Department for Environment, Food & Rural Affairs
Public Consultation on the Regulation of Genetic Technologies

Summary of views submitted by the Microbiology Society

We note that our response reflects the views expressed by thirteen members of the Microbiology Society who have responded to our call for input and share different perspectives on the regulation of genetically modified organisms (GMOs) which could have been developed using traditional breeding. Therefore, our response is by no means comprehensive and it is not our intention to speak on the behalf of the microbiology community. Rather, we highlight anecdotes and examples of where genetic technologies are impacting on microbiology and its applications. We are currently consulting members to inform further explainers on these scientific issues. The evidence will be submitted for consideration to Defra in due course.

Introduction

1. The Microbiology Society is a membership charity for scientists interested in microbes, their effects and their practical uses. It is one of the largest microbiology societies in Europe with a worldwide membership based in universities, industry, hospitals, research institutes and schools. Our members have a unique depth and breadth of knowledge about the discipline. The Society's role is to help unlock and harness the potential of that knowledge.
2. We welcome the opportunity to inform Defra's timely consultation. Techniques for sequencing and modifying genomes have been an integral part of fundamental and applied microbiology since genomics studies began. Consequently, genome sequencing and engineered microbes contribute greatly to the significant impacts being seen within microbiological research. These innovations span many areas, including health, agri-food, environmental science and industrial biotechnology. Fundamental microbiology underpins the discovery and development of many transformative, widely-used tools for genomics such as CRISPR/Cas.

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

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

3. Thirteen members responded to this question in total. Five members responded that **no**, organisms developed using genetic technologies such as GE **should not continue to be regulated as GMOs** if their genetic change(s) could have been produced through traditional breeding. To the contrary, four members responded that **yes**, organisms developed using genetic technologies such as GE **should continue to be regulated as GMOs** even if their genetic

change(s) could have been produced through traditional breeding. Four members required more information or were in favour of a different definition. Their perspectives are presented below.

No – they should not continue to be regulated as a GMO

4. The European Union (EU) definition of a GMO is where "the genetic material of the resulting organisms has been altered in a way that does not occur naturally"[1]. The existing legislation needs to be amended to account for the fact that the kinds of modifications introduced using GE techniques can indeed introduce natural type mutations (e.g. single base pair deletions, introduction of stop codons, targeted deletions).

5. The mechanisms by which GE work are well understood and if the targeted edited change is verified by sequencing (i.e. accuracy and lack of off-targets effects) then, the change could not be distinguished from one that would be affected by traditional breeding.

6. The current GE technology allows highly precise and controlled changes in an organism's DNA. This could be as precise as the alteration of one nucleotide in a genome. Such changes happen randomly in all organisms and are unavoidable. Nature selects for beneficial mutations that confer a fitness benefit to the individual, and humans have for thousands of years applied 'unnatural selection' to select for mutations that generate desired characteristics in agriculture and livestock. Currently, scientists can irradiate potato embryos to induce random mutation and, if lucky, select for one beneficial mutation. Alternatively, GE enables precise changes. The end result is safer and more efficient as no other mutations are introduced.

7. A clearer distinction is needed between transgenic and edited organisms. Transgenic cells form the basis of GMOs – new donor DNA sequence is transplanted from one species into a different species that lacked it. In contrast, edited cells receive no novel donor DNA sequence - changes are made to DNA code native to cells.

8. Traditional breeding methods (i.e. non-GMO) combine mutagens and selection pressure to develop desirable mutant traits. This edits DNA code already native in cells without new donor DNA. The mutagens randomly speed up natural processes that underpin molecular evolution, and selection for a trait gives directionality to the outcome. CRISPR methods should be viewed in the same way. In particular, post-2018 base-editing and primed-editing strategies[2] do not use donor DNA, but with greater precision than using mutagens. A desired mutation is made at a specific site to achieve the desired phenotype, based on prior knowledge of the genetic system being edited[3].

