AUSTRALIAN ACADEMY OF TECHNOLOGY AND ENGINEERING

AUSTRALIAN ACADEMY OF SCIENCE

JOINT SUBMISSION TO THE FSANZ CONSULATION ON FOOD DERIVED USING NEW BREEDING TECHNIQUES

The Australian Academy of Technology and Engineering and the Australian Academy of Science (collectively, the Academies) welcome the opportunity to provide a submission in response to the Consultation Paper issued by Food Standards Australia New Zealand (FSANZ) on food derived using 'new breeding techniques', which are technological developments arising from new understandings around breeding, genetics, and genetic modification.

In accordance with the legislated procedure under the *Food Standards Australia New Zealand Act 1991*, FSANZ is undertaking a review of the Australia New Zealand Food Standards Code (the Code) to consider its application to the food products of new breeding techniques as there is uncertainty as to whether these techniques are captured by Standard 1.5.2 of the Code – *Food produced using gene technology* – and, if not, whether they should be.

The specific techniques under consideration by FSANZ are genome editing, GM rootstock grafting, cisgenesis and transgenesis, and techniques involving null segregants.

The Academies' submission is guided by the following general principles:

- **The regulatory system for gene technology and new breeding techniques in Australia should be consistent and mutually supportive.** FSANZ's treatment of gene technologies should be remain consistent with that of other government regulatory agencies, particularly the Office of the Gene Technology Regulator (OGTR).
- **Agencies involved in the regulation of gene technology and new breeding techniques should not act as an undue impediment to research, development and commercialisation in these fields.** The regulation should not impose costs or barriers to taking food derived from new technologies to market beyond what is necessary to ensure safety.
- **Regulation of food should be commensurate with the risk presented to human health.** The involvement of gene technology does not necessarily present a greater risk than other technologies currently in use without regulation. Gene technologies and new breeding techniques may warrant scrutiny not because they are inherently dangerous, but because the range of potential applications is very broad.
- **A food which is derived from an organism modified by gene technology but is biochemically indistinguishable from a food derived from an unmodified organism does not present a greater risk than the food derived from an unmodified organism.** The products of GM rootstock grafting, and of null segregants, would fall within this category.
- **Labelling of the products of gene technology assists consumers in making informed choices.**

The Consultation Paper provides a number of questions to direct responses. The Academies have provided responses to these questions below.

3.1.1 Questions

Do you agree, as a general principle, that food derived from organisms containing new pieces of DNA should be captured for pre-market safety assessment and approval?

Should there be any exceptions to this general principle?

Response: In their submission to the review of the Gene Technology Scheme, the Academies indicated support for a risk-tiering approach to facilitate movement of safe technologies to market. The Academies would support exceptions from pre-market safety assessment and approval for technology applications with a long history of safe use. Exemptions should be considered for low risk GM foods, in particular for foods where the modified gene is not expressed in the edible part of the food crop.

3.1.2 Questions

Should food from null segregant organisms be excluded from pre-assessment and approval?

If yes, should that exclusion be conditional on specific criteria and what should those criteria be?

If no, what are your specific safety concerns for food derived from null segregants?

Response: Food from null segregant organisms should be excluded from pre-assessment and approval. Null segregants as described in the Consultation Paper contain no modified genetic material and are biologically and biochemically indistinguishable from unmodified organisms. The idea that null segregants might be "contaminated" by the involvement of gene technologies earlier in their development is not scientifically supportable.

3.1.3 Questions

Are foods from genome edited organisms likely to be the same in terms of risk to foods derived using chemical or radiation mutagenesis? If no, how are they different?

If yes, would this apply to all derived food products or are there likely to be some foods that carry a greater risk and therefore warrant pre-market safety assessment and approval?

Response: Where gene editing is used to alter genomes without introducing any new DNA, such foods are likely to pose the same level of risk as foods derived using chemical or radiation mutagenesis which are exempt from regulation on the basis of their history of safe use.

Chemical- or radiation-induced mutation generates non-specific changes randomly throughout the genome, whereas modern gene editing methods are more precise and generate fewer off-target (unintentional) changes. As this enables targeted changes to be made with greater ease, efficiency and specificity there is no increased risk from genome edited organisms. The Gene Technology Regulator recently proposed exempting such simple gene edits from being considered as gene technology on the basis that they are indistinguishable from both random mutations and changes that can be made with unregulated mutagenic techniques.

3.2 Questions

Are you aware of other techniques not currently addressed by this paper which have the potential to be used in the future for the development of food products?

