinformatic analyses and then experimentally assessed. Various bioinformatic tools have been developed to screen for potential off-target sites in a particular genome and predict the probability of off-target alterations. For some species, individual organisms can be selected that do not contain off-target changes, or the unintended modification may be removed in a subsequent generation by sexual crossing." [655]	"The efficiency of creating a desired genomic alteration has to be weighed against the probability of generating unintended effects at off-target sites." [151]
Example 2: Broothaerts et al., 2021, p. 28		
"In some cases, cytotoxicity of ZFNs has been observed, which may be related to off-target cleavage of the DNA." [109]	"Several approaches have been successfully described to reduce such effect, including making them more specific by use of more zinc fingers (4 to 6 per monomer) or using preferentially heterodimerising ZFNs (Miller et al., 2007). Other strategies to lower off-target activity include decreasing their binding affinity (Pattanayak et al., 2011), or lowering ZFN expression, e.g. through directly delivering ZFN mRNA or protein to the cells instead of the DNA expressing the proteins inside the cells (Bilichak et al., 2020)." [522]	"In plants, limited successes have been obtained with ZFN technologies due to the typically low rate of HR in plants (reviewed in Weinthal et al., 2010). In one successful study with maize, no off-target effects were identified in the potential ZFN off-target sites of five plants resulting from a sequence insertion in a phytate biosynthesis gene (Shukla et al., 2009). Also in pig fibroblast cell editing, a nuclease assay showed that the ten most likely off-target cleavage sites were not modified (Hauschild et al., 2011)." [525]
Example 3: Broothaerts et al., 2021, p. 34		

DESCRIPTION OF		Context, additional information etc.
off-target effects	**possible counter-strategies against off-target effects**	
"Three major types of off-target regions have been described, including those with substitutions or mismatches compared to the target region (particularly in the non-seed region), those with insertions and/or deletions (indels) in comparison with target DNA or sgRNA spacer (which may result in a small bulge of unpaired nucleotides), and those with a different PAM sequence (Manghwar et al., 2020). A fourth type may be the unexpected off-targets in genomic regions which are not related to the target, such as initially reported for mice, but later contested (Montoliu and Whitelaw, 2018). In plants, off-target modifications may not necessarily result in a modified phenotype and may be segregated out in subsequent generations. Such effects may be much more critical for therapeutic and clinical applications (Zhang et al., 2015b)." [834]	"The identification of such off-target effects in initial CRISPR-Cas experiments has prompted investigations to mitigate or reduce such effects. Several approaches have been employed, including more careful target selection and sgRNA design, reducing the expression of Cas9 through use of weaker promoters, spatial or temporal control systems for Cas expression, introduction of Cas-mRNA or ribonucleoproteins (RNPs) instead of vector DNA, or use of high-fidelity Cas proteins (Wu and Yin, 2019; Hajiahmadi et al., 2019; Gangopadhyay et al., 2019; Broeders et al., 2020; Manghwar et al., 2020). Others have diverted from using the DSB-generating SDNs toward deactivated versions with partially or completely impaired nuclease functions (e.g. nickases or dCas), which have demonstrated to be less prone to off-target activity (Ran et al., 2013). An interesting very recent addition to enhance specificity is the linking of a dCas9 to the obligate dimerising Clo51 nuclease, a proprietary technique called Cas-CLOVER reported to be void of off-target activity (https://www.geneng-news.com/resources/webinars/cas-clover-the-clean-alternative-to-crispr-cas9/). Another recent development with potential for reducing off-target activity is the use of anti-CRISPR proteins found in bacteriophages to tailor Cas activity to specific cells or tissues (Hwang and Maxwell, 2019), or use of anti-CRISPR agents that can switch the CRISPR-Cas system on and off (Dolgin, 2020)." [1460]	

3.3.2.6 Types of changes

An essential prerequisite for correct handling of the technical developments of new genomic techniques is a systematic naming and/or description of the central processes involved in NGT interventions. The analysis of the COM study by the present expert opinion reveals various inconsistencies, for example in the description of changes or mutations and the wording used. In the course of the present expert opinion respective inconsistencies of the wording "same type of" have been analysed. However, the inconsistencies are not limited to this.

The COM study leaves important questions open regarding molecular characterisation. This is – at the very least – unfortunate, not least because the molecular changes are often at the centre of the COM study's consideration (see Chapter 3.3.1.1 above). These inconsistencies in the handling of molecular changes result partly from the different sources and partly from a

lack of distinction. The report by Broothaerts et al. (2021) was prepared to describe the state of the art of the new genomic techniques.

Paraskevopoulos & Federici (2021), as part of the supplementary material of the COM study, by contrast, elaborate on the different views on risk assessment of EFSA and EU Member States. They also describe basics of the techniques. They show that there are examples for a more detailed molecular characterisation of mutations, changes et cetera induced by NGT (Paraskevopoulos & Federici, 2021, p. 16f.). They quote the work of Hilscher et al. (2017)[118], who describe different types of mutations known so far. The following is taken from Hilscher et al. (2017), the authors write with respect to types of mutations produced with SDN-1 techniques:

- "In *Arabidopsis* and rice, based on to date available data, the *most frequently* detected mutations are insertions of a single adenosine or thymidine nucleotide,
- followed by small deletions of *predominantly* one nucleotide and deletions of <10 nucleotides [107, 112, 119, 120, 123-125].
- Other detected mutations are nucleotide replacements and
- [nucleotide] insertion of >1 nucleotides, *but to a lesser extent*.
- Based on the data available at present from *Arabidopsis* and rice, the mutation spectrum *may be generalised* over experimental systems, mutations detected in protoplasted cells, transgenic lines CRISPR-Cas generated by floral dip transformation (*Arabidopsis*) or somatic embryogenesis after agro-inoculation (rice).
- In soybean, the *most frequently detected* mutations were deletions <10 nucleotides [118, 121, 122]. There is the indication that dependent on the sgRNA or the targeted locus the mutation spectrum *may differ* in some instances.
- In the study of Jacobs et al., one sgRNA induced *predominantly* single nucleotide insertions, independently of the experimental system (soybean hairy root and somatic embryogenesis) [121]. Similar observations were made in rice [124, 125]. The location of the generated mutations *predominantly* occur starting three nucleotides off the PAM in the proto-spacer sequence (for example [118-121])" (Hilscher et al., 2017, p. 25f.; emphasis and insertion of indents by authors).

The italicised phrases show that no definitely typical changes can be described with SDN-1 interventions. "[P]redominantly occur" at the end of the quote suggests that initial molecular changes are possible as well. The question arises what prevented Paraskevopoulos & Federici (2021) from following the approach of Hilscher et al. (2017), and carrying out more precise characterisations of changes and collecting them systematically? Hilscher has not yet found the best of all conceivable forms of representation. Nevertheless, a consistent characterisation of the changes can be an important step towards being able to systematically investigate the possible consequences of certain molecular changes in the long term. Imprecise phrases such as "same type as" or "similar alterations" (see Chapter 3.3.1.1 above) could then be avoided.

[118] In the context of Paraskevopoulos & Federici, 2021, "opinion 3".

3.3.2.7 Broothaerts et al. (2021) sort NGTs in four groups

Sorting NGTs into four groups, as done by Broothaerts et al. (2021) (see Chapter 3.3.1.4.1 above), raises certain questions. As such there is nothing incorrect in this order, content-wise. It is presented in a technically comprehensible manner. If anything, the question arises as to how compatible this approach is with regard to the ongoing (public) discussions. There, the categories SDN-1, SDN-2 and SDN-3 are widely used. The lack of connection to the public discussions is also evident in the following aspects:

- (1) In the COM study itself, the sorting of the NGT in four groups as proposed by Broothaerts et al. is not used (see for example in the discussion chapter and the references to EFSA there (COM study, 2021, p. 53)
- (2) The EU Commission did not use the proposal of Broothaerts et al. in the communication regarding its considerations for a possible future regulation following the publication of the COM study.[119]
- (3) The sorting proposal of Broothaerts et al. (2021) has also not taken up or reflected in the public debate, for example in the Policy Forum of the journal Science (Gould et al., 2022).

A minimum variant would have been e.g. a table with the corresponding – clear – classifications of the most important techniques with concrete examples into the systematics with the proposed four groups. Unfortunately, Parisi & Rodríguez-Cerezo have not published their database. The information requested on the NGT plants and organisms respectively indicates that corresponding allocations to the two systems could be part of the database Parisi & Rodríguez-Cerezo (2020 and 2021, p. 8f.).

It remains to be asked, however, whether the technical order is helpful for the ongoing discussions. If the classification presented here by Broothaerts et al. were relevant for the ongoing discussions on a future regulation of NGTs, the Commission should have adapted and applied it in the communication following the publication of the COM study. With the multitude of variants of NGTs, a good, systematic and scientifically based classification can certainly be helpful to support a discussion. Since the EU Commission itself did not follow the systematics suggested by Broothaerts et al. (2021), it must be concluded that it did not derive such a positive effect itself.

> "From a conceptual point of view, SDN applications have been categorised into SDN-1 [...], SDN-2 [...] and SDN-3 [...]. While such a grouping may be informative for regulatory purposes, it does not reflect intrinsic characteristics of the different SDN techniques and cannot be used for their description. From the review presented here it will become clear that many techniques described here may be used in the form of SDN-1, -2 or -3. Moreover, repair pathways typical for one SDN category may induce alterations representative of another one" (Broothaerts et al., 2021, p. 24).

In fact, this already indicates that the COM study will not succeed in presenting a consistent system for a possible new regulation of European genetic engineering legislation. The present expert opinion sees this indecision in dealing with the categorisation of NGTs as part of an attempt of the COM study. This attempt has failed so far and is interpreted by the present

[119] See for example European Commission, 2021a.

expert opinion as an indication that the COM study has not succeeded in establishing a scientific basis for the deregulation of certain groups of NGT.

3.3.2.8 Speed of development

In the public statements of the developers of NGT plants and products, speed is often cited as a major reason for using the new techniques. It is said that this advantage is all the more important because current problems (e.g. climate change, growing world population with increasing demands) require rapid action. However, the present expert opinion cannot detect any attempts by the COM study or its supplementary material to verify this thesis. Against the background of only two commercial plant-based NGT products in nine years after the first description of the "game-changer" CRISPR in 2012 (COM study, 2021, p. 51), such a test should have been evident. In this respect, the thesis of the higher speed of development – compared to other techniques or breeding methods – is only moderately convincing.

In this context, the COM study refers to the note of the SAM HLG from 2017:

> "However, mutations can often be introduced more quickly using NGTs than with conventional breeding or established genomic techniques, in particular when using the CRISPR[37]-Cas genome editing system, mainly due to the reduced need for time-consuming screening procedures and/or back-crossing" (p. 11f.; fn. 37 says "Clustered regularly interspaced short palindromic repeats.").

Only one year earlier, the researcher Karl-Heinz Kogel from the University of Gießen (Germany) was asked about the use of CRISPR. He admits: "In practice, it is much more inefficient and imprecise than is generally claimed." Kogel continues: "According to textbook knowledge, the CRISPR technique would be very easy to use here now, but we have been struggling for a year to produce optimal CRISPR plants. In reality, this is not as easy as one would expect" (Fittkau, 2016).

3.3.2.9 Broothaerts as a co-author of a supplementary material

Wim Broothaerts is leading author of "New Genomic Techniques: State-of-the-Art Review". It is frequently cited as JRC review in the COM study and as Broothaerts et al. (2021) in the present expert opinion. The review is published as part of the supplementary material of the COM study and as a "JRC Technical Report". Broothaerts is as well co-author of another explanatory note (Emons, 2018) that is relevant in the course of the COM study (see Chapter 3.3.3.7 below). As Table 10 shows he changed his affiliation between the European Commission's Joint Research Centre and the Seed and Biotech Company Pioneer/Corteva Agriscience several times. He worked three times for the JRC, from 2005 to 2008, in 2017 and from 2021 to 2023, when the COM study has been published. In between he worked for the international company DuPont Pioneer (since 2015 part of Corteva Agirscience™), at least between 2008 to 2014 and in 2018 (see Meunier, 2021; supplemented by own findings of the present expert opinion[120]).

From the perspective of the present expert opinion, it is not particularly farsighted to select an author with such professional credentials in the context of the COM study. The COM study and the supplementary material are of particular importance for the further process. The impression that the balance between the different poles of the discussion may already has been

[120] See profile at www.researchgate.net/profile/Wim-Broothaerts. In part the information can be found in connection with the listed publications and the mentioned affiliations (accessed 31 October 2022).

lacking in the preparation of the material should be urgently avoided. For the political process, this balance is extremely important.

Table 10: Affiliations of Wim Broothaerts, lead author of the COM study's supplementary material "New Genomic Techniques: State-of-the-Art Review".

Year/Period	Affiliation	Source
2005-08	JRC	2005-08 https://www.researchgate.net/profile/Wim-Broothaerts (https://archive.ph/bPvkB)
2008-14	Pioneer	https://www.researchgate.net/profile/Wim-Broothaerts (https://archive.ph/bPvkB)
2017	JRC	https://www.researchgate.net/publication/315837131_Recommendation_for_the_unit_of_measurement_and_the_measuring_system_to_report_traceable_and_comparable_results_expressing_GM_content_in_accordance_with_EU_legislation (https://archive.ph/8Hlzs)
2018	Pioneer *	JRC (2018): Explanatory Note – Challenges for the detection of genetically modified food or feed originating from genome editing (with affiliation from ResearchGate). https://www.infogm.org/IMG/pdf/comeur_note-detection-nveaux-ogm_nov2018.pdf
2021-2023	JRC	2021 https://www.researchgate.net/publication/351481928_New_genomic_techniques_State-of-the-art_review (https://archive.ph/KnDL3) 2022 https://www.researchgate.net/publication/364459813_Proficiency_of_European_GMO_control_laboratories_to_quantify_MON89788_soybean_in_a_meat_pate_matrix (https://archive.ph/VQUTG) 2023 https://www.researchgate.net/profile/Wim-Broothaerts (https://archive.ph/bPvkB)
* Pioneer is part of Corteva Agirscience™ since 2015. Internet sources accessed 31 January 2023.		

3.3.3 How well researched and substantiated are the COM study's statements about the technical developments of NGTs?

3.3.3.1 Changes – molecular characterisation in the COM study

Unfortunately, Broothaerts et al. (2021), and consequently the COM study, fall short in their analysis of the changes obtained by NGTs. The presentation in Table 1 in Broothaerts et al. in particular is quite comprehensive, but also leaves important questions unanswered. A more detailed presentation would have been possible and desirable. For example, the table should have shown which scientific papers are referred to in the various descriptions – even if this part is reproduced in the publication. A more important aspect would have been to note if a particular research paper has addressed the question of physiological or structural consequences of the changes listed in the table. This raises the question of whether it is always clear what consequences follow from specific molecular changes. Furthermore, it would have been important to indicate what types of consequences result from different modifications. Most sequence modifications made with new genomic techniques intentionally lead to gene silencing (knockout). But, whether the molecular changes in Table 1 of Broothaerts et al. (2021) have yielded further consequences remain unclear and will most likely be determined on a case-by-case basis.

In view of the very numerous and very different changes in Table 8 it becomes all the more clear that a better view and categorisation of the changes is needed. A simple formulation such as "same type of" is not sufficient.

Another level of analysis focuses on how products are compared from a technical point of view. Again, the COM study lacks a systematic explanation (and definition), what is actually meant by this. For example the similarity due to a specific trait, such as insect toxicity to a particular pest or the expression of a particular defence molecule, as it is typical for many Bt crops modified with the current genetic engineering techniques. The unanswered question is: What makes products similar? This is connected with a second question: What makes risk-levels – in the sense of the Commission's study – similar? Both questions will be dealt with in chapter 3.5.1.1.1.

3.3.3.2 Changes – accessible regions of the genome

Following Ossowski (2010; after Kawall, 2019, p. 4) "[e]volutionary pressure enriches mutations at certain genomic regions over many generations". Different molecular DNA repair systems help to limit those changes. It has been shown, that they can work differently depending on the location in the genome. Kawall herself describes the consequences in her publication as follows:

> "Thus, mutations are spread randomly throughout the genome of MMR-deficient [121] strains, while they are non-randomly distributed throughout the genome of MMR-proficient strains. This is a clear indication that MMR preferentially protects genes, rather than non-genic regions of the genome, from mutations. How targeting of MMR to genic regions of the genome works in plants still remains to be answered" (Kawall, 2019, p. 5).

The author has shown, that changes, induced by genome editing techniques (CRISPR/Cas) had been found in other and/or more regions of the genome, than those induced by conventional breeding techniques:

> "New genome editing technologies, such as CRISPR/Cas9, are now making the entire genome accessible for any desired change by the researcher and breeder. These new techniques circumvent mechanisms that protect certain areas of the genome by targeting nucleases to specific genomic regions, thereby increasing the probability of the induction of genomic alterations" (Kawall, 2019, p. 6).

The new possibility for access of the whole genome for molecular changes has been completely overlooked by the COM study. It fundamentally calls into question the treatment of the COM study and EFSA. These had been restricted to superficial molecular descriptions of the changes (see 3.3.3.1) and their number.

From the perspective of the present expert opinion, this aspect should be investigated much more closely in the future. It is highly relevant for the risk assessment of NGT plants and products because the expanded opportunities obviously affect particularly protected areas of the genome. It must be assumed that these areas have special significance for the plants – the MMR systems protect strongly conserved areas of the genome, which can be found both in bacteria and in eukaryotes. Another question arises in this context: It should be investigated whether this aspect also needs to be applied to the investigation of off-target alterations.

3.3.3.3 Off-target changes – unintended effects

Off-target alterations are discussed in the context of unintended changes of the genome. Those could lead to unintended changes of the physiology or other parameters of the

[121] MMR stands for mismatch repair. Kawall uses the term for DNA repair systems, that repair mismatches after replication.

metabolism of NGT plants and products (unintended effects). Changes might lead to risks for health and/or environment. The COM study says:

> "EFSA concluded, on the basis of recent experimental evidence, that the off-target mutations potentially induced by SDNs are of the same type as, and fewer than, those in conventional breeding, including spontaneous mutations and those produced by physical and chemical mutagenesis" (COM study, p. 53).

The Commission's study and the supplementary material lack a comprehensive description of the off-target mutations. From this it also follows that it remains unclear to the reader which details are used as a basis for the work of the authors of the COM study. This is also the case with the scientific report of Paraskevopoulus & Frederici (2021).

It is very important to note, that the Commission's study follow EFSA with respect to off-target changes in three aspects:

1. Further parameters for the investigation of off-target mutations – besides the type ("same type") and the number ("fewer than") – are not necessary. At least the COM study does not go beyond the assumptions of EFSA (and SAM HLG), both of which limit their comments to these two aspects.
2. The "recent experimental evidence" is strong enough to show that. This evidence is based on outcomes of three scientific papers. (Tang et al., 2018; Lee et al., 2019; Li et al., 2019; quoted following EFSA GMO Panel, 2020). In these three papers, conclusion of research with 164 single gene edited plants/plantlets from three crop species (maize, cotton, rice) are present (see Chapter 3.3.3.4 below and COM study, p. 53).
3. And last but not least Commission's authors do follow EFSAs conclusion, that the "analysis of potential off-targets would be of very limited value for the risk assessment" (EFSA GMO Panel, 2020, p. 9f.). In any case, the COM study does not conclude – unlike some Member States and stakeholders – that off-target changes should be given special attention in the context of risk assessment.

Investigation of off-target changes

The Commission's study does not spend much energy on off-target changes. "Off-target alterations following the use of NGTs have been reported in the literature" (COM study, p. 13). This is basically everything, that the Commission's study has to say with respect to the state of the art of the NGTs. The authors seem to be more in favour of the diverse "optimisation strategies [that] are employed for enhancing the specificity of the technique and for minimising off-target effects" (COM study, p. 13; for details see Chapter 3.3.2.5 above). The COM study completely ignores the consequences of off-target changes. The Commission's study is satisfied with the purely quantitative data – off-target effects are observed less frequently than (for example) with non-directed mutagenesis (see also 3.3.2.2 above).

3.3.3.4 Recent experimental evidence for the types of off-target changes

What the authors of the Commission's study call the "recent experimental evidence"

> "EFSA concluded, on the basis of recent experimental evidence, that the off-target mutations potentially induced by SDNs are of the same type as, and fewer than, those in conventional breeding, including spontaneous mutations and those produced by physical and chemical mutagenesis" (COM study, 2021, p. 53).

is based on three papers, all of them had been conducted with CRISPR-Systems.[122] Table 11 below gives an overview.

Lee et al. (2019)

Lee et al. (2019) worked with maize lines. They concluded: "our results suggest that the CRISPR/Cas9 system used in this study is highly efficient and specific for genome editing in maize, while CRISPR/Cas12a needs further optimisation for improved editing efficiency." The work was meant to test for "efficacies" (Lee et al., 2018, p. 366) of CRISPR systems, including a comparison of two CRISPR systems. Additionally, they did research on the potential prediction of off-target mutations and the potential passing of off-target mutations from T0 to T1 progenies (p. 367). With respect to possible limitations of their work, the authors wrote: "One limitation in this maize study is its small sample size" (p. 366).

Li et al. (2019)

Li et al. (2019) conducted whole genome sequencing (WGS) of 14 Cas9-edited cotton plants targeted to three genes, and three negative (Ne) control and three wild-type (WT) plants. In the sense of the detailed description of the changes caused by NGTs – which is missing in the COM study but desirable in principle – they write:

> "We detected 11 mutation types in the two sgRNAs of AP2, nine mutation types in the two sgRNAs sites of MYB44 and four mutation types in the two ARC sgRNAs between WGS and Sanger sequencing. The WGS and Sanger sequencing data revealed that most of Cas9-generated mutations are deletions (Figure 2e–g). [...] These results confirmed that six on-target sites exhibited multiple mutation types and different mutation frequencies from three target genes" (p. 859).

According to Li et al. (2019), somaclonal effects play a much more significant role compared to the off-target effects caused by NGTs. Somaclonal effects are changes due to cell culture steps during processing in the laboratory workflow of the application of NGTs. Furthermore important: "These results indicated that the low frequency off-target mutations were low in Cas9-edited cotton plants, even there were some unpredicted mutations in the regions that were not homologous to sgRNA target sites" (p. 860). And with a view to the general state of knowledge: "The CRISPR/Cas9 system has been extensively applied for crop improvement. However, our understanding of Cas9 specificity is very limited in Cas9-edited plants" (Li et al. 2019).

Tang et al. (2018)

Tang et al. (2018) show "WGS analysis of 34 plants edited by Cas9 and 15 plants edited by Cpf1 in T0 and T1 generations along with 20 diverse control plants in rice"; and further on:

> "Our results clearly show that most mutations in edited plants are created by the tissue culture process, which causes approximately 102 to 148 single nucleotide variations (SNVs) and approximately 32 to 83 insertions/deletions (indels) per plant. Among 12 Cas9 single guide RNAs (sgRNAs) and three Cpf1 CRISPR RNAs (crRNAs) assessed by WGS, only one Cas9 sgRNA resulted in off-target mutations in T0 lines at sites predicted by computer programs. Moreover, we cannot find evidence for bona fide off-target mutations due to continued expression of Cas9 or Cpf1 with guide RNAs in T1 generation."

[122] For details see EFSA GMO Panel et al., 2020, p. 9.

Tang et al. also comment on the state of knowledge:

> "In plants, only limited studies have used whole-genome sequencing (WGS) to test off-target effects of Cas9. The cause of numerous discovered mutations is still controversial. Furthermore, WGS-based off-target analysis of Cpf1 (Cas12a) has not been reported in any higher organism to date" (p. 1).

Table 11: Recent experimental evidence off-target mutations.

Publication	Crop species	CRISPR systems	Number of Cas edited plants
Lee et al. 2019	Maize	Cas9 + Cpf1	58 + 43
Li et al. 2019	Cotton	Cas9	14
Tang et al. 2018	Rice	Cas9 + Cpf1	34 + 15
		Total	164

Within the scope of the present expert opinion, it is not possible to go into the details of this issue. But it should be comprehensible even without them that experimental evidence looks different. The knowledge about the various changes in the genome mapped here by the COM study are at best hints, but not evidence. This is all the more true as the COM study repeatedly emphasises how versatile the CRISPR technique is (see for example 3.3.1.4.2). In addition, as can be seen from Table 11 only three crops are dealt with in the three publications described. Against these three there are more than fifty plant species on which, according to Parisi & Rodrígez-Cerezo (2021) changes have been made with NGTs. Moreover, a close look at the three publications mentioned above (Lee et al., 2019; Li et al., 2019; Tang et al., 2018) makes it clear that their authors do not share the view on off-target changes than the COM study (and others e.g. SAM HLG). Especially they show interests in details. However, the question of the consequences of off-target effects remains unaddressed here as well.

3.3.3.5 Details of the NGTs in the COM study

CRISPR (multiplexing, off-target changes)

A well-known example of multiplexing with the CRISPR system is a wheat that was extensively genome-edited. In total, the researchers changed 35 genes to reduce the gluten content. Broothaerts et al. (2021, p. 20) refer to this gluten-free wheat, but point to a review article by Seedek, Mahas and Mahfouz (2019) as the source. What does not become clear in this review article, however, can be found in the original publication by Sánchez-León et al. (2018): "Transgene-free lines were identified, and no off-target mutations have been detected in any of the potential targets" (Sánchez-León et al., 2018). A check of the method of how the off-target changes were tested leads to this result: "However, analysis of unintended effects was restricted merely to looking for off-target activity at 6 sites" (GeneWatch UK, 2021, p. 7). GeneWatch UK points in this context of "experiments aiming to perform editing of multiple genes at once (multiplexing)" to Liu et al. (2021) and van Overbeek et al. (2016), who warn that "would induce tremendous translocations between any two target sites" (quoted following GeneWatch UK, 2021, p. 7).

In fact, the COM study only minimally addresses this feature or capability of NGTs, namely on its page 12 (see 3.3.1.4.2 above) and on its page 49. In this context, it is surprising that the COM study does not use the term "multiplexing" (instead speaking of "multiple changes" or

similar). Also the possibilities for changing organisms, as well as for finding or identifying them, are not explicitly considered. It is obvious that the probabilities of changing several gene loci simultaneously with the methods of undirected mutagenesis tend towards zero. Why the COM study estimates this aspect so low cannot be determined within the scope of the present expert opinion (see also 3.3.1.2 above and in Chapter 3.3.3.6 "Alterations of genes or genomes and matrices" directly following here).

3.3.3.6 Alterations of genes or genomes and matrices?

NGTs and the plants and products produced with them are special from various points of view. As already outlined in the present expert opinion, one special feature is that NGTs enable changes to be inserted at specific locations in the target genome (see Chapter 3.3.1.3 above). The molecular tools, the NGTs, address specific DNA sequences in the genome. These sequences are not unique, but can exist several times. On the one hand, because certain genes or sequences can be found several times – in the genome, on individual chromosomes or even on different chromosomes. On the other hand, the polyploidy of the genome can have the effect that certain chromosomes – and thus the sequences on them – occur several times in a genome. (See chapter 3.3.2 for another aspect of the sequence-specificity of the NGTs.)

All of the same sequences can be altered by NGTs in one application. Weeks (2017) focuses on

> "the use of these technologies [[123]] with polyploid plants [...] whose more complex genetic composition make them often more challenging to manipulate [...]. Indeed, an immediate recognition for those wishing to edit genes in a polyploid plant is that instead of two copies (alleles) of any particular gene present in a diploid plant, there are four copies of the same gene in a tetraploid plant or six in a hexaploid plant. While this may have been a define concern in the early days of gene editing, more recent studies outlined in this chapter provide ample evidence that for several polyploid plant species, rapid and efficient modification can be achieved for most, if not all, chromosomes in the multiple chromosome sets of polyploid plants. Examples are presented in which gene editing technologies have been successfully applied to triploids (apple, citrus), tetraploids (pasta wheat, potato, cotton, apple and peanut), hexaploids (Camelina, bread wheat) and octaploids (sugar cane) for both academic studies as well as for potential commercial applications" (Weeks, 2017, Chapter 4)

In practice, it is not always the case that all the same sequences are changed. Different factors determine this. Weeks reports two different laboratories working on the fatty acid composition in *Camelina* (FAD2 genes). One group (Morineau et al., 2016; following Weeks, 2017) reported that none of their plants had been modified in all six genes (that a knockout had not been inserted in each of the six genes). The other group (Jiang et al., 2016; following Weeks, 2017), on the other hand, had succeeded in switching off all six gene copies that were significant for the experiment with a knockout.

Th great potential to alter several if not all copies of a plant gene – although characteristic for the NGTs and essential for their functioning – remains practically unmentioned in the COM study. This is all the more astonishing because this peculiarity can be seen as a potential for tackling current challenges. But: Even if there is no certified method for the detection of NGT plants and products so far, solutions are emerging precisely through the use of the

[123] Zinc finger nucleases (ZFNs), single-stranded oligo DNA nucleotides (ssODNs), TALE effector nucleases (TALENs) or CRISPR/Cas9/sgRNA.

aforementioned peculiarities. The use of several gene loci is essential here. ENGL has so far focused on single gene loci that can be identified on the basis of their DNA sequence. This concept runs like a red line through the COM study.[124] In the future other sources of information will be used additionally. These can be, for example, other types of molecules that are used with the help of proteomics or metabolomics techniques. But also document-based information can complement the matrix approach (Agapito, 2021; Bertheau, 2018).

3.3.3.7 Detection and identification of NGT plants and products

Detection and identification of NGT plants and products is one of the key issues of the Commission's study. The issue plays a crucial role in the replies of Member States and stakeholders to the targeted consultation – not least because it is asked about in the questionnaires. That there are challenges associated with detection and identification of NGTs has been known for a long time. See for example Lusser et al. (2012) or the New Technologies Working Group of the EU Member States (New Technologies Working Group, 2012).[125] The above-mentioned reports, and not least ENGL (2019), are characterised by an attitude that a large part of the problems negotiated in the context of detection and identifiability of NGT plants and products cannot be solved.[126] More constructive contributions are to be found recently, as for example in the work of Ribarits et al. (2021 and 2022), Agapito (2021), Chhalliyil et al. (2020) or Bertheau (2018).[127] These contributions are characterised by methodical attempts to capture systematically the problems related to detection, quantification and identifiability. This is true even if they do not solve the existing problems in an all-encompassing way. At least, the problems related to detection, quantification and identifiability are made clear and accessible to future research and development work.

A major shortcoming of the COM study is that it only superficially reviews what kind of research has been conducted on this topic so far and what research is considered necessary for the future. Since ENGL (2019) is the essential basis of the COM study in terms of detection and identification, it is not surprising that the mentioned can already be found here. The two main questions asked by the EU Commission to ENGL for its report were

- "[W]hether and under what conditions current analytical possibilities allow detection and quantification of all types of mutagenesis events and other new breeding techniques (NBTs); and
- [I]f not, what possibilities exist to overcome any issues identified" (quoted following the COM study, p. 25)

[124] This is not least due to the fact that ENGL has invested too little in research and development in recent years - both financially and conceptually. The present expert opinion shows this in Chapter 3.3.3.7.

[125] "A New Techniques Working Group was founded due to a request by the National Competent Authorities of the EU for clarification of the legal state of these new techniques. The New Techniques Working Group completed its work in 2012, summarizing its findings as a report to the National Competent Authorities (New Techniques Working Group, 2012)". Hartung, F. & Schiemann, J.; The Plant Journal, Volume 78, Issue 5 p. 742-752. Online: https://doi.org/10.1111/tpj.12413.

[126] See Chapter 3.3.1.4 above for details.

[127] In particular, the work of Chhalliiyil et al. must be highlighted here. They are the first attempt for a specific method to detect and quantify a commercialised genome-edited plant. As the COM study does not discuss this effort, it is included in the present expert opinion under 3.3.5 "What issues and challenges of NGT plants and products" below.

In the follow up of the July 2018 ECJ ruling, "diverging views emerged on the detectability of products obtained by new mutagenesis techniques, both among Member States and stakeholders" (COM study, 2021, p. 25).[128] Accordingly, it was also foreseeable that time that the topic would be of particular importance. "In October 2018, the JRC received a mandate from DG SANTE to elaborate, together with the ENGL, on the implications of this ruling for the detection of such organisms" (ENGL, 2019, p. 4) Unfortunately the ENGL report failed on this point. The report makes the growing number of new plant breeding techniques an issue and refers in this context to in a footnote to SAM HLG (2017). However, a look in the so called explanatory note of the SAM HLG reveals that the description of the new breeding techniques remains only very cursory and hardly constitutes a comprehensive review. ENGL continuous:

> "These DNA alterations [single nucleotide variants (SNV) or sequence insertions or deletions (InDels)] may be present either in a homozygous or heterozygous state in the genome, i.e. all or only a fraction of the copies of a given gene (called the alleles of a gene) may carry the alteration (e.g. in a tetraploid (4n) plant the same DNA alteration can be present as DNA copy between one and 4 times)" (ENGL, 2019, p. 3).

At this point, the ENGL report misses the opportunity to highlight the importance of alterations of alleles of a gene for the detection and identifiability of NGT plants and products. Later the ENGL report comes to this question again (see ENGL, 2019, p. 12f.). There, the report emphasises the difficulties that could arise in later generations: "Event-specific detection methods would be required to target all different alterations in the genome in case they may segregate in subsequent generations" (ENGL, 2019, p. 13). It would also have been possible to emphasise the possibilities that lie in this characteristic. It is difficult to understand from the perspective of the present expert opinion, why the COM study did not request an update of the ENGL report from 2019. The COM study also does not sufficiently investigate the molecular clues that make detection and identification possible or appear possible in the future. This may be due to the fact that the COM study deals with the topic under the aspect of regulation, more precisely under the aspect of "4.3 Implementation and enforcement of EU GMO legislation with regard to NGTs" (COM study, 2021, p. 25) – and not under technical-scientific aspects.

Only little efforts have been made in investigating the detection and identifiability of NGT plants and products. Of 356 million Euro NGT related funds over the past 5 years, 1.6 percent was spent on detection methods, risk assessment and monitoring and 1 percent was spent on regulatory, ethical and communication-related issues (COM study, 2021, p. 35). 1.6 percent of 356 million Euro would be 5.7 million in five years (distributed all over EU) for detection methods, risk assessment and monitoring alltogether. The funds of the EU – 271 million Euro for 78 projects in plant biotech under the umbrella of bioeconomy – are not broken down in the COM study according to their detailed topics or objectives (see COM study, 2021, p. 34). A rather small amount of money for a problem that has been known for years and that many

[128] Making diverging views an issue, if necessary even clearly contrasting them and resolving them in a plausible way is often not an issue for the COM study. In this specific case, the COM study refrains from presenting the different arguments. See Chapter "3.3.4 Stakeholder and Member States views on research and innovation".

stakeholders consider to be of central importance.[129] It would have been the task of the EU Commission to ensure higher budgets at an early stage.

As mentioned before (see 3.3.1.4) the COM study took account of past evaluations of the EU GMO legislation. In certain cases it would be impossible to determine whether the end product of NGT applications was based on "old" or "new" techniques. Another aspect of the discussion on the procedures for detection, identification and quantification remains unmentioned in the COM study. The current approaches used for the genetically modified organisms also leave questions unanswered (in the context of the established genome techniques). This applies, for example, to unauthorised GMOs that use molecular elements that are not covered by the screening methods. Another reason why a genetically modified organisms escapes the European control system is that the plant species in question has not been tested. The example of genetically modified petunias found in Finland in 2017 became more widely known to the public (Servick, 2017). Other examples concern products that may have been produced from genetically modified organisms but which cannot be detected by molecular methods. These include, for example, refined sugar or highly processed soy lecithin. The problem also arises outside the GMO issue, for example in the labelling of foods with a special origin or with products from organic farming. Moreover, this aspect is also addressed in the 2010 evaluation.

The lack of detailed aspects of detection and identification of NGT plants and projects in the COM study is all the more spectacular as both issues are seen as the central topic or one of the central topics by practically all those involved. At the same time, however, it is not evident – with few exceptions – that the actors who consider detection and identification to be important have themselves become active in closing knowledge gaps through their own research and development projects.

An article published by the French NGO Inf'OGM (Meunier, 2021) sheds light – at least partially – on the unclear situation in which a separate European expertise does not materialise. So also in the question how it comes that the ENGL report still in 2019 writes that "at the current state, own experimental work on detectability of genome-edited food or feed products of plant origin has not been conducted" (ENGL, 2019, p. 4). The Inf'OGM article describes a number of occasions when EU Member States could have launched R&D programmes in the areas of detection and identification of NGT plants and products. This applies in particular to the European Network of Laboratories (ENGL),[130] at least since June 2013 (Meunier, 2021). Also other players mentioned in the present expert opinion – e.g. the European Commission or SAM HLG – have not taken steps to fill the knowledge gaps, neither through theoretical nor with laboratory studies. In addition, according to Inf'OGM, the European Commission influenced the draft version of the report, which was later published as ENGL (2019). Inf'OGM also

[129] For more details on research funds see Chapter "3.3.4 Stakeholder and Member States views on NGT-related research" below. For details on detection and identification see 3.3.3.7 above.

[130] The European Network of GMO Laboratories (ENGL) assists the EU Reference Laboratory for Genetically Modified Food and Feed (EURL GMFF), hosted by the Joint Research Centre (JRC) of the European Commission (ENGL, 2019).

refers to an explanatory note from the European Commission's JRC (Emons et al., 2018)[131] on the challenges of detecting genetically modified or genome-edited food and feed.

In the paper, the authors play out a case study in rough terms ("A ship arriving at the harbour of Rotterdam is carrying 20,000 t of bulk grain maize from outside the EU. There is no declaration in the accompanying documents that the maize consignment is genetically modified"). The authors conclude among others that it is not possible to reliably detect and identify NGT plants and products without prior information. The present expert opinion could not go into details. Nevertheless the question arises, why the note is not accessible at the website of the JRC. Meunier criticises e.g. that only a single detection approach had been considered and concludes that the note "is seen more as a political paper than as a scientific study" (Meunier, 2018).

All in all, the presentation of the issues of detection, identification and quantification in the COM study is not satisfactory. The main reason for this is that it does not reflect the latest state of science. According to the assessment of the present expert opinion, it also plays a role that the very technical questions are dealt with primarily from the point of view of the implementation of law.

3.3.4 Stakeholder and Member States views on NGT-related research

Section 4.5.2 of the COM study "Member States' and stakeholders' activities in NGT-related research" is a very short section with two paragraphs (see COM study, 2021, p. 35f.).

Table 12: Questions in the targeted consultations on activities in NGT-related research. Presumably evaluated in section 4.5.2 "Member States' and stakeholders' activities in NGT-related research" in the COM study, 2021.

Number of question/ Questionnaire*	Wording of the question
Q8/MS	Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?
Q10/SH	Are your members carrying out NGT-related research in your sector?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*	

The section provides information on Member States' and stakeholders' activities in NGT-related research. This information was obtained through the questionnaires of the targeted consultations (see Table 12).

The evaluation of the questionnaires had shown that the Member States had funded research on NGT with 356 million euros in the last five years. According to the COM study, 44 percent of this funding was spent on medical research, 32 percent on agriculture and 19 percent on basic research. Furthermore, 2 percent had been spent in the field on industrial applications,

[131] This note was co-authored by Wim Broothaerts, among others. It is available from the website of the French NGO Inf'OGM (Meunier, 2018), but not from the JRC. In contrast to Broothaerts et al. (2021) the note of Emons (2018) has not been specially commissioned for the COM study. In this respect, the present expert opinion classifies Broothaert's co-authorship in Emons (2018) as less significant. However, the criticism mentioned above regarding the authorship of documents from the European Commission's JRC remains fundamentally valid. See Chapter 3.3.2.9 above for details.

1.6 percent in the field of detection methods and risk assessment and 1 percent for research in the regulatory, ethical and communication-related field.

In addition, many stakeholders reported research with new genetic technologies in the various areas of application (Agricultural Biotechnology, Industrial Biotechnology and Pharmaceutical Biotechnology/Human health), but also on risk assessment and ethical issues.

3.3.4.1 Stakeholder and Member States views on research and innovation

Section 4.5.3 of the COM study, titled "Member States' and stakeholders' views on research and innovation" analyses the views on research and innovation of the Member States and stakeholders (see COM study, 2021, p. 36). The section is divided into three subsections in which the respective questions in the questionnaire are evaluated. The following Table 13 provides an overview.

Table 13: Questions in the targeted consultations on research and innovation. Presumably evaluated in section 4.5.3 "Member States' and stakeholders' views on research and innovation" in the COM study, 2021.

Unnumbered subsections	Number of question/Questionnaire*	Wording of the question
Benefits and concerns relating to NGT research	Q11/MS	Could NGT-related research bring opportunities/benefits to science, to society and to the agri-food, medicinal or industrial sector?
	Q13/SH	Could NGT-related research bring benefits/opportunities to your sector/field of interest?
	Q12/MS	Could NGT-related research bring challenges/concerns to science, to society and to the agri-food, medicinal or industrial sector?
	Q14/SH	Is NGT- related research facing challenges in your sector/field of interest?
Impact of the CJEU ruling and the GMO regulatory framework on NGT research	Q12/SH	Could NGT-related research bring challenges/concerns to science, to society and to the agri-food, medicinal or industrial sector?
Research needs	Q10/MS	Have you identified any NGT-related research needs from private or public entities?
	Q15/SH	Have you identified any NGT-related research needs/gaps?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

In the subsection **"Benefits and concerns relating to NGT research"**, the COM study states that "all" Member States reported benefits from the application of NGT in the medical sector (see COM study, 2021, p. 36). "Most" also see a contribution of NGT to sustainable agriculture and some (or "several") see a benefit for the industrial sector. The COM study emphasises that "many" Member States see research as being linked to ethical issues. These ethical issues are, on the one hand, the responsible use of NGT (who uses the techniques and for what purpose) and, on the other hand, specific cases related to human applications (embryos, germ lines). "Some" Member States indicated in the targeted consultation that research should be subject to public debate.

