GE Free New Zealand

In Food And Environment Inc.

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3 December 2021.

RE: **Proposal P1055 – Definitions for gene technology and new breeding techniques**

Tēnā koe Food Regulation Modernization team,

GE Free NZ in Food and Environment is a NGO voluntary public organisation, public stakeholder representing a large consumer base. We regularly make submissions to FSANZ and other government bodies. We regularly inform our members about the current research on genetic engineering.

GE Free NZ in Food and Environment would like to comment on your proposal to re define the process-based definition for 'gene technology' to capture all methods for genetic modification other than conventional breeding; and 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.

These definitions are

- **Food produced using gene technology** means a food, which has been derived or developed from an organism, which has been modified by gene technology.
- **Gene technology** means recombinant DNA techniques that alter the heritable genetic material of living cells or organisms.

1. As part of the proposal, FSANZ has considered process and non-process based definitions and the need to ensure that NBT foods are regulated in a manner that is commensurate with the risk they pose.

   We agree with the proposal that the definition should be updated to include genetically engineered NBTs. As NBT's are new and emerging technologies and do not have a history of safe use. Food produced from them have not been subject to any long-term feeding trials and have no safety record to enter the food chain; therefore it is timely to ensure they are fully regulated under the FSANZ Act GMO regulations, standard 1.5.2.

We suggest that the updated definition of gene technology reads -

- **Food produced using gene technology** means a food, which has been derived or developed from an organism, which has been modified by gene technology.
- **Gene technology** means – The scientific manipulation using molecular biology tools, which deletes, replaces, or inserts RNA/DNA molecular sequences (synthetic or natural), altering the heritable genetic material of living cells or organisms.

2. The FSANZ assertion that

> *"NBTs can be used to introduce a range of genetic changes to food organisms. The vast majority of these changes are the same as those that happen naturally or from breeding. This means we can predict what types of NBT food can be produced based on our extensive knowledge of conventional food. It also means it is valid to compare NBT food to conventional food."*

FSANZ is incorrect as until the foods created from NBTs are tested or undergo rigorous ingestion studies there can be no prediction as to their safety. Until carefully designed procedures and comprehensive measuring of the profiles of the all the genome (transcriptomics) proteins (proteomics) or small molecule metabolites (metabolomics) within the cells tissues is conducted, there is no scientific base to make any assertion on whether these engineered changes might have produced new proteins or toxic compounds altering the safety profile. As can be seen in the simplest of GE manipulations, SDN1, there are unexpected mutations. Biswas et al (2020) data detected how imprecise the technology is. He found that not only "on-and off-target insertions or deletions in the mutations but also exogenous elements in T_2 plants and these mutations were passed on stably to T_3 or T_4 generation".[1] Unless these mutations are understood they pose a direct threat to health of consumers. This has been further supported by Kirwall K. (2021)[2] who concluded -

> *"that nearly half of plants with so-called market-oriented traits contain complex genomic alterations induced by SDN-1 applications, which may also pose new types of risks. It further underscores the need for data on both the process and the end-product for a case-by-case risk assessment of plants derived from SDN-1 applications."*

Regarding animals, Kosicki M et al (2018)[3] discovered large deletions and more complex genomic rearrangements at the targeted sites in mouse embryonic stem cells that were not expected. Gene edited hornless bovine had errors overlooked by the developer as the complexity of the down stream procedures were disregarded.

Dr B. Skryabin reported that "conventionally applied PCR analysis—in most cases—failed to identify such multiple integration events, which led to a high rate of falsely claimed precisely edited alleles". This finding is confirmed by the Hornless GE Bovine development. In 2016 the developer and breeder, Recombinetics Inc, reported that none of their primer sets detected the template plasmid integration and that there were no introgression into the

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[1] Biswas S, Tian J, Li R et al (2020) Investigation of CRISPR/Cas9-induced *SD1* rice mutants highlights the importance of molecular characterization in plant molecular breeding. *J Genet Genom* S1673–8527(20):30091–30096. https://doi.org/10.1016/j.jgg.2020.04.004

[2] Kawall, K. (2021) The Generic Risks and the Potential of SDN-1 Applications in Crop Plants. *Plants,10*,2259. https://doi.org/ 10.3390/plants10112259

[3] Kosicki , M., Tomberg, K., Bradley A. (2018) Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements. *Nature Biotechnology,* 36: 765–771

bovine embryo cells from the GE process [4]. The Office of the New Animal Drug evaluation scientists at the FDA, however, on assessing the application in 2019 found the plasmid bacterial template had integrated into the genetic material of the cattle. Amongst other things, they found complete DNA-fragments able to confer resistance to antibiotics in the genomes[5]. This was only picked up because of the diligence of the regulator who used screening techniques for off target complex rearrangements including insertions, deletions, inversions, and translocations that are difficult to detect by standard PCR and DNA sequencing methods. Food safety must at all times have third party assessment through regulation.

3. **FSANZ** proposal process declares that they will ensure there is open communication and active engagements with all interested parties and also explore ways to raise awareness about GM and NBT foods.