[1] Van Der Meer *et al* (2021). The status under EU law of organisms developed through novel genomic techniques. Cambridge Core. DOI: 10.1017/err.2020.105

[2] Anzalone *et al* (2019). Search and replace genome editing without double-strand breaks or donor DNA. Nature. DOI: 10.1038/s41586-019-1711-4 ; Marzec & Hensel (2020). Prime Editing: Game changer for modifying plant genomes. Trends in Plant Science. DOI: 10.1016/j.tplants.2020.05.008; Molla *et al* (2020). Base editing landscape extends to perform transversion Mutation. Nature Genetics. DOI: 10.1016/j.tig.2020.09.001

[3] Aznar-Moreno & Durrett (2017). Simultaneous targeting of multiple gene homeologs to alter seed oil production in camelina sativa. Plant Cellular Physiology. DOI: 10.1093/pcp/pcx058 ; Koblan *et al* (2021). In vivo Base editing rescues Hutchinson-Gilford Progeria syndrome in mice. Nature. DOI: 10.1038/s41586-020-03086-7.

Yes – they should continue to be regulated as a GMO

9. Micro-organisms can adapt to environmental changes via mutations, this occurs constantly in the natural environment[4]. In addition, these mutations can occur naturally by the acquisition of foreign DNA or by mutations in the DNA of the micro-organism. An example of this is the acquisition of antimicrobial resistance by being exposed to antibiotics, which can occur due to DNA mutations (which could be generated using CRISPR technology) or the acquisition of antimicrobial resistance genes from foreign DNA, such as plasmids. Technically, as this can occur naturally overtime without direct manipulation of the micro-organisms' DNA, it could be called 'traditional breeding'.

10. Similarly, when using antibiotics, we select for the antibiotic resistant organisms, like we select for more productive plants when doing traditional breeding. Therefore, it could be argued that using GE to produce genetic changes in micro-organisms that could be produced overtime with the correct environmental stimulus and selection would allow GE micro-organisms to fall under the 'traditional breeding' category.

11. The fundamental principal behind the regulation of GMOs is that the techniques used define the GMO status, regardless of whether or not these could have happened by other means. GE does not change this.

12. GE is a mode of genetic modification that although does not imply the production of transgenic organisms, will transmit their genetic modifications to the progeny with implications of unpredictable extension and gravity. Separating out GE and GM as different approaches is pointless and confusing.

13. It would be more beneficial to update the current GMO regulations rather than generate a new category (i.e. GE due to 'traditional breeding') that is effectively a loophole for the current regulations.

14. Deliberate genetic change through molecular manipulation should be described as resulting in a genetically modified organism. No matter how small the alteration is in terms of number of base pairs changed, the phenotypic change on the individual organism can be large, as could the impact on ecosystems. For reasons of sustainability and to maintain healthy ecosystems it is important to record and regulate activities that impact biodiversity. Expert review of any proposal to molecularly engineer a GMO is advisable and the panel of experts consulted should cover a broad range of expertise, for example molecular biology, ecology, animal husbandry or plant science.

Other comments

15. A more precise definition of GE than the one provided in the consultation document is needed to assess whether current legislations should be amended. Is Defra referring to the deletion of a gene which could happen naturally or to the replacement of a faulty gene with a correct copy of the same gene?

[4] Koskella & Vos (2015). Adaptation in natural microbial populations. Annual Review of Ecology, Evolution, and Systematics. DOI: 10.1146/annurev-ecolsys-112414-054458.

16. Regulation should depend on the hazard group. For example, the engineering of cat 1 microbes (e.g. Bifidobacterium) which are GRAS, might not require strict regulations. However, a form of regulation as well as knowledge and transparency as to how microbes are being engineered (e.g. are beneficial or virulence traits added in?) remain imperative.

17. Any difference between a change made by GE and the same change made by any other means is purely philosophical. In the majority of cases, it will be easy to argue a logical case that the targeted change could occur in nature (e.g. through deletion, deregulation, point mutation), although it could be possible to push the boundaries.

18. GE is a methodology rather than an end product/organism. Each GE product/organism should be considered individually as an end-point rather than based on how it was made.