The COM study refers to section 4.10.4 for a further discussion of ethical issues ("please refer to Section 4.10.4", COM study, 2021, p. 36). This section is not included in the COM study.

Presumably an error was made and the reference should have been to section 4.11.1 of the COM study, which evaluates Member States' views on ethical issues. As there is no explicit question on ethical issues in the Member States' questionnaires, it could be that the authors of the COM study moved the content on ethical issues there.

Subsequently, the study points to different views in the surveys regarding the benefits of NGT research. "Some" stakeholders ("mainly food entrepreneurs and scientists") saw benefits from NGT research in many application areas. "Other" stakeholders ("mainly NGOs and non-GM food entrepreneurs") thought that no benefit could be expected in the agricultural sector. In this context – according to the COM study – the concern is raised that research using new genetic technologies is not participatory and decentralised, and that such modes of innovation need to be established. The COM study then refers to section 4.6., for a further discussion of the benefits concerns regarding products developed through NGT.[132]

In the subsection titled **"Impact of the CJEU ruling and the GMO regulatory framework on NGT research"**, the various perspectives of the Member States are presented first (see COM study, 2021, p. 36f.). "Many" Member States reportedly see challenges in the regulation of NGT research activities, but "some" do not. Among the stakeholders, those in the fields "food business operators, academics and researchers, biotechnology industry" in particular reported negative effects (e.g. funding of projects, halting the implementation of projects) of the ruling, while others ("other") – specifically in the fields related to "NGOs" – reported positive effects on agricultural research. "Some" NGOs indicated that there had been lobbying for NGT research. "One" scientific actor had extended a research programme regarding risk assessment. Other "GMO-free/organic operators and NGOs" saw no impact of the CJEU ruling on their activities.[133]

In the sub-section **"Research needs"**, the questions on the need for research on NGTs are evaluated (see COM study, p.37). According to "many" Member States, a major challenge for research is the development of detection methods. "Several" Member States would see a need for research in risk assessment and "some" in relation to unintended effects at the molecular level.

A prominent feature of the stakeholder survey was respondents' expression of a need for research into safety and environmental risks, and related detection methods. Independent research in particular was demanded. This is followed by an uncommented list of areas for further research, including questions around public perception, farmers' rights, other ethical issues, the loss of biodiversity, socio-economic consequences, and other basic research into the specific applications of plant and animal breeding. These suggestions from the stakeholder survey remain uncommented by the COM study.

What is evident here are the knowledge gaps identified by Member States and/or stakeholders. The present expert opinion reports on this (among others) in Chapters 3.3.2.3 "Detection

[132] It should be noted here that the COM study effectively posed questions about benefits and concerns about NGT twice. It did so first in relation to NGT research and secondly in relation to NGT-produced products. It might have made more sense to evaluate both questions together.

[133] It should be noted that the Member States' questionnaire did not contain an explicit question on the ECJ ruling. However, from the wording of the survey, it can be assumed that the sub-question to question 2 in the Member States' questionnaire was evaluated in this section: "Have you taken specific measures (other than inspection) related to the application of the GMO legislation to NGT-products? – If yes or no, have you encountered any challenges or limitations, including administrative burden or costs?"

and identification – methodological issues with respect to current and future technical developments of NGTs" and 3.5.1.1.4 "How much information is needed for a risk assessment?".

However, the suggestions put forward from the stakeholder survey remain uncommented by the COM study. In doing the COM study does not succeed in presenting a coherent procedure for different positions from different stakeholders.

3.3.5 What technical issues and challenges were not investigated?

3.3.5.1 Chhalliyil et al. (2020)

It is obvious that the COM study did not satisfactorily investigate the issues of detection, identification and quantification of NGT products. This is particularly evident in the lack of discussion of the publication of Chhalliyil et al. (2020).[134] Chhalliyil et al. had presented for the first time a method for the detection and quantification. It targets a certain variety of rapeseed, that had been discussed in the European Union as one of the first possible NGT plants (BVL, 2015). In 2021, a scientific evaluator at Health Canada stated in a personal communication that "the plant was actually the result of a mutation that arose during tissue culture and not due to the gene editing process".[135] Health Canada is the competent authority of the country, where the plant had been developed. Taking this clarification into account, the present expert opinion follows the evaluation of Health Canada (2016) and categorises the Cibus rapeseed as a non gene edited plant. Nevertheless, the discussion on the detection method delivers important aspects, especially the attitude of the developers of the method. Important is also that the progress in this field will not take place if no one starts with practical steps.[136] In fact different authors and organisations (e.g. ENGL, 2020; BVL, 2022; Weidner et al., 2022) commented on the case. BVL for example stated:

> "The published assessment shows that the method does not meet the minimum performance requirements of ENGL for qualitative PCR methods and is therefore not suitable for official control of GM products in the EU" (BVL, 2022).[137]

The present expert opinion cannot conclusively clarify to what extent the method developed by Chhalliyil et al. ultimately works. Nor can it be decided here on whether the Cibus rapeseed is actually the result of somaclonal variation (for more details see 3.3.2.3).

3.3.6 Interim summary of current and future technical developments of NGTs

Chapter 3.3 of the present expert opinion investigates the current and future technical developments of NGTs in the Commission's study. The COM study puts a lot of effort into placing NGTs in line with of other plant development techniques by emphasising similarities at the molecular level. The study states that the changes in the genome caused by NGTs are similar to those that can be achieved, for example, by means of non-directed mutagenesis techniques or cross-breeding. However, since the COM study only provides superficial descriptions of the changes and only makes isolated comparisons, its descriptions are not convincing. This is all

[134] See as well the correction, Chhalliyil et al. (2022).

[135] Health Canada, personal communication, E-Mail dated 13 May 2021 (in the context of another project).

[136] For details regarding the legal status see Chapter 3.4.3.1 "Commercialised plants obtained with NGT" of this expert opinion.

[137] Original in German: "Die veröffentlichte Bewertung zeigt, dass die Methode die Mindestleistungsanforderungen des ENGL für qualitative PCR-Methoden nicht erfüllt und daher für die amtliche Kontrolle gentechnisch veränderter Produkte in der EU nicht geeignet ist."

the more true as it does not take into account essential special features of the NGTs. For example, the COM study does not mention that NGTs can modify areas of plant genomes that are not accessible to other methods.

Off-target changes and effects respectively are practically ignored by the COM study. The justification for this follows the assessments of EFSA. It ignores the positions of Member States and stakeholders – who voted partly in favour of the consideration of off-targets with respect to risk assessment. The justification of the COM study also remains unsatisfactory because the COM study does not consider the diversity of NGTs. On the basis of specific molecular biological reviews, it derives – unjustifiably – a relatively broad evidence base for the own argument, that off-targets are of the same type in NGT plants and products as in those obtained by other means. With regard to off-target changes, the COM study draws a comparison of NGTs with other techniques and procedures, for example, non-directed mutagenesis. The present expert opinion criticises this comparison as there are no off-target changes at all in the plants modified with non-directed mutagenesis at that time. In this respect, it is also not as meaningful if NGTs cause fewer off-target effects than undirected mutagenesis as the COM study presents it. Unintended effects are also not sufficiently considered by the COM study – regardless of whether they result from intentional or unintentional changes.

The COM study does not make it sufficiently clear whether and, if so, how it takes into account the criticism of the Member States and stakeholders (see 3.1.2.2.4 above). The lack of clarity about the COM study's consideration of the critique is unfortunate as such and also in terms of content. One stakeholder stated for example: "[A]ll genomic alterations or allelic combinations generated by CRISPR/Cas9 generally are identical to naturally occurring variations is a misleading oversimplification." The present expert opinion supports this argument, while the COM study writes in its conclusions (yet again): "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis" (p. 59).

The COM study has a problem with the issues of detection and identification of NGT plants and products. On the one hand, the COM study is not up to date with the current discussion. What is at least as important is the attitude of the study in dealing with these issues: To put it in a comparative perspective: The COM study displays too much optimism regarding the realisable potentials of NGT plants and products (see chapter 4 below), and it lacks this optimism when it comes to the issues of the possible future methods for detection. Those methods for detection and identification do currently not exist (for specific NGT products). Regarding the question, what possibilities exist to overcome the identified problems, the COM study does not come up with much. It notes that an amount of 5.7 million Euro was spent in five years for detection methods, risk assessment and monitoring distributed all over EU alltogether. A rather small amount of money for a problem that has been known for years and that practically all Member States and stakeholders consider to be of central importance.

3.4 State of the utilisation of NGTs in the agri-food sector

The COM study purports to provide a broad overview of the mentioned economic areas: Agriculture, industry, and medicine. As highlighted in the Commission's study's Chapter 2.2. ("Scope and objectives of the study"), it "covers the use of NGTs in plants, animals and micro-organisms, in a broad variety of potential applications, including in the agri-food, medicinal and industrial sectors." The main basis for this component of the Commission's study is the JRC "Science for Policy report", titled "Current and future market applications of new genomic

techniques" (Parisi & Rodríguez Cerezo, 2021), and its respective dataset presented in parts online as a dashboard (Parisi & Rodríguez Cerezo, 2020[138]). Additionally, the COM study took into account the answers of the Member States and the stakeholders to the respective questionnaires of the targeted consultation. In fact, neither the COM study nor Parisi & Rodríguez Cerezo (2020 and 2021) achieves a "broad variety of potential applications". All focus on plants and plant-based products – respectively agriculture and the production of food, feed, and fibre.

Chapter 3.4 of the present evaluation refers to plants and plant-based products that had been developed with new genomic techniques – or those which are under development.[139]. Chapter 3.4.1 will present the new and known outcomes and challenges. In Chapter 3.4.2, the methodological approach of the COM study regarding NGT utilisation is criticised. The question of how well and substantially the COM study has researched its analyses and findings on the use of NGTs is addressed in Chapter 3.4.3.

The complete dataset prepared by Parisi & Rodríguez Cerezo includes 645 examples: plants (426), human cells (119), animals (99), and mushrooms (1). Unfortunately, the raw data (referred to as the "Excel database", see COM study, 2021, p. 8) are not accessible. Authors present their outcomes in charts and give access to corresponding (selected) data. The background is: "Since much of the data was obtained under conditions of confidentiality, the report shows data aggregated into species groups and trait/disease categories. The detailed content of the database will not be made public" (Parisi & Rodrígez-Cerezo, 2021, p. 8f.).

3.4.1 New or known outcomes and challenges

The COM study found that "NGTs have developed rapidly in the past two decades and will continue to do so, while NGT products are becoming a reality in many parts of the world" (COM study, 2021, p. 59). In summary, the COM study states that "tens of applications potentially reaching market stage in the next 5 years and even hundreds in the next 10 years" (COM study, p. 51). The statement refers not only to applications for plants as Parisi & Rodrígez-Cerezo (2021, p. 11f.) categorise applications according to four development stages: commercial, pre-commercial, advanced R&D, and early R&D (or proof of concept).

Some NGT "applications are already on the market outside the EU" (COM study, 2021, p. 59). The authors found two plants, "a high-oleic soybean variety with healthier fatty acid profile, modified with transcription activator-like effector nucleases (TALENs), and a tomato variety fortified with gamma-aminobutyric acid, modified with CRISPR/Cas" (COM study, 2021, p. 14f.[140]). The dashboard (Parisi & Rodrígez-Cerezo, 2020) with the selection "development stage" shows only one organism, i.e. an oil and fibre crop made with TALENs.

More "applications, across different sectors, are expected in the years to come" (COM study, 2021, p. 59). This is not in the least due to the fact that 15 more plants and products were able to be classified in their pre-commercial stage. The COM study states that some of the NGT plants and products in this group of 15 are known as they had "already been developed with

[138] The online dashboard is an interactive tool, which enables selection with various filters (Parisi & Rodríguez Cerezo, 2020a).

[139] For details regarding the non-plant developments and applications see Chapters 3.4.1.2 - 3.4.1.4 of the present expert opinion.

[140] Footnote 38 of the COM study (being part of the quote above) says: "Gamma-aminobutyric acid is commonly sold as a dietary supplement."

established genomic techniques" (COM study, 2021, p. 15); the mentioned traits are herbicide tolerance, fungal resistance, modified oil or starch composition and non-browning properties. But there are also new combinations of crops and traits (even though these are not presented in detail – see Table 15 below).

117 plants are in the group of advanced projects and 292 in the one with early stages of development (COM study, 2021, p. 15). Subsequently, the COM study presents various further evaluations of the data set, see for example on genome-edited crop varieties in Table14. The COM study also found a mushroom, that was categorised in the pre-commercial stage. It was genome edited so that it would not turn brown during processing.[141]

Table 14: Crop plants in which NGTs are used, from early R&D to commercial stage (Table quoted af-ter COM study, 2021, p. 15; fn. 28: Current and future market applications of New Genomic Techniques https://doi.org/10.2760/02472; original from Parisi & Rodrígez-Cerezo, 2021, p. 15).

Plant groups	Plants included (not exhaustive)
Cereals	Maize, wheat, rice, barley, sorghum, millet
Forage and grasses	Alfalfa, ryegrass, switchgrass, *Setaria viridis*
Fruits	Apple, banana, orange, groundcherry, grapefruit, grapevine, kiwifruit, melon, watermelon, berries, stone fruits, avocado
Legumes	Beans, chickpea, peanut, pea, pigeon pea
Oil and fibre crops	Soybean, rapeseed, cotton, camelina, flax, pennycress, sunflower, mustard, strawberry
Ornamentals	Chrysanthemum, dandelion, orchid, petunia, poinsettia, poppy, Japanese morning glory, wishbone flower (*Torenia fournieri*), jasmine tobacco
Sugar crops	Sugar beet, sugar cane
Trees	Poplar, softwood trees
Tubers and root vegetables	Potato, sweet potato, cassava, beetroot
Vegetable crops	Tomato, broccoli, cabbage, cucumber, aubergine, lettuce, pepper, chicory
Plants (aggregated)	Only 'plants' or a list of diverse plants were identified
Other plants	Cocoa, coffee, tobacco, sage

Regarding the goals of genome editing in plants, the COM study found that "[e]specially in the R&D stage, most traits under development relate to modified composition, biotic and abiotic stress tolerance, and plant yield. Similarly, beyond cereals and oil crops, there is a greater focus on vegetables, fruits and legumes" (COM study, 2021, p. 51). Unfortunately, the presentation of the results in the COM study does not provide any insight into concrete projects. A specific crop with a particular new trait is only identifiable as an absolute exception.[142] For the types of traits see Table 15.

[141] The present expert opinion follows the approach of the COM study to present plants and the mushroom together.

[142] See for example the already commercialised NGT plants (COM study, 2021, p. 14f. and Chapter 3.4.3.1 below).

Table 15: Types of trait introduced in NGT plants, from early R&D to commercial stage (Table quoted after COM study, 2021, p. 15; original from Parisi & Rodrígez-Cerezo, 2021, p. 15).

Trait category	Description
Biotic stress tolerance	Resistance to biotic stressors such as nematodes, fungi, bacteria, viruses and other pests, pathogens or parasites
Abiotic stress tolerance	Resistance to abiotic stressors such as drought, heat, salt, rain and UV radiation
Herbicide tolerance	Tolerance to different types of herbicide
Modified colour/flavour	Modified colour or flavour
Modified composition	Modified content of substances such as starch, oil, proteins, vitamins, fibres, toxic substances, allergens, etc. to improve food/feed quality for better industrial use. This includes seedless fruits as a quality characteristic.
Plant yield and architecture	Yield increase (or stability) related to higher number of flowers/seeds/fruits to fruit size/weight and to photosynthetic efficiency. This includes other changes in plant architecture, e.g. plant height and shape, fruit shape and growth pattern.
Storage performance	Improvement of characteristics such as shelf-life and storage requirements (e.g. cold storage), including non-browning and reduced black spot
Other traits	Remaining traits (not previously classified), e.g. production of molecules of industrial interest, flowering time for agronomic purposes and nitrogen use
Breeding tools	Reproductive/flowering characteristics, e.g. induction of sterility, early flowering and haploid techniques

With respect to the available new genome techniques, Parisi & Rodrígez-Cerezo (2021) found that the greatest number of plants had been developed via CRISPR (68.5 percent), followed by TALEN (8.4), and zinc finger nucleases (6.9). A group of 9.1 percent had been labelled as "genome editing" without further specification. These are shown in the categories of Broothaerts, et al. (2021; for details see 3.3.2.7). The results were 90.6 percent for group 1 and 7.7 percent for group 2.

3.4.1.1 Contributions of future NGTs to political sustainability strategies

In Chapter 2.2 (Scope and objectives of the study) the COM study highlights that the Commission considered it important to take into account major political objectives under the European Green Deal, the Farm to Fork Strategy, and the pharmaceutical strategy. Its executive summary, discussion and conclusions all mention the potential importance of plant NGT products in the context of the Biodiversity Strategy and the SDGs:

> "A more sustainable agri-food system, is a key objective of the European Green Deal and in particular of the 'farm to fork' and biodiversity strategies. To enable NGT products to contribute to sustainability, an appropriate mechanism to evaluate their benefits should be considered. At the same time, NGT applications in the agricultural sector should not undermine other aspects of sustainable food production, e.g. as regards organic agriculture" (COM study, 2021, p. 59).

The COM study pays particular attention to the question to which extent NGT crops can contribute to achieving the goals of the European Green Deal. The EU's Biodiversity Strategy and Farm to Fork Strategy are also expected to benefit:

> "Several plant NGT products identified in the JRC review, from R&D to the market stage, could contribute to the Green Deal, and more specifically to the 'farm to fork' and Biodiversity

Strategy objectives of a more resilient and sustainable agri-food system, and to the UN SDGs" (COM study, 2021, p. 52).

Nevertheless, there are "indications about both benefits and concerns associated to NGT products and their current and future applications" (European Commission, without date, a).

3.4.1.2 NGT applications with animals

The presentation of the state of the art of NGT in animals in the COM study is limited to two paragraphs of fifteen lines of text and two tables. The first table gives an "[o]verview of animals in which NGTs are used (from early R&D to commercial stage)" and the other table shows the "[t]ypes of trait introduced in NGT animals (from early R&D to commercial stage)". Both tables like those for the NGT plants, are the result of the COM study's own research work (COM study, 2021, p. 17, Tables 3 and 4).

Accordingly, the focus of the development of NGT applications on animals is on farm animals for food production. In particular, the COM study identified cattle, pigs, chickens and various fish species. The use of so-called gene drives in insects is also briefly mentioned. On the state and progress of NGT applications in animal NGT developments, the COM study reports four examples in the "pre-commercial stage" category. These include: "yield-enhanced/fast-growing tilapia, disease-resistant pigs, hornless cattle and heat-resistant cattle" (COM study, 2021, p.17).[143] Combined 59 NGT applications can be found in "advanced and early R&D stage" (COM study, 2021, p. 17). The COM study devotes a good part of its – short – explanations (six of the fifteen lines) on the presentation of projects from the fields of medicine, the use of NGT animals as model organisms for human diseases and so-called xeno-transplantation, i.e. the development of animal organs for transplantation into humans (for all quotes see COM study, 2021, p. 16).

Further analysis of these results on the NGT animals is not included in the present expert opinion for the reasons stated above (see Chapter 2 "Methodical procedure of the present expert opinion"). In fact, the EU Commission has announced that for the application of NGT to animals it will "continue to build up scientific knowledge" (European Commission, without date, b). The COM study itself also refers to future reports, but only in relation to the issue of detection and identification (see COM study, 2021, p. 26.).

3.4.1.3 NGT applications with microorganisms (including industrial utilisation)

Regarding the use of NGT applications with microorganisms, the COM study writes: "In industrial micro-organism applications, it appears that NGTs are already a reality" (COM study, 2021, p. 17).

A distinction must be made between, on the one hand the use of products, that had been produced with NGT microorganisms. According to the COM study, these would be more easily taken up by industry. On the other hand, these NGT microorganisms can also be the products themselves. The COM study cites an example that has already been commercialised: Bacteria for the fertilisation of agricultural soil (see COM study, 2021, p. 17). Further distinctions in this context relate to the range of uses. These can be, as shown in the COM study with the table, firstly, in a closed system or as a deliberate release, or secondly, intended for the food or non-

[143] In the meantime, at least two genome-edited fish products are actually commercialised: "In December 2021, Regional Fish Institute Ltd. began selling both the '22nd Century Sea Bream' and '22nd Century Tiger Puffer,' online through its website" (Matsuo & Tachikawa, 2022).

food and feed sector (see COM study, 2021, p. 18, Table 5). The EU Commission is planning to build up further scientific knowledge in this area as well (see EU Commission, without date, b).

The table also gives examples of various uses that are to be made possible with NGTs in microorganisms. However, these again remain very general, for example: Production of: "food enzymes (for baking, starch products, [...]), feed enzymes (to increase nutritional value), biofuels, pharmaceuticals, other bio-based chemicals, and others" (see COM study, 2021, p. 18).

The present expert opinion only comments on these results or their presentation in exceptional cases. The reasons were explained above (see Chapter 2 "Methodical procedure of the present expert opinion"). The COM study itself again, refers to future reports, but only in relation to the issue of detection and identification (see COM study, 2021, p. 26).

3.4.1.4 NGT applications in medical research and development

The COM study devotes two paragraphs, eight lines in total, to NGTs in medical research. It emphasises that "NGTs are employed widely in the development of medicinal products for human use" (COM study, 2021, p. 18). The medical projects are assigned according to the usual testing steps there. The COM study was able to classify 64 clinical studies that were in phases I or I/II. The majority of these (56) are aimed at NGT applications in the context of cancer therapies, followed by hereditary diseases (31) and projects concerning blood (16). T cells, stem cells and cancer cells are modified.[144]

However, the present expert opinion will comment on the NGT applications in medical research and development only in exceptional cases. The reasons have already been explained above.

3.4.2 Methodological critique of the chapters on the NGT utilisation

The JRC market review (Parisi & Rodríguez, 2021), which is the basis of the COM study on this issue, collected data from various sources: "[S]earches of publicly available online information and consultation of experts through videoconferences, written communication and targeted surveys of public and private technology developers" (COM study, 2021, p. 9). The JRC review focuses on "products that are marketed in non-EU countries, in near-market development or in the pipeline stage", wherein these data are based on applications of NGTs globally. The so called "Excel database" included where available, an application ID, technique, technique details, technique group (following Broothaerts et al., 2021), organism and species group, species, trait/disease description, trait/disease category, and development stage and the developer. The review covers the following areas: "applications in agri-food, industrial and medicinal sectors" at different development stages, including "any kind of plant, mushroom, animal or microorganism or human cells altered with NGTs" (Parisi & Rodríguez-Cerezo, 2021, p. 7). The term "application" refers here "to organisms in which an NGT is applied to obtain a trait of interest. It has no regulatory implications" (Parisi & Rodrígez-Cerezo, 2021, p. 4, fn. 1).

[144] See Chapter 3.4.1.2 above with respect to the medical NGT projects with animals, that are part of medical research and development, e.g. as modell organisms.

3.4.2.1 General scope of the COM study including animals, microorganisms and human health

Neither Parisi & Rodríguez-Cerezo (2021) of the use of NGT applications nor the COM study covers the full range of NGT applications, as claimed.

The essential results in the medical sector, as reproduced in particular in the COM study, are presented so superficial that the significance of NGTs is hardly recognisable.[145] From the perspective of the present expert opinion, it can only be speculated what the reason for this might be. One possible cause is that the COM study did not have the resources to deal with this topic area in a sufficiently comprehensive manner. A lack of data material or access to information may also have played a role.

Missing data are apparent in various passages of the COM study and in its supplementary material (see COM study, 2021, p. 11, Parisi & Rodrígez-Cerezo, 2021, p. 11). Results for the industrial sector are also presented unsatisfactorily. The COM study chooses formulations which are difficult to understand, as for example a passage which reads: "In industrial micro-organism applications, it appears that NGTs are already a reality, facilitated by the contained use of micro-organisms as bio-factories and the fact that the final product is usually not the target of the modification" (COM study, 2021, p. 17). Here, it is unclear why the COM study chooses such ambiguous phrasing, such as "it appears that NGTs are already a reality" to describe the progress of their utilisation. The fact that the NGT microorganisms are primarily used in the production process and not in the end product is also only partially convincing. This, again, is especially the case because the data are not comprehensible and the sources are not transparent. With respect to pharmaceutical and cosmetic product applications derived from microorganisms Parisi & Rodrígez-Cerezo (2021, p. 40) see a data gap in their study. They write in their general conclusions: "The field of pharmaceutical and cosmetic products derived from microorganisms represents a data gap in this study, but we believe that it is also a very important field of application of NGTs in products that may have already reached the market". In fact, in the corresponding section of their review ("3.4.3. Data gaps in microorganisms"), they state – regarding microorganisms in general, not only pharmaceutical and cosmetic products – that "the resulting data cannot be aggregated in a similar way to those for plants, animals and human cells, because of scarcity and heterogeneity. Therefore, no figures (and no visualisation in the web dashboard) are presented" (Parisi & Rodrígez-Cerezo (2021, p. 31). For the present expert opinion it is not possible to clearify, why the data gap is not presented in full in the conclusion. At the same time, however, it should be acknowledged that the authors make an effort to deal openly with the issue of data gaps.[146] Due to the data gaps (and other reasons layed out above[147]) the COM study should have decided to work only on NGT plants and products.

For the NGT plants and products, it is of great importance that readers of the COM study and the market review of Parisi & Rodrígez-Cerezo have access to the original data – the "Excel file" (Parisi & Rodrígez-Cerezo, 2021, p. 11). This is not the case in the COM study, nore in the market review.

[145] For illustration see p. 18 of the COM study. Under the subheading "Human health", the corresponding results with respect to the state of the art of the NGTs in the medicinal sector are summarised in eight lines.

[146] See Parisi & Rodrígez-Cerezo (2021, Chapters 3.1.1., 3.3.1., 3.4.3. and 3.5.2).

[147] See Chapters 2 and 3.4.1.2-3.4.1.4 above.

3.4.2.2 Classification with four development stages

The authors of the COM study use procedures (methods), that do not always fit to the known literature. Or, to put it another way: It is not clear why the authors of the COM study – or those of the supplementary material – chose their approach, why they selected a particular method. One respective example is the use of a classification for the NGTs with four development stages as an important tool (see Parisi & Rodrígez-Cerezo, 2021, p. 11). In the context of the presentation of the chosen method, it would have been important to show on what basis this method was chosen. This is relevant against the background of discussing the results of the COM study in the context of past/earlier research.[148]

Table 16 below contrasts the four-stage method chosen by the COM study with a six-stage representation by Monsanto. As can be seen, there is a risk that certain development stages can be upgraded in the four-stage system. This is the case, for example, with the grouping into the category "Early R & D stage", as happened in the COM study. A look to the review of Parisi & Rodrígez-Cerezo (2021, p. 21) illustrates this very clear. There the fourth stage is called "4. Early R & D stage", but "proof of concept", what is part of the definition at page 11, remains unmentioned). At the very least, the COM study, and the JRC review, misses out on a meaningful differentiation.

Table 16: Comparison of development stages for plants used by the COM study (supplementary ma-terial: Parisi & Rodríguez-Cerezo, 2021, p. 11, Chapter 2.5.) and Monsanto (2011), cited after Mumm (2013), see Figure 2 below.

COM study	Monsanto (today part of Bayer)
Commercial stage	Marked launch
Pre-commercial stage	Phase IV pre-launch
Advanced R & D stage	Phase III advanced development
Early R & D stage	Phase II early development
	Phase I proof of concept
	Discovery

[148] This applies to many of the selected methods: the COM gives no, or only very few, references to the sources in which the methods have already been described (see "2 Methodical procedure of the present expert opinion" above).

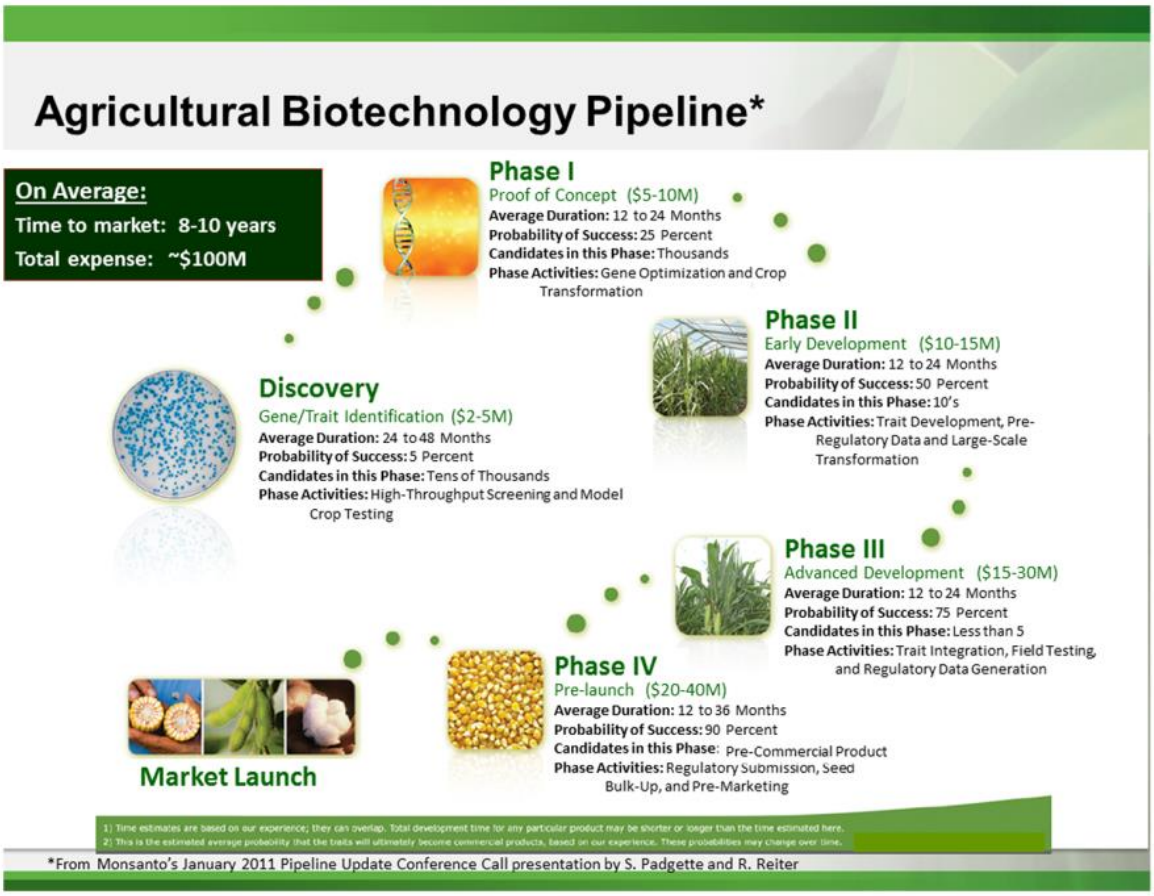

Figure 2: Agricultural Biotechnology Pipeline with six-stage system of development stages (Monsanto, 2011, cited after Mumm, 2013).

3.4.2.3 Utilisation of the dashboard

3.4.2.4 Utilisation of the dashboard

The database created by Parisi & Rodrígez-Cerezo (2020) (the "Excel database") is a useful resource.[149] It is however obscured by the JRC market review (and consequently also by the COM study). Nevertheless, the related online dashboard tool is helpful even in its artificially reduced form, that is, without a presentation of the full database. The limited use of the dashboard by Parisi & Rodrígez-Cerezo (2021) (see p. 15ff.) – and the COM study – is difficult to understand, precisely because the COM study and the JRC market review use a series of ambivalent statements regarding the current use of NGT:

> "As NGT-related research is increasing, so too are its potential applications in plants, animals and micro-organisms for the agri-food, industrial and medicinal sectors, with tens of applications potentially reaching market stage in the next 5 years and even hundreds in the next 10 years" (COM study, 2021, p. 51).

[149] To avoid misunderstandings: In the present expert opinion, the JRC market review by Parisi & Rodrígez-Cerezo (2021) is referred to as "Parisi & Rodrígez-Cerezo (2021)", the (Excel) database and online dashboard as "Parisi & Rodrígez-Cerezo (2020)". For details see References below.

A more comprehensive use of the dashboard by Parisi & Rodrígez-Cerezo (2021) and the COM study would have allowed for a clearer and more data-driven statement.

The present expert opinion nevertheless attempted to extract certain information for its own analysis of the COM study by way of this online dashboard. Accordingly, the present expert opinion entered individual queries. For example, activating the filter "Development stage" alone with "Commercial products" results in exactly one application: TALEN, oil and fibre crops, private company (what should be the genome-edited soy from Calyxt, mentioned in Gelinsky, 2022). The GABA tomato was only found after the finalisation of the review of Parisi & Rodrígez-Cerezo (2021). Against this background the wording "with some applications already on the market" (COM study, 2021, p. 2) does not seem appropriate.[150] As far as it can be reconstructed, this formulation is a consequence of the applications of genome-edited microorganisms in industry as reported by experts (see Parisi & Rodrígez-Cerezo, 2021, p. 6). However, it is also noteworthy that not a single microorganism has been named by the industry as already having been commercialised.

This group, the microorganisms, is not available for selection in the filter "organism" in the online dashboard. Parisi & Rodrígez-Cerezo (2021) write that the nature of the use of NGTs in combination with EGT makes it "difficult to provide a meaningful list of organism + NGT + trait combinations, as has been done for plants" (Parisi & Rodrígez-Cerezo, 2021, p. 30). In turn the decision against microorganisms being represented in the online dashboard raises questions about the formulation as it appears in the COM study: "In industrial biotechnology, NGT micro-organisms appear already to be a reality, producing compounds of interest as micro-organism cell factories" (COM study, 2021, p. 51). This is especially true due to the fact that the readers of the COM study and the work of Parisi & Rodrígez-Cerezo (2021) have no insight into the original data of the market review. Without this insight, the data can hardly be distinguished from the experts' narratives. Thus the representation of the COM study is only partly convincing. It should be noted that the list of organism + NGT + trait combinations, that had been presented for plants, was not that meaningful as it might seem from the wording above.

3.4.2.5 Sources of the data

Parisi & Rodríguez-Cerezo (2021) collect their data in different ways. These include publicly available sources such as scientific publications, but also a questionnaire sent to private and public institutions. These institutions may develop NGT plants and products themselves, or be involved in the approval process. In this respect the two authors find themselves being prisoners of their own sources and their approach, respectively. This is true for over 40 percent of the data set (184 out of 426 plant projects), namely the data from the private sector. Asking the developing companies directly is of course obvious because it seems to provide the greatest possible proximity to the source of the relevant information. But there remains a relatively high degree of uncertainty, since the firms themselves are players in the debate over NGT regulation, which may lead them to make the outlook seem somewhat nicer – or more optimistic – in order to ensure a favourable regulatory environment. This is all the more true as calls for consideration of the positive effects of NGT-based crops and products have grown louder in the EU since 2012 (see for example ESA, 2012). Moreover, companies in the Commission's research for the 2021 published COM study insist that the details must be treated

[150] This result of the dashboard query also contradicts the statement that two NGT plants are commercialised (see COM study, 2021, p. 51; see Chapter 3.4.1 above).

as confidential business information. "Scientific literature is mostly produced by academia, while private companies are generally reluctant to disclose early information, as they wish to protect their business and intellectual property" (Parisi & Rodríguez-Cerezo, 2021, p. 18). Whether or not the analysis of the role of the academic sources would lead to comparable outcomes, would be an interesting research question for the future. A cursory view of contributions by academics to this discussion suggests that they too are taking a clear position here – at least in part also regardless of whether they themselves are working in the context of genome-edited plants or researching the regulation of genetic engineering (cf. Nüsslein-Volhard, 2021; Leopoldina et al., 2019; ENSSER, 2017). A critical reflection on the sources and their roles in the debate on the future regulation of NGT plants and products would have been the very least for the COM study.

In addition to the sources mentioned above, Parisi & Rodrígez-Cerezo (2021, p. 10f.) consulted experts listed under section "2.2 Consultation of new genomic technique experts". These are not mapped personally, but in the form of their affiliation. It remains unclear according to which criteria these experts were selected. This is particularly important in light of the fact that the COM study was expected to provide a balanced, open-ended account. Last but not least, it should be emphasised here that it is also of considerable importance which sources are not used. One particular source is to be presented here as an example: Gelinsky (2022) presents in her research which plants developed with the help of "new genetic engineering methods"[151] are already in cultivation or are part of the development pipeline. She also presents licensing agreements in the field of new genetic engineering techniques. In the current version of the research, the author provides information on similarities and differences between her findings and those of the JRC market review (Parisi & Rodríguez-Cerezo, 2021), which was published as part of the supplementary material of the COM study. The following features of Gelinsky (2022) are particularly worth highlighting here: 1) The data come from public sources, which means that they can also be published in full – and this publication is not restricted or prohibited by the companies involved (as it is the case with Parisi & Rodríguez-Cerezo, 2021). 2) Consequently, Gelinsky's data are accessible free of charge and in full. 3) Thus, concrete plants with specific properties can be described and subsequently also discussed. 4) The research has been repeated for several years,[152] which means comparisons between versions offer possibilities that go far beyond a JRC market review-style snapshot. In the current version of the research, the author indicates that:

> "[S]ince the JRC survey is only a momentary overview, it does not take into account the fact that private companies in particular (especially the smaller startups) adjust their project portfolios from year to year: Compared with the 2020 survey alone, six projects had to be deleted from Table 1 and twelve from Table 2 because they were no longer in the companies' development pipeline" (Gelinsky, 2022, p. 93, English by the author of the present expert opinion[153]).

[151] In the course of the present expert opinion: new genomic techniques – NGTs.

[152] See for example Gelinsky (2017).

[153] From the original document in German: "Da es sich bei der JRC-Erhebung jedoch nur um eine zeitliche Momentaufnahme handelt, bleibt z. B. unberücksichtigt, dass v. a. die Privatunternehmen (hier insbesondere die kleineren Start-Ups) ihr Projektportfolio von Jahr zu Jahr anpassen: Allein im Vergleich zur Recherche 2020 mussten in Tabelle 1. sechs Projekte, in Tabelle 2. zwölf Projekte gestrichen werden, weil diese nicht mehr in der Entwicklungspipeline der Unternehmen auffindbar waren" (Gelinsky, 2022, p. 93).

3.4.3 How well researched and substantiated are the COM study's statements about the utilisation of NGT plants and products?

An important outcome with respect to the future applications of NGTs is represented in the following quote: "[T]ens of applications potentially reaching market stage in the next 5 years and even hundreds in the next 10 years" (COM study, 2021, p. 51). This is important with respect to different aspects. First of all the context of this quote says:

> "As NGT-related research is increasing, so too are its potential applications in plants, animals and micro-organisms for the agri-food, industrial and medicinal sectors, with tens of applications potentially reaching market stage in the next 5 years and even hundreds in the next 10 years" (COM study, 2021, p. 51).

It must be said that it is not easy to map the basis of this statement. It remains overly cautious, and above all vague on essential aspects by way of phrasing such "potential applications", "tens of", "potentially reaching the market" or "even hundreds". Nevertheless, if the content is taken literally as, two conclusions can be drawn:

1. NGT-related research is increasing.
2. The number of potential applications is increasing – and will do so in the future.

A look into Chapter 4.5 ("New genomic techniques research and innovation") of the COM study shows no special (detailed) analysis of the development of the NGT related research or research funding, neither EU, nor stakeholder or EU Member States. What can be found is a very general overview of the EU funds related to NGTs. COM study authors wrote it on the basis of an "analysis of EU funding for NGT-related projects", that had been conducted by the Commission's Directorate-General for Research and Innovation (DG RTD). The Commission's study calls this overview "the key findings of the analysis" (COM study, 2021, p. 9), unfortunately, the analysis of DG RTD is not publicly available.

Even though the most important basis for this issue within the COM study are the market review and the online dashboard of Parisi & Rodrígez-Cerezo (2021 and 2020), a quote from Broothaerts et al. (2021) should be highlighted. In addition to the potential of NGTs, the difficulties associated with their application are also emphasised: "The developmental processes from the individual cell of which the genome has been successfully altered through a NGT to a functioning living organism harbouring the same alteration could be long and difficult" (Broothaerts et al., 2021, p. 3).

3.4.3.1 Commercialised plants obtained with NGT

Calyxt soy and GABA tomato

Calyxt soy and GABA tomato are the only two NGT commercialised plants. The COM study did no research on the extent of the actual cultivation of either of these plants. This is in contrast to the – albeit very brief – explanation of the COM study on the likewise commercialised mushroom (see below). The present expert opinion sees this as an example of a general disinterest of the COM study in the exact circumstances of the commercialisations. The COM study is also not interested in the commercialisations that have not yet taken place. Gelinsky can, for example, state that she had to cancel six projects, compared to her 2020 research alone, because they could no longer be found in the companies' development pipelines (Gelinsky, 2022, p. 93).

With respect to the identified soybean variety from the US company Calyxt the internet portal "seekingalpha.com" had reported on the commercial development of the product and the company's further ideas already in 2020. Issa (2020) summarises the findings as follows:

- "Project delays and slower than anticipated growth contradicts CLXT's business model that claim a speedy development cycle using novel gene-editing technologies."
- "After unprofitable commercialisation of the high oleic soybean oil, CLXT is shifting strategy to focus solely on seed production and tech licensing."
- "The simplification of the business model will allow CLXT to focus on scientific innovations and lower the demand on working capital funding" (Issa, 2020).

