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Biotechnology

Deregulation of New GE: Reasonable? Proportional?

Critical assessment of possible changes in EU GMO law to deregulate plants derived from new genomic techniques (genome editing)

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Summary

The EU Commission has published a report setting out plans to change EU GMO regulation (EU Commission 2021). According to this report, plants derived from New GE (new genomic techniques, genome editing) could be exempt from EU regulation if their intended characteristics are already known from conventional breeding and no transgenes have been inserted. In addition, it proposes that potential benefits should be taken into consideration in the respective approval processes.

However, a Testbiotech analysis calls the proportionality of the planned changes into question: the planned changes in regulation will have a serious impact on the interests of consumers, farmers, breeders and food producers. On the other hand, any potential benefits are likely to be minor or insignificant.

In addition, the proposals in the report appear to be ill-considered and not purposeful. There is no scientific justification for declaring whole groups of genetically engineered plants safe. The reason: apart from the intended genetic changes and traits, including their possible combinations, the unintended effects arising from the multistep processes of New GE and their impacts must also be taken into account.

This Testbiotech backgrounder provides a tabular overview of various risk categories. It concludes that, independently of whether there is a change in legislation, every approval of an organism

derived from New GE – both now and in future - must include thorough in-depth risk assessment to avoid damage to health or the environment. Substantial risks to health and the environment would be an inevitable consequence if this were to be ignored.

The overview also shows that the European Food Safety Authority (EFSA) has not sufficiently considered unintended effects caused by New GE processes, even though such effects play a key role in EU Commission argumentation to justify possible deregulation.

Testbiotech therefore concludes that the EU Commission report is too one-sided or, at the very least, incomplete.

Testbiotech further recommends that the EU Commission first of all examines existing legislation to determine whether it currently includes enough flexibility to achieve its aims. The EU Commission can, for example, already take potential advantages of genetically engineered plants into consideration in its decisions on EU approvals. In addition, risk assessment standards can, amongst others, be precisely regulated through implementation rules, without having to change the legal framework.

Testbiotech additionally draws attention to the considerable need for research to be carried out in regard to risks and risk assessment methodology. In many cases, current standards of risk assessment need to be significantly raised in order to assess the often highly complex genetic changes.

This all underlines the need to strengthen the precautionary principle, precisely because New GE has a huge potential to generate technical interventions associated with complex risks and potential damage, which often only become apparent after a longer period of time.

EU Commission report proposes changes in EU GMO regulation

At the end of April 2021, the EU Commission (2021) published a report on new genomic techniques (genome editing, New GE, NGT). The Commission comes to the conclusion that existing GMO regulation should be changed and adapted to reflect more recent developments. Their goals are to promote New GE applications in agriculture as well as actively encourage international trade, technology and product development. The Commission is also demanding that market approval decisions should consider the potential benefits in regard to policies such as the ‘Green Deal’ and the ‘Farm to Fork’ strategy. Safety for health and environment should nevertheless be guaranteed.

The EU Commission appears to be considering new regulations for specific categories of New GE organisms and exempt them (partially) from current GMO regulation. As the Commission summarises: *“For certain NGTs, EFSA has not identified new hazards compared to both conventional breeding and established genomic techniques (EGTs). EFSA has also noted that random changes to the genome occur independently of the breeding methodology. Insertions, deletions or rearrangements of genetic material arise in conventional breeding, genome editing, cisgenesis, intragenesis and transgenesis. In addition, EFSA has concluded that off-target mutations potentially induced by site-directed nuclease (SDN) techniques are of the same type as, and fewer than, those mutations in conventional breeding. Therefore, in certain cases, targeted mutagenesis and cisgenesis carry the same level of risk as conventional breeding techniques.”*

Technically, these plants could be derived from a broad range of techniques, such as gene knockout, changing natural gene functions (SDN-1 or SDN-2) or the insertion of additional genes from the same species (SDN-3).

