Claire Robinson & Dr Michael Antoniou – Written Evidence (UST0068)

This evidence addresses the following points in the Call for Evidence.

1) "The Government has stated it would 'uphold the UK's high levels of public, animal, and plant health, including food safety' and 'any trade agreement with the US must work for UK consumers, farmers and companies and the Government will strongly defend our right to regulate in these areas in the public interest'.

2) Question 20
"… what might be the consequences of a deal with the US that included agricultural goods for Sanitary and Phytosanitary Standards (SPS) and animal welfare standards domestically in the UK?"

Introduction

1. This evidence addresses the safety of genetically modified (GM) (including gene-edited) crops and foods. Under a US-UK trade deal, GM (including gene-edited) crops and foods could be imported into the UK, and such crops and foods could even be grown and produced here. The US has an inadequate system of regulation for such products, including patchy and weak safety assessments and no meaningful labelling for the farmer or consumer who may wish to avoid purchasing them. We are therefore concerned that human and animal health and environmental safety, as well as the UK's high farming standards, will be undermined by the import of poorly controlled US GM (including gene-edited) products.

2. The purpose of GMO regulations and labelling is to protect human and animal health and the environment. Process-based as well as product-based regulation and risk assessment must continue to be applied to all imported and (in future) domestically produced GM crops and foods, including those made using gene-editing techniques – as is the case under current EU and UK law. In addition, all GM products, including gene-edited ones, must carry a clear on-package GM label, as is currently the case under EU and UK law.

3. This is because GM (including gene-edited) products pose risks to health and the environment that must be assessed on a case-by-case basis under regulation that is sufficiently stringent to detect problems.

4. Such regulation needs to be process-based because this takes account the genetic manipulation process used to develop the organism and its unintended, as well as intended, effects. Labelling is crucial because it allows consumer choice and traceability in the event that something goes

wrong.

5. Regulation needs to be stringent because gene editing causes unintended mutations in plants, which in turn results in changed gene function, leading to altered biochemistry, which could include the production of unexpected toxins and allergens, higher levels of existing toxins and allergens, or altered nutritional value.

6. Controlled laboratory animal feeding studies show that the above food safety problems have arisen with the first generation of GM crops (see Krimsky S (2015). Science, Technology & Human Values. http://sth.sagepub.com/content/early/2015/08/05/0162243915598381; Hilbeck A et al (2015). Env Sci Europe 27(1):4. http://www.enveurope.com/content/27/1/4/abstract; and references collected in Robinson C, Antoniou M, and Fagan J (2018), GMO Myths and Truths, 4th edition. Chelsea Green Publishing. https://www.amazon.com/GMO-Myths-Truths-Citizens-Genetically/dp/0993436722).

7. We are not asking for a ban on these products, but for them to continue to be risk assessed under GMO-specific process-based regulation and labelled. Regulation is the moderate middle ground, in contrast to the free-for-all that is demanded by those who wish to de-regulate gene-edited crops, animals and foods.

Gene editing: Scientific research showing unexpected outcomes and risks

8. Many more scientific papers have been published on unintended outcomes and risks of gene editing in medical research involving human and animal systems compared with plants. The results have implications for the gene editing of farm animals. However, the problems found with human and animal gene editing are increasingly being confirmed in plant gene editing. A list of references is below.

9. The unintended mutational (DNA damaging) outcomes detailed below occur after the gene-editing tool has completed its task of inducing a double-strand DNA break. The mutations are caused by the cell's DNA repair machinery, which the genetic engineer cannot control. Thus even if in the future, scientists succeed in avoiding off-target mutations, most of the unintended mutations described can still occur at the intended gene-editing site.

10. This lack of control of the gene-editing procedure, as well as gaps in scientists' knowledge of outcomes, point to the need for strict regulation of gene editing in food crops and farm animals. Regulation must be process-based, so that regulators can better understand where things can

go wrong and which outcomes, both expected and unexpected, they should look for.

11. It cannot be assumed that developer companies will breed out all unintended mutations via backcrossing with elite varieties of non-GM crops. Studies on first-generation GM crops (Mesnage R et al (2016). Scientific Reports. http://www.nature.com/srep/2016/161219/srep37855/full/srep37855.html) and gene-edited cattle (Norris AL et al (2020). Template plasmid integration in germline genome-edited cattle. Nat Biotech 38(2): 163-164. https://www.nature.com/articles/s41587-019-0394-6) show that companies cannot be relied upon to ensure that GM products are indeed "substantially equivalent" to non-GM counterparts and contain no potentially harmful unintended changes. They will not check products carefully unless they are forced to do so via regulation.

12. Moreover, only mutations that are visible – for example, those that cause deformities or poor growth – are generally targeted by developers for breeding out. Mutations that cause more subtle changes to the organism's biochemistry, which can cause production of toxins or allergens, are not easy to spot and could easily go undetected without stringent regulation.

13. Yves Bertheau, director of research at the French National Institute for Agricultural Research (INRA), has pointed out (Bertheau Y (2019). Encyclopedia of Food Chemistry. https://www.sciencedirect.com/science/article/pii/B9780081005965218349) that numerous changes intentionally or unintentionally induced by gene-editing techniques can be transmitted to offspring and appear in the final marketed seed variety. Also, the number of backcrosses performed with elite varieties for marketed products is generally below the six that are theoretically necessary to obtain the desired minimum 95% level of genomic "purification".

