IHER Inc.
Institute of Health and Environmental Research Inc

Submission to FSANZ

1st Call for submissions – Proposal P1055

Definitions for gene technology and new breeding techniques

December 2021

1 About IHER

The Institute of Health and Environmental Research Inc. (IHER) is a not-for-profit research institute with an interest in genetically modified (GM) organisms, particularly those destined for food.

Dr Carman is a Director of IHER and the author of this submission. She has an Honours Degree in Organic Chemistry, a PhD in Medicine and a Master of Public Health. She has taught at an agricultural college, worked at the CSIRO in food and nutrition and was the Senior Epidemiologist in the Communicable Disease Control Branch of the SA government, investigating outbreaks of disease for the SA government, most of which were outbreaks of food-borne disease. She has training and expertise in agriculture, medicine, chemistry, biochemistry, nutrition, epidemiology and biostatistics.

2 Submission

IHER thanks Food Standards Australia New Zealand (FSANZ) for developing Proposal P1055 (FSANZ, 2021a) and for asking for comments on the proposal. IHER also thanks FSANZ for the opportunity to comment on the Proposal.

IHER also thanks FSANZ's sincere attempts to work through the complexities of the issues involved with NBTs in order to develop a definition of gene technology that tries to capture all current and future techniques, with the aim of providing greater certainty about assessments and approval requirements for NBT foods, and to better regulate NBT foods in a manner that matches the risk they pose.

However, IHER would like to suggest changes to the Proposal.

2.1 Support for other submissions

IHER supports the submission written by Consumers SA on this matter. IHER also supports the submission written by the Centre for Integrated Research in Biosafety (INBI, 2021) on this matter.

In addition to those submissions, IHER would like to make the following comments.

2.2 Principles upon which this submission is made

This submission concentrates on the three objectives in subsection 18(1) of *The Food Standards Australia New Zealand Act 1991 (FSANZ Act)*, being:

1. Protection of public health and safety.
2. The provision of adequate information relating to food to enable consumers to make informed choices.
3. The prevention of misleading or deceptive conduct.

The submission is therefore based on the principle that the food regulatory system should be based on these objectives, and that, while other policy drivers such as the commercial demands of industry should be recognised, they should not be permitted to displace or relegate these objectives.

Therefore, for example, while FSANZ considers that the current definitions may "discourage innovation and investment" and that changing the definitions may allow "new products [to] have clear

and predictable pathways to market" (FSANZ, 2021a), it should be noted that encouraging innovation and investment, and providing a clear and predictable pathway to market are not FSANZ's objectives under the *FSANZ Act*.

Indeed, it is the conclusion of this submission that the current pathway favoured by FSANZ favours innovation, investment, and a clear and predictable pathway to market over the objectives of the *FSANZ Act* and hence pushes the proposed regulation of foods produced using genetic technologies in general, and NBT foods in particular, uncomfortably away from the objectives of the *FSANZ Act*.

2.3 Proposal 1055 and Objective 1 of the *FSANZ Act*

Objective 1 of the FSANZ Act is to protect public health and safety. Most of this submission is based upon considerations relating to this Objective.

2.3.1 Measuring risk

IHER agrees with FSANZ stated desire "to regulate NBT foods in a manner that matches the risk they pose" (FSANZ, 2021a). However IHER disagrees with FSANZ's understanding of "risk" in relation to NBT foods and public health. As those working in public health know, there is a significant difference in quality between a risk that has been decided-upon through theory, belief or assumption, compared to a risk that has been measured or mathematically calculated using experimental data. Public health is littered with examples of exposures that were assumed to have low or nil risk, until studies on animals and humans showed otherwise. These include exposures to lead, tobacco, asbestos and certain pharmaceutical drugs.

It is therefore of concern that much of the risks of NBT foods seem to have been largely determined by FSANZ based on assumption rather than experimental evidence.

The Public Health Association of Australia (PHAA) is recognised as the principal non-government organisation for population health in Australia. It has written numerous submissions to various reviews tasked with considering deregulating these new GM techniques, urging that they be regulated. The PHAA considered that these organisms cannot be considered to be safe for human health, for many reasons, including the following (PHAA, 2017):

- There seems to be uncertainty and debate about how these new techniques actually work.
- These new techniques are in their infancy and are constantly changing as techniques evolve.
- These techniques might unintentionally interfere with the functioning of an organism's genes.
- There is little experimental evidence to be found in the peer-reviewed scientific literature where the risks of these new techniques have actually been measured. Consequently, any decision that is made now that products of these new techniques are safe, must be based on opinion and assumption rather than evidence. Consequently, a decision about deregulation should be deferred until the risks have actually been measured.
- If some of these organisms are later found to be unsafe, then these organisms may cause a huge health and financial burden for Australia.