This statement is based on a previous (EFSA 2020) opinion, which suggests that exemptions from EU GMO Regulation could be applied, in particular, to plants with intended characteristics already known from conventional breeding and where no transgenes are inserted. As EFSA (2020) states: *„On the one end, 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. In this case, the risk assessment may focus on the knowledge of that variety (the history of safe use) and specific data on the edited gene and its product may not be needed.”*

The tabular overview presented in this backgrounder shows that the European Food Safety Authority (EFSA) has not sufficiently considered unintended effects caused by New GE processes. At the same time, EFSA (2020) stated that no comprehensive literature research was conducted on this issue. Instead, they make the general assumption that there is no need to assess many of these effects in detail. Scientific publications presented during the consultation which came to conclusions different to those of EFSA are not mentioned in the opinion. This is not in accordance with the usual basic scientific standards.¹

Nevertheless, the report of EFSA (2020) plays a key role in EU Commission argumentation to justify possible deregulation.

Proportionality: Advantages and disadvantages of potential changes in EU law

Testbiotech also sees the need for some adjustments. One reason: in many cases, the risk assessment of the New GE applications is much more complex compared to ‘Old GE’ (Testbiotech 2020).

At the same time, Testbiotech also points out that current regulation provides enough flexibility for adjustments. This is not only relevant for standards in risk assessment. For example, the EU Commission can already take potential benefits into account in its decisions on market approvals. However, these aspects must not be confused with scientific questions of risk assessment.

Against this backdrop, there needs to be a discussion on the benefits that might be expected from a partial exemption of New GE plants from GMO legislation. For example, the specific benefits of plants with traits that do not go beyond what could be derived from conventional breeding might appear questionable in regard to the goals of the EU’s ‘Green Deal’ or ‘Farm to Fork’ strategy.

The questionable benefits of potential deregulation must be weighed against factual negative impacts: as became evident from input to the consultation as part of the EU Commission report², deregulation would be contrary to the interests and expectations of many consumers, institutions and organisations representing the food production, agriculture and breeding sectors. These stakeholders are for various reasons in favour of continuing with clear boundaries between production with and without genetically engineered plants. According to recent opinion polls, a huge majority of consumers is against the kind of deregulation currently being discussed by the EU

1 <https://www.testbiotech.org/aktuelles/efsa-verwirrung-um-risiken-der-neuen-gentechnik-bei-pflanzen>

2 https://ec.europa.eu/food/plant/gmo/modern_biotech/stakeholder-consultation_en

Commission.³ Furthermore, substantial investments have been made in markets without GE plants, based on reasoned expectations of current legislation.⁴ In conclusion, the question of the proportionality of the planned measures is highly relevant and must be carefully considered by the EU Commission.

In regard to the potential benefits of genetically engineered plants, existing experience with agricultural has to be taken into account: for decades industry and experts with affiliations to industry have repeatedly stated that the cultivation of transgenic plants would bring many benefits for the environment due, in particular, to a reduction in pesticide use. However, there have never been any sufficiently defined criteria to request reliable data that would allow verification of the claimed advantages. Instead, decisions on desirable benefits were left to the markets whose aim was to generate profits. The consequence was a substantial increase in the pesticide load in the environment.⁵ In addition, and more recently, further scientific findings have been published in regard to environmental damage caused by transgenic plants. The enhanced spread of specific pest insects⁶ and damage to the centres of biodiversity for wild cotton⁷ were reported in this context.

Purpose: Is it possible to market GE plants without risk assessment?

In regard to the purpose of the measures being discussed, Testbiotech is emphasising that from a scientific point of view, the deregulation of specific groups of New GE plants is problematic. To explore the issue, Testbiotech has provided a tabular overview of categories which might be discussed in the context of potential exemptions from current GMO regulation (see table below).

Clearly, general exclusions from mandatory approval process cannot be justified, as there are no sufficiently reliable scientific criteria that make it possible to declare specific categories of New GE applications to be safe. Safety of specific organisms can only be concluded after a ‘case by case’ examination of the risks – but not in advance or solely by taking the intended characteristics of the GE organisms into account. The same applies even when no additional genes are inserted.

For example, if equivalence is claimed in comparison to traits derived from conventional breeding, then sufficient data must be made available in each case to prove such a claim. This request must be mandatory and the data must be made transparent. In this regard, it is not sufficient to establish systems such as those used by USDA (APHIS)⁸ or the Joint Research Center (JRC)⁹, where there is no detailed information on exactly what and how changes in the plants were made. This crucial information relevant to risk assessment is treated as confidential business information.

