European Parliament

New genomic techniques

European Commission study and first reactions

SUMMARY

On 29 April 2021, the European Commission presented a study on the status of new genomic techniques (NGTs) under EU law. The Council had asked for this study in the context of a 2018 European Court of Justice judgment and the practical questions raised by it.

The Commission study examines the implementation of EU legislation on NGTs, based on consultations with the Member States and stakeholders. It provides information on the status and use of NGTs in plants, animals and micro-organisms for agri-food and for industrial and pharmaceutical applications. The study defines NGTs as 'techniques capable of changing the genetic material of an organism and that have emerged or have been developed since 2001', that is, after the existing EU legislation on genetically modified organisms was adopted.

The main conclusions of the study point to 'limitations as to the capacity of the legislation to keep pace with scientific developments', stating that this causes implementation challenges and legal uncertainties. According to the study, there are strong indications that the legislation is not fit for purpose for some NGTs and their products, and that it needs to be adapted to scientific and technological progress.

According to the Commission, the study confirms that NGT products have the potential to contribute to sustainable agri-food systems in line with the objectives of the European Green Deal and the 'farm to fork' strategy.

Stakeholders have mixed reactions to the study: while some industry associations and researchers welcome its content and conclusions, others appear more cautious, and some environmental NGOs strongly oppose it. In the European Parliament, the Environment and Agriculture Committees (ENVI/AGRI) have organised public hearings, and the initial views of the Parliament are taking shape in the context of the 'farm to fork' strategy.

IN THIS BRIEFING

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Introduction

New genomic techniques (NGT) have evolved rapidly in the past 20 years. The 2020 Nobel Prize in Chemistry was awarded to the developers[1] of a novel innovative technique for genome editing, CRISPR-Cas9. This quick, precise and cheap-to-use gene-editing technique, described as 'genetic scissors', has revolutionised genome editing since 2012. According to the Nobel Committee, these technologies have resulted in innovative crops, but will also lead to ground-breaking new medical treatments, such as innovative cancer therapies.

The legal status of these new techniques has raised questions in the EU as well as worldwide. In November 2019, the Council asked the Commission to submit a study in light of a judgment by the Court of Justice of the EU (CJEU) in Case C-528/16 on the status of new genomic techniques under EU law. The Commission study (the study), published on 29 April 2021, covers the use of NGTs in plants, animals and micro-organisms, and in agri-food, industrial and medicinal applications.

The study concludes that the EU legislation on GMOs has clear implementation challenges and that there are legal uncertainties as regards new techniques and new applications. The Commission says that it will discuss the outcome of its study with the Council, the Parliament and the stakeholders, to gather their views on the proposed follow-up. What the EU decides to do will also have implications for its international trade. Diverging regulatory requirements for NGTs could place technical barriers to trade and thus lead to disputes between the EU and its trade partners.

The study in a nutshell

Context

The EU definition of GMOs is contained in Directive 2001/18/EC and reflects the scientific and technical knowledge at the time of its adoption in 2001. Since then, biotechnologies and novel techniques, such as the above-mentioned CRISPR-Cas technique, have emerged at a fast pace. This has led to uncertainty as to whether the techniques and the products developed through them are covered by the GMOs definition and therefore subject to the obligations imposed by the directive, such as prior authorisation, labelling and traceability rules.[2]

In July 2018, the CJEU delivered a judgment in which it held that organisms obtained by the new mutagenesis techniques are GMOs and fall within the scope of EU legislation on GMOs. The Commission study underlines that the judgment concerns only mutagenesis techniques and no other NGTs.

While the CJEU ruling focused on new mutagenesis techniques, the Council's request for the Commission to prepare a clarifying study was broader and referred to NGTs in general. As there is no definition for NGTs, for the purposes of the study these were defined as **techniques that are capable of altering the genetic material of an organism and that have emerged or have been mainly developed since 2001**.

Study methodology; consultations done ahead of the study

To prepare its study, the Commission held a targeted consultation of the EU-27 competent authorities and EU-level stakeholders (food chain, animal and plant health, and pharmaceuticals, cosmetics and environmental sectors). Of the 107 stakeholders invited to participate, 58 replied. The European Food Safety Authority (EFSA) provided an overview of the risk assessment and the Commission's Joint Research Centre (JRC) delivered two reports: on the scientific and technological developments and on the current and future market applications of NGTs. In addition, the study took into account opinions submitted by the Group of Chief Scientific Advisors and the European Network of GMO Laboratories, and an opinion on the Ethics of Genome editing by the European Group on Ethics in Science and New Technologies (EGE).

