Contribution ID: 0d2655b6-49e5-4b79-8f61-11b5f56ccb49
Date: 28/04/2020 18:57:27

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?

Ireland

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

The Health Products Regulatory Authority (HPRA) had an innovation query in relation to the development of a medicinal product using CRISPR/Cas9 to correct a gene mutation.
As referenced under question 10, several plant breeding companies based outside the EU have contacted Teagasc seeking clarity on the current legal status.
The Health Products Regulatory Authority (HPRA) had an innovation query in relation to the development of a medicinal product using CRISPR/Cas9 to correct a gene mutation.
As referenced under question 10, several plant breeding companies based outside the EU have contacted Teagasc seeking clarity on the current legal status.

* **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

To date, GMOs generated using NGTs have been consistently regulated under EU GMO legislation.

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

- ( ) Yes
- (●) No

* Please explain why not

No challenges or limitations have been encountered to date however that does not preclude that there will be in the future. The current legal issue is the primary challenge. Potentially identical products may be obtained by different techniques and may then fall under different regulatory regimes. Directive 2001/18/EC needs to be reviewed and updated to accommodate the new circumstances with respect to NGTs. Definition, including but not limited to, GMO and mutagenesis need to be addressed as well as the rapid development of NGTs.

* **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

It is proposed to carry out similar controls and checks on products produced from NGTs as those currently in place for GMOs. Until such time that official identification and quantification methods are established, the controls will be based on documentary checks.

We do not have the technical capacity to detect and identify organisms generated using NGTs.
We have not made an assessment of NGT products available in third countries or their availability in the EU. Is the full extent of international trade of products generated using NGTs known?

No specific measures are being undertaken.
The nature of the modification is not known in advance and there is a lack of validated detection, identification and quantitation methods. If there is no new or foreign DNA or if there is no sequence information on the mutation, then there is no detection method. Furthermore, it is not possible to distinguish between plants produced by new mutagenesis techniques or by conventional mutagenesis or natural mutation. Unauthorised releases are even more problematic if there is no general screening or information available on what to look for.

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

- (●) Yes
- ( ) No

* Please describe

Owing to limited availability of resources (in terms of monitoring costs, financial and human resources) we are reliant on the industry developing detection methods in respect of GMOs to be placed on the market.

* How could these challenges or limitations be overcome?

Greater availability of resources

* **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

We have no experience

* **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?**

☑ **Medicinal sector?**

Agri-food sector

There are no experimental releases involving products generated using NGTs

Industrial sector

There are no experimental releases involving products generated using NGTs

Medicinal sector

There are no clinical trials involving products generated using NGTs

* **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

aa9039e6-55ad-47cc-8ca3-b0d5c34e336b/Question_7.docx

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 data provided (title of project and cost) is contained in Appendix 1. It has been pointed out that there may only be a fraction of these monies that are actually used to support the NGTs.
In addition to the information provided in Appendix 1, Teagasc are currently conducting research around the potential impact of utilizing gene editing as a means to prove/disprove gene functionality tests. In essence, the gene editing that is currently being conducted is being used for proof-of-concept purposes.

The establishment of a Virtual Irish Centre for Crop Improvement (see Appendix 1) has at its core two

principle objectives:
1. to exploit the output of recent/current research programmes to effectively interconnect the application of biotechnology tools to varietal improvement goals and
2. to build sufficient capacity in Ireland to lead to the identification and development of improved crop varieties for the Irish agri-industry.
The data provided (title of project and cost) is contained in Appendix 1. It has been pointed out that there may only be a fraction of these monies that are actually used to support the NGTs.
In addition to the information provided in Appendix 1, Teagasc are currently conducting research around the potential impact of utilizing gene editing as a means to prove/disprove gene functionality tests. In essence, the gene editing that is currently being conducted is being used for proof-of-concept purposes.

The establishment of a Virtual Irish Centre for Crop Improvement (see Appendix 1) has at its core two principle objectives:
1. to exploit the output of recent/current research programmes to effectively interconnect the application of biotechnology tools to varietal improvement goals and
2. to build sufficient capacity in Ireland to lead to the identification and development of improved crop varieties for the Irish agri-industry.

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

Challenges encountered at present are technical. The technology is developing rapidly and tools are coming on line to assist in overcoming the existing challenges. The primary challenge is the fact that any plant material that is edited must be considered a GMO following the ruling of the ECJ in 2018. This is at odds with the guidance and reports published by the European Commission's Scientific Advisory Mechanism, EFSA, EASAC as well as a multitude of national scientific organisations and academic/industry institutions. The current legal issues are the primary challenge, and this must be addressed within the confines of current GMO legislation.

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

NGT techniques are likely to become an integral part of biological research. Over the past 10 or more years this has already largely taken place in many fields of discovery research, in particular in fields such as biochemistry, genetics and immunology. This trend will continue to accelerate with the advent of CRISPR and other increasingly accessible genetic manipulation techniques. This trend is being supported by significant decreases in the cost of genome sequencing, and when combined this is resulting is a future trend towards moving these techniques from discovery to translational work. This includes advanced therapy medicinal products (ATMPs), and to a lesser extent agri-food.