In addition, further questions arise, for example, regarding the genetic background in which a trait is expressed. Where already existing traits are newly combined in one plant, the resulting characteristics can raise complex questions in regard to risks to health and the environment. Even

3 https://www.bmu.de/fileadmin/Daten_BMU/Pools/Broschueren/jugend-naturbewusstsein_2020.pdf
<https://www.greens-efa.eu/en/article/news/opinion-poll-on-the-labelling-of-gm-crops>

4 https://ec.europa.eu/food/sites/food/files/plant/docs/gmo_mod-bio_stake-cons_stake-reply-04.pdf
https://ec.europa.eu/food/sites/food/files/plant/docs/gmo_mod-bio_stake-cons_stake-reply-34.pdf
https://ec.europa.eu/food/sites/food/files/plant/docs/gmo_mod-bio_stake-cons_stake-reply-93.pdf

5 www.testbiotech.org/en/news/transgenic-plants-failing-fields

6 <https://www.testbiotech.org/en/news/how-do-genetically-engineered-crops-speed-spread-plant-pests>

7 <https://www.testbiotech.org/en/news/disturbance-interactions-between-ge-cotton-and-environment>

8 www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated/Regulated_Article_Letters_of_Inquiry

9 https://datam.jrc.ec.europa.eu/datam/mashup/NEW_GENOMIC_TECHNIQUES/index.html

more questions arise concerning potential further crossings of the New GE plants, these would require an additional system for post-market monitoring of breeding activities.

The tabular overview given here clearly shows that EFSA (2020 and 2021a) did not sufficiently take the unintended effects such as resulting from the multistep processes in CRISPR/Cas applications into account. Indeed, EFSA (2020) states that no comprehensive literature research was conducted on this issue. Nevertheless, the findings from EFSA in this report (EFSA 2020) play a key role in EU Commission argumentation to justify possible deregulation.

Testbiotech concludes that the proposal to generally exclude specific categories from mandatory approval process cannot be implemented unless a high level of protection for health and the environment is ensured.

Therefore, the factual advantages of potential deregulation are unlikely to fulfill the expectations of the biotech industry. The requirement to provide data and the need to assess the data in a transparent way before any market approval is given cannot be omitted.

Table: Overview of different categories of genetic modifications in plants with regard to the necessity of risk assessment

	Categories	Problems / Reasons for risk assessment	Required levels of risk assessment	EFSA assessments
1	Intended changes	The subject of the analysis is intended traits with regard to intended genetic alterations and unwanted side effects.		
1.1	Traits are known from previous breeding and are already expressed in similar varieties of the respective species.	If it is assumed that the traits of NGT plants can be equated with those from conventional breeding, this must be proven by appropriate data.	DNA Alterations of ingredients, metabolism and gene expression (Omics techniques) Phenotypical characterisation	EFSA does not provide any information on how an assumed equation of plants should be checked.
1.2	Traits are known from a cultivated variety, now expressed in a new genetic background.	Example: Wild tomatoes were adapted to traditionally cultivated tomatoes (i.e. <i>de novo</i> domestication) (Zsogon et al., 2018). However, the concentration of various ingredients is different.	Comprehensive environmental and health risk assessment. Tomatoes, for example, have many ingredients that, depending on their concentration, can also have a negative effect on health. Among other things, metabolomics processes should be used here.	EFSA does not specifically address known traits that are expressed in a new genetic background.
1.3	Traits are known from previous breeding, but as yet they could not (or	An example: in an experiment with rice eight different target genes were changed at the same time and the already known	Comprehensive environmental and health risk assessment.	EFSA does not specifically address new combinations of known