State of affairs regarding NGTs

The study presents the current situation regarding NGTs, referring to the scientific advisors' note and the JRC reports. The Commission notes that the scientific advisors recognised the heterogeneity of NGTs and the fact that this was reflected in the variety of NGT products; consequently, it may not be ideal to group NGTs in a single category. Furthermore, the scientific advisors pointed to similarities between some NGTs and some conventional breeding and established genomic techniques. The advisors concluded that while genome editing may produce 'off-target' effects,[3] the frequency of these effects is generally much lower than in the context of conventional breeding techniques and established genomic techniques.[4] The scientific advisors also considered that, due to the precision and efficiency of use of certain NGTs, they are the only realistic means of obtaining certain products. According to the scientific advisors, the safety of these products can only be assessed on a case-by-case basis and depends on the products' characteristics, intended use and receiving environment. Moreover, it is generally not possible to determine whether the changes are the result of natural causes or the use of any breeding technique.

The JRC review on scientific and technological developments notes that the deployment of these techniques can be expected to increase 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. The most prominent set of NGTs, according to the JRC, is based on the CRISPR-Cas technology that has exponentially expanded the opportunities for modifying many genomic targets in diverse organisms.

The JRC review on market applications covers applications in plants, mushrooms, animals, micro-organisms and human cells in the agri-food, industrial and pharmaceutical sectors. The review notes that most NGT applications have been developed in the United States or China. In the EU, Germany has produced the biggest number of applications. Due to the flexibility and affordability of NGTs (especially CRISPR), several developing countries are also active in the field. Both private and public/academic entities are actively developing NGT products.

The JRC review identifies two plant applications that are already on the market: a high-oleic soybean variety with a healthier fatty acid profile, and a tomato variety fortified with gamma-aminobutyric acid. Another 15 plant applications are at a pre-commercial stage.[5] Some of these are similar to plant/trait combinations that have already been developed with established genomic techniques (e.g. maize, soybean, rice and potato with herbicide tolerance, fungal resistance, modified oil or starch composition and non-browning properties), while others have not been reported before (e.g. herbicide-tolerant pigeon peas and flax; pennycress and camelina with modified oil content). A non-browning white button mushroom, obtained with CRISPR-Cas9, is in the pipeline.

In the medium term (by 2030), the JRC envisages the creation of plants tolerant to drought, salinity and heat, the applications now being at an advanced or early R&D stage. Improving the nutrition profile of crops (for example, fibres, vitamins), reducing the content of gluten or harmful substances (toxins, allergens, acrylamide precursors), or obtaining higher and more stable yields and bigger sizes of fruits and grains are among the further possible applications.

Table 1 – Traits introduced in NGT plants (being in early R&D stage up to commercial stage)

Trait category	Description
Biotic stress tolerance	Resistance to biotic stressors (fungi, bacteria, viruses, pathogens or parasites)
Abiotic stress tolerance	Resistance to abiotic stressors (drought, heat, salt, rain, UV radiation)
Herbicide tolerance	Tolerance to different types of herbicides
Modified colour/flavour	Colour or flavour modified

Modified composition	Modified content of starch, oil, protein, vitamins, fibres, allergens etc.; seedless fruits
Plant yield and architecture	Increased yield through higher number of flowers/seeds/fruits; changes in plant height or shape
Storage performance	Improved shelf-life characteristics (for example non-browning or reduced black spot)
Breeding	Reproductive/flowering characteristics (sterility, early flowering etc.)
Other traits	Traits not previously classified (e.g. production of molecules, flowering time, etc.)

Data source: European Commission study on new genomic techniques, 2021 (Table 2, p. 17).

As regards **animals**, the Commission study notes that research on NGTs mainly focuses on the livestock sector for food production purposes: cattle, pigs, chickens and various fish species, with desired traits such as resistance to bacteria, viruses and other pathogens; resistance to high or low temperature; hypoallergenic properties, higher and faster meat production or modification in meat quality. The study also mentions gene-drive technology, which seeks to pass a genetic modification to the whole offspring, usually to eliminate pathogen-carrying insects (such as mosquitos spreading the Zika virus), or control invasive species.

According to the study, no NGT animals are yet commercialised, but there are four examples at the pre-commercial stage: yield-enhanced/fast-growing tilapia, disease-resistant pigs, hornless cattle and heat-resistant cattle. The study notes that one particular use of NGTs in animals is R&D work on human diseases: i.e. using animals as disease models for gene therapy studies or for making transplants. For example, mice are used in human gene therapy studies for cancer and genetic diseases, and pigs for making organs that do not cause transplant rejection in humans.

