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Stakeholder 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

Discussed and finalised in the Ad-hoc Stakeholder meeting on 10 February 2020

Background

The Council has requested [1] the Commission to submit, by 30 April 2021, "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).

To respond to this Council's request, the Commission is collecting contributions from the stakeholders through the questionnaire below. The study covers all new genomic techniques that have been developed after 2001.

Instructions

For the purpose of the study, the following definition for new genomic techniques (NGTs) is used: techniques that are capable of altering 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-organisms and derived food and feed products obtained by NGTs for agri-food, medicinal and industrial applications and for research.

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 specific NGTs/organisms, please indicate this in the reply.

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

Guidelines

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 15 May 2020 (close of business) to submit the questionnaire via EUsurvey.

QUESTIONNAIRE

Please provide the full name and acronym of the EU-level association that you are representing, as well as your Transparency Registry number (if you are registered)

If the name of the association is not in English, please provide an English translation in a parenthesis

European Fermentation Group (EFG), a sector group of Cefic

Please mention the sectors of activity/fields of interest of your association

Chemicals. In particular, fermentation products used as specialty food and feed ingredients (i.e. additives, flavourings and processing aids) or in pharmaceuticals applications. Examples: vitamins, amino-acids, lactic acid, critic acid, etc.

If applicable, please indicate which member associations (national or EU-level), or individual companies /other entities have contributed to this questionnaire

DSM, Jungbunzlauer, Evonik, Ajinomoto, Corbion, Novartis, Citrique Belge

If applicable, indicate if all the replies refer to a specific technique or a specific organism

Not applicable

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

* **1. Are your members developing, using, or planning to use NGTs/NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide details

Due to the higher precision and ease of genome editing, all genetic engineering work is currently transitioning rapidly from the older “cloning” techniques to state-of-the-art genome editing techniques, be it for single base substitutions or the introduction of entire heterologous genes. It is a matter of fact that for some, genome editing is already now the norm rather than the exception; accordingly, providing specific examples from the fermentation industry seems obsolete. Examples of (potential) applications of genome editing for the benefit of consumers are provided in answers 3, 13 and 17.

* **2. Have your members taken or planned to take measures to protect themselves from unintentional use of NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide details

This question can be interpreted in two different ways: if the focus is on protection and relates to biosafety, then indeed, the same biosafety standards and measures are applied for genome editing as for genetic engineering (“GMO”) work.

If, on the other hand, the focus is on unintentional use (i.e. receiving and using a product, assuming it is non-genetically engineered because – due to local legislation – the genome-edited product is not subject to GMO legislation), then measures are in place at least partially. Every company has a quality system in place and, as part of that, needs to request information from its suppliers and to provide information to its customers, about the compliance of a product with all applicable legislation. GMO statements and GMO questionnaires are an integral part of these quality systems, for regulated products. However, both statements and GMO questionnaires may not (yet) contain specific wording on the use of genome editing.

* 2 bis. Have you encountered any challenges?

- (●) Yes
- ( ) No

* Please provide details

Supply chains in the food industry are often long and complex. To get all required information on the (potential) use of genome editing transmitted all along the supply chain is a significant administrative and technical challenge, due to non-harmonized regulatory standards on genome editing globally.

*** 3. Are you aware of initiatives in your sector to develop, use, or of plans to use NGTs/NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide details

Genome editing techniques are used to improve microbial strains for the production of food and feed additives and processing aids. Such improvements may include: (a) the targeted deletion of genes that are of potential safety concern (such as antibiotic resistance genes or genes involved in mycotoxin biosynthesis); (b) the targeted duplication/multiplication of intrinsic genes of an organism, to increase production of, e.g., amino acids, vitamins, or other compounds of interest; or (c) the targeted introduction of a (heterologous) gene from another organism, to allow sustainable production of human or animal products (such as human milk oligosaccharides or bovine chymosin).

*** 4. Do you know of any initiatives in your sector to guard against unintentional use of NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide details

Currently, compliance is secured at the company level (through each company’s quality system), and is not coordinated across an entire industry sector.

* 4 bis. Are you aware of any challenges encountered?

- (●) Yes
- ( ) No

* Please provide details

See response to Q2bis.

* **5. Are your members taking specific measures to comply with the GMO legislation as regards organisms obtained by NGTs?**

Please also see question 8 specifically on labelling

- ( ) Yes
- (●) No
- ( ) Not applicable

* Please explain why not

The authorization system of Directive 2001/18 as applied to the deliberate release of genetically modified microorganisms has become virtually unusable. Therefore, operators simply abstain from requesting an authorization for, and from placing on the market, live microorganisms that might be under the scope of the Directive.

* 5 bis. What challenges have you encountered?

