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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?

Estonia

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

* Please provide details on the request

Yes and no. The public authorities have not been consulted. However, the public authorities have asked advice from our Gene Technology Advisory Board and universities. In addition, the research institutions have been contacted by public authorities, other universities, schools and NGOs. Estonian representatives from Universities have participated in OECD discussion on new genomic methods in Paris in 2018 and in a meeting lead by EPSO (European Plant Science organization) in Brussels in 2019.

* **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

Currently, all research in Estonia with NGTs has been done in contained use. There has been no applications for field trials and no NGTs have been registered in national catalogues.

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

- ( ) Yes
- (●) No

* Please explain why not

Currently, all research in Estonia with NGTs has been done in contained use. There has been no applications for field trials.

* **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

The NGTs referred here are new mutagenesis methods.
In contained use, the inspections do not depend on the methods used in the lab, therefore the inspection practices do not need adaptations.
In other controls, we have not adapted the inspection practices for the products produced by new

mutagenesis technologies, as we do not know about reliable, cost-effective identification methods. The only method of identification we have heard of is whole genome sequencing, but it may not be reliable (as the changes may be results of traditional or natural mutagenesis) and we do not have the capacity (funds, computational and personnel) to do it.

* 3 bis. Have you encountered challenges or limitations, including administrative burden or costs?
- ○ Yes
- ◉ No

* Please explain why not

We have not yet encountered challenges, however, in case, there is an unauthorized environmental release of products made by new mutagenesis methods, we are currently not able to identify whether the changes in the organism are caused by natural mutations, traditional mutation or new mutation methods.

* **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 describe

The NGTs referred here are new mutagenesis methods.
General information we have: some NGTs are based on changing DNA sequences in a very precise way without inserting foreign genetic material. Latter being the major concern regarding classical GMO techniques. At the same time it makes tracing practically impossible, as it is not possible to find one changed nucleotide in the genome, unless there is the specific info about the change. Using WGS (whole genome sequencing) and having a good sequence as reference genome (not the case for complicated genomes like common wheat) makes it in theory possible to detect small changes. However, it is impossible to assert with certainty if the change was produced via new mutagenesis methods or natural mutation. Sometimes, depending on the species and the information available, bioinformatics and statistics can help to calculate the probability that the change occurred naturally or not. We do not consider it feasible right now to apply WGS, bioinformatics and statistics in a routinely way to test plants at large scale: no certainty in most of the cases and expensive.

* How could these challenges or limitations be overcome?

We do not practical solutions, however, we are open for discussions.

* **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:**
- ☑ **Agri-food sector?**
- ☐ **Industrial sector?**
- ☐ **Medicinal sector?**

Agri-food sector

There have been no experimental releases in our country, neither with conventional GMOs nor with NGT-products, therefore, we do not have any experience to share. However, there are labs that would wish to carry out field experiments with NGT-products (plants) but they have not yet done it due to possible bureaucratic burden regarding applying for field trials with GM organisms.

* **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 specify

There is no specific information required in the application. However, in the technical questionnaires there are questions about breeding methods (ie. What is the formula for hybrids).

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

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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 provide an overview of the project/program including title of project, a brief summary with scope and objectives, the amount of national funding received and possibly specify if the receiving entity is public or private

The Estonian Research Council has funded several projects of the University of Tartu that use NGTs to achieve the set objectives.
PSG404 - Improving plant productivity and water use efficiency via simultaneous modification of stomatal density, aperture and photosynthesis. It is a start-up project funded for 4 years, 01.01.2020 to 31.12.2023, with 104 500 € yearly funding. The objectives of the project are:
1) simultaneous modification of stomatal development and aperture, with the aims to i) identify the mechanisms of possible coordination and co-regulation of stomatal development and aperture and ii) identify trait combinations that could be applied in breeding crops for improved water use efficiency (WUE), drought tolerance or yield

