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Member State questionnaire on new genomic techniques to contribute to a Commission study requested by the Council

Fields marked with * are mandatory.

Questionnaire on new genomic techniques to contribute to the study requested by the Council

endorsed in the Joint Working Group of GMO competent authorities on new genomic techniques on 15 January 2020

Introduction

With this questionnaire the Commission is collecting contributions from Member States competent authorities to respond to the Council's request[1] for "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" (i.e. Directive 2001/18/EC, Regulation (EC) 1829/2003, Regulation (EC) 1830/2003 and Directive 2009/41/EC). The scope of the study goes beyond new mutagenesis techniques, as there are other new techniques, for which the Council seeks clarification. Therefore, the study covers all new genomic techniques, which have been developed after 2001.

For the purpose of the study, the following definition for new genomic techniques (NGTs) is used: techniques, which are capable to alter the genetic material of an organism and which have emerged or have been developed since 2001[2].

Unless specified otherwise, the term "NGT-products" used in the questionnaire covers plants, animals, micro-organims and derived food and feed products obtained by NGTs for agri-food, medicinal and industrial applications and for research. GMO competent authorities are invited to seek input from other competent authorities when appropriate.

The questionnaire is meant to provide information primarily, but not exclusively, at national level. Please substantiate your replies with explanations, data and source of information as well as with practical examples, whenever possible. If a reply to a specific question only applies to a specific NGT, please indicate this in the reply. With regard to agri-food applications, replies may include considerations on specific sectors, such as the organic sector.

Please indicate which information should be treated as confidential in order to protect the commercial

interests of a natural or legal person. Personal data, if any, will be protected pursuant to Regulation (EU) 2018/1725 [3].

[1] Council Decision (EU) 2019/1904, OJ L 293 14.11.2019, p. 103-104, https://eur-lex.europa.eu/eli/dec/2019/1904/oj
[2] Examples of techniques include: 1) Genome editing techniques such as CRISPR, TALEN, Zinc-finger nucleases, mega nucleases techniques, prime editing etc. These techniques can lead to mutagenesis and some of them also to cisgenesis, intragenesis or transgenesis. 2) Mutagenesis techniques such as oligonucleotide directed mutagenesis (ODM). 3) Epigenetic techniques such RdDM. Conversely, techniques already in use prior to 2001, such as Agrobacterium mediated techniques or gene gun, are not considered NGTs.
[3] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC, OJ L 295, 21.11.2018, p. 39–98

Instructions

Please note that the survey accepts a maximum of 5000 characters (with spaces) per reply field. You might be able to type more than 5000 characters, but then the text will not be accepted when you submit the questionnaire. You will also receive a warning message in red colour below the affected field.

You have the option to upload supporting documentation in the end of each section. You can upload multiple files, up to the size of 1 MB. However, note that any uploaded document cannot substitute your replies, which must still be given in a complete manner within the reply fields allocated for each question.

You can share the link from the invitation email with another colleague if you want to split the filling-out process or contribute from different locations; however, remember that all contributions feed into the same single questionnaire.

You can save the draft questionnaire and edit it before the final submission.

You can find additional information and help here: https://ec.europa.eu/eusurvey/home/helpparticipants

Participants have until 30 April 2020 (closure of business) to submit the questionnaire via EUsurvey.

QUESTIONNAIRE

* Which Member State are you representing?

Luxembourg

A - Implementation and enforcement of the GMO legislation with regard to new genomic techniques

* **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 ?**

- ○ Yes
- ◉ No

* **2. Have you taken specific measures (other than inspection) related to the application of the GMO legislation to NGT-products?**

- ○ Yes
- ◉ No

* Please explain why not

Unlike transgenic plants, which fall under Directive 2001/18/EC, NGT-products with no foreign DNA in the genome are difficult to trace in the final product. And if so, they cannot be distinguished from products in which mutations have been introduced in a “classical’ manner”. Although altered genetic composition induced by NGTs can theoretically be traced, it will not be possible to establish with certainty whether the mutated plant product resulted from the application of an NGT, from the application of an exempted technique of mutagenesis or indeed from natural mutations.