Safety assessments of organisms made using these new techniques take time and therefore lag behind the development of the techniques themselves. For example, a review of histopathology studies of the gastro-intestinal tracts of rats where the rats were fed GM crops containing one or more of three commonly-used GM genes, found that there were no published histopathology studies for 81% of the 47 approved crop varieties. In addition, of the studies that were done, half were published at least nine years after approval (Zdziarski et al, 2014). As a result of this type of lag, there is currently little

experimental evidence to be found in the peer-reviewed literature where the risks of these new techniques have actually been measured in animals or humans.

The gold standard of determining the risk to the population from a new substance is informed by the processes of the pharmaceutical industry. First, animal studies are conducted to determine benefits and harms. Then the four phases of human clinical trials are conducted, where Phase I looks at harm in a small number of volunteers, Phase II looks at benefits in a small number of volunteers, Phase III studies benefits and harms in a much larger number of people using a double-blind randomised controlled trial, and then the substance is monitored in the community (Phase IV).

For Phase IV to occur, or indeed any epidemiological studies into the effects of NBT foods on public health to occur, it is important to identify those who are exposed and those who are not exposed to a given NBT food. If NBT foods are released into the food supply without labelling, then it is almost impossible to determine who has been exposed and who has not, thereby making it almost impossible to undertake an epidemiological study. Therefore, without labelling, there will be no mechanism to do surveillance for any potential effects on human or animal health and to subsequently withdraw any NBT foods which are found to be potentially dangerous to human or animal health. As the PHAA has noted (PHAA, 2017), “It would be profoundly unwise to, at this stage, through a lack of regulatory oversight, approve a process that would prevent later epidemiological studies into the health of these new organisms”.

Consequently, the process that FSANZ has followed in order to decide that NBTs pose no harm to the population, falls well short of the gold standard. It should be noted that when these new techniques are used in medicine, it is understood that they can result in unexpected and unprecedented genetic modifications. Because of this, these new techniques are heavily regulated for medical applications, and assessed according to the gold standard. Yet when applied to plants, animals and microbes, apparently these techniques are so precise, predictable and safe that they do not need regulation (PHAA, 2017).

To decide now, without these safety assessments, that NBT foods do not need regulation, is to effectively decide that **every** product of such techniques is safe, before an adequate safety assessment is done on **enough** products of the new techniques to determine if **any** product is safe.

There is no consensus that organisms produced by NBTs are safe for public health.

2.3.2 Scalability and risk

IHER supports the statements made by INBI on scalability and risk. In addition, IHER would like to make the following comments.

It would appear that FSANZ may believe that only those with significant laboratories and training would be able to use these new techniques to make an NBT food, thereby restricting their use to large market players. However, as reported in PHAA (2017), kits to make such organisms have been available for years (New Scientist, 2016). For example, in February of 2016, “Amino Labs showed off the Amino One”, a briefcase-sized “table-top lab for the consumer market”, where “beginners will be able to modify bacterial cells to create medicinal chemicals, scents and even foodstuffs such as yogurt, beer and bread.” In addition, “Amino Labs wants people to improvise, hacking together different scents and materials” (New Scientist, 2016). In a second example, Indiegogo hosted a crowd-funding project that promised "Everything you need to make precision genome edits in bacteria at home including Cas9, gRNA and Donor DNA template for an example experiment" for as little as $130. And for $3000, "We will set you up with everything you need to start your own extensive home lab doing molecular biology and genetic engineering. We will guide you through setting it up and we will

also provide you with a CRISPR kit and other kits to get you started!" and that "everyone will be able to use these kits (they contain everything you need, no extra equipment is required), even if you have had zero experience with Biotechnology (there will be extensive written protocols and videos available)".

Examples such as this show how easy it is for people with little training and experience to make these organisms and bring them into the food supply. For example, a brewery could alter yeast, use it to make beer, and not filter-out the yeast before serving, in the same way that Coopers Brewery makes some of their beer. Alternatively, a yoghurt-maker may alter the bacteria it uses to make their yoghurt, with consumers eating the bacteria in the final product. FSANZ's favoured approach would allow such use to occur without a safety assessment on the NBT food.

Another aspect of scalability is that the same technique can be used repeatedly on the same organism. This can result in a final organism that can be very different to the starting organism. Under FSANZ's proposal, the final organism would not require a pre-market safety assessment even if the final changes were of a similar nature and scale to those obtained using previous GM techniques, which **would** have required a pre-market safety assessment. By recommending that such serially-treated organisms do not need a pre-market safety assessment, FSANZ appears to ignore the possibility of such extensive changes and the potential harm that could result from eating such organisms.