Comparable information cannot be found in the COM study.

Gelinsky (2022) reports about free seed distribution in spring 2021 by Sanatech Seed, the developer of the GABA tomatoes. The latest GAIN Agricultural Biotechnology Annual report for Japan of the US Department of Agriculture writes that Sanatech Seed had saled online fresh tomatoes, puree and seeds after completing a voluntary consultation in Japan (USDA, 2022). More up-to-date details are currently not to be found – after cursory examination by the present expert opinion.

Cibus canola

The history of the so-called Cibus canola constitutes an important episode in the commercialisation of genome-edited plants. The herbicide-tolerant oilseed rape was engineered with Cibus's own genomic technique RTDS™,[154] according to the documents of the German Federal Office of Consumer Protection (BVL, 2015). The relevant German authority

> "stated that the herbicide-resistant oilseed rape lines produced by means of the Rapid Trait Development System (RTDS™) described in the application of the company Cibus do not constitute genetically modified organisms within the meaning of the Genetic Engineering Act and are therefore not subject to the provisions of the Genetic Engineering Act" (BVL, 2015; translation by the author; for German original see below[155]).

When asked, Health Canada made the following statement in May 2021:

> "When Health Canada originally assessed this particular herbicide tolerant canola, we identified that, while the developer attempted to use their proprietary gene editing process to produce this canola, the plant was actually the result of a mutation that arose during tissue culture and not due to the gene editing process. Health Canada completed our assessment of this canola and accurately reflected the nature of this plant variety in our Decision Document published online here [[156]]. Health Canada has not altered our document for this plant at any time" (Health Canada, personal communication[157]).

[154] An ODM variant, see Chapter 3.3.1.4.5 above.

[155] Original in German: "Es wird festgestellt, dass die mittels des im Antrag der Firma Cibus beschriebenen Rapid Trait Development Systems (RTDS) hergestellten herbizidresistenten Rapslinien keine gentechnisch veränderten Organismen i.S.d. Gentechnikgesetzes darstellen und damit nicht den Vorschriften des Gentechnikgesetzes unterliegen."

[156] Link as found in the original document: https://www.canada.ca/en/health-canada/services/food-nutrition/genetically-modified-foods-other-novel-foods/approved-products/novel-food-information-cibus-canola-event-5715-imidazolinone-sulfonylurea-herbicide-tolerant.html (accessed 31 October 2022).

[157] Health Canada, personal communication, E-Mail dated 13 May 2021 (in the context of another project).

Meunier (2020) has looked at the process and comes to a different conclusion than the Canadian authority:

> "Today, this presentation has changed. In the version currently online, last modified in July 2020, there is no longer any hypothesis or uncertainty about the origin of the mutation. The agency now writes that 'the mutation […] has been created as a result of a spontaneous somaclonal variation'".

In any case, the Cibus canola can still be found in the literature as one of the first commercialised gene-edited products (Li, 2022). Above all, the example shows that many of those involved themselves have difficulties describing (or understanding) with equal precision the often-praised precise workings of NGTs. It apparently does not always matter whether they are employees of regulatory authorities or companies, scientists or other experts.

Non-browning white button mushroom (*Agaricus bisporus*)[158]

Parisi & Rodríguez-Cerezo's research states that no information is available on the current status of commercialisation. Even the wording about the approval for commercial use in the USA appears uncertain: "According to the information available, these mushrooms were approved for commercialisation in the United States in 2016 and can be sold without further oversight" (Parisi & Rodríguez-Cerezo, 2021, p. 22). As a result, the authors classify this mushroom as pre-commercial, since they could not find any signs of commercialisation in any country.

3.4.3.2 Contributions to the European Union's Green Deal hypothetical

To show which plants are suitable in supporting the achievement of the goals of the EU's Green Deal, EU's Biodiversity Strategy or even those of the United Nations' Sustainable Development Goals, the COM study refers to the report of Parisi & Rodríguez-Cerezo (2021) (see COM study, 2021, p. 52). But the COM study does detail which new traits introduced into the plants with NGT are likely suitable to these political initiatives. Examples mentioned are "plants that are more resistant to diseases and environmental conditions or climate change effects in general, improved agronomic or nutritional traits, reduced use of agricultural inputs, including plant protection products, adaptation of varieties to local needs, or preservation of traditional or niche varieties". Additionally, it is questionable whether it is possible at all to infer any outcomes regarding individual plants or products from the general and abstract ("aggregated") representations within the market review of Parisi & Rodríguez-Cerezo (2021). As shown in Table 15 the details of the traits are not presented. This is all the more the case, since Parisi & Rodríguez-Cerezo (2020 and 2021) does not mention the European Green Deal (EGD). More specifically, for example, the term "sustainability" ("sustainable" ...) in the Parisi & Rodríguez-Cerezo market review can be found only in names of sources (companies, networks ...). "Pesticide" (as the relevant keyword for pesticide reduction – a central goal of the Farm to Fork Strategy, being part of the EGD) is mentioned once, in the context of NGT microorganisms.

As mentioned above, the focus of the present expert opinion is on plants and plant-based products which have been developed using new genomic techniques. To examine this aspect

[158] The COM study presents mushrooms together with plants; that categorisation is followed here.

of the COM study and to interpret its results, the present expert opinion undertook a targeted query through the online dashboard (see Table 17).

Regarding the goals of genome editing, the COM study found – among other things – that "[e]specially at the R&D stage, most traits under development relate to modified composition, biotic and abiotic stress tolerance, and plant yield" (COM study, Chapter 3.4.1). The aforementioned database query made by the present expert opinion (see Table 17) does not (fully) support this finding. Notably, it does not reflect the relative importance of new traits which are designed to improve tolerance to abiotic stress. Herbicide tolerance (HT) should have at least been mentioned in this listing. HT at the early R&D stage counts for more projects as for abiotic stress tolerance (24 against 23). At the advanced stage fewer HT-projects (4 against 15) could be found, and at the pre-commercial stage 6 projects (against 0 for the abiotic stress tolerance). Klaus Berend, acting director for food safety and innovation with DG SANTE considered herbicide tolerance not as sustainable in a recent discussion event.[159]

Because the COM study refers only to the general statements of the JRC market review (Parisi & Rodríguez-Cerezo, 2021), its statement that NGT plants could contribute to the goals of the Farm to Fork Strategy, the Biodiversity Strategy, and the UN SDGs remains unsubstantiated. However, the listings of NGT plants and used traits (COM study, 2021, Table 1, p. 15 and Table 2, p. 16) already indicate that a benefit for the strategies mentioned or the UN SDGs cannot be assumed in general. For example, poplars and rapeseed have a high hybridisation potential. Various species such as rapeseed and alfalfa, moreover (including transgenic ones) can be found proliferating in the wild naturally, which may be problematic in terms of preserving genetic diversity. Various traits, such as herbicide tolerance, can also have a negative impact on biodiversity under certain circumstances (see Chapter "3.5.3.1 Environmental risks" below).

Despite the limited willingness of private companies to provide information, it would have been possible to look at individual plants and their traits modified by NGT. This indicated by the report New genetic engineering techniques: Commercialisation pipeline in plant breeding and licensing agreements,[160] which has been available since 2017 and was last updated in January 2022 (Gelinsky, 2022). A total of 60 different products, spread over 15 crops and one ornamental plant, are listed in this document; an intention to commercialise them can be assumed. For at least 21 developments (concerning the crops rapeseed, soybean, maize, rice, wheat, camelina, lettuce, and alfalfa), field trials have already been carried out; for a further 25 developments, no reliable statement can be made, as the relevant information is not available. A look at the traits modified by NGTs shows that, in addition to altered composition (e.g. fatty acids, protein, glycoalkaloids) or increased plant yield, biotic stress tolerance [11 mentions: disease resistance (7), nematode resistance (4)], and herbicide tolerance (8) are also important traits. Increasing abiotic stress tolerance is targeted in five products [drought tolerance (3, each in conjunction with other traits), salt tolerance (1), cold tolerance (1)]. Three other applications target more effective nitrogen utilisation by the crop.

[159] "Gene-editing revamp: the solution to climate change and food security?". Organised by Politico magazine in June 2022. www.politico.eu/event/gene-editing-revamp-the-solution-to-climate-change-and-food-security (accessed 23 October 2022).

[160] Original in German: "Neue gentechnische Verfahren: Kommerzialisierungspipeline im Bereich Pflanzenzüchtung und Lizenzvereinbarungen".

Table 17: Database query made by the present expert opinion with the dashboard of Parisi & Rodríguez-Cerezo (2020): Plants at a certain development stage (own research).

Number of row ↓	Development stage (column) → Traits (row) ↓	Pre-commercial (relative position)	R&D advanced (relative position)	R&D early (relative position)
1	**Applications as indicated in the online dashboard**	16	117	292
2				
3	**Herbicide tolerance**	6 (1)	4 (8)	24 (5)
4	**Modified composition**	5 (2)	38 (1)	71 (2)
5	**Storage performance**	2 (3)	11 (5)	12 (7)
6	**Biotic stress tolerance**	2 (3)	37 (2)	74 (1)
7	**Plant yield and architecture**	1 (4)	31 (3)	56 (3)
8	**Abiotic stress tolerance**		15 (4)	23 (6)
9	**Modified colour/flavour**		10 (6)	11 (7)
10	**Other traits**		9 (7)	11 (7)
11	**Breeding tools**		3 (9)	31 (4)
12	**NA**		1 (10)	
13				
14	**Number of single applications represented in this table (sums of row 3 to 13)**	16	159	313
15	**Differences row 14 minus row 1**	0	42	21

Row 1 shows the number of applications (organisms) as indicated in the dashboard. **Rows 3-12** correspond to the results in the online dashboard when two filters are activated. The first filter is always "plants", the second corresponds to the information in the column "Development stage".
NA is not specified in the Dashboard.

The extent to which crops with the above traits can actually contribute to the goals of the European Green Deal or the UN SDGs cannot be answered blanketly. Such an answer depends on numerous factors and can therefore only be assessed as part of a comprehensive case-by-case assessment. The seven specific areas of concern identified by EFSA in its guidance (EFSA, 2010) for GMOs are largely also present for NGT products (see Chapter 3.5.3.1 "Environmental risks"). Therefore, in addition to the method used to produce the desired change in the plant's genome, the risk assessment must also consider the modified trait itself.

The COM study itself is limited to emphasising the potential benefits of NGT products and pointing out that some stakeholders consider that "these benefits are hypothetical and

achievable by means other than biotechnology" (COM study, p. 2). As it is the case in the study overall, a risk-benefit discussion is not included here.

In addition, only a few goals from the Farm to Fork Strategy, the Biodiversity Strategy and the UN SDGs are mentioned, to which the NGT products are supposed to contribute. The COM study does not provide a comprehensive consideration of the extent to which the goals addressed here may conflict with other goals also mentioned in these strategies, nor does it consider other sustainability goals. In examining the Farm to Fork Strategy, for example, it states that:

> "As such, even though the EU's transition to sustainable food systems has started in many areas, food systems remain one of the key drivers of climate change and environmental degradation. There is an urgent need to reduce dependency on pesticides and antimicrobials, reduce excess fertilisation, increase organic farming, improve animal welfare, and reverse biodiversity loss" (COM(2020) 381 final, p. 3).

The EU Biodiversity Strategy (COM(2020) 380 final) lists targets for "bringing nature back to agricultural land". These include, for example, reversing the alarming decline in farmland birds and insects, especially pollinators; restoring at least 10 percent of agricultural area under high-diversity landscape features; farming at least 25 percent of the EU's agricultural land organically by 2030; and reversing the loss of genetic diversity (including by facilitating the use of traditional varieties of crop and breeds).

Similarly, a look at the 17 UN SDGs and their targets shows that the use of NGT products can also negatively affect some of these targets. Goal 1 (no poverty: "end poverty in all its forms everywhere"), for example, includes access to natural resources and appropriate new technologies. Goal 2 (Zero hunger: "End hunger, achieve food security and improved nutrition and promote sustainable agriculture") formulates as target 2.5 the maintenance by 2020 of the genetic diversity in seeds, cultivated plants, farmed and domesticated animals and their related wild species, and the promotion of access to the benefits arising from the utilisation of genetic resources and associated traditional knowledge. According to target 2.4, by 2030, food production should be sustainable and implement resilient agricultural practices that increase productivity and production that help maintain ecosystems, strengthen capacity for adaptation to climate change, extreme weather, drought, flooding and other disasters, and that progressively improve land and soil quality. Goal 14 (Life below water: "Conserve and sustainably use the oceans, seas and marine resources for sustainable development") and 15 (Life on land: "Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss") represent biodiversity targets that may be negatively affected by NGT products if they pose risks to species or habitats (e.g., lethal/sublethal effects on non-target species, hybridisation of NGT plants with wild relatives, invasion of drought-tolerant NGT plants into xerothermic habitats) (all quotes: United Nations, 2015).

The COM study concludes in its executive summary that a purely safety-based risk assessment may not be enough to promote sustainability and contribute to the objectives of the European Green Deal and in particular the Farm to Fork and Biodiversity Strategies. By proceeding in such a way the COM study fails to recognize that both the sustainability goals and the aforementioned strategies encompass different aspects that need to be considered holistically (COM study, 2021, p. 4). This means that not only "the benefits contributing to sustainability would need to be evaluated, so an appropriate mechanism to accompany the risk assessment

may be required," as the COM study goes on to write, but also that those risks that may negatively impact sustainability aspects need to be comprehensively evaluated as well.

3.4.3.3 NGTs can or could contribute to the EU goals?

The conclusion that NGT-crops and products could help achieve current European Union goals is not tenable. The argumentation found in the COM study is largely too general to a support EU goals in the future use of NGTs. All the more astonishing is a small but subtle and important linguistic shift between the study and its presentation in April 2021: The COM study itself states "NGT products and their applications *could* provide benefits for EU society and address major challenges" (COM study, 2021, p. 59). But Commissioner for Health and Food Safety, Stella Kyriakides replaced the subjunctive by the indicative, when she presented the study: "The study we publish today concludes that New Genomic Techniques *can* promote the sustainability of agricultural production, in line with the objectives of our Farm to Fork Strategy" (European Commission, 2021d, emphasis by authors).

3.4.4 Stakeholder and Member States views on the utilisation of NGT plants and products

The perspectives of the EU Member States and the stakeholder on the possible use of NGTs and the plants and products produced with them are largely addressed in the COM study under the headings "[o]pportunities and benefits" and "[c]oncerns and challenges". The present expert opinion has dealt with these contents of the COM study in Chapters 3.3.4 and 3.6.1 in order to consider a connection with other related topics, for example general research questions the socio-economic aspects.

3.4.5 What issues and challenges were not investigated in the context of the utilisation of NGTs?

3.4.5.1 Utilisation of genetically modified crops obtained with EGTs

The COM study leaves unanswered how it assesses the developments and the experiences with genetically modified plants and products over the last 30 years. Even in the early 2000s, many different projects used genetically modified plants (Vogel & Potthof, 2003; Sauter & Hüsing, 2005). At that time, such plants were modified with the "established genome techniques (EGT)", as they are referred to in the context of the COM study; the bollistic and the *Agrobacterium*-technique in particular were used. There has been no systematic investigation by the COM study into which of the plants and projects from the early 2000s have come onto the market, which techniques have been used, or even which approaches have had a lasting effect on agricultural systems. A corresponding evaluation could form a template for the assessment of the prospects of NGT plants and products. First experiences with commercial NGT plants already show that economic success is not only determined by technical aspects.[161]

It should be noted that the adoption rate of transgenic crops is limited to relatively few crop species. Following ISAAA the commercially available biotech crop species are: soy, corn, cotton, canola, sugar beets, papaya, potato, eggplant, pineapple, alfalfa, squash, apples, sugarcane, safflower (ISAAA, 2022); most of these, with – in global terms – predominantly relatively

[161] See Chapter 3.4.3.1 above.

small acreage. Exceptions are the three crops soy, maize and cotton. In the EU, the cultivation of genetically modified crops plays practically no role.

3.4.5.2 Assessment of sustainability and goal conflicts

Closely related to the previous topic is the question of assessing sustainability. This applies to the assessment of NGT crops and products in particular, as well as agricultural systems in general. Research on these issues is complex. In some cases, systems – for example, for evaluation at the company level – are in place. In other cases, the data situation is thin. The extent to which studies are already possible today depends on the specific questions (Meyer, Priefer & Sauter, 2021). In addition, the European Union is facing a political debate on this issue that is no less complex than the scientific assessment.

Special challenges arise with foreseeable goal conflicts of various kinds. Without the present expert opinion being able to deal with this question in detail, they are already becoming apparent today. The political question is: To deregulate certain NGT plants and products as quickly as possible, without considering the risks in detail – or rather not? The question stands against the backdrop of climate change and biodiversity loss. And can be seen as an example for the mentioned goal conflict. It must not be forgotten in this context that most of the NGT plants and products that might need to be assessed for their sustainability do not yet exist. This means that it is in no way clear that NGT plants and products have any positive effects on climate change and biodiversity, or that they are better able to cope with the consequences of climate change. The COM study does not address these questions.

3.4.6 Interim summary of utilisation of NGTs

Chapter 3.4 of the present expert opinion investigates the representation of the utilisation of NGTs in the agri-food sector in the COM study. The focus on the agri-food sector follows the assessment of the present expert opinion that the other sectors are not adequately covered by the COM study. Neither the JRC technical review of the use of NGT applications nor the COM study covers the full range of NGT applications, as claimed. Regarding the goals of genome editing in plants, the COM study found that "most traits under development relate to modified composition, biotic and abiotic stress tolerance, and plant yield. Similarly, beyond cereals and oil crops, there is a greater focus on vegetables, fruits and legumes" (COM study, 2021, p. 51). The present expert opinion has made its own queries to an online dashboard provided by the authors of the supplementary material to the COM study (Parisi & Rodríguez-Cerezo, 2020). According to the results of these queries, the information provided by the COM study is only partially supported. Notably, the results of the mentioned queries do not reflect the relative importance of new traits which are designed to improve tolerance to abiotic stress. Herbicide tolerance, on the contrary, should have been classified by the COM study with a higher relative importance. The COM study pays particular attention to the question to which extent NGT crops can contribute to achieving the goals of the European Green Deal. The EU's Biodiversity Strategy, the Farm to Fork Strategy and the UN Sustainable Development Goals are also expected to benefit. The COM study stated that Parisi & Rodríguez-Cerezo (2021) had identified several plant NGT products that *could* contribute to the Green Deal. In this context, the communication of EU Commissioner Stella Kyriakides is significant: At the day of the presentation of the COM study she already said that the NGT plant products *can* contribute to the Green Deal. The extent to which crops with the above traits can actually contribute to the goals of the European Green Deal or the UN SDGs cannot be answered blanketly. Such an answer depends on numerous factors and can therefore only be assessed as part of a

comprehensive case-by-case assessment. Unfortunately, the COM study does not provide any insight into concrete projects. A specific crop with a particular new trait is only identifiable as an absolute exception. Because the COM study refers only to the general statements of Parisi & Rodríguez-Cerezo (2021), even the statement that NGT plants could contribute to the goals of the Farm to Fork Strategy, the Biodiversity Strategy, and the UN SDGs remains unsubstantiated. In this respect Parisi & Rodríguez-Cerezo (2021) find themselves being prisoners of their own sources and their approach, respectively. This is true for over 40 percent of the data set (184 out of 426 plant projects), namely the data from the private sector. Asking the developing companies directly is of course obvious because it seems to provide the greatest possible proximity to the source of the relevant information. However, there remains a relatively high degree of uncertainty, as the companies themselves are players in the debate over NGT regulation, which may lead some of them to make the outlook seem more optimistic in order to ensure a favourable regulatory environment. In addition, companies in the Commission's research for the 2021 published COM study insist that the details must be treated as confidential business information. It would have been reasonable for Parisi & Rodríguez-Cerezo (2021), respectively the COM study, to critically reflect on the sources and their roles in the debate on the future regulation of NGT plants and products.

The COM study does not seem to be interested in the commercialisation process. This applies to the experiences gained with the commercialisation of transgenic plants in the past decades as well as to those with the first commercialised NGT plants and products. The COM study either presents very little information or it is outdated. There is also nothing in the COM study about projects with NGT plants and products that were started but then cancelled. According to the assessment of the present expert opinion, this could have been important information for the presentation of the possible future development of NGT plants and products.

In any case, it is important to note that the COM study can only present hypothetical contributions to the above-mentioned policies.

3.5 Risk assessment of plants and products developed with NGTs

This chapter will summarise and discuss the ideas, principles, and concepts of risk assessment systems for the utilisation of NGT plants and products as presented in the COM study. It is neither intended nor feasible to address the complete EU system of risk assessment regarding genetically modified plants and products within the scope of the present expert opinion. As mentioned above, the risk assessment of the new genomic techniques and the respective plants and products is closely connected with their technical developments. The focus of this section is on regulation. Technical aspects of risk assessment can be found in Chapter 3.3 above.

As a basis for the COM study's work on risk assessment, the EFSA compiled an analysis of the Member States' and their own work titled "Overview of EFSA and European national authorities' scientific opinions on the risk assessment of plants developed through New Genomic Techniques" (Paraskevopoulus & Federici, 2021). This "scientific report" had been requested by the European Commission and is listed at the end of the Commission's study as one component of the supplementary material provided there. Additionally, the JRC report from 2011 (Lusser et al., 2011) and SAM HLG work from 2017 (SAM HLG, 2017) were both used by the COM study (see COM study, 2021, p. 9f.).

Inputs from Member States on risk assessment and safety aspects of NGTs, NGT plants and products could – at least theoretically (see below) – find their way to the COM study secondarily, due to the various steps in the analysis and research connected to the preparation of the COM study. In addition to the above-mentioned review (Paraskevopoulus & Federici, 2021), Member States also integrated their own views on risk assessment into their responses to the questions posed over the course of the targeted consultations. The assessments of the stakeholders on risk assessment were also taken into account in the COM study. The corresponding sections in the views of the latter two – Member States and stakeholders – presented by the COM study's Chapter 4.4.2. are dealt with separately in Chapter 3.5.5 of the present expert opinion. However, the COM study leaves open to what extent the contributions of the Member States and stakeholders were taken into account if they were submitted as independent documents (or annexes) to the targeted consultation.

Chapter 3.5.1 presents new or known outcomes and challenges. The present expert opinion takes into account the unusual fact that, although segments of the COM study are marked in its table of contents (as for example, the section titled "4.4. Safety of new genomic techniques of the COM study"), little can be learned about the regulation of risk assessment. Instead, implicit references to the regulation of risk assessment are (repeatedly) found throughout the COM study. These are mapped in sections 3.5.1.1.1 to 3.5.1.1.7 of the present expert opinion. Methodological criticisms of the COM study's coverage of the topic of risk assessment are presented in Chapter 3.5.2. In Chapter 3.5.3, the question is raised as to how well the COM study researched the topic of risk assessment. And the positions of Member States and stakeholders can be found in Chapter 3.5.4.

3.5.1 New or known outcomes and challenges

As already discussed in Chapter 3.3 above, the following paragraph demonstrates an important outcome of the Commission's study on NGTs:

> "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59).

To recapitulate, this conclusion is a mixture of technical analysis and risk assessment. The Commission's study combines a far-reaching demand with its technical basis, and is formulated neutrally: to "apply different levels of regulatory oversight to similar products with similar levels of risk" – that is, the actual EU regulation of genetic engineering – "may not be justified". This is in fact a strong demand. Even when formulated in a circuitous manner, the authors refrain from relativising any restrictions. This approach is novel, and is in contrast with previous statements made by the Commission on this issue.[162] This is significant in that it is more comprehensive than any other finding in the COM study. Consequently, it is the most important outcome with respect to risk assessment, and it constitutes the core of the discussion in the EU.

[162] The Commission has been struggling for years to meet the demands of the EU Member States for a clear statement on the regulation of NGTs, specifically regarding the interpretation of existing European law. See for example Commission's letter to Competent authorities of the Member States (European Commission, 2015). Subsequently, after the European Court of Justice had announced case C-528/16, a statement of the Commission's would no longer have been appropriate.

In the context of this outcome it would, of course, be interesting to understand which "certain genome editing techniques" the Commission's study had in mind by the time of its publication. Today we know that the SDN-1, the SDN-2, the ODM technique and cisgenesis would be the prime candidates for a new regulation – see for example the first formal step of the new initiative "Legislation for plants produced by certain new genomic techniques". Here, the Commission writes that it

> "will prepare a policy initiative on plants obtained by targeted mutagenesis and cisgenesis, accompanied by an impact assessment. It will also cover food and feed derived from such plants (hereinafter, references to plants obtained by targeted mutagenesis and cisgenesis will refer as well to their food and feed products)" (European Commission, 2021b).

The explanation for "targeted mutagenesis (SDN-1, SDN-2 and ODM)" can be found in the COM study (see p. 31).

When the Commission's study was published, the qualification for "certain genome editing techniques" was not as clear. SDN-1, SDN-2 and cisgenesis (without ODM) are mentioned together explicitly only once,[163] and the context is rather different from one in which a special group is characterised: "The above conclusion (i.e. that SDN-1, SDN-2 and cisgenesis techniques present similar hazards to conventional plant breeding) assumes that no exogenous genetic material is present in the product derived from these techniques " (COM study, 2021, p. 54). Online, at the European Commission's website it reads "The Commission plans to initiate a policy action on plants produced by targeted mutagenesis and cisgenesis, which will involve an impact assessment including a public consultation" (European Commission, without date, a).

The new initiative started in September 2021. Details can be found on a special website (European Commission, 2021c). The initiative is only very marginally relevant to the present expert opinion.

From a risk assessment perspective, the outcome mentioned at the beginning of this section 3.5.1 raises at least two questions: What determines if risk-levels – in the sense used by the Commission's study – are similar? This will be discussed below in Chapter "3.5.1.1.1 Similarity of risk-levels and risk profile – comparability". Secondly, a question arises with respect to the wording of the COM study. The quote "[i]t may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59) has been discussed as a strong demand in the course of the present expert opinion (see Chapter "3.5.1 New or known outcomes and challenges" above). Nevertheless the wording suggests that other systems of regulatory oversight might not be fundamentally excluded by the COM study.

3.5.1.1 The COM study's chapter on the risk assessment and safety

The COM study deals explicitly with the topics of "safety" and "risk assessment" in one chapter, which is the Chapter "4.4. Safety of new genomic techniques" with the Subchapters "4.4.1 EFSA's overview on risk assessment opinions of plants developed through NGTs " (including

[163] A second joint mention of the respective NGTs (including ODM) is in footnote 4 (COM study, 2021, p. 3). It is made without reference to any policy initiative.

"SDN techniques and ODM", "Cisgenesis and intragenesis" and "Other considerations on risk assessment") and "4.4.2. Member States' and stakeholders' views regarding safety".[164]

"SDN techniques and ODM"

The COM study explains here (COM study, 2021, p. 29) again in a rather general, non-specific manner that NGTs are used for different purposes. Subsequently, the position of EFSA is stated: "EFSA did not identify new hazards specifically linked to the genomic modification produced via SDN-1, SDN-2 or ODM, compared with conventional breeding and techniques introducing new genetic material"[165] (COM study, 2021, p. 29).

EFSA and the Member States agree – according to the presentation of the COM study – that SDN techniques are a major advance over random genetic modifications, especially in terms of their specificity. Nonetheless, there are considerations on off-target modifications (types, frequency and their consequences) in the statements of the Member States, which argue that a risk assessment is necessary. "However", the Commission's study goes on, "direct comparison is difficult due to the varied nature of the opinions" (COM study, 2021, p. 29).

With regard to mutations, the COM study refers to EFSA, which for its part considered only recently published evidence: The off-target mutations possibly caused by SDN techniques were of the same type, but occur less frequently than in conventional breeding, including spontaneous mutations and mutations triggered by physical and chemical mutagenesis (see COM study, 2021, p. 30; see "3.3.3.3 Recent experimental evidence" above). According to the COM study, less information is available on the ODM technique, especially with regard to its molecular details and for the occurrence of off-target mutations (see COM study, 2021, p. 30). The two aspects under which ODM techniques are addressed in this subchapter should be noted. They could help answer the question "How much information – and which – is needed for a risk assessment? (see Chapter 3.5.1.1.4 for further details).

"Cisgenesis and intragenesis"

Following EFSA the COM study noted that cis- and intragenesis use the same gene pool as conventional plant breeding. Only desired genes are transferred, there is no risk of linkage drag. The "hazards associated with the introduced genes" are "similar to those from conventional breeding" (COM study, 2021, p. 30). But in the case of intragenesis, new traits and new hazards might be possible, comparable to transgenesis. With respect to the understanding of the potential gene pool, EFSA uses the idea of a "tertiary gene pool i.e. from species that can only be crossbred using advanced techniques", while one Member State sees in this view a violation of the "basic definition of a cisgene (i.e. a gene from a cross-compatible species)" (COM study, 2021, p. 30).

Although one Member State disagrees, EFSA sees a general understanding that plants produced with cisgenesis are "not substantially different" (COM study, 2021, p. 30) from conventionally bred plants when it comes to "phenotypic characteristics and risks for human and animal health". The Member State believes that this can only be determined through

[164] For the considerations on Chapter 4.4.2. of the COM study see Chapter 3.5.4 of the present expert opinion.

[165] As shown already in Chapter 3.3.2.7, among others, the COM study does not follow the sorting of the NGTs according to Broothaerts et al. (2021).

"comprehensive comparative analyses between the cisgenic plant and its conventional counterpart" (COM study, 2021, p. 30).

Intragenesis and transgenesis can involve new DNA combinations and new open reading frames. With cisgenesis and conventional breeding this is usually not the case. With respect to the regulatory elements, EFSA stated that regulatory elements can also lead to altered expression of genes in cisgenesis. Intragenesis can be used to significantly increase the options of altering gene expression and the evolution of traits because the genes, promoters and regulatory elements can be exchanged within the element (see COM study, 2021, p. 30f.).

"Other considerations on risk assessment"

The COM study reports a "general agreement that the risk assessment may benefit from any knowledge on the history of safe use of the modification(s) and trait(s) introduced" (COM study, 2021, p. 31). Unfortunately, the COM study cannot clarify who exactly assents to this "general agreement". With such an agreement, the COM study continuous, a guarantee to certain flexibility in the risk assessment would be justified. Examples of a possible reduction in the demands on data and simplification of the risk assessment are given. The COM study identifies a second agreement: "existing risk assessment guidance is adequate for the assessment of plants obtained through SDN-based and cisgenesis/intragenesis techniques" – again unfortunately, without clarifying who shares it.

Furthermore, the COM study highlights at this point an EFSA finding that for an NGT product to be classified as non-transgenic, evidence should be provided, "that no exogenous DNA is retained" (COM study, 2021, p. 31).[166]

3.5.1.1.1 Similarity of risk-levels and risk profile – comparability

As already explained above (see 3.5.1), the COM study states that "It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59). In this, the COM study masks an implicit demand to change this unjustified regulation. The COM study puts this forward as a conclusion. It does so on the basis of the principle of comparability of risk assessments, in this case the comparison of different genetically modified – or genome-edited – plants with those that have been bred using conventional methods. The principle is found, for example, in the EFSA guidance for environmental risk assessment (EFSA, 2010) under the title "Comparative safety assessment as a general principle for the risk assessment of GM plants". The COM study applies this principle as follows:

> "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59).

To focus on one aspect, the COM study assumes that "similar products with similar risk profiles "can be obtained" with conventional breeding techniques, certain genome editing techniques and cisgenesis" (COM study, 2021, p. 59).

[166] In the COM study, this part is followed by the presentation of the "Member States' and stakeholders' views regarding safety" (COM study, 2021, p. 31, Chapter 4.4.2.). Due to the structure of the present expert opinion, this part can be found below in section 3.5.4.

3.5.1.1.2 Novelty in the sense of new and advanced possibilities to change DNA

What is technically possible?

Because the technical description of NGTs in the COM study starts with the SAM HLG, the present expert opinion follows this approach in addressing the question of whether NGTs meet the claim of being "new". The SAM HLG argues from the perspective of the new – and never before seen – potentials that could open up with the application of NGTs. SAM HLG refers less to the question "New or not?": "The SAM HLG considered that, due to the precision and efficiency of use of certain NGTs, they are the only realistic means of obtaining certain products" (SAM HLG, 2017; quoted here according to COM study, 2021, p. 11).

This perspective, for its part, is suitable for characterising the NGT as actually new. In the representation of Broothaerts et al. (2021), the COM study also makes the new possibilities afforded by NGTs a topic of analysis. The authors place it in the context of other new scientific findings, especially concerning the "functional properties in various organisms and their genetic basis". The COM study argues that:

> "Whereas several established GM techniques generate random sequence alterations in the genome, new technological developments mean that changes can be directed to a selected genomic location, thus enabling more precise editing of the genome. Sequence variations to the genome may be entirely novel or may occur already in other individuals of the species" (COM study, 2021, p. 12).

The novelty applies in particular to the most important new genomic techniques that work with the CRISPR system, or – as the COM study puts it – that are part of the CRISPR platform. CRISPR was first described as a genetic engineering tool in 2012 (Jinek et al., 2012).

The concept of NGTs

Conceptually, the heart of the new genomic techniques is that they work in a targeted way, in terms of the site of change. This is the essential difference to the techniques considered as EGTs in the COM study.[167] Although some genomic techniques have been used or developed since the early 2000s (for example ZFN and ODM), the breakthrough for directed mutagenesis came with the techniques of the CRISPR platform. The COM study calls CRISPR a "true game-changer" (COM study, 2021, p. 51). The constantly growing knowledge about the genome sequences of various crops plays a decisive role in this context. Knowledge of this kind is crucial for successful work with the new genome techniques. This is because the molecular tools needed to change a specific location in the genome are guided by the sequence information of this location.

The novelty of NGT stems not least from the expectation that the new techniques will make it possible to produce a large number of NGT plants and products in the future that would not be possible – or only very much slower – with the current genetic techniques and conventional breeding. In line with the above-mentioned perspective of the SAM HLG.

3.5.1.1.3 Case-by-case assessments

In sum, the position of the COM study based on case-by-case assessments in GM regulation is quite clear: "Embedding rigid risk-assessment guidance in legislation limits case-by-case

[167] At this point, cis-genesis falls out of view – at least as long as it is not used in connection with the SDN-3 technology.

assessment and makes it difficult to adapt risk-assessment requirements to scientific progress; this appears to be very much the case for NGTs" (COM study, 2021, p. 59). The emphasis here falls on the problems caused by the fact that the "rigid risk assessment guidance" is part of the European GMO regulation. At the same time, the COM study does not refer to a certain argument for regulation. It should be noted that the section on case-by-case assessments in the discussion chapter of the COM study reads quite differently:

> "Case-by-case assessment is widely recognised as the appropriate approach. EFSA and the Member State opinions agree on the need for flexibility and proportionality in risk assessment methodologies and data requirements, to take account of available knowledge on the history of use of the modification(s) and the trait(s) introduced. On these points, not all stakeholders share the expert body opinions. Several Member States and stakeholders see a need to develop specific risk-assessment procedures for NGTs. Some stakeholders called for research on safety and environmental risks linked to unintended adverse effects and NGT products' interaction with the environment" (COM study, 2021, p. 53).

In other parts of the COM study the positions are even more divergent: an unspecified number of stakeholders ("others") argue that the case-by-case approach should be applied at least as rigorously as in the current GMO risk assessment and that more information should be requested to assess the safety of NGT products (see COM study, 2021, p. 33).[168]

3.5.1.1.4 Information for a risk assessment

There is no fixed quantity of information that is necessary to carry out a risk assessment. At the same time, there are empirical values from the assessment of genetically modified plants which can inform such judgments, even when there no unanimity exists regarding the details of the risk assessment in the EU. Directice 2001/18/EC, for example, gives clear instructions on the aim of such information. It states the following:

> "The criteria and the information requirements shall be such as to ensure a high level of safety to human health and the environment and be based on the scientific evidence available on such safety and on the experience gained from the release of comparable GMOs" (Article 16, 2).

The COM study does not pose this question and accordingly does not give an answer. Nevertheless, the question is touched in the COM study at several points. For example, other stakeholders ("others") argue that the case-by-case principle should be at least as stringent as in the current GMO risk assessment – and "it should require more information to assess the safety of a NGT product" (COM study, 2021, p. 33). Unfortunately, the study does not clarify how many stakeholders support this demand. Another example concerns the ODM technology. First, the COM study states: "EFSA did not identify new hazards specifically linked to the genomic modification produced via [...] ODM, compared with conventional breeding and techniques introducing new genetic material" (COM study, 2021, p. 29). But only three paragraphs further on, it becomes clear that knowledge about the technique is assessed as limited: "As regards ODM, it was generally recognised that less information is available in the literature, in particular on its molecular mechanism and off-target modifications" (COM study, 2021, p. 30). Strictly speaking, it remains open whether there is only "less information" or too little. Broothaerts et al. (2021, p. 47) write "[t]he presence of off-target mutations has not been well studied for this NGT (Sauer et al., 2016)". All authors of Sauer et al. named the US company

[168] See Chapter 3.1.2.2.4 "Lack of transparency" above.

Cibus as affiliation. An automated search for the term "off-target" does not yield a single hit in the paper. A look at Modrzejewski et al. (2019, p. 23) shows how large the knowledge gap is in this specific case.[169] The authors found a single research paper on the topic of off-target changes in the context of the use of the ODM technique.

What is considered sufficient later becomes clear (but only in one specific example), although this is not directly a question of risk assessment itself. In the example where the COM study refers to EFSA, a certain point is justified by way of the most recently published experimental evidence. In this concreteness, however, this passage remains an isolated one for the COM study (COM study, 2021, p. 30). Furthermore, the present expert opinion shows that this example is not convincingly presented by the COM study (see Chapter 3.3.3.3 above).

In the discussion and conclusion sections, the topic arises again: here, the COM study makes the assessment that most "expert opinions" and most "views" are related to SDN techniques and deployment on plants (see COM study, 2021, p. 53). Furthermore, the COM study recommends that future policies should address the knowledge gaps identified in the study. It continues: "Safety data are mainly available for genome editing in plants, making it difficult to draw relevant conclusions on other techniques and applications in animals and micro-organisms" (COM study, 2021, p. 59). It remains unspecified how the COM study's authors assess the situation regarding the accessibility of relevant data in genome-edited plants, but they do emphasise that with respect to animals and microorganisms, it "would be prudent to generate relevant information in these areas too" (COM study, 2021, p. 59). From this quote, it may be inferred that the authors of the COM study do not see a priority problem regarding the relevant data for the genome-edited plants. With respect to technique, it is important to note that the same question arises, thereby "making it difficult to draw relevant conclusions on other techniques" so that it "would be prudent to generate relevant information in these areas too" (COM study, 2021, p. 59). The present expert opinion interprets this to mean as follows: The COM study considers it justified to draw relevant conclusions for the techniques mentioned – genome editing techniques applied to plants. Those are the only techniques mentioned by the COM study in this context, and in this paragraph specifically.

3.5.1.1.5 Transparency and access to the relevant data

The COM study and the supplementary material show that access to relevant information on NGTs is limited. Risk assessment is an important perspective for the discussion of this issue in the present expert opinion, even though it is also relevant in the other subject areas. This topic in this context is unique because it is unclear what exactly is known only to the developers of NGT plants and products, and what knowledge is also available, for example, to the authorities or the broader public.[170] Only with knowledge of these details regarding NGT plants and products is an unbiased risk assessment possible. The clearest indication of the limited access to information on NGTs and NGT plants and products in the context of the COM study arises from the presentation of the findings of the JRC market review: "Since much of the data was obtained under conditions of confidentiality, the report shows data aggregated into species groups and trait/disease categories. The detailed content of the database will not be made public" (Parisi & Rodríguez-Cerezo, 2021, p.9). As a result, those properties of plants produced

[169] An important review that has not been recognised by Broothaerts et al. (2021).

[170] The phrase "confidential business information" and blacked out areas in documents are somehow standard, at least well known in freedom of information inquiries.

with new genomic techniques are only found in the JRC review in a very general and aggregated form. This makes an evaluation in the sense of a risk assessment practically impossible. Any evaluation is dependent on detailed descriptions of the new properties of the genome-edited plants. This is particularly true since developers and companies emphasise how well NGT is suited to incorporating properties into plants that were or are not possible with previous breeding methods. It is not insignificant, that there is a general problem regarding access to the data necessary for a thorough risk assessment.[171]

3.5.1.1.6 Presence and absence of foreign DNA

The COM study itself makes the presence of foreign DNA an issue in three different contexts:

- First at the level of regulation. Here, the absence of foreign DNA is a criterion for classifying NGT plants and products as non-genetically engineered in the sense of the law (see COM study, 2021, p. 24 and 31).
- Second, in what may be termed the reverse case, the presence of foreign DNA is cited as an example of how the characterisation "genetically modified" can be demonstrated molecularly (see COM study, 2021, p. 55).
- The third context is the quality of the molecular changes – "the formation of sequence combinations and open reading frames that would normally not occur with conventional breeding or cisgenesis" (COM study, 2021, p. 30). This can be caused by the introduction of foreign DNA. However, the COM study does not clarify the relevant differences and problems, i.e. what the risks or possible hazard are introduced alongs is with the foreign DNA.

The levels are in any case clearly connected.

