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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 Federation of Biotechnology (EFB)

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

The European Federation of Biotechnology (EFB) is Europe's non-profit federation of National Biotechnology Associations, Learned Societies, Universities, Scientific Institutes, Biotech Companies and individual biotechnologists working to promote biotechnology throughout Europe and beyond. As the independent "Voice of Biotechnology in Europe", EFB promotes the safe, sustainable and beneficial use of fundamental research and innovation in life sciences, while providing a forum for interdisciplinary and international cooperation.

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

Executive Board of the European Federation of Biotechnology

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

No

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

NTGs are defined as any technique developed after 2001 that can be used to alter the genetic material of an organism. It is understood that the year 2001 is the basis of this definition as the EU GMO directive (Directive 2001/18) was implemented that year, and that the Court of Justice of the EU (CJEU) in case C-528 /16 ruled that any genome modification performed using techniques developed after the directive was implemented are to be considered as leading to a GMO. However, we would like to stress that this definition lacks any sound scientific basis. 2001 was not a year of significant new technique developments. The groundbreaking techniques now used for gene editing, such as CRISPR, were developed significantly later. Therefore, from both a technical and scientific view, the definition is wholly arbitrary. This is further affirmed by the given example techniques that are either considered NGTs or not considered NGTs in footnote [2]. Here it is specified that, for example, CRISPR is an NGT, but that Agrobacterium-mediated techniques or gene guns are not considered NGTs. However, the Agrobacterium or gene gun are merely delivery systems used for plant transformation, similar to electroporation, heat/osmotic shock, lipofection, etc., used with other organisms. Therefore, to perform CRISPR modifications that are considered NGT modifications, there would be the need to also apply one of the "non-NGT" methods. This means that the resulting organism will be the product of both NGT and non-NGT and this is likely to cause confusion in relation to the meaningful use of the NGT term throughout the questionnaire.
As explained above, the definition of NGTs is arbitrary from both scientific and technical points of view, so in most cases, companies from our federation will use both NGTs and other recombinant technologies that would not be considered NGTs. It is more relevant to ask about the genotypic and phenotypic modifications a developer intends to introduce rather than how they are introduced.

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

- ○ Yes
- ◉ No
- ○ Not applicable

* Please explain why not

Again, it is not important which technologies have been used to modify an organism. It is rather much more important what the new properties of the organism are to provide a meaningful reply. For example, if you ask if the unintentional use of a yeast strain developed using NGTs would be a concern, then that is not possible to answer per se. If you ask if unintentional use of a yeast for biofuel production that has a deletion of a gene responsible for glycerol formation using NGTs is a matter of concern, then the answer would likely be no. If you ask if unintentional use of a yeast that has been engineered to produce opioids using NGTs would be a concern, then the answer would likely be that such a yeast would have to be protected and only used for intentional drug manufacturing. Both yeast strains have already been constructed.
It is not possible to tell from the WGS if an organism has been constructed using NGTs or if it has been constructed using non-NGTs. So unless there is full traceability from strain construction to a product it is not possible to judge if the product is the result of NGT modifications or not.

* 2 bis. Have you encountered any challenges?

- ○ Yes
- ◉ No

* **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

We do not discriminate if a technology is NGT or non-NGT. Technology development by academic labs is by definition NGTs. Biotech companies from our federation choose the best technology for a given purpose and the same changes can be introduced using either technology that would be characterized as NGT or non-NGT. So, most products developed today will be based both on NGTs and other methods.