2) simultaneous modification of stomatal and photosynthetic parameters, with the aims to i) gain insight into coordination and regulation of stomatal physiology and photosynthesis ii) identify trait combinations that could be applied in breeding crops for improved WUE or yield
Within the frames of the project, NGTs will be applied to generate mutations in genes of interest.
PRG433 - Unlocking the potential of guard cell CO2 signalling for designing drought-tolerant plants. It is a team grant funded for 5 years, 01.01.2019 to 31.12.2023 with early funding 257 125 € year. The objectives of the project are:
1) To identify molecular details of the guard cell CO2-signaling and to apply this knowledge for improving plant drought tolerance.
2) To identify new components of guard cell CO2 signalling and study their function in modulating plant water-use.
With the project the scientists are already analysing NGT tomato plants that have significantly higher water use efficiency and on the basis of laboratory experiments withstand better drought conditions. Next step will be to study possible effect on yield and dependent on results introduce these modifications to various tomato varieties to reduce water use in commercial greenhouses. Similar approach is been scheduled also with barley, a common crop in Estonian fields and thus eventually the plan is to make these NGT-products available to Estonian farmers.
PRG719 - Stomatal regulation due to reduced air humidity and its links to abscisic acid and temperature. It is a team grant funded for 1 year, 01.01.2020 to 31.12.2020 with 183 250 € funding.
The project studies: 1) dry air-induced stomatal closure, its dependence on the plant stress hormone abscisic acid and leaf hydraulics, missing links and proteins in the pathway and 2) the responses of production-related gas exchange traits of Arabidopsis and agricultural plants to reduced air humidity and increased temperature, applied either singly or together.
Within the frames of the project, NGTs will be applied to generate specific mutations in genes of interest.
Enterprise Estonia has funded a project by University of Life Sciences.
Project “Development of cloning technology for the production of biopharmaceuticals from the transgenic cattle” (1.04.2009–28.02.2014). The amount of funding was 985 609.59 EUR. The aim of the project was to produce transgenic cows with somatic cell nuclear transfer and from the milk of these animals purify human pharmaceuticals for medical use. The project was followed by a follow-up project “Supporting the development of transgenic cloning technology” (25.10.2015–31.03.2016) that received public funding from University Development Funds (22 100.00 EUR).

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

We did not encounter any challenges when funding the NGT related research. As the studies are all done in contained use, they have to follow the corresponding rules. To receive the funding, they have to follow the rules of the grant application process and compete with other applicants.

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

The NGTs referred here are new mutagenesis methods unless stated otherwise.
NGT-research is evolving very well. By now, NGTs have become standard in research labs working with model organisms and they are continually adapted for application in a wide range of species. For example, PubMed.gov scientific database gives at the moment over 8000 CRISPR-Cas related entries. The precision of the NGTs is improving daily, with technologies like prime editing that enables targeted controlled changes of specific nucleotides in DNA being developed. Number of plant species in which NGTs can be applied for genome editing is already high and it is growing rapidly. NGT-related research has and will have many opportunities for studying basic mechanisms and functions in microorganisms, plants and mammals. Moreover, it has very important role in applied sciences, such as plant breeding. Especially in the light of