Additional to the above answer, the technology-based approach of the Directive makes it challenging to even determine whether an organism would fall within the scope or not. An approach based on the characteristics of organisms instead of the technologies used to develop it would make authorization and compliance straightforward and robust.

* **6. Has your organisation/your members been adequately supported by national and European authorities to conform to the legislation?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please describe what type of support and what best practices you can share

We did not need support by authorities to comply with the current, outdated GM legislation (as applied to NGTs). We would however very much appreciate their commitment and support towards a future legislation that will be fit-for-purpose. We expect such future legislation to be science-based, risk-proportionate, and product-centric (instead of the current process-centric approach).

* **7. Does your sector have experience or knowledge on traceability strategies, which could be used for tracing NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please describe the traceability strategy, including details on the required financial, human resources and technical expertise

Companies have a traceability system already in place, namely the quality system they use to secure that their products are fully compliant with applicable legislation. GM statements/questionnaires are used to secure compliance with (GM) legislation.

* **8. Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?**

- ○ Yes
- ◉ No
- ○ Not applicable

* Please explain why not

Please see the answer to Q5. The EU GM labelling regulation (No. 1830/2003) is an integral part of the EU GM Food and Feed regulations, so the answers to questions 5 and 8 necessarily need to be identical.

* 8 bis. What challenges have you encountered?

Please see the answer to Q5. The EU GM labelling regulation (No. 1830/2003) is an integral part of the EU GM Food and Feed regulations, so the answers to questions 5 and 8 necessarily need to be identical.

* **9. Do you have other experience or knowledge that you can share on the application of the GMO legislation, including experimental releases (such as field trials or clinical trials), concerning NGTs/NGT-products ?**

- ○ Yes
- ○ No
- ◉ Not applicable

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 on NGTs/NGT-products

* **10. Are your members carrying out NGT-related research in your sector?**

- ◉ Yes
- ○ No
- ○ Not applicable

* Please specify including subject, type of research, resources allocated, research location

In the fermentation industry, for targeted improvement of production strains, genome editing is already now rather the norm than the exception and is used to make improvements to such strains as outlined in the answer to Q3.

*** 11. Are you aware of other NGT-related research in your sector?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please specify

Rather than providing specific examples, it seems more appropriate to express EFG firm belief that genome editing techniques are used rather as a norm rather than an exception by those doing targeted improvements of production strains in the fermentation industry.

Again, if one can choose between the use of 'old-fashioned' GMO techniques (requiring GM labelling), vs. the use of state-of-the-art, precise genome editing (also requiring GM labelling), it is most likely the latter approach would be followed.

*** 12. Has there been any immediate impact on NGT-related research in your sector following the Court of Justice of the EU ruling on mutagenesis?**

Court of Justice ruling: Case C-528/16 http://curia.europa.eu/juris/documents.jsf?num=C-528/16

- ( ) Yes
- (●) No
- ( ) Not applicable

* Please explain why not

There was no immediate, negative impact on the running business, as no product involving the use of genome editing was developed and/or placed on the market, interpreting and claiming that it can be considered a non-GM product in the EU.

Nevertheless, there was an immediate negative impact by preventing that innovative concepts could be pursued that would have benefitted both the conventional and non-GM markets. For some products intended for non-GM applications, industry needed to resort to classical mutagenesis rather than using more appropriate genome editing approaches. So, as a bottom line, the verdict of the EU Court of Justice prevented the use of innovative approaches of genome editing in some markets. One example is the potential use of genome editing in generating bacteriophage-resistant dairy cultures (Börner et al., FEMS Microbiol. Lett. 366:fny291, 2019; Stuer-Lauridsen & Janzen, European Patent No. EP 1 838 839 B1). As dairy cultures are traditionally a non-GM business, the “GM classification” of such phage-resistant strains plays an important role in determining market access and market success.

*** 13. Could NGT-related research bring benefits/opportunities to your sector/field of interest?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide concrete examples/data

As already outlined in the answer to Q3, potential benefits/opportunities may include the targeted deletion of mycotoxin gene clusters (or other sequences of potential safety concern); the targeted deletion of sequences contributing to strain instability, thereby securing even better consistency in product quality; or the targeted deletion of antibiotic resistance genes (some microorganisms intrinsically contain such resistance genes!). In addition, competing pathways resulting in unwanted side products in the final commercial preparation may be deleted in a targeted manner.

*** 14. Is NGT-related research facing challenges in your sector/field of interest?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide concrete examples/data

The most significant and impactful challenge is the potential regulatory burden to commercialize products obtained through genome editing, dependent on the applicable regulatory framework, including the challenges of non-harmonized regulatory systems in different countries, with a product obtained by genome editing potentially being considered "GM" in one country, but "non-GM" in another country.