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

- ○ Yes
- ◉ No
- ○ Not applicable

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

- ◉ Yes
- ○ No

* Please provide details

Academic labs from our federation develop NGTs and publish their progress in publicly available journals. That is their mission and it is not their task to decide if a given technology should be regulated. Companies from our federation work according to regulations, securing that products are marketed following appropriate regulatory assessments. If a company brings unauthorized products to the market it is difficult to tell if the product is based on NGTs or not. Methods for the detection of some genetic modifications, like gene deletion or gene insertion, can be developed. However, each such method is DNA sequence-specific and cannot distinguish between e.g. a gene deletion obtained using classical or CRISPR-based methods. Indeed, for CRISPR-based SDN1/SDN2, it is not possible to determine whether a mutation was introduced by CRISPR, classical mutagenesis or occurred as a spontaneous event. Moreover, new methods and concepts are developing very rapidly, e.g. prime editing that emerged just recently (Nature 2019;576:149). The development of any detection method is dependent on DNA sequence information provided by the developer of the organism in question. In some cases, it will not be possible to distinguish whether a mutation was introduced by NGT or occurred without any form of human intervention.

* **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

As previously mentioned, companies from our federation do not discriminate between technologies developed before and after 2001, and very often both technologies that would be considered NGTs and traditional genetic modification methods have been used. The companies are legally obliged to follow the law and must secure authorization of products before putting them on the market, but do not consider if technologies applied are considered NGTs or not.

* 5 bis. What challenges have you encountered?

We are strongly advocating for a regulatory framework that is based on the properties of the organism developed rather than on the technologies used to develop it. This is not a revolutionary idea, but a practice that is becoming standard elsewhere.

* **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

This question is not applicable to academic members of our federation.
Companies from different sectors of biotechnology have experienced different levels of support, but generally support from EFSA and other regulatory bodies in the EU is of high quality. Thus, it is not the level of support that prevents authorization of necessary products in the EU but rather the regulatory requirements themselves.

* **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

See also reply to question 4.
Academic members of our federation develop analytical tools and methods that can be applied for the purpose. Companies develop methods for the detection of DNA from the organisms used to produce the products. These methods can be used to detect the presence of the organism or DNA from the organism in the product. They can also be used by a company to detect if the product in question is produced by a competitor using an organism developed by that company.
However, all these detection strategies can only be applied if detailed sequence information on the genetic modifications is known. Since new methods and techniques are developing very rapidly, in some cases, it will not be possible to distinguish whether a mutation was introduced by NGT or occurred without any form of human intervention.

* **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 describe the measures and their effectiveness including details on the required financial, human resources and technical expertise

That depends on the scope and extent of labelling.

* What best practices can you share?

See text below

* Please explain why not

Clarification is needed. Is this question about GMO labelling or a proposal that a new labelling system is required for NGTs (e.g. a “Gene-edited” labelling)? As indicated previously, the definition of NGTs is arbitrary. Therefore, any labelling would also be arbitrary or even misleading at this point.
As there are no safety concerns with the use of NGTs per se, an NGT labelling should only be introduced to secure consumers’ right to choose. However, as the definition of NGTs is arbitrary, such labelling would confuse consumers rather than providing them with a tool to choose according to preferences and conviction.
It should be stressed that EFB members live up to all legal requirements, so companies do label products that must be labelled according to existing legislation.

* 8 bis. What challenges have you encountered?

Explained in 8 main text.

* **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 describe for the:

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

Agri-food sector

Both companies and academic members of our federation experience that a release of genetically modified plants is not practically possible in the EU due to EU regulation and member state veto right.

Industrial sector

As all NGT products are considered GMOs or produced by GMOs according to the EU court of justice ruling in 2018, it makes no difference if a product is produced using NGTs or other GM technologies. Under current regulations, production and sales of products produced using a GMO and/or NGT organisms under contained use is possible. For GMOs or NGT organisms to be sold as live products (deliberate release), the issue is the same as for the Agri-food sector.

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 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

Both academic and industrial members of our federation work intensely on the development of NGTs and use them for the development of new products. It is not possible to do relevant biotechnology research or development without NGTs, because it would have to exclude all technological progress that has been made after 2001. Our members do not discriminate between NGTs and non-NGTs but must comply with the law.

