BioIndustry Association response to Defra's consultation on the regulation of genetic technologies

March 2021

This consultation was submitted to Department for Environment, Food and Rural Affairs (Defra) via email in response to its consultation on the regulation of genetic technologies.

Questions 1-4 form Part 1 of the consultation and address the regulation of GMOs produced by gene editing (GE), or other genetic technologies, but which could have been developed using traditional breeding methods. Questions 5-6 form Part 2 of the consultation and address Defra's approach to regulating novel organisms in the longer term. All text below in bold is copied verbatim from Defra's consultation.

Introduction

1. The BioIndustry Association (BIA) is the trade association for innovative life sciences in the UK. Our goal is to secure the UK's position as a global hub and as the best location for innovative research and commercialisation, enabling our world-leading research base to deliver healthcare solutions that can truly make a difference to people's lives.
2. Our members include:
    - Start-ups, biotechnology and innovative life science companies
    - Pharmaceutical and technological companies
    - Universities, research centres, tech transfer offices, incubators and accelerators
    - A wide range of life science service providers: investors, lawyers, IP consultants, and communications agencies
3. The BIA's members are at the forefront of innovative scientific developments targeting areas of unmet medical need. This innovation leads to better outcomes for patients, to the development of the knowledge-based economy and to economic growth. Many of our members are small, pre-revenue companies operating at the translation interface between academia and commercialisation.
4. We welcome Defra's timely consultation on the regulation of genetic technologies. Most of our members are working in human health, and as such we focus on gene editing in human medicines in our response. However, the BIA recognises the benefits of gene editing and GMOs in the other areas which are covered in this consultation, including crop plants, breeding farmed animals, human and animal food, and veterinary medicines. It is vital that current and future approaches to the regulation of these areas ensure that the UK is an attractive destination for foreign investment and top global talent to conduct their research and innovative companies to start-up and grow. Ultimately, this will safeguard the UK as a country in which science and technology can be developed to the benefit of society.

Part 1: The regulation of GMOs which could have been developed using traditional breeding methods

This part of this consultation addresses the regulation of GMOs produced by gene editing (GE), or other genetic technologies, but which could have been developed using traditional breeding methods.

Question 1: Currently, organisms developed using genetic technologies such as GE are regulated as genetically modified organisms (GMOs) even if their genetic change(s) could have been produced through traditional breeding. Do you agree with this?

- ~~Yes – they should continue to be regulated as a GMO~~
- **No – they should not continue to be regulated as a GMO**

Please explain your answer, providing specific evidence where appropriate. This may include suggestions for an alternative regulatory approach.

5. Gene editing is a range of techniques used to make precise changes at specific locations in an organism's genome to improve its functionality. Together with the study of genomics, gene editing enables truly personalised medicines, designed to effectively address patients' disease with as few side-effects as possible. It is also paving the way for more accurate, convenient diagnostic products that help characterise and potentially prevent disease, by picking up signs much earlier. Beyond health benefits, gene editing holds the potential to help society tackle environmental challenges by, for example, improving food security by developing crops that are resistant to blight, and reduce the economy's reliance on petroleum-based products by enabling the efficient manufacturing of bio-degradable bioplastics and renewable chemicals. As such, gene editing is key in enabling a transition to a sustainable bioeconomy.
6. As consumers are increasingly demanding sustainable products, there is also a strong economic argument for gene editing. Countries with science-led gene editing and GMO regulations, such as the US, are capturing the economic benefits of this growing industry. For example, the US engineering (also known as synthetic) biology sector, which largely consists of companies working with and developing new gene editing technologies and GMOs, raised nearly $8bn USD in 2020.[1]
7. With its strong science base and thriving life sciences ecosystem, the UK is also well-positioned to benefit economically from gene editing technologies beyond healthcare. The UK has strong expertise in plant science at institutes such as the Earlham Institute, the John Innes Centre and The Sainsbury Laboratory on Norwich Research Park, as well as many others nationwide - from Rothamsted Research in Harpenden to the James Hutton Institute in Dundee. In 2020, the UK's growing biotech sector raised a record £2.8bn in equity finance, an increase of over 1000% since 2012.[2] While most of the companies driving this growth are developing new medicines that do not necessarily rely on gene editing

[1] Synbiobeta (2021), "Synthetic Biology Investment Reached a New Record of Nearly $8 Billion in 2020 — What Does This Mean For 2021?": https://synbiobeta.com/synthetic-biology-investment-set-a-nearly-8-billion-record-in-2020-what-does-this-mean-for-2021/

[2] BIA (2021), "The science of success: UK biotech financing in 2020": https://www.bioindustry.org/uploads/assets/bbf42256-e162-461f-bb171ae6272f974d/The-science-of-success-WEB-small.pdf

technologies, the sector's immense growth demonstrates the strength of the UK life sciences ecosystem.