If the regulatory system is not adequate, risk-proportionate, and is not creating the required legal certainty, this will prevent investments to be made in promising approached to address the global environmental, health, and socio-economic challenges that our modern society is currently facing.

*** 15. Have you identified any NGT-related research needs/gaps?**

- ( ) Yes
- (●) No
- ( ) Not applicable

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 potential opportunities and benefits of NGTs/NGT-products

*** 16. Could NGTs/NGT-products bring benefits/opportunities to your sector/field of interest?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

There are many opportunities and benefits from modern biotechnology, incl. NGTs. In general, up-to-date technologies materialize these benefits through higher accuracy, and often through less impactful changes needed to obtain the desired effect in the modified organism.
For instance, microorganisms used in Food and Feed as cultures/probiotics/silage agents: the genetic basis for e.g. antibiotic resistance and or toxigenic/virulence factors can be accurately and easily eliminated. The benefits include assured food safety as well an improved use of feed by animals, supporting less use of raw materials and less production of waste.

Microorganisms used in Agriculture: several agronomical properties such as increased nutrient uptake and resistance to heat or draught and protection against plant pests can be introduced into a single microorganism, which would in many cases be very challenging with “pre-2001” technology. The benefits are an improved use of nutrients and a more consistent yield of crops under challenging pest pressures and climate conditions, without additional or with reduced use of mineral fertilizers or chemical plant protection products.

* Are these benefits/opportunities specific to NGTs/NGT-products?

- (●) Yes
- ( ) No

* Please explain

The opportunity of advanced understanding of the microbial genomes, the ability to modify these with high accuracy, the laboratory selection tools, and the characterization methods (e.g. sequencing) have been tremendously improved over the past 10-20 years. This also led to a much better in-depth understanding of the genomic characteristics that have to be taken into account when performing risk assessments.

* **17. Could NGTs/NGT-products bring benefits/opportunities to society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic benefits?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Through the precise and targeted deletion of (a) mycotoxin gene clusters (or other sequences of potential safety concern) and (b) pathways resulting in the formation of unwanted side products, the intrinsic safety of production strains used in industrial fermentations, as well as the consistency in final product quality can be further improved.

In addition, the use of precise and targeted techniques to improve production strains, combined with whole-genome sequence analysis to confirm the correctness of the targeted mutations will allow to continuously reduce the need for animal experimentation to confirm the safety of fermentation products, thereby contributing to animal welfare. An example of clear-cut environmental benefits is, for instance, the fermentative production of riboflavin (vitamin B2) using genetically engineered production strains. While the current industrial production strains for vitamin B2 were generated using traditional genetic engineering approaches, it is conceivable that further improved production strains can be obtained by genome editing. Vitamin B2 is an indispensable, mandatory component of infant food, and biotechnological production is the most environment-friendly approach to produce it.

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

There needs to be a political acceptance of the fact that industrial biotechnology provides benefits that are crucial to society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic benefits.
That commitment needs to be implemented explicitly in policies such as the Green Deal and Farm to Fork.

It must result in a legislation that secures consumers' and environmental safety, while allowing innovative products of industrial biotechnology to reach the market in a timely and proportionate way

* Are these benefits/opportunities specific to NGTs/NGT-products?

- ○ Yes
- ◉ No

* Please explain why not

Benefits are not unique to genome editing, but they can be realized with higher precision, using more subtle genetic changes, and with greater ease.

* **18. Do you see particular opportunities for SMEs/small scale operators to access markets with their NGTs/NGT-products?**

- ◉ Yes
- ○ No

* Please describe and provide concrete examples/data

Certain technologies developed in the last ten years are less complex or costly to implement than older gene technology tools. This makes them in principle more accessible to SMEs. However, the same regulatory obstacles as for larger companies apply to SMEs (current legislative framework and /or EU policy and associated perceptions on the use of these current techniques).

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

- ○ Yes
- ◉ No

* Please explain why not

The question of genome editing has little to do with the question of patenting. For patenting, a set of boundary conditions need to be fulfilled: (a) there must be an inventive step; (b) the invention must provide a benefit; (c) and the patent disclosure needs to allow a person skilled in the art to reproduce the invention. Whether genome editing is used or not has no impact on the functioning of the patent system.

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 potential challenges and concerns on NGTs/NGT-products

* **20. Could NGTs/NGT-products raise challenges/concerns for your sector/field of interest?**

- ○ Yes
- ◉ No

* Please explain why not

We do not associate any particular and/or new challenges or concerns with the use of genome editing techniques and for commercial products developed with such techniques, when compared to those observed /known for the more traditional techniques of genetic engineering.

The most significant challenge and concern is the potential regulatory burden, dependent on the future regulatory framework for biotechnological products. As already outlined, an overly demanding regulatory framework, both in terms of process to be followed and potential labelling needs, will risk to seriously stifle innovation in this field.