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

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

* Please specify

There have already been about 20,000 scientific papers on CRISPR from all over the world. As described at question 17, NGT organisms have been or are being developed for a large number of different applications.

* **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 describe

Before the Court of Justice ruling there was a belief that certain NGTs that introduced modifications that were essentially identical to naturally occurring mutations, or mutations generated by classical mutagenesis, would be considered exempt from GMO regulation in the EU. That opened a window of opportunity for modification of plants and microorganisms that could then actually be brought to the market in the EU. That window of opportunity was closed with the ruling.

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

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

* Please provide concrete examples/data

The development of NGTs rapidly continues and that creates new opportunities for new modifications that can lead to beneficial products such as those described under question 17. For example, a recently developed prime editing technique, which has a great potential in medical genetics, mediates targeted insertions, deletions, and base-to-base conversions without the need for double strand breaks or donor DNA templates (Nature 2019;576:149).

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

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

* Please provide concrete examples/data

Following the Court of Justice ruling, it became difficult to see a path forward for an EU regulation enabling the potential of genetically modified organisms outside of contained use. Other countries, such as the USA and China, have embraced the gene-editing technologies and are actively encouraging their use for new necessary product development. This has already resulted in the reduction of the activities of several biotechnology companies within the EU, and difficulties for academics to see a future for such biotechnology in Europe. Therefore, investments and funding opportunities for NGTs are drying up in Europe but are increasing in competitor countries. It is a paradox that many EU funded projects still aim at developing NGT products while the EU regulation does not facilitate these products to be used, once developed. One example of that is the Horizon 2020 supported project CHIC that is funded with 7,3 MEUR with the purpose of developing better and more sustainable chicory crops using NGTs (http://chicproject.eu/what-is-chic/). Despite the fact that society impact and consumer interests are integrated into this project, the resulting chicory cultivars can only be used in agriculture outside of Europe if used at all. In summary, it is completely illogical that the EU invests huge amounts of money in research and development projects but prevents Europe from benefitting from the results. The EU should keep investing in this but secure that the results can be used.

* **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

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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

See the answer to question 17 for details.

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

- ◉ Yes
- ○ No

* Please explain

The emergence of gene editing technologies such as CRISPR has greatly accelerated the biotechnology field. It is now possible to make modifications in virtually any organism with unprecedented speed and accuracy, and it is possible to introduce a large number of such modifications simultaneously.
NGTs combined with other techniques developed in modern biotechnology hold great promise to address some of the very large global problems identified in UN's SDGs. We believe that it is important to discuss the ethics of action or inaction, the obligation or prevention to use all the tools at our disposal that may prove essential for saving our planet.

* **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

Plants
Coeliac disease is an autoimmune disorder caused by the ingestion of gluten proteins from wheat, barley and rye. Spanish and US scientists used a CRISPR-based gene editing to delete corresponding alpha-gliadin genes from the wheat genome to produce a gluten-free wheat. Up to 35 out of 45 different alpha-gliadin genes were mutated, which reduced the immunoreactivity by 85% (Plant Biotechnol J 2018;16:902).
The US company Calyxt has gene-edited soybean using TALEN technology to produce a “high oleic” oil with no trans fats and less saturated fat, which should make the oil more heart-healthy and improve its shelf life (https://www.the-scientist.com/news-opinion/gene-edited-soybean-oil-makes-restaurant-debut-65590).
In a rainy season, wheat grains start germination in spikes before harvest, which greatly reduces yield. By mutating all three copies of the QSD1 gene in hexaploid bread wheat genome using CRISPR, Japanese scientists produced a rain-resistant wheat variety that produces high-quality flour even under moist conditions (Cell Rep 2019;28:1362)
By editing several genes responsible for tomato branching and growth, compact and high yield tomato plants were developed by a US group. These plants can save space and resources needed for growth, being great for urban gardening, or could one day even be used in long-distance space missions (https://www.cshl.edu/a-new-tomato-ideal-for-urban-gardens-and-even-outer-space/).