3.5.1.1.7 Naturalness

The COM study discusses the naturalness of the introduced changes obtained by NGTs from different points of view:

- Are the products distinguishable from products that had been produced with "hybridisation techniques, or occurring naturally"? (COM study, 2021, p. 13) Here, the COM study in many respects follows the findings of the ENGL group.[172]
- This means that the COM study would argue that similar changes be possible in nature, with NGTs or with conventional breeding. The COM study brings this aspect forward several times and in different variations – like EFSA does.[173]
- A direct reference to Directive 2001/18/EC must not be missed in this context: "The EU GMO legislation applies to GMOs as defined in Article 2(2) of Directive 2001/18/EC, i.e. 'an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination'" (COM study, 2021, p. 19; Article 2 of the Directive).
- With reference to some stakeholders, the COM study writes that they raise ethical concerns about the concept of naturalness, which is partly associated with NGT (see COM

[171] See Chapter 3.5.3.2 "Case-by-case assessments as part of a risk assessment".
[172] For details see Chapter 3.3.1.3 of the present expert opinion.
[173] The main aspects of this argument can be found in Chapter 3.3.3.1 of this expert opinion.

study, 2021, p. 47). However, this is not further elaborated in the COM study.

Taking these references into account, the COM study implicitly – but not explicitly – argues that greater proximity to natural conditions results in greater safety of NGT plants and products. However, it remains open how this can be proven.

With regard to molecular changes in particular, the COM study – as shown in Chapter 3.3.3.1 above – fails to provide evidence that the changes caused by NGT are indeed similar to those that occur naturally.

3.5.2 Critique of the methods of the chapter on risk assessment

3.5.2.1 Wording of "risk level" and "risk profile"

The comparison of plants produced with different techniques and methods is well known in risk assessment. In European regulation, for example, transgenic plants are also compared with their unmodified isoline. The comparative approach is simple: the modified and the unmodified organism are compared with the aim of determining the consequences of the modification. What is unusual in the conclusion drawn in the COM study is the use of unclear terms. This applies in particular to "risk level" and "risk profile" in this example. Apparently, the term is to be understood synonymously with "same level of risk". However, this can only be assumed at this point. The use of this term ("level of risk" or "same level of risk") in the COM study remains a puzzle: it only appears in the Executive Summary and in the Discussion.

In contrast, the phrase "safety of NGTs" (or "safety of products developed by NGTs" or comparable formulations respectively) can be found more frequently in the COM study. This is probably a consequence of the (summary of the) questionnaires to the Member States and the stakeholders. Most of the mentions (12 out of 19) can be linked to the questionnaires, the answers to them or corresponding paraphrases by the authors of the COM study. But that, too, can only be assumed here.

All in all, the use of these terms in the COM study does not provide a clear picture of a system of meaning.

3.5.2.2 Confusion around EFSA and Member States

Chapters 4.4.1 and 4.4.2 of the COM study discuss contributions to the question of risk assessment of NGT. On the one hand, EFSA was mandated to present an overview of the relevant work of the Member States and its own work (see Paraskevopoulus & Federici, 2021; in the COM study supposedly Chapter 4.4.1). On the other hand, the Member States had the opportunity to communicate their opinions within the framework of the targeted consultation. In addition, the Member States could upload their own documents, for example their own scientific reports, as part of the consultation (COM study, ostensibly Chapter 4.4.2, there together with the assessments of the stakeholder's contributions).[174] The presentation in the COM study is not convincing. For example, under 4.4.1 it is not even clear whether the phrases "EFSA did" or "EFSA was" mean EFSA in general or the review (Paraskevopoulus & Federici, 2021). The latter would – as described – also include the assessments of the Member States.

[174] Here again arises the problem, that it is not clear, whether or not the COM study reflects the contributions of the Member States and stakeholders. This especially the case for the attachments to the answers in the context of the targeted consultation (see Chapter 3.1.2.2.4 and Chapter 3.5 above).

A more precise naming of the sources in the COM study could have provided much more clarity here.

3.5.2.3 (No) EFSA conclusions on risk assessment

Looking at the "Conclusions" of Paraskevopoulus & Federici (2021) it is apparent that the authors do not present any content-related conclusions. Instead, they present again the various sources of the work and their approach. In addition, there is a "summary" in the scientific report. Here, too, the presentation of the underlying sources takes up a lot of space. Emphasis of content is searched for in vain. Once again, it is worth recalling that this scientific report was intended to provide an overview of the work carried out to date by EFSA and Member States on the risk assessment of plants produced using new genomic techniques. The mandate explicitly stated: "EFSA was not requested to carry out any critical appraisal of the reviewed scientific opinions" (Paraskevopoulus & Federici, 2021, p. 3).

At the very least, this raises the question of how/on what basis the authors of the COM study, for their part, build up a summary presentation of the essential aspects of the risk assessments.

3.5.3 How well researched and substantiated are the COM study's statements about the risk assessment of NGT plants and products?

A preliminary remark: the present expert opinion has already referred at various times to the COM study's statement that "EFSA did not identify new hazards specifically linked to the genomic modification produced via SDN-1, SDN-2 or ODM, compared with conventional breeding and techniques introducing new genetic material" (see Chapters 3.5.1.1 above and 3.8 below). The statement is taken up several times in the COM study, and also partially in a modified form (cf. for example p. 29 and p. 32). However, a critical discussion of this statement does not take place within the COM study itself.

Paraskevopoulos & Federici (2021) provide a compilation of the previous work on risk assessment as undertaken by EFSA and EU Member States. This compilation was not intended to serve as a critical review, nor, as expressed in the COM study, did "EFSA [...] conduct a critical appraisal of the Member State scientific opinions" – rather, "it commissioned an evaluation and summary of them"[175] (COM study, 2021, p. 10). But the critical discussion takes place at the Member States and stakeholder level. However, as the present expert opinion shows in Chapter 2 above, the COM study does not succeed in bringing the various positions into scientific competition with each other. The COM study shows its true colours when it states that "direct comparison is difficult due to the varied nature of the opinions" (COM study, 2021, p. 29).

Stakeholders' and Member States' views on the safety of NGT plants and products and on the risk assessment respectively are presented separately in Chapter 3.5.4 of the present expert opinion (see below). However, one further statement from the COM study should be highlighted here. The COM study states that "[s]ome stakeholders (mainly NGOs and organic/GM-free food business operators) raised concerns regarding the safety of NGT products, while others (mainly food business operators, NGT developers and academics) consider that NGT

[175] It should be noted, that the title of the work of Paraskevopoulos & Federici (2021) is "Overview of EFSA and national authorities' scientific opinions on the risk assessment of plants developed through New Genomic Techniques". It is not only about concerning the scientific opinions of the Member States.

products are safe" (COM study, 2021, p. 31). In this context, the phrase "consider [...] as safe" can only be understood in the sense that the other stakeholders (mainly food business operators, NGT developers, and academics) consider the NGT products to be safe, but not that they consider them likely or possibly safe. This statement – "consider that NGT products are safe" – violates every rule of risk assessment at the time it was made. There is virtually no basis for it, in particular because there are no specific examples of NGT plants or products to which this assessment could be applied. It stands alone and absolute – and it must be seen in this context as a carte blanche for all NGT products. If the statements of the stakeholders were as described here, then it is of course the task of the Commission to include this in the COM study. Yet it would have been necessary to contextualise such statements, to compare opposing positions and to evaluate them explicitly on the basis of their arguments. The present expert opinion is only able to check this process in a cursory manner. Stakeholders who consider that NGT products are safe in fact violate the principle of a scientific risk assessment on at least one point. The guidance document on ERA supports a list for a case-specific problem formulation: "Consider knowledge gaps (such as scientific uncertainties)" (EFSA, 2010, p. 16). At least the COM study writes in its Discussion: "[A]s demonstrated in this study, NGTs and NGT products vary considerably [...] so it is not possible to draw generalised conclusions as to their safety" (p. 52).

In Chapter 3.5.3.1 environmental risks are first presented as a cross-sectional topic.

3.5.3.1 Environmental risks

According to Article 4 of Directive 2001/18/EC, all appropriate measures must be taken "to avoid adverse effects on human health and the environment which might arise from the deliberate release or the placing on the market of GMOs". The Directive therefore requires that an environmental risk assessment (ERA) be carried out beforehand. According to Annex II of the Directive "the objective of an environmental risk assessment is, on a case by case basis, to identify and evaluate potential adverse effects of the GMO, either direct and indirect, immediate or delayed, on human health and the environment which the deliberate release or the placing on the market of GMOs may have. The ERA should be conducted with a view to identifying if there is a need for risk management and if so, the most appropriate methods to be used".

When mentioning risks, the COM study otherwise always uses the general term "risk assessment", without actually considering all relevant aspects[176] of such an evaluation. In fact the impact on the environment is hardly considered. Rather, the focus is – if mentioned at all – on the risk of off-target effects and unintended mutations associated with the various new genomic techniques. Furthermore, the statement by EFSA that no new hazards were identified specifically linked to the genomic modification produced via SDN-1, SDN-2 or ODM, as compared with conventional breeding and techniques introducing new genetic material (COM study, 2021, p. 29 and p. 53), was made in the context of this – genetic – perspective. Despite their relatively high targeting accuracy, currently available NGTs are not fully specific, so unintended molecular changes may occur. These unintended changes can cause phenotypic effects and affect the properties of the modified plant (SAM HLG, 2017). Method-related

[176] In general, the term covers the unintended effects of the genetic engineering process, the unintended effects of the intended modification(s) on the metabolism of the genome-edited organism and its overall composition, and the ecological effects on the environment (Kawall, 2021a).

considerations are therefore essential for a comprehensive environmental risk assessment to identify potential negative effects on the environment, the more as even the modification of a single gene can have an impact on the environment, as shown by Barbour, Kliebenstein & Jordi (2022). They experimentally imitated a naturally occurring food web consisting of a plant (*Arabidopsis thaliana*), two aphid species (*Brevicoryne brassicae* and *Lipaphis erysimi*) and a parasitic wasp (*Diaeretiella rapae*). In this study, a single allele of a single plant defence gene was shown to be critical for species coexistence and the level of their extinction risk.

Looking at the 16 scientific opinions of the European Member States evaluated by EFSA and the scientific opinion of EFSA itself on the risk assessment of plants developed through NGTs (van der Vlugt 2021, Paraskevopoulos & Federici 2021), it becomes apparent that they regard a consideration of environmental risks to be necessary.[177]

It is also mentioned that it might be possible to specify and, if applicable, to reduce the data requirements for risk assessment case-by-case (van der Vlugt 2021, p. 18). Paraskevopoulos & Federici (2021, p. 10) emphasise that all elements described in the guidance on the environmental risk assessment of GM plants (EFSA, 2010) can apply to cisgenic/intragenic plants, and the relevance of applying specific elements of the guidance is defined on a case-by-case basis. For plants generated via SDN-1 approaches, EFSA (Paraskevopoulos & Federici 2021, p. 19) concluded that this guidance document is sufficient but only partially applicable to the risk assessment; in the absence of transgenes, intragenes or cisgenes, the amount of experimental data needed for risk assessment will mainly depend on the modified trait introduced. It is clear that the EFSA also considers a trait-related risk assessment to be necessary. And the COM study as well explicitly emphasises that "there is agreement that existing risk assessment guidance is adequate for the assessment of plants obtained through SDN-based and cisgenesis/intragenesis techniques" (COM study, 2021, p. 31).

It therefore is astonishing that the COM study concludes in the following manner: "[A]s concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (p. 59).

Paraskevopoulos & Federici (2021) refer to the guidance document on the environmental risk assessment of GM plants. This document (EFSA, 2010, p. 3) lists the following specific areas of concern which should be addressed by applicants and risk assessors during the environmental risk assessment:

- (1) Persistence and invasiveness of the GM plant, or its compatible relatives, including plant-to-plant gene transfer.
- (2) Plant-to-microorganism gene transfer.
- (3) Interaction of the GM plant with target organisms.
- (4) Interaction of the GM plant with non-target organisms, including criteria for selection of appropriate species and relevant functional groups for risk assessment.

[177] E.g., for ODM: "Food safety aspects have to be evaluated, in particular if the expression of proteins is increased due to the modification. The characteristics of the modified protein have to be considered and are also important for evaluating potential environmental risks" (van der Vlugt 2021, p. 18).

- (5) Impact of the specific cultivation, management and harvesting techniques; including consideration of the production systems and the receiving environment(s).
- (6) Effects on biogeochemical processes.
- (7) Effects on human and animal health.

With exception of point (2), which is relevant in cases where transgenes, intragenes or cisgenes remain in the plant, the listed areas of concern all relate to the modified traits introduced by NGTs.

The COM study points out that the risk assessment may benefit from any knowledge on the history of safe use of the modification(s) and trait(s) introduced and that therefore data requirements may be reduced and only parts of the risk assessment may be implemented on a case-by-case basis (European Commission 2021, p. 31). As shown by EFSA (Paraskevopoulos & Federici 2021, p. 17), this might be possible in some cases (e.g., for SDN-1, if "the new allele obtained by genome editing and the associated trait characterising the final product are already present in a consumed and/or cultivated variety of the same species"). Directive 2001/18/EC already involve the possibility of using existing knowledge about similar organisms and traits.[178] However, if a modified allele introduced by NGTs and its associated trait have not yet been described, appropriate data are needed to perform the risk assessment (Paraskevopoulos & Federici, 2021, p. 17). For example, considering SDN-1 techniques, numerous applications have already demonstrated, that plants with novel genotypes can be produced "resulting in traits unlikely to be achieved by conventional breeding techniques" (Kawall, 2021a, p. 2). According to EFSA, those plants do not have a history of safe use and specific data on the edited gene and its product are required for risk assessment (Paraskevopoulos & Federici, 2021, p. 17). This includes a trait-based ERA to be carried out (Paraskevopoulos & Federici 2021, p. 19). In view of this, a general reduction of the risk assessment requirements related to specific NGTs, as currently being discussed for SDN-1, SDN-2 and cisgenesis, does not seem justified.

Looking at the types of traits introduced in NGT plants,[179] risks to environment and health cannot *a priori* be ruled out.

Herbicide tolerance

Herbicide tolerance is used as a tool for weed control in agricultural production. Cultivating herbicide-tolerant crops allows the application of a broad-spectrum herbicide during crop growth without harming the crop. Direct and indirect effects on the environment have been demonstrated in scientific studies. For example, glyphosate-based herbicides can affect aquatic microorganisms negatively (Schütte, et al. 2017). Also, negative impacts on nitrogen-fixing symbionts may occur and result in changes in the soil microbial communities and changes in the use of nitrogen fertilizer (EFSA, 2012).

[178] "Information from releases of similar organisms and organisms with similar traits and their interaction with similar environments can assist the ERA", Directive 2001/18/EC, Annex II C.1.

[179] E.g. biotic stress tolerance (stressors such as nematodes, fungi, bacteria, viruses and other pests, pathogens or parasites), abiotic stress tolerance (stressors such as drought, heat, salt, rain and UV radiation), herbicide tolerance, modified content of substances such as starch, oil, proteins, vitamins, fibres, toxic substances, allergens, etc., and other traits such as nitrogen use (European Commission 2021, p. 15)

Of great concern are the indirect effects on biodiversity resulting from the changes in weed management, and the occurrence of herbicide resistant weeds, which can be observed (EFSA, 2010; Schütte, 2017; Eckerstorfer et al., 2020):

- Repeated applications of the same herbicide across crop rotations lead to the development of herbicide resistant weeds and changes in weed community diversity.
- Herbicide tolerant NGT-crop volunteers and weed relatives, which acquire the trait by plant-to-plant gene transfer,[180] may require additional measures for control in other crops (e.g., use of specific herbicides) and result in additional environmental impact, in particular in cases of multiple herbicide resistance. Novel genes have the potential to create weed issues by providing novel traits that enable weeds to compete better, produce more seeds, and grow widely (Sohn et al., 2022).
- Changes in weed management associated with the cultivation of herbicide-resistant crops result in fewer weeds and/or weed shifts, which can negatively impact the biodiversity of farmland flora and fauna.

As weeds are reduced by herbicides, the food availability for wild bees and other pollinators also decreases, which can lead to altered abundance and population declines of pollinators, especially when herbicides are used on a large scale. In addition to the associated species conservation aspects (resulting, for example, from the Biodiversity Convention or the Habitats Directive), this is also negatively correlated with the ecosystem services provided by pollinators. Negative impacts may also occur to seed-eating farmland birds, as the herbicide application to herbicide tolerant plants leads to less weeds and therefore to a loss of food resources. Watkinson et al. (2000) modelled the effects of the introduction of a transgenic herbicide-resistant sugar beet on the population dynamics of an annual weed, *Chenopodium album* and its consequences for skylarks (*Alauda arvensis*).

While the indirect effects that occur with herbicide applications are not limited to their use on transgenic or NGT crops, they do promote herbicide use during crop growth, which can lead to sustained reductions in pollen plants or seed production from wild plants and decreases in biodiversity. NGTs also make it easier to introduce multiple herbicide resistances or combine herbicide resistance with other traits (such as abiotic stress tolerance), which could significantly increase the invasiveness of modified plants and thus impact biodiversity. Such impacts can only be assessed through an appropriate environmental risk assessment.

Disease resistance

Plant diseases are caused by numerous organisms, such as nematodes, fungi, bacteria, viruses, pathogens or parasites. Therefore, different approaches are pursued, an overview is given in Eckerstorfer et al. (2020). Environmental risks resulting from virus resistance may be shown as increased persistence, weediness and invasiveness of the GM plant or wild relatives which acquired virus resistance, as well as impacts on non-target organisms; potential environmental impacts of plants with resistance to bacterial pathogens can result in comprise effects on plant-associated bacterial communities, in particular in the rhizosphere (Eckerstorfer et al., 2020). Scientific studies also describe pleiotropic effects associated with knocking-out or silencing plant genes. For instance, loss-of-function mutations of mildew resistance locus o

[180] A plant-to-plant gene transfer from transgenic plants to wild plants was observed e.g. for transgenic oilseed rape (*Brassica napus*) to its wild relative *Brassica rapa* (Sohn et al. 2022).

(Mlo) genes are used to protect plants from infection by powdery mildew fungi. Mlo is coexpressed with genes involved in plant defence, so Mlo seems to exert a function in plant immunity (Kusch & Panstruga, 2017). For gene-edited plants with powdery mildew resistance, pleiotrophic effects such as reduced plant size or premature senescence have been reported, most likely because the silenced plant genes encode multiple functions rather than a single function (Kusch & Panstruga, 2017, Eckerstorfer et al., 2020).

Compositional changes

Plants with altered composition are developed in a broad range of plant species using NGTs. As the resulting organisms are "substantially different" from the parental plants or existing crops, there might be no history of safe use as food and feed products and if key metabolic functions are modified, also unintended compositional changes may occur (Eckerstorfer et al., 2020).

The fact that the targeted changes made by NGTs in the plant genome can lead to unintended effects in the gene-edited plants and in the environment is illustrated by the example of Camelina (*Camelina sativa*, family Brassicaceae, tribe Camelineae). *Camelina sativa* is an allohexaploid plant composed of three sub-genomes and therefore with multiple alleles of homologous genes. SDN-1 technique is being applied to camelina to generate high oleic acid plants. Oleic acid is desaturated to linoleic acid by the fatty acid desaturase (FAD2) in the endoplasmic reticulum (ER). Three FAD2 genes (*Cs*FAD2-1, -2 and -3) were identified in *Camelina sativa* (Kawall 2021). When CRISPR/Cas9 was targeted to conserved regions in the sub-genomes of *Camelina sativa* to alter all CsFAD2 genes, plants with mutations in all three FAD2 homoeologs in the T3 generation showed drastic developmental defects, such as impaired growth, twisted leaves, and delayed bolting (Morineau et al., 2017; Kawall, 2021a). In a field experiment with genome-edited *C. sativa* containing CsFAD2 double and triple knockouts, the observed phenotypic defects were even more evident (Faure & Napier 2018). As these examples show, minor changes introduced via genome editing can lead to major changes in plant physiology and/or phenotype (Kawall 2021a). Kawall (2021a) has shown, that the intended altering of fatty acid biosynthesis can have unintended impacts on stress response and influence the synthesis of secondary metabolites of genome-edited plant, as well as having an impact on the plant-associated food web. For example, in the closely related *Arabidopsis thaliana* a mutation in the fatty acid desaturase (FAD2) genes results in an alteration of the fatty acid profile and causes severe impairments under abiotic stress conditions (like affected root growth, impaired seed germination and a reduced survival rate under high salt conditions) (Zhang et al., 2012, Kawall, 2021a). If novel plant components are produced by NGT-plants (like long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in oilseed rape) this could result in potential hazards for food webs for instance, by changing the growth and fecundity of the organisms that feed on them (Columbo et al., 2018, Bauer-Panskus et al., 2020).

Other aspects mentioned by Kawall (2021a) show a further possible impact on the environment: plants such as *Camelina* could escape from cultivation, persist and propagate in the agricultural environment, hybridise with closely related species,[181] enter new habitats and infiltrate new phytosociological contexts. If gene flow to closely related native or non-native

[181] *Camelina sativa* is sexually compatible with closely related species such as *Camelina microcarpa*, *Camelina rumelica* and *Camelina alyssum*, but can also hybridize with shepherd's purse (*Capsella bursa-pastoris*).

wild species occurs, this may result in a selection advantage, especially if the gene codes for traits that enhance reproduction and survival.

Abiotic stress tolerance

Inducing resistance to abiotic stressors such as drought, heat, salt, rain and UV radiation usually requires changes in the endogenous metabolic pathways of the genetically modified crop. Thus, beside the intended effect also unintended effects might occur, as has already been outlined in the context of compositional changes.

Another aspect is, that resistance to abiotic stressors can enhance the fitness of NGT-plants, and in case of gene flow or hybridisation the fitness of their wild relatives, too. If invading ruderal, semi-natural and natural habitats, this could lead to a displacement of native plants. Since these are often rare and endangered plant species that specialize in certain ecological niches, negative impacts on biodiversity might be caused. If wild plants adapted to the habitat are displaced by the spread of more competitive plants, this can also result in changes in the spectrum of animal species characteristic for these habitat types. Even minor changes in vegetation can result in animal species no longer being able to use the habitat.[182]

The fact that even small changes to the genome can lead to far-reaching changes in environmentally relevant properties is also evident in the production of genetically modified animals: fruit flies (*Drosophila melanogaster*) were modified by CRISPR/Cas (SDN-2) at three locations in the genome by a total of less than 10 base pairs. As a result, the flies gained higher fitness and resistance to a class of plant toxins, the cardiac glycosides. On the one hand, this has increased their potential food supply, and on the other hand, they now can protect themselves against predators by absorbing and storing the toxin (Karageorgi et al., 2019).

As the few examples cited here show, the deliberate release of plants modified by NGTs may be associated with direct, indirect, immediate, and delayed effects on the environment.[183] Environmental risks from the release of gene-edited plants into the environment can therefore not be ruled out per se, which is why EFSA also considers an ERA to be necessary (Paraskevopoulos & Federici, 2021). In order to be able to evaluate such risks properly, a comprehensive risk assessment, as prescribed in the Directive 2001/18/EC, appears to be indispensable.

3.5.3.2 Case-by-case assessments as part of a risk assessment

Case-by-case assessments are mentioned in the Directive on deliberate release of GMO:

> "Member States and where appropriate the Commission shall ensure that potential adverse effects on human health and the environment, which may occur directly or indirectly through gene transfer from GMOs to other organisms, are accurately assessed on a case-by-case basis. This assessment shall be conducted in accordance with Annex II taking into account the environmental impact according to the nature of the organism introduced and the receiving environment" (2001/18/EC, Art. 4).

The annexes to the Directive also indicate the use of a case-by-case principle, as for example in Annex VII C, where the design of the monitoring plan is characterised by the injunction to

[182] As has been documented, for example, for vegetation changes due to eutrophication, resulting in the loss of the lepidopteran species *Euphydryas aurinia* and *Maculinea arion*, Ministerium für Umwelt, Klima und Energiewirtschaft Baden-Württemberg, 2019, p. 23.

[183] As defined in Directive 2001/18/EC, Annex II, paragraph 2.

"be detailed on a case by case basis taking into account the e.r.a." and to "take into account the characteristics of the GMO, the characteristics and scale of its intended use and the range of relevant environmental conditions where the GMO is expected to be released". At the same time, the guidance document from 2010 allows for the possibility that the scope of the information found necessary for a risk assessment can be adapted to the each genetically modified plant under assessment:

> "The [e.r.a.] should be carried out on a case-by-case basis, meaning that the required information may vary depending on the species of GM plants concerned, the introduced genes, their intended use(s) and the potential receiving environment(s), taking into account specific cultivation requirements and the presence of other GM plants in the environment" (EFSA, 2010, p. 12).

EFSA's recommendation for an approach based on the case-by-case principle continues into the steps of a given risk assessment. This holds, for example, in the problem formulation – which is covered under the recommended step 1 of an assessment. Here, EFSA lists various tasks which must be developed specifically on NGT plants and products, i.e. the properties of these plants. The criteria also include a determination of an endpoint for the assessment of possible damage (EFSA, 2010, p. 16).

In sum, the two aspects – sufficient information, but no more – may be presented as follows: case-by-case assessments are applied at the level of individual GMO events in order to make fit-for-purpose environmental impact assessments without collecting superfluous information. However, the case-by-case assessments are firstly the implementation of an abstract principle. They are part of a risk management protocol and are intended to ensure that the diversity of genetically modified (or genome-edited) plants is taken into account. In this context – and in this sense – the case-by-case assessments are primarily intended to ensure that sufficient information is collected in the course of general, non-specific examination and assessment regimes.

By contrast, the COM study takes a fundamentally different position in its concluding sections. The conclusion cannot be derived from the substance of the COM study itself, nor from the relevant legal framework. This is especially true for the sentence "Embedding rigid risk-assessment guidance in legislation limits case-by-case assessment and makes it difficult to adapt risk-assessment requirements to scientific progress" (COM study, conclusions, p. 59). This is because it is ultimately claimed that a strict risk assessment, as provided for under current law, undermines the case-by-case principle, with the consequence that the rules on risk assessment must be relaxed – according to the Commission – in order to be able to give effect to the case-by-case principle. Moreover, this statement is also wrong in itself. It creates a contradiction between strict rules for risk assessment and the case-by-case principle, which does not exist. Rather, the case-by-case principle is already an integral part of risk assessment under current law and not a contradiction to it. This already follows from the basic standard for this in Art. 4 (3) sentence 1 of Directive 2001/18/EC, which reads:

> "Member States and where appropriate the Commission shall ensure that potential adverse effects on human health and the environment, which may occur directly or indirectly through gene transfer from GMOs to other organisms, are accurately assessed on a case-by-case basis".

3.5.3.3 Presence and absence of foreign DNA – well researched?

In the context of the discussed amendment of the EU genetic engineering legislation, the presence or absence of foreign DNA is important in different ways.

The following levels must be distinguished, there are implications for

- (1) the risk assessment,
- (2) the detection an identification,
- (3) the regulation of one and/or the other techniques and organisms produced with them.[184]

(1) As mentioned before the COM study does not clarify the relevant differences and problems, i.e. what risks or possible hazard are introduced along with the foreign DNA. Neither the COM study, nore the SAM HLG or the EFSA ask for the safety of the cisgenesis (and intragenesis technique) as such in detail.

> "However, EFSA noted that transgenesis involves exogenous, non-host (and even non-plant) DNA, possibly leading to the formation of sequence combinations and open reading frames that would normally not occur with conventional breeding or cisgenesis. Similarly, intragenesis could give rise to new combinations in open reading frames, due to reconfiguration of the host sequences" (COM study, p. 30).

The COM study does not explore these arguments further. The safety assumed for cisgenesis (and intragenesis) plants seems to be primarily borrowed from conventional breeding. This can be seen, for example, in the fact that the COM study places cisgenesis close to the cross-breeding in nature and conventional breeding (see Chapter 3.5.1 above).

In terms of the presence or absence of foreign DNA, Paraskevopoulos & Federici (2021) formulate an explicit proposal for the regulatory handling:

> "Overall, two possible scenarios were envisaged depending on whether or not any nucleic acid sequence intentionally deployed during the genome editing process (e.g. the full SDN module or part of it) is present in the plant genome; if present, the product would be risk assessed as a transgenic plant with regard to the genome-integrated exogenous DNA and as a gene-edited plant with respect to the target sequence(s) modified via SDN-1; if not present, the assessment will only focus on the modification(s) resulting from the SDN activity" (p. 17).

(2) The ENGL report highlighted implementation challenges for certain plant products that contain no foreign genetic material. Although existing detection methods may be able to detect even small specific DNA alterations, this does not necessarily confirm the presence of a genome-edited plant product. The same DNA alteration could have been obtained by conventional breeding or random mutagenesis techniques, which are exempted from the GMO legislation. With the current state of knowledge, enforcement laboratories are unlikely to be able to detect the presence of unauthorised genome-edited plant products in food or feed entering the EU market without prior information on the altered DNA sequences.

3.5.3.4 Naturalness and safety – well researched?

As mentioned before, the COM study discusses the naturalness of NGT plants and projects in different aspects. The COM study implicitly – but not explicitly – argues that greater proximity to natural conditions results in greater safety of NGT plants and products, but leaves the reasoning for this argumentation open. Arguing along this line is very common in the current discussion on NGTs, including the fact that the thesis as such, i.e. safety follows from naturalness, is not further substantiated. E.g. Euroseeds, the voice of the European seed industry,

[184] For more on (3) see Chapter3.2.3.4 above.

states: "[P]lant varieties developed through the latest breeding methods should not be subject to different or additional regulations if they could also be obtained through earlier breeding methods or result from spontaneous processes in nature" (Euroseeds, 2019, p.1). But, by repeatedly stating the thesis, it does not become more convincing, if the thesis is not simultaneously strengthened in terms of content – which is not the case. Apart from that, the present expert opinion shows that the changes produced with NGTs cannot be equated with the changes induced by random mutagenesis or traditional breeding by crossing – nor can changes in genome sequences in nature simply be presented as the same or as similar.[185]

3.5.4 Stakeholder and Member States views on risk assessment

In section 4.4.2 of the COM study ("Member States' and stakeholders' views regarding safety"), various aspects regarding the safety of NGT are addressed (see COM study, 2021, p. 31ff.). It is not always possible to reconstruct to which sections of the questionnaire the evaluation refers. There are two questions on safety, but they are only included in the questionnaire for the stakeholders, and not in the one for Member States (see Table 18). Similarly, it might be that the statements made by Member States and the material provided by them – as part of the collection of Member States' expert opinions (see Paraskevopoulus & Federici, 2021) – had already been incorporated in the previous sections in the COM study.

Five subsections organise the overall section thematically into the following components: (1) general views on the safety ("General views on the safety of NGTs and specific considerations for plant applications") and specific considerations for (2) animal, (3) microorganism, and (4) medical applications. The last subsection (5) refers to the need for risk assessment ("Stakeholders' and Member States' view regarding the need for risk assessment"), although it is unclear where in the questionnaire this topic was introduced.

Table 18: Questions in the targeted consultations on safety. Presumably evaluated in section 4.4.2 "Member States' and stakeholders' views regarding safety" in the COM study, 2021.

Number of question/Questionnaire*	Wording of the question
Q24/SH	What is your view on the safety of NGTs/NGT-products? Please substantiate your reply.
Q25/SH	Do you have specific safety considerations on NGTs/NGT-products?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*	

The study states that "most" stakeholders consider safety to be indispensable for bringing products developed using NGT to the market. However, the study contends that different views exist, and that therefore there is no consensus on whether NGTs are safe or whether a risk assessment is necessary. The study states that "many" stakeholders would focus primarily on the mutagenesis techniques, only "a few" on other types of NGT and "some" on gene drive modified organisms.

In the first subsection, titled **"General views on the safety of NGTs and specific considerations for plant applications"** (see COM study, 2021, p. 31), the study first presents the views of "some" Member States. These see the possibility of off-target and unintended effects, with

[185] See e.g. Chapter 3.3.3.3 "Off-target changes – unintended effects".

potentially negative effects on human, animal and plant health, and deleterious effects on the environment. "Some" Member States reportedly referred to the possibility of long-term risks. As only stakeholders, but not Member States were asked about safety, it is unclear to which sources in the questionnaire the COM study refers here.

The COM study then analyses the stakeholders' responses and distinguishes between two fundamentally opposing positions. "Some" stakeholders from the group of "NGOs/organic/GM-free food business operators" would express concerns about the safety of NGT products. "Other" stakeholders from the group of "food business operators, NGT developers and academics" would emphasise the safety of NGT.[186]

The COM study then presents some concerns and risks expressed in the stakeholder consultation. These include unintended effects such as the presence of new toxins or allergens; on-target and off-target effects; the lack of a history of safe use, and in general an insufficient scientific understanding of NGT. Also raised are concerns about negative environmental consequences, such as gene flow and interaction with wild species, and impacts on the food chain. "Some" stakeholders point to the fact that NGTs might not be retrievable from the environment, possibly due to the release of gene-drive organisms.

This list of critical aspects is followed by a presentation of the arguments from the stakeholder survey which speak for the safety of NGT. Stakeholders claimed that NGT was more precise than conventional breeding methods, which do not have to undergo a mandatory risk assessment. In addition, NGT would allow a better understanding of genetic modification.

Other subsections examine the use of NGTs in animals, microorganisms and in medical applications. The subsection with titled **"Stakeholders' and Member States' view regarding the need for risk assessment"** (see COM study, 2021, p. 33f.) is especially relevant for the purposes of this present expert opinion. It is not known to which questions in the questionnaire the arguments presented in these passages refer. In principle, however, there are various questions where corresponding answers may be located, e.g. question 20 or 21 in both questionnaires – and possibly the open question found at the end of each questionnaire.

Regarding the opinion of "several" Member States and stakeholders that a risk assessment is necessary and needs to be adapted to the NGT, there were – according to the COM study – different ideas about the format: "Most" stakeholders from the field of "NGOs organic/GM free food business operators" wanted a risk assessment designed according to current GMO legislation.

"Some" stakeholders, including NGOs, felt that the requirements for a risk assessment should be decided on a case-by-case basis. According to "most" stakeholders, risk assessment should be "science-based" and proportional to risk. "Some" stakeholders are of the opinion that risk assessment should not be "process-based, but product-based". "Others" thought that the case-by-case approach should be more strictly enforced. All these approaches to risk assessment are listed in the COM study, but are not elaborated upon. Still, according to the COM study, a "few" stakeholders from "agricultural and plant breeding sector" argued that no additional risk assessment should be carried out, and argued that the products might also be developed using conventional methods. Finally, "some" stakeholders felt that a risk

[186] See for an interpretation section 3.5.3 "How well researched and substantiated are the COM study's statements about the risk assessment of NGT plants and products?" in this expert opinion.

assessment of gene drives was only possible to a limited extent. Since there is only limited knowledge about the impacts on the environment, the only way to expand this knowledge, according to these stakeholders, would be to release the organisms.

The viewpoint of this present expert opinion is, that the arguments the COM study takes from its targeted consultations are reproduced only very briefly. They are neither explained nor discussed. However, the COM study attempts to organise the arguments from the targeted consultations in terms of content and to identify opposing positions.

3.5.5 What issues and challenges were not investigated?

3.5.5.1 Legal requirements for risk assessment

Risk assessment not only is a scientific and technical issue, but also a legal requirement, stemming from the European genetic engineering law. So if one – like the Commission in its study – intends to deregulate certain NGTs, legal obligations and requirements need to be followed and considered. As the following chapters show, the Commission did not address these requirements.

Overview of the rules of European Genetic engineering law

As the basic legal act of European genetic engineering law, the Deliberate Release Directive 2001/18/EC contains requirements for risk assessment. Cornerstone for this is Art. 4 para. 3 sentence 1 of Directive 2001/18/EC, according to which "potential adverse effects on human health and the environment, which may occur directly or indirectly through gene transfer[187] from GMOs to other organisms, are accurately assessed on a case-by-case basis".

This risk assessment obligation explicitly applies not only to the Member States but also to the European Commission. According to Art. 4 para. 3 sentence 2 of Directive 2001/18/EC, this assessment[188] must be carried out "taking into account the environmental impact according to the nature of the organism introduced and the receiving environment". Specifically for the risk assessment of food and feed Art. 5 and 6 as well as Annex II of Regulation 503/2013/EU[189] contain specific requirements.

[187] As genetic modifications by the certain NGTs the Commission wants to deregulate in many cases do not result in classical transgene transfers, one might argue that those requirements cannot apply to NGT-derived organisms with no exogenous genes. But this view jumps too short. The Deliberate Release Directive dates back to 2001, when only classical transgenic genetic engineering was known. Techniques such as genome editing, which in many cases does not involve the insertion of foreign DNA, had not yet been developed. It was therefore clear that the guideline only referred to transgenic genetic engineering at that time. However, the basic statement that a comprehensive risk assessment is required before genetically modified plants are released into the environment also applies, of course, to plants without exogenous genes, since these can, in certain cases at any rate, pose just as great a risk as classical transgenic plants; see Chapter 3.5.5.1. (Principles of risk assessment).

[188] In the Directive, this is referred to in somewhat abbreviated form as "environmental impact assessment", abbreviated because it is explicitly concerned not only with risks to the environment but also with risks to human health.

[189] Commission Implementation Regulation 2013/503/EU of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006, OJ L 157/1 of 8.6.2013.

Current risk assessment rules as minimum standard

The requirements in Annex II to Directive 2001/18/EC, last amended by Commission Directive 2018/350/EC, and in Regulation 503/2013/EU represent a minimum standard for the risk assessment of GMOs required by the precautionary principle in Article 191 (2) sentence 2 TFEU. Thus, they are constitutionally binding as primary law and therefore cannot be undercut by the ordinary EU legislator. Admittedly, according to the principle of separation of powers, it is always possible for the legislator to amend simple law. In this respect, it has a certain leeway, which means that the legislator has the power to change European genetic engineering law. However, it must observe the limits of the precautionary principle as overriding law.

Deregulation of certain NGTs by law

In concrete terms, this means that the EU legislator is free to decide in which way it regulates certain NGTs. In particular, it is also free to deregulate entire groups of NGTs such as cisgenesis, SDN1 and SDN2, either in the form of a complete or partial exemption from the rules of European genetic engineering law or in particular with respect to risk assessment. However, since this in substance amounts to a kind of blanket approval by the legislator itself, the legislator can only undertake such deregulations if he observes the European requirements on risk assessment for GMOs. He can therefore only make such blanket relaxations if he has previously carried out a risk assessment in accordance with the requirements of Annex II of Directive 2001/18/EC and – as far as food and feed are concerned – in accordance with the requirements of Regulation 503/2013/EU, which shows that the deregulation does not give rise to any risks for humans or the environment.

Compatibility of deregulation with current risk assessment requirements

Principles of risk assessment: As mentioned above Art. 4 para. 3 sentence 2 of Directive 2001/18/EC foresses, that the risk assessment is carried out taking into account the effects on the environment depending on the type of organism introduced and the environment receiving the organism. In any case, this has not yet been done with regard to the CRISPR/Cas gene scissors or any other of the certain genome editing techniques. With this technology, interventions in the genome are possible that cannot occur in nature or conventional breeding.[190]

Natural populations mostly have a whole range of different gene variants which can help to stabilize the ecosystems. However, CRISPR/Cas applications usually change all the variants (alleles) of a gene within an organism at the same time and in the same way, for example by blocking the gene function. That can have far-reaching consequences for food-webs and ecosystems.

This recently has been demonstrated by a study published in the journal Science. The authors showed that even a reduction in the diversity of a single gene caused species interacting with the plants to become extinct. They experimentally tested the effect of three plant defense genes on the persistence of an insect food web and found out that the reduction in the genetic diversity was fostering destabilization of the food. In the study for example a disturbation of the population of aphids and wasps was observed (Barbour et al. 2022).

Not all such effects must pose a problem. But they do if so-called keystone gene are changed. Keystone genes are genes that influence the persistence of interacting species in an ecological

[190] In this respect, the premise of similar risks as conventional breeding is not correct.

community. This can already be the case if only one gene is altered and it can exacerbate heavily if lots of such altered plants exist. However, it remains a matter of uncertainty which genes under which conditions can be considered as keystone genes. It is exactly this situation of uncertainty, when the precautionary principle enshrined in Art. 4 para 1 Dir. 2001/18/EC requires a risk assessment before releasing such plants into the environment. In other words: As long as it is not clear, which genes are keystone genes, the use of the gene scissor CRISPR/Cas cannot be deregulated.

Examination of indirect or delayed adverse effects: According to Annex II section A objective of Directive 2001/18/EC, not only the direct and immediate, but also the indirect and delayed adverse effects must be examined. Annex II defines indirect effects as

> "effects on human health or the environment occurring through a causal chain of events, through mechanisms such as interactions with other organisms, transfer of genetic material, or changes in use or management".

Delayed effects are defined in Annex II as

> "effects on human health or the environment which may not be observed during the period of the release of the GMO, but become apparent as a direct or indirect effect either at a later stage or after termination of the release".

Such consideration of indirect and delayed effects has not taken place to a sufficient extent for NGTs. With regard to effects that may arise from the CRISPR/Cas gene scissor, this has already been addressed above ("Principles of risk assessment"). But even beyond this, no sufficient investigations have taken place. This is quite simply due to the fact that risk assessments are usually only obligatory for regulations or release applications. Even independently of mandatory measures, the developers of NGTs have not provided risk relevant data voluntarily. However, due to the examination methods commonly used today, it can be assumed that they do have a certain amount of risk relevant data material. Another reason for the lack of – especially publicly available – risk relevant data is that only very few NGT plants and products are ready for commercialisation or are already commercialised. Also, and according to retrievable data, NGTs have not been studied closely enough by genomics, proteomics or metabolomics technologies.

