Consultation

ACNFP Consultation Response to the DEFRA consultation on regulation of New Genetic Technologies

16th March 2021

Dear Consultation Coordinator,

Defra consultation on the regulation of New Genetic Technologies

I am writing to offer thoughts on the consultation on behalf of the Advisory Committee on Novel foods and Processes (ACNFP). The outcomes of this consultation will directly impact the work of the ACNFP.

The ACNFP is an independent Scientific Advisory Committee who provide advice to the Food Standards Agency, comprising specialist experts from a wide range of scientific disciplines as well as consumer and food sector representatives. The ACNFP advise the Food Standards Agency on matters relating to the safety of novel foods and processes, traditional foods and genetically modified food and feed. Through a series of discussions, the ACNFP have produced the following response to the Defra genetic technologies consultation. The ACNFP have responded only to questions in section 2, part 1 as the other sections are outside of the remit of the Committee.

The response is as follows:

Response to Section 2, Part 1, Question 1

In responding to question 1, it is first necessary to have clarity on what constitutes ‘traditional breeding’. Only then can decisions be made as to whether

specific outcomes from genome editing or other genetic technologies could also have been obtained through traditional breeding techniques. A clear definition and technical description of the types of genome editing technologies and processes that lead to outcomes that could also be achieved by traditional breeding could then be provided. The considerations in part 1 question 4 are relevant here. We believe that the generic yes/no answer requested is too simplistic with regards to the science.

For example, the answer might be ‘yes’, for some genetic technologies which produce extensive changes that are very unlikely to be achieved by traditional techniques. These should remain within the GMO regulation.

Conversely, for some forms of simple genome editing in plants, animals and microbes, where the same outcome could have been produced through traditional breeding, it may be feasible for the resulting products not to be regulated in the same way as GMOs. Traditional plant and animal breeding have a long history of safe use, giving confidence that similar outcomes obtained through genome editing should not lead to additional or new risks. However, traditional plant and animal breeding techniques have resulted in significant variations, both positive and deleterious. It should be noted that current breeding processes have ensured that unwanted variation is not selected or included in final varieties or breeds. Genome editing has the potential to reduce the risk of harmful changes, with a better prediction of trait outcomes, but a case by case assessment of outcomes, deliberate and unintended, would still be needed. For example, it is worth noting that the allergenic potential of crops including those produced through traditional breeding methods is not always predictable. There have been demonstrated differences in allergen content between samples of the same crop cultivars grown in different areas due to the influence of environmental factors. This would be applicable for genome edited crops also, and therefore considerations should be made on a case-by-case basis.

Traditional breeding encompasses the accumulation and selection of genetic variation within a crop variety or animal breed. As part of any new policy going forward, it is important to define clearly the range of genetic variation that could be obtained through traditional breeding methods. Genome editing techniques can be used to make changes that could be found within this genetic variation. However, genome editing allows these changes to be introduced more quickly than traditional breeding, in a matter of a few years. The characteristics of the final product may be more appropriate for assessing risk to the consumer rather than the method of production. Some form of safety assessment on a case by

case basis is considered necessary as the use of genome editing technology emerges, to give confidence that the more rapid breeding process did not increase risk. However, the committee agreed that this safety assessment would not need to encompass all the aspects of the current GM assessment framework. It would need to include, as examples, the demonstration of the absence of a transgene or nucleases used in the editing process, and the monitoring of allergen and toxin levels in species with a known history, for example glycoalkaloid levels in Solanaceae species.

Conclusion

The ACNFP recognises the many benefits this transformative technology may bring to consumers and society. It is recommended that a scientifically robust safety assessment should continue to be performed for all novel foods produced using genome editing technologies, even in cases where the full current safety/risk assessment process required for a GMO product may not be considered appropriate. In cases where outcomes from the use of genome editing can be demonstrated to be the same as those that could be obtained from traditional breeding, an appropriate risk assessment process should be established to ensure consumer safety.

Response to Section 2, Part 1, Question 2

Genome editing can allow for the introduction of genetic changes that could occur through traditional breeding, so in principle the risks presented could be similar if the outcomes are similar. However, it would not be possible to say categorically that any modification made via genome editing will present a similar risk to a product from traditional breeding unless it was clearly demonstrated that an equivalent outcome had been achieved.

For example, traditional breeding in plants could include the use of a mutation breeding approach that has been in use for many years, where numerous mutations are introduced throughout the plant genome using chemicals or radiation in an untargeted way. These are undefined genetic changes from which individual outcomes are selected and subjected to further crossing. Genome editing allows a more targeted approach to facilitate genetic modifications at

predetermined sites in the host genome, with fewer background mutations and more clarity on the genetic changes that have taken place. Both approaches may introduce changes that affect wider metabolic or other biological networks, and lead to unintended effects such as the accumulation of toxic intermediates. However, after further crossing and testing to produce a new variety for trialling, the risks presented by both methods would be similar. It does not mean, however, that the risks would be zero.

In animals, genome editing currently involves microinjection into an embryo with the editing reagents or with edited cells (cloning technology) then genotype screening is usually carried out on the resulting live births. From the microinjection stage, animals are still 5-6 generations away from a farming environment, during which time, any deleterious genotypes should have been identified, especially since TALENs, ZFN and CRISPR can be precise in animals. Full sequencing of the genomes will allow unintended changes to be identified, reducing the chances of unintended effects reaching a farming environment. However, careful monitoring and assessment of safety would still be needed to ensure minimal public risk.

