FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Consultation paper

Food derived using new breeding techniques

February 2018

How to make a submission

Submissions must be in writing and should be sent electronically where possible.

All submissions must be received by **12 April 2018**. If there is an extension to the due date this will be advised on the Food derived using new breeding techniques[1] web page.

If you have any difficulties lodging your submission online please contact NBTConsultInfoRequest@foodstandards.gov.au

What should my submission include?

Your submission should include:

- the title of the Consultation paper you are commenting on
- your name and contact details including: position, address, telephone number, fax and email address
- for organisations, the level at which the submission was authorised.

Your submission may have greater impact if it:

- comments on the specific issues raised and responds to the questions in the paper
- provides as much supporting evidence as possible.

Your submission should:

- be simple, clear and concise
- be supported by relevant, reputable and current data where possible
- use appropriate and specific case examples
- include a brief summary, especially if the submission is lengthy.

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What happens to my submission?

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Under the Information Publication Scheme, your submission will be published on our website unless you provide appropriate reasons for FSANZ to treat it as confidential. Submissions will be published as soon as possible after the end of the consultation period. Details such as

[1] http://www.foodstandards.gov.au/consumer/gmfood/Pages/Review-of-new-breeding-technologies-.aspx

direct phone numbers, personal email addresses or addresses of private individuals are redacted from documents before publication.

Under our legislation, FSANZ is required to treat information as confidential if it identifies trade secrets relating to food and any other information relating to food, the commercial value of which would be or could reasonably be expected to be destroyed or diminished by disclosure. Confidential commercial information should be clearly identified and separated from your submission. If FSANZ does not agree that the information meets the criteria for confidential information, you will be given an opportunity to withdraw the submission before it is made public.

You may want to keep only parts of your submission confidential. If this is the case, this should also be indicated in your submission.

All relevant issues raised in submissions will be considered by FSANZ. Subsequent reports will address these issues.

Any enquiries about making submissions or the consultation process should be emailed to NBTConsultInfoRequest@foodstandards.gov.au.

Contents

1. Introduction

Food Standards Australia New Zealand (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 (NBTs).

Specifically, the review is to consider the definitions for '*food produced using gene technology*' and '*gene technology*'. The review is being undertaken in accordance with section 113 (s.113) of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act)[2].

The s113 review will not consider issues related to labelling, nor will it directly result in changes to the Code. As soon as practicable after completing the review, FSANZ will decide whether to prepare a proposal to amend the Code. Any subsequent proposal to amend the Code will be done separately and involve additional public consultation.

FSANZ has established an Expert Advisory Group on New Breeding Techniques (EAG NBT) to assist with the review. This group will provide advice on relevant issues, such as the current science, potential food safety issues and stakeholder concerns associated with NBTs.

The purpose of this Consultation Paper is to seek views from a broad range of stakeholders on some of the specific issues and questions raised by the review.

1.1 The issue

Section 1.1.1—10 of the Code provides that a food produced using gene technology cannot be sold or used as an ingredient unless it has been assessed and listed in Schedule 26. Section 1.1.2—2 includes interacting definitions for '*food produced using gene technology*' and '*gene technology*'. The definitions refer to gene technology techniques that result in inserting new pieces of DNA into a genome (see also Appendix 1), producing what is commonly referred to as a genetically modified (GM) organism. The technique most commonly used to introduce new DNA into an organism is called transgenesis[3]. All the approved foods listed in *Schedule 26 – Food produced using gene technology* of the Code have been derived from plants modified by inserting new DNA.

New DNA means a piece of DNA that is new to the host organism in terms of its nucleotide sequence, genome location or orientation of insertion