Examination of cumulative long-term effects: Annex II to Directive 2001/18/EC further requires an assessment of cumulative long-term effects prior to authorisation.[191] By this, Annex II understands the "accumulated effects [...] on human health and the environment, including inter alia flora and fauna, soil fertility, soil degradation of organic material, the feed/food chain, biological diversity, animal health".[192]

Such a study was also not possible for the same reasons, because there are only two plants on the market for cultivation at all so far.[193]

Case-by-case approach: The case-by-case principle is one of the most important principles of risk assessment in European genetic engineering law and has therefore found expression in numerous places.[194] For example, recital 18 of Directive 2001/18/EC states: "It is necessary to establish harmonised procedures and criteria for the case-by-case evaluation of the potential

[191] Introductory remarks just before section A as well as section C.1,1 and recital 19.
[192] Introductory remarks just before section A.
[193] See above 3.5.5.1 ("Examination of indirect or delayed adverse effects" at the end).
[194] Cf. 3.5.1.3 and 3.5.3.2.

risks arising from the deliberate release of GMOs into the environment". Recital 19 reads: "A case-by-case environmental risk assessment should always be carried out prior to a release. It should also take due account of potential cumulative long-term effects associated with the interaction with other GMOs and the environment".

The basic standard of Art. 4 para. 3 sentence 1 of Directive 2001/18/EC requires a case-by-case assessment and Annex II also emphasises this principle.[195]

In concrete terms, this means that each genetic event (a particular genetic modification in a particular plant species) is examined individually. A blanket classification of GMOs – as the Commission intends to do with the techniques cisgenesis, SDN1 and SDN2 – is not only incompatible with this, but also turns this principle on its head.[196]

Furthermore, the case-by-case principle requires experience with every genetic event in the field with commercial cultivation and not only in strictly supervised releases or even only in the greenhouse. This is because the conditions under interactions with the ecosystem in free cultivation are different and often involve effects that would never have been detected in the greenhouse or in experimental releases. This is precisely why the recital 24 of the Directive prescribes the step-by-step approach according to which the release into the environment should only take place after the gradual gathering of experience, first in the laboratory, then in the greenhouse and then under controlled release trials. Specifically with regard to the need for experience with commercial cultivation, the decision of the ECJ on the second referral from France (Mutagenesis II) will then also have to be taken into account (ECJ, 2021).

Finally, the approach based on alleged similar risks in the case of mutations in nature and in conventional breeding also violates the case-by-case principle, since it removes genetic engineering events from consideration across the board and does not look at them on a case-by-case basis.

Checking whether risk management is required: Annex II of Directive 2001/18/EC also requires an assessment of the need for risk management prior to authorisation.[197] Specifically, risk management is required if risks are identified which, due to their characterisation, require measures for their management.[198] The aim of this risk management is also to quantify the resulting reduction of the overall risk.[199]

There are no considerations in the COM study as to whether risk management is required for certain NGTs, nor is there any idea of what such risk management might look like and how it might reduce overall risk.

Comparison with adverse effects of unmodified organisms: Annex II further requires a comparison of the effects of NGTs with the effects of unmodified organisms prior to approval,[200] with this comparison to be made in a transparent manner based on scientific and technical data.

[195] Annex II, section A as well as section C.3, 1 letter b, indent 3 Directive 2001/18/EC.
[196] The wording "Embedding rigid risk-assessment guidance in legislation limits case-by-case assessment" on page 59 of the COM study therefore turns the legal situation upside down.
[197] Annex II, A. Dir. 2001/18/EC.
[198] Annex II, C.3, 5 Dir. 2001/18/EC.
[199] Annex II, C.3, 5 Dir. 2001/18/EC.
[200] Annex II, B, first indent Dir. 2001/18/EC.

None of these requirements are met. The COM study claims as a reason for the intended deregulation of certain NGTs that they have the same risk profile as plants bred by natural crossing or conventionally (COM study, p. 59). However, given the current state of knowledge, this is not much more than a political claim. This is evident from the use of the term "risk profile" alone. The concept of risk profiles is completely foreign to the current regime for risk assessment in Annex II of Directive 2001/18/EC and is also not defined in more detail in the COM study. Such a diffuse term cannot serve as a scientific basis for a deregulation.

Apart from this vagueness, the equation of certain organisms derived by NGTs with organisms resulting from natural crossing or conventional breeding is not based on any scientific criteria. Only the modified gene is considered and thus only a very small part of the entire organism. Not considered are the interactions with the rest of the organism, let alone the interactions of the entire modified organism in food webs and ecosystems.[201]

Additional Requirements for Food and Feed

Regulation 2013/503/EC contains numerous additional requirements for risk assessment before GMOs are allowed on the market. These have also not been met. In detail:

Comprehensive assessment of the modified plant: According to Recital 10 to Regulation 2013/503/EC

> "the safety assessment of the genetically modified food or feed should include studies related to new components resulting from the genetic modification, the molecular characterisation of the genetically modified plant, the comparative analysis of the composition and the phenotype of the genetically modified plant compared to its conventional counterpart"

depending on the characteristics of the genetically modified plant and on the outcome of that first set of studies, the EFSA guidance indicates that it may be necessary to perform additional studies. According to Annex I, Part II, No. 1.2 to the Regulation 2013/503/EC, the genetic stability and the phenotypic stability has to be examined.[202]

Admittedly, this regulation still assumes classical transgenic genetic engineering because it speaks of recipient plants. However, this is simply due to the fact that NGTs had not yet reached the public consciousness at the time of the work on this regulation. The regulation today must therefore be interpreted in the sense of the precautionary principle according to altered Article 191 (2) sentence 2 TFEU in such a way that these risk assessment principles – mutatis mutandis – do not only apply to transgenic plants. This must apply if only because – as described above[203] – even the slightest point mutations by NGT can have harmful effects.

Lack of toxicological studies: Furthermore, Annex I, Part II No. 1.4 to the Regulation prescribes toxicological studies *prior* to the authorisation of genetically modified food and feed. Thus, an investigation of possibly newly or altered proteins must be carried out.[204] In addition, it is expressly stipulated that an investigation of the entire genetically modified food or feed must be carried out[205] and that it is not sufficient – as the COM study implies – to consider only the

[201] See above 3.5.5.1 (Principles of risk assessment).
[202] Annex II, II, 1.2.2.4 lit. a to Reg. 2013/503/EU.
[203] See 3.5.5.1 (Comprehensive assessment of the modified plant).
[204] Annex II, No. 1.4.1 to Reg. 2013/503/EU.
[205] Annex II,II, 1.4 lit.d) to Reg. 2013/503/EU.

individual modified gene. Furthermore, 90-day feeding studies with rodents are prescribed,[206] and explicitly also for only one single event.[207] Here, too, the regulation only refers to transgenic genetic engineering. However, the fact that these requirements must also apply to non-transgenic mutations follows for the same reasons as already explained above[208] in the context of the obligation to comprehensively test plants.

Post-marketing monitoring as a minimum standard

Preliminary remark: It was comprehensively shown above that deregulation of certain NGTs is not compatible with the risk assessment principles of European genetic engineering law given the current state of knowledge. Such plants must therefore not be placed on the market without approval and risk assessment, as required under current genetic engineering law. A lack of risk assessment cannot be replaced by market monitoring either, because that would then be mere aftercare and therefore also not compatible with the precautionary principle under Article 191 para 2 sentence 2 TFEU.

However, since scenarios must be expected in which there is a political majority in favour of deregulation of NGTs, the following section examines whether European genetic engineering law then requires at least post-market monitoring[209] as a minimum standard.

Requirements of European genetic engineering law for post-market monitoring: Article 13 para 2 lit. e of Directive 2001/18/EC contains an obligation to draw up a monitoring plan for all GMOs that are to be placed on the market. Annex VII to Directive 2001/18/EC specifies the requirements to be met by this monitoring plan. According to this, the aim of the monitoring plan is, among other things, to determine the occurrence of adverse effects of the GMO or its use on human health or the environment.[210] If changes in the environment are observed, these must be evaluated.[211] This monitoring plan shall be tailored to each individual case[212] and shall take into account the relevant conditions of the environment into which the GMO is to be released[213] and shall detect any unexpected adverse effects.[214] This shall include systematic monitoring of the release into the receiving environment.[215]

Specifically for food and feed, Regulation 1829/2003/EC[216] contains provisions for post-market monitoring. These general provisions are supplemented by Art. 7 para. 1 lit. c of Regulation 2013/503/EU.[217] According to this, there is an obligation for post-market monitoring if the relevance and intensity of the effects and unintended effects can only be further defined by in-market monitoring.

[206] Annex II,II, 1.4.4.1 to Reg. 2013/503/EU.
[207] Recital 11 to Reg. 2013/503/EU.
[208] See 3.5.5.1 (Comprehensive assessment of the modified plant).
[209] Which according to current law even has to be conducted after a risk assessment and authorisation procedure has been gone through.
[210] Annex VII, A, indent 2 to Dir. 2001/18/EC
[211] Annex VII, B, UA 2 sentence 2 to Dir. 2001/18/EC
[212] Annex VII, C, 1. to Dir. 2001/18/EC.
[213] Annex VII, C, 2. to Dir. 2001/18/EC.
[214] Annex VII, C, 3. to Dir. 2001/18/EC.
[215] Annex VII, C, 4. to Dir. 2001/18/EC.
[216] Art. 5 para 3 lit. k and Art. 17 para 3 lit. k.
[217] Art. 7 para. 1 lit. c.

Transfer of these rules to deregulated NGTs: It could now be argued that the primary purpose of the above described monitoring is to determine whether the assumptions made in the risk assessment are correct[218] and that those monitoring requirements therefore cannot apply to deregulated plants where there has been no risk assessment at all.

However, such an argument fails for several reasons. Firstly, the argument is only valid in the case of complete deregulation, i.e. when there is no obligation for authorisation and risk assessment at all. In the case of a merely relaxed risk assessment, the argument does not apply from the outset. Furthermore, monitoring is not limited to checking the risk assessment. On the contrary, monitoring should also be carried out independently of the risk assessment in order to determine the occurrence of harmful effects.[219]

The most important argument, however, is the precautionary principle according to Article 191 para 2 sentence 2 TFEU. As already explained above,[220] a waiver of precaution by means of a risk assessment prior to market authorisation cannot be compensated by monitoring after market authorisation. If, however, against this requirement no risk assessment has been conducted before marketing, the precautionary principle as a minimum standard requires at least monitoring of the plants placed on the market without risk assessment.

3.5.5.2 The role of unintended effects in the risk assessment

As described above, the COM study did not systematically investigate the unintended effects of NGT use, in some cases ignoring them completely.[221] Off-target changes, which only account for a part of unintended effects, are apparently considered irrelevant by the COM study. It seems as if it follows EFSA's assessment at this point. However, this can only be assumed in the context of the present expert opinion due to methodological deficiencies of the COM study. The deficiencies concern the lack of weighing of arguments. In this specific case, for example, the COM study leaves open why it follows EFSA's position and not that of the Member States and stakeholders. In sum, it follows from this situation that unintended effects become unnoticed effects.

3.5.5.3 How much information is needed for a proper risk assessment?

How much and what information is needed for a good risk assessment of NGTs? The COM study only marginally addresses this question. As the present expert opinion shows, the contributions of the COM study are not satisfactory. On the contrary, there is a whitewash in the presentation (see Chapter "3.5.1.1.4 How much information is needed for a risk assessment?" above). The amount of information that needs to be known in order to evaluate an NGT product or plant concerns various areas: These include in particular the case-by-case principle in general, as well as, for example, detailed information about an organism and its molecular make-up in particular.

The Bigger Conversation (2021) highlighted as particular effect in a comprehensive consultation process in the UK that

[218] Annex VII, A, indent 1 to Dir. 2001/18/EC.
[219] Annex VII, A, indent 2 to Dir. 2001/18/EC.
[220] See 3.5.9.1.
[221] As outlined in Chapter 3.3.2.2 "How the COM study considers unintended effects?" of the present expert opinion.

> "perhaps surprising to some, the British Veterinary Association 'strongly supports retained EU law which requires that all gene-edited organisms are classified as genetically modified organisms.'
>
> It goes on to say that 'As gene-editing is still a relatively new process we consider that the risks are currently difficult to quantify, which is why it is essential that regulation and transparent reporting of data continues such that an evidence base can be built. If gene-editing is deregulated then the opportunity to gather data, continually improve on techniques, and achieve better outcomes, will be lost.'" (p. 21)

Even though the UK has now left the EU, the important point remains that only the regular and continuous flow of information makes evidence-based decisions possible.

3.5.5.4 Unintended effects of established genomic techniques

The established genome techniques (ETGs) are not the subject of the COM study. However, they are mentioned repeatedly, as the NGTs are usually used together with established genome techniques. The ETGs are used in particular as 'delivery systems'. Testbiotech has compiled an overview of the use of ETGs. Two techniques are used: the gene gun and the *Agrobacterium* method.

> "The applications of 'old' methods of genetic engineering (such as biolistic methods or transformation using *Agrobacterium tumefaciens*) used in most cases to introduce the CRISPR/Cas component into the plant cells can cause a broad range of unintended effects" (Testbiotech, contribution to the targeted consultation, p. 13).

Apparently, the COM study sees no need to examine the risks associated with ETGs. Various stakeholders disagree. This is not only evident from the contributions to the targeted consultation (e.g. VLOG completed questionnaire, Testbiotech completed questionnaire), but also from scientific literature (Hilbeck et al., 2015).

> "All these technical details which determine the precision as well as the efficiency of an intervention, go along with specific risks which exceed those resulting from conventional breeding" (Testbiotech, contribution to the targeted consultation, p. 13).

However, Broothaerts et al. (2021) also suggest that unwanted off-targets can be observed in connection with ETGs:

> "Although the occurrence of unwanted off-target alterations following the use of NGTs is often not negligible and needs careful evaluation during the design of the experiments, the frequency of such modifications is generally much lower compared *to the range of potential unintended effects resulting from the use of EGTs*, [...] (Anderson et al., 2016; SAM, 2017)" (Broothaerts et al., 2021, p. 22; emphasis by author).

The COM study remains true to itself in not taking aspects of the ETGs into account: These points of criticism do not find their way into its corresponding Chapter "4.4. Safety of new genomic techniques".

3.5.6 Interim summary of risk assessment

Chapter 3.5 of the present expert opinion analyses the COM study with regard to the risk assessment of NGT plants and products. The COM study largely refers to a document prepared by EFSA (Paraskevopoulus & Federici, 2021) and to the responses of EU Member States and stakeholders to the targeted consultation. The present expert opinion identifies the following as the central findings of the COM study on risk assessment:

> "Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59).

Certain aspects of this finding have already been criticised by the present expert opinion in the section on technology. These include, for example, the attempts of the COM study to present the molecular changes in the genome – caused by NGTs or arising by other means – as similar (see Chapter 3.3 above). The present expert opinion decries the above results because the COM study uses terms here – risk profile and risk level – in which it does not provide a clear picture of a system of meaning. Another point of criticism is that the COM study does not consider environmental risks. As shown in the present expert opinion, current research illustrates the relationships between intended and unintended changes or effects in the NGT plants and products with – for example – ecological effects. The release of genetically modified plants into the environment can be associated with negative impacts on other organisms, biodiversity, and ecosystem services.

It is noteworthy that the only conclusion of the COM study regarding the case-by-case approach is that "[e]mbedding rigid risk-assessment guidance in legislation limits case-by-case assessment and makes it difficult to adapt risk-assessment requirements to scientific progress" (p. 59). This is especially important, since the case-by-case approach is currently used in the EU for the risk assessment of GMOs and has been demanded by Member States and stakeholders for the assessment of the risks of genome-edited plants and products (see chapter 3.5.4 above). Thus, it remains unclear for the present expert opinion how the COM study comes to exactly this conclusion. From the substance of the COM study itself and from the relevant legal framework the conclusion cannot be derived in this way.

Paraskevopoulus & Federici (2021) summarise various reports and scientific opinions from the Member States and EFSA's own work. However, differences that may arise between the positions are not adequately taken into account – an approach that runs like a red thread through the entire COM study.

The COM study does not raise the question of how much and what information is needed for a risk assessment. At the same time, it states that ODM – among other techniques – does not lead to new risks in connection with off-target effects. It also states that less information is available on this technology. An examination by the present expert opinion revealed that just one single scientific paper formed the basis of the assessment of ODM regarding the presence of off-target alterations undertaken by EFSA and the COM study – far too little to be able to comment in a qualified manner.

The present expert opinion also analysed whether the deregulation of certain NGTs is compatible with the exigencies of the European engineering law regarding risk assessment. In doing this the overall approach was a different assessment regarding complete or partial deregulation. As it seems to be the intention of the Commission that certain NGTs should be deregulated by law the starting point was, that this can only be legal if the deregulation itself lives up with the requirements of the European genetic engineering law regarding risk assessment. The result of the analysis was that this for a number of reasons is not the case. For instance a broad release into the environment only is legal after an examination of the indirect or delayed adverse effects and the cumulative long-term effects. Both is not possible at this stage as there is nearly no experience with cultivation regarding those NGTs. Further a central

principle of risk assessment, the case-by-case principle, is infringed by deregulating whole groups of NGTs without looking at each single event. Regarding food and feed toxicological studies are required which also have not been conducted so far.

If all those requirements of the European genetic engineering law regarding risk assessment are disregarded and the marketing of such products without risk assessment is allowed, the precautionary principle at least demands a post-market monitoring of those products as a compensation. But even this is not intended.

3.6 Ethical and socio-economic implications of new genomic techniques

The COM study also addresses the socio-economic consequences of an application of NGT. This topic results from the extended question of the COM study.[222] Four sections of the COM study are devoted to socio-economic impacts: the opportunities and benefits of NGT (section 4.6); the concerns and challenges of NGT (section 4.7); small and medium-sized enterprises (SMEs) and intellectual property rights (4.8); and labelling (4.9). Furthermore, information on forums for public dialogue and surveys on NGT are presented in section 4.10, and ethical considerations are discussed in section 4.11.

The topics addressed in the sections and highlighted by the section structure of the COM study are shown in Table 19 below.

Table 19: Overview of the topics and the sections of the COM study with socio-economic and ethical aspects.

Topic	Section in the COM study
Opportunities and benefits of NGT	4.6 Member States' and stakeholders' views on potential NGT-related opportunities and benefits
Concerns and challenges of NGT	4.7 Member States' and stakeholders' views on potential NGT-related challenges and concerns
Small and medium-sized enterprises	4.8 Views relating to Small-Medium-Enterprises and intellectual property
Patenting	4.8 Views relating to Small-Medium-Enterprises and intellectual property
Labelling	4.9 Stakeholders' views on the labelling of NGT products
Public dialogue forums and surveys on NGT	4.10 Public dialogues and surveys on NGT
Ethics	4.11 Ethical aspects of NGTs

The COM study's analysis of the ethical and socio-economic implications of NGT draws primarily on the results of the two surveys conducted as part of the targeted consultation. The expert opinion from the Expert Group on Ethics (EGE), the content of which is summarised in section 4.11.4 of the COM study, is used as an additional source. The following section 3.6.1 "New or known results and challenges" of this expert opinion discusses how these issues are addressed in the COM study. This section therefore provides an analysis of the presentation of the targeted consultations in the COM study. The process was the same as described in

[222] See section 3.1.2.2.1 "Focus of the COM study" of this expert opinion, which discusses the research question of the COM study.

section 2 "Methodical procedure of the present expert opinion" and as used in the previous sections here to present the views of Member States and stakeholders.

The subsequent section 3.6.2 "Methodological critique of the chapters on socio-economic consequences and ethics of NGTs" contains critical comments on the methodological approach of the COM study that go beyond the aspects mentioned in section 3.1 of this present expert opinion, "General evaluation of the COM study's methodological approach". Section 3.6.3 "How well researched and substantiated are the COM study's statements about the ethical and socio-economic implications of NGTs?" offers starting points for a more in-depth analysis of socio-economic consequences and their ethical dimensions. The comments from the targeted consultations clearly indicate which problems for action confront stakeholders and Member States. These have been elaborated, and further questions have been posed regarding the manner in which they might be addressed substantively. Due to the complexity of the issues raised, the present comments can only be cursory. They should serve primarily to illustrate what the COM study did not achieve, namely a substantive discussion.

3.6.1 New or known outcomes and challenges

This section presents the arguments of the COM study regarding socio-economic consequences and the ethical aspects of NGT. The presentation focuses on the agricultural sector. Arguments concerning medical applications are considered only marginally.

The COM study focuses on SMEs, patenting, and labelling through its questionnaire and the thematic structure of its sections. No justification is given as to why these issues are highlighted. The sections "Opportunities and benefits" and "Concerns and challenges" address varied topics. Some of them relate to consequences to the environment and to animal welfare and therefore do not qualify primarily as socio-economic consequences. The COM study indicates in its summary presentation of its arguments how many respondents voiced each respective argument or represented each respective point of view as found in the two surveys. Additionally, the presentation of the arguments and views of the stakeholders indicate from which stakeholder group they originate.

3.6.1.1 Opportunities and benefits of NGTs

In **section 4.6, "Member States' and stakeholders' views on potential NGT-related opportunities and benefits"** of the COM study, the question of what opportunities and benefits are associated with NGT is answered on the basis of the targeted consultations (see COM study, 2021, p. 37ff.). The responses of the Member States and stakeholders are presented in two separate subsections. A third subsection addresses the arguments of the stakeholders who deny any benefit. This topic was not explicitly posed in the targeted consultations, and presumably emerged out of the stakeholders' responses themselves.

Table 20 below shows how the sections in the study correspond to those in the questionnaire. It should be noted that although the questions in both questionnaires address the same topics, they do differ slightly. Question 16 asks about the opportunities and benefits of NGT for Member States in rather general terms, while stakeholders are asked directly about their sector or client base. Question 17, on the other hand, is general for both groups of respondents, with the exception of the phrase "in the short, medium and long term", which is missing for stakeholders. As mentioned in section 3.1 of this expert opinion, our general methodological critique, the COM study does not provide a rationale for differences in research questions.

Table 20: Questions in the targeted consultations on potential NGT-related opportunities and benefits. Presumably evaluated in section 4.6 "Member States' and stakeholders' views on potential NGT-related opportunities and benefits" in the COM study, 2021.

Subsections	Number of question/Questionnaire*	Wording of the question
4.6.1 Member States' views	Q16/MS	Could the use of NGTs and NGT-products bring opportunities/benefits to the agri-food, medicinal or industrial sector?
	Q17/MS	Could the use of NGTs and NGT-products bring opportunities/benefits to society in general, such as for the environment, human, animal and plant health, consumers, animal welfare as well as social and economic benefits, in the short, medium and long term?
4.6.2 Stakeholders that see benefit in NGTs	Q16/SH	Could NGTs/NGT-products bring benefits/opportunities to your sector/field of interest?
	Q17/SH	Could NGTs/NGT-products bring benefits/opportunities to society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic benefits?
4.6.3 Stakeholders that do not see benefits in NGTs		*No corresponding question*
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

In **section 4.6.1 "Member States' views"**, expected benefits as expressed by the Member States are broken down into the three sectors: "agri-food sector", "medicinal sector", and "industrial biotechnology sector" (see COM study, 2021, p. 37f.). It should be noted that this classification according to these three labels is already included in the question posed by the Member States.

For the agri-food sector, the expected benefits expressed by many Member States are listed as follows:

- Tolerance to biotic stress (such as plant diseases) and to abiotic stresses (temperature, drought)
- Tolerance of climate change effects
- More precise and faster plant breeding
- Greater efficiency in nutrient consumption, water consumption
- Higher yields
- Better nutrient properties
- Reduced use of pesticides
- Fewer allergens and toxins
- Lower development costs

For the sector of industrial biotechnology, which is relevant for the agricultural and food industries through the production of additives, the results of the consultation with Member States are summarised in one sentence: NGT are said to be important for the "production of a broad array of substances and fields of application". As examples, the COM study mentions

the recycling of contaminated soils and the production of special chemicals for paper, biofuels, and plastics.[223] Here it is clear that the study refers to a broad repertoire of expected benefits, but these are in fact often not new, and have already arisen in relation to current genetic technologies.[224]

In **section 4.6.2, "Stakeholders that see benefit in NGTs"**, the questionnaires of the stakeholders are analysed (see COM study, 2021, p. 38f.). "A number of" stakeholders here are reported to have stated expectations of certain benefits. These stakeholders are "food business operators, biotechnology and pharmaceutical industry actors; academic/scientific organisations". On the one hand, these stakeholders expect benefits for their respective sectors, but on the other, they refer to the EU Green Deal and Farm to Fork Strategy in order to justify the benefits of NGT. Those benefits expected by the stakeholders are also briefly presented by the COM study, according to areas of application. Besides the "agri-food sector", these are the "medicinal sector", the "sector of microorganisms and industrial biotechnology" and "animal NGT application". It should be noted that the latter sector was not present in the analyses of the Member States.

According to the COM study, the most frequently named benefits were in the "agri-food sector". In the view of this expert opinion, this finding is not particularly surprising, due to the predominance of stakeholders surveyed from this sector.[225] In addition to the arguments already mentioned by the Member States, which the COM study lists again here, the stakeholders had above all stressed the necessity of using NGT in order to achieve the EU's pesticide reduction targets.

If stakeholders had answered "yes" to question 17, they were then asked to provide not only concrete examples, but also those conditions under which the benefit expectations are to be realised.[226] The following conditions were mentioned as those under which any expected benefits would might be realised:

- "[…] adapting the regulatory framework to make it fit for purpose for NGTs […]"
- "[…] greater public acceptance, transparent authorisation procedures, increased political acceptance" and
- "[…] treating NGTs as one tool in an integrated, holistic approach, rather than a solution by themselves" (COM study, 2021, p. 39).

The obstacles to the unfolding of the benefits are described so briefly in the COM study that it is to reconstruct or even describe them properly here. This is because the COM study does not provide answers to the following questions: Which stakeholders wish to use NGTs for their respective practice? For what reasons do they want to use them? What do they then state in each case as a condition that must be met so that they can benefit from NGTs? Answers to

[223] For other expected benefits that were mentioned less frequently by the Member States, the COM study refers to Annex D, Table 8. In the following sections, the COM study always refers to similar tables in Annex D. It is unclear to what extent these arguments are only documented here or are included in other forms.

[224] See for a listing Peuker, 2010, p. 215ff.

[225] See section 3.1.2.2.3 "Selection of stakeholder" in this expert opinion.

[226] In addition, they were asked whether these benefit expectations were specific to NGTs. See the additional questions in the stakeholder questionnaire: "If yes, please describe and provide concrete examples/data"; "If yes, under which conditions do you consider this would be the case?"; "If yes, are these benefits/opportunities specific to NGTs/NGT-products?". These supplementary questions were also put to the Member States, with the exception of the last question.

these questions could have been extracted from the replied questionnaires, but the COM study only provided generic statements.[227]

Another section in addition to those two mentioned, addresses expected benefits by presenting the arguments of those stakeholders who deny any such benefits (see **section 4.6.3 "Stakeholders who see no benefit in NGTs"**, COM study, 2021, p. 39f.). "A number of" stakeholders from the fields designated as "NGOs and GM-free/organic operators" argue that the expected benefits might also be achieved by way of alternative agricultural techniques. These stakeholders reportedly believe that the benefits expected from NGTs remain hypothetical and that there is no evidence that NGT contributes to sustainable agriculture. Furthermore, these stakeholders question whether the expected benefits of NGT can be achieved at all. These stakeholders claim that the problems addressed by the claimed benefits are too complex to be solved by one technology alone. They maintain that the expected benefits of the current genetic technologies have not materialised either. Similarly, these stakeholders believe that traits such as drought resistance require more complex changes in the genome and are therefore more difficult to achieve than, for example, herbicide resistance. In addition, they argue that both earlier and new genetic technologies are linked to an agricultural system that relies on uniform seeds, monocultures, and low genetic diversity, rather than genetic diversity and resilience. Furthermore, these stakeholders believe that only big companies would benefit from genetic engineering.[228]

It should be noted here that there is not a section on "hypothetical concerns" in the COM study, although in debates on risk they are often termed "hypothetical risks" from a perspective of proponent's of a technology. It is therefore positive that the COM study takes these concerns seriously and acknowledges them in a separate section. Nevertheless, there is no explanation as to why the contrary allegation was not addressed. The question then arises, as to whether the topic came up in the targeted consultations. Furthermore, the arguments denying a benefit are only listed, but are not discussed in the context of the expected benefits mentioned above.

3.6.1.2 Challenges and concerns of NGTs

The COM study then moves to highlight challenges and concerns (see **section 4.7, "Member States' and stakeholders' views on potential NGT-related challenges and concerns"**, see COM study, 2021, p. 40ff.). In two subsections, the arguments of the Member States and those of stakeholders are addressed. Table 21 below shows which questions in the questionnaires correspond to the content of the section in the COM study.

Again, as with the section on "opportunities and benefits", a slight difference in the questions as conveyed by the two surveys can be observed. Question 21 is similar for Member States and stakeholders, but the phrase "in the short, medium and long term" is only addressed to Member States.

[227] Arguments less frequently expressed are presented in Annex D of the COM study, Table 10.
[228] For further arguments, the COM study refers to Annex D, Table 10.

Table 21: Questions in the targeted consultations on potential NGT-related challenges and concerns. Presumably evaluated in section 4.7 "Member States' and stakeholders' views on potential NGT-related challenges and concerns" in the COM study, 2021.

Subsections	Number of question/Questionnaire*	Wording of the question
4.7.1 Member States' views	Q20/MS	Could the use of NGTs and NGT-products raise challenges/concerns for the agri-food, medicinal or industrial sector?
	Q21/MS	Could the use of NGTs and NGT-products raise challenges/concerns for society in general, such as for the environment, human, animal and plant health, consumers, animal welfare as well as social and economic challenges, in the short, medium and long term?
4.7.2 Stakeholders' views	Q20/SH	Could NGTs/NGT-products raise challenges/concerns for your sector/field of interest?
	Q21 /SH	Could NGTs/NGT-products raise challenges/concerns for society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic challenges?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

Section 4.7.1 in the COM study, titled "Member States' views" evaluates the views of the Member States (see COM study, 2021, p. 40). According to the COM study, "many" Member States express concerns or noted challenges. In the targeted consultations, the acceptance of NGT as well as verifiability and traceability were "mentioned most" as important challenges. Furthermore, challenges with regard to risk assessment were indicated. "Many" Member States see negative impacts on the environment, biodiversity, and ecosystems due to NGT generally. The COM study does not specify what these negative consequences might be. The evaluation is dealt with in only one sentence: "Many are also concerned about potential negative environmental impacts on biodiversity and ecosystems in general" (COM study, 2021, p. 40).

The COM study goes on to say that for "many" Member States, a further challenge lies in the different legal and administrative requirements that exist with regard to NGT in the EU and non-European trading partners. "Several" Member States expressed concerns that because of the regulatory requirements, industry would have difficulties commercialising NGT-related applications. As this paraphrases shows, the mention of possible negative consequences for the environment is followed without transition by the discussion of challenges presented by applications of NGT. Importantly, any expectation of negative consequences in the application of a technique must be distinguished from the practical difficulties of its application. The COM study should have addressed these issues separately for the purpose of clarity.

The COM study then continues by addressing the coexistence of different agricultural systems, as revealed in the targeted consultations. "Several" Member States had mentioned the co-existence of various crop systems as a challenge related to NGTs ("expressed concern on the co-existence of different types of agricultural production", COM study, 2021, p. 40). These respondents see the GMO-free market as being particularly threatened. The COM study elaborates on this point by indicating that certain difficulties with respect to traceability and labelling exist. But in the paragraph which introduces this point, negative economic consequences

are presented without linking them to negative ecological consequences: "some" Member States referred to the displacement of wild plants and the loss of agrobiodiversity through the "massive use of improved NGT varieties" as reasons for concern. Other ("several") stakeholders address freedom of choice and labelling as an issue in this context. The COM study does not elaborate on this point. The relation of the above-mentioned economic challenges presented by applications of NGT to environmental and consumer protection is likewise not explored.

The COM study proceeds by indicating selected concerns expressed by the Member States on these issues, especially those which have been classified as ethical aspects; the study refers to the fact that the ethical arguments are listed in a separate section. The content of these arguments is not indicated at this point by the COM study. A cursory evaluation of the relevant section shows that these are arguments that relate NGT to concentration processes of companies in the agri-food sector.[229]

Section 4.7.2 in the COM study "Stakeholders' views" presents the concerns and challenges expressed by stakeholders (see COM study, 2021, p. 40f.). According to the COM study, the "major concern for several stakeholders" is differences in regulation of NGT in the EU and non-EU countries and resulting competitive disadvantages. This concern was mainly mentioned by "food business operators, scientific and research associations, and academics". This was also a widespread concern among Member States, as outlined above. The COM study omits the importance of a coherent legal framework, even though this point emerged as a key concern in both targeted consultations. As will be shown later, this aspect is also not sufficiently acknowledged in the two final chapters of the COM study.[230]

According to the COM study, another "major concern" among stakeholders is the lack of reliable detection methods. The disadvantages are recapitulated by the COM study: among the reasons are cost, consumer confidence, and the like. Furthermore, the study introduces two further arguments, presented in a single sentence, and which deal with the concerns around the legal burden of NGT and the general prejudice against herbicide-resistant crops: "Finally, some stakeholders are concerned about the potential regulatory burden on NGTs and their products; others argued that herbicide-tolerant traits should not be rejected just on principle" (COM study, 2021, p. 41). Neither the relation with the aforementioned problem, nor the exact nature of the respective stakeholder's concern is made clear. It is also at this point in the COM study impossible to trace these arguments to their sources in the questionnaires, as no reference is made to them.

The COM study then identifies a specific group of stakeholders, the "organic/GM-free operators and NGOs", and considers their arguments. "Several" stakeholders from this group see the GMO-free sector in agriculture and food as threatened. Among the reasons cited are the rising costs of segregating commodity chains, additional controls and certification, and a loss of consumer confidence.

The COM study proceeds to turn to another stakeholder group comprised of "mainly business associations". Some stakeholders in this group reported a fear that the rejection of current

[229] See COM study, 2021, p. 48. See also section 3.6.1.6 "Ethics" in this expert opinion. Reference is also made to Annex D, Table 9 for these additional arguments.

[230] See section 3.8 "Evaluation of the overall structure and argumentation of the COM study" in this expert opinion.

genetic engineering techniques would be transferred to the new genetic engineering techniques, and that therefore the market for NGT products would be reduced. They also feared that "prohibiting the use of NGTs" would result in the loss of an important tool for the agri-food sector.

The COM study does not address the fact that different economic actors see different benefits in the application of NGT, and it likewise does not refer to the problem of the coexistence of the use of GMO and GMO-free production chains. Similarly, some of the paraphrases transposed from the source questionnaires are difficult to understand across these passages in the COM study.

The study goes on to mention – in a short, one-sentence paragraph – two further concerns: the loss of consumer choice and "undetected NGT products". These findings from the targeted consultations are again too short and not well-connected to the rest of the text, making them difficult to follow.

The COM study also lists general concerns expressed by stakeholders. "Some" stakeholders from the field of food producers and NGOs ("food business operators and NGOs") expressed concerns about concentration processes and monopolies in the NGT sector (the study does not specify which sectors are meant here: seeds, agrochemicals, or food traders). The study highlights various reasons for the formation of monopolies. In particular, "food business retailers" see the regulation of genetic engineering as a reason for the formation of monopolies. By contrast, according to the "NGOs", monopolies arise from the technology itself. Furthermore, NGOs point out that NGTs are linked to industrial agriculture and patenting, thereby impeding access to genetic resources, and furthermore affect "farmers' and breeders' rights". In mentioning this, the COM study does not refer to any of the subsequent sections of the study concerning patents. Moreover, it is notable that the same section discusses arguments on those monopoly practices that were previously were identified as ethical concerns in the discussion of Member States' views and moved to a corresponding section on ethics. Stakeholder arguments on the same issue are not understood and presented here as ethical. It remains unclear how this difference in assessment came about.

In subsequent paragraphs, the COM study discusses the conditions required for the above concerns to be realised. The COM study points to a discrepancy in the stakeholders' answers to this question.[231] For "food business operators, industry, academics and scientific stakeholders", their concerns would persist if NGT were regulated under the existing legal framework. For stakeholders from the "NGOs and organic/GMO-free operators" sector, their concerns would remain if NGT were regulated differently from conventional genetic engineering or even completely unregulated. Similarly, different opinions are expressed on the question of whether such challenges are specific to NGT or already present with earlier genetic technologies. The COM study does not draw any conclusions from these different perspectives, nor does it refer to earlier sections, e.g. on law and the various new genetic technologies.[232]

[231] There are two additional questions in the stakeholder questionnaire on question 21: "If yes, under which conditions do you consider this would be the case?"; and "If yes, are these challenges/concerns specific to NGTs/NGT-products" (see questionnaire stakeholders COM study, Annex B, p. 73). It is reasonable to assume that the answers to the respective questions were summarised at this point by the COM study.

[232] Finally, the study refers to Annex D, Table 12 for further concerns.

Summary assessment for the two sections "Opportunities and benefits" and "Challenges and concerns"

In general, both sections appear quite compact in terms of their content. Many arguments are only mentioned and presented generally, where lines of argumentation are only developed superficially. Cross-references and interpretations of the findings are lacking. Thus, the COM study in these sections amounts to not much more than a simple juxtaposition of arguments. Nevertheless, the COM study does contain interpretative approaches, as for example where its presentation is organised according to content, even if inconsistently, and where different perspectives are emphasised. Yet the COM study fails to develop the concept of "risk", which must involve evaluating both negative and positive consequences of applying NGT.[233] One consequence of this procedure is an accumulation of inaccuracies, as seen in the "Challenges and concerns" section. Negative consequences of a technology's application are conflated with the obstacles or practical difficulties of its application. The study would have been better served by separating the discussions of possible consequences from that of practical problems.

3.6.1.3 Small and medium-sized enterprises (SME) and intellectual property rights

The questions for sections "information on potential opportunities and benefits from the use of NGTs and NGT-products" and "information on potential challenges and concerns of NGT products" also dealt with the impact on small and medium-sized enterprises (SMEs) and intellectual property rights. The results are summarised in **section 4.8 of the COM study, titled "Views relating to Small-Medium-Enterprises and intellectual property"** (see COM study, 2021, p. 42ff.). Table 22 shows the chapter structure and the corresponding sections in the questionnaires.

Table 22 shows that the questions for the Member States and for the stakeholders differ slightly regarding SMEs. Stakeholders are asked about SMEs and "small scale operators", Member States about SMEs only (Q18 and Q22). Furthermore, questions posed to Member States do not differentiate between NGT and NGT products. An explanation for the different lines of questioning is not given by the COM study.

The advantages and disadvantages of NGT for small and medium-sized enterprises are presented in **section 4.8.1 of the COM study, "SMEs".** "Many" Member State and stakeholder respondents see advantages for SMEs in the agricultural sector, due to lower costs and an easier handling of technology there. However, they also stress that regulation is a heavy burden for companies, making market access difficult. Various reasons are given for this statement, such as the difficulty of creating an authorisation dossier, the cost and effort of security testing, and obtaining cultivation approvals. High costs are also associated with patenting. "Others" see an economic risk for SMEs in low public acceptance and high research and development costs.[234]

Section 4.8.2 in the COM study discusses **"Intellectual Property"** (see COM study, 2021, p. 43). "Many" stakeholders from the agricultural sector see advantages in patenting. However, according to "some" Member States, access to new patented genetic technologies should be facilitated for competitive reasons. The COM study then emphasises that there is a different

[233] See also section 3.6.2.2 "No risk-benefit debate" in this expert opinion.

[234] Arguments are also made in relation to the pharmaceutical sector. The COM study refers to Annex D, Table 8-12 for further arguments.

view on this ("on the other hand"). "Many" Member States and stakeholders expressed concerns about patenting, especially with regard to SMEs. Patents, for example, could limit access to new technologies and also affect the rights of breeders. There are also reported concerns about concentration in the seed sector, which risks higher prices, limited choice, and less independence for farmers. Because of the increased complexity in patenting CRISPR technology, restrictions on corporate freedom are also envisaged. All stakeholders from the pharmaceutical sector as well as some Member States were of the opinion that patent protection is a prerequisite for innovation.[235]

This section of the COM study ties together strands of argumentation from previous sections regarding opportunities/benefits and concerns/challenges, which are repeated as some new features are added. Thematically bundled argumentation would have benefited the presentation. The topics of SMEs and intellectual property are tightly intertwined in their content, but are nevertheless presented separately. As a result, cross-references cannot be easily made. A well-founded evaluation of risks and benefits is therefore difficult.

Table 22: Questions in the targeted consultations on small-medium-enterprises and intellectual property. Presumably evaluated in section 4.8 "Views relating to Small-Medium-Enterprises and intellectual property" in the COM study, 2021.

Subsections	Number of question/Questionnaire*	Wording of the question
4.8.1 SMEs	Q18/MS	Do you see particular opportunities for SMEs on the market access to NGTs?
	Q22/MS	Do you see particular challenges for SMEs on market access to NGTs?
	Q18/SH	Do you see particular opportunities for SMEs/small scale operators to access markets with their NGTs/NGT-products?
	Q22/SH	Do you see particular challenges for SMEs/small scale operators to access markets with their NGTs/NGT-products?
4.8.2 Intellectual property	Q19/MS	Do you see benefits/opportunities in patenting or accessing patented NGTs or NGT-products?
	Q23/MS	Do you see challenges/concerns in patenting or accessing patented NGTs or NGT-products?
	Q19/SH	Do you see benefits/opportunities from patenting or accessing patented NGTs/NGT-products?
	Q23/SH	Do you see challenges/concerns from patenting or accessing patented NGTs/NGT-products?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

3.6.1.4 Labelling

Positions on labelling are presented in the study in **section 4.9, "Stakeholders' views on the labelling of NGT products"** (see COM study, 2021, p. 43f.). The questionnaire for stakeholders contained two questions on labelling (see below Table 23). Although question 8: "Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?" was probably evaluated in section 4.3.2 of the

[235] For further arguments, the COM study refers to Annex D, Table 8-12.