Furthermore, new [plant] varieties have been developed for all major crop species with enhanced efficiencies to combat abiotic stressors, existing pests/pathogens and/or utilize fertiliser to reduce run off potential. The impact of editing is real in that it can make a positive contribution to crop (tillage and grassland) production, which could assist Ireland meet its environmental goals. Unfortunately, the current legal status on editing within Europe makes this challenging and unlikely.

In the area of medicine there are a considerable number of diseases which could potentially be treated by gene editing techniques, by correcting at genomic level, mutations that are associated with producing the pathophysiological phenotype of the disease.

* **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

Several plant breeding companies based outside the EU have contacted Teagasc seeking clarity on the current legal status.

Research funding bodies have indicated that while there are a number of programmes where research using these advanced techniques can be applied to make scientific and societal advances, they are not specifically tailored to respond to research needs in this domain. There is no dedicated NGT strategy. Funding programmes operate on a bottom-up basis, where applications are assessed on their scientific excellence and their potential for impact. NGT related research needs have not been identified or addressed as such. This does not preclude the funding of NGT related research in the future provided of course a relevant proposal is submitted.

* **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

This area of research has already brought enormous benefits to early-to-mid stage research, such as their use to develop induced pluripotent stem cells. 15 years later, and with a number of improvements to techniques used, many of the leading genetic technologies are now making the transition from lab to market /society. Significant medical advances that are on the cusp of creating a very sizeable impact on the pharma industry and on human health include gene therapies, CAR-T/CAR-NK therapies, and others. By making these techniques easier to use and adapt by a wide range of scientists around the world, new genetic manipulation techniques also have the potential to make significant strides in agri-food, to the benefit of society and industry.

Novel varieties with tolerance to diseases e.g. late blight resistance in potato, septoria resistance in wheat, Rhynchosporium and ramularia resistance in barley, BYDV (barley yellow dwarf virus) resistance in wheat /barley, cereal and potato varieties with increased nitrogen and phosphorous use efficiency, plus grass with enhanced agronomic and nutritional composition. The cultivation of these varieties would dramatically reduce the level of synthetic pesticides used in Ireland and reduce the need for fertiliser. This would be in line with the overall goals of the EU's Green Deal.

From a medicines perspective, NGTs can edit and correct mutations at a DNA level and thereby provide long term benefit

* **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

In the medical/pharmaceutical sectors a number of challenges exist. These include the potential cost of ATMPs and related challenges around health budgets, insurance coverage and national reimbursements. Industrial production of these products is also a significant challenge, with many products moving into the market being highly patient specific. Scientific challenges (and also potential solutions) in this area include how to use allogeneic cells for CAR-T, or other methods to mass produce and bring down costs. Related to this are challenges to society, including questions of potential income-based access to medical treatment. These challenges already exist in society but could be exacerbated by new genetic treatments. Cost is also an issue in agri-food, as is societal acceptance.

Ethical concerns in that any DNA sequence in the body can potentially be altered. Prior ethical clearance of projects is given in research institutes.

In the medical/pharmaceutical sectors a number of challenges exist. These include the potential cost of ATMPs and related challenges around health budgets, insurance coverage and national reimbursements. Industrial production of these products is also a significant challenge, with many products moving into the market being highly patient specific. Scientific challenges (and also potential solutions) in this area include how to use allogeneic cells for CAR-T, or other methods to mass produce and bring down costs. Related to this are challenges to society, including questions of potential income-based access to medical treatment. These challenges already exist in society but could be exacerbated by new genetic treatments. Cost is also an issue in agri-food, as is societal acceptance.

Ethical concerns in that any DNA sequence in the body can potentially be altered. Prior ethical clearance of projects is given in research institutes.

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

ab03251c-7aa0-449b-9089-b62ddae5b69f/Question_12.docx
30afd5bf-dfbf-47c0-828e-380c37a8cd91/Question_8_Appendix_1.docx

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

The maximum file size is 1 MB

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

From a medicines perspective, NGTs can edit and correct mutations at a DNA level and thereby provide long term benefit as the edited DNA is inheritable when the cells divide etc. This could offer potential therapeutic options for diseases which have limited or ineffective alternative treatment options.
Research into disease resistance without the use of chemicals
Crop enhancement (disease resistance, nutrient use efficiency and productivity)
Reduction of use of plant protection products
The challenges presented by climate change
Refer to Question 11

* **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

See response to Question 16 above

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

Where there review/amendment of the legislation and public engagement

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

- ○ Yes
- ◉ No

* Please explain why not

The legislation is restrictive. The costs associated with the authorisation procedure are high for public research bodies and SMEs. This places public research bodies / SMEs / plant breeders at a competitive disadvantage in relation to their equivalents in other non-EU countries. Their capacity to avail of this scientific progress is challenged.

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

- ○ Yes
- ◉ No

* Please explain why not

We have no concrete examples re NGT patenting

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

Acceptance would be an issue with regard to agri-food.