The study states that in **industrial biotechnology**, NGT micro-organisms already appear to be a reality. Facilitated by the contained use of micro-organisms,[6] the industrial biotechnology sector 'is quick to apply technological innovation, and NGTs are used alone or in combination with established genetic techniques to improve specific strains'. Most commonly, CRISPR in particular is used to knock out undesirable genes affecting toxins, antibiotic resistance or unwanted by-products. Examples of applications include food enzymes (for baking, plant-based proteins, dairy products); probiotics for animal and human health; and bio-control substitutes for pesticides.

As regards **human health**, the study observes that NGTs are widely used for developing medicinal products for human use. NGT applications were identified in 64 clinical trials, and there is 'extensive activity' at early R&D stage. Cancer was found to be the main target of therapeutic NGT applications, followed by hereditary diseases and viral diseases. The biggest group of medicinal products in development is based on the genetic modification of T-cells, followed by stem cells and cancer cells.

The study concludes that in the short term, about 30 applications in plants, animals and micro-organisms are at a pre-commercial stage and could reach the market in the next five years. In the medium term, over 100 plants, several dozen animals and medicinal applications that are now in the advanced R&D stage could reach the market by 2030.

Legal status of organisms developed through NGTs

The study reminds that the EU legislation on GMOs has two main objectives: i) to protect human and animal health and the environment in accordance with the precautionary principle; ii) and to ensure the effective functioning of the internal market. Therefore, there are strict procedures for the safety assessment, risk assessment and authorisation for GMOs before they can be placed on the market. To enable consumers as well as professionals (farmers, food chain operators, etc.) to make informed choices, labelling and traceability must be ensured.

EU legislation applies to GMOs as defined in Article 2(2) of Directive 2001/18/EC on the deliberate release into the environment of GMOs: 'genetically modified organism (GMO)' means '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'. The GMO definition is further refined by a list of GM techniques (set out in Part 1 of Annex IA to the directive) and by excluding certain techniques (listed in Part 2 of Annex IA) that are not considered to result in genetic modification. Also, the directive excludes GMOs that result from certain techniques/methods (mutagenesis and cell fusion), on the basis that these techniques/methods have a long history of safe use.

In its judgment of July 2018 in case C-528/16 (*Confédération paysanne and Others)*, the CJEU ruled that 'Article 3(1) of Directive 2001/18/EC, read in conjunction with point 1 of Annex IB to that Directive and in the light of recital 17 thereof, must be interpreted as meaning that only organisms obtained by means of techniques/methods of mutagenesis which have conventionally been used in a number of applications and have a long safety record are excluded from the scope of that Directive' (paragraph 54). According to the Commission study, this judgment clarifies that organisms obtained through new mutagenesis techniques that have appeared or have been mostly developed since the adoption of Directive 2001/18/EC are GMOs subject to the provisions of that directive.[7]

For the purposes of its study, the Commission also screened the GMO and NGT legislation in 31 non-EU countries, concluding that around two thirds have no specific legislation for NGTs and/or their products, as these are regulated in the same way as conventional GMOs. However, half of these countries are debating whether to adapt their legislation specifically to NGTs.

Detectability of NGTs

The EU Reference Laboratory (EURL) and the European Network of GM Laboratories (ENGL) produced a report on the difficulties in detecting NGT products. The report considers that it would be very hard for laboratories to detect the presence of unauthorised genome-edited plant products entering the EU market without prior information on the altered DNA sequences. According to the report, the polymerase chain reaction (PCR)-based screening methods commonly used to detect conventional GMOs cannot be applied to, nor could they be developed for, genome-edited plant products. This is because they target common sequences generally present in transgenic organisms, which do not occur in genome-edited plants. DNA sequencing may be able to detect specific DNA alterations in a product, but this would not necessarily confirm genome-editing, as the same alteration could have been obtained by conventional breeding or the traditional random mutagenesis techniques.

Safety assessment of NGTs

The European Food Safety Authority (EFSA) provided an overview of the risk assessment of plants developed with the use of NGTs, based on its previous scientific opinions and those of the Member States' competent authorities[8] since 2012. The Commission did not ask EFSA to develop new opinions on plants developed through specific NGTs.

For NGT applications in plants, EFSA concluded that there are no new hazards specifically linked to targeted mutagenesis[9] and cisgenesis[10] compared with conventional breeding. EFSA furthermore concluded that the unintended effects of modification with targeted mutagenesis are of the same type as, and fewer than, the unintended effects occurring with conventional, non-GM breeding techniques. The Commission notes that the types of modifications introduced with targeted mutagenesis and cisgenesis can also take place naturally in the environment without human intervention. No safety assessment beyond plant applications has yet been made.

