This response was submitted to the Call for Evidence held by the Nuffield Council on Bioethics on *Genome editing* between 27 November 2015 and 1 February 2016. The views expressed are solely those of the respondent(s) and not those of the Council.

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Dear Nuffield Committee,

1. GARNet is a community network that acts as an advocate and supporter of plant science research in the UK and worldwide. The network has existed for the past decade and has recently obtained funding from the BBSRC to ensure its continuation until 2020.

2. Our primary goal is to ensure that the plant science community remains competitive and productive at the national and international level. Therefore we have a broad interest in the technological advances that surround the development of gene-edited (GE) plants.

Summary:

3. We believe that gene editing should be an important contributory technology in future strategies that enable scientists to generate new plant varieties both for commercial exploitation and for challenges associated with a climate change and with food and nutritional security.

4. Given the breadth of genetic changes that can be made using gene-editing techniques, we believe that the most effective method of regulation will involve the assessment of traits on a case-by-case manner and not by use of blanket legislation that is based on the method of transformation. This mirrors a recent BBSRC position statement on this topic (1).

5. We believe that providing a science-led regulatory framework for the use of gene-edited crops is critically important for the future development of plant science in the UK. A permissive regulatory environment will encourage technology transfer between academics and industrial collaborators, therefore maintaining the UK as a worldwide leader in plant science.

6. We believe that it is important for all scientists to engage with policy makers, educators and the public in order to increase scientific literacy within the UK. This will

provide a higher level of understanding and allow for policy makers to develop regulations based on current scientific evidence.

** What is the current state of the art in the field? What are the current technical limitations and constraints/ bottlenecks?*

7. The application of gene editing technology is at an advanced state in plant systems, for example in the past six months effective gene editing using the CRISPR-Cas method has been demonstrated in Arabidopsis, potato, tobacco and barley amongst others (2-4). It is not our remit to provide a detailed description of the technology but rather we will focus on its future regulation.

8. Regulating GE plants on a case-by-case basis is important given the different types of GE that is possible. It is, for example, critical to make the distinction between plants that have been edited to remove the function of an endogenous gene and those where homology-directed repair (HDR) has introduced a new element into the genome. We believe that the latter case should be considered the same as a conventional GM crops albeit that they should be assessed on a case-by-case basis as stated above. However the use of GE technology to produce *transgene-less* edited plants needs to be regulated in a new manner that reflects the genetic makeup of these organisms.

9. Recently good progress has been made to improve the specificity of gene editing. However the principle concern during the generation of GE plants is in the off-target effects that might occur. This concern is particularly relevant when considering the complex, duplicated genomes of many crop species. However the falling price of next generation sequencing (NGS) and improvements in bioinformatics will reduce the difficulty and cost in the identification of off-target mutations created by gene editing. Therefore identification of any off-target mutations that have been generated will not be a significant bottleneck in the future generation of GE plants.

10. For many researchers the true bottleneck in the generation of gene-edited crops occurs in the efficiency of the transformation process (5). Even though transgene DNA has been introduced to plants for decades, we are still lacking methods for the efficient and cost-effective transformation of many crops species. Use of editing technology will in theory, reduce the burden of this bottleneck compared to other *cis* or *trans*genic GM approaches. Use of HDR allows the precise targeting of a transgene to a genomic locus, which will overcome any genome 'position effects' that might occur during non-targeted transformation.

** What are the main directions of travel? What are the envisaged endpoints/ applications?*

11. The applications of gene editing are similar to those with conventional GM approaches. The technology provides an opportunity to alter a plants phenotype by precisely changing an area(s) of its genome. However whereas conventional GM usually requires the continued presence of the introduced DNA, gene-editing can allow for a separation of the editing process from the altered gene(s)(4). These plants contain no transgenic DNA and ostensibly, assuming the lack of off-target mutations, will be genetically equivalent to an organism that contains a single naturally occurring mutation. This process of '*focused evolution'* results in a plant that differs significantly

from those generated by most conventional GM approaches, and therefore we believe should be regulated in a different manner. This is the regulatory approach taken by the US Department of Agriculture (UDSA), who have judged that transgene-less plants should be regulated differently to conventional GM plants (6).

12. The type of genetic alterations made during the gene editing process are distinct from those used in conventional GM so there is an opportunity to represent these plants in a different manner. It is critical to engage with policy makers on a fact-based level that will provide a solid platform to encourage decisions to set a new regulatory framework for these plants.