* 2 bis. Have you encountered any challenges or limitations, including administrative burden or costs?

- ◉ Yes
- ○ No

* Please describe

Since other countries (USA, Canada, …) have exempted NGT-products, breeders and farmers that invest in and use NGTs, thereby increase their competitive advantage. NGS approaches could only be used if considerable efforts would be done to establish references sequences of plants of interest to which analysed samples can be compared to. But even those techniques would not be able to distinguish SNV or InDel caused by genome editing, by classical breeding techniques or by natural mutations. The national control plan has thus not been adapted to NGT-products. Food, feed and seeds have been analysed for known and unknown GM products except those obtained by NGT as explained above. This approach requires considerable investments in bioinformatics tools. For the moment, the NRL does not have the money, expertise or equipment to carry out such assays.

* How could these challenges or limitations be overcome?

A legislation that can be applied to NGT-products and taking into account the technical limitations to detect and quantify unknown genome-edited plant products is urgently needed.

* **3. Have you adapted your inspection practices to cover all NGT-products and to ensure the enforcement of traceability requirements?**

- ○ Yes

- (●) No

* Please explain why not

Too little information is available to cover all NGT-products. A register could help collecting data about NGT-products. Therefore, no changes to the actual practices have been made. Food, Feed and seeds have been sampled according to the national control plan. Information about NGT-products already potentially present on the market is missing.

Luxembourg does not produce products obtained by NGTs for the EU market. Imports from other MS have to comply with the EU regulations and will have to be controlled in the respective MS prior export. The existing controls (documentary checks) have been applied to food or feed regardless of the method of production (NGT or classical GMOs).

* 3 bis. Have you encountered challenges or limitations, including administrative burden or costs?

- ( ) Yes
- (●) No

* Please explain why not

Too little information is available to cover all NGT-products. Since no specific detection methods are available it would be questionable legally do declare a product to be produced by NGTs and subsequently refuse import.

* **4. Do you have experience or information on traceability strategies, which could be used for tracing NGT-products?**

- ( ) Yes
- (●) No

* 4 bis. Have you encountered any challenges or limitations, including administrative burden or costs?

- ( ) Yes
- (●) No

* Please explain why not

To our knowledge, no harmonized detection methods and reference materials are available for detecting NGT-products. Validation (and implementation in OCLs) of quantitative event-specific methods such as required by regulation 1829/2003 is only possible for NBT plant products where a known DNA alteration has been identified and shown to be unique.

Other than documentary checks, no specific traceability strategies have been described.

* **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 the:**

- [x] **Agri-food sector?**
- [x] **Industrial sector?**
- [x] **Medicinal sector?**

Agri-food sector

According to the coalition agreement 2018-2023 the ban on genetic engineering in agriculture and food, including NGTs, will continue to be supported by the LU government. No field trials or cultures with plants produced by NGTs or transgenic plants have been or will be authorized in LU.

Industrial sector

After the vitamin B2 incident, industries using enzymes will be controlled more thoroughly in 2020.

Medicinal sector

No notifications for clinical trials using GM or NGT medication have been received

* **6. Have plant varieties obtained by NGTs been registered in national catalogues?**

- ○ Yes
- ◉ No

* **7. Do you require specific information in national catalogue when registering plant varieties obtained by NGTs?**

- ○ Yes
- ◉ No

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

The maximum file size is 1 MB

B - Information on research and innovation

* **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?**

- ○ Yes
- ◉ No

* Please highlight the potential challenges encountered when supporting/funding NGT-related research and any consequences from these challenges.

N.A.

* **9. How do you see NGT-related research evolving?**

The development of NGTs allows an acceleration of modifications to the genetic material without proportion compared to mutations, which are likely to occur in a natural or random manner or which have otherwise been induced by physical or chemical means..

The crops grown and harvested today, whether in organic or conventional fields, are all products of artificial selection (i.e., the identification of individual plants with desirable traits conferred by variations in genome sequences and further breeding to combine beneficial variants). Since the initial description of gene editing in crops, NGTs have been applied to more than 50 plant species. More applications will follow. Given the moderate price of the transformation process, more players are likely to put their NGT-products on the market.