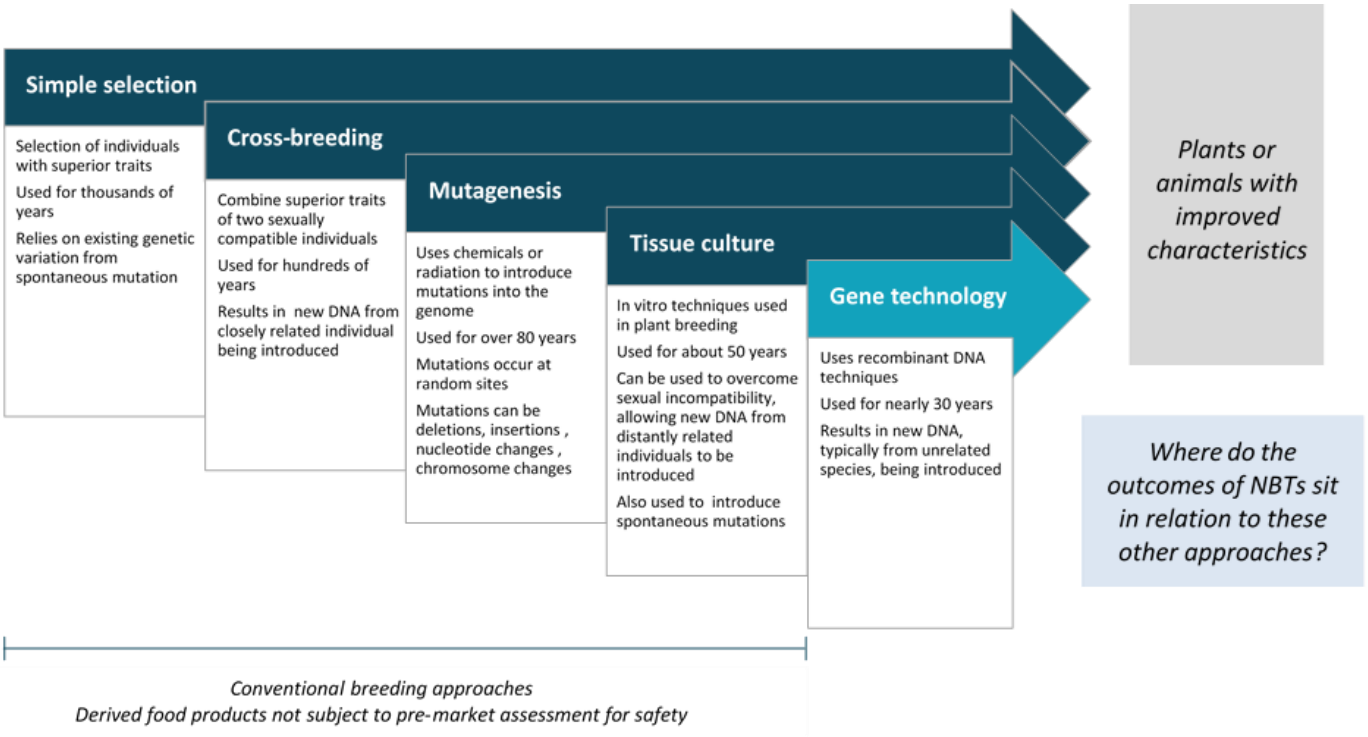
NBTs are a highly diverse set of new technologies being developed and applied in plant and animal breeding, with similar techniques being applied to medical therapies. Some of the products of NBTs are foods. A degree of uncertainty exists about whether foods produced using NBTs are '*food produced using gene technology*' because some of the new techniques can be used to make defined changes to the genome of an organism without permanently introducing any new DNA, although it may be present in the genome initially. The organism from which the food for sale is obtained may therefore contain genome changes but these will not include new DNA.

[2] Available from the Federal Register of Legislation (https://www.legislation.gov.au/Details/C2016C01118)

[3] Transgenesis involves transferring DNA between unrelated organisms, e.g. transferring a gene from a bacterium to a plant.

As a result, some foods produced using NBTs can be similar to foods that have been produced using conventional methods of plant and animal breeding that do not involve gene technology (Figure 1).

Figure 1: Different approaches used in plant and animal breeding



Foods derived using conventional breeding, referred to as 'conventional foods', are generally considered to have a long history of safe use and are not typically subject to pre-market safety assessment before entering the food supply. The Code makes a clear distinction between conventional breeding techniques and techniques involving gene technology described by the current definitions[4].

There has been ongoing scientific and public debate about the nature of the risks associated with foods produced using NBTs and whether pre-market assessment and approval is appropriate for those foods.

The issue being considered for this review is whether (and the extent to which) the food products of NBTs require pre-assessment for safety, before they can be sold as, or used as ingredients in, food.

1.2 Background

FSANZ has been considering the issue of NBTs for some years. The techniques were considered at workshops in 2012 and 2013[5]. These workshops were held to gain more understanding of how the techniques were being used and the types of foods that may result

[4] Under Schedule 26 of the Code, conventional breeding means all methods used to produce plants, excluding techniques that use gene technology.

[5] Reports from both workshops are available from the FSANZ website (http://www.foodstandards.gov.au/consumer/gmfood/Pages/New-plant-breeding-techniques-in-the-spotlight.aspx)

from their use.