19. If a change made by GE can be made by 'traditional' means, how will a regulating body tell the difference and what sort of legislation would be set-up? Would we require specific 'owning-up' declarations for any product made using GE, or would everyone using traditional breeding and mutation techniques need to declare, or even provide evidence, that they have not used GE? Similar outcomes can be obtained using non-GM/GE techniques such as TILLING, where molecular biology is used to direct conventional mutagenesis. There is potential for escalation of regulation across applied biology in general, for no specific benefit.

20. The regulation should be assessed based on the type of editing (e.g. germ-line mutation or somatic mutation) and there needs to be better education about the benefits of GE, regardless of the method.

Additional comment from the Microbiology Society Council

21. The nuanced nature of the responses may be missed. For example, when members responded that organisms developed using genetic technologies such as GE should continue to be regulated as GMOs, they stated that any genetic modification in an organism can occur naturally and therefore that the concept of 'GMO' does not exist. This suggests that while they responded that GE should be regulated as GMO, they are instead putting forward the argument that there is no sound scientific basis to separate GE and GMO and therefore traditional or genetic engineering should not be distinguished by regulation.

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?

22. Ten members responded to question 2 in total. Seven members responded that organisms produced by GE or other genetic technologies pose a **similar or lesser risk** of harm compared with their traditionally bred counterparts as a result of how they were produced. To the contrary, two members responded that organisms produced by GE or other genetic technologies pose a **greater risk** of harm compared with their traditionally bred counterparts as a result of how they were produced. Finally, two members estimated that the risk had to be assessed on a case-by-case basis. Their perspectives are presented below.

Lesser risk

23. In plants and mammals, the newly developed GE methods of primed[5] and base-editing[6] are likely to be more predictable methodologies than traditional mutagenic breeding or 'traditional' CRISPR-Cas9 editing. Each can target a mutation to a desired locus. Though not without risk, and there are not yet enough case studies, these methods look likely to be an improvement for containing unintended negative effects of GE.

24. Current methods generate many random mutations, often never discovered, in the pursuit of one 'desired' mutation. GE can cut out all the mutational 'noise', which must have a safety benefit. Nevertheless, GE is very powerful and there is no doubt that it could be used to generate more dangerous organisms if not properly regulated. Risk analysis for any GE project should be subject to rigorous ethical review.

25. In addition, the slow nature of traditional methods can also pose a potential risk to human health. If an emergency situation ever occurred where a rapid change was needed to be introduced (e.g. a new crop variety was needed due to an untreatable crop pathogen), 'traditional methods' would take years to decades to generate a new variety, while GE would have the potential to produce a change within months to a year. While admittedly an unlikely scenario, it is still worth consideration.

Similar risk

26. Traditional breeding of plants can already be used to generate hybrid plants (i.e. 'offspring' generated from combining qualities of two different species, such as wheat and cotton[7]), but hybrids can occur naturally too. As with the example of micro-organisms gaining antimicrobial resistance genes from foreign DNA [see point 9], these hybrids acquire improved traits by combination of 'foreign' DNA. In both cases, 'traditional breeding' methods could be employed to gain these outcomes and GE could be used to generate hybrids. As these events can occur naturally, the risk is similar. That does not mean that the risk is not great, as we can have changes that occur naturally and have a great impact on the other organisms (e.g. mutations obtained by SARS-CoV-2 occur naturally overtime as the virus replicates, but the impact on human transmission is great and therefore increases risk[8]).

27. In plants traditional breeding methods for GE rely on seed mutagenesis using UV/gamma/chemical agents to create the mutations that are selected for in the desired trait. This can result in off-target and pleiotropic effects that had not been anticipated. Similarly, pre-2018 CRISPR GE methods are hampered by undesired off-target effects from the methodology used (i.e. Cas9-gRNA). The deleterious and potentially risky effects of this CRISPR-based GE is

[5] Marzec & Hensel (2020). Prime editing: game changer for modifying plant genomes. Trends in Plant Science. DOI: 10.1016/j.tplants.2020.05.008
[6] Molla *et al* (2020). Base editing landscape extends to perform transversion mutation. Nature Genetics. DOI: 10.1016/j.tig.2020.09.001
[7] Goulet *et al* (2016). Hybridization in plants: old ideas, new techniques. Plant Physiology. DOI: 10.1104/pp.16.01340.
[8] Conti *et al* (2020). The British variant of the new Coronavirus-19 (Sars-Cov-2) should not create a vaccine problem. J Biol Regul Homeost Agents.DOI: 10.23812/21-3-E.

well documented, but it is not worse than that of traditional breeding[9]. However, this level of risk may not be tolerable at present for studies in human cells[10].