* **10. Have you identified any NGT-related research needs from private or public entities?**

- (●) Yes
- ( ) No

* Please specify which needs and how they could be addressed

Development of traceability strategies are needed.

* **11. Could NGT-related research bring opportunities/benefits to science, to society and to the agri-food, medicinal or industrial sector?**

- (●) Yes
- ( ) No

* Please provide concrete examples/data

Medicinal sector:
NGTs are a matter of great interest to the scientific community, but also as well to the general public. Their potential for clinical applications in the prevention and treatment of genetic diseases, oncology, cardiovascular disease, diabetes, HIV/AIDS, and mental and neurological disorders should be further investigated. By offering increased opportunities for improving diagnoses of diseases and developing targeted drugs, NGTs complement increased global efforts to implement precision or personalized medicine in medical practice.

Industrial sector:
NGTs can increase the number of chemicals and products that are accessible through fermentation and broaden the diversity of strains suitable for industrial production.

Agri-food sector:
According to the coalition agreement 2018-2023 the ban on genetic engineering in agriculture and food, including NGTs, will continue to be supported by the LU government.

* **12. Could NGT-related research bring challenges/concerns to science, to society and to the agri-food, medicinal or industrial sector?**

- (●) Yes
- ( ) No

* Please provide concrete examples/data

Genome editing can be used to make genetic alterations identical to naturally occurring variants. Regulatory systems help society find a balance among the potential benefits, risks and concerns associated with new technologies. However, regulatory effort should be proportional to the risk posed by the product being

evaluated. Genome editing allows relatively precise changes to be made in the genomes of agricultural organisms without the introduction of DNA from other species. Without clear safety and testing guidelines, and public engagement and discussion, the public's trust in the safety of NGT-products will be low. It is not unreasonable to think that, in the wrong hands, NGTs could be used to make dangerous pathogens even more potent. Ethical and safety recommendations are necessary to guide development and use of NGTs.

Agri-food sector:
According to the coalition agreement 2018-2023 the ban on genetic engineering in agriculture and food, including NGTs, will continue to be supported by the LU government. If there is a product authorized or legally traded around the globe, there is some possibility that it will eventually show up in goods imported from third countries.

Medical sector:
- Ethical concerns for applying NGTs to human germ cells and embryos raise some concern.
- Delivery and ability to target specific cell types in the body with high editing efficiency is a key step for successful human therapies.

Environment:
The use of gene drives, though, also poses a much larger risk to the environment, as they can induce imbalance in ecosystems and possible disappearance or alteration of entire species of useful animals and plants. This stands in sharp contrast to the conservation of biological diversity.

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

The maximum file size is 1 MB

C - Information on public dialogues and national surveys

* **13. Have you or other institutions/bodies/entities organised national dialogues concerning NGTs?**

- ○ Yes
- ◉ No

* **14. Have you or other institutions/bodies/entities organised national surveys, which assessed public opinion on NGTs?**

- ○ Yes
- ◉ No

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

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D Information on ethical aspects

* **15. Have any national bodies or expert groups discussed or issued opinion on the ethical aspects of NGTs?**

- ○ Yes
- ◉ No

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

The maximum file size is 1 MB

E - Information on 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?**

- ◉ Yes
- ○ No

* Please provide concrete examples/data

The simplicity of NGT has led to its rapid adoption in various sectors. Current applications of genome editing include some with potential impact on the world food supply and on clinical therapies. Genome editing will not provide general solutions to these broader issues, but there are some areas where the technology could help and should be at least considered.

Medical sector:

- NGTs could help curing genetic diseases by reversing the responsible mutations.
- NGTs could provide the tools that are needed for the development of immunotherapies.
- NGTs could potentially speed up the drug discovery process.
- NGTs could help fighting multi-drug resistant bacteria.

However, the durability of NGT-induced functional effects has yet to be extensively tested, and thus the optimal delivery strategy as well as potential side effects thorugh unitended off-target-mutations/alterations remain unknown.