The Commission reports that some Member States expressed concern about the possibility of off-target, unintended effects in the genome of the edited organism and their potential negative consequences for human, animal and plant health, and the environment. The main safety concern raised was the risk of unintended effects linked to the intended genetic modification: for example, the production of new toxins or allergens. The study reminds that EFSA has noted that random changes to the genome occur independently of the breeding methodology: insertions, deletions or rearrangements of genetic material also arise in conventional breeding and potential new proteins are created at random also during conventional breeding.

Some stakeholders also highlighted the potential negative consequences for the environment, such as the introduction of new traits; interactions with wild species; influence on food webs and interaction between plants and pollinators; and the potential uncontrolled spread into the environment. Most NGOs, as highlighted by the Commission, are particularly concerned about NGT animals and their welfare: some mentioned the potential risk of cancer in animals; others pointed out that experimenting on animals often causes unnecessary animal suffering and death, and that genetically modified animals often have health issues at birth. Concerns were also expressed about gene drive-modified organisms, in particular their impact on the environment, ecosystems and biodiversity preservation.

According to the Commission, several Member States consider that the current risk assessment procedures and guidelines need to be adapted for NGTs. Most NGOs and organic food business operators state that NGT products require risk assessment under the current GMO legislation or that they require more stringent risk assessment, whereas other stakeholders believe that risk assessment requirements should be decided on a case-by-case basis.

Research activities

The study confirms that there is considerable interest in research on new genomic techniques in the EU, but development is mostly taking place outside the EU. The EU as well as Member States and stakeholders have increasingly funded NGT-related research: EU funding under the research programmes FP7 (2007-2014) and Horizon 2020 (2014-2020) amounted to €3.2 billion, distributed among 1 021 projects. Health and medical-oriented research accounted for most of the funding; the rest was bioeconomy research, which includes agri-food applications.

Many Member States mentioned that the current regulatory framework presents challenges to NGT research, putting EU academics and public and private research institutions at a competitive disadvantage internationally. Moreover, there is a risk of NGT research shifting to places outside the EU. Many Member States pointed to a need to develop reliable detection and traceability methods.

Challenges and concerns regarding NGTs

The study notes that a number of stakeholders are not enthusiastic about the opportunities offered by NGTs. They do not believe that NGTs would bring particular benefits in the agri-food sector: any benefits, in their view, can also be obtained through other forms of agriculture. They also argue that the benefits of NGTs are largely hypothetical, and that to date, there is no proof of their potential to contribute to the sustainability of the agri-food system. Finally, they point out that there is not enough knowledge about the health, environmental, economic and social impacts of NGTs.

The Commission reports that the Member States' most common concerns are about the negative public perception of NGTs in the agri-food sector; difficulties with effective detection, identification and traceability of NGT products; safety issues; and potential negative environmental impacts. The EU trade partners' diverging legal requirements are a concern as well: this may lead to unauthorised products entering the EU, and EU farmers and businesses facing an uneven playing field. Several Member States also express concern about the ethical aspects of using NGTs.

Several stakeholders see NGT products as a major threat to the viability of the organic and GM-free sectors, due to difficulties with controls and certification, the potentially unavoidable presence of NGT products in their supply chains, and a potential loss of consumer trust.

Stakeholders from the pharmaceutical sector are concerned about the application of the GMO legislation to medicines: as the GMO legislation is not specifically designed for medicinal products, it hinders the conduct of clinical trials, delaying patient access to them and affecting the EU's competitiveness as a place where advanced therapy medicinal products are developed.

Labelling NGT products

Several stakeholders note that there being no reliable detection or differentiation methods, labelling NGT products creates not only a challenge and a legally untenable situation for operators but also problems in dealing with imports from countries regulating NGTs differently or not at all. Others emphasise that NGT labelling is crucial for organic and GMO-free agriculture farmers and value chains, and that consumers have a right to information under EU food law and the Treaties.

Other topics in the Commission study

This briefing gives an overview of the content of the study and the issues that are likely to come up during the forthcoming public discussion about the steps to be taken. Among the issues addressed in the study but not in detail here (due to their technical complexity) are different types of new genomic techniques and characteristics of genetic modifications (Section 4.1.2 of the study), application of EU GMO legislation to organisms developed through different kinds of techniques (Sections 4.2.2. to 4.2.5 and Chapter 4.3 of the study); and intellectual property rights and patents (Chapter 4.8 of the study). The study also gives a short overview of the principles guiding the regulation of NGTs in non-EU countries (Section 4.2.6).