8. The Court of Justice of the European Union (CJEU)'s ruling to regulate gene edited products as GMOs raised widespread concern from the scientific community, including from the European Commission's own Group of Scientific Advisors.[3] The UK's Agricultural Biotechnology Council, which consists of four global agricultural science companies, also noted that the decision "effectively signals that the EU is an unfavourable location to undertake plant genetics research, development and commercialisation of new crop innovations."[4] The decision was particularly perplexing to the scientific community because the decision was not logical from a scientific perspective. By diverging from the CJEU's unscientific ruling, the UK would send a positive international message that the UK wants to have a science-based regulatory system, which in turn would enable more start-ups to be created from our excellent science base, attract global investment, and help deliver on the Government's levelling up agenda and ambition to make the UK a global life sciences cluster.

9. For these health, environmental and economic reasons, we do not think that products of gene editing should continue to be regulated as a GMO. The wider GMO regulations on the UK's statute are burdensome and ineffective. Without addressing the underlying problems of these regulations, the UK will not be able to reap the benefits of gene editing and GMOs. We therefore welcome the second part of this consultation, as the UK should adopt an innovation-friendly regulatory framework by regulating the product instead of the process.

Question 2: Do organisms produced by GE or other genetic technologies pose a similar, lesser or greater risk of harm to human health or the environment compared with their traditionally bred counterparts as a result of how they were produced?

- **Similar**
- Lesser
- Greater

Please provide evidence to support your response including details of the genetic technology, the specific risks and why they do or do not differ. Please also state which applications/areas your answer relates to (for example: does it apply to the cultivation of crop plants, breeding of farmed animals, human food, animal feed, human and veterinary medicines, other applications/ areas).

10. Gene edited changes are targeted, often to just one or a few genes of interest, and with a clear objective as to intended effect. Since many applications of gene editing result in plants without foreign DNA that could be achieved by conventional breeding, gene edited varieties are as safe as conventionally bred varieties.[5] In addition, because gene edited techniques produce precise changes at targeted sites of the genome, they enable better genomic characterisation which is important for risk assessment.

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[3] Statement by the Group of Chief Scientific Advisors (2018), "A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive": https://ec.europa.eu/info/sites/info/files/2018_11_gcsa_statement_gene_editing_2.pdf

[4] Agricultural Biotechnology Council (2018), "UK urged to 'bring back' sound science as the basis for regulating crop genetic innovation post-Brexit": https://abcinformation.org/uk-urged-to-bring-back-sound-science-as-the-basis-for-regulating-crop-genetic-innovations-post-brexit/

[5] See e.g.: Lassoued et al (2019), "Risk and safety considerations of genome edited crops: Expert opinion": https://www.sciencedirect.com/science/article/pii/S2590262819300024

11. By contrast, traditional breeding techniques are semi-random and make many changes of often unknown impact; some will help the crop (with whatever feature we are selectively breeding for), but there will also be 'hitchhiking' unintended changes that get propagated to the final product - and these introduce a secondary risk factor not present in the gene edited process. This means that unintended or off-target effects with gene edited products are less of a risk than with other traditional breeding methods such as mutation breeding: both the EU's Scientific Advice Mechanism[6] and European Food Safety Authority (EFSA)[7] have concluded that these will be fewer than observed for mutation breeding. They further conclude that, as with traditional breeding, these effects do not need to be assessed to conclude on the safety of the product. In the absence of concrete, identifiable risk induced by use, gene edited products should not be treated differently from conventional products.
12. For human medicines, gene delivery systems routinely used in the manufacture of advanced therapy medicinal products (ATMPs) contain built in features to ensure the absence of replication competent genetic vectors, for example third and fourth generation self-inactivating, replication deficient lentiviral vector systems. Furthermore, significant experience with these gene delivery systems in the manufacture of commercial and investigational ATMPs provides demonstrable evidence of the lack of increased risk of harm to human health or the environment posed by organisms produced by gene editing, compared with their traditionally bred counterparts.
13. ATMPs manufactured using gene delivery systems, for example patient-derived autologous cell therapies, are typically unable to survive or persist in the environment outside of patients.