The NBTs considered most likely to be used in food production, and which were the subject of discussion at the workshops are:

- **genome editing** – techniques that can be used in both plants and animals to make changes at specific targeted locations in the genome (see Appendix 1 for detailed description)
- **GM rootstock grafting** – involves joining the vegetative (upper) part of a conventional plant to the rootstock of a GM plant
- **cisgenesis and intragenesis** – involves introducing DNA obtained from the same or a cross-compatible species into the genome of an organism
- **techniques producing null segregants** – null segregants are the progeny of GM plants or animals that have not inherited the new DNA (see Appendix 1).

Of these, genome editing, GM rootstock grafting and techniques producing null segregants are the NBTs generating the most uncertainty with respect to the definition for '*food produced using gene technology*'.

1.3 Relationships to other reviews

FSANZ's review is separate to two other reviews currently being undertaken by the Office of the Gene Technology Regulator (OGTR)[6] and for the Legislative and Governance Forum on Gene Technology[7]. Any decisions or actions taken as a result of these reviews, including changes to the Gene Technology Act and its Regulations, will not change the parts of the Code that relate to food produced using gene technology.

2. Gene technology and FSANZ

2.1 Role of FSANZ and the food regulatory system

FSANZ is a statutory authority in the Australian Government Health portfolio, established under the FSANZ Act. FSANZ is responsible for developing food standards for Australia and New Zealand.

Food standards developed and gazetted by FSANZ are compiled as the Code. These standards apply to food produced for sale in, or imported into, Australia and New Zealand.

FSANZ is one part of the food regulatory system. Policy is set by the Australia and New Zealand Ministerial Forum on Food Regulation (the Forum). Australian state and territory and New Zealand government agencies are responsible for implementing, monitoring and

[6] Information about the OGTR's Technical Review of the Gene Technology Regulations is available from the OGTR website (http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/reviewregulations-1).

[7] Information about the Third Review of the National Gene Technology Scheme is available from the Australian Government Department of Health website (https://consultations.health.gov.au/health-systems-policy-division/genetechreview2017/).

enforcing food regulation through their own Food Acts and other food-related legislation. The Australian Government Department of Agriculture and Water Resources is responsible for enforcing food regulation at the border.

2.2 Food produced using gene technology

Food produced using gene technology cannot be sold unless expressly permitted by, and listed in, Schedule 26 of the Code. It is an offence under Australian Commonwealth, state and territory and New Zealand food laws to not comply with the Code.

The key definitions in the Code 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.*

Foods are captured according to the process used to develop them.

These definitions were drafted with the intent of capturing only those foods derived from organisms modified using gene technology, while at the same time excluding foods derived from organisms modified using conventional breeding. Gene technology is limited to recombinant DNA techniques, which are not defined[8] although the practical effect has been the capture of foods derived from organisms which contain new pieces of DNA in their genome derived from any source, including the same species.

Since the adoption in 1999 of pre-market assessment and approval arrangements for food produced using gene technology (under Standard 1.5.2 – Food produced using gene technology), more than seventy foods have been approved and listed in Schedule 26 of the Code. For a variety of reasons, not all of these foods end up in the food supply.

2.3 Pre-market safety assessment and labelling

Food that meets the definition of '*food produced using gene technology'* is assessed by FSANZ under Standard 1.5.2. The safety assessment is done according to procedures outlined in the FSANZ *Application Handbook*[9]. These procedures are consistent with internationally agreed guidelines and principles developed by the Codex Alimentarius Commission for conducting GM food safety assessments[10]. The Commission is the international food standards setting body established by the United Nation's Food and

[8] There is no single definition for recombinant DNA techniques but generally it is taken to mean the recombining or joining of DNA from two or more sources and inserting it into an organism.

[9] Part 2.3 (page 30) and Guideline 3.5.1(page 97) of the March 2016 edition of the Handbook, available from the FSANZ website (http://www.foodstandards.gov.au/code/changes/pages/applicationshandbook.aspx).

[10] Codex (2009) Foods derived from modern biotechnology, second edition. Available from the Food and Agriculture Organization website (http://www.fao.org/3/a-a1554e.pdf)

Agriculture Organization[11] and World Health Organization[12].