** What is the rate of travel? What are the expected timescales for realising the envisaged endpoints?*

13. It is now relatively straightforward to generate gene-edited plants that are free from off-target mutations. Currently any plants generated in this manner exist in a "legal limbo" as their regulatory status is debated and so are not eligible for field-testing (7,8). Given the opportunity to conduct the appropriate field trials on these plants, a fully-tested gene-edited variety can be available to a potential consumer within 3 years of conceiving the initial idea. This represents a shorter time scale than is possible with marker-assisted breeding or even with conventional GM.

CONDITIONS OF RESEARCH AND INNOVATION

** What are the main 'drivers' and 'obstacles' for plant genome editing in relation to envisaged endpoints?*

14. Use of this technology is motivated by the same reasons as those that directed the generation of GM plants; the technology is used as an aid to discovery, to improve productivity or quality. Preliminary research using gene-edited crops has been ongoing in the UK for the past few years but the main obstacle to further exploration of this technology and its application is the existing uncertain regulatory landscape. Future work will require a more permissive regulatory environment that will examine the merits of each plant on a case-by-case basis to determine whether it is appropriate for the proposed work.

** What direct or indirect influence does historical public discussion surrounding genetic modification of plants have? What is (and what should be) the current level and focus of public debate?*

15. This is arguably the most significant area of concern when considering the future use of gene-edited plants. As mentioned above, it is critical that the debate separates the technology used to generate GE or GM plants and instead focuses on newly developed plants on a case-by-case basis. This was the recommendation of the multi-party Science and Technology Committee report on '*Advanced Genetic Techniques*' (9). Importantly, organisations involved in science communication such as 'Science about Science' are engaging with the public in order to inform this future debate (10).

OUTCOMES

· What are the main anticipated benefits and costs (including safety and other risks) of

genome-edited plants? In what ways, if any, are they significantly different from alternative GM technologies?

16. We anticipate that the main benefits gained from the use of GE technology will be dependent on the manner in which they are regulated, particularly if that is different from the restrictive regulation that currently exists for GM plants. If policy makers can be convinced that this type of technology should be regulated on a case-by-case basis then this will open up the benefits of discovery, production and quality that are outlined above. In principle we agree with five-step set of guiding principles for the future regulation of GE plants, as recently proposed by a worldwide group of eminent plant scientists (11).

- Are there particular issues raised by genome editing in ….. technology transfer between countries, and equitable sharing of the benefits of research?

17. Technology transfer will be dependent on establishing coordinated regulatory policies between countries. The current GM regulations make it more difficult for collaboration to occur between EU countries. Therefore it is important that regulators develop common policies that facilitate the sharing of materials across borders. This will encourage the submission of collaborative grants and, in the case of the EU, allow funding bodies to take advantage of the breadth of talent across the continent.

18. The restrictive GM regulations discourage agricultural companies from investing in the UK and/or EU, which prevents an effective technology transfer pipeline for many UK academics. RCUK has funded research that has resulted in the generation of both fortified GM tomatoes (12) and disease research GM potatoes (13). However in order to bring these products to market, the UK researchers now collaborate with non-EU companies. By allowing regulation of future GE/GM plants in a trait and not method-based manner this will encourage investment from UK and EU companies, allowing the UK consumer to benefit from the excellent research currently undertaken by UK plant scientists.

- To what extent, and in what way, does and should the distribution of anticipated benefits and costs of using genome editing in plants influence research and innovation?

19. We believe this is a key issue that will be greatly influenced by the legislation that determines how GE is regulated. The cautious regulatory policies that govern the use of GM plants negatively influences the ability of UK plant scientists to explore the impact of their research outside of the greenhouse. This both provides a limit on what is experimental possible but also impacts the ability of UK researchers to form collaborative relationships with industrial partners. We would hope that gene edited plants will be governed within a more permissive regulatory framework that will ultimately reduce the cost of developing new GE varieties. This is key for facilitating the technology transfer pipeline. The UK is a world leader in plant science research so we hope that a different regulatory framework will encourage further investment into this area, which will improve both basic and applied research.

- To what extent are public and commercial interests in genome editing in plants complementary? In what circumstances might they come into conflict?

20. Altering the current GM regulations and therefore reducing the cost of conducting field trials on gene edited plants will lower the barriers that prevent new products making to the market. This will encourage the exploration of new commercial opportunities whilst reducing the costs to the consumer. Secondarily it will allow the rapid generation of plants with traits that may have an impact on food security. This will encourage UK researchers to partner with collaborators in developing nations to generate varieties that can provide solutions to specific local problems.

Yours,

The GARNet Advisory Board.

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