Green Deal, where Europe needs to lessen the amounts of pesticides and mineral fertilizers. Currently the other countries (USA, Canada, Argentina etc) have moved on with NGT research quite fast, as for they have decided, that the potential benefit is more important than potential risks. It is very likely that NGT will be driving plant breeding research in future, as they enable controlled, fast and efficient mutagenesis and selection of varieties, contrary to the established methods of classical plant breeding.
There are concerns, that as long as products made by new mutagenesis methods are categorized under EU GMO legislation, the new mutagenesis methods related research will be done only for basic research in academic setting and that majority or all agriculturally grown varieties developed by new mutagenesis methods will be developed outside of Europe using foreign varieties and species that might not be cultivatable in Estonia. Any NGT-variety developed abroad and officially registered in Europe will have to be very profitable, therefore it is likely that the NGT-varieties will be primarily engineered for very high yield with intensive practices. In longer run, global demand for high quality produce using minimal chemical plant production will increase with global population and public ecological awareness.
This is likely to lead to deregulation of NGTs as GMOs and NGT-products will be treated as regular varieties needing no special regulation. This will enable the development of NGT-varieties with ecologically beneficial traits with less emphasis on high profitability.
There are international discussions about the use of NGTs in nature conservation, however, there are no such discussions in Estonia. On international level, it is discussed that the organism made by NGTs, especially gene drive organisms might be used for example for eradication of invasive species. However, this work is still theoretical and raises ethical concerns in addition to legal concerns as under current legislation it is not allowed to introduce GMOs that will spread in nature.

*** 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

The NGTs referred here are new mutagenesis methods.
NGTs help to breed and develop crop plants that are more resistant to biotic stresses (diseases and pests) and abiotic stresses (heat, drought, frost, winter damages). Since the new Green Deal has aimed to reduce the chemical pesticide use in agriculture, then there is a need for many more varieties that are resistant. Another goal is to reduce the amount of mineral fertilizers used. One way out could be the use of crop varieties that can use nutrients in more efficient manner. We also need to improve other crops (pulses, other legumes, vegetables), that can improve the crop rotations (by adding more nutrients to the soil, by breaking the crop cycles and thus diseases; enriching the ecosystem biodiversity), but also they can improve the variety of foods and thus improve human health. Farmers and breeders in Estonia have expressed concerns that traditional crop breeding is too slow to provide climate ready varieties fast enough. They have stated that application of NGTs would be welcome to solve these urgent needs. Of course, other technologies, such as genomic prediction and selection will also remain important. Especially as for many required traits, there is no info about the resistance genes and their functionality.
NGTs in principal are low cost methods and therefore they could be very useful for small countries, like Estonia, to improve the crops suitable for the Nordic climate. When most of the world needs crops tolerant to drought, then Nordic countries need crops that can tolerate too wet soils, as well as winter and frosts. Estonian crops have to be adapted to short vegetation period.
Already present example in the world, that can be useful in Estonia, is the powdery mildew resistant wheat, where MLO 1 or/and TaEDR1 locus modification gives 40-100% resistance. However, Estonian farmers need also varieties that are resistant to septoria leaf blotch, tan spot disease of wheat (Pyrenophora tritici-repentis), Fusariums, net blotch of barley Pyrenophora teres, Drechslera teres), snow mold (Typhula incarnata, Typhula itoana). These are the most important diseases for Estonian farmers. There are also

problematic pests. In Estonia, there is a need for varieties resistant for Oscinella frit, thrips, stem weevils (Ceutorhynchus pallidactylus).
One more important question is how to avoid or minimize the off-target effects and how to make gene knock-in more effective using NGTs. Because using the NGTs for production of commercial products, the offtarget effect question is most important, the safety of the technique.
The other research area in human medicine is how to use the NGTs in gene therapy, how they can be delivered in to the body. Medical research also needs to focus on curing hereditary monogenic diseases using NGTs.