Microbes
Several NGT microbes are currently in use for production of sustainable products like enzymes, amino acids and vitamins in contained use.
Live microbes are used for a range of different purposes such as human or animal probiotics, inoculants for agriculture, Biocontrol in agriculture or biopesticides in agriculture.
Non GMMs are currently used for these purposes to varying extent but they can be dramatically improved using NGTs e.g. by:

- Deletion of antibiotic resistance genes or other genes of concern. This is important to improve safety, but it is also important for strictly regulatory reasons as no microorganisms with non-intrinsic antibiotic resistance can be market authorized in Europe. This is particularly important for probiotics for animal or human use. CRISPR has been demonstrated to be an efficient technology for modifying probiotics both to delete genes of concern but also to improve the properties of the probiotics (van Pijkeren et al, Microbiol Spectr. 2017;5(5)). Examples of use of such probiotics are treatment of:
  - Ileitis in pigs (Jobin C, Gut Microbes. 2010;1(3):196–199)
  - Bovine mastitis (Rainard P, Foucras G. Front Vet Sci. 2018;5:251)
  - Ulcer without the use of other drugs (Khoder G et al. Exp Ther Med. 2016;12(1):3–17)
  - IBD (Quigley A. B.Frontline Gastroenterology 2020;11:62-69)
- Upregulation of genetic pathways e.g. nif gene clusters to improve nitrogen fixation or phosphorous solubilization of inoculants to improve the effect either of these properties or to enable one organism to do both (Surovy M. Z. et al. In: Islam et al (eds) Bacilli and Agrobiotechnology: Phytostimulation and Biocontrol. Springer, 2019)

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

NGTs combined with other techniques developed in modern biotechnology hold great promise to address some of the very big global problems identified in UN’s SDGs. We believe that it is important to discuss the ethics of action or inaction, the obligation or prevention to use all the tools at our disposal that may prove essential for saving our planet. Above we provided examples of biotechnology solutions that can significantly contribute to meeting UN’s SDGs.

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

- (●) Yes

No

* Please explain

Non-transgenic low-gluten wheat lines can be produced only with the NGT methods (https://www.scientificamerican.com/article/scientists-genetically-engineer-a-form-of-gluten-free-wheat/)
Rain-resistant wheat variety that produces high-quality flour even under moist conditions can be produced only with the NGT methods (http://www.asahi.com/ajw/articles/AJ201908210010.html).
Special tomato for urban agriculture can be only produced with the NGT methods (Nature Biotechnol 2019; 38:182).
NGTs can be used to remove genes of concern like antibiotic resistance markers from naturally occurring probiotics, but by doing so the resulting organism is genetically modified and needs to be approved, released and labelled as such. In the EU the regulatory process is tedious to the extent that it cannot be considered an operational opportunity. So, such probiotics cannot not be offered to the EU at current regulatory status. Using NGTs or other recombinant technologies it will be possible to develop a probiotic that can efficiently eradicate H. pylori without the use of other drugs.
New nitrogen fixing microbes can be developed using NGTs that can reduce the need of fertilizers.

* **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

In general, NGT technologies like CRISPR are significantly less resource demanding to use than older methods or genetic modifications. Hence, it is possible to develop new biotechnology products for small companies today. However, since the GMO regulation in Europe is no longer fit for purpose and very significant resources are needed to get regulatory approval, the products developed by SMEs are very unlikely to be marketed in Europe. It is much more likely that the SME will move its activities to the USA when they approach success. This point is illustrated by the CRISPR patent landscape. In June 2019, 2072 CRISPR patent families were identified in a study by Martin-Laffon et al (Martin-Laffon et al Nat Biotechnol 37, 613–620 (2019)) For plant biotechnology, 259 of these patent families originate from China, 61 families originate from the USA and only 18 originate from the whole of Europe (3 from the UK)

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

Yes
No

* Please describe and provide concrete examples/data

Developing a biotech product represents a huge investment. Therefore, it is critical for academics or companies that develop new technologies or products to have the possibility to protect these by patenting, but the complexity and duration of patent conflict proceedings are becoming a limitation. As demonstrated under question 18, it is clear that Europe is falling dramatically short of China and the USA.