In plants, genome editing may be used to introduce novel combinations of characteristics. This is achieved by making several simultaneous small changes to the host genome. These combinations may not have previously been considered commercially viable, due to the time it would take to produce these individuals through traditional breeding. These novel combinations would need to be assessed on a case by case basis to determine whether they posed a greater risk. Classical plant breeding is slow, which allows any unwanted traits to be identified, and individuals with those traits to be removed from the breeding population over time. Plants within the Solanaceae group provide an example of traditionally bred plants with known toxins or allergens (glycoalkaloids). As genome editing speeds up the breeding process, it may also remove some of the check points. Specific testing of these crops should be carried out on a case-by-case basis, to check for unintended effects in specific genes and pathways leading to such toxins or allergens.

Both genome editing and traditional breeding methods may alter endogenous allergen and toxin levels. However, the risk factor is not necessarily associated with the production method, but rather is linked to the induced change in an organism and the characteristics of the product. Existing checks and procedures are in place to screen for known toxins and allergens and these should be used for genome edited foods as with any other novel food. Genome edited foods, if

removed from the definition of GM organisms, would no longer require the same risk assessment under the GMO regulations. Genome edited foods would need to undergo a pre-market safety assessment on a case by case basis, and this process would need to be defined. Current novel food safety assessments could provide a basis but would require some specific modifications and new guidance to be developed to define fit-for-purpose safety assurance of foods produced by genome editing.

Conclusion

The ACNFP consider that a case by case risk assessment approach could and should be employed for all genome edited foods at least in the early years of the adoption of this transformative technology. This could be based on that currently undertaken for novel foods. However, the exact process will need some modification to adequately assess the safety of genome edited foods.

Response to Section 2, Part 1, Question 3

If simple genome edited products were available, that could in principle have been formed naturally or via traditional breeding, and were to have a different regulatory framework, it may have impacts in the following areas.

Rush to market and need for safety evaluation

There may be a rush to use genome edited techniques by the food and farming industries. This could lead to an increased number of genome edited products that would require safety evaluation as these new transformative technologies emerge for use in the market. It will be important to ensure that there is time and the facilities to assess their safety properly, keeping the public safe and maintaining the high standards of food safety and animal welfare in the UK

Animal welfare

There could be both positive and negative impacts on animal welfare, and these would need to be reviewed and assessed fully. The process of genome editing does not have an impact on animal welfare itself, but it’s consequences may do. There are areas where genome editing technology could be used to improve animal health and welfare, for example in disease reduction. However, as with

traditional breeding, there may be unintended animal welfare or environmental consequences to the introduction of some animal traits. The UK has some of the highest animal welfare standards in the world. These would need to be maintained for genome edited animals. The ethical implications of genome edited animals would also require careful consideration.

Transparency & traceability

There may be issues related to transparency and traceability. For example, some genome edited products will contain genomic changes that cannot be distinguished, even by molecular testing, from products obtained through traditional breeding techniques. Thus, there would be technical challenges to trace genome edited products through the food chain without an audit trail, raising both regulatory and consumer choice issues.

Consumer awareness

It would be beneficial to build consumer confidence by explaining transparently and clearly how genome editing technologies differ from GMO and describe the traditional breeding approaches that are currently accepted by society. Consumers should also be kept informed of when genome editing approaches have been used through use of a transparent audit trail.

Conclusion

There are several non-safety areas where issues may be raised by a change in the regulation of some genome edited products. These include a ‘rush-to-market', animal welfare, transparency and traceability and consumer awareness.

Response to Section 2, Part 1, Question 4

A clear definition of the changes that could be induced through traditional breeding would be needed, before a decision could be made on the criteria that could be used. The scale of genetic changes that could be produced through traditional breeding is quite large and simplifying this to one definition is difficult. For plants and animals, a loss, duplication or recombination of DNA **in the host genome** can be achieved using existing (non-GMO) methods of breeding. Thus, if there is no recombinant DNA randomly integrated (e.g. transgenes from another

species) into the host genome then it could be regulated as non-GMO.

Traditional breeding has occurred for thousands of years and the scale of the changes that may be introduced can be huge. Examples of some of the large-scale genetic changes selected for through traditional breeding include; changes in total chromosome number, or movement of large sections of chromosome. Traditional breeding also includes chromosome translocations from other species; for example, part of a rye chromosome was introduced through traditional breeding into modern wheat to increase disease resistance. Allelic replacements or copies of alleles at a natural locus, may also be made by traditional breeding. These changes could also be introduced by genome editing techniques and should perhaps also be considered as outside of GMO regulation, but would need checking closely, to identify the scale of the changes made. Some more complex genetic technology mediated changes may also need further consideration. For example, genes from a cross-compatible species inserted randomly such as in cisgenic/intragenic approaches but these approaches are outside of the scope of genome editing.

As future genetic technologies develop and expand, it will be increasingly challenging to define regulatory boundaries based on the methods used to produce a new food type. There is a strong argument to move away from technology-based triggers for regulation and to adopt a more holistic approach based on the novelty and risk profile of the final product, regardless of the methods used to develop it.

It could be argued that, if the end product is undistinguishable from something that could be found in nature, but has been produced through editing of the hosts' own genome, then this could be considered outside of the definition of a GMO. The end product must be demonstrated as something that could be produced through nature or traditional breeding, even if this would require a lengthy breeding process, regardless of production method.

Conclusion

The ACNFP consider that a clear definition of "traditional breeding methods" is required before this can be answered fully. Some traditional breeding methods can produce large changes in the genome, albeit over a long timeframe, which could pose concerns for safety or nutritional composition, should these products reach the market. Likewise, some genome editing could generate products with small precise changes that can be controlled more efficiently than with traditional

breeding methods. The Committee considered that current controls on breeding and registration of new cultivars provide a degree of reassurance on the traceability and safety of such products but recommend a move towards **a case-by-case fit-for-purpose safety assessment of the final products** to be consumed, regardless of the method of production.

Yours sincerely,

Dr Camilla Alexander-White

Chair

Advisory Committee on Novel Foods and Processes