Should food derived from other techniques, such as DNA methylation, be subject to pre-market safety assessment and approval?

Response: The Academies have identified two techniques which will need to be accommodated within any new regulatory scheme or exempted from regulation, depending on their perceived level of risk. Note that these techniques would not trigger a product-based regulatory scheme based on the introduction of 'foreign' DNA.

- **Disabled Cas9 enzymes (dCas9)**

  Disabled Cas9 enzymes (dCas9) bind to DNA using their specific guide RNAs but do not cut the DNA. This generates potential new uses for the gene editing machinery in both plants and animals beyond the initial application of making double stranded breaks and repairing them with or without a DNA repair template.[1]

  One such application is to fuse the dCas9 with chromatin modification or methyltransferase enzymes to make epigenetic changes to specific parts of a genome. This will lead to generational consequences on gene expression without actually changing DNA sequence per se.

  Another application is the fusion of dCas9 to deaminase enzymes to specifically deaminate cytosines close to the guide RNA binding site, thus converting them to thymines. This effects a C → T base change without cutting the DNA or using a DNA repair template.[2] Other systems allow different edits, such that it is now possible to achieve all four transitions–C → T, A → G, T → C, and G → A–in the genomic DNA of any species.[3]

- **Cas9 ribonucleoproteins**

  There are a number of systems for the delivery of Cas9 ribonucleoproteins (RNPs) into cells, including transient (viral) delivery systems or systems involving in vitro assembly of RNPs and injection into cells.[4] These gene editing systems do not require the initial production of a transgenic cell or organism and do not integrate any novel DNA into the final host. Genome outcomes are similar to existing methods involving transgenics, with a higher specificity due to the rapid turnover of the RNP complex relative to that produced in a transgenic organism. The risks posed are therefore similar or less, and may not need any different regulation.

[1] See Thakore PI, Black JB, Hilton IB, Gersbach CA. Editing the Epigenome: Technologies for Programmable Transcriptional Modulation and Epigenetic Regulation. Nature methods. 2016;13(2):127-137. doi:10.1038/nmeth.3733.

[2] For example, see Zong, Y et al., Precise base editing in rice, wheat and maize with a Cas9-cytidine deaminase fusion. Nat. Biotechnol. 2017, 35:438–440. doi:10.1038/nbt.3811.

[3] See Gaudelli et al., Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. Nature 2017, 551:464–471. doi:10.1038/nature24644.

[4] See Kim, Sojung, et al. Highly efficient RNA-guided genome editing in human cells via delivery of purified Cas9 ribonucleoproteins. Genome research 2014, 24(6):1012-1019. doi:10.1101/gr.171322.113

3.3 Questions

Do you think a process-based definition is appropriate as a trigger for pre-market approval in the case of NBTs? If no, what other approaches could be used?

If yes, how could a process-based approach be applied to NBTs?

Are there any aspects of the current definitions that should be retained or remain applicable?

Response: A process-based trigger for regulation carries the implication that the process itself presents a risk requiring regulatory oversight. While this approach is beneficial in ensuring that the development and application of certain technologies are closely scrutinised it can have a distorting effect on the adoption and commercialisation of such technologies, particularly when the extent of regulatory oversight is not moderated in the light of experience with their safe use. This is unfortunate when the new techniques may provide improvements over earlier or alternative methods and results in limited examination of developments in technologies that are not regulated. Hence there is an argument that a product-based regulatory trigger (which is neutral regarding the method of production) could provide more effective health and safety outcomes. The Academies discussed the pros and cons of process and product triggers in their submission to the review of the National Gene Technology Scheme (referenced in Question 3.1.1).

In the context of the current regulatory structures in Australia, as acknowledged in Question 1, the most meaningful trigger for the regulation of foods modified by gene technology would remain the presence in the parent organism of novel DNA. The trigger should then be tempered by other factors including the history of use of the parent species in human activities (is it domesticated and well-characterised, for example, and is it therefore predictable in its properties?) and experience with consumption of similar products from other sources. These factors would inform assessments of the level of risk.

As noted in the Consultation Paper, the present definition is some twenty years old and is somewhat unclear in scope. The Academies recommend harmonisation of definitions with the Office of the Gene Technology Regulator and other agencies involved in the regulation of gene technology.

3.4 Question

Are there other issues not mentioned in this paper, that FSANZ should also consider, either as part of this Review or any subsequent Proposal to amend the Code?

No response.

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