Approved foods are also subject to labelling provisions under section 1.5.2—4 of Standard 1.5.2. Subject to certain exceptions[13], GM foods and ingredients (including substances used as food additives and processing aids) must be identified on labels with the words 'genetically modified', if novel DNA or novel protein (as defined in Standard 1.5.2) is present in the food. Some foods may also be required to be labelled with the words 'genetically modified', as well as other additional labelling, regardless of the presence of novel DNA or novel protein in the foods[14]. These foods are considered to have an altered characteristic, such as an altered composition or nutritional profile, when compared to the existing counterpart food that is not produced using gene technology.

If the food for sale is not required to bear a label (for example, the food is displayed in an assisted service display cabinet or is made and packaged on the premises from which it is sold), Standard 1.2.1 requires the labelling information to accompany the food or be displayed in connection with the display of the food.

Foods that do not meet the definition for '*food produced using gene technology*' are not required to undergo pre-market safety assessment and approval or comply with the mandatory labelling requirements in Standard 1.5.2. Such food must still however comply with the general provisions of Australian, state and territory, and New Zealand food laws relating to safe food as well as general labelling provisions. It is the legal responsibility of those who trade in food to ensure it is safe and suitable and complies with relevant labelling requirements.

3. Issues to consider and questions

3.1 NBT outcomes

NBTs are a diverse range of techniques for modifying genomes. To help consider the issues further, FSANZ has grouped the various techniques according to the types of outcomes they produce in the genome of the organism from which the food for sale is obtained (Figure 2). These different outcomes are discussed separately below.