2.3.3 Unintended changes and risk

In its document (FSANZ, 2021a), FSANZ states that these new techniques are precise. Such a view may have developed due to the workshops it conducted (for example FSANZ, 2012). However, it should be noted that these occurred almost 10 years ago, and there have been a substantial number of peer-reviewed scientific papers published in scientific journals since, to show that they are not precise. These imprecisions include unintended alterations and deletions at the site of the intended change, and alterations and deletions at sites distant from the site of intended change.

Two glaring and worrying examples of such changes have been given in submissions by Consumers SA and INBI (INBI, 2021). There are many others. Briefly, Consumers SA described research showing chromothripsis in NBT-treated organisms, while INBI (2021) described significant off-target effects in hornless cattle, intended for human consumption. It should be noted that the developers of the cattle had repeatedly made public statements about their cattle having no off-target effects. The cattle had essentially been held-up as a poster-child of the technology, to show how accurate and useful the technology could be. Yet all the time, the DNA of the cattle contained significant unintended changes, including about 4,000 new nucleotides inserted during the application of the new techniques, including antibiotic resistance genes, that were not "found" until an independent assessment was conducted on the cattle (Heinemann et al, 2021).

While it would be easy to undertake a literature search and provide numerous other examples in this submission, it would appear that doing so may be irrelevant to FSANZ. That is, from FSANZ's documents (FSANZ, 2021a; FSANZ, 2021b), it appears that FSANZ may be aware of such examples, and that FSANZ may not consider them to be important when assessing the safety of foods produced using these techniques. This concern is based on statements by FSANZ, such as:

> *"The method used to induce a genetic change; the size of the genetic change; or whether the change was intended or unintended, is irrelevant to food safety."* (FSANZ, 2021a)

> *"For determining risk, the assessment shows the focus should be on the food itself and its characteristics, not the types of genetic change occurring in a food organism or whether the changes were intended or unintended."* (FSANZ, 2021a)

"Substantial genetic changes exist in all organisms used for food" (FSANZ 2021b).

FSANZ further argues (FSANZ, 2021b) that any unintended changes will naturally be picked up by the developers of the new organism, even if FSANZ does not require a developer to look for such changes. FSANZ argues (FSANZ, 2021b) that the developer would naturally screen the resulting organism for any undesirable traits. It is wishful thinking to believe that every developer would spend substantial amounts of money on thoroughly screening every organism made using new breeding techniques for anti-nutrients, allergens, toxic substances and completely novel substances if they are no longer required to do so by FSANZ. Why **would** a developer spend thousands of dollars on such screening if they are not required to, especially a small producer of NBT food?

If these concerns are correct, and FSANZ does truly believe that off-target effects are not relevant to the safety of the food produced, then FSANZ is ignoring the ability of such changes to alter the function of the organism receiving the changes. These changes include possible reductions in the production of nutrients in the food, possible increases the production of anti-nutrients, allergens, and toxic substances, and also the possible production of completely novel substances in the food.

A suitable analogy would be for health authorities to regarded random changes in another micro-organism, the SARS-CoV-2 virus that causes COVID-19 disease, to be irrelevant to the safety profile of the organism, when in fact, we have been anxiously watching the development of new variants, such as delta and omicron, to determine their impact on health. In short, intended and unintended alterations to the genetic material of an organism **do** matter to public health.

2.3.4 Food from null segregants

FSANZ considers that food from null segregants should not be regulated because "the final organism used to produce the food has not itself inherited the genetic modification introduced using gene technology" (FSANZ, 2021a). FSANZ therefore appears to assume that if an attempt to genetically modify an organism has been attempted, but has "failed" because the specific, desired genetic modification has not successfully occurred, then the resulting organism must still be safe to eat. In this regard, there is an assumption that the organism cannot have undergone any other changes during the genetic modification process. That is, there is an assumption that there could not have been any unintended or unexpected consequences in the organism, either at the intended site of the genetic modification or elsewhere in the organism. FSANZ also assumes that any such changes have not been inherited. Because GMOs are not thoroughly checked for unintended or unexpected consequences at the site of insertion or elsewhere (Carman, 2004), it is unsound to conclude that "there is no risk justification for subjecting such foods to pre-market assessment as GM food as the foods will be equivalent in risk to conventional food" (FSANZ, 2021a).

Consequently, null segregants should undergo a through pre-market assessment.