   FSANZ is charged with protection of the public food chain not industry pressures to adopt GM or NBTs. It is imperative that FSANZ engagement is balanced and not biased toward the applicant views. The comment by FSANZ must also openly communicate and raise issues of the unexpected outcomes, mutations and "off target" effects that occur with NBTs.

   FSANZ must have an expert body of independent scientists and consumer advocates to fully examine the safety of NBTs, using appropriate "omics" diagnostics, to see if there are any deleterious health effects for the animal or consumer from the GE food.

   It is imperative that the appropriate independent regulatory expertise is put in place to fully assess all processes in producing NBTs (SDN1, SDN2 and SDN3) and that all case-by-case applications are open to public submissions.

   Regulation should at all times be accompanied by long term (minimum 90 days) feeding study on the animals and people that are going to consume the product. The raw data from any NBT ingestion tests that are evaluated on peer reviewed and published science and all raw data open to all scientists and public to comment on.

   Gene-Edited (GE) organisms are prone to unintended and unexpected effects at the molecular level that may pose a threat to human health and the environment if commercialized without comprehensive mandatory safety assessment and oversight.

4. **FSANZ posits** -Because many changes introduced using NBTs will be similar to changes from breeding; some NBT food will be similar or even identical in product characteristics to conventional food. It is also possible that some NBT food will have new or altered characteristics compared to conventional food.

   It is correct that NBT food could have altered characteristics that pose dangers to health. The severing of the DNA helix has been observed to lead to complex chromosomal rearrangements. The repairs result in off target insertions of base pairs can occur causing chromothripsis and deletions of whole chromosomes.[6] This has diverse phenotypic

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[4] Carlson, D., Lancto, C., Zang, B. *et al.* Production of hornless dairy cattle from genome-edited cell lines. *Nat Biotechnol* **34,** 479–481 (2016). https://doi.org/10.1038/nbt.3560

[5] Norris, A.L., Lee, S.S., Greenlees, K.J. *et al.* (2020) Template plasmid integration in germline genome-edited cattle. *Nat Biotechnol* **38,** 163–164 https://doi.org/10.1038/s41587-019-0394-6

[6] Henry I.M., Comai L., Tan E.H. (2018) Detection of Chromothripsis in Plants. In: Pellestor F. (eds) Chromothripsis. Methods in Molecular Biology, vol 1769. Humana Press, New York, NY. https://doi.org/10.1007/978-1-4939-7780-2_8

outcomes, resulting in and transmissible disorders in the germ and the somatic cells with unknown health dangers. The results of on a food cannot be understood until it is subject to trials on its safety.

5. **FSANZ has declared** that if an NBT food is similar or identical in product characteristics to a conventional food, and that conventional food has a history of safe use then it is safe... The vast majority of these changes are the same as those that happen naturally or from breeding.

   This is an extraordinary statement as there is no scientific proof to deduce that a similar or identical characteristic to a conventional food has a history of safe use. There can be, then, no conclusion that the NBT food is as safe as conventional food.

   This is because if a food can be changed identically then why use a NBT to alter the characteristics when nature has done it? The only reason is to patent the trait and this then becomes a novel invention that confers a change to the DNA that makes it different and not similar to nature.

   If a NBT food or product has come from a patented[7] process it must be regulated, as they cannot be created in nature and it therefore will have to have unique characteristics that are not identical or similar to nature. The patenting of animals is prohibited along moral and ethical grounds so no food from a patented animal should be approved.

   All NBT food products in Proposal P1055, developed from a genetically engineered parent plant, including those developed by ODM, SDN1, SDN2 and SDN3 regardless of the levels of backcrossing to remove and obscure the fact that they are genetically engineered must be fully regulated and assessed on a case-by-case basis and open to public consultation.

   The interference of industrial technological breeding cannot be seen as "natural". The products are patented and for this to occur there need to be proof that it cannot happen naturally.

In Summary –

1. If a NBT uses a patented novel inventive molecule to engineer an organism it must be fully regulated.
2. NBT regulation covers all forms of manipulation using *in-vitro* technologies.
3. An independent scientific and consumer committee using carefully designed, appropriate "omics" diagnostics on any "off target" effects must carry out evaluation of NBTs.
4. If a food developed from any NBT process that uses a patented technology it must be fully labelled.
5. Any food developed by NBT resulting in the harming of sentient animals is morally and ethically abhorrent and should be disallowed into the food chain.
6. If a NBT escapes regulation it must be labelled and carry a warning that it is untested.
7. Post monitoring of NBT must be undertaken for five years once the product is commercialised.
8. Before release diagnostic tools for health professionals must be developed to trace the NBT in case of allergic reactions.

[7] https://www.legislation.govt.nz/act/public/2013/0068/latest/DLM1419043.html#DLM1419359

9. If any food using NBT is developed to withstand synthetic pesticide applications then it must be regulated.
10. Independent experts knowledgeable in understanding the unintended mutations due to "off target /on target" effects must evaluate all NBTs to look at exemptions to regulation.
11. Consumers must have clear labelling to be able to exercise their choice in buying.
12. Therefore if created through a genome editing process and can show that there is no damage to the whole DNA chromosomes then it must be labelled as such

We recommend that the updated definition of gene technology is

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Nāku iti noa, nā,

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Cc: Claire Bleakley