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

NGT products would not raise challenges different from other products that are GMOs or produced using GMO technologies. The EU regulations of GMOs and the EU labeling requirements bring about the situation that practically only the products obtained using NGTs in contained use that require no labeling can be put on the market in the EU.

* **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

NGTs or NGT-products do not raise concerns or challenges that are any different from challenges and concerns from other GMOs or GMO products. Owing to the targeted nature of many NGTs, the final product contains far fewer unspecific changes compared to some routinely used GMO products such as radiation breeding produced crops.
It is a challenge that there is a perceived risk of the technology per se meaning that substantial parts of the public perceive GMO/NGT products as having inherent risks, simply because GMO/NGT methods have been applied, irrespective of the genetic modifications that were introduced.
GMOs/NTGs can be used for several highly useful purposes as described under question 17. They can enable the biobased society to replace non-renewables with renewables, increase crop yields while reducing environmental food print and contribute new drugs to fight diseases that cannot be cured today. It is a concern if EU societies end up in a situation of not utilizing these options and rather relying on existing technologies simply because of widespread negative perceptions of these technologies. This would cause Europe to become non-competitive, unsustainable and in deep dependency on the rest of the world.

* **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

In practical life it is not possible even for large enterprises to market products based on NTGs (or other GMO technologies) due to the current regulatory system in the EU unless the NGT organism is grown in contained use and the product does not contain any residuals of the NGT organism. This challenge is even greater for SMEs/small scale operators that simply do not have the capacity to prepare and push a dossier for EFSA for regulatory approval.

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

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Certain NGTs, like CRISPR, have become very problematic to utilize due to a very locked IP situation. Several companies and even academics refrain from using CRISPR/cas9 due to the ongoing patent dispute. Hence freedom of operation analysis is significantly more complicated for some of the NGTs than for older technologies for genetic modification.

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The maximum file size is 1 MB

E - Safety of NGTs/NGT-products

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

This question does not have a meaningful answer. The safety of an organism or a product cannot be assessed based on the technologies used to develop the organism or the product, but only by assessing the genetic modifications that have been introduced. For some NGTs like the SDN1 format of CRISPR, the genetic modifications introduced are no different from mutations that can be introduced by evolution or classical mutagenesis. In principle, identical modifications can be developed using e.g. classical mutagenesis and CRISPR SDN1. Yet, they are currently subject to a different type of safety risk assessment and so the safety risk assessment is unrelated to NGTs.

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

- ( ) Yes
- (●) No

* Please explain why not

As argued under question 24, the safety assessment of an organism or product has nothing to do with its NGT status. Safety assessments can only be made considering the final organisms developed based on the safety of the recipient organism and the genetic modifications introduced. How these genetic modifications were introduced is of no consequence to the risk assessment. NGTs can be used to develop perfectly safe and useful organisms or they can be used to develop inherently unsafe organisms e.g. for chemical warfare.

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**

As with safety, the use of NGTs is not the determining factor when it comes to ethical aspects of NGTs. The important thing is the purpose of changing the genetic properties of an organism.
For the biotechnology applications discussed in this questionnaire, we do not see any ethical concerns about the use of the NGTs (or other gene technologies), excluding modifications of human germline cells.
If products can be developed that can significantly contribute to meeting the UN SDGs, then we believe it is unethical not to promote such products. Using such technology, European academics and companies can fight some of the world's biggest problems and with that ability comes responsibility and obligation. This is for example very much in line with the conclusions that the Danish Ethical Committee advised the Danish government in ethical questions (https://www.etiskraad.dk/english/publications/gmo-and-ethics-in-a-new-era)
It is obviously possible to undertake unethical activities using NGTs and there will be borderline cases. Is it for example ethical to eradicate an entire species by gene drive? What if that species is mosquitoes spreading zika virus? What if the gene drive components could spread to more benign mosquitoes? Such controversial cases with a potentially large impact on natural communities should be subject to a thorough evaluation by the regulatory officers.