2.3.5 NBT food that is the same as conventional food

FSANZ states: "FSANZ's assessment is that NBT food should not be GM food for Code purposes if the NBT food is equivalent in its characteristics and risk to conventional food." (FSANZ, 2021a). Of these two items (characteristics and risk), FSANZ also states that "When the characteristics of a NBT food are equivalent to those in conventional food with a history of safe use, the NBT food is also equivalent in risk to conventional food." Consequently, of these two items (characteristics and risk), FSANZ appears to be relying almost entirely on the **characteristics** of the organism produced using an NBT, essentially saying that NBT food should be considered to have the same risk as conventional

food if it has the same characteristics as conventional food.

It is therefore important to know how FSANZ defines "characteristics", because this definition acts as the trigger as to whether an NBT food will require a pre-market food safety assessment or not. We were not able to find a clear definition. FSANZ did state that "the same characteristics" means the same "product characteristics" (FSANZ, 2021a), without providing a definition of what was meant by "product characteristics". In another document (FSANZ, 2021b), FSANZ seems to refer to characteristics as the yield of a plant, the flavour of a plant, the growth of a plant or how quickly fruit ripens on a plant.

If this is the case, then FSANZ seems to be suggesting that as long as an organism produced using NBTs is not markedly different in how it grows or yields compared to a conventionally-bred organism, then it has the same "characteristics" as the conventional organism, and it does not need to undergo a pre-market safety assessment. That is, any unintended changes to the genome of the organism do not need to be assessed for safety unless they alter how the organism grows or reproduces. Given the risks to public health from unintended changes to the genome of the NBT organism, it is argued that FSANZ's definition of "characteristics" should include actual measurements of any reduction in nutrients in the food, any increase in the production of anti-nutrients, allergens, or toxic substances, and any possible production of completely novel substances in the food.

In addition, while FSANZ provides a list of criteria to determine if a NBT food could be excluded from a pre-market assessment (FSANZ, 2021a), FSANZ does not seem to say **how** the developer of the NBT food would satisfy those criteria without providing evidence that would amount to a pre-market safety assessment. That is, the only way that FSANZ can reassure itself that those criteria are met for a given NBT food is to require the developer to provide information to show that the criteria are met, which would amount to a type of pre-market safety assessment. Or does FSANZ intend to simply accept a developer's assurances that the NBT food does not require a pre-market safety assessment without checking the basis of those assurances? The example of hornless cattle shows that self-assessments by developers should not be trusted.

It is also important to note that you can change how genes are regulated without changing the base pairs (Heinemann et al, 2013; Heinemann, 2019; Huang et al, 2018). And you can further do that in a way that allows the changes to be inherited. One such method is called methylation. And that method will be deregulated.

2.3.6 GM rootstock grafting

While FSANZ prefers to no longer regulate NBT foods produced as a result of GM rootstock grafting (FSANZ, 2021a), it is noted that in 2012, (FSANZ, 2012) FSANZ stated that food obtained from a GM rootstock plant "may contain novel RNA and/or protein as a result of the genetic modification to the rootstock. Depending on the genetic modification, the food may also have altered composition or other characteristics." The report also stated that: "It was the view of the panel that foods produced using these techniques [including GM rootstock grafting] should be regarded as GM food and undergo premarket safety assessment."

Consequently, the PHAA concluded (PHAA, 2018) that GM rootstock plants should undergo pre-market safety assessment and approval, and as part of that assessment, the composition of the edible part of the plant should also be assessed to determine if it has changed as a result of the GM rootstock.

2.4 Proposal 1055 and Objectives 2 and 3 of the *FSANZ Act*

Objective 2 of the *FSANZ Act* is to provide adequate information relating to food to enable consumers to make informed choices. Objective 3 of the *FSANZ Act* is to prevent misleading or deceptive conduct.

FSANZ's explanatory document (FSANZ, 2021a) does not adequately address how FSANZ's proposed way forward will satisfy these objectives.

Australia's food system depends on consumer confidence in the food supply. FSANZ's preferred pathway forward will mean that NBT foods will enter the food supply without labelling. There is therefore a concern that the lack of labelling will remove choice from consumers who, for whatever reason, choose not to eat NBT foods. There is therefore a concern that FSANZ's preferred way forward may be inconsistent with Objective 2 of the *FSANZ Act*.

It should also be considered that many consumers would consider NBT food to be GM food, and may therefore consider that allowing NBT food to enter the food supply without labelling, to be misleading and deceptive, in contradiction to Objective 3 of the *FSANZ Act*.

2.5 Proposal 1055 and Option 3

IHER welcomes FSANZ's preference for a process-centred definition, but is concerned that FSANZ has then removed techniques from the definition on what appears to be an *ad hoc* basis.