* **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

The NGTs referred here are new mutagenesis methods.
NGT-related research would bring benefits to all listed sectors by providing a great tool for basic sciences. For science NGT-related research provides rapid techniques to introduce various alterations into the genome and test their relevance for organism form and function in every scale. As a specific example, the scientists have used NGTs to create mutations in target genes of interest that they think are implicated in plant stomatal regulation. This has enabled them to test, whether the genes of interest have a role in stomatal function in several organisms, such as Arabidopsis thaliana, tomato, rice and barley.
Our scientists have generated tomato plants by CRISPR method, where HT1 gene function is missing, that lose less water and are more tolerant to drought. These plants could easily be developed for application in agriculture and benefit the agri-food sector, if NGTs were not regulated in the EU as they currently are. With current regulation, the scientists do not have sufficient resources to carry through the process of taking the drought tolerant plants they have developed to practical application.
For society, NGT-related research brings new knowledge about how the world functions and thus provides ideas for solutions to the problems the society at large faces, such as climate change and diseases.
For agri-food sector. The NGTs will speed breeding process and possibly enable creating or transferring beneficial traits into organisms that cannot be created by classical breeding methods. There is an urgent need to speed plant breeding process as climate is changing in several agricultural regions and this poses a risk for global food security. Furthermore, NGTs can reduce the use of toxic chemicals as pesticides since they provide methods for acquiring plant intrinsic genetic systems for pest management and this in turn will have positive effect on farmers' health and the environment. NGTs can make more sustainable and environmentally friendly agriculture that can help with several SDGs (no hunger, health, clean water, sustainable production, climate change, ecosystems).
Animal research has examples of edited farm animal genes to make them more muscular or resistant to certain virus. There have also been research how to increase animal welfare to make, for example, dairy cows naturally without horns, so they do not have to go through the painful procedure of the removal of the horns.
For medicinal sector, NGTs can help in treating genetic diseases for which there is no alternative cure, or that is currently very expensive. NGTs can also be applied for the production of drugs or other compounds with medicinal activity by microorganisms or plants. There are also edited chicken eggs that can produce vaccines or pharmaceutical components for human medicine. This solution decreases the waste of eggs at the same time. From the industrial point, there are opportunities to increase sustainability in production, which is closely linked to bioeconomy.
For industry, NGTs would create new opportunities for small enterprises, if they were not regulated as GM-technologies, as application of the NGTs is relatively cheap and would thus be accessible for small

companies that could bring to the market products needed by the agricultural or medical sector, currently accessible only to large corporations.

* **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

The NGTs referred here are new mutagenesis methods.
The major challenge with the NGT-related research is that the research done in laboratories will not lead to practical applications, because the regulation of NGTs is as slow, costly and inefficient as it is for GMs. Thus, although the benefits of the plant varieties or treatments developed by NGTs could be immense for agriculture and medicine, they will not happen, because it is too time consuming and costly to bring these solutions to the market. So EU research is currently lagging behind.
In respect to concerns to society: all stakeholders need to be well-informed. The societal discussions need to be undertaken in the timely manner. In other European countries, the open discussion has helped. Active discussions are still missing in Estonia.
Challenges regarding ethics are important. How far we can go with the edits and how to regulate them. How to make sure everyone follows these guidelines.
The challenges and concerns are already there: EU is lagging behind in this field, scientists and industry are already moving to other countries.
There are also concerns related patenting NGT-varieties that will lead to restrictions in plant breeding. It is important that new NGT-varieties are available for plant breeding under plant breeder's rights.

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

* Please describe briefly the content, methodology and conclusions

The ministries have not organised a national dialogue. However, there have been newspaper articles, public presentations, debates, and discussions between different stake-holders, researchers and public authorities. Universities have introduced and discussed NGTs to/with the public at every opportunity. As researchers and teachers, they school the next generation of scientists, officials and citizens through their courses in the university, where they introduce, explain and discuss NGTs. In addition, in agricultural sector two bigger presentations to farmers (Future of plant breeding, Evelin Loit, 07.02.2019; Precision breeding, Evelin Loit,

20.03.2020) have been made, explaining the mechanisms of NGTs, which were followed by discussion. Conclusion by farmers was that the new technologies are very useful and they need to be used more and faster in the agricultural sector.

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

- (●) Yes
- ( ) No

* Please describe briefly the content, methodology and conclusions

University of Tallinn has made surveys as part of teaching on different topics (i.e. personal medicine), which have included questions about NTGs (data not available).
The most recent public perceptions study was done in 2009 by national economic research institute. The survey did not distinguish GMOs and NGTs. It was a typical consumer survey carried out within 1 month, the results were based 1000 written replies. The main conclusion was that the population is poorly informed on GMOs.

