Response to the Court of Justice of the European Union (CJEU) ruling of 25th July 2018 on the regulation of products developed using genome editing techniques.

This letter presents the response of the Synthetic Biology Leadership Council (SBLC) and its Governance Subgroup (GSG) to the CJEU ruling that "**organisms obtained by mutagenesis are GMOs and are in principle subject to the obligations laid down by the GMO Directive**"[1]. Please note that the content of this letter reflects the consensus view of the UK SBLC and its GSG, as summarised by its authors, but may not be assumed to reflect the specific views of any constituent organisation or its individual representative on the council or the governance sub-group.

The CJEU ruling affects products developed using new techniques for genetic modification having the potential to play a major role in the future UK bioeconomy. "Directed mutagenesis" techniques, including the use of the CRISPR-Cas9 system, enable gene editing ("GE") of such precision, ease of execution and cheapness, that it has quickly overtaken conventional approaches using recombinant nucleic acids (which lead to "GM" products). Until the ruling, products of these new mutagenesis techniques ("GE" products) were explicitly exempted from the considerable obligations that the GMO Directive imposed upon recombinant products. The judgment means that products of new *precision* mutagenesis lose this exemption, while products of *random* mutagenesis (e.g. caused by exposing seeds to ionising radiation) remain exempted and therefore unregulated: an inversion of the EU's own principles of risk and regulation[2].

The impact of the ruling is entirely negative at a time of multiple threats to global food security. Such is the importance of directed mutagenesis techniques like CRISPR-Cas9 as a potential technological revolution, that the ruling will have a negative influence on innovation in crop and animal production, in which the UK has internationally recognised scientific expertise. It will increase significantly the costs and timescales for regulatory approval, preventing innovative small companies from developing viable businesses and discouraging altogether the development of products suited for European agricultural systems. These techniques could contribute to future global food security while maintaining food safety and quality and protecting the natural environment through, for example: resistance to pests, diseases, drought and flooding; reduction in the need for fertiliser inputs; increases in the nutritional quality of foods; and disease resistance in animals.

The current EU GM regulatory system has already prevented the emergence of European production and trade based on the products of GM recombinant techniques. By allowing the Directive to extend to the now-dominant GE techniques, the CJEU ruling will stifle the emergence of this technological revolution in Europe. The judgment fails to reflect the rapid progress in knowledge of natural systems acquired in recent decades, or the increasing need to rebalance regulatory frameworks to better reflect global challenges as identified in the UN's Sustainable Development Goals. It is not the job of a court to forge policy, but the decision illuminates the EU's sloth in regulating this vital new technology despite the mounting body of evidence and advances in understanding. By contrast, some countries are considering, or have adopted, different regulatory approaches for GM and GE products with a view to realising these benefits, including Canada, USA, Japan, Argentina, Chile, Brazil, Australia, China and several African nations.

[1] https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf
[2] See Article 191 of the Treaty on the Functioning of the European Union.

The Brexit context, the potential benefits to the economy, food security and the environment, and the lack of current EU trade in the products of these techniques have created a potential opportunity for the UK Government, as one of several possible responses to the CJEU ruling.

We propose that the Government should be prepared to act promptly should an opportunity arise to adapt the UK regulatory system for GM and GE techniques to be more in tune with those of other major global trading blocs, by developing a new model for their future UK regulation, bringing together all interested parties (industry, government/policy makers, experts in international trade, regulatory bodies, citizens).

The proposed new model could also form a basis for indirect influence on the expected future reform of the EU regulatory/governance framework for these products and also on wider international thinking, for example by convening an international conference on harmonising the law for GM/GE products.

The process, as elaborated in the Annex to this letter, will build on the Industrial Strategy[3], and will help to foster a new internationally trading sector in the UK economy, to contribute to the Export Strategy target of 35% of GDP[4].

Yours Sincerely,

Lionel Clarke, SBLC Co-Chair,

Joyce Tait, SBLC member and Chair of the GSG.

[3] https://www.gov.uk/government/publications/industrial-strategy-building-a-britain-fit-for-the-future

[4] https://www.gov.uk/government/publications/export-strategy-supporting-and-connecting-businesses-to-grow-on-the-world-stage

ANNEX

Background

For over twenty years the EU regulatory system for GM crops and related products and the politicised nature of its implementation have prevented almost all biotechnology-based innovation for European agriculture and, through trade-related impacts, in much of the developing world. A 2015 report on the EU GMO regulatory system (Directive 2001/18/EC) from the House of Commons Science and Technology Committee recommended "… that the Government make a long-term commitment to achieving more substantial regulatory overhaul and a more meaningful repatriation of national decision-making"[5].