	only to a much lesser extent) be combined in a variety.	traits were recombined through multiplexing (Shen et al., 2017). Intended alterations included yield, growth and fragrance. Possible new combinations that correlate with risks can also be made after market approval through further crossings; this would require appropriate monitoring.	For example, intended alterations of plant ingredients can significantly disrupt or even destroy the interaction of plants with their environment (such as with microbiomes, communication with insects, defence against pests, resistance to diseases) or the respective food webs and ecosystems.	properties.
1.4	Traits are known from previous breeding, but can far not be expressed separately from others, as both are linked genetic characteristics.	Example: Over 25 percent of genes relevant for breeding are genetically linked in tomatoes (Lin et al., 2014).	Comprehensive environmental and health risk assessment (see above).	EFSA does not mention the separation of genetic traits that have always been inherited together.
1.5	Properties are <u>not</u> known from previous breeding. With the help of the CRISPR/Cas gene scissors, specially protected genomic areas and a large number of gene copies can be changed at the same time.	Properties of plants can go far beyond those achieved with previous breeding (even if no additional genes have been inserted). Examples: Wheat with a modified gluten content (Sanchez-Leon et al., 2018), camelina with a modified oil quality (Kawall 2021), tomatoes with increased concentrations of GABA. (Nonaka et al., 2018)	Comprehensive environmental and health risk assessment (see above). Among other things, whole genome sequencing and omics methods must be used here.	EFSA considers an assessment of NGT plants with complex genetic changes or new traits to be necessary even if no additional genes have been inserted. However, it is unclear which methods EFSA considers to assess the risks.
2.	Unintended effects	The subject of the assessment are unintended alterations induced by the incorrect or imprecise use of the gene scissors that are caused by the respective methods.		
2.1	Multi-staged process for application of the gene scissors (e.g. introduction of the gene scissors DNA via transgenic intermediate stages)	The process to introduce the gene scissors into the plant cells can cause many unintended effects. The effects depend on the respective process and are often described in publications. Many effects are still relevant for risk assessment even if there are no (complete) transgenes left (for references see below the	DNA analysis Investigation of epigenetic effects	EFSA seems to no longer consider a detailed examination if no (complete) transgenes are detected in the end product. However, this is not justified in detail.

		table).		
2.2	Unintended alterations of the genome	<p>Through the use of the gene scissors, unintended genetic alterations can occur in the respective target regions (on-target), regions that are similar to the target regions or in other parts of the genome (off-target). The main influencing factors are the respective target region and the processes used (for references see below the table).</p> <p>These effects are documented in numerous publications and can differ significantly in their pattern and resulting effects from those in previous breeding. For example, several DNA areas that have a sequence similar to the target area can be cut unintentionally at the same time ('mistaken targets').</p>	DNA analysis and, if necessary, further tests (ingredients, investigation of newly formed biologically active molecules, etc.)	<p>EFSA does not seem to consider an in-depth examination, but gives no detailed explanation.</p> <p>So far, only off-target effects have been discussed.</p> <p>However, EFSA has not submitted any systematic analyses of the risks..</p>
2.3	Unwanted formation of 'gene products' or metabolic products relevant to nutrition	<p>Genetic changes induced in the target region due to use of gene scissors can lead to the formation of new biologically active molecules (such as new proteins or regulatory RNA). The main influencing factors are the respective target region and the processes used.</p> <p>These effects (e.g. induced by 'exon skipping' or frameshift mutations) are documented in numerous publications and can differ significantly in their pattern and effects to those from previous breeding.</p> <p>Some of these effects appear after several metabolic steps. One example is wheat, where dozens of alpha-gliadin genes have been knocked out to reduce gluten content (Sanchez-Leon et al., 2018).</p>	<p>DNA analysis and omics techniques (transcriptomics, proteomics, metabolomics).</p> <p>In the case of wheat with a reduced gluten content, checks must be carried out, for example, to find out whether new precursors (prolamins and glutelins) of gluten have been formed. These can have negative effects on food safety. Actual changes in the composition of gluten only show up in the further metabolism through the combination of prolamins and glutenins.</p>	EFSA has not yet discussed in detail the formation of unwanted gene products relevant to nutrition.
2.4	Unintended effects on the environment and unexpected effects of genetically engineered organisms on the environment.	Unintended alterations at the level of the genome, the epigenome, gene products or in the metabolism can affect the interaction of plants with their environment (such as the microbiome, communication with insects, defence against pests, resistance to diseases) or	Among other things, investigation of interactions with the environment and responses to stressors.	EFSA has not yet discussed in detail unintended changes at the level of the genome, the epigenome, gene products or in the metabolism of plants, that are

		<p>the respective food webs and significantly disrupt or even destroy ecosystems (see Kawall, 2021).</p> <p>The respective effects, which have as yet not been well researched, can differ significantly in their effects from those resulting from previous breeding.</p>		<p>relevant for the environment.</p>
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The impact of unintended effects

As Testbiotech has already shown in detail in the context of the STOA consultation (Testbiotech 2021), the risk assessment of organisms derived from New GE cannot be restricted to investigating the intended modifications as proposed by EFSA (2020 and 2021a) and the EU Commission (2021).