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 describe briefly the content, methodology and conclusions

In July 2019, more than 160 European (including Estonian) scientist wrote a letter to the EC and European Parliament to ask for a change in the legislation. The letter dealt with NGTs related to agriculture and explained the need for these techniques in this sector. The letter was echoed in the media with a positive feedback, as if there were no ethical concerns. Vice-versa: the call on EC to amend legislation was perceived as the ethical choice. Before that, in 2018, the case of He Jiankui experiment with human germline was largely commented in the press, as a scandal going against ethical rules.
In national level specifically ethics has not been discussed, however, university of Tartu and University of Tallinn researchers have participated in European level forums where these topics have been discussed. There has been a question whether allowing foreign GMOs would have adverse effects on the availability and use of local varieties. During a public debate about genetically modified food crops a question was raised whether it is ethical to restrict the use of NGTs if they could improve plant resistance.

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 NGTs referred here are new mutagenesis methods.
The use of NGTs and NGT-products would bring positive effects to all sectors.
The benefits are covered in questions 10 and 11. In addition, for the agri-food sector, in the conditions of climate change the speed of traditional breeding is not sufficient to keep up with the increasing demands of the more extreme weather conditions, as developing new varieties through several generations of crossings takes too long time and too many resources. NGTs enable to achieve similar effects within one or two generations, reducing the time to develop a new variety 5-10-fold, and decreasing the costs remarkably.
If the plants obtained by NGTs could be commercialized faster and with less costs, agri-food sector would benefit as varieties with improved stress tolerance and yield obtained in laboratories would reach the fields and contribute to farmers and consumers welfare. Local potato varieties made resistant to potato cyst nematodes would enable to restrict the spread of potato cyst nematodes in Estonian fields and ensure higher yields without being forced to abandon local popular varieties. Local variety of field pea made semi-leafless would enable to improve the lodging resistance of that variety and enable combine harvesting. Varieties could also be made more suitable for human consumption by reducing the expression of toxic glycoalkaloids in potato or common allergens in other food crops.
Furthermore, several valuable traits cannot be delivered by classical breeding methods. NGTs enable fast targeting of specific genes underlying the traits that farmers and consumers are interested in (drought tolerance, disease resistance, yield quality and quantity, nutrient content etc). If the plants obtained by NGTs could be commercialized faster and with less costs, agri-food sector would benefit as varieties with improved stress tolerance and yield obtained in laboratories would reach the fields and contribute to farmers and consumers welfare.
As for the medicinal sector, there are many genetic diseases, which either cannot be cured to date or are extremely expensive to treat. Application of NGTs for gene therapy would help in combating these genetic diseases.

* **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 NGTs referred here are new mutagenesis methods.
NGTs and NGT-products could bring many benefits. In addition to the answer to question 10 the biggest gain would be for environment and plant health. NGTs enable faster plant breeding with less generations, they would reduce the environmental footprint of breeding. By NGTs, plants that have improved disease or pest resistance can be generated, thus reducing or removing the need to apply fungicides or pesticides, reducing the costs and mitigating the environmental impacts of agriculture. Healthier plants and lessening of pesticide residues will improve human health.
Water-saving varieties can be developed by NGTs, reducing the amount of water applied for agriculture and therefore being more environmental friendly. NGTs could also be applied in phytoremediation to generate plants that can take up and/or metabolize toxic compounds from the environment.
Better selection of varieties suitable for Estonian conditions would support strongly the farming sector in general. When we have farmers, then we will have food security and strong and lively rural communities.
In farm animals, it could be possible to make them more resistant to certain diseases, like for example African Swine Fever, this would again reduce the cost for farmers and prevents food shortages.
For human medicine, it could be possible to develop new gene therapy methods to cure some diseases or at least make the symptoms milder.

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

The NGTs referred here are new mutagenesis methods. NGT-products could provide the above said benefits, if it would be easier and more cost-effective to have them commercialised.