* **21. Could NGTs/NGT-products raise challenges/concerns for society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic challenges?**

- ○ Yes
- ◉ No

* Please explain why not

Use of advanced technologies will inevitably raise concerns in parts of society. Therefore, next to a science-based, risk-proportionate, and product-centric future regulatory framework, also open and transparent information and education of the public should be encouraged to secure buy-in and support for innovative, future-proof approaches to biotechnology that best support the ambitious EU Green Deal and Farm-to-Fork strategy.

Products should be assessed on their safety as and when placed on the market, not on the technique used to create them, to create a clear and trustworthy system based on science.

* **22. Do you see particular challenges for SMEs/small scale operators to access markets with their NGTs /NGT-products?**

- ◉ Yes
- ○ No

* Please explain and provide concrete examples and data

The regulatory burden and near impossibility to obtain authorizations for release of NGT developed products are an even bigger issue for SMEs compared to bigger companies. If the regulatory burden is reasonable, SMEs could have an advantage in entering the market as the NGTs offer speed to R&D, as already mentioned.

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

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Please refer to the answer to Q19.

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

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E - Safety of NGTs/NGT-products

*** 24. What is your view on the safety of NGTs/NGT-products? Please substantiate your reply**

First, it should be emphasized that most of the purported safety risks assigned in the early years of traditional genetic engineering could not be substantiated upon closer examination using increasingly powerful analytical techniques over the ensuing years and decades.

In addition, two aspects cannot be emphasized enough in the discussion on the safety of products obtained with genome editing: (a) the intrinsic higher precision and accuracy of state-of-the-art genome editing approaches to achieve a desired improvement of a strain as compared to the more traditional approaches of genetic engineering; and (b) the availability and ease of whole-genome DNA sequencing to confirm that the strain improvements have happened as planned and did not lead to unintentional side effects. The combination of both provides a sound basis for a scientific risk assessment, based on which meaningful conclusions can be drawn on the intrinsic safety of a particular production/commercial strain.

*** 25. Do you have specific safety considerations on NGTs/NGT-products?**

- ( ) Yes
- (●) No

* Please explain why not

See the answer to Q24.

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

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F - Ethical aspects of NGTs/NGT-products

*** 26. What is your view on ethical aspects related to NGTs/NGT-products? Please substantiate your reply**

Our views are not any different with products sourced via other processes/technologies than NGTs. The ethical aspects of innovation in biotechnology should not be viewed in the light of the technologies used – but rather by looking at the product/organism and its intended uses. Therefore, we do not have specific views on the ethical aspects of the technologies in question.

*** 27. Do you have specific ethical considerations on NGTs/NGT-products?**

- (●) Yes
- ( ) No

* Please explain

A number of challenges are presently facing our planet and societies: global warming and climate change, food security, scarcity of land and resources, (plastic) pollution, etc. In this context, one could consider unethical that European authorities would not do their utmost to promote technologies and products that can offer solutions and safely address some of these challenges. NGTs are among such existing technologies, and the commitment to use all modern technologies through the promotion of adequate policies and legislation at European Union level would be very much welcomed. As a conclusion, it is unfortunate to recognise that, on NGTs, the European Union appears to be lagging behind other regions in the world.

Please upload any supporting documentation for this section here

The maximum file size is 1 MB

G - Consumers' right for information/freedom of choice

*** 28. What is your view on the labelling of NGT-products? Please substantiate your reply**

Increasing transparency is a continuing, reasonable and justifiable trend. It is laudable if final customers /consumers are interested in how products they enjoy are made, and what impact they may have (in terms of benefits and potential risks) on the environment, nutritional quality, and health. Thus, we could support to make meaningful information on production methods available to customers.

However, labelling requirements should be restricted to what it is truly meaningful in terms of food quality, food safety, and food sustainability. Again, food labels should contain science-based, meaningful information for the target use of a product, and should not contain elements that may politically motivated, and not reflecting what the science say.

In any event, any initiative in the field of labelling should primarily aim at not misleading consumers on products quality and safety. This is relevant criteria to consider about NGTs labelling.

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

H - Final question

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

- (●) Yes
- ( ) No

Please provide your comments here

The present questionnaire seems to imply that it remains uncertain whether products of up-to-date gene technology / industrial biotechnology provide benefits to society. Such premises would be inappropriate and outdated as it is already state of art and used potentially for each and any new innovative product from biotechnology.

Industrial biotechnology is here to stay, as it is essential if the EU wants to fight resource scarcity and climate change while playing a role in meeting the UN SDGs. The present GMO legislation, as well as the singling out of post- vs. pre-2001 technologies, currently prevent this essential tool from being used more effectively and more broadly.

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

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