The study also summarises a March 2021 opinion of the European Group on Ethics on genome editing. Concerning NGTs in plants, the opinion recommends that regulation should be proportional to the risk; light-touch regulation should be used where the change in the plant could have been achieved naturally, or where genetic material from sexually compatible plants has been introduced. Where genes from non-sexually compatible organisms or multiple changes have been introduced, there should be a comprehensive risk assessment. Member States' and stakeholders' views on ethical aspects are further presented in Chapter 4.11 of the study.

Main conclusions of the study

The Commission concludes that there are challenges as concerns the capacity of the EU legislation to keep pace with scientific developments. According to the Commission, there are strong indications that the current GMO legislation is not fit for purpose for some NGTs and their products, and that it needs to be adapted to scientific and technological progress.

The Commission says that it will soon initiate policy action specifically focused on plants derived from targeted mutagenesis and cisgenesis. An impact assessment, including a public consultation, will be done to examine potential policy options. As for the other NGTs, and their use in animals and microorganisms, the Commission says it will 'continue to build up scientific knowledge'.

The study also notes that in general, the use of NGTs in the pharmaceutical sector is viewed more positively than in other areas: NGTs can be used to develop therapy for seriously debilitating and life-threatening diseases, as well as vaccines and treatments for controlling zoonoses. The Commission specifies that the use of NGTs in medicinal products will be addressed in the context of the pharmaceutical strategy.[11]

The Commission also concludes that NGT products have the potential to contribute to sustainable agri-food systems in line with the objectives of the European Green Deal[12] and the 'farm to fork' strategy.[13] Both of these seek to improve the sustainability of the agri-food system, while also highlighting climate change challenges and noting that biotechnology can play a role, for example, in reducing dependency on pesticides, developing plants that are more resistant to climatic conditions, as well as contributing to food security and a more sustainable food chain.

However, the study notes that the safety of NGTs is key, and that as both the new NGT techniques and products vary considerably, drawing generalised conclusions about their safety is impossible. Case-by-case assessment, the study argues, is widely recognised as the appropriate approach. Furthermore, as EFSA concluded, similar products with similar risk profiles can be obtained both

with conventional breeding, certain genome editing techniques and cisgenesis: it may not be justified to apply different regulatory oversight to similar products with similar levels of risk.

As for the legal status of NGTs, the study notes that, while the CJEU judgment has provided important elements of legal clarity, open questions remain: e.g. developments in biotechnology, combined with a lack of definitions (or clarity of the meaning) of key terms in the legislation, are giving rise to ambiguity in the interpretation of some concepts, potentially leading to regulatory uncertainty. As examples of lacking definitions the study mentions key concepts such as 'mutagenesis' (whether EU legislation covers all mutagenesis techniques or only conventional ones); 'long safety record' and 'altered' genetic material.

Stakeholders, as the study notes, are divided on whether the current legislation should be kept and its implementation reinforced or whether the legislation should be adapted to scientific and technological progress and the level of risk of NGT products.

European Parliament and Council

Parliament

On 10 May 2021, the Committee on Environment, Public Health and Food Safety (ENVI) held a public hearing where experts from academic, EU and other institutions as well as consumer organizations discussed the potential risks and impacts of NGTs. During its presentation of the study at the event, the Commission noted the existence of strong indications suggesting that the current GMO Regulation is not fit for purpose for some new genomic techniques. It went on to explain that current risk assessments are very rigid, and that it 'might not be justified to apply different levels of regulatory oversight to similar products with similar level of risk'. At the same time, new techniques should not undermine other aspects of sustainable food production, such as organic agriculture. The Commission also reminded that the new techniques can also help to develop vaccines and treat patients, and confirmed that it will initiate policy action on plants derived from targeted mutagenesis and cisgenesis. The study was also presented at the meeting of the Committee on Agriculture and Rural Development (AGRI) on 22 June 2021. In December 2015, during the previous Parliament's term, AGRI had already organised a hearing on new techniques for plant breeding and, together with ENVI, a hearing in May 2018. In its January 2020 and June 2021 resolutions[14] the Parliament called for a global moratorium on releases of gene drive organisms into nature, including field trials.