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

- ○ Yes
- ◉ No

* Please explain why not

Our considerations would be based on specific organisms developed and their properties, but not on the technologies used to develop them. See question 26.

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**

Products should be labeled in line with EU policy of transparency, safety and ethics. However, the labeling should be based on the properties of the final organism used to produce the product in question rather than on the technologies used to develop that organism. If you go back to the example of the two identical organisms developed by different technologies in question 24, then it is very hard to argue that the one developed using classical mutagenesis should not be labelled whereas the one developed using CRISPR

SDN1 should be labelled.
One relevant labeling requirement could be if the health properties of food have been changed, then that has to be labelled. If e.g. a potato is engineered to have very low asparagine levels so that no acrylamide is formed when it is fried, then it is reasonable to label that particular potato as engineered to prevent the formation of acrylic amide. If rice is engineered to produce higher amounts of vitamins, then that could be a labeling requirement. Companies producing such products may use labeling such as “Healthy chips”, “Vitamin rich rice”…, which will actually show the advantage of their product.
Some consumers also want to know about GMO status. However, as discussed throughout this questionnaire, GMO status is no longer easily determined. Thus, it could be relevant e.g. to label if DNA from a different species (transgenesis) has been applied rather than basing labeling on the use of technologies. This is not to hide anything from the consumers but given that NGT per default lead to GMO, GMO labeling will encompass all modifications that can be done and not just modifications that were originally intended as modifications to trigger labelling. Based on the EU court of justice ruling in sensu stricto, we would soon end up in a situation where practically all food products would need to be labeled as GMO, which would provide no meaningful guidance for the consumer.

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H - Final question

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

- (●) Yes
- ( ) No

Please provide your comments here

The EU is, similar to the rest of the world, facing huge environmental and societal challenges. Radical changes need to be implemented to reverse climate changes, erosion of farmland, globally increasing population and the unsustainable drain of resources that cannot be recycled.
One such change is to promote the bio-based society where the use of scarce natural resources is replaced by the production of renewables using biotechnology, where more and healthier agricultural products can be produced on less land in a sustainable way.
For that to happen, a biotech revolution needs to take place and the technologies used for the advancement of biotechnological products need to be further developed. All of these necessary new technologies are by definition NGTs. With existing technologies, we can develop many products that can all contribute to the EU economy and sustainability, thereby creating new jobs and a clean Europe in balance.
However, the current EU regulatory system, for approval of organisms and products developed by NGTs and other gene technologies, is no longer fit for this purpose and is effectively blocking any gene-based developments in biotechnology.
The result of that is that only NGT based products for contained use are developed for production in Europe. Still huge amounts of NGT derived plant products are being imported from the USA and other countries with a large transportation environmental food print. So, the EU consumers are exposed to NGT products being imported from abroad, but Europe do not harvest any of the environmental and economic benefits that the NGTs offer.
The current regulatory system from 2001 that is based on the technologies that existed at the time needs to

be replaced by a science-based system reliant on objective risk assessment of the final organisms rather than on the technologies used to develop the organism. It needs to focus on the genetic modifications introduced and a science-based risk assessment of these modifications.
Moreover, programs to educate the wide public to understand the potential of the biotech revolution are needed. Even if the technologies are further developed and the regulatory system is fit for purpose, products based on NGTs will not have any impact unless the EU citizens understand the potential of these products and trust that the regulatory system guarantees their safety.

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