COM study.[236] Member States were asked about traceability strategies only and not about labelling. As the title suggests, this section of the COM study presents the views of the stakeholders alone and not those of the Member States.

Table 23: Questions in the targeted consultations on the labelling of NGT products. Presumably evaluated in section 4.9 "Stakeholders' views on the labelling of NGT products" in the COM study, 2021.

Subsection	Number of question/Questionnaire*	Wording of the question
4.9 Stakeholders' views on the labelling of NGT products	Q28/SH	What is your view on the labelling of NGT-products? Please substantiate your reply.
4.3.2 Member States' and stakeholders' views on implementation and enforcement	Q8/SH	Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*		

This section begins by stating that "all" stakeholders recognise the importance of consumer protection. However, according to the COM study, there are divergent views on labelling. On the one hand, "several" stakeholders from the field of "NGOs, food business operators, including those specialising in non-GM foods and retailers" would regard labelling as an essential precondition for their freedom of choice. Some of these stakeholders would like to use labels according to the current legal framework. Stakeholders from the field of "NGOs and non-GM food business operators" in particular see labelling as vital for the survival of organic and GMO-free agriculture. One stakeholder indicated that the EU "Green Deal" strategy includes greater consumer transparency. Eliminating the labelling of GMOs or NGTs would therefore be contradictory.

The COM study then emphasises that other stakeholders in the survey expressed a different view. The arguments in favour of labelling are opposed by "several" stakeholders from the field of "food business operators", who note that as there are no reliable detection methods and labelling would be a major challenge. They argued that labelling should not be applied to NGT products, which could also be achieved through conventional methods. "Some" stakeholders from this group said that the label should also highlight the benefits of the product produced through NGTs. Labels could also be misleading, and would need to be understandable and based on scientific facts. Some stakeholders reported concerns that labelling products from NGTs would be equivalent to banning the technology. The COM study then refers to the arguments of "some" stakeholders: Firstly, respondents indicated that traceability of NGT is important for companies for monitoring and potential recalls; and secondly, respondents report that an NGT-specific labelling scheme would waste resources, as other labelling schemes already exist.[237]

[236] For a summary and analysis of this section see section 3.2.7 "Stakeholder and Member States views on GMO legislation" in this expert opinion.

[237] For further arguments, the COM study refers to the list in Table 13 in Appendix D.

This section of the COM study largely presents the different points of view thematically and clearly. Even if some of the information and arguments are presented in such an abbreviated way that they are difficult to follow, the reader is given a good overview of the debate.

3.6.1.5 Public dialogues and surveys on NGTs

Section 4.10, "Public dialogues and surveys on NGT" of the COM study is informative. This section refers to questions in the Member States' questionnaire concerning public events and surveys. Accordingly, the section is divided into two subsections. Table 24 below provides an overview of the sections and the corresponding questions in the Member States' questionnaire.

Table 24: Questions in the targeted consultations on public dialogues and surveys on NGT. Presumably evaluated in section 4.10 "Public dialogues and surveys on NGT" in the COM study, 2021.

Subsection	Number of question/ Questionnaire*	Wording of the question	Supplementary material
4.10.1 Public dialogues reported by Member States	Q13/MS	Have you or other institutions/bodies/entities organised national dialogues concerning NGTs?	
4.10.2 National and EU-wide surveys	Q14/MS	Have you or other institutions/bodies/entities organised national surveys, which assessed public opinion on NGTs?	Eurobarometer 2019
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*			

In **section 4.10.1, "Public dialogues reported by Member States"**, the COM study states that 67 public dialogues and surveys related to NGT were reported by the Member States. These were conducted in various formats – open or targeted, in seminars or workshops. There is no content-related or more differentiated evaluation of the dialogue forums, but in Appendix D, Table 14, all reported events are listed by country, year, event form, event title and content, audience, and sector. It would have been possible for the COM study to extend the analysis further in terms of specifying which sectors and for which Member States the dialogue events were held. It might also have been possible to cluster the topics in order to give an overview of the topics discussed and the problems which are prominent in each respective country. In its present form, the evaluation of the COM study is only of limited use.

In **section 4.10.2, "National and EU-wide surveys"**, the COM study reports that six Member States responded to 11 surveys.[238] This would make it difficult for the COM study to draw general conclusions. Consumers were the main target group, but two of the surveys focused on farmers, food producers, and other stakeholders. The main topic of these surveys was public knowledge and perception of NGTs. The surveys are summarised in Annex D, Table 15, by country, year, organisation, participants, and target. The results are also summarised in the table in the appendix. Again, no comparative analysis is given in the COM study.

As a substitute, the COM study presents the results of a survey from Eurobarometer. The results of the 2010 Eurobarometer survey are compared with 2019's results. The COM study

[238] The surveys were not always quantitative surveys, but also represented citizen forums.

shows that the proportion of critical voices in the population has fallen. It also finds that the population tends to see 'natural' aspects in cis-genesis techniques.

3.6.1.6 Ethics

The study deals with ethical dimensions as its final main topic (**section 4.11, "Ethical aspects of NGTs"**, see COM study, 2021, p. 46ff.). In the targeted consultation, a question on ethics was included for both Member States and stakeholders. However, the question is posed to each group at different points in the questionnaire, and its formulation concerns different aspects of the ethical problem. Under the thematic heading "information on ethical aspects" in the questionnaire, Member States were asked whether there are any published statements on the ethical aspects of NGT. However, stakeholders were explicitly asked for their views on ethical aspects related to NGT and products made with them. In addition to the analysis of the questionnaires, the COM study included an expert opinion from the Expert Group on Ethics (EGE 2021).

Table 25 below shows how each section in the study corresponds with the questionnaire and supplementary material.

Table 25: Questions in the targeted consultations on ethical aspects of NGTs. Presumably evaluated in section 4.11 "Ethical aspects of NGTs" in the COM study, 2021.

Subsection	Number of question/ Questionnaire*	Wording of the question	Supplementary material
4.11.1 Member States' views	*Source cannot be reconstructed*		
4.11.2 Public dialogue initiatives and Member State expert opinions	Q15/MS	Have any national bodies or expert groups discussed or issued opinion on the ethical aspects of NGTs?	
4.11.3 Stakeholders' views	Q26/SH	What is your view on ethical aspects related to NGTs/NGT-products? Please substantiate your reply.	
4.11.4. Opinion of the European Group on Ethics			EGE
** Q = Question; MS = Questionnaire of the Member States; SH = Questionnaire of the stakeholders*			

In **section 4.11.1, "Views of the Member States"**, the ethical arguments of the Member States are first briefly summarised according to the three areas of application: human, animal, and plant (see COM study, 2021, p. 46). It is unclear which questions in the questionnaire correspond to this section, as there is no direct question on ethical views in the Member States' questionnaire. Accordingly, "some" Member States expressed general ethical concerns about the use of the technique in relation to the human germ line and embryos. With regard to animals, "some" Member States expressed concerns about animal welfare. The COM study does not elaborate on the details of these concerns. With regard to the application of NGT to plants, the COM study highlights a tension between different views. "Some" Member States consider the non-application of NGT ethically problematic if benefits are expected. "While another" position emphasises NGT's negative impacts on developing countries. The application of NGTs would lead to rising agricultural prices, malnutrition, migration and war. In principle,

the arguments do not represent counter-positions, since with regard to negative impacts, they only refer to the situation in the developing countries. Similarly, the impression is given that there are negative impacts only in the developing world and not in the developed world.

The following **section, 4.11.2, "Public dialogue initiatives and Member State expert opinions"**, presents content-related results of the public dialogues and expert opinions on ethical aspects as reported by the Member States in their surveys (see COM study, 2021, 46f.). This is accomplished by unnumbered separate subheadings for agricultural applications ("Agri-Food-Applications") and medical applications ("Medicinal application and other potential uses in humans"). In what follows below, the argumentation made by the COM study under the subheading "Agri-Food-Applications" is discussed.

With regard to applications in agriculture, several **experts or in public dialogue forums** pointed out that NGT may solve various problems in plant breeding. They contend it would be immoral to forego use of these techniques if they could solve such problems as biodiversity and climate change. In terms of animal welfare, the forums suggest that NGT might expand the use of laboratory animals. The COM study does not elaborate to what extent. Likewise, animals that are already extinct might be recreated. These findings are listed sequentially by the COM study without cross-reference and without any reference to what moral considerations might be relevant.

According to the COM study, two **expert opinions** submitted by the Member States emphasised that the precautionary principle should always be applied to innovations; one expert opinion held that social values should also be taken into account for an extended risk assessment approach. The COM study then mentions that two Member States were of the opinion that a ban on NGTs might not be unjustified. The presentation does not clarify whether the Member States expressed this opinion or whether they had submitted an expert opinion from which this recommendation was derived. These statements are also only summarised by the COM study and listed without reference to each other.

Following the analysis of this survey of Member States, an evaluation of the stakeholder survey on ethical aspects of the application of NGT is to be found in **section 4.11.3, "Stakeholder's views"** (see COM study, 2021, p. 47f.). "Some" stakeholders from "NGOs and GM-free/organic food business operators" raised several points regarding ethical concerns. These are as follows: Concerns about freedom of choice with regard to seeds, breeding techniques and agricultural practices; further negative impacts on ecosystems, biodiversity, and animal welfare. Farm animals might well be harmed, as the aim of genetic modification through NGTs is an increase in productivity.

By contrast, "other" stakeholders from the field of "food business operators, academics" would argue that it is immoral to stop scientific progress. The NGTs promise to be a solution to the problem of sustainability. In this section, the COM study contrasts concerns about the application of NGTs with their non-application. This juxtaposition then also appears in the conclusions of the COM study – as the only one drawn from the field of ethics.

The COM study then turns to highlight another line of conflict between different views, namely that occurring between "some" actors from the NGO sector on the one hand, who consider the precautionary principle to be an ethical or moral principle, and other stakeholders from the area of "academics and food business operators" who would argue that scientific findings must play a greater role, and that therefore the proportionality principle should be applied to NGT use. The COM study then presents different perspectives on political decision-

making. "Some" stakeholders from the NGO sector would like to include moral concerns in decision-making processes. The COM study does not elaborate on how moral concerns could be incorporated into such decisions. "Other" stakeholders from the field of "food business operators, academics" believe that it is not so much the technology itself that should be evaluated, but the products or organisms produced with it. Again, "some" food entrepreneurs ("food business operators") express moral concerns about a scenario in which science no longer plays a role in decision-making processes. It is not addressed to what extent this includes questions of morality. Considerations on technological assessments are connected to questions of risk assessment, which are in turn considered in greater detail elsewhere in the COM study (namely in **section 4.4.2, "Member States' and stakeholders' views regarding safety"**, COM study, 2021, p. 31ff.) The COM study includes no cross-reference to this section.

As mentioned above, the COM study proceeds systematically, and assigns corresponding questions from the two targeted consultations to its content sections. In the section "Member States' and stakeholders' views on potential NGT-related challenges and concerns", the COM study identified some responses on this topic expressed as ethical arguments, and promised to report them in relevant sections.[239] The COM study does deliver on this promise: "some" stakeholders from the NGO sector indicated that genetic engineering might lead to a concentration of property rights and power in the agri-food sector through patents and licences, and thus impact the quality of democratic rule. The mention of this argument occurs outside the preceding context of argumentation, and the topic of concentration is dealt with in greater detail elsewhere in the COM study (see section 4.8, "Views relating to Small-Medium-Enterprises and intellectual property", see COM study, 2021, p. 42ff.). This particular organisation shows once again that in the COM study inconsistencies arise in the reproduction of the arguments from the questionnaires, and that the arguments are partly ordered in terms of content but often also reproduced incoherently so that the substantive points informing statements are lost in a mass of information.[240]

Section 4.11.4 briefly presents the recommendations of the European Group on Ethics in Science and New Technologies from the expert opinion "Ethics of Genome Editing" (EGE 2021, see COM study, 2021, p. 48f.). The EGE opinion was completed in March 2021, shortly before the publication of the COM study in April 2021. The COM study states that the EGE refers to the importance of discourses and narratives, especially on notions of naturalness, humanity, and humanisation. With regard to plants, the EGE (2021) recommends that companies should carry out risk assessments, including on the impact on biodiversity and the environment ("Companies introducing new varieties, regardless of method or provenance, should be required to identify the impact of their use on both biodiversity and environment", COM study, 2021, p. 49). The EGE also recommends a systemic approach which takes into account the influence of existing agricultural practices. According to the COM study, the EGE also recommends that regulation of NGT should be proportionate to risk. Regulation should be less restrictive if those changes brought about by the technique may also occur naturally. A comprehensive risk assessment should therefore be carried out. For this purpose, detectability and labelling are to be made possible ("[…] regulation should be proportional to the risk; light touch regulation should be used where the change in the plant could have been achieved

[239] See also section 3.6.1.2 "Challenges and concerns of NGT" in this expert opinion.

[240] After the evaluation of the ethical arguments in relation to the agricultural sector, there follows a very brief presentation in relation to medical applications.

naturally, or where genetic material from sexually compatible plants was introduced. Where genes from non-sexually compatible organisms or multiple changes are introduced, there should be a comprehensive risk assessment", COM study, 2021, p. 49).[241] The EGE also recommends that greater attention should be focussed on "small" players, on public debate, and the potentially higher prices and availability that might result from stricter regulation. The COM study lists these last points, but does not elaborate on them.

3.6.2 Methodological critique of the chapters on socio-economic consequences and ethics of NGTs

The sections on the socio-economic aspects of NGTs refer to the benefits and challenges that stakeholders and Member States see for particular actors and society in general. In addition, more specific questions are asked about the consequences for small and medium-sized enterprises. The COM study bases its presentation of the socio-economic impacts primarily on its surveys (or target consultations). It does not conduct its own analyses, unlike in sections 4.1 and 4.5 concerning issues of technology development, legal regulation, safety, and innovation.

However, some sections on public dialogue and surveys, as well as those on ethics are supported by supplementary material (section 4.10 and section 4.11 in the COM study). These consist of surveys from Eurobarometer and the EGE expert opinion (see Eurobarometer, 2019, EGE 2021). The evaluation of the Eurobarometer replaces the comparative analysis of national surveys and dialogue forums reported by Member States as part of the targeted consultation. As mentioned above, the COM study refrained from this analyse because it was "difficult to draw general conclusions" (COM study, 2021, p. 45).

The analyses of socio-economic impacts and ethics therefore remain only assertions. The COM study more or less reproduces the arguments from public debates via targeted consultations. However, it does not provide any justifications for these arguments. Thus, the COM study does not make any statements about the socio-economic impacts of NGT, but only reproduces the opinions of stakeholders and the Member States on this topic.

Stakeholders and Member States had the opportunity to support their statements with evidence. They were able to upload supporting material and provide references to relevant literature along with their answers to the questionnaires. However, this material is not analysed in the COM study in connection with the survey results. It is unclear whether this material was evaluated et all.[242] In any case it is not cited as evidence for the various assertions made over the course of the targeted consultations.

As the methodological critique advanced in section 3.1.2 of this expert opinion showed, the analysis of the targeted stakeholder consultation may be criticised both in terms of sociological criteria and in terms of the criteria required for conducting stakeholder consultations in accordance with the Better Regulations Guidelines of the European Union. The discussion of the argumentation of the COM study in the previous sections of this expert opinion on the socio-economic impacts showed that the complex argumentations, which were obviously given by the surveyed Member States and stakeholders in the questionnaires, are often only presented in a highly abbreviated form. This presentation makes the argumentation of the COM study difficult to follow.

[241] See also the discussion on law and risk assessment in section 3.5 of this expert opinion.
[242] See also the methodological critique in section 3.1.2 of this expert opinion.

For the sections on the socio-economic consequences and the ethics of NGT, three further points can be highlighted, to supplement the general methodological critique found in section 3.1.2 of this expert opinion. These three points relate to the content of the targeted consultations, the choice of words regarding the consequences of NGT and NGT products, and the perspective taken with regard to consumers.

3.6.2.1 Practical problems are only touched upon and not discussed

On the subjects of SMEs and intellectual property,[243] the Commission has set thematic priorities in its questionnaire. Potential benefits and concerns with respect to NGT for small and medium-sized enterprises (SMEs), and patenting's potential consequences were grouped as aspects of the use of NGT in the questionnaire. The COM study does not give a reason for the focus on SMEs and patents. The "Better Regulation Guidelines", which call for a reference to small and medium-sized enterprises, might explain this feature of the study (see European Commission, 2021a, p. 11f.).[244] Yet the COM study does not find a conclusive answer to the question of the impact of NGT on SMEs. In its conclusions, it emphasises that there is a need for further research on this issue (COM study, 2021, p. 59).

Another shift in the setting of topics in the COM study concerns the topic of labelling of NGT plants and NGT products. Questions on this topic are asked explicitly only in the stakeholder questionnaire and are therefore rendered marginal. The evaluation in the COM study is carried out in an extra section and is thus emphasised here. However, the issue is closely linked to the question of detectability of NGT, which is dealt with in detail elsewhere in the study and also in the questionnaire.[245] The COM study abstains from a consideration of both problems. It would have been better to treat them as a single practical problem and discuss them in one section so as to recommend possible solutions. This indicates a possible inconsistency, but it also demonstrates that solving practical problems regarding NGTs was not the main focus of the COM study.

3.6.2.2 No risk-benefit debate

The term "risk" is not used by the COM study. Instead of using the term and contrasting it with certain benefits, the study redefines the positive and negative aspects of a technological application. On the one hand, the COM study focuses on the "opportunities and benefits". On the other hand, it lists "challenges and concerns".

As this present expert opinion has demonstrated, "challenges" means not only those potential negative consequences for health, the environment and the economy, but also obstacles to the realisation of any benefits. This is shown by the analysis of arguments in the COM study by this expert opinion.[246] In the chapter section 4.7, "Member States' and stakeholders' views on potential NGT-related challenges and concerns" (see COM study, 2021, p. 40ff.), the COM study mentions negative impacts on biodiversity and ecosystems as concerns. Without a

[243] The heading of the section in the COM study is "intellectual property", but the two questionnaires in the targeted consultation ask about patenting.

[244] Interview 5 also points out that it is due to the new approach of the European Commission that there are questions on small and medium-sized enterprises. According to interview 5, it is a standard question of the European Commission that is asked in such surveys (see Interview 5).

[245] Namely in section 4.3.2 of the COM study "Member States' and stakeholders' views on implementation and enforcement", COM study, 2021, p. 26ff., as well as in section 4.1.1 "SAM explanatory note on new techniques in agricultural biotechnology", COM study, 2021, p. 11.

[246] See section 3.6.1.2 "Challenges and concerns of NGT" in this expert opinion.

transition to the next topic, obstacles to the realisation of the technology are mentioned. This conflates two separate issues: namely, the consequences of technology use, especially for those who do not use the technology, and the practical difficulties faced by the technology user. For the purpose of clarity, the expectation of negative consequences in the application of a technique must be distinguished from the practical difficulties of its application. The COM study should have addressed these issues separately.

A large part of the risks is not named as such, but are treated as part of the topic of safety and concerns.[247] Some classic risk arguments, especially those concerning the environment (for example biodiversity) and socio-economics (for example monopolisation), appear in the section on ethics. This presentation scatters the discussion of potential negative consequences of NGT, viz. the risks associated with its application. The result is that potential benefits are not contrasted with potential risks and measured against one another systematically.[248] For example, although the COM study indicates that many Member States anticipate certain environmental risks and attach high importance to risk assessment and risk management of NGTs,[249] it does not engage in a risk-benefit debate in this regard. This is surprising, given that the COM study calls for "further policy action" aimed at "reaping benefits from innovation while addressing concerns" (COM study, 2021, p. 4). The COM study states, that a purely "safety-related risk assessment" may not be sufficient "to promote sustainability and contribute to the objectives of the European Green Deal and in particular of the Farm to Fork Strategy and the biodiversity strategies" (COM study, 2021, p. 4). Since the COM study does not compare benefits and risks, it is difficult to comprehend how these statements are justified by the European Commission.

A lack of comparison or weighing up of benefits and risks is further complicated by the structure of the sections of the study. Statements on opportunities/benefits and challenges/concerns are each presented by way of an extra section. A presentation in a joint section would have been better, as is the case in the COM study's discussion of small and medium-sized enterprises in relation to patents.[250] There, benefits and concerns were considered in one section and those contradictions resulting from a technology application – positive effects with simultaneous negative effects – were made clear.

An interview conducted in the context of this expert opinion reveals that the concept of risk is a key concept in genetic engineering law (see Interview 5). For unknown reasons, the European Commission apparently deliberately decided against the term "risk" when preparing the COM study. "We had said several times that the word 'risk' is a central concept in genetic

[247] At this point, reference should be made to the FoEE 2021 discussion paper. The criticism of the COM study included in it also states that there were no questions on risks in the questionnaire and only three questions in the questionnaire referred to concerns (see FoEE, 2021, p. 5).

[248] Compare, for example, the actuarial risk calculus, in which the expected negative consequences of an object are estimated in connection with the expected benefit and depending on the probability of occurrence. See Zwick/Renn, 2008, p. 77. The concept of risk thus contains both the expectation of positive and negative consequences. Negative consequences can include not only negative consequences for the technology users, but also negative consequences for those who do not use the technology. These are, for example, consumers and the natural environment.

[249] "Member States see a challenge relating to the mechanisms that are in place to ensure the risk assessment and risk management of NGTs in all their applications. Many are also concerned about potential negative environmental impacts of NGTs on biodiversity and ecosystems in general" (COM study, 2021, p. 40).

[250] See above, section 3.6.1.3 "Small and medium-sized enterprises (SME) and intellectual property rights" in this expert opinion.

engineering legislation [...] – this was simply completely rejected" (Interview 5). This decision impacted the COM study's insufficient discussion of negative consequences for the environment and for environmental protection (Interview 5).

3.6.2.3 Perspective on the consumer

The COM study employs a narrow conceptualisation of the population in a democratic society. People are not presented as citizens but rather as consumers. In the study, consultation processes are explicitly seen as procedures to gain acceptance by the consumers and in public debate, and not as part of a democratic participation process. Exemplary of this viewpoint is the Executive Summary of the COM study, which asserts that "[p]ublic perception of new biotechnologies is key to their market uptake" (COM study, 2021, p. 4). Findings of the Eurobarometer on public acceptance and knowledge of NGTs are reported in detail in order to show that acceptance has increased. This framework is deployed to indicate that consumer acceptance of NGT will facilitate the technology's application.

3.6.3 How well researched and substantiated are the COM study's statements about the ethical and socio-economic implications of NGTs?

In its description of the socio-economic consequences of NGT, the COM study mainly refers to its two targeted consultations. In its section on ethics, the COM study draws on the findings from the two targeted consultations as well as the expert opinion of the European Group on Ethics in Science and new Technologies (EGE 2012), entitled "Ethics of Genome Editing".

For the most part, therefore, the COM study reflects assertions on the questions of socio-economic consequences and ethics of NGT. These assertions about the potential consequences of new genetic technologies could be (scientifically) tested to see if they are valid on a factual level. These problems at the factual level are then presented in subsequent sections, broadening the perspective of the COM study.

One assumes the existence of studies substantiating or refuting the opinions expressed in the social debate regarding substantive problems with NGT. A review of the state of research should have been carried out within the framework of the COM study. Although the present expert opinion cannot provide a systematic re-analysis, it can highlight certain indications on the basis of the COM study's findings.

3.6.3.1 Options for small and medium-sized enterprises

The potential benefits of NGTs are central to the COM study's discussion of the socio-economic consequences of NGT technology in relation to small and medium-sized enterprises.[251] The questionnaires of the two targeted consultations employed by the COM study poses the following questions: what are the opportunities and what are challenges for SMEs to access markets with their NGTs/NGT products?

Answers to this question can be derived from the responses of the stakeholders and the Member States listed in the COM study:[252]

[251] See section 3.6.2.1 "Main thematic focuses of the COM study" in this expert opinion, above.

[252] See also section 4.8 of the COM study "Views relating to Small-Medium-Enterprises and intellectual property" (see COM study, 2021, p. 42ff.) Its summary and analysis are to be found in the present expert opinion, in section 3.6.1.3 "Small and medium-sized enterprises and intellectual property rights".

- (1) Easier handling of the technology and lower costs will facilitate market access for SMEs.
- (2) SMEs are hampered in their market access by the regulation of NGTs.

These two points are considered in more detail in the following subsections.

3.6.3.1.1 Easier handling of the technology and lower costs

One argument reproduced in the COM study from the targeted consultations refers to the lower costs and easier handling of NGTs, a possible advantage for small and medium-sized enterprises. The COM study does not indicate the particular sector of those small and medium-sized enterprises for which NGTs would be an advantage. As is shown in section 3.1.2.2.3 of this expert opinion, the COM study surveyed organisations, companies, and business associations at various points in the value chain. Companies and organisations in research, the seed industry, farmers, wholesale, and retail are among those queried. At each of these levels, there may be small and medium-sized enterprises. The first question is therefore at which stage of the value chain do the advantages of NGT emerge? Furthermore, the question arises as to how the lower costs are achieved compared to the alternatives and what it means that NGTs are easier to handle.

The relevant sections of the COM study which discuss the above argument refer to the "agricultural sector". The COM study refers to companies that develop plants with certain characteristics so as to contribute to sustainable agriculture. It can thus be assumed that the statements of easier handling and lower costs refer to small and medium-sized companies in the seed sector and small research companies.[253]

3.6.3.1.2 Regulation of NGTs as a burden for SMEs

The COM study also states that the regulation of NGT is a burden for small and medium-sized enterprises. Here, too, the question arises as to which enterprises in the value chain this statement should apply. In this context, the COM study mentions an "authorisation dossier", which refers to the authorisation documents for GMOs. Furthermore, difficulties in obtaining cultivation approval are reported (see COM study, 2021, p. 42). The COM study therefore concludes that regulation is a burden for breeding companies and agricultural enterprises. Subsequently, the question arises as to whether this is also the case for the other enterprises in the value chain, and whether small and medium-sized enterprises from certain sectors could possibly benefit from a regulation of NGT.

In fact, there is also evidence in the COM study that regulation is not a burden but a help for some companies. This scenario is implied at times in the COM study. For example, the study mentions that enterprises from the organic and GMO-free agriculture and food sector benefit from a regulation of new genetic engineering. These companies could even be threatened if the regulation of NGT no longer existed (see COM study, 2021, p. 44).

[253] One argument in this context is that NGT could shorten the development times for new NGT products. This argument plays less of a role in the COM study with regard to SMEs. However, this can also be taken as an opportunity to ask for which applications the development times are shortened and what benefit SMEs can derive from this. With regard to plant breeding, Interview 2 states that certain development steps could be shortened, but that no general statement can be made about whether the breeding process as a whole could be shortened (see Interview 2).

3.6.3.2 Patents and intellectual property rights

Following the questions in the questionnaires, the question of the COM study in relation to patenting or in relation to intellectual property rights in general is which "benefits/opportunities" and which "challenges/concerns" are associated with it. The arguments mentioned in the COM study can be ordered according to which practical possibilities and problems are addressed in each case, so that four aspects can be distinguished from each other to answer the above question:[254]

- (1) Patents may make it more difficult for plant breeding companies to access new technologies and thus to carry out breeding work.
- (2) Patents could increase concentration in the seed industry.
- (3) Patents are a precondition for innovation.
- (4) The role of intellectual property rights in access to genetic resources is discussed.

These four aspects are considered in more detail in the following subsections.

3.6.3.2.1 Access to new technologies

The COM study deals with the question of what opportunities and challenges patents offer in the context of new genetic technologies; a similar question was posed more generally in the questionnaires for the targeted consultations, and was not restricted to the topic of SMEs. Responses indicate that the topic of patents was then critically received, especially with regard to SME access to the New Genetic Technologies. It can be concluded from these exchanges that the topic is of vital importance for the surveyed stakeholders.

In an interview conducted by the authors of this expert opinion, examples were also given indicating that patents hamper the application of genetic engineering. Certain methods, such as TALEN, are owned by one company, Calyxt (see Interview 2). Furthermore, the interviewee points out that access to NGTs is hampered by patenting, and that such a problem is publicly known. The problem concerns licence fees that must be paid to use a given technology, as well as a lack of knowledge among breeders regarding the patent status of such technologies; this impedes breeders' work.

The interview refers to the Pinto database from the ESA, in which companies can voluntarily register which of the varieties they have developed are protected by patent.

> "The problem that many smaller, even conventional breeders have in Europe is that when they work with certain varieties, they don't know, for example, if they have any resistance, whether this resistance is not patented. And this database should create a bit of transparency, but it is not obligatory as far as registration is concerned" (Interview 2).

These comments suggest that the situation regarding patents and access to NGTs is more complex than presented in the COM study. The relationship between patents and the work of breeding companies requires a different study design than that of the COM study, which only reflects opinions pertaining to the impact of patents.

[254] See also section 4.8 "Views relating to Small-Medium-Enterprises and intellectual property" of the COM study, 2021, p. 42ff., and the paraphrase and analysis of this section in section 3.6.1 "Small and medium-sized enterprises and intellectual property rights" of this expert opinion.

3.6.3.2.2 Patents and concentration processes in the seed sector

Concentration in the seed sector is closely linked to the issue of access to NGTs. The COM study discusses monopolisation in both its challenges and concerns section and the ethics section.[255] The COM study states that different views on the formation of monopolies exist. Regulation of genetic engineering is thought to be a reason for the formation of monopolies, but it is also argued that industrial agriculture and patents increase monopolisation.

These arguments are also found in public debates. For example, Leopoldina et al. (2019, p. 3) suggest that restrictive genetic engineering law could lead to "cost-intensive approval procedures" and thus foster monopolisation tendencies.

This contention is opposed by the argument that that CRISPR tools require laboratory infrastructure, which are only owned and operated by larger enterprises (see ENSSER/CSS, 2021, p. 46). Thus, so this argument holds, small breeder companies require larger partners. Larger companies, in turn, might use small start-ups as innovation hubs. From this viewpoint, new genetic technologies are not in fact easier to employ, but rather more difficult and complicated.

One NGO reports a similar connection. In a brochure published by the *Arbeitsgemeinschaft bäuerliche Landwirtschaft* (ABL, Working Group for Rural Agriculture), the organisation reports a concern that if patents are held by only one company, monopolisation could intensify in the seed sector (see ABL, ed., 2021, p. 72). The large companies would not only hold licences to a technology's use, but also own laboratories and capital as well as maintain the necessary know-how, all of which would solidify the imbalance between smaller and larger companies (see ABL, ed., 2021, p. 19). The interplay between larger and smaller companies, their partnerships and their cooperation seem more complex than the COM study suggests.

The authors of this expert opinion addressed the topic of monopolisation and the relationship between large and small companies over the course of an interview with a relevant expert (Interview 2). This interview revealed that there are a large number of small breeding and research companies, "new companies that actually only came into being in connection with this new genetic engineering" (Interview 2). However, the seed market is dominated by "four giant companies" (Interview 2). The small start-up companies tried to get into the market dominated by the big companies. But this would be very difficult because of the market power of the big companies (see Interview 2). In general, there seems to be a hope among some actors in the debate that by making methods cheaper, the dominance of large companies could be reduced (GEAP3 2020). Small and medium-sized enterprises could weaken the monopoly position of a few seed companies, once the technology is made easy to employ (Leopoldina et al., 2019, p. 3).

It therefore remains to be seen to what extent the NGTs can affect tendencies toward monopolisation. The problem requires a more detailed analysis of the processes, and should be based on an analysis of the interplay of economic processes as well as the opinions of stakeholders.

The extent to which NGTs play a role in monopolisation cannot be explored fully here. However, the COM study clarifies that positions both critical of genetic engineering and those in favour of it view the monopolisation of the seed market critically and seek to a means of

[255] See section 3.6.1.2 "Challenges and concerns of NGT" and section 3.6.1.6 "Ethics" in this expert opinion.

mitigating this development. The topic thus lies outside the hardened fronts between proponents and opponents of current and new genetic technologies. An article in the journal *Forum Wirtschaftsethik* (Forum on Business Ethics), for example, argues that proponents and opponents should stand together against monopolisation (see DNWE, ed., 2018, p. 123). Nonetheless, the COM study indicates that the reasons given by supporters and opponents of monopolisation rationalise their positions differently. The outstanding question is whether alliances can be formed out of these different perspectives.

The COM study furthermore does not specify in which sector monopolisation tendencies are identified or anticipated. In the examples mentioned above, reference is often made to breeding companies and thus only to one stakeholder group that was consulted in the COM study. Are other stakeholders, such as agricultural cultivation companies, wholesalers or retailers, also affected by NGTs? The study does not answer these questions.

3.6.3.2.3 Patents and Innovation

Answers to the targeted consultations, as reported in the COM study, show that patenting both promotes and protects technological development, but can also hinder it. Yet the role of patents in plant breeding is insufficiently dealt with in the COM study. The issue of breeding new plant varieties is complicated by the fact that the relationship between patenting and plant variety protection would have to be discussed. A report by the Federal Ministry of Food and Agriculture in Germany (BMEL, 2017) which summarises the results of a dialogue on the new genetic technologies, states that one problem with patent protection is that it can also extend to conventional products and thus undermine the breeder's privilege. Patent and plant variety protection law would have to be adapted to each other (see BMEL, 2017, p. 10). The final report of the Future Commission on Agriculture of the Federal Ministry of Food and Agriculture also concludes that plant variety protection should be preferred to patent protection and strengthened (ZKL, 2021, p. 114). A report by the Office of Technology Assessment at the German Parliament (TAB), which describes the effects of the use of transgenic seeds on the economic, social and political structures in developing countries, points out that the answer to the question of whether patents promote innovation and increase prosperity can only be answered in a well-founded manner by studies which compare countries and differentiate among them according to types of protection systems and those objects protected (see TAB, 2008, p. 14).

Limitations of space in this expert opinion only allow for a reference to these discussions. But the COM study should have comprehensively analysed these facts in order to prepare a detailed description of the problem, so as to make well-founded and factual statements.

3.6.3.2.4 Appropriation of genetic resources

The appropriation of genetic resources, a prominent aspect of the debate on genetic engineering and new genetic technologies, is not included in the COM study (see for a social science perspective for example Görg 2003, Boyer 2022). In this debate, the issue of patents is not only related to the promotion of innovation, but is also related to securing access rights to genetic resources.

An analysis of the relationship between patents in plant breeding and access rights to genetic resources would provide a good analytical framework.

3.6.3.3 Labelling and consumer protection

The section in the COM study on labelling is also based exclusively on the targeted consultations. Only the stakeholders were asked questions about labelling. The questions were general and aimed to assemble the stakeholders' opinions on this topic. From the stakeholder responses presented in the COM study,[256] the following points, relevant for solving practical problems, can be derived:

- (1) Consumer protection is generally recognised.
- (2) The link between labelling of NGT and NGT products and consumer choice can be seen in opposing ways.
- (3) Labelling of NGT and NGT products has an impact on the farming system in which production takes place.
- (4) The technical possibilities for labelling must be ensured. Similarly, labelling of NGT and NGT products involves costs.

These four aspects are considered in greater detail below.

3.6.3.3.1 Consumer protection

According to the COM study, consumer protection or the consumer right to information and freedom of choice is a generally recognised value among all surveyed stakeholders. Furthermore, consumer protection occupies a central place in the Green Deal strategy of the European Union. The COM study also mentions this, but only by quoting a statement from the targeted consultation. Consumer protection's constitutional status at the EU level is not given equivalent emphasis.[257]

Based on this legal and political dimension of consumer protection, the question arises as to how consumer protection is specified in individual documents, and how labelling or non-labelling of NGT might correspond to this or contradict it. The COM study reflects the assertion of some stakeholders that non-labelling of NGT would contradict the Green Deal strategy. This point should be examined in detail substantively.

3.6.3.3.2 Consumers choice and transparency

Analysis of the different views in the COM study reveals conflicting views on the relationship between NGT and consumer choice in stakeholder consultations on labelling. One statement holds that labelling of NGT products is a prerequisite for freedom of choice. Another contends that labels might mislead consumers. The latter claim is justified by the fact that labels do not necessarily contribute to greater transparency for the consumer and to greater freedom of choice. These contradictory statements raise the question of whether there are studies on the effect of labels for consumers generally, and on NGT labelling in particular.

In this context, the COM study refers to a separate idea expressed in the targeted consultations: a label might also present the benefits of NGT. The question should be asked: what would such a label look like, and would it signify more or less transparency for consumers?

[256] See section 4.9 "Stakeholders' views on the labelling of NGT products" in COM study, 2021, p. 43f. and the summary and analysis of this section in section 3.6.1.4 "Labelling" of this expert opinion.

[257] Consumer policy has a comprehensive legal framework in the EU. See also the new consumer agenda adopted in 2020 (see European Commission, 2020).

Furthermore, it is important to note that labels may refer to products that are produced from NGT (agricultural biotechnology) but also to products that were produced with the help of NGT (industrial biotechnology). In the production of food, for example, genetic engineering is more often used for the production of additives that are not directly incorporated into the product. The direct use of NGT products as food, on the other hand, does not currently take place. A differentiated consideration of freedom of choice depending on the role of NGT in food production would deepen the analyses and help to make the connection between freedom of choice and transparency clearer.

3.6.3.3.3 Agricultural production

The COM study indicates that from the point of view of some stakeholders, labelling is important for the continuation of organic and GMO-free agriculture. This point could be analysed in more depth. The traceability of NGT and the separation of commodity flows need not necessarily lead to a consumer label. On the other hand, the COM study reflects the fear of some stakeholders that labelling NGT products is equivalent to banning them. Again, the question arises as to what justifies this alleged link. Both statements should be seen in the context of current surveys on consumer acceptance: if consumers reject genetic engineering, then labelling would be tantamount to a ban, as consumers would not buy the correspondingly labelled products. For the same reason, consumers could strengthen GMO-free agriculture with their purchasing behaviour. Consumer choice as a means of politics, whether for strengthening ecological or social values, is endorsed and supported by many actors.[258] This concept also reinforces a connection between consumer choice and the coexistence of different agricultural systems. In this context, it must be considered whether consumers should decide, through purchasing behaviour, which agricultural system is promoted and supported.

Two main opposing options are being discussed in the current public and political debate on agriculture. One position favours industrial agriculture, while the other supports ecological agriculture, or agro-ecology (see SCAR 2011). There is also a question of whether there are not more alternatives available.

The discussion in the COM study regarding the sustainability of NGT crops should be viewed in this context. A central argument repeatedly put forward by the COM study is that NGT and NGT products have the potential to contribute to the goals of the Green Deal. This question cannot be answered without considering the agricultural system in which they are used. The several interviews conducted as part of this expert opinion supports this.

Interview 4, for example, raises the question of whether a drought-tolerant and disease-resistant plant would in reality make agriculture more resilient. The interviewee reported that "[s]uch a plant in itself" would "certainly not, if the soil is damaged" (Interview 2). The COM study, by contrast, focusses on a narrower inquiry into the sustainability of specific crops.

The COM study also deals with regulation of NGT as related to either specific products or to processes. In general, from the perspective of sociological technology studies, it can be stated that every instrument or product is always integrated into a social context (Rammert 2016, Weyer 2008, Degele 2002). Especially in high-tech, socio-technical infrastructure is always required for the function of an individual technical artefact. In an interview conducted within the framework of this expert opinion, the idea is illustrated as follows: it is relevant under

[258] For example, the Competence Center for Sustainable Consumption in Germany (Kompetenzzentrum nachhaltiger Konsum, nachhaltigerkonsum.info).

which conditions production takes place, "[...] because the process is one that does not fall from the sky, but requires infrastructures, which requires certain support and socio-economic power and money structures, and so on and so forth" (Interview 4).

With regard to genetically modified plants, the point is illustrated as follows: "In which [...] comprehensive model of agriculture are they actually integrated? [...] If [...] the new genetic technologies are used [in a] – let's say – industrial, pesticide-etcetera patent-based agriculture, if they are integrated there, then they are also problematic from a nature conservation point of view with regard to the associated, perhaps not even consciously intended destruction of soils, reduction of biodiversity and so on and so forth" (Interview 4).

The COM study did not discuss the environmental impact of agricultural systems using genetically modified crops, according to the assessment of an interviewee who had studied the COM study (see Interview 5). Even among the critical public, the use of genetically modified plants was and still is associated with a model of industrial agriculture and monoculture. The current and new genetic technologies would strengthen this model, which is neither sustainable nor future-oriented.[259] This present expert opinion recommends that this debate be taken into account. Accordingly, positions asserting the sustainability of NGT crops first need to substantiate how such technology can be integrated into a system of sustainable agriculture. A claim regarding the sustainability single crop varieties is not sufficient.

3.6.3.3.4 Technical options and costs

The COM study suggests that labelling also requires certain resources. Furthermore, the practical implementation of labelling is linked to the discussion about detection methods. The concrete possibilities for this are seen differently across the stakeholder surveys. Considerations of this content are included in this expert opinion.[260]

3.6.3.4 Findings of dialogues and surveys

The COM study gathered information on public forums and national surveys in the Member States' targeted consultation. This information was listed in the COM study's annex. However, no evaluation of the dialogue forums and national surveys is included. A brief view of the compilation of national surveys in appendix D of the COM study (Table 15, p. 98) shows the following:

- Member States reported 11 national surveys, as also mentioned in the body text of the COM study. Links to some of these reported national surveys are included in the table. The documents found there were reviewed in this present expert opinion. It turned out that the reported national surveys do not always represent quantitative surveys. Some were qualitative in nature, such as the study reported by the Netherlands, conducted in 2017 by InSite Consulting commissioned by the Netherlands (see COM study, 2021, p. 101).
- The surveys refer to different areas of application of genetic engineering and thus not only to agriculture. One example is the study from France conducted by the Institute of Public Opinion (IFOP) on behalf of Alliance VITA on medical applications (see COM study, 2021, p. 99).