The Parliament outlines its initial views on NGTs in its resolution on the farm to fork strategy, under joint committee procedure between AGRI and ENVI. A joint committee meeting to vote on the draft own-initiative report was held in September 2021, and the plenary vote took place in October 2021. On NGTs, the compromise amendment adopted states that Parliament takes note of the Commission's plans to initiate a regulatory policy action on plants derived from certain new genomic techniques, aimed at maintaining a high level of protection of human and animal health and the environment, while reaping potential benefits from science and innovation, in particular to contribute to sustainability goals of European Green Deal and the farm to fork strategy. The Parliament 'highlights the precautionary principle and the need to ensure transparency and freedom of choice to farmers, processors and consumers, and stresses that this policy action should include risk assessments and a comprehensive overview and assessment of options for traceability and labelling with a view to achieving proper regulatory oversight and providing consumers with relevant information, including for products from third countries in order to ensure a level playing field'.

Council

The Agriculture and Fisheries Council held a debate on the conclusions of the study in its meeting of 26-27 May 2021. The ministers responded positively to the study and appreciated the need to modernise the current legislation, while also recognising the particular challenges presented by such modernisation. They discussed the importance of reflecting the latest scientific developments

when conducting risk assessments on new genomic techniques, and also the need to raise awareness and provide education on these issues.

Stakeholder reactions

EuropaBio, the European association for the biotechnology sector, sees the NGT study as a positive step. The association observes that the current GMO legislation does not reflect the advances in technology and has impacted Europe's global competitiveness. 'New genomic techniques are major innovative tools in the biotechnology sector and can provide breakthrough solutions for a healthy planet', says EuropaBio. Euroseeds, representing European plant breeders, argues in its press statement that the Commission study confirms the urgent need for policy change: 'urgent action from Commission and Member States is needed to allow for a differentiated approach to products derived from innovative plant breeding methods'.

In May 2021, more than 20 agri-food trade groups called on EU agriculture ministers to support the findings of the study. They insisted that '[a] differentiated regulatory approach is needed', saying that it is important to address the topic from a global perspective while also taking into account trade-related challenges. While they strongly welcomed the prospect of policy action in the area of plants, they also encouraged the Commission to initiate discussions on the review of the regulatory approach in other sectors. 'These techniques hold great potential for the animal breeding sector and for the development of new/further development and improvement of existing strains of microorganisms to support the transition to more sustainable food systems', the groups stated.

On a different note, in March 2021 organic farmers' group IFOAM, in a coalition with 162 civil society, farmers and business organisations, addressed a letter to the Commission Vice-President, Frans Timmermans, calling on him to ensure that all new genetic engineering techniques continue to be regulated in accordance with existing EU GMO standards. 'There are no scientific or legal reasons to exempt new genomic techniques from risk assessment, traceability and labelling', argues the coalition, warning that weakening the regulation of these powerful techniques would contradict the objectives of the EU Green Deal, farm to fork and biodiversity strategies. According to the coalition, new genetic modification techniques can cause a range of unwanted genetic modifications that can result in the production of novel toxins or allergens, the transfer of antibiotic resistance genes, or in traits that could raise food safety, environmental or animal welfare concerns.

Environmental groups insist on the need to rigorously apply current GMO regulations to the new techniques. Friends of the Earth Europe argues in its December 2020 briefing that these new forms of genetic modification, despite being portrayed as a magical solution, would not make the farming system more resilient to extreme weather, or result in healthier food. 'So far, neither the new nor the old generations of GMO technologies have been able to produce crops with significant health benefits', the NGO observes. Moreover, multiple studies have shown that gene editing can have unintentional 'off-target' effects. Furthermore, because cell DNA repair mechanisms play an important part in the process and involve a certain amount of randomness, it is impossible to reliably predict the exact outcome even in the targeted gene(s). Friends of the Earth also reminds that biotech companies are legally obliged to deliver a testing method for any GMO that is authorised in the EU, so that unapproved GMOs can be identified in imports.

Environmental advocates also point to issues about the patentability of plants and genetic material of plants, warning that patenting a plant or a plant's traits restricts farmers from sowing, planting, harvesting or breeding the variety without permission. This threatens farmers' rights to store, use and sell seeds from their own harvests and increases their dependency on a few big seed producers.

In an April 2021 press release, the environmental watchdog Test Biotech stresses that no general exclusions from the mandatory approval process can be justified, as there are no scientific criteria making it possible to declare specific categories of new gene-editing applications safe. 'Safety of specific organisms can only be concluded after a case by case examination of the risks – but not in advance or solely taking the intended characteristics of the GE organisms into account', Test Biotech

says. The watchdog also refers to an EFSA opinion of February 2021 evaluating the existing guidelines for making a risk assessment of plants obtained through synthetic biology. The EFSA opinion evaluates, among other things, the risk assessment of a low-gluten wheat produced using CRISPR/Cas9 genome editing. Test Biotech argues that the EFSA opinion shows that detailed risk assessment must be carried out even if no additional genes are inserted. According to Test Biotech, EFSA rightly concludes that the complex patterns of genetic change go beyond what has been achieved in genetic engineering and conventional breeding thus far.