As already outlined problems exist with regard to detection and identification. This will likely impact on inspection and control systems, particularly in terms of identifying the possible import of unauthorised feed /seed from third countries that do not consider such products produced using NGTs to be GM. This problem is likely to be exacerbated as NGTs become easier and cheaper.

*** 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

No concrete examples that we have experience of but one which has been well documented has been the application of gene editing for reproductive purposes and embryo edits by rogue users.

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

Where there is a disregard for ethics and human/patient safety

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

- (●) Yes
- ( ) No

* Please explain under which conditions

Generally the legislation is restrictive, costly and lengthy. It places public research bodies / SMEs / plant breeders at a disadvantage in relation to their equivalents in other non-EU countries where NGTs are not subject to regulation. This will likely impact competitiveness and innovation within the EU.

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

- ( ) Yes
- (●) No

* Please explain why not

Patents provide an incentive to continue to invest in research and development

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

G - Final question

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

- (●) Yes
- ( ) No

Please provide your comments here

We support a review and amendment of Directive 2001/18/EC to accommodate the new circumstances with respect to NGTs as well as to support finding some solution to the detection and identification problem that exists.

EU authorities must address the legislation to provide clarity and to keep up to date with evolving science

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

Contact

SANTE-NGT-STUDY@ec.europa.eu

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

No, however the Minister shall, where a GM variety has been accepted, indicate it as such in the National Catalogue.

Q8

Appendix 1

Proposal Title	Public/Private	Direct Costs / €
The establishment of a Virtual Irish Centre for crop improvement	Public	2,992,994.00
The ATR and ATM kinases: new roles in maintaining genome stability	Public	1,385,058.00
Multiparticulate Technology Development for Enhanced Oral Delivery of Pharmaceuticals	Public	34,515.82
Understanding biopharmaceutical production at subcellular resolution: The application of ribosome footprint profiling to optimise therapeutic protein synthesis in mammalian cell factories	Public	480,030.00
Development of GDFS neurotrophic factor therapy for Parkinson's disease	Public	494,278.00
Development of an Aspergillus niger strain for industrial heterologous protein expression	Public	57,341.00
Evaluating the potential of EMT, a novel gene transfer technology, to overcome the industrial challenge of genotype dependency, which limits the engineering of multiple varieties of important crop species	Public	71,577.75
Mechanisms & consequences of HDACs in the NCoR Complex, in controlling the activity of MutSb in trinucleotide repeat expansions	Public	221,050.00
Quantitative and systems of analysis of (patho)physiological signaling networks	Public	1,299,917.00
Uncovering the fundamental roles of the CDC7 kinase and of its regulatory subunits through genome editing technology	Public	1.323,591.00
A new avenue for crop protection; generating Brassica cultivars with supernumerary trichomes	Public	447,348.50
Development of Continuous Spatially Distributed Diafiltration for Pharmaceutical Synthesis	Public	93,498.43
miRNA knockout using CRISPR/Cas9 to enhance recombinant protein productivity in CHO cells	Public	93,203.10
Uncovering the role of ER-shaping proteins in neurodegenerative disease	Public	32,474.00
CHO cell process characteristic profiling and modelling in fed-batch and continuous perfusion cell culture platforms	Public	72,605.00
Development of a biocomputing platform to screen bifidobacteria for the food industry	Public	5,272.58
BacTrans - Natural DNA Transfer systems for Bacterial Starter Cultures	Public	848,098.34
A Disruptive, Non-Viral Gene Editing Platform Technology for Treating Genetic Conditions	Public	217,070.00
Discovering non-protein coding vulnerabilities in lung cancer with CRISPR-Cas9	Public	1,246,311.00
CD39/HGF Modified CD362+Stromal Cell Therapy for Ischemic Muscle Injury	Public	79,160.02
Assessment of functionality of immune cells following Solupore® mediated engineering	Public	48,210.67
Type VII collagen restoration for RDEB using a non-viral non-invasive CRISPR system	Public	58,179.17
Targeting underlying disease mechanisms in cancer using targeted protein degraders, a novel class of molecular therapeutic	Public	423,816.00
READER LOST IN TRANSLATION - An epi-transcriptomic-based approach for development of high producer Chinese Hamster Cells	Public	96,315.00

Validating promising RIP2 inhibitors as a new therapeutic option in triple negative breast cancer	Public	98,800.33
New yeast strains for production of low -FODMAP baked products	Public	83,990.00

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

No

- o If yes, please provide concrete examples/data.
- o If no, please explain why not.

NGT for plants (in its simplest sense) is a form of targeted mutagenesis. Mutagenesis is outside the regulatory remit of 2001/18. Therefore, varieties that are generated through mutagenesis are not deemed GMO and hence do not require a risk assessment to be completed. NGT derived crops, from a scientific perspective, fall into this category but based on a legal interpretation they are to be considered GMO and hence require the completion of risk assessments, but this is not due any greater risk compared to material developed through conventional breeding practises