[259] "And genetic engineering is made now always for monocultures and relatively large-scale agriculture, in which we do not see that this is the agriculture of the future" (Interview 5).

[260] See section 3.3.3.7 Detection and identification of NGT plants and products in this expert opinion.

Instead of systematically analysing these eleven studies, the COM study refers to Eurobarometers from 2010 on "Food-related risks" (Special Eurobarometer 354), "Biotechnology" (Special Eurobarometer 341), and a Eurobarometer from 2019 on "Food safety in the EU " (Special Eurobarometer Wave EB91.3).[261]

The exact figures referred to in the body text of the COM study (2021, p. 45) are as follows:

- "2010 Eurobarometer on biotechnology, a large majority (84 percent) had heard of GM foods and **61 percent felt uneasy** about them".
- "EFSA 2010 Eurobarometer on food-related risks, where **66 percent of respondents** were worried about GMOs in food and drink".
- "In 2019, a special Eurobarometer on food safety in the EU (requested by EFSA) showed that 60 percent of EU respondents had heard about GM ingredients in food and drinks, and **27 percent were concerned about them**".
- "Specifically on NGTs, the 2019 Eurobarometer reported that only 21 percent of EU consumers had heard of genome editing and **4 percent were concerned about genome editing in foods**".

The COM study does not interpret these figures. It would be incorrect to understand these figures as signifying an increase in acceptance of current and new genetic technologies. The Eurobarometer of 2019 on food security underscores this point:

> "As noted in the Introduction to this report, the Special Eurobarometer survey in 2010 (SP354) asked a similar question. Although the comparison of these results should be taken with caution, as the question wording and response categories were different, respondents' main concerns were similar in 2010 as in the current survey" (Eurobarometer, 2019, p. 39)

The Eurobarometer of 2010 showed that 66 percent of respondents expressed concerns. The question was:

> "Please tell me to what extent you are worried or not about the following issues". Answers: Very worried; Fairly worried; Not very worried; Not at all worried; Don't Know. (see footnote 18, Eurobarometer 2019, p. 39).

Whereas in the 2019 Eurobarometer, which came to a 27 percent disapproval, respondents were first asked what food safety issues they were aware of and then asked:

> "Please tell me which of these topics you have heard about concern you most when it comes to food? Firstly? And then? Total (Max. 5 Answers)". (see Eurobarometer 2019, p. 39, fn. 17).

Respondents were presented with 16 different food safety topics.

In general, both the 2010 Eurobarometer and the 2019 Eurobarometer find large differences between countries' responses to their questions, and thus in their approval of genetic engineering. For the Eurobarometer 2019, the following country differences are cited:

> "Concern about genetically modified ingredients in food or drinks is highest in Lithuania (45 percent), Bulgaria and Greece (both 42 percent) and Latvia (41 percent), while

[261] Special Eurobarometer Wave EB91.3 "Food safety in the EU": https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/Eurobarometer2019_Food-safety-in-the-EU_Full-report.pdf.
Special Eurobarometer 354 "Food-related risks": https://europa.eu/eurobarometer/surveys/detail/1476;
Special Eurobarometer 341 "Biotechnology": https://europa.eu/eurobarometer/surveys/detail/755.

> respondents express the lowest levels of concern in Malta (12 percent) and Finland (13 percent)." (Eurobarometer, 2019, p. 42).

This is emphasised here, as it will help to better understand and contextualise further country-specific studies on the acceptance or rejection of genetic engineering and GMOs mentioned below.

From the list of results of the 11 national surveys in the annex of the COM study it becomes obvious that in some countries a large part of the respondents positions itself against genetic engineering in agriculture and food.

Germany reported four national surveys. Of these, the results of two quantitative surveys are reproduced:

- A study by the Federal Ministry of the Environment, Nature Conservation and Nuclear Safety (BMU) and the Federal Agency for Nature Conservation (BfN) has shown that "**81 percent** of those surveyed **were in favour of banning genetic engineering in agriculture**." (COM study, 2021, Annex D, Table 15, p. 98)
- A survey by the Natural History Museum concludes that **69 percent of visitors to the supermarket project have a problem eating genetically modified food**. They do not agree at all or tend not to agree with the statement "I have no problem eating genetically modified food". (Museum für Naturkunde/YOUSE GmbH, 2019, p. 17)[262]

Lithuania reported one national survey. Table 15 of the COM study does not include figures and only refers to the survey result that rejection of GM food is lower for new genetic technologies. However, reference is made to a document in which these are included.

- According to the survey, more than half (58 percent) of the respondents had a negative or very negative attitude towards genetically modified food. In contrast, 42 percent had a negative attitude towards the new genetic technologies in food. The evaluation then carried out by the study points out that the differences are significant and assumes that the reason for the different rejection rates is the different familiarity of the respondents with the new genetic technologies (see Bašinskienė, 2019, p. 40).
- Less than half of the respondents said that they would buy such food in the future. For genetically modified foods, 42.85 percent and for new genetic technologies, 42.34 percent of consumers said they were likely and very likely to buy such products in the future (see Bašinskienė, 2019, p. 43).

The **Netherlands** reported two national surveys. One survey is qualitative in nature and refers to statements obtained in online citizen interviews. Another survey contains quantitative questions on attitudes towards genetic engineering. The submitted article, however, only gives the mean scale values across all the application areas (environmental, food, medical domains). The article concludes that attitudes towards GM applications are "reasonably positive" (see Hanssen et al., 2018).

As the COM study also notes, the results of the surveys are quite difficult to compare. Not only are there major national differences, but the surveys also cover different issues and applications. This leads to the following questions:

[262] The COM study refers to a link where the results reproduced above can be accessed. Online: https://www.museumfuernaturkunde.berlin/sites/default/files/mfn_broschuere_komplett_erbundgut.pdf.

- In which EU countries is the approval or rejection of genetic engineering traditionally high or low?
- How does the approval or rejection develop in the countries for the individual areas of application? Traditionally, approval rates are higher for medical applications. Applications in the production of additives in food are also less widely criticised.

Investigating the question of whether the population's approval of current genetic engineering techniques is higher than that of new ones seems to be difficult, as surveys from the Netherlands and Lithuania show (see Hanssen et al., 2018, Bašinskienė, 2019). In particular, Bašinskienė (2019) indicate that the new genetic technologies are still little known among the population and that this could have an influence on attitudes towards the new genetic technologies.[263]

3.6.3.5 Key ethical issues

The main arguments from the COM study on the ethics of the new genomic techniques relate to the following issues:

- Ethical concerns about applying the technique to the human germ line and embryos.
- Moral concerns about not applying techniques that bring benefits.
- Legal concepts of precautionary principle vs. proportionality principle as ethical guidelines for action represent two alternatives.

In the paraphrase of the EGE opinion by the COM study, the following was emphasised:

- In a pluralistic society, small stakeholders should also be consulted.[264]

These questions – with the exception of the first, which relates to medical applications and is thus not the focus of the present expert opinion – are discussed in the following sections.

3.6.3.5.1 Moral concerns about not using a technique

A key argument put forward by the COM study is that not using a technique when it brings benefits is morally questionable. The specific benefit referred to here is claimed in relation to the application of NGT to plants and states that NGT plants could contribute to the preservation of biodiversity and the mitigation of climate change. This point raises the question of the extent to which one-sided positive aspects should play a role in a discussion of moral

[263] Furthermore, it should be pointed out at this point that population surveys are also communicated in the public debate. Sometimes surveys are also commissioned by NGOs and associations. One recent example is a survey conducted by Civey, commissioned by the German Association Food without Genetic Engineering (Verband Lebensmittel ohne Gentechnik e.V.) [VLOG] 2022 on eggs from genetically modified chickens (see https://www.ohnegentechnik.org/artikel/versteckte-gentechnik-im-osterei). Another is a survey by Greenpeace conducted by Kantar Public in 2022 (https://cdn.greenpeace.fr/site/uploads/2022/06/Greenpeace_Sondage-OGM_2022.pdf). Another example is a survey in Austria commissioned by ARGE Gentechnikfrei from the market and opinion research institute Marktagent. Online: https://gentechnikfrei.at/studie-gentechnik-freie-produktion-wichtiges-motiv-beim-lebensmitteleinkauf. All three surveys refer to different issues and are country-specific.

[264] Furthermore, the COM study refers to other recommendations on the regulation of new genetic engineering from the EGE report (see section 3.6.1.6 "Ethics" in this expert opinion). The regulation of genetic engineering is discussed in section 3.2 of this expert opinion.

behaviour, without considering negative outcomes. A balance is already established in the concept of risk.[265]

The discussion of negative and positive consequences could be taken as ethical arguments, according to an interview conducted for this present expert opinion, even if they represent factual arguments at their core (Interview 4). The reasoning is that the assessment of whether a specific consequence is a positive or a negative consequence is always dependent on values, and thus represents a value judgement (see Interview 4). Accordingly, a well-founded weighing of positive and negative consequences would be the prerequisite for acting ethically and undertaking political decisions.

This particular expert interview provides a reason to reflect on whether the fact that something might have come into being naturally at all releases humans from their responsibility for their actions: "First and foremost, we are responsible for what we do" (Interview 4). A technology that imitates nature still qualifies as human action. And "the fact that something is natural does not make it better" (Interview 4). Accordingly, there may well be concerns about not acting or not using a technology. However, these would have to be weighed against any risks or negative outcomes. This sequence of considerations could then form the basis for a responsible use of technology.

3.6.3.5.2 Precautionary principle vs. proportionality principle

In the weighing of different arguments, the study discusses the precautionary and proportionality principles. The COM study offers two legal facets of these principles as ethical guidelines for action:

> "Some stakeholders (NGOs) were of the view that the *precautionary principle is a moral action-guiding principle for regulating new biotechnology*. However, others (academics and food business operators) think that, particularly in plant breeding, *it has to be taken together with the proportionality principle* to strengthen the use of scientific evidence and tackle future uncertainties" (emphasis by the authors, COM study, 2021, p. 48).

This presentation of legal principles as ethical guidelines for action is however not justified. Both principles constitute binding law and are not merely non-binding ethical guidelines. The question of the relationship between ethics and politics will be addressed in more detail in the following section.

3.6.3.5.3 Pluralistic society and political action

The EGE opinion points out that in a pluralistic society, small stakeholders must also be heard from. In this context, the question arises as to how attitudes in the population relate to political action. This question also arises because, as was made clear in the section on dialogue procedures and population surveys (see section 3.6.3.4 "Dialogues and surveys" in this expert opinion), popular consent is often used as an argument to justify particular policies.

Interview 4, which was conducted as part of the present expert opinion, offers a commentary on this problem. It contends that there is a difference between acceptance and acceptability (Interview 4). Acceptability refers to what is considered morally correct in a society, whereas acceptability refers to the moral justification for certain actions. Accordingly, certain moral concepts that are widely regarded as right socially can therefore also be translated into legal

[265] See section 3.6.2.2 "No risk-benefit debate" of this expert opinion.

regulations. However, it is also justifiable to make legal regulations that are not yet considered morally correct by a majority of the population when good reasons can be given for doing so (Interview 4). "In some places, politics has to do something differently even against the voice of the people – to put it polemically" (Interview 4).

The attitudes of the population collected in participation processes or the views of stakeholders cannot be translated immediately and literally into specific policies. For this reason, especially regarding socially controversial fields, although diversity of opinion is sought, ethics reports are also prepared in order to establish the reasoning behind each position. Ultimately, however, democratically elected representatives must make the key decisions (see Interview 4). The European Commission followed both lines of approval the context of the study: it "sought the plurality of opinions" and obtained an ethics report. From an ethical perspective, however, the Commission should inquire further so as to justify why one position is more desirable than another. "On what basis do we now say: We have preserved the plurality of opinions, but is this position now plausibly justified or not and how do we now deal with it? And that is then the actual decisive question" (Interview 4).

Consequently, in modern society there are complex relationships between moral concepts, attitudes in the population, social debates with a pluralistic diversity of opinions, and political regulation. A careful balancing in the sense of the common good is a task that the COM study also demands of political actors. This is shown by the following quotation:

"Stakeholders have different and often opposing views on NGTs and their products. Any further policy action should aim to reap the benefits of innovation while addressing concerns; efforts should be made to reconcile opposing views in order to find common ground to address the issues identified in this study" (COM study, 2012, p. 59).

3.6.3.6 Development policy argumentation

A classic line of argument to support the claim of benefits of genetic engineering is to present it as an important tool for fighting world hunger. The benefit of agricultural genetic engineering is thus seen as bringing advantages to developing countries and small farmers. However, these arguments are only mentioned in the margins of the COM study. Only in Annex D, Table 8 is reference made to world hunger. Furthermore, in section 4.11.1 "Member States' views" of the COM study, which includes the views of the Member States on ethics, a developmental policy argument is presented.[266]

Thus, although the developmental policy line of argumentation is missing from the COM study, it is nevertheless present both among the stakeholders surveyed and in the public debate.

- The following stakeholders refer to the argument that genetically modified plants can contribute to alleviating world hunger in their questionnaires:
  - Plants for the Future' European Technology Platform, p. 22;
  - International Confederation of European Beet Growers (CIBE), p. 16
  - Euroseeds, p. 36
  - European Plant Science Organisation (EPSO), p. 32
  - The Committee of Professional Agricultural Organisations of the European Union,

[266] See also section 3.6.1.6 "Ethics".

called "Copa", p. 4

- In some cases, explicit reference is made to SDG 2 (Zero Hunger).

The COM study thus rehearses an existing debate and gives the impression that the discussion could now revolve around the realisation of sustainable agriculture. Some actors are of the opinion that this is only possible with genetic engineering, while others hold its prohibition is required. This line of conflict is also highlighted in the conclusions of the COM study (see COM study, 2021, p. 59f.).

> „A more sustainable agri-food system, is a key objective of the European Green Deal and in particular of the "farm to fork " and biodiversity strategies. To enable NGT products to contribute to sustainability, an appropriate mechanism to evaluate their benefits should be considered. At the same time, NGT applications in the agricultural sector should not undermine other aspects of sustainable food production, e.g. as regards organic agriculture" (COM study, 2021, p. 59).

3.6.4 Interim summary of ethical and socio-economic implications

Chapter 3.6 aims to analyse the ethical and socio-economic implications of NGTs in the COM study. During the preparation of the present expert opinion, it became apparent that there are no statements at the substantive level on the ethical and socio-economic implications in the COM study. The COM study only reflects the statements of the two targeted consultations – the stakeholder consultation and the consultation of the Member States. The approach of the COM study in this respect has already been criticized in other parts of the present expert opinion.

Other criticisms of the COM study, which emerged particularly in the analysis of the socio-economic and ethical aspects, were firstly that practical problems were only touched on and not discussed. One focus of the COM study was, for example, the impact of NGT on SMEs. This question could not be answered with the methods used; rather, a need for further research was identified. Secondly, the COM study avoids talking about risks. Instead of using the term "risk" and contrasting it with certain benefits, the study redefines the positive and negative aspects of a technological application. On the one hand, the COM study focuses on "opportunities and benefits". On the other hand, it lists "challenges and concerns". It can be shown by this expert opinion that "challenges" means not only the possible negative consequences for health, the environment and the economy, but also obstacles to the realisation of benefits. This conflates problems of technology users with problems of those affected by a technology application. A final problem is the view of the consumer. When looking at surveys and citizen dialogues on NGTs, people are not portrayed as citizens but as consumers. This is done under the overarching assumption that consumer acceptance of NGT will facilitate the technology's application. This denies them the right to have a say.

Moreover, an important drawback of the COM study is that it does not move from the presentation of the arguments to the central problems at the substantive level. For example, stakeholders express specific problems and challenges in dealing with NGT plants and products in their responses in the targeted consultations. The COM study presents the challenges and problems with NGT plants and products via the stakeholder survey. However, for each of these problem areas, there is also a scientific debate that is not addressed in the COM study. This expert opinion refers to these debates wherever possible to highlight this shortcoming of the COM study (see Section 3.6.3 "How well researched and substantiated are the COM study's

statements on the ethical and socioeconomic implications of NGT"). Within the scope of the present expert opinion, neither a systematic evaluation of the completed questionnaires nor a systematic review of the scientific debate was possible. This would have been a task of the COM study.

3.7 Considering ECJ-Judgement C-528/16

As it was the express wish of the Council of the European Union to prepare a study "in light of the ECJ's decision C-528/15" (COM study, 2021, p.2), the following remarks will scrutinize the extent to which the Commission complied with this request. The evaluation of this point is structured in two separate sections according to aspects of the decision.

3.7.1 Which issues of this decision were considered?

3.7.1.1 Interpretation of the exemption

First, the COM study deals with the interpretation of the exemption according to Art. 3 para 1 in conjunction with Annex I B of Directive 2001/18/EC (COM study, p. 5) and quotes the court according to which "only organisms obtained by means of techniques/methods of mutagenesis which have been conventionally used in a number of applications and have a long safety record are excluded from the scope of that Directive". However, the study lacks the necessary precision. It does not distinguish between directed mutagenesis (to which the Directive applies) and random mutagenesis (to which the Directive does not apply). Nor does the COM study list the most important use cases for the latter, namely chemical or physical mutagenesis, in contrast to the ECJ (ECJ, 2018).

On the other hand, the study interprets the decision unilaterally by claiming that it only applies to mutagenesis, but not to other NGTs. From a purely procedural point of view, this view may be correct, since the subject matter of this request for a preliminary ruling was indeed mutagenesis alone. However, the study disregards the fundamental reason for the ECJ's decision, according to which only a history of safe use justifies an exclusion from the Directive. (see Chapter 3.7.2.2 below).

Particular attention must be paid to the fact that, "as a provision derogating from the requirement to subject GMOs to the obligations laid down in Directive 2001/18, Article 3(1) thereof, read in conjunction with point 1 of Annex I B to that Directive, must be interpreted strictly" (ECJ, 2018, para. 189).

In this respect, the hurdles for a possible exemption of NGTs from obligations of the Directive are high. The COM study does not succeed in sufficiently justifying why the ruling should be limited to the specific applications of directed mutagenesis.

3.7.1.2 Consequences of the ruling for research

The study furthermore refers to the fact that the decision would have negative consequences for public and private research on NGTs (COM study, p. 2, 36, 51). It cites as examples applications for field trials which had to been withdrawn in the wake of the ECJ decision (COM study, p. 28). However, the study also indicates that elements of the food industry also see this development as an opportunity to investigate less risky alternatives to NGTs more (COM study, p. 37).

3.7.1.3 Scope and objectives of the study

The COM study deals with the ECJ decision in its description of its own scope and objectives (COM study, p. 6). In doing so, the COM study narrows down the ECJ ruling by only referring to its decision on mutagenesis. When the study correctly states that the Council's mandate is broader and concerns all NGTs, it thereby gives the impression that the main reasons for the ECJ's decision regarding the history of safe use apply exclusively to mutagenesis and do not apply to the remaining NGTs, which are in fact covered by the study.

3.7.1.4 Applicability of the ECJ ruling to contained uses

In another chapter, the COM study addresses the question of whether the ECJ ruling also applies to limited contained use involving microorganisms. From a legal point of view, it thus raises the question of whether the judgment applies not only to releases under the Deliberate Release Directive 2001/18/EC, but also to contained uses under the Systems Directive 2009/41/EC. This question is justified, given the fact that only the application of the Deliberate Release Directive has been disputed, which has led to some Member States deciding that the Directive does not apply to contained uses.[267] In contrast to its position on the question of the applicability of the judgment to NGT to other than mutagenesis, the study here takes a broad interpretation of the scope of the decision and seeks to apply it also to the Systems Directive 2009/41/EC. This view is consistent given the GMO definition in Article 2 lit. b Directive 2009/41/EC, which is identical in essence to the definition in the Deliberate Release Directive.

3.7.1.5 Interpretation of the term "altered"

The study also refers to the ECJ judgment in the context of the definition of the word "altered" according to Art. No. 2 Dir. 2001/18/EC (COM study, p. 22). According to the Commission, this point should be an issue when it comes to genetic modifications that do not lead to a change in the nucleic acid sequence, which is often the case with NGTs. Here, the COM study discusses the question of whether such genetic modifications by NGTs still fall within the scope of the Directive at all. As a result, it argues that such alterations should no longer be covered by the Directive from the outset, citing judgment C-528/16. Specifically, the study states that the restrictive interpretation of the word "mutagenesis" also implies a restrictive interpretation of the word "altered " (COM study, p. 22).

This conclusion cannot be based on any legal methodology. One searches in vain for its reasoning; it appears simply to be an unsupported assertion. An attempt to conclusively define the interpretation of one term – namely the term "mutagenesis" in Annex I B of the Directive – from an interpretation of a completely different term – namely the term GMO in Art. 2 No. 2 of the Directive – does not make sense from a legal point of view.

Above all, the study's conclusion does not comply with the ECJ's findings. The ECJ advocated a narrow interpretation of the exemption for mutagenesis in order to give the Directive the broadest possible scope of application for reasons of the precautionary principle. However, a narrow interpretation of the term "altered", in which genetic modifications by NGTs fall outside the scope of the Directive if there is no change in the nucleic acid sequence, would lead to a considerable reduction in the scope of the Directive and thus weaken the precautionary principle. This conclusion of the COM study is also surprising because the COM study even explicitly mentions the precautionary principle in its considerations (COM study, p. 22).

[267] Questionnaire Finland, Annex 1, B, p 3 (4).

3.7.1.6 Clarification of undefined legal terms

Finally, the study cites decision C-528/16 as evidence that numerous indeterminate legal concepts related to NGTs must be clarified (COM study, p. 54) and highlights the concept of mutagenesis, of all things, for this purpose.

Here, too, the study interprets the result of the ECJ's decision differently, as the ECJ had eliminated any ambiguity regarding the term "mutagenesis" in this decision. Since this objection[268] was likely anticipated, an alternate reason was given as to why this term had to be "clarified"; the study then criticised the ECJ for having been forced to clarify this term on the basis of other elements of the Directive, given the ambiguity of the term mutagenesis itself (COM study, p. 54). Clarifying legal terms on the basis of other elements of a legal instrument, however, has been found in nearly every decision of the ECJ for decades. It is one of the most important methods of legal interpretation, called "systematic interpretation" and it is a natural part of all modern legal systems. To cite this as a reason for the need for clarification fails to recognise fundamental methods of legal interpretation.

3.7.2 Which issues of this decision were not considered?

The main basis for the ECJ's decision is to be found in the precautionary principle and the need for a history of safe use for deregulation through sectoral exemptions such as Annex I B to Directive 2001/18/EC. In the following, it is shown that both key reasons for the decision were only marginally considered in the COM study.

3.7.2.1 Precautionary principle

The precautionary principle is mentioned from time to time in the COM study. However, in the study's own considerations, this principle appears only six times, and is only mentioned at these points without reference to the central importance that the ECJ attached to the principle in its decision.

The court emphasises in numerous places that the precautionary principle requires, that products developed with such technology should not be released into the environment without an extensive risk assessment, especially in situations where too little known about the risks of a technology (ECJ, 2018).

Applied to NGTs, this basic statement means that deregulation can only be considered at all if the risks posed by NGTs are first clarified. The COM study does not address this point, however, but rather claims that certain NGTs are harmless because of their similarity to natural changes. The study even dismisses the precautionary principle as potentially harmful when dealing with the challenges of climate-change mitigation and sustainability:

> "A purely safety-based risk assessment may not be enough to promote sustainability and contribute to the objectives of the European Green Deal and in particular the 'farm to fork' and biodiversity strategies; benefits contributing to sustainability would also need to be evaluated, so an appropriate mechanism to accompany risk assessment may be required" (COM study, Executive Summary, p. 4).

It is also striking that the explanations in which the study deals with the alleged benefits of NGTs are disproportionate to the explanations of the precautionary principle. For example, in the Commission text itself, the precautionary principle is mentioned superficially only six

[268] The objection that there is no need for any clarification of this concept after the ECJ decision.

times, while the study alone deals 15 times with the alleged benefits of NGTs for the farm-to-fork strategy, 11 times with the supposed benefits of NGTs for combating climate change, and 4 times with the benefits of NGTs for the pursuit of the SDGs. In other words, the study does not consider it necessary to address the ECJ's considerations on the precautionary principle.

A further disregard of the precautionary principle lies in the lack of consideration of the rapid development in the field of NGTs, which the Commission notes in several places (COM study, p. 2). If a technology, whose ecosystem effects in particular have hardly been researched to date and which can also bring about precise changes, develops at a rapid pace, this increases the potential risks. In its ruling in case C-528/16 the ECJ brought forward this argument explicitly. The court states

> "that the direct modification of the genetic material of an organism through mutagenesis makes it possible to obtain the same effects as the introduction of a foreign gene into that organism and, secondly, that the development of those new techniques/methods makes it possible to produce genetically modified varieties at a rate and in quantities quite unlike those resulting from the application of conventional methods of random mutagenesis" (ECJ, 2018).

This once again calls for the precautionary principle to be taken into account regarding NGTs.

3.7.2.2 History of safe use

Similar striking is the COM study´s passing over statements of the ECJ's on the history of safe use, i.e., the findings based on recital 17 of the Directive that only mutagenesis methods that have long been considered safe are exempt from the Directive (ECJ, 2018, para 54). This statement, which is most central to practical policy, is mentioned only twice in passing, without substantive explication. Indeed, if the ECJ states that only those mutagenesis procedures that have long been considered safe may be deregulated, this obviously applies to all other NGT procedures as well. A study whose explicit mandate was to investigate the legal status of NGTs in light of the ECJ decision should have first and foremost have investigated whether and for which other NGTs there is a history of safe use. This omission does not do justice to the study´s mission or the significance of the ECJ ruling.

3.8 Overall structure and argumentation of the COM study

In this present expert opinion, two possible approaches have been mentioned regarding the evaluation of the results of the COM study (see section 3.1 "General criticism of the methodological approach of the Commission's study", above). Firstly, such an evaluation requires an analysis of the presentation of the study's arguments and, secondly, the identification of those arguments from the main body of the COM study which reappear in the two closing chapters and the executive summary.[269] It is therefore of particular interest which of the themes, arguments and strands of discussion presented in the study are emphasised in the two concluding chapters and which are considered secondary. In the following, we will first assess how the arguments are presented in the study (section "Presentation of the arguments"), and then follow up with an analysis of the two final chapters (section "Presentation of the topics"), and a brief evaluation of the findings (section "Evaluation of the overall structure and argumentation of the COM study").

[269] Another possible approach is to analyse the existing questionnaires and show how the arguments expressed there were taken up in the COM study. Such a re-analysis of the two targeted consultations could not be carried out by this expert opinion.

3.8.1 Presentation of the arguments

In general, the study strives for a balanced presentation of the debate on the NGTs. This corresponds to the self-formulated claim of the COM study to analyse "all views collected [...] on their own merit" (COM study, 2021, p. 8). However, when reproducing arguments from the cited expert opinions and studies as well as the targeted consultations, it is not always clear whether it is a statement from the study, a paraphrased statement from one of the expert opinions or a statement from the targeted consultation.

The COM study also tries to make transparent by whom and how often certain arguments were expressed in the targeted consultations. At some places, the COM study refers to opposing positions or discussion fronts. How many of the stakeholders or Member States made each respective argument (use of the frequency statements "some", "most" and "several") is also mostly consistently indicated, though not in all cases. The presentation does not appear to follow a systematic analysis and lacks a fixed scale. Assignments of stakeholders to specific groups and the group boundaries are likewise ambiguous. The study's division of participants into groups often changes depending on the section and argument presented. Labelling the lines of division in the debate also does not seem to be a systematic process. The analysis therefore at many points appears quite arbitrary.

In the COM study, as has already been mentioned, levels of reality are not clearly separated.[270] Not all statements by stakeholders and Member States are marked as such. Instead, they are presented as facts. This approach, which presents opinions as facts, is observed especially when the study paraphrases positions of NGT proponents. Critical statements tend to be presented as opinions of a stakeholder group, and additional relativising arguments are then often introduced. The following example from one of the final chapters of the COM study illustrates.

1. "Several plant NGT products [...], could contribute to the Green Deal, [...]."
2. "Examples of benefits include plants that are more resistant to diseases and environmental conditions or climate change effects in general, improved agronomic or nutritional traits, reduced use of agricultural inputs, including plant protection products, adaptation of varieties to local needs, or preservation of traditional or niche varieties."
3. "In contrast, it has been claimed that the proposed benefits of NGTs in agriculture are hypothetical and that they could be achieved by means other than biotechnology."
4. "Particularly strong concerns were expressed by several Member States, operators in the organic/GM-free premium market sector and NGOs. They argued that the organic/GM-free value chain could face severe threats from certain NGTs, which runs counter to the Green Deal […]."
5. "Nonetheless, the organic sector uses seeds that may also result from conventional mutagenesis and are hence GMOs not subject to the obligations of the Directive." (COM study, 2021, p. 52; Numbering of sentences by the authors of the present expert opinion).

[270] By levels of reality was meant that there are, on the one hand, scientifically based statements concerning processes in nature or the material basis of society, and, on the other hand, scientifically based statements concerning the opinions or attitudes of citizens or stakeholders. See section 3.1.2.2.5 "Evidence is not distinguished from opinion" in this expert opinion.

In the first sentence, the form "could" is still used. In the second sentence, the prospective benefits are listed as if they have already been confirmed. A promised benefit thus is transformed into a known property. In the third sentence, the opposing argument is presented in such a way that its correct qualification of a promised benefit as hypothetical is dismissed as a mere assertion. The argument is credited to a specific author in the fourth sentence and is thus presented as opinion rather than fact. In the fifth sentence, this opposing argument is undermined by an unsubstantiated claim by the COM study. Thus, although the study presents both lines of argument, it clearly takes the side of expected benefits (which it presents as more real than concerns).[271] In the first two sentences, the arguments appear anonymous and universally valid; in the fourth and fifth sentences, they are tied back to a specific author and thus presented as personal opinions.[272]

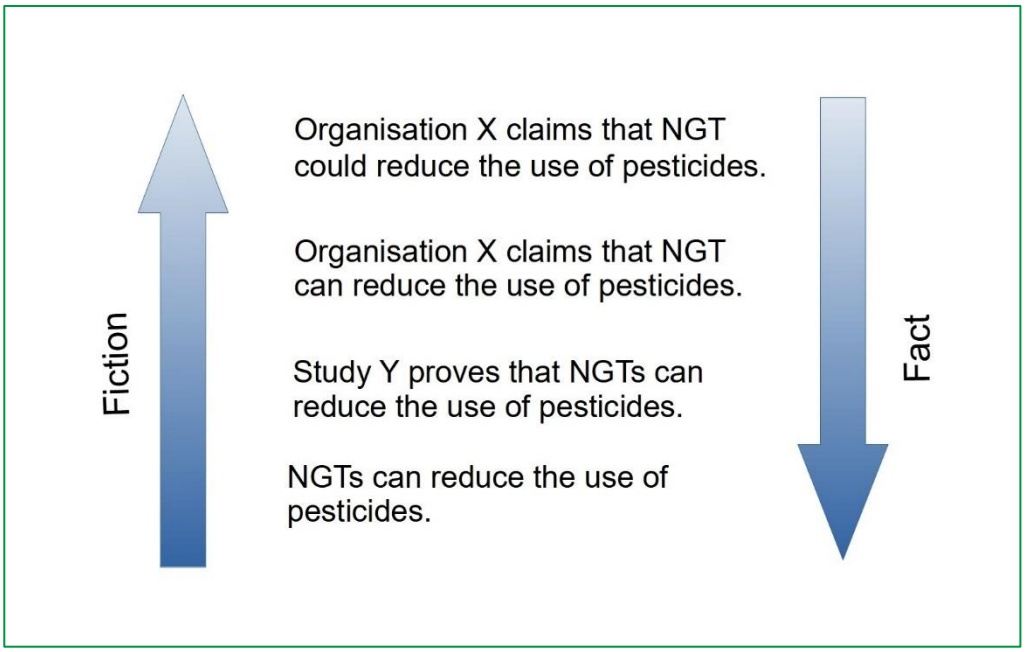

Figure 3: Rhetorical strategy: Implicitly, some arguments are presented as more real than others. Own illustration, inspired by Latour 1987, p. 44.

3.8.2 Presentation of the topics

In the two concluding chapters, the COM study discusses the results of the presented material and reaches its conclusions:

[271] This procedure of analysing and interpreting an excerpted text follows the approach of Latour 1987, p. 21ff. Latour argues that in (scientific) controversies, a common rhetorical strategy is to present competing statements as arbitrary observations of an individual at a certain place and time. Statements only appear to be facts when they are made in a generally valid manner without reference to an author and a specific situation.

[272] This line of argument also makes the study appear one-sided to observers of the debate from the NGO sector. See interview 5, which was conducted as part of this expert opinion: "[This is] one thing about this study that is really, that's what I mean by it, extremely one-sided. [In] the press release about it says that the new genetic engineering can contribute to sustainability, not 'could'. But it could be that there are risks, yes? So one is communicated as fact, with 'can' (contribute to sustainability) and the other is 'may'" (Interview 5).

> "(…) the objective of this study is to provide clarity on NGTs, in the form of updated and comprehensive information, on a broad variety of topics and assist in deciding, if appropriate, any further action in this policy area." (COM study, 2021, p. 6)

Chapter 5, "Discussions", of the COM study begins with a paragraph on research and potential applications of NGT (see COM study, 2021, pp. 51-52). In particular, it deals with the role of CRISPR/Cas technology as a "game changer" and it highlights the dynamics of certain developments. The COM study discusses the influences of regulation on these dynamics based on the comments of Member States and stakeholders. There seems to be some concern that EU regulation could have a negative impact on research and development. The description of the dynamics itself remains vague (for example, it employs multiple qualifiers, as in the phrase, "appear already to be a reality", COM study, 2021, p. 51), and some of the formulations are difficult to understand:

> "As NGT-related research is increasing, so too are its potential applications in plants, animals and micro-organisms for the agri-food, industrial and medicinal sectors, with tens of applications potentially reaching market stage in the next 5 years and even hundreds in the next 10 years" (COM study, 2021, p. 51, see also section 3.4.3, above).

In sum, the Commission study tries to render a positive picture of NGT, which it justifies mainly through anticipated developments. Those doubts expressed by ("some") stakeholders are mentioned only briefly.

Following the presentation of research and potential application of new genetic technologies, reference is made to the two EU strategies Green Deal and Farm to Fork Strategy (see COM study, 2021, p. 52). The claim is made that plants developed with NGT will contribute to realising these strategies. The JRC review on the use of NGT (Parisi & Rodríguez-Cerezo, 2021) is cited in this case as evidence. Certain expected benefits of NGT-produced products, especially of plants, are then presented. These expected beneficial traits include resistance to diseases, resilience under changing environmental conditions such as those induced by climate change, improved agronomic and nutritional properties, reduction of agricultural inputs, improved crop protection, adaptation to local conditions, and preservation of traditional and niche varieties.

It is not clear to the reader here how the currently formulated expected NGT benefits relate to the actual development stages of NGT plants. In the JRC Review on which the COM study essentially bases itself here, the presentation of concrete plants or crop species with concrete properties is practically omitted in its entirety. The review describes above all which plant groups (e.g. cereals) or which properties (e.g. tolerance to biotic stress) are being researched and developed. Projects which combine these different aims (for example, maize tolerant to pests such as the corn rootworm) is not the subject of the review. Consequently, there is also no speculation about the concrete benefits of individual NGT plants that may be available in the future.

The UN SDGs, the European Green Deal, the EU Farm to Fork Strategy and Biodiversity Strategy are not mentioned at all in the JRC report. Accordingly, the wording in the Commission study that

> "[s]everal plant NGT products identified in the JRC review, from R&D to the market stage, could contribute to the Green Deal, and more specifically to the 'farm to fork' and biodiversity strategy objectives of a more resilient and sustainable agri-food system, and to the UN SDGs" (see COM study, 2021, p. 52)

is misleading. This is all the more true as it remains unclear in this quotation whether this is the assessment of the COM study or that of the JRC review.

The list of expected benefits is followed by a presentation of the opposite side. The opposite arguments hold that expected benefits are hypothetical and that the same product characteristics could also be achieved with other methods (see COM study, p. 52). The negative impact on GMO-free agriculture is held to be a problem for many Member States and stakeholders. In their opinion, such a policy would contradict the two EU strategies mentioned above, the Green Deal and Farm to Fork Strategy.

The disagreement is clearly emphasised here. However, in conclusion, the study renders the juxtaposition of what was initially two equal viewpoints in a manner decisively favouring one over another:

> "Nonetheless, the organic sector uses seeds that may also result from conventional mutagenesis and are hence GMOs not subject to the obligations of the Directive." (COM study, 2021, p. 52)

This sentence effectively asserts that organic farming also uses genetic engineering, and so ultimately implies that mutagenesis should not be a problem for organic farming. This is, however, misleading. In 2001, the European legislature deliberately excluded only random mutagenesis (i.e. mutagenesis using chemicals or radiation) from the scope of the Directive,[273] as this had already a history of safe use.[274] However, this exception does not apply to targeted mutagenesis which uses genetic engineering, precisely because it has not yet been established that it has a safe history of use. This point been explicitly decided on by the ECJ (ECJ 2018).

The complete section on hypothetically beneficial expectations can therefore be seen as an example of how the arguments of the proponents are more likely to be supported by the COM study than those of the critics.[275] Furthermore, multiple issues are conflated in the study. Can the expected benefits be realised? If they can be realised, do they help to implement the EU strategies or not? These are two separate questions.

In the subsequent sections, the study discusses questions pertaining to NGT safety (see COM study, 2021, pp. 52-53). The study states that safety cannot be definitively assessed. It then notes that there are different views among Member States and stakeholders as to whether NGT especially "SDN-based" techniques used in plant applications (COM study, 2021, p. 53) and its products are safe and require a risk assessment.

Partly, however, the comparisons of different views are unsorted, so that the reader is left with at best a clue of the existing differences. For example, this is the case with the discussion of the case-by-case assessment. Here, first of all, are the corresponding five sentences from the discussion chapter of the COM study:

1. "Case-by-case assessment is widely recognised as the appropriate approach."
2. "EFSA and the Member State opinions agree on the need for flexibility and proportionality in risk assessment methodologies and data requirements, to take account of available knowledge on the history of use of the modification(s) and the trait(s) introduced."

[273] Annex I.B (1) of Directive 2001/18/EC.
[274] Recital 17 of Directive 2001/18/EC.
[275] See also the example in the previous section of this expert opinion 3.8.1 "Presentation of the arguments".

3. "On these points, not all stakeholders share the expert body opinions."
4. "Several Member States and stakeholders see a need to develop specific risk-assessment procedures for NGTs."
5. "Some stakeholders called for research on safety and environmental risks linked to unintended adverse effects and NGT products' interaction with the environment." (COM study, 2021, p. 53; Numbering by the authors of the present expert opinion).

In the first sentence, the COM study makes a relatively broad statement in support of case-by-case assessment. In the second sentence, this statement is concretised by means of examples. Subsequently, in the third sentence, differences are expressed with regard to the concretisations formulated in the second sentence. In the fourth sentence, it remains open whether it should be read more in the sense of supporting sentence one or supporting sentence three. The last sentence (five) opens up a new topic, which, however, can also be understood as a concretisation of sentence three. Moreover, the COM study undercuts in sentence five that the investigation of off-target effects is not only demanded by "[s]ome stakeholders", but also by Member States (see below). The change of the respective groups (Member States, stakeholders, EFSA) mentioned in each case between the sentences also does not contribute to a better understanding for the reader. An essential point in this context is also the following: The COM study does not establish clarity about what exactly the individual actors associate with the term case-by-case assessment.

For example, it is not explicitly addressed at which point a case-by-case assessment comes into play. For example, whether as part of a mandatory environmental impact assessment in the context of an equally mandatory authorisation procedure. Or does it already come into play, for example, as part of the decision as to whether a licensing procedure is considered necessary at all for a particular NGT application? (Instead of the trigger genetic engineering/NGT) Further details remain completely open. It also remains open what information is necessary for such an assessment, or how the nature and extent of the necessary information is to be determined. The reason for this approach can only be speculated within the scope of the present expert opinion. One possible reading is that the COM study artificially creates consensus this way. What follows is a series of findings, usually from EFSA, which together form a substantial part of the basis of the COM study. Each finding in itself can hardly be criticised. However, important connections remain unsaid. As a result, a misleading picture emerges overall. To put it in an example: "Some expert opinions consider that genetically and phenotypically similar products deriving from the use of different techniques are not expected to present significantly different risks" (COM study, p. 53). This quote naturally raises the question of what other experts have to say about it (since the COM study already specifies the restriction "some"). Another example: "In particular, EFSA did not identify new hazards linked to SDN-1, SDN-2 or ODM, as compared with conventional breeding and established genomic techniques" (COM study, p. 53). In the COM study (and in the present expert opinion) it is emphasised elsewhere (see COM study, 2021, p. 30 and section 3.5.1.1.4 above) that with regard to ODM techniques "less information is available in the literature, in particular on its molecular mechanism and off-target modifications". And it is not clarified to what extent this information is sufficient to draw a qualified picture of the risks associated with this technology. The specificity of genome editing techniques is a key aspect for their safety, writes the COM study. Subsequently, the COM study emphasises the concordant assessments of Member States and EFSA that the [development of] SDN technology is a substantial advance over random mutagenesis. This is also supported by SAM HLG and the JRC, as the COM study goes on

(see COM study, p. 53). However, the combination of the sentences here is at least problematic, because the statement of the first sentence seems to be supported by the second sentence. Although there is agreement between Member States and EFSA on the development of NGT, there is no agreement on the significance of the specificity of NGT for safety. On this point, the assessments diverge in part very clearly (see COM study, 2021, p. 31f.).