Meantime, given the continuing stalemate in EU regulatory decision making, some national regulators, including DEFRA in the UK, had given guidance that GE products are excluded under the mutagenesis exemption and therefore would not be subject to the EU legislation. This raised scientists' hopes and expectations for applications of their work that will contribute significantly to addressing global challenges related to food security and climate change.

The CJEU ruling that the products of these more advanced biotechnologies will be subject to the requirements of the EU GMO Directive is a serious disappointment to all those working in the area. The recommendations of the 2015 House of Commons Science and Technology Committee, quoted above, seem more relevant than ever, particularly given the widespread concerns generated by the CJEU ruling and the additional Brexit context for the UK.

Consequences of the CJEU Ruling

Maintaining food security for the future global population is one of today's most important challenges and the EU, as one of the most productive agricultural regions in the world, has a responsibility to contribute to the required increases in productivity, while maintaining food safety and quality and protecting the natural environment. Products of the new advanced biotechnology techniques, among our most important tools in achieving these goals, will be unavailable in the EU, but will be developed and applied elsewhere.

The expected consequences of the CJEU ruling for companies planning to develop products based on these new biotechnologies in Europe, or for those targeting EEA markets, are:

- Substantial increases in the costs and timescale for developing an innovation, limiting investment to large companies that can meet the costs of regulatory compliance;
- A relative lack of the path-breaking innovations that are typically developed by small companies;
- Difficulty in attracting investment into the area, as market and regulatory barriers are increased;
- Investment and innovation will be redirected to countries outside the EU, particularly the US and China;
- Reduced prospects of developing effective solutions for Europe to challenges such as food security, climate change, and protection of biodiversity.

The scale of the UK bioeconomy in 2015 was estimated to be least £150 Bn Gross Value Added (GVA), potentially increasing by a further £40 Bn over the coming decade and supporting approx. 600K jobs[6], and synthetic biology and gene editing are expected to transform the sustainability and

[5] House of Commons Science and Technology Committee (2015) *Advanced Genetic Techniques for Drop Improvement: regulation, risk and precaution.* Fifth Report, Session 2014-15. https://publications.parliament.uk/pa/cm201415/cmselect/cmsctech/328/328.pdf

[6] Chambers, G., Dreisin, A. and Pragnell, M. (2015) *The British bioeconomy: an assessment of the impact of the bioeconomy on the UK economy.* Capital Economics, Report to BBSRC. (http://www.bbsrc.ac.uk/documents/capital-economics-british-bioeconomy-report-11-june-2015/)

productivity of the industries that contribute to the bioeconomy. The movement of companies and intellectual property from the UK to the USA and China will therefore impact negatively on the future prospects for the UK economy and will undermine our current exceptionally high international standing in this area. Also at risk will be private investment in synthetic biology-based start-ups in the UK (£564M compared to £56M public investment from 2002-16[7] plus a further £880M private investment in the past 18 months[8])

Proposed response to the CJEU ruling

Gene editing/mutagenesis was the target of the CJEU ruling because it had been identified by some EU national regulators as not being captured by the EU definition of a GMO, offering an opportunity to enable commercial developments based on this limited, but powerful, set of techniques.

Many commentators on the CJEU ruling see it as reinforcing the case for a wider reform of Europe's regulatory approach[9]. Several UK government and other reports have already advocated such reforms, for example: the Advisory Committee on Releases to the Environment (ACRE)[10]; the House of Commons Science and Technology Committee[11]; the House of Lords Science and Technology Select Committee[12]; and the Council for Science and Technology[13, 14]. While these recommendations for a fundamental reform of the EU regulatory system have not gone unchallenged, the stimulus of the CJEU ruling, combined with the UK's scheduled departure from the EU, may open up an opportunity for us to implement these proposed reforms and to align UK regulation of GM and GE products more closely with those of other major trading blocs.

Given the lack of EU markets for the products of GM and GE techniques and the scale of the potential alternative markets, the positive impact of such a change on the UK economy, by permitting domestic development of GM and GE organisms, could be significant. Countries that are considering or have adopted approaches to gene editing that are different from the EU include Canada, USA, Japan, Argentina, Chile, Brazil, Australia and China. Also, African countries (including South Africa, Nigeria, Egypt, Sudan, Ethiopia, Ghana, Tanzania, Mozambique, Uganda), most with previously negative positions on GM crops that were dictated by the trade-related requirements of EU markets, are now developing strategies focused on the adoption of GM and related techniques[15] with local needs and other markets in mind. The trade-related benefits to the UK of building on our world class expertise in these new biotechnology areas to provide products and processes that we can export across the globe would contribute significantly to the Export Strategy Target of 35% of GDP (Note 4), and to the aims of the Industrial Strategy, helping the UK to meet the Grand Challenges (particularly Clean Growth and Healthy Aging) (Note 3).