28. Gene edited crop plants have no exogenous DNA in them and are therefore targeted, more rapidly created versions of the kinds of plants that arise through traditional crop breeding. Indeed, often these natural crop breeding experiments are used to introduce multiple beneficial mutations in to single crop plant genomes. Given this, they offer no more risk than traditional crop bred plants when entering the food chain.

29. In terms of production of medicines, gene editing of producing organisms will have little effect on products as these generally do not contain DNA from the host; gene editing will simply expedite the process of generating high yielding strains.

Greater risk

30. Unlike transgenic organisms, genome edition may have less impact on the individual fitness, thus not affecting the survival in the environment and eventually even extending it. Also, contrary to transgenes, genome edition events may be much more stable in the genome, persisting over generations and it might not be impaired by incompatibility defence mechanisms occurring in the genomes. Both facts will contribute to the perpetuation of these man-made modifications.

31. A potential threat exists if molecular genetic technologies speed up the time to impact on biodiversity, whether crop or farmed animals. Homogeneity in either case could result in increased susceptibility to extensive losses due to infectious disease, for example.

Other comments

32. The risk of harm to human health or the environment depends on the modification and must be dealt with on a case-by-case basis. Natural or selective breeding has caused safety issues such as the lethal Africanised honeybee, animal welfare problems such as oversized cattle having problems giving birth unaided, and crop cultivation issues such as the almost universal use of the Cavendish banana variety making it susceptible to disease. By contrast, there have not been adverse effects from GMOs, partly due to the scrutiny of the regulatory process prior to their generation.

33. Also worth considering are issues surrounding the criteria used to assess the risks of genetic modification, which risks should be considered acceptable and in which type of products might such modifications be eventually acceptable?

[9] Graham *et al* (2020). Plant genome editing and the relevance of off-target changes. Plant Physiology. DOI: https://doi.org/10.1104/pp.19.01194

[10] Rayner *et al* (2019). CRISPR-Cas9 causes chromosomal instability and rearrangements in cancer cell lines, Detectable by Cytogenetic Methods. CRISPR Journal. DOI: 10.1089/crispr.2019.0006

Are there any non-safety issues to consider (e.g. impact 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?

34. Ten respondents have highlighted non-safety issues to consider if organisms produced by GE or other genetic technologies were not regulated as GMOs. Their views are presented below.

Ecological and physiological impacts

35. From a biology perspective, it is imperative that we consider and assess the ecological and physiological impact of any changes: What happens to the organism's microbiome? How does it affect ecological interactions? What happens to the overall physiology of the organism? Does it affect any fitness traits?, are all important questions.

Impacts on trade

36. Any country that regulates organisms produced by GE as GMOs and that does not allow for the sale of GMO products would ban trade of UK's GE organisms. For example, the EU does not allow for the consumption by humans of fresh fruit or vegetables produced by GM[11]. The current stance of the EU is extremely hard-line and, if this does not change, there are real risks any GE products would be banned.

37. There could be potentially adverse effects on organic food producers if GE/GMOs were to find their way into the supply chain or cross-pollinate crops.

38. A major driver not to use GE for commercial applications where other techniques could achieve the same result relates to the complex framework of Intellectual Property, where basic techniques and their specific applications and technical variations all potentially require licensing and payment of royalties. In many cases CRISPR/cas9 and its many variants may be used for research purposes, but different techniques will be used to generate biological systems for commercial use. Against this, it needs to be borne in mind that at some stages the patents will expire and CRISPR will become much more attractive for commercial application.

Animal Welfare

39. GE has proven that it has the potential to have a positive effect on animal welfare. In 2019, hornless cattle were created using GE. It has proved difficult to create hornless cattle by 'traditional breeding methods'. At present cattle horns are removed surgically at an early age. This dehorning is a quite traumatic process for them, so creating cattle without horns would improve their wellbeing. There is also the potential that GE could lead to negative animal welfare outcomes, in the same way that 'traditional breeding methods' already do.