The European Network of Scientists for Social and Environmental Responsibility (ENSSER) warns in its press release that the relative ease of use and low cost of the ingredients of CRISPR, the best-known and most widely used genome editing tool, give rise to a considerably higher potential for dual use, abuse and accidental misuse. It also criticises the claim that this technology would be crucial to help fight hunger by raising food crop yields, pointing out that the root causes of hunger are related to social and economic problems (poverty, conflict and exclusion) rather than yields. The precautionary principle requires that genome editing remains stringently regulated, ENSSER states, in particular as there is no history of safe use for any of these new techniques.

Some academics point out that a main element of the discussion is and has been the phrase that is a part of the GMO definition in Directive 2001/18, 'altered in a way that does not occur naturally by mating and/or natural recombination'. The main discussion is whether it refers to the technique used, to the resulting genetic alterations or to both. The academics stress that in its 2018 judgment the CJEU only ruled on the scope of the mutagenesis exemption. The challenge thus remains to determine the precise scope of the GMO definition itself, the academics say, arguing that under the existing definition, the requirements regarding both process (genomic techniques employed) and product (genetic alteration realised) need to be cumulatively met.

Researchers also warn about the economic and environmental consequences of the choices that the EU will make, pointing out that since in some cases it is impossible to distinguish genome-edited from non-genome-edited plants, EU importers may fear that they would risk violating EU legislation. They may choose not to import products based on crops for which genome-edited varieties are available. As a consequence, crop products of which the EU is currently a net importer (such as soy) would become more expensive in the EU. Intense substitution of products covered and not covered by genome editing would occur in consumption, production and trade, the researchers say, resulting in dramatic effects on agricultural and food prices as well as on farm income.

Some academics have expressed hope that the coronavirus pandemic could be a game changer in GMO regulation – given the contribution of modern biotechnology to the creation of a vaccine against the disease – and also regarding the possibilities to address food shortages induced by pandemics or other threats of similar magnitude.

Developments in other international organisations

The OECD organised a conference on genome editing applications in agriculture in June 2018. An OECD genome-editing hub was established as a result of a project of the OECD Working Party on Biotechnology, Nanotechnology and Converging Technologies. The OECD's Working Party on the Harmonisation of Regulatory Oversight in Biotechnology aims to assist countries in evaluating the potential risks of genetically engineered organisms.

The Cartagena Protocol on Biosafety to the UN Convention on Biological Diversity (CBD) is an international agreement aiming to ensure the safe handling and use of living modified organisms (LMOs) resulting from modern biotechnology. International discussions in the frame of the Nagoya Protocol include, inter alia, the regulatory status of genome-editing techniques. A peer review process for the CBD Technical Series on Synthetic Biology went on from May to July 2021; a revised draft will be made available for the 15th meeting of the Conference of the Parties (COP15), to be held in October 2021 and April-May 2022.

Since early 2021, the WHO has been developing a Global Guidance Framework for the Responsible Use of Life Sciences, with a view to updating guidance in light of advances in the life sciences since 2010. The aim is to promote responsible use of life sciences and to protect against potential risks caused by accidents and misuse. In May 2021, the WHO issued new guidance for research on genetically modified mosquitoes to fight malaria and other vector-borne diseases. In July 2021, the WHO published global recommendations on human genome editing.

In November 2018, the US raised concerns at the WTO Committee on Sanitary and Phytosanitary Measures regarding the CJEU judgment on organisms obtained by mutagenesis. The US said that the implementation of this judgment will 'place unjustified barriers to trade on products of genome editing as well as stifle the agricultural research and innovation necessary to prevent hunger and malnutrition in the coming decades while ensuring environmental sustainability of agricultural activities'. The delegations of 10 countries[15] also signed a statement on agricultural applications of precision biotechnology, asserting that cultivars derived from genome editing should be regulated in a way similar to conventional cultivars, due to the high similarity between the two. Differing regulatory approaches for products derived from precision biotechnology may create potential trade issues that could impede innovation, the statement cautions.

Outlook

On 24 September 2021, the Commission published its roadmap on Legislation for plants produced by certain new genomic techniques, stating that the regulation it plans to propose will put forward a legal framework for plants obtained by targeted mutagenesis and cisgenesis and for their food and feed products. Feedback could be submitted until 22 October 2021, and the Commission should adopt its proposal during the second quarter of 2023. On 29 November 2021, the Commission is organising a high-level event on NGTs to discuss the follow-up of its NGT study.