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[7] https://synbiobeta.com/investment-fuels-cutting-edge-synthetic-biology-in-uk/

[8] https://synbiobeta.com/category/synthetic-biology-news/funding-investments

[9] https://blogs.royalsociety.org/in-verba/2018/07/26/when-is-genetic-modification-not-genetic-modification/ https://royalsociety.org/news/2018/07/ecj-genome-editing-ruling-john-skehel/

[10] ACRE, (2013) *Report 1. Towards an evidence-based regulatory system for GMOs*. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/239839/an-evidence-based-regulatory-system-for-gmos.pdf

[11] House of Commons Science and Technology Committee (2015) *Advanced genetic techniques for crop improvement: regulation, risk and precaution.* Fifth Report of Session 2014-15. https://publications.parliament.uk/pa/cm201415/cmselect/cmsctech/328/328.pdf

[12] House of Lords Science and Technology Select Committee (2015) *Genetically Modified Insects.* 1st Report, Session 2015-16. https://publications.parliament.uk/pa/ld201516/ldselect/ldsctech/68/68.pdf

[13] Council for Science and Technology (2013) *GM Technologies – Letter to the Prime Minister.* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/288823/cst-14-634-gm-technologies.pdf

[14] Baulcombe, D., Dunwell, J., Jones, J., Pickett, J. and Puigdemenech, P. (2014) *GM Science update: a report to the Council for Science and Technology* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/292174/cst-14-634a-gm-science-update.pdf

[15] https://geneticliteracyproject.org/2017/03/06/led-nigeria-africa-gradually-opening-door-genetically-modified-crop-cultivation/

As advised in the documents referenced above, the regulatory system for products developed using these new biotechnologies should:

- Be based on the properties of the final product rather than focusing primarily on the technique used to modify the organism;
- Consider and balance the potential benefits and risks of the product;
- Consider the risks of not developing the product;
- Be informed by scientific experience and understanding gained from the adoption of GM crops and animals worldwide since the original GMO regulations were put in place;
- Reflect technological advances in the ability to measure and monitor the impact of new products in the field and marketplace.

Beyond these aspects of product registration there will also be a continuing need to ensure the safety of laboratory research-based and industrial production processes.

The requirement for regulatory adaptation to meet the needs of new techniques is increasingly widely recognised[16], but there has been little guidance on how to implement such changes. With this in mind, a recent report, funded by BEIS/British Standards Institution and endorsed by the Synthetic Biology Leadership Council[17], introduced a framework for the creative use of standards and guidelines as a means to adapt existing regulatory systems and to make them more proportionate to the needs of innovative technologies. This report includes a case study on synthetic biology and gene editing, and could contribute to the process recommended in the covering letter.

Many of the Parliamentary and other reports referenced above comment on the need for regulatory reform to be accompanied by stakeholder dialogue involving citizens, farmers, industry and other interested parties to enable them to inform themselves about the proposed regulatory changes and to have an opportunity to discuss them with other key players in the process. The report referenced in Note 16 includes a case study on *Responsible Governance*[18] that addresses the problems of conducting such a dialogue on a topic where there is a number of pre-existing entrenched positions among stakeholder groups, as would be the case here.

The course of action proposed in this letter thus addresses an important problem and associated opportunity for the UK Government. It builds on decades of scientific research and regulatory experience and is congruent with current major political and policy developments.

[16] https://ec.europa.eu/epsc/sites/epsc/files/strategic_note_issue_15.pdf
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/735587/better-regulation-framework-guidance-2018.pdf

[17] Tait, J., Banda, G. and Watkins, A. (2017) *Proportionate and Adaptive Governance of Innovative Technologies (PAGIT): a framework to guide policy and regulatory decision making (Final Report and Summary Report).* Innogen Institute Report to the British Standards Institution. https://www.innogen.ac.uk/reports/1222

[18] Tait, J., Banda, G. and Watkins, A. (2018) *Proportionate and Adaptive Governance of Innovative Technologies (PAGIT). Case Study: Responsible Governance of Innovative Technologies (Final Report and Summary Report).* https://www.innogen.ac.uk/reports/1302.