Public and media perceptions

40. Recent history shows that there is a part of the population that will never accept that a technology like GE should be considered as equivalent to traditional methods. This will be given the full glare of the news and social media which will have ramifications. The worry is that

[11] Royal Society (2016). Where are GM crops being eaten? https://royalsociety.org/topics-policy/projects/gm-plants/where-are-gm-crops-being-eaten/

allowing GE has a knock-on effect that weakens the position of science generally, beyond the debate around GMO/GE.

41. Any introduction on novel genotypes needs to be very carefully handled and promoted in the right way. Transparent and accurate communications are required to shift away from the fear appeals that frequently appear in the mass media.

42. The consumer should be informed if a product derives from a GMO so they can make an informed choice as to whether to support such initiative or not.

Ownership

43. There are concerns over ownership and control of any GE/GM products, such as crops. Many of the arguments against GM crops were not related to the science or safety but to ownership of big businesses (e.g. multinational agribusiness Monsanto). These issues can also arise with organisms produced through traditional breeding methods.

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?

44. Ten members responded to question 4 in total. Four members responded that the term of '**traditional breeding' needs to be further defined** before criteria can be decided. On the contrary, three members responded with **potential criteria suggestions**. Three members raised further **issues related to the question** itself. Their perspectives are presented below.

Defining traditional breeding

45. The aim of GE methods, as well as clearly defined GM methods, is to produce a new organism with defined and controlled genetic change. However, during traditional breeding methods, uncontrolled and unpredictable off-target effects can occur, including the reactivation of dormant biochemical pathways and induction of viruses. Therefore, the definition of what may be obtained by traditional breeding can become problematic.

46. Genetic changes that have been acquired naturally over time within an organism are complex and include changes occurring within the same species, between related species and between species that are not closely related. Whereas genetic change in animals and plants is mainly limited by the traditional species barrier, horizontal gene transfer across species can occur in micro-organisms, which adds complexity to the term 'traditional breeding'. For example, gene transfer between unrelated species, based on naturally occurring mechanisms such as conjugation and virus-mediated transduction, can occur in both fungi and bacteria[12].

47. The issue of introduction of DNA from related strains and species needs to be considered carefully. There is evidence to support successful crossing of strains or species by traditional breeding methods and therefore transgenes could provide the first test of the criteria. However, including transgenes could lead to pushing the boundaries of this definition, for example when trying to introduce a drought resistance gene from rice into wheat or barley. This may be

[12] Boto (2010). Horizontal gene transfer in evolution: facts and challenges. Proceedings of the Royal Society. DOI: https://doi.org/10.1098/rspb.2009.1679.

acceptable to the public, as it will help sustain food production. On the contrary, the public may not accept introduction of genes that encode plant toxins being introduced to crops, except where they clearly only target pest species. Therefore, moving genes between plants must be carefully controlled. One option could be to restrict the transfer of genes between related, established crop species or livestock species. This might be scientifically justified in terms of safety but could still elicit a negative response in the public imagination.

48. The criteria for whether an organism produced by GE or another genetic technology, could have been produced by traditional breeding, should be if (even in theory) the genetic changes that are made could have been acquired naturally overtime within that organism. However, using that definition raises the issues [see point 9] and the term 'traditional breeding' is not recommended when defining whether GE could be used. Rather than focusing on determining whether an organism produced by gene editing could have been produced by traditional breeding, determining whether the GE organism has an environmental impact, or raises issues relating to animal welfare, could be more suitable. For example, when trying to improve a crop's resistance to fungal diseases such as Fusarium ear blight, determining whether it would outcompete natural flora within the region would provide more value than determining whether it could be produced by traditional breeding.

Criteria suggestions

49. A clearer distinction is needed between transgenic and edited organisms [see point 7]. Criteria may be (a) no novel donor DNA sequence is required to generate the edit (the resulting cells are therefore not transgenic (b) the edit made is a mutation confined to a single open reading frame, or possibly even a single codon.