Specific patterns of unintended changes observed in New GE organisms occur because, amongst others, CRISPR/Cas typically prevents the cells from restoring the original gene function: if the target site is restored to its original condition, CRISPR/Cas can bind and cut again, making it very likely that the target site will eventually be altered (Brinkmann et al., 2018). This is different to the processes occurring in the cell during physical or chemical mutagenesis where, in many cases, the original gene function will be restored by natural repair mechanisms. In response, depending on the number and structure of the targeted genes, the number of unintended changes is also likely to increase.

However, not only number, but also the site of the unintended changes caused by the processes can be specific. Technical tools used in ‘New GE’ make the genome available for changes that go beyond those which can be derived from processes of physical and chemical mutagenesis: CRISPR/Cas also enables alterations in parts of the genome where fewer mutations occur and where they are very unlikely to occur naturally or through conventional breeding (Belfield et al., 2018; Kawall, 2019; Kawall et al., 2020; Monroe et al., 2020; Testbiotech, 2020). Therefore, unintended effects, in many regions of the genome, will also occur with a higher likelihood compared to conventional breeding.

A broad range of unintended effects caused by CRISPR/Cas has already been published (mostly ignored by EFSA, 2020): Several publications describe how CRISPR/Cas causes unintended changes, including off-target effects, on-target effects and chromosomal rearrangements (Kosicki et al., 2018; Lalonde et al., 2017; Kapahnke et al., 2016, Haapaniemi et al., 2018; Wolt et al., 2016; Cho et al., 2014; Sharpe, 2017; Adikusuma et al., 2018; Kosicki et al., 2020; Biswas et al., 2020; Tuladhar et al., 2019; Ono et al., 2019; Leibowitz et al., 2020; Skryabin et al., 2020; Weisheit et al., 2020; Michno et al., 2020; Norris et al., 2020; Grunewald et al., 2019; Burgio et al., 2020; Liu et al., 2021). These unintended changes can cause a variety of unwanted effects. For example, the integrity of a non-target gene may be compromised if its coding region is cleaved by CRISPR/Cas (e.g. cleavage at off-target-sites). This could lead to changes in the metabolism of the organism that could affect its safety for health and the environment. Such effects are highly dependent on the genomic context within which such unintended alterations occur (e.g. within a gene, loss of function mutations; outside of genes, unintended alterations in promoters could alter gene expression).

In addition, a process-oriented risk assessment and mandatory approval process is necessary because genome editing is a multi-step process, with inherent and specific risks which are independent from the purposed traits. For example, in plants, New GE is typically combined with old genetic engineering techniques ('Old GE', such as non-targeted biolistic methods or *Agrobacterium* transformation) to deliver the DNA for the nuclease (gene scissors) into the cells. Thus, in most cases, the result of the first step of the CRISPR/Cas application is a transgenic plant. Only at the end of the multistep process is further breeding applied to remove the transgenic elements from the plant genome. At each stage of the process, such as (i) insertion of the DNA of the gene scissors into the cells, (ii) target gene recognition and cutting and (iii) cellular repair, specific unintended alterations can occur, with associated risks. For example, alterations caused by the non-targeted insertion of transgenic elements in the first step of the process may remain in the plants and impact safety, even if the transgenic elements are removed by further breeding at the end of the process.

There are a number of publications reporting unintended effects arising from the application of 'Old GE' (see for example Liu et al., 2019; Gelvin et al., 2017; Forsbach et al., 2003; Jupe et al., 2019; Makarevitch et al., 2003; Windels et al., 2003; Rang et al., 2005). These alterations can only be detected by considering each case separately using appropriate analytical tools, e.g. long-read next generation sequencing for detecting chromosomal rearrangements or whole genome sequencing for detecting off-target effects, in combination with methods such as transcriptomics, proteomics and metabolomics (Burgio et al., 2020; Enfissi et al., 2021).

In summary, the specific unintended effects arising from the overall process (also due to lack of precision of the gene scissors)¹⁰ include

- off-target effects,
- on-target effects (i.e. large deletions, insertions, translocations, inversions around the target site),
- unintended integration of DNA-sequences (e.g. from plasmid DNA, DNA templates, endogenous DNA, exogenous DNA),
- exon skipping (e.g. causing the unintended production of new proteins from the altered genes) and
- epigenetic alterations

Consequently, it is not only the intended genotypes typical of New GE that can go beyond what is achieved in conventional breeding, but also the patterns of unintended changes and their associated effects. These findings are relevant for most GE organisms, no matter whether additional genes are inserted or not.