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

- (●) Yes
- ( ) No

* Please explain under which conditions

The NGTs referred here are new mutagenesis methods.
NGTs in principal are low cost methods and therefore they could be very useful for small countries, like Estonia, to improve the crops suitable for the Nordic climate. Estonian plant breeding is funded nationally, but NGTs can provide opportunities for SME-s to develop some varieties (like neglected crops, vegetables).
If plant breeders can selectively improve old varieties and landraces then there will be a new market for large selection of improved old varieties. There is already public interest in genetically blue potatoes, green tomatoes and other varieties with interesting taste, appearance or texture. These varieties are often expensive to grow and they lack resistance to new plant diseases. If old varieties could be improved with a few carefully selected traits then more old varieties would be profitable to be produced by SMEs.
If NGT-products would be classified as products obtained by classical breeding, then this would significantly reduce cost for bringing new (improved) varieties into the market and this would make it possible for SMEs to contribute to breeding process. Currently, it is likely that they cannot afford it due to high cost and big risk in bringing GM-products to the European market.

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

- ( ) Yes
- (●) No

* Please explain why not

The NGTs referred here are new mutagenesis methods.
The opportunity to patent NGTs or NGT-products would increase attractiveness of agri-sector and this in turn should attract investments from private sector. However, this would likely help larger companies and not so much small enterprises, breeding centres and universities. Thus, patenting may instead hinder breeding process, as it would deny wide access of breeders to patented varieties and limit further breeding opportunities. It would be better, if NGTs and NGT-varieties were freely available for use in plant breeding, as traditionally bred registered varieties are, as this would lead to a larger improvement of desired traits in shorter time. The patent system has proved to slow increase in yield per hectare in the USA. NGTs and NGT-varieties must be freely available for use in plant breeding because patents will slow down plant breeding and make NGT-varieties more expensive for farmers to grow. Restrictions and rules for growing a patented variety limit the free choice of a farmer over his production process.
The patents should not protect the NGTs as methods. The initial idea behind CRISPR/Cas system was to create simple and accessible method, which can be used by all researchers and enterprises despite the size of the lab and budget. However, novel plant varieties bred by NGTs should be protected as any other variety.

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

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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

The NGTs referred here are new mutagenesis methods.
Challenges and concerns will always be there. It is a matter of coping with them in the proper way: well established market policy, communication with all stakeholders (especially with direct consumers), updates in the legislation if needed, transparency at all levels.
One of the challenges is the trust in the community and public perception. The examples from the other countries show, that if something is done for purpose that is understandable to the consumer, they accept the method, as well (ie. Arctic Apple, non-browing mushrooms). So the main challenge is proper marketing and correct consumer information. The legislation needs to be updated accordingly.
A potential challenge is public perception, but this is unlikely to change when NGT is heavily regulated in EU as potentially dangerous, even though the risks have been shown to be no greater than for conventional breeding. If NGT is used to upgrade local varieties for maintaining their propagation in the same region, no inconveniences can be foreseen for the farmers as they are already familiar with the growing techniques for these particular varieties.
Potential problems are related with verifying NGT-products which are difficult (or even impossible) to discriminate from those obtained by mutagenesis. This is major question, when Europe wants to protect its market.

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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