50. Testing of GE organisms using molecular and genomic tools including next-generation sequencing, quantitative polymerase chain reaction and fluorescence in-situ hybridisation, is required to validate the accuracy of GE and the lack of off-target effects. Performing this analysis for a plethora of GE derived lines would allow the identification of genetic changes that fit with the established mechanisms that are well-known for traditional methods.

51. Criteria could be determined by comparing the modified organism to records from existing breeding programmes, including studies on existing breeding programmes and genome databases.

Other comments

52. No additional genetic material is inserted when using precise GE technologies, such as transient introduction of the Cas9, and it is therefore difficult to distinguish between organisms produced through GE, rather than traditional breeding methods.

53. Drawing a distinction between GE organisms and organisms produced by traditional breeding is a dangerous move for the scientific community, as it splits the basically equivalent approaches of GE and GM into perceived 'good' and 'bad' modifications. This has the potential to backfire and do more harm than good to scientific R&D in the UK.

54. Defining the criteria depends on whether the desired beneficial functional trait generated by traditional breeding can be defined by a single gene or whether it is multi-factorial. If the function can be defined by single genes, organisms can be produced using precise GE

technologies. If the function is multi-factorial, then it would require repeated or multiplexed editing, which may be a much harder sell ultimately to the consumer.

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

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?

55. Five members responded to question 1 in total. Four members responded that **non-GM legislation is not sufficien**t to deal with all organisms irrespective of the way that they were produced, and additional legislation is needed for all areas. One member responded that non-GM legislation is **not sufficient in cultivation of crop plants, breeding farmed animals and human food**, whilst non-GM legislation is sufficient in animal feed, human and veterinary services, and other sectors. Their views are presented below.

No – non-GM legislation is not sufficient to deal will all organisms irrespective of the way that they were produced and additional legislation is needed for all areas

56. Current non-GMO legislation does not capture all the considerations required to determine if a GE organism fits the criteria for safe use and therefore existing legislation needs to be amended. Change would be needed to convince the general population that GE organisms have been fully and appropriately vetted.

57. Non-GM methods are in general designed to target specific genetic events, mainly transgenes that may be detected at trace levels. In GE, the genetic modifications may be difficult to detect using such approaches and in situations of non-compliance or of illegal use of GE, modifications can be difficult to detect.

58. Guidelines and legislation should be regularly reviewed. Awareness and understanding of the importance of sustainable practices, the interdependence of organisms within an ecosystem and potential for unintended consequences when we intervene, has grown and should be drawn on in a review of governance measures.

No – Non-GM legislation is not sufficient in cultivation of crop plants, breeding farmed animals and human food, whilst non-GM legislation is sufficient in animal feed, human and veterinary services, and other sectors

59. Any new product that is consumed directly by humans, or with the potential to cause animal welfare issues, should have higher levels of regulation initially as are required by GMO regulations, since the healthcare sector is already tightly regulated.

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).

60. New legislation is required to ensure that the genotype (accuracy and lack of off-target effects) of any GE organisms were appropriately verified and shown to be equivalent to a 'traditional' method. Non-GMOs should be subject to (a) full genome sequencing at the point of clonal cell production to ensure accuracy and lack of off-target effects, and (b) evaluation that typical chemical/nutritional composition of cells/material is altered only for the targeted characteristics

61. Risk assessments for human and animal health using evidence-based guidelines are needed (e.g. biodiversity impacts, assessing fitness/spreading of new GE organism, invasion capacity of GE varieties, development of resistance mechanisms). Whilst more research on organisms produced by genetic technologies – and the associated risks - is being carried out, precautionary measures should be implemented. Other measures should ensure that independent and transparent research are funded.

62. After a period of safe use, products classified as GMOs should revert to the non-GMO levels of control. This would be a more appropriate regulatory framework than trying to differentiate GE from GMO.

63. Expert opinion is required to consider on a case-by-case basis whether a given GE approach could indeed be achieved by traditional breeding approaches and therefore additional regulatory measures are required. A degree of humility is required in terms of recognising gaps in knowledge such as impacts on the environment and potential unintended impacts on animal welfare (e.g. risk of unintended off-target effects of GE).