NEED FOR REGULATION

14. Gene-edited GM plants do not have a history of safe use and should not be exempted from biosafety assessments.
Kawall K et al (2020). Environ Sci Europe 32:106 (2020). https://enveurope.springeropen.com/articles/10.1186/s12302-020-00361-2

Eckerstorfer MF et al (2019). Front Bioeng Biotechnol 7:31. https://www.frontiersin.org/articles/10.3389/fbioe.2019.00031/full

Gelinksky E and Hilbeck A (2018). Environ Sci Europe 30(1):52. https://enveurope.springeropen.com/articles/10.1186/s12302-018-0182-

CHANGES INDUCED BY GENE EDITING ARE NOT THE SAME AS HAPPEN IN NATURE

15. Gene editing makes the whole genome accessible for changes – unlike naturally occurring genetic changes.

Kawall K (2019). Frontiers in Plant Science 10:525.
https://www.frontiersin.org/articles/10.3389/fpls.2019.00525/full

UNINTENDED MUTATIONS

16. Below are some studies showing different types of unintended mutations resulting from gene editing that can affect the functioning of multiple gene systems. The consequences are an alteration in the plant's protein and biochemical function, which could lead to poor crop performance and/or the production of novel toxins and allergens, or higher levels of existing toxins and allergens.

Off-target mutations

17. Gene-editing tools, especially CRISPR, are prone to causing mutations (damage) to the organism's DNA at locations other than the intended edit site ("off-target mutations"). This can alter the function of other genes, with unknown consequences to biochemical composition and gene function.

Wolt JD et al (2016). The Plant Genome 9(3):10.3835/plantgenome2016.05.0047.
https://acsess.onlinelibrary.wiley.com/doi/full/10.3835/plantgenome2016.05.0047

Zhu C et al (2017). Trends in Plant Science 22(1):38–52.
https://www.ncbi.nlm.nih.gov/pubmed/27645899

Large deletions and rearrangements of DNA at both off-target and on-target gene editing sites

18. Large deletions and rearrangements of the plant's genome, which can involve thousands of base units of DNA, have been found following CRISPR gene editing. These mutations can affect the functioning of many genes, leading to alterations in the plant's protein and biochemical composition.

Biswas S et al (2020). Journal of Genetics and Genomics. May 21.
https://www.sciencedirect.com/science/article/pii/S1673852720300916

Kosicki M et al (2018). Nature Biotechnology 36:765–771. https://www.nature.com/articles/nbt.4192

Mou H et al. (2017). Genome Biology 18:108. https://genomebiology.biomedcentral.com/articles/10.1186/s13059-017-1237-8

Shin HY et al. (2017). Nature Communications 8, 15464 (2017). https://www.ncbi.nlm.nih.gov/pubmed/28561021

Creation of new gene sequences leads to new RNA and protein products

19. Alteration of the genetic code of the targeted gene can produce mutant forms of the protein it encodes for, new RNA, and new protein products. These outcomes can lead to changes in the plant's biochemistry.

Mou H et al. (2017). Genome Biology 18:108. https://genomebiology.biomedcentral.com/articles/10.1186/s13059-017-1237-8

Tuladhar R et al (2019). Nat Commun 10, 4056 (2019). https://www.nature.com/articles/s41467-019-12028-5

Smits AH et al (2019). Nat Methods 16, 1087–1093. https://www.nature.com/articles/s41592-019-0614-5

Gene-editing process-induced mutations

20. The gene editing process, taken as a whole (including plant tissue culture and the GM transformation procedure), induces hundreds of unintended mutations throughout the genome of the plant. This can affect multiple gene functions, with unknown consequences for protein biochemistry and metabolic activity.

Tang X et al (2018). Genome Biology 19:84. https://genomebiology.biomedcentral.com/articles/10.1186/s13059-018-1458-5

Insertion of foreign and contaminating DNA into genome at editing sites

21. Following creation of a double-strand DNA break by the CRISPR gene-editing tool, the repair can unexpectedly include the insertion and rejoining of the broken DNA ends of the recombination template DNA

used in SDN-2 (gene modification) and -3 (gene insertion), or the insertion of contaminating DNA present in materials used in the plant tissue culture. This insertion of extraneous DNA in the genome of the plant, which can take place at off-target sites as well as the intended on-target edit site, results in the introduction of new gene functions, as well as disrupting the function of host genes. These effects can combine to alter the biochemical function of the plant in unexpected ways.

22. Studies (Norris et al., 2020; Skryabin et al., 2020; Molteni 2020) describe the unintended insertion of the whole plasmid DNA molecules that acted as the recombination template for the SDN-2 or SDN-3 procedure. The insertion of these plasmid DNA templates will result in at least one antibiotic resistance gene being incorporated in the genome, as these are a component of plasmids. There is a real risk that antibiotic resistance genes could be transferred to disease-causing bacteria in the environment and more worryingly, in the gut of the consumer. This could compromise the medical use of antibiotics.

Norris AL et al (2020). Nat Biotech 38(2):163-164.
https://www.nature.com/articles/s41587-019-0394-6

MEDIA ARTICLE: Molteni M (2020). WIRED, 24 July.
https://www.wired.com/story/a-crispr-calf-is-born-its-definitely-a-boy/

Skryabin BV et al. (2020). Science Advances 6(7), eaax2941.
https://advances.sciencemag.org/content/6/7/eaax2941

Ono R et al (2019). Communications Biology 2: 57.
https://www.nature.com/articles/s42003-019-0300-2.pdf?origin=ppub

Conclusion

23. GM (including gene editing) of crops, animals and foods leads to several different types of unintended genetic mutations, which unpredictably alter the function of multiple gene systems of the organism. Altered patterns of gene function will unpredictably change the biochemistry of the organism, which in the case of plants can lead to the production of novel toxins and allergens, or increased levels of known toxins and allergens. Thus, due to the risks that GM (including gene-edited) products pose to health and environment, they must continue to be regulated under GMO-specific process-based and product-based laws. All such products must carry clear on-package GMO labels to preserve consumer and farmer choice.

25 September 2020