Question 3: Are there any non-safety issues to consider (e.g. impacts on trade, consumer choice, intellectual property, regulatory, animal welfare or others), if organisms produced by GE or other genetic technologies, which could have been produced naturally or through traditional breeding methods, were not regulated as GMOs?

- **Yes**
- ~~No~~

Please provide evidence to support your response and expand on what these non-safety issues are.

Environmental benefits

14. As climate change escalates, developing new ways of reducing our environmental footprint for a more sustainable economy is becoming more pressing. Gene editing has many benefits to the environment. The widespread adoption of agrichemicals in food production has been detrimental to biodiversity, but gene edited crops could help reduce our reliance on agrichemicals by developing crops resistant to diseases.[8] Gene editing can also be used to sustainably improve farming productivity and yields while at the same time supporting the natural environment. For example, by using cutting edge genetic editing technologies, Norwich-based SME Tropic Biosciences develops high-performing commercial varieties of tropical crops which promote cultivation efficiencies, enhance consumer health, and improve

[6] Scientific Advice Mechanism (2017), "Explanatory Note, New techniques in agricultural biotechnology: https://ec.europa.eu/research/sam/pdf/topics/explanatory_note_new_techniques_agricultural_biotechnology.pdf
[7] EFSA (2020), "Applicability of the EFSA Opinion on site-directed nucleases type 3 for the safety assessment of plants developed using site-directed nucleases type 1 and 2 and oligonucleotide-directed mutagenesis": DOI:10.2903/j.efsa.2020.6299
[8] See e.g.: Borel (2017), "CRISPR, microbes and more are joining the war against crop killers": https://www.nature.com/news/crispr-microbes-and-more-are-joining-the-war-against-crop-killers-1.21633

sustainable environmental practices. Another UK SME, Phytoform Labs, based at Rothamsted Research, is working to minimise the damaging impact of agriculture on the environment and to make food crops healthier for consumers.

Trade and investment

15. As noted in para 7, the UK has a world-renowned science base and a rapidly growing life sciences sector. By no longer regulating gene edited products as GMOs and providing a clear route to market for gene edited products, the UK could attract inward investment from global companies and make the UK a go-to destination for innovative plant breeding technologies, much in the same way that the UK is a global destination for innovative medical technologies. A science-based regulatory approach would also enable more start-ups to be created in areas beyond healthcare, which would further attract investment from global companies and investors.

16. The Government should carefully consider how a new regulatory approach for gene edited products would affect its new trading relationships with the EU and global partners. A new regulatory approach would enable UK companies to export to markets with similar regulatory requirements, but it would also close markets which have more stringent regulations. The Government should also consider the route to market for gene edited products in the UK and the regulatory costs associated with this, as global companies may not deem the UK a favourable R&D location if regulatory costs are high and export opportunities are low.

17. It is important to note that the GMO legislation was adopted primarily for agricultural applications to protect food consumers and the environment. The authorisation procedure for clinical trials with investigational ATMPs requires additional steps to comply with the GMO legislation, leading to prolonged approval timelines and making Europe less attractive for conducting clinical trials with gene therapies. See our response in paras 20-24 below.

Public perception of gene editing

18. As consumers increasingly demand sustainable products, the Government, industry, and academia have important roles to play in informing the public of the benefits of gene editing. While historically there has been a common perception that the public is not supportive of gene edited products, there is evidence to suggest that this is no longer the case. For example, according to YouGov survey in 2020 commissioned by the Agricultural Biotechnology Council, 52% of people expressed support for the use of new agricultural innovations such as new plant breeding techniques like gene editing to make crops more nutritious and resistant to pests and diseases.[9] In addition, polling of UK farmers undertaken in January 2021 also found that 65% of cultivators backed greater use of innovations such as gene editing, with 72% of farmers believing they have a responsibility to tackle the environmental footprint of farming.[10]

[9] Agricultural Biotechnology Council (2020), "Two thirds of Britons fear impact of second wave of COVID-19 on UK food supplies": https://abcinformation.org/two-thirds-of-britons-fear-impact-of-second-wave-of-covid-19-on-uk-food-supplies/

[10] Polling of farmers conducted by YouGov, January 2021 – full data available from Agricultural Biotechnology Council on request

Question 4: What criteria should be used to determine whether an organism produced by gene editing or another genetic technology, could have been produced by traditional breeding or not?

Please provide evidence to support your response.

19. To address this question, Defra must clarify how 'traditional breeding' is defined. This is because traditional methods to generate genetic variation in plants and animals have included techniques such as radiation-induced mutagenesis, which can induce multiple, significant changes in genomes, as well as methods by which it is possible to move genes between closely related crop species.