Above, the missing of the demand for consideration of off-target effects has already been presented. In addition, with regard to off-target effects, it is repeated that the COM study presents the arguments of Member States and stakeholders who express concerns about the off-target effects of NGTs as opinions. Strictly speaking, the arguments are not mentioned here. The COM study writes of "some concerns on off-target modifications" (COM study, p. 53). In contrast, it presents EFSA's position – in short: there are no problems with off-target effects – with "recent experimental evidence" as scientific fact. The EFSA position is quantitatively much more extensive (in a ratio of one to three) and detailed. The fact that, for example, the "views" of Member States and stakeholders also refer – at least in part – to scientific publications remains unmentioned. As already formulated above, the impression is created that the more NGT-friendly EFSA position is preferred by the COM study.

Another inaccuracy shines through this section on risk assessment and safety of NGT plants and products: The COM study argues with terms such as "similarity" (for example with "genetically and phenotypically similar products", with "similarities between cisgenesis and conventional plant breeding" or with "similar hazards to conventional plant breeding"), or "same type as" (COM study, p. 53 and 54, see also Chapter 3.3.1.1 of the present expert opinion). The terms, the similarities (but also the differences), are not explained in a sufficiently differentiated way – neither here nor elsewhere in the COM study. This inaccuracy comes into play, for example, in the following paragraph of the discussion chapter of the COM study. In it, the COM study reports "similarities between cisgenesis and conventional plant breeding" (COM study, 2021, p. 53) noted by EFSA and other Member states [sic!] expert opinions.

The COM study then comes to the request of the Council of the EU to prepare a study on NGT and to address the EU's GM legislation (Council of the EU, 2019). The COM study emphasises two things in this context: First, the Council of the EU recognised that the definition of genetically modified organisms in Directive 2001/18/EC and the associated list of techniques had been drafted in the light of the techniques available at the time. Based on this, the COM study formulates its reading of which techniques lead to the application of the Directive: "the GMO legislation applies to organisms obtained through new mutagenesis techniques, cisgenesis and intragenesis, and organisms in which the genetic material is altered without changing the nucleic acid sequence" (COM study, p. 54).

Second, the COM study provides a list of terms and concepts which, even after the ruling of the EU Court of Justice of 25 July 2018 (Case C-528/16), "have given rise to ambiguity" (COM study, pp. 54-52). Due to the particular importance of the relationship between the ECJ ruling in Case C-528/16 and the COM study (the Council formulated "a study in light of the Court of Justice's judgment in Case C-528/16"; Council of the EU, 2019), this is discussed in detail in a separate section of the present expert opinion (see Chapter 3.7 above).

The COM study refers in a kind of interim conclusion of the discussion chapter to certain aspects of the evaluations of the GMO legislation of 2010 and 2011. It stated that the COM study had shown – like the evaluations of 2010 and 2011 – that "some new techniques create new

challenges for the regulatory system" (COM study, p. 55). At this point in the discussion chapter, however, the COM study leaves open the nature of these challenges.

A glance at the 2011 evaluation shows:

> "Some of the new techniques available create new challenges for the regulatory system because there is no recombinant DNA in the product placed on the market. The biotech industry is against expansion of the legislation's scope. Certainly, expansion of the system's scope to new techniques without improvements to its efficiency would, in effect, automatically bar any products produced with those techniques from the EU market" (EPEC, 2011, p. 74).

However, it also says: "But some consultees are concerned about the potential impacts of the products derived from new techniques" (EPEC, 2011, p. 74). In this context, the COM study states that many stakeholders complained about the lack of reliable detection methods (see COM study, 2021, pp. 55-57). These reliable detection methods are seen as a precondition for applying the existing GMO legislation. The issue of proof, identification and related traceability is important for both Member States and stakeholders. In general, stakeholders are concerned because they cannot see how compliance with current rules will be met. At the same time, the COM study demonstrates the feasibility of paper-based documentation. One objection to this alternative is financial. In this context, the COM study shows that one third of the non-EU states examined in the COM study have introduced new regulations. This might lead to problems, as "many" Member States believe. "In certain cases", so the COM study reports, it is to be expected that traces of unauthorised NGT plants will not be determined in a court of law. However, the COM study does not provide a detailed characterisation of such cases. Attempts to solve the problem are not discussed by the COM study (see, for example, Chhalliyil et al., 2020 and Chapter 3.3.5.1 in the present expert opinion; Chhalliyil et al. present a method for detection and identification).

The COM study highlights the concern from the targeted consultations that regulation could lead to trade barriers subject to sanction by the WTO (see COM study, 2021, p. 57). Furthermore, the COM study points out that its findings from the targeted consultations are not clear whether regulation is more likely to harm or benefit SMEs and under which conditions monopolisation processes are more probable (see COM study, 2021, p. 57). It is also unclear what effects patenting has on innovation, whether patents are rather a motor or an obstacle for innovation. The COM study bases these statements entirely on its two targeted consultations.

This is followed by a brief presentation on ethics (see COM study, 2021, p. 57). The study states that many concerns expressed in the targeted consultations only concern products and not the technology itself. There are very different and contradictory views on ethical aspects and furthermore, for some respondents it is unethical to use NGT and for others to not use it. Finally, some respondents understand the precautionary principle and also the proportionality principle as ethical guidelines for policy. Yet both principles are binding law and not just non-binding ethical guidelines.

Another important issue that the COM study emphasises in the concluding section is consumer acceptance (see COM study, 2021, pp. 57-58). In their view, a positive view is important for market access, but public opinion is negative. However, the Eurobarometer indicates that there is only limited knowledge about genetic engineering among the population. Public dialogue could increase awareness and understanding of the new techniques. The COM study claims that more research is needed in this area.

One of the authors of the present expert opinion has participated in several dialogue events brought into the process by the German federal government. It can be reported here that criticism of possible deregulation of NGTs at such events was at best noted (Potthof, 2017). However, as the documentation of the respective event makes clear, the criticism was not received there (Bundesministerium für Ernährung und Landwirtschaft, 2017). This suggests that little of this input reached the European Commission – as for example, in the context of the research and collection of material for the COM study. But this can only be speculated in the context of the present expert opinion.

The study concludes that it is a task of policy makers to reconcile these views. NGT could contribute to sustainable agriculture, but they should not undermine other applications that have sustainability effects. With regard to the two topics of SMEs and patenting, knowledge gaps are identified and further research efforts are called for. Further consultation processes are also called for. For the socio-economic aspects of NGT, the conclusion of the COM study is that the sustainability potentials of NGT should be exploited without compromising the use of other sustainability strategies. The conclusion regarding ethics and socio-economic aspects refers to the finding that there are different views among stakeholders on the benefits and risks of earlier and new genetic technologies.

The complex arguments in the sections on the advantages and disadvantages of NGT are reproduced in abbreviated form in the COM study's final chapters. The study strives for a balanced picture, which sometimes leads to a juxtaposition of competing views. On the other hand, important issues raised in the targeted consultations are not mentioned in the final chapters. Regarding the problem of legal uncertainty, for example, was expressed in particular by wholesalers who prefer that there should be uniform (global or European) legislation. But no consistent picture or argumentation on this point appears in the study's "Discussion" or "Conclusions" section.

The COM study does not give criteria for judging the superiority of the various opinions and positions it identifies. At some points in the argumentation the perspective of the authors is implied by way of presenting of some arguments as statements of fact, and others as opinions.

4 Challenges and Measures (Work Package II)

4.1 Examination and evaluation of the proposals

4.1.1 The reform discussion

An examination and evaluation of the proposals only can be made if precise proposals in form of drafts are presented. As this so far is not the case, it first is necessary to sift through the circulating documents of the EU-Commission for clues in which direction the reform could go.

4.1.1.1 Statements in the COM study itself

In the Discussions (COM study, 2021, Chapter 5) and even in the Conclusions (COM study, 2021, Chapter 6) of the study itself, there are only a few tangible concrete proposals. Apart from that one finds only generalities such as the formulation: "any future measures (as requested by the Council) should address how they should be interpreted and implemented in synergy" (COM study, 2021, p. 57).

The Commission's repeated claim that the current regulations would not be fit for purpose (COM study, 2021, p. 57) also is not very fruitful. It is not clear from this formulation what exactly the regulations are not fit for purpose: not fit for enforcement? not fit for ensuring a high level of protection? not fit for achieving legal certainty?

Looking at one of the main causes of the Commission's communication, which is the maintaining of the competitiveness of the European biotech industry (COM study, 2021, p. 51) one cannot escape the impression that the Commission considers the current NGT regulation not fit for the interests of the biotech industry. The same is true for emphasising the alleged benefits of NGTs regarding the European Green Deal, sustainable agriculture and the UN sustainable development goals (COM study, 2021, p. 59). With the latter, the Commission is adopting the biotech industry's promises without any critical appraisal. If this suspicion of being too close to industry were true, it would be a serious violation of the EU Commission's duty of neutrality as a state institution.[276] The reform process would then be burdened with a mortgage from the outset. In two places does the COM study at least hint at the direction it wants to take. For example, it reads "Embedding rigid risk-assessment guidance in legislation limits case-by-case assessment" (COM study, 2021, p. 59). This formulation can only be understood as meaning that the application of the current rules on risk assessment[277] tends to result in a violation of the case-by-case principle and – taken further – that risk assessment for NGTs must therefore be scaled back. The case-by-case principle is thus used as an argument for the alleged need for less rigid risk assessment regarding NGTs. However, this turns the case-by-case principle of the European genetic engineering law on its head. According to this "an environmental risk assessment should always be carried out in each individual case".[278] However, if – as the Commission wants – the requirements for risk assessment are to be reduced across the board for certain NGTs,[279] the case-by-case principle is violated, as it requires an assessment of each individual event. This statement in the COM study is therefore

[276] The discussion of the extent to which the EU already has the quality of a state or rather the character of a supranational community is not to be conducted here. Regardless of how one classifies this entity, its organs must in any case be neutral.

[277] Stipulated in Annex II Dir. 2001/18/EC.

[278] See reasoning 18 of the Dir. 2001/18/EC.

[279] Especially genome editing and crisgenesis.

inconsistent and telling at the same time. At any rate it cannot be used as a justification for deregulation. The other semi-tangible statement in the COM study reads:

"Furthermore, as concluded by EFSA, similar products with similar risk profiles can be obtained with conventional breeding techniques, certain genome editing techniques and cisgenesis. It may not be justified to apply different levels of regulatory oversight to similar products with similar levels of risk" (COM study, 2021, p. 59). [280] This statement ultimately implies that certain genome editing techniques (SDN-1 und SDN-2) and cisgenesis should be considered similar as conventional breeding. Since conventional breeding is not covered by genetic engineering law at all, this would amount to a complete deregulation of such NGTs. But it also has to be kept in mind that the other way round also would be possible: Extending the genetic engineering law to the conventional breeding.

4.1.1.2 Comments in the Inception Impact Assessment

In its Inception Impact Assessment Paper however, the Commission is more specific. So the reform proposal is due in the second quarter 2023 (European Commission, 2021b) and will initially only affect SDN-1, SDN-2 and cisgenesis techniques. As reasons for the necessity of a reform, the Commission cites unmanageable vague legal terms such as "mutagenesis" or "long safety record" (European Commission, 2021b). But those reasons are not convincing. The legal term "mutagenesis" has been determined in a very clear way by the ECJ in its mutagenesis decision 2018[281] and thus is not unmanageable vague any more. Apart from that both the European and not only the German public law is full of such grey legal concepts. They take shape by decisions of courts and thus can be handled very well. So the reason of the alleged unmanageable vague legal terms seems to be a pretext. Furthermore, the Commission believes that the application of the current law would hamper the major benefits of NGTs for climate protection, sustainable agriculture and biodiversity, citation:

> "It therefore lacks mechanisms to incentivise the development and placing on the market of products that contribute to the sustainability objectives of the European Green Deal and Farm to Fork and Biodiversity strategies" (European Commission, 2021b).

According to the Commission it would therefore be necessary to adapt the rules on risk assessment and approval requirements accordingly (European Commission, 2021b).

Finally, the Commission considers it necessary to label NGTs in a way that shows how valuable those products, at least according the Commission, were for climate protection, sustainable agriculture and biodiversity (European Commission, 2021b).

4.1.1.3 Derivable reform proposals

Although the Commission will not make a concrete proposal until the second quarter 2023, the broad outlines can already be seen from the above mentioned statements.

4.1.1.3.1 Regulatory technology

From a regulatory point of view, there are many indications that both the Deliberate Release Directive 2001/18/EC and the Food and Feed Regulation 1829/2003/EC is intended to be adapted by an amending regulation. The regulation type is obvious because the Commission

[280] Whether the basis for this statement, that certain NGT techniques are not riskier than classical breeding, is correct, will not be discussed here; cf. 3.3.1.1 and 3.5.

[281] C-528/16 of 27 July 2018.

wants to prevent different practices in the various Member States (European Commission, 2021b), which is best achieved by this legal act because it has direct effect in the Member States.[282] In the case of an amendment in form of a directive, the Member States could still have legal leeway in implementation. Furthermore, the fact that the Commission uses terms like "mechanisms for rapid adaptation to technical progress" (European Commission, 2021b) speaks much in favour of the Commission envisaging a two-step procedure. This means that it first wants to be empowered for the issuing of implementing acts and then make the actual changes on this basis in the comitology procedure.[283] It could therefore be that the reform proposal announced for the second quarter of 2023, which is very much in the political spotlight, will not itself bring the substantial new rules in terms of content. Rather they would then be made "quietly" by the Commission, possibly even without the need for the European Parliament's approval. In this scenario, the Commission would be able to act largely on its own with regard to NGTs deregulation and could, for example, unilaterally remove other NGT methods such as further advanced genome editing or other techniques from the scope of European genetic engineering law.

4.1.1.3.2 Regulatory content

In terms of content, everything speaks for deregulation of certain NGTs. How far this will go in detail is not yet clear. Central statements, which run through both the COM study and the Inception Impact Assessment in numerous places, speak of certain forms of genome editing like SDN-1, SDN-2 and cisgenesis being classified just as safe as plants bred using conventional methods. This suggests complete deregulation. Certain forms of genome editing (SDN-1, SDN-2) and cisgenesis would then be completely excluded from the scope of European genetic engineering law e.g. by inclusion in Annex I B to Directive 2001/18/EC. As a result, there would e.g. no longer be a risk assessment or an authorisation requirement, and the regulations on labelling and traceability would no longer apply.

However, it would also be possible not to deregulate SDN-1, SDN-2 and cisgenesis completely, but to subject them to a simplified approval procedure with a slimmed-down risk assessment (partial deregulation). How traceability and labelling would be dealt with in such a scenario is a look into the chrystal ball. However, it would then be consistent to maintain the traceability rules and the labelling obligation, the latter, however, perhaps not with the label "genetically modified", but "produced with SDN-1, SDN-2 or cisgenesis" or similar.

In the following chapters, if need be, both scenarios (complete deregulation – partial deregulation) are considered.

4.1.2 Compatibility with the precautionary principle

As the compliance of the reform proposals with the precautionary principle currently is extensively being assessed by a scientific project at Bonn University), regarding this issue it is referred to this project.[284]

4.1.3 Compatibility with the polluter pays principle

This principle means that polluters should bear the costs of their pollution including the cost

[282] Art. 288 para. 2 TFEU.

[283] Comitology refers to a set of procedures that enable EU countries, via special committees, to oversee how the European Commission adopts implementing acts.

[284] Spranger, 2021.

of measures taken to prevent, control and remedy pollution and also the costs it imposes on society. By this cost attribution polluters are incentivised to avoid environmental damage and held liable for the pollution that they cause, which also means, that they have to bear the costs of remediation.

4.1.3.1 Complete deregulation

In the case of complete deregulation, the NGTs concerned[285] would fall on its whole outside the regulatory scope of European genetic engineering law. In particular, they would not be subject to any risk assessment with the consequence that any potential damage to humans and the environment could not be detected. In the absence of rules on identifiability and traceability, it would also not be possible to establish that such damage was caused by NGTs in the event of damage to humans, animals or the environment. However, the EU Environmental Liability Directive 2004/35/EC provides in Art. 3 para. 1 in conjunction with Annex III No. 11 for liability of the polluter for all ecological damage caused by GMOs, be it by their release into the environment or even during transport, regardless of fault.[286] However, this liability is only imposed in cases involving genetically modified organisms as defined in the Deliberate Release Directive 2001/18/EC. So if certain NGTs were to be excluded from the scope of the Directive, this liability would thus run empty. Deregulation of NGTs would therefore mean that the user or developer of these NGT plants would not be liable for any resulting ecological damage. That is why such deregulation would not be compatible with the polluter pays principle enshrined in European law. This principle states that the costs must be borne by those who damage the environment, regardless of fault. This is also a general cost allocation principle and a principle aimed at preventing environmental damage from the outset. All these incentives to protect the environment would no longer exist under deregulated NGTs.

If NGTs were to cause damage to human health, the situation would be somewhat different. This is because, in contrast to the Environmental Liability Directive, the civil liability systems of the Member States apply not only to damage caused by certain explicitly enumerated activities, but to any damage to human health, although fault is a prerequisite here.[287] In the absence of identifiability and traceability, however, it would at least be very difficult both to detect damage caused by NGTs and to attribute it to a specific polluter, and also to establish fault. This also would not be compatible with the polluter pays principle.

4.1.3.2 Partial deregulation

In the case of partial deregulation, i.e. basically leaving NGTs within the scope of European genetic engineering law but with a slimmed-down risk assessment, the realisation of the polluter-pays principle would depend on whether or not the regulations on identifiability and traceability would continue to apply. If no, the same would be true as mentioned above.[288] If yes, the polluter pays principle would not be violated.

[285] I.e SDN-1, SDN-2 and cisgenesis.
[286] Art. 3 Abs. 1 lit. a RL 2004/35/EG.
[287] Cf. for instance for the German civil law section 823 para 1 Civil Code.
[288] See Chapter 4.1.3.1.

4.1.4 Identifiability and traceability

Regarding the issue of identifiability and traceability it also is referred to current assessment by project of Spranger.[289]

4.1.5 Preservation of the principle of coexistence

Whether the principle of coexistence can be safeguarded, also depends on the level of deregulation (Complete or partial deregulation).

4.1.5.1 Complete deregulation

Complete deregulation would also have an impact on the legal provisions for safeguarding coexistence, i.e. in particular safeguarding GMO-free agriculture.[290]

This already starts at the level of Union law. Article 26a para 1 of Directive 2001/18/EC[291] leaves the task of ensuring coexistence with the Member States. The EU thus restrains itself from a regulatory point of view and authorizes the Member States to make appropriate regulations. But this empowerment is also linked to the concept of GMO. Thus, if certain NGTs such as SDN-1, SDN-2 and cisgenesis were excluded from the scope of the Deliberate Release Directive and thus no longer constitute GMOs within the meaning of this Directive, that authorisation for the Member States will no longer apply to these NGTs. The safeguarding of national coexistence regulations under European law would cease to exist and there would be a risk that such measures would then be regarded as inadmissible interference in the free movement of goods.[292]

Irrespective of this, there would be a risk that also the national regulations on coexistence safeguards for NGTs would be undermined. For example, the German regulations on coexistence protection, i.e. the rules on site registers,[293] on good professional practice,[294] and the special neighbour defence and liability claims[295] are all based on the concept of GMO. And this GMO concept must be interpreted in conformity with European law. So if the EU were to exclude certain NGTs from the GMO concept of the Deliberate Release Directive, these coexistence rules would no longer be valid and could be challenged in court by users of NGT products.

4.1.5.2 Partial deregulation

If only the regulations on licensing requirements and risk assessment were relaxed for certain NGTs, but otherwise the regulations of European genetic engineering law like e.g. the rules on site registers[296] continued to apply, the rules for ensuring coexistence described above would still be possible, since NGTs would continue to fall under the GMO concept.

4.1.6 Compliance with the requirements of the Cartagena Protocol

Both the European Union and Germany are members of the Cartagena Protocol (CP).[297]

[289] Spranger, 2021.
[290] Section 1 Nr. 2 GenTG.
[291] The reading of Art. 26 para 1 Dir. 2001/18/EC is: Member States may take appropriate measures to avoid the unintended presence of GMOs in other products.
[292] Art. 34 ff. TFEU.
[293] Sect. 16a GenTG.
[294] Sect. 16b GenTG Genetic Engineering Plant Production Regulation.
[295] Sect. 36a GenTG.
[296] Art. 31 para 3 Dir. 2001/18/EC.
[297] Cartagena Protocol on Biosafety to the Convention on Biological Diversity of 20 January 2000.

According to Art. 4 CP, this protocol applies to "the handling and use of all living modified organisms that may have adverse effects on the protection and sustainable use of biological diversity". Since there is no exemption in the Cartagena Protocol for certain types of genetic engineering such as NGTs, the Protocol also applies to organisms developed through NGTs.

According to Art. 15 para 1 CP, risk assessments must be carried out in a "scientifically sound manner" and be based on "available scientific evidence". Thus, the Cartagena Protocol sets a strict standard for risk assessment. This means for the risk assessment of NGTs that not only those areas of the genome should be looked at, where modifications occured, but that a more detailed and comprehensive approach must be taken. In any case, a risk assessment is only then scientifically sound and based on available scientific evidence if not only the modified areas are looked at, but the entire genome is assessed. The practice of EFSA, which only looks at the modified areas selectively, is not compatible with this exigency.

4.1.7 Protection of ecologically sensitive areas

The reform proposals, depending on the precise extent of the deregulation, also could have negative effects on protected areas.

4.1.7.1 NGTs and protected areas

One of the most discussed risks of genetic engineering are adverse effects on biodiversity. Biodiversity is defined as the "variability among living organisms from all sources including, inter alia, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part, including diversity within species, between species and of ecosystems".[298]

Ecologically and thus also in their biodiversity particularly sensitive areas are protected at European level by the Natura 2000 network. This network consists of the protected areas according to the Wild Birds Protection Directive 2009/147/EC[299] and the protected areas according to the Fauna-Flora-Habitat (FFH) Directive 92/43/EEC (Habitats Directive).[300] These areas enjoy a particularly high level of biodiversity protection and cover[301] 18.5 percent of the land area of all Member States.[302] Any damage caused by NGTs use could therefore be considerable.

In addition,[303] there also are ecologically sensitive areas protected under national law[304] in each Member State like e.g. nature reserves[305] in Germany.

It must therefore be clarified whether deregulation will have an impact on the level of protection of such areas, because the use of NGTs can also cause such damage:

Looking at the mutations induced by NGTs, scientists observe that very precise modifications can be made in the genome of the target organisms. The new techniques also can access areas

[298] Art. 2 enumeration 1 of CBD.
[299] Directive 2009/147/EC of the European Parliament and of the Council of 30 November 2009 on the protection of wild birds, OJ No. L 20, 26.1.2010, p. 7–25.
[300] Council Directive 92/43/EEC of 21 May 1992 on the protection of natural habitats and of wild fauna and flora, OJ Nr. L 206, 22.7.1992, p. 7–50.
[301] As of 2020.
[302]. https://www.bfn.de/natura-2000-gebiete (accessed: 31 October 2022).
[303] I.e. in all cases where the national nature reserves not already are protected by the EU provisions of the Natura 2000 network.
[304] Cf. for Germany sections 22 ff. BNatSchG.
[305] Section 23 BNatSchG.

of the genome that are naturally well protected against mutations and therefore are hardly accessible by classical plant breeding or by "classical" genetic engineering. Via NGTs, the traits of organisms can thus (potentially) be strongly modified. The COM study (Executive Summary, p. 2) mentions here, for example, plants that are more resistant to diseases and environmental conditions or to the effects of climate change in general. Plants with induced herbicide resistance, for example, are mentioned to be in the pre-commercial phase (six applications); in the medium term, plants with tolerance to drought, salinity or heat might be developed and brought to market (COM study, chap. 4.1.3).

As with the use of "classical" genetic technologies, the deliberate release of plants modified by NGTs may be associated with direct, indirect, immediate, and delayed effects on the environment.[306]

For example, potential impacts on ecologically sensitive areas might be caused by genetically modified crops that have an increased tolerance to abiotic environmental factors (such as drought or soil salinity). These plants might have greater competitive vigour and could be able to migrate and spread into sensitive ecosystems. Plants native to these habitat niches (often highly endangered specialists) could be displaced and the entire biodiversity impoverished. Such impacts have been scientifically documented, for example, for numerous invasive neobiota that prove to be more competitive with native species, leading to local species extinctions and ecosystem changes.

Furthermore, plants that have been modified (through classical genetic engineering or NGTs) to produce insecticide themselves can potentially have a toxic effect not only on the pest itself, but may also affect protected endangered species.

Indirect impacts may occur with the cultivation of herbicide-resistant crops, where herbicides such as glyphosate can be used throughout the growing season without harming the crop. If resistant weeds develop, they are in turn controlled with other herbicides. Increased herbicide use could then lead to negative effects on biodiversity, soil and water bodies. The loss of pollen resources (e.g., for wild bees) and food resources (e.g., for butterfly caterpillars) associated to weed control contributes to the insect mortality observed worldwide.

Such damages related to ecologically sensitive areas cannot be examined in a general risk assessment of NGTs for the environment as a whole, as one always has to look area-specific. Therefore, in addition to the general risk assessment of NGTs, specific assessments are needed in relation to individual protected areas.

4.1.7.2 Deregulation and European nature conservation law

4.1.7.2.1 FFH impact assessment – current legal situation

The most efficient instrument for the protection of FFH sites is the so-called FFH impact assessment. According to this, "any […] project […] likely to have a significant effect thereon […] shall be subject to appropriate assessment of its implications for the site in view of the site's protection objectives".[307]

Thus, it can also be checked whether the use of NGTs leads to biodiversity damage.

[306] Definitions of the terms used, see Directive 2001/18/EC, Annex II, paragraph 2.
[307] Art. 6 para 3 Dir. 1992/43/EEC.

However, a prerequisite for this assessment always is that the activity is a "project"[308] within the meaning of the Habitats Directive. The ECJ has always defined this term very broadly and explicitly included agriculture, even conventional agriculture[309] that does not use genetic engineering.

However, there is an important exception with regard to conventional agriculture. According to this, activities that were already approved before the Habitats Directive came into force and continue to be carried out in an unchanged manner at the same location are not subject to the obligation to carry out an impact assessment. Such activities are therefore considered to be one and the same project due to their recurring nature. Thus, if agriculture[310] was already carried out in a protected area before May 21, 1992,[311] it may be continued without having to carry out an impact assessment. However, the general prohibition of deterioration[312] also applies here.

With regard to NGTs, all this means, as with conventional transgenic genetic engineering, that the use of such plants constitutes a project within the meaning of Directive 1992/43/EEC due to its potential for impairment and therefore requires an impact assessment.

4.1.7.2.2 FFH impact assessment in case of complete deregulation

It is questionable what effects a complete deregulation of certain NGTs would have on this obligation to carry out an impact assessment.

On the one hand, it could be argued that the GMO concept of European nature conservation law is independent in relation to European genetic engineering law. This could be justified by the fact that the risk assessment prescribed by European genetic engineering law only applies to environmental impact assessment in general. Ecologically sensitive areas, however, enjoy a particularly high level of protection and must be considered very specifically in each case due to their individuality. However, the general risk assessment in European genetic engineering law is not capable of doing this. If one follows this line of argument, deregulation would not lead to a lowering of the protection standard for FFH areas, at least in theory. However, enforcement would be difficult in practice because NGTs might not even be detected[313] due to lack of identification as genetically modified.

More likely, however, is the scenario in which there would be no independent GMO term in European nature conservation law. In that case, the use of NGT plants in nature conservation law would be treated the same way as conventional agriculture. The corollary would be that the use of NGTs would not be considered a project within the meaning of the Habitats Directive triggering an impact assessment. All that would remain would be the general prohibition of deterioration.[314] However, this would reverse the burden of proof: If an impact assessment has to be carried out, the user of the NGT product has to prove that the area will not be adversely affected. If only the general prohibition of deterioration applies, the nature

[308] Art. 6 para 3 Sentence 1 Dir 1992/43/EEC.

[309] Cf. ECJ, judgement of 7th November 2018 – C-293/17 and C-294/17, points 67 ff.; according to this decision merely the fertilization of agricultural sites is looked upon as *project* within the meaning of the Habitats Directive; see also ECJ, judgement of 10.1.2006 – C-98/03, Rdnr. 41 ff.

[310] Be it conventional or organic agriculture.

[311] The day where the Dir. 1992/43/EEC came into effect.

[312] Art. 6 para 2 Dir. 1992/43/EEC; cf. ECJ, judgement of 10th November 2016 – C-504/14.

[313] E.g. because there were no site registers according to Art. 31 para 3 Dir. 2001/18/EC.

[314] Art. 6 para 2 Dir. 1992/43/EEC.

conservation authority would have to prove this deterioration before it could intervene.

A complete deregulation of NGT would thus mean a deterioration of the protection of FFH areas by NGTs.

4.1.7.2.3 FFH impact assessment in the case of partial deregulation

The effects of partial deregulation would depend on its exact design.

If the GMO status of certain NGTs were retained and the changes were limited to a relaxation of the requirements for risk assessment, the current protection status would not change.[315] This is because NGTs would then continue to be identifiable, labelled and traceable, so that they could be subjected to an impact assessment as a project within the meaning of the Habitats Directive without any problems.

However if, in addition to a relaxation of the risk assessment for NGTs, the rules on identification, labelling and traceability were also abolished, the situation would be different. It then may be true that from a purely legal point of view there would still be no change in the protection status. Because due to the continued status of NGTs as GMO, the use in FFH areas as a project would trigger an impact assessment.[316] However, even in this scenario, there are likely to be significant practical enforcement deficits due to the difficulty in detecting the use of NGT plants.[317]

4.1.7.3 Deregulation and federal nature conservation law

4.1.7.3.1 Problem outline

From a purely legal point of view, it would have to be said that the effects on European nature conservation law described above would also have to be reflected 1:1 in German nature conservation law. This is because German nature protection law must be interpreted in conformity with the EU-Directives[318] and in accordance with the requirements of European nature conservation law. However, difficulties are likely to arise in practice, because deregulation would at least initially have very clear effects to the detriment of site protection against NGTs:

Because, in contrast to European law, in which the concept of a project is generally not defined,[319] and certainly not in relation to the use of GMOs, there are very precise definitions on this in German law. So for the areas of the Natura 2000 network, there is an extra provision on the use of GMOs in section 35 BNatSchG. The provision explicitly clarifies that the use of GMOs in these areas is to be regarded as a project within the meaning of the Habitats Directive triggering an obligation for an impact assessment. And that is true both for experimental releases of GMOs[320] and their cultivation after placing on the market.[321]

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[315] I.e. the same would apply as outlined above 4. 1.7.2.1 for the current legal status.

[316] See above 4.1.7.2.1.

[317] So this would be the same as in case of a complete deregulation, see above 1.7.2.2.

[318] Art. 288 para 3 AEUV.

[319] See above 4.1.7.2.1.

[320] Section 35 No. 1 BNatSchG in connection with section 3 No. 5 GenTG

[321] Section 35 No. 2 BNatSchG in connection with section 3 No. 6 GenTG respectively regarding food and feed Art. 3 ff. and Art. 15 ff. Reg. 1829/2993/EC. In contrast to experimental releases, where the impact of plants located outside the area, such as from pollen drift, is also covered, in the case of plants approved for cultivation, only the use in the area itself is considered a project.

4.1.7.3.2 Complete deregulation

In the case of complete deregulation, the provision of section 35 BNatSchG would initially be rendered obsolete. This is because the provision is based on the concept of GMO, which must be interpreted in conformity with European law. If certain NGTs were to be excluded from the GMO concept of the Deliberate Release Directive, the basis for the application of section 35 BNatSchG would cease to exist.

The risk could occur that the biotech industry would take advantage of this. The industry could hold the legal position that the German legislator only wants to regard the use of genetic engineering as a project within the meaning of the Habitats Directive in cases where the plants are to be classified as *GMO* under European genetic engineering law. The previously secure protection status of such areas would thus be threatened.

It is true that the nature conservation authorities would then most likely refer to the fact that section 35 BNatSchG is only of a clarifying nature and that, if the application of this specific provision were to cease, the general rules on impact assessment would apply directly. However, a possible argumentation of the biotech industry, according to which the German legislator wanted an impact assessment only in the presence of *GMO*s, could also be justified from a legal system point of view.

The nature conservation authorities would then have to go through a lengthy preliminary ruling procedure at the ECJ to try to clarify that the use of NGTs is also to be regarded as a project within the meaning of the Habitats Directive. Whether this path would be successful is anyone's guess, because it could well be that the ECJ would adopt the view of the amended Deliberate Release Directive not to regard NGTs as a GMO into the nature conservation law also and would then no longer regard the use of NGTs as a project.

4.1.7.3.3 Partial Deregulation

In the case of partial deregulation, i.e., retaining the GMO status for the NGTs, section 35 BNatSchG would maintain its meaning and the use in FFH areas would still be subject to an impact assessment. However, the extent to which this would then be enforceable in practice without difficulty would again depend on whether the rules on identifiability, labelling and traceability were also relaxed.

4.1.7.4 Deregulation and state conservation law

4.1.7.4.1 Initial situation

In Germany, the federal legislator created a precise regulation on the use of GMOs through section 35 BNatSchG only for FFH areas, i.e. areas already protected under European law. For purely nationally protected areas, the federal government left such regulations to the states.[322] In most cases, these have also issued corresponding regulations at the state level and regularly prohibited the use of GMOs in protected areas in principle.[323]

4.1.7.4.2 Complete deregulation

In the case of complete deregulation, this reliable protection of purely national protected

[322] I.e. Bundesländer.

[323] Cf. for example Section 35 para. 1 NatSchG BW, according to which any use of GMOs in nature conservation areas, core and maintenance zones of biosphere areas and areal natural monuments is prohibited in principle.

areas would cease to exist, because the GMO regulations under state law are also based on the European GMO concept. The nature conservation authorities would then only be left with the laborious task of checking whether the use of NGTs would be compatible with the protection objectives of the respective protection regulation, which would considerably reduce the possibilities for intervention.

In practice, this is likely to result in a complete lack of protection due to too many hurdles. First, the protected area ordinances would have to provide for appropriate intervention options. Second, the nature conservation authority would have the burden of proving that NGTs have harmful effects. Thirdly, the NGTs would not even be detected, because they would not have to be labelled as such. And last but not least, the biotech industry could here also take the position that the protection standards under national law should only apply to GMOs as defined in the Deliberate Release Directive.

4.1.7.3.3 Partial Deregulation

In the case of partial deregulation, the same would apply mutatis mutandis as in the case of European protected areas:[324] in principle, protection would remain in place. In practice, however, much would depend on whether the rules on identifiability, labelling and traceability were also relaxed.

[324] See above 4.1.7.2.

5 Options for action (Work Package III)

5.1 Identification of individual needs for action

5.1.1 Methodological issues

First of all, there is a fundamental need for action with regard to the methodological procedure of the study. One can only speak of a study if it meets certain standards of social science criteria. For example, a certain degree of representativeness, systematicity and comprehensibility must be present. However, these methodological requirements are not met. For example, it is often not clear which sources the Commission refers to. The criteria for the selection of supplementary material remain in the dark. The same applies to the criteria for the selection of the 31 non-EU legal systems presented. The survey concept is missing, i.e. a justification for why certain questions were asked and others not. The selection criteria are insufficient and only presented in an untransparent way. The analysis concept regarding the questionnaires is not presented. Also, rhetorical tricks are used, such as presenting certain arguments as more real than others. For all these reasons one cannot speak here of a serious study.

5.1.2 Ensuring identifiability and traceability

The proposals must be examined to what extent identifiability and traceability[325] like e.g. the rules for site registers[326] are further ensured.

In the case of complete deregulation, this would not be the case.

In the case of partial deregulation, this would not be the case if the intention was to no longer apply the rules on identification and traceability to certain NGTs.

5.1.3 Maintaining the polluter pays principle

Directly related to identifiability and traceability are the effects of changes in this area on the polluter pays principle.[327] These can vary depending on the depth of deregulation.

For example, complete deregulation would completely disregard the polluter-pays principle, as this would mean that the use of NGTs would no longer be traceable and thus no costs could be attributed in the event of damage.

In the case of partial deregulation, on the other hand, one must look closely at which areas would be deregulated. For example, if only risk assessment were relaxed, but traceability and labelling rules were retained, the polluter pays principle would be preserved. It would be different if (also) the traceability and labelling rules for NGTs would no longer apply.

5.1.4 Preservation of the coexistence principle

It is of vital importance for organic agriculture and the label “without genetic engineering” to what extent the regulations to ensure GMO-free production are affected by the reform proposals.[328]

In the case of complete deregulation of certain NGTs, the protection of GMO-free agriculture

[325] See above 3.2.2.3.
[326] Art. 31 para 3 Dir. 2001/18/EC.
[327] See above 4.1.3.
[328] See above 4.1.5.

from these NGTs would be eliminated across the board.

In the case of partial deregulation, it would depend on which regulations would be affected. If there were only a relaxed risk assessment and the other regulations were maintained, securing coexistence would also be possible with respect to the certain NGTs. If the coexistence protection clause of Art. 26a of Directive 2001/18/EC were to be repealed for certain NGTs, this would deprive national regulations on coexistence protection of their basis. If the regulations on labelling and traceability were repealed and the rules on coexistence protection were retained, the latter would remain formally in force, but in practice would be virtually empty due to the lack of recognizability of certain NGTs.

5.1.5 Compliance with the Cartagena Protocol

It would have to be examined whether the Commission's proposals are compatible with the Cartagena Protocol.[329]

In the case of complete deregulation, this would not be the case because the Cartagena Protocol implicitly assumes a risk assessment for all LMOs and makes no exception for certain NGTs.

In the case of partial deregulation, one would have to look primarily at the amendments related to risk assessment. If they would go so far that the requirements in Art. 15 para. 1 CP would no longer respect that the risk assessment is carried out in a scientifically sound manner and is based on available scientific evidence, this would no longer be the case.

5.1.6 Protection of ecologically sensitive areas

From the Federal Agency for Nature Conservation´s point of view, a particularly important issue would be the extent to which deregulation of certain NGTs would affect protected areas, especially the Natura 2000 network.[330]

In the case of complete deregulation, the general decision of the legislator in the area of genetic engineering law to regard certain NGTs as safe would very probably have an effect on European nature conservation law in such a way that protection of protected areas from these certain NGTs would also no longer be regarded as necessary.

In the case of partial deregulation, it would again depend on which regulations exactly would be relaxed. If the risk assessment were merely relaxed while all other regulations were retained, the protection of areas from certain NGTs would continue to be guaranteed. If, on the other hand, the rules on labelling and traceability were (also) dropped, the situation would be the same as for coexistence safeguards:[331] the rules for the protection of Natura 2000 sites would remain formally in force also with respect to certain NGTs, but would largely run empty in practice due to lack of detectability.

5.1.7 Halting the loss of biodiversity: sustainable agricultural practices and natural restoration

As the European Union and its Member States are parties to the International Convention on Biological Diversity they are committed to the protection of biodiversity (i.e. diversity within

[329] See above 4.1.6.
[330] See above 4.1.7.2.
[331] See above 4.1.5.

species, between species and of ecosystems). So far, the European Union has not succeeded in halting biodiversity loss. The EU Biodiversity Strategy for 2030 (COM(2020) 380 final) therefore provides for further measures to protect biodiversity in the European Union. As "certain agricultural practice " have been identified as "a key driver of biodiversity decline", one starting point of the strategy is "to support and incentivise the transition to fully sustainable practices" (COM(2020) 380 final).[332] Therefore, the legal rules for the release and cultivation of genome-edited plants must be designed in such a way that they do not conflict with the goal of halting biodiversity loss through sustainable land management. In this context, attention must also be paid to the protection of crop genetic diversity. The Biodiversity Strategy therefore points out that the "decline of genetic diversity must also be reversed, including by facilitating the use of traditional varieties of crops and breeds". In contrast, NGT plants are based on exceptionally narrow germplasm in breeding and especially a large-scale cultivation could lead to a loss of genetic biodiversity.

It is of central importance to stop the loss of biodiversity, including the restoration of intact ecosystems. As announced in the Biodiversity Strategy, a proposal for a regulation on nature restoration was presented by the European Commission in June 2022 (COM(2022) 304 final) that is intended to establish a framework for legally binding EU nature restoration targets to restore degraded ecosystems. Proposed is that Member States shall undertake effective and area-based restoration actions that together cover at least 20 percent of the Union's land and sea areas by 2030 and all ecosystems in need of restoration by 2050. According to Article 8 of the proposed regulation, the obligation to restore pollinator populations should lead to a reversal of the trend by 2030, after which pollinator populations should increase again. Article 9 addresses the restoration of agricultural ecosystems: Member States shall put in place the restoration measures necessary to enhance biodiversity in agricultural ecosystems. The improvement of biodiversity in the agricultural landscape will be measured by the following indicators: Grassland butterfly index, stock of organic carbon in arable mineral soils, proportion of agricultural land with species-rich landscape features, and index of common farmland birds.

Since these regulations are intended to implement international requirements from the CBD, to which the EU and its Member States are committed, the regulation of NGTs must also be aligned with these requirements.

[332] Such as precision agriculture, organic farming, agro-ecology, agro-forestry, low-intensive permanent grassland, and stricter animal welfare standards, COM(2020) 380 final, p. 7.

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