New GE wheat (Sanchez-Leon et al., 2018) is a good example with which to illustrate these findings. The wheat is intended to have a reduced gluten content (see table above). The intended genetic changes introduced with CRISPR/Cas aim to knock out dozens of alpha-gliadin genes responsible for gluten protein content in wheat. Specific forms of gluten are thought to trigger chronic inflammatory processes in the intestines, therefore several projects aim to reduce its content in wheat.

EFSA (2021b) referred to these plants as an example of highly complex alterations in plant genomes (SDN-1 applications). However, potential unintended effects associated with the technical

¹⁰ for more details see also Kawall et al., (2020).

processes were never investigated in detail. Therefore, this example (Sanchez-Leon et al., 2018) requires further analysis:

In a first step, the DNA for the nuclease (CRISPR/Cas) was inserted into the wheat genome. As a result, many unintended genetic changes may persist in the plants even if the transgenes are removed by further breeding (see above).

In a second step, dozens of genes belonging to the alpha-gliadin gene family were knocked out to prevent production of the respective proteins. This was successful in most, but not all of the targeted genes. As a result, each of the intentionally altered genes must be assessed to investigate whether unintended new proteins are produced which, for example, may contribute to inflammatory cascade. In addition, metabolic processes that ultimately produce gluten need to be analysed.

This example shows that it is simply not sufficient to assess intended traits. Furthermore, it is not sufficient to risk only on the level of DNA. Rather, risk assessment must also consider gene products (the transcriptome and proteome). Finally, it needs to include risk assessment of the changes in metabolic processes involved in the production of gluten (the metabolome).

In general, the results presented here show that, due to the complexity of genome editing technology, it is impossible to reduce risk assessment to intended changes. Instead, the unintended genetic changes resulting from the process and the unintended effects triggered by the intended genetic changes need to be taken into account. For this purpose, and as required in current GMO regulation, the starting point for risk assessment must always be the process (and the technology that was applied), irrespective of the level of intended genetic changes.

Recommended actions

The EU Commission, in its plans to adapt EU GMO Regulation to the challenges of New GE, should use the existing legal framework that already provides considerable flexibility:

- 1. Standards of risk assessment:** Risk assessment standards could, with respect to different categories of New GE organisms, be defined by the EU Commission in a new Implementing Regulation. In this respect, the Commission should be aware that, in the light of the technical potential of New GE, higher standards of risk assessment will become necessary in many cases. In addition, specific precautionary measures should be implemented for organisms able to persist and propagate in the environment.
- 2. Assessment of potential benefits:** The EU Commission is currently able to consider all relevant aspects and other criteria within the framework of Directive 2001/18. There is, however, an urgent requirement for sufficiently well-defined and reliable criteria to assess potential benefits before market approval and post-market monitoring after approval.
- 3. Improving traceability:** The EU Commission should take action to establish an international register for all New GE organisms and methods so that they can be tracked and traced if necessary (see Ribarits et al., 2021).
- 4. Reducing costs for approval processes:** Projects for whole genome sequencing, -omics methods and establishing reference genomes could be funded within the framework of EU Regulation 178/2002, and could subsequently be used by the companies to prepare their approval applications.

5. Empowering independent risk research: There is an urgent need for systemic and long-term risk research driven by the precautionary principle and carried out from the perspective of the protection goals (health, environment, nature). This risk assessment should be completely independent of any interests in developing new technologies, or specific applications, or marketing of the resulting products.

6. Access to the technology: The EU should restrict the scope of patents to the specific technical processes, with the aim of preventing absolute product protection on plants, animals and the relevant traits.¹¹

Conclusions

Given the low expectations in regard to potential advantages and consequent negative impacts, the measures proposed by the EU Commission are neither proportional nor purposeful.

Rather than change existing GMO regulation, the EU Commission should use the existing legal framework to meet and adapt to the challenges presented by New GE.

Special implementing regulations can, amongst other things, be put in place to define risk assessment standards. The consideration of potential benefits, the development of adequate methodology for risk assessment, establishment of independent risk assessment and the restriction of the scope of patent protection are all relevant issues, but do not require any change in the legal framework of the EU GMO regulations.

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¹¹ This is especially relevant for patents granted in context of Article 4 of EU Patent Directive 98/44 EC. Absolute product protection covers plants and animals and their traits independently of the method used to generate them.

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