Due to political decisions, the LU government will not support NGT-products in agriculture and food.

* **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?**

- ◉ Yes
- ○ No

* Please provide concrete examples/data

The application of NGTs require ethical standards and the resulting products need to guarantee the consumers freedom of choice and must be as safe as conventional products.

Question 16

* Under which conditions do you consider this would be the case?

NGT products will need to be regulated, traceable and labelled.

*** 18. Do you see particular opportunities for SMEs on the market access to NGTs?**

- ○ Yes
- ◉ No

* Please explain why not

Medicinal sector:
Therapeutic developers have strong interests to develop therapeutics affecting the greatest number of people. Rare diseases are typically woefully under-researched. By definition, the therapeutic market for rare diseases is smaller and, consequently, therapeutics developers have fewer incentives to cure or treat patients suffering from them. As long as the regulatory system of NGT-products remains unchanged, only the big industries have the budget to push products through the expensive authorization process. The ease of use of NGTs can probably not break the monopole of the big industries.

*** 19. Do you see benefits/opportunities in patenting or accessing patented NGTs or NGT-products?**

- ○ Yes
- ◉ No

* Please explain why not

Patent issues surrounding NGT-products may have important implications for the public health sector. Patents maintain high prices for novel therapies, limiting patient access. The pricing of drugs remains one of the most significant issues to the public interest and public health. This stands in sharp contrast to a cheap, precise mechanism to edit the genome in living tissue.

Moreover “patent wars” between research teams can even prevent or delay that a new product hits the market.

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

The maximum file size is 1 MB

F - 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?**

- ◉ Yes
- ○ No

* Please provide concrete examples/data

Development and application of new genetic engineering methods in agriculture, medicine, and industry raises the issue of legal regulation by the norms of national and international law that ensure biological and ecological safety and efficient risk management and prevent the abuse of such technologies. Therefore, it is necessary to study all the potential risks for ecosystems and humans and to resolve the emerging ethical issues related to the application of this technology.

Medical sector:
In applications to human therapy, we need to be assured that the treatment will not cause a new condition while curing the one intentionally addressed. The effect of off-target can alter the function of a gene and may result in genomic instability, hindering it prospective and application in clinical procedure. Evidence for the safety and effectiveness of this technology can only be obtained through basic and preclinical research, on the basis of strictly following technical standards and ethical norms.

Ever since the first gene-edited baby was “created” to be naturally immune to the human immunodeficiency virus (HIV), discussions were immediately triggered over the scientific and ethical legitimacy of genetic experiments. The incident highlights the need for urgent improvement of ethics governance at all levels, the enforcement of technical and ethical guidelines, and the establishment of laws relating to such bioethical issues.

Agri-food sector:
It is highly improbable for enforcement laboratories to be able to detect the presence of unauthorized genome-edited plant products in food or feed entering the EU market without prior information on the altered DNA sequences (see point 2 and 4). European regulators might need to rely on companies to voluntarily share that data. The creation of a registry of gene-edited crops developed in different countries could be a possible solution and should be considered.

* **21. Could the use of NGTs and NGT-products raise challenges/concerns 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?**

- (●) Yes
- ( ) No

* Please provide concrete examples/data

Question 12

* Under which conditions do you consider this would be the case?

/

* **22. Do you see particular challenges for SMEs on market access to NGTs?**

- (●) Yes
- ( ) No

* Please explain under which conditions

Question 18

* **23. Do you see challenges/concerns in patenting or accessing patented NGTs or NGT-products?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Due to the ease of use of NGTs, the time between new product conception and its actual existence can be relatively short. Whereas basic research is less restricted through intellectual property rights, generation of a commercial application of NGT-products requires a license from the owner of the relevant intellectual property. Again, beneficial application may not be used to their full extend.

Please upload any supporting documentation for this section here. For each document, please indicate which question it is complementing

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G - Final question

* **24. Do you have other comments you would like to make?**

- ( ) Yes
- (●) No

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Contact

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