Part 2: Questions on broad reform of legislation governing organisms produced using genetic technologies

This part of the consultation is designed to start the process of evidence gathering to inform how Defra should reform its approach to regulating novel organisms in the longer term. There are two questions that focus on areas where views and evidence would be welcome.

These questions do not apply to the use of genetic technologies in contained use conditions (e.g. in laboratories) or to the use of genetic technologies in humans (e.g. gene editing of human embryos).

Question 5: There are a number of existing, non-GM regulations that control the use of organisms and/or products derived from them. The GMO legislation applies additional controls when the organism or product has been developed using particular technologies. Do you think existing, non-GM legislation is sufficient to deal with all organisms irrespective of the way that they were produced or is additional legislation needed? Please indicate in the table whether, yes, the existing non-GMO legislation is sufficient, or no, existing non-GMO legislation is insufficient and additional governance measures (regulatory or non-regulatory) are needed. Please answer Y/N for each of the following sectors/activities:

	Cultivation of crop plants	Breeding farmed animals	Human food	Animal feed	Human and veterinary medicines	Other sectors/activities
Yes (sufficient governance)	Y		Y	Y	Y	
No (insufficient governance)						

Please provide evidence to support your response.

<u>Human and veterinary medicines: Advanced therapy medicinal products</u>

20. ATMPs are innovative medicines which have the potential to bring highly transformative value to patients, by either correcting the underlying cause of their disease (e.g., a genetic defect) or by modifying a function in the body to cure or significantly ameliorate their disease. Some ATMPs, such as gene therapies that contain or consist of GMOs, need to comply with the GMO legislation. Such

requirements come on top of the requirements for the authorisation of clinical trials in accordance with the Clinical Trials Regulation.

21. Gene therapies using genome editing technologies, such as CRISPR-Cas9 or TALENs, have the potential to radically transform the standards of care for patients who currently lack treatment options. However, the ruling of the CJEU may inadvertently delay access to new treatments, also entailing a negative impact on the research and innovation landscape in Europe.

22. Given that both the GMO and Clinical Trials legislations apply, without defining a *modus operandi* for how they should interoperate, different approaches have been taken by EU Member States - either applying the GMO approval regime before, or in parallel with the clinical trial authorisation application to national regulatory authorities, making the EU less attractive than the US for conducting clinical trials with gene therapies.

23. The recent decision by the European Commission to temporarily exempt investigational medicinal products containing or consisting of GMOs to treat or prevent COVID-19 from complying with some provisions of the GMO legislation is a clear recognition of delays to clinical development and access to life-saving treatments and vaccines caused by GMO legislation.[11] The measures taken to save lives during the COVD-19 pandemic can also save lives in other circumstances. Time is also of the essence for people with cancer, inherited diseases, and other life-threatening conditions.

24. Therefore, the BIA calls on Government to put in place an exemption scheme for ATMPs containing or consisting of GMOs undergoing clinical trials, considering that their environmental risk is often negligible. This will ensure the UK remains a global competitive place for clinical development and allow more rapid patients' access to these potentially curative medicines, as well as clinicians getting experience with these medicines when they come to market.

<u>Cultivation of crop plants, human food, and animal feed</u>

25. As noted in para 4, since most of the BIA's members are focused on human health, we are not able to comment in detail on crops, human food, and animal feed. However, we do believe that existing non-GMO legislation provides sufficient controls for the cultivation of crop plants, human food and animal feed developed through gene editing and other techniques that could have been produced via conventional breeding or natural processes.

26. We reiterate that it is vital that current and future approaches to the regulation of these areas ensure that the UK is an attractive destination for foreign investment and top global talent to conduct their research. By adopting a science-based regulatory system that regulates the product instead of the process, the UK would enable more start-ups to be created from our excellent science base, attract global investment, and help deliver on the Government's levelling up agenda and ambition to make the UK a global life sciences cluster.

[11] Regulation (EU) 2020/1043: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32020R1043

Question 6: Where you have answered no (existing, non-GMO legislation is insufficient to deal with organisms produced by genetic technologies), please describe what additional regulatory or non-regulatory measures you think are required to address this insufficiency, including any changes you think need to be made to existing non-GMO legislation. Please explain how any additional measures you identify should be triggered (for example: novelty, risk, other factors).

Please provide evidence to support your response.

27. We are leaving this blank as we answered 'no' above.

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