The NGTs referred here are new mutagenesis methods.
All new technologies have some risks and it is impossible to know all consequences especially at long term. At the same time, NGTs have so many advantages and are not dangerous per se, that it is logical to seek development and accept a certain level of risk. As always, it is a matter of reacting adequately with policies and legislation as soon as a risk appears.
For agri-food sector, the NGTs and NGT-products do not raise challenges that would be different from traditional breeding in terms of obtained results. Most, if not all results that can be obtained by traditional breeding could be also obtained by NGTs. The difference is much improved speed and precision of NGT. If anything, they pose less challenges, as NGTs enable directed control over mutagenesis, which has never been possible or controlled in traditional breeding, where thousands of unknown changes in genomes are present in the varieties developed. With NGT-products, the potential risks arising from these unknowns have been mitigated by controlled changes in DNA.
Adverse public perception could cause time-consuming public debates but the benefits of NGTs and NGT-products may outweigh these challenges. Also, if NGT is used to upgrade local varieties for maintaining their propagation in the same region, no adverse effects on the environment are expected.
If the organisms made by NGTs for agri-food sector, are leading to agriculture that uses less fertilizers and plant production products then this would be more beneficial to environment compared to conventional agriculture. However, when developing the organism by NGTs, the potential harmful effects to environment should be avoided.

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

When public is not adequately informed or involved in discussions.

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

- (●) Yes
- ( ) No

* Please explain under which conditions

The NGTs referred here are new mutagenesis methods.
If the NGT-products are regulated as GM-products, the SMEs have difficulties in market access, as the development of the products is time consuming and costly. Furthermore, due to current regulation of GMproducts in European market, it is unlikely that SME-s could afford using them. If the NGT-products were regulated as traditionally obtained varieties, the SMEs would likely have better market access, as NGTs enable faster and cheaper development of new varieties than classical methods and thus SMEs would be more likely to afford it.
If the patent system is applied to NGTs and NGT-products, then yes. If the patent system is avoided, then NGTs create many new opportunities for SMEs. NGTs are highly technology and know-how demanding, thus the use of these methods might not be accessible to SME breeders and it is very important that NGT-varieties are also available for conventional plant breeding even for SMEs.
The SMEs in Europe are moving to other places due to the EU legislation. Even if the regulation in the EU

changes, the challenge is to have a balance in the market so that the SMEs have their own place beside the big seed/biotech multinational companies.

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

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

The NGTs referred here are new mutagenesis methods.
Yes, patenting and maintaining the patents is expensive and therefore the entire process is hard for both the start-ups and the SMEs to access. Challenges related to patenting NGTs and NGT-products lye in the hindrance to the possibility to use developed varieties as a basis for further breeding, when they have been patented. For efficient and accessible breeding, NGTs should be treated as conventionally bred registered varieties that are freely accessible to breeders under plant breeder's rights. This approach would give the best chance for achieving breeding goals and give opportunities for small companies, breeding centres and universities to contribute to this process. Otherwise there is a danger of having the big seed companies getting the market (IP rights, patents) and leaving the SMEs with minor possibilities.

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

Please provide your comments here

The NGTs referred here are new mutagenesis methods.
Professionals working with the new mutagenesis methods find that EU needs to change the legislation related to NGT-products. Otherwise, technological development and the utilisation of applications will be inhibited for decades as happened with the stem-cell technologies in some regions of the world and which has cut the legs of regenerative medicine. Europe cannot stay behind in the research and application of these techniques. Researches and companies are already moving to other countries to develop their ideas.
All plant breeding is based on changes in plant genome. Conventional breeding changes plant genome enormously: each crossing changes half of the genome. For wheat, this is half of six times 15 billion DNA bases. Contrary to traditional plant breeding that applies chemicals and radiation to introduce a large array of unknown mutations in genomes, NGTs enable fast controlled changes of genomes and thus provide the opportunity to carry out targeted precision breeding that has never been accessible before. Therefore, NGTs are currently the best and most controlled technology for breeding that could bring vast benefits to agriculture and environment, if their application were not unnecessarily complicated as it is under current EU regulation that classifies NGTs as GM products.
Using NGTs can advance plant breeding and help breed high yielding crops better suited for less intensive

agronomical practices. However, NGTs will only help if the new NGT-varieties are not restricted from plant breeders by excessive regulations, patents or any other loopholes (i.e. classifying them as synthetic varieties).
In discussions about the use of the organisms made by with NGTs in addition to potentially negative effects also potentially positive effects should be considered.

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