Gene-edited crops in the EU are currently only grown on test fields, for example in Belgium, Spain and Sweden. The United Kingdom recently approved the first field trials of wheat created with CRISPR-Cas, where the aim is to reduce the levels of carcinogenic acrylamide in wheat products. On 29 September 2021, the UK government published plans to ease research and testing requirements for gene-edited crops in England.[16] The next step, according to the press release, will be to review the regulatory definitions, 'to exclude organisms produced by gene editing'. There had already been indications that the UK wishes to diverge from EU legislation on this matter after Brexit: in January 2021, the UK launched a public consultation on gene editing. According to the press release by the Environment Secretary, George Eustice, the potential of gene editing was 'blocked by a European Court of Justice ruling in 2018, which is flawed and stifling to scientific progress. Now that we have left the EU, we are free to make coherent policy decisions based on science and evidence'.

FURTHER READING

New techniques in biotechnology, European Commission website.

Kritikos M., What if gene editing became routine practice? EPRS, European Parliament, October 2018.

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Menz J., Modrzejewski D., Hartung F., Wilhelm R., Sprink T., Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment, *Front. Plant Sci.*, October 2020, https://doi.org/10.3389/fpls.2020.586027.

Purnhagen K., Wesseler J., EU Regulation of New Plant Breeding Technologies and Their Possible Economic Implications for the EU and Beyond, *Applied Economic Perspectives and Policy*, September 2020, https://doi.org/10.1002/aepp.13084.

Van der Meer, P., Angenon, G., Bergmans, H., Buhk, H., Callebaut, S., Chamon, M., . . . Zimny, T. (2021). The Status under EU Law of Organisms Developed through Novel Genomic Techniques. *European Journal of Risk Regulation,* 1-20. doi:10.1017/err.2020.105.

ENDNOTES

[1] French microbiologist Emmanuelle Charpentier and American biochemist Jennifer A. Doudna.

[2] For a detailed description of legislation, see 'Annex E - EU regulation on GMOs' in the Commission study.

[3] 'Off-target modifications' are DNA modifications occurring at an unintentional location in the genome (see Annex A – 'Glossary of scientific terminology' in the Commission study).

[4] With 'established genomic techniques', the Commission refers to genomic techniques developed prior to 2001, when the existing GMO legislation was adopted.

[5] Applications ready to be commercialised in at least one country but not yet on the market.

[6] Contained use of micro-organisms as bio-factories, and the fact that the final product is usually not the target of the modification.

[7] Therefore, the Commission study concludes that micro-organisms developed through new mutagenesis techniques are genetically modified micro-organisms (GMMs) subject to the provisions of Directive 2009/41/EC on the contained use of genetically modified micro-organisms, if used under containment, and of Directive 2001/18/EC if deliberately released or placed on the market.

[8] 16 scientific opinions, submitted by eight Member States (AT, BE, DE, DK, ES, FR, LT and NL).

[9] 'Targeted mutagenesis' or 'site-directed mutagenesis techniques' are umbrella terms used to describe newer techniques of mutagenesis that induce mutation(s) in selected target locations of the genome without insertion of genetic material. The process usually results in a 'knock-out' (i.e. the disruption of the functioning) of a gene that is responsible for an unwanted effect (See Annex A - 'Glossary of scientific terminology' in the Commission study).

[10] 'Cisgenesis' means insertion of foreign genetic material (e.g. a gene) into a recipient organism from a donor that is sexually compatible (crossable). The foreign genetic material is introduced without modifications or rearrangements. (Annex A - 'Glossary of scientific terminology' in the Commission study).

[11] The Commission adopted a pharmaceutical strategy for Europe in November 2020.

[12] The Commission's communication on the European Green Deal states that 'the EU needs to develop innovative ways to protect harvests from pests and diseases and to consider the potential role of new innovative techniques to improve the sustainability of the food system, while ensuring that they are safe'.

[13] The communication on the 'farm to fork' strategy states that 'new innovative techniques, including biotechnology and the development of bio-based products, may play a role in increasing sustainability, provided they are safe for consumers and the environment while bringing benefits for society as a whole. They can also accelerate the process of reducing dependency on pesticides'.

[14] Resolution on COP15 to the Convention on Biological Diversity and resolution on the EU biodiversity strategy for 2030.

[15] Australia, Argentina, Brazil, Canada, the Dominican Republic, Guatemala, Honduras, Paraguay, the United States of America, and Uruguay.

[16] Following the announcement, the Welsh and Scottish governments have declared that they have no plans to relax their rules on gene-edited crops.

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