For all of the reasons given in this submission, IHER supports INBI's conclusion and recommendations (INBI 2021), being:

> *We **do** support (Option 3) a "revised and expanded process-based definition for 'gene technology'". We **do not** support the definition that FSANZ prefers.*
>
> *We do **not** support "Product-based pre-market safety assessment exclusions for certain foods" based on exclusion criteria focussed on food characteristics alone. We do not believe that the proposed non-regulatory approaches are a satisfactory way to mitigate risk.*
>
> *We submit that the proposed product-based exclusions are actually process-based exclusions in disguise. FSANZ is proposing to deregulate processes that result in products that have characteristics similar to other products that may have been created using arbitrarily deregulated processes, for example chemical and radiation mutagenesis or heritable double-stranded RNA treatments, and never assessed for risk. The product-based exclusion is therefore likely to lead to risk creep.*
>
> *We support Option 3 with the deletion of the sentences "revise the definition for 'food produced using gene technology' to include specific product-based criteria for excluding certain foods from pre-market safety assessment and approval as GM food. Foods not meeting all relevant exclusion criteria would require an application to FSANZ." Those sentences could be replaced with "Foods produced by NBTs require an application to FSANZ."*
>
> *We advocate a heuristic definition that describes the properties of gene technology. We submit that a new draft definition should be developed for further consultation. The definition should not exclude technology that increases the scale of potential harm with use. The definition should not be limited to nucleic acids. The use of any agent intended to accelerate the overall*

or specific mutation rate and rate of creating new phenotypes should be included. The definition should not be limited to the persistence of the causative agent, nucleic acid or otherwise, in a product for the product to be within scope.

In addition, IHER also calls for:

- A clear definition by FSANZ of the term "characteristics", because this definition acts as FSANZ's trigger to determine if an NBT food will require a pre-market food safety assessment or not. It is argued that the measurement of "characteristics" should include a measurement of key nutrients, anti-nutrients, allergens, and toxic substances in the food, and the measurement of the possible production of completely novel substances in the food.
- Labelling of NBT foods to allow for consumer choice and for post-market epidemiological studies.

References

Carman J (2004). 'Is GM Food Safe to Eat?' in *Recoding Nature Critical Perspectives on Genetic Engineering*, ed. Hindmarsh R & Lawrence G, UNSW Press, Sydney, p. 82-93.

FSANZ (2012). New plant breeding techniques: report of a workshop hosted by Food Standards Australia New Zealand. http://www.foodstandards.gov.au/publications/Pages/New-plant-breeding-techniques-workshop-report.aspx

FSANZ (2018). Consultation paper: Food derived using new breeding techniques. Food Standards Australia New Zealand, February 2018. http://www.foodstandards.gov.au/consumer/gmfood/Pages/Review-of-new-breeding-technologies-.aspx

FSANZ (2021a). Food Standards Australia New Zealand (FSANZ). 1st Call for submissions – Proposal P1055. Definitions for gene technology and new breeding techniques. FSANZ, Canberra, ACT.

FSANZ (2021b). Supporting document 1. Safety assessment: full technical report. P1055 – Definitions for gene technology and new breeding techniques. FSANZ, Canberra, ACT.

INBI (2021). Submission on Proposal P1055 Definitions of Gene Technology. Centre for Integrated Research in Biosafety, School of Biological Sciences, University of Canterbury, Canterbury, New Zealand.

Heinemann JA, Agapito-Tenfen SZ, Carman JA (2013). A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. Environment International, 55: 43-55.

Heinemann J (2019). Should dsRNA treatments applied in outdoor environments be regulated? Environment International https://doi.org/10.1016/j.envint.2019.05.050.

Heinemann JA, Paull DJ, Walker S, Kurenbach B (2021). Differentiated impacts of human interventions on nature: Scaling the conversation on regulation of gene technologies. Elem Sci Anth 2021;9

Huang S, Iandolino AB, Peel GJ, Office, USP (2018). Methods and compositions for introducing nucleic acids into plants. Monsanto Technology LLC, United States.

New Scientist (2016). Make your own life form, New Scientist, 13 February 2016, page 20

PHAA (2017). Public Health Association of Australia submission on the 2017 Review of the National Gene Technology Regulatory Scheme. Public Health Association of Australia, Canberra, ACT.

PHAA (2018). Public Health Association of Australia submission to Food Standards Australia New Zealand on Food Derived using New Breeding Techniques. Public Health Association of Australia, Canberra, ACT.

Zdziarski IM, Edwards JW, Carman JA, Haynes JI (2014). GM crops and the digestive tract: A critical review, Environment International, http://dx.doi/10.1016/j.envint.2014.08.018.