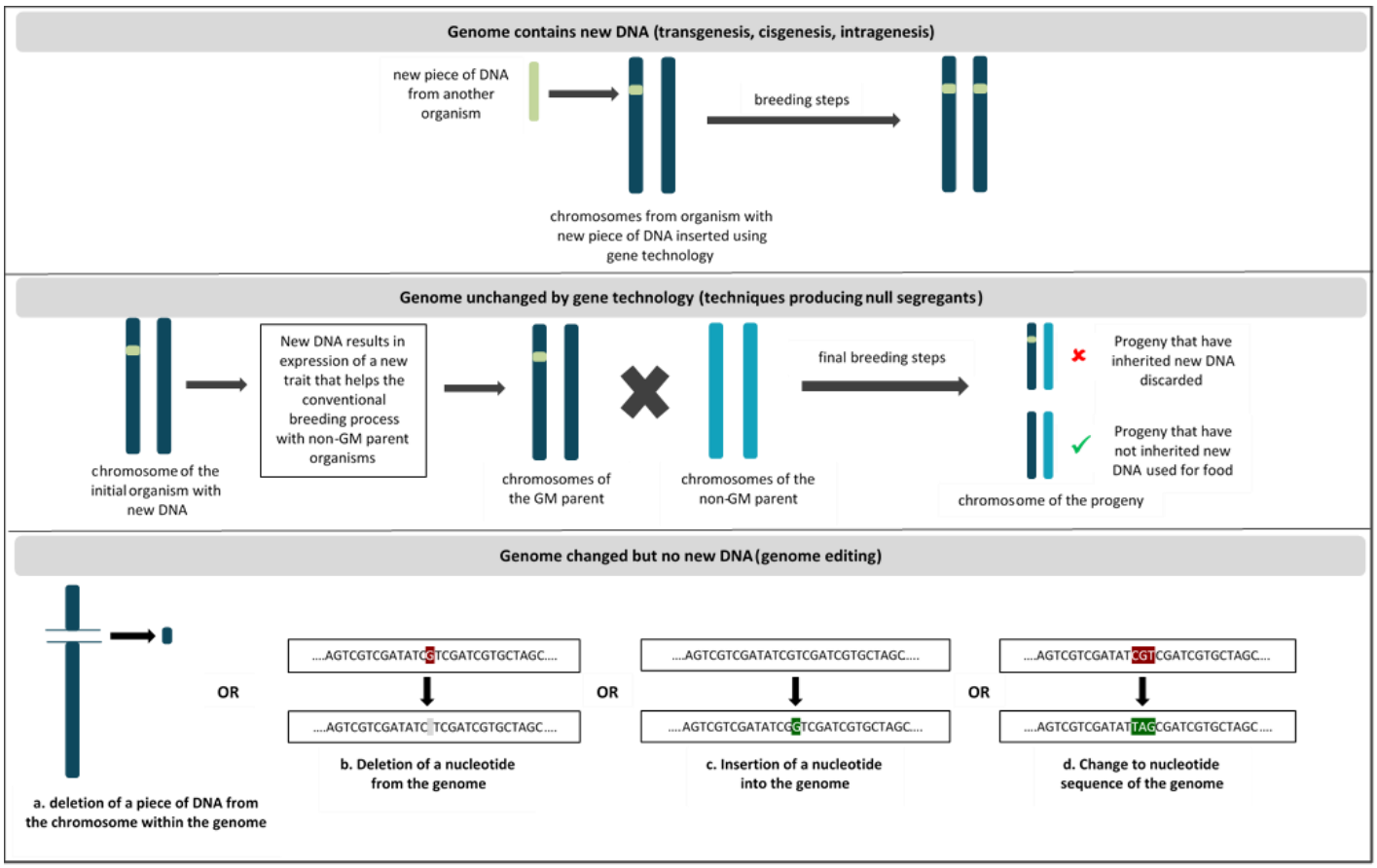
[11] http://www.fao.org/home/en/

[12] http://www.who.int/en/

[13] A number of exemptions from the requirement to label food as 'genetically modified' apply. These exemptions are listed in Standard 1.5.2, which can be accessed from the FSANZ website (http://www.foodstandards.gov.au/code/Pages/default.aspx).

[14] Schedule 26 lists the foods that require labelling as 'genetically modified' or other additional labelling regardless of the presence of novel DNA or novel protein. The Schedule can be accessed from the FSANZ website (http://www.foodstandards.gov.au/code/Pages/default.aspx.

Figure 2: Outcomes of techniques on the genome of the organism from which food is obtained



3.1.1 Genome contains new DNA

NBTs producing this outcome include intragenesis and cisgenesis. Although not a NBT, transgenesis would also belong in this group. The new DNA that is inserted typically gives rise to the expression of a new or modified form of a protein. However, this will not always be the case, for example where an RNA interference approach is being used to silence the expression of a specific gene.

New pieces of DNA are inserted into the genome and remain in the organism from which food for sale is obtained

Capturing food derived from organisms with new DNA inserted would be consistent with the types of approved foods already listed in Schedule 26. While FSANZ has yet to receive an application for a food derived using cisgenesis, applications for foods derived using intragenesis have been received and subsequently approved[15]. From a technical perspective there is no distinction between cisgenesis, intragenesis and transgenesis as all three techniques involve introducing new pieces of DNA into the genome using gene technology[16].

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?

Yes. I believe the introduction of new DNA sequence that could not be achieved through traditional breeding strategies should require pre-market safety assessment and approval.

Should there be any exceptions to this general principle?

GM rootstock grafting has a long history of safety and should be excluded from this category.

One technique that involves inserting new DNA but does not fit neatly into this category is GM rootstock grafting. Grafting is a very old plant propagation technique that involves joining the rootstock of one plant variety to the upper part (scion) of a compatible plant variety, creating a composite plant. Grafting enables plants with superior characteristics to be combined into one plant without the need to undertake complex and often time consuming breeding.

GM rootstock grafting is somewhat unusual compared to the other techniques in this category because the new DNA that is inserted is confined to the rootstock[17]. The scion, from which food, such as fruit would be obtained, will not contain any new DNA. In some cases, the expression of new DNA in the rootstock may be used to alter the characteristics of the scion, including derived food. Changes to the food, should they occur, would not however be heritable/transmitted through the seed as the DNA of the scion would remain unchanged.

The issue to be considered for this technique is whether the absence of new DNA in the upper part of the plant, from which food is obtained, changes the risk, given the potential for

[15] Application A1128 Food derived from potato line E12 and Application A1139 Food derived from potato lines F10, J3, W8, X17 & Y9.

[16] This was the conclusion of the technical workshop hosted by FSANZ in 2012. The report of that workshop is available from the FSANZ website (http://www.foodstandards.gov.au/publications/Pages/New-plant-breeding-techniques-workshop-report.aspx)

[17] Typically the rootstock is transgenic, but cisgenic or intragenic rootstocks could also be used.

the characteristics of the food to be influenced by the expression of new DNA in the rootstock.

3.1.2 Genome unchanged by gene technology

The NBTs in this group are those producing null segregants. The techniques are highly diverse but they all have in common the use of an initial organism into which new DNA has been inserted. The new trait that results is used to facilitate the breeding process or breeding objective but serves no purpose in the final organism from which food will be obtained. Towards the end of the breeding process progeny are selected that have not inherited the new DNA. These progeny are referred to as "null segregants".

New DNA is inserted into an initial organism but is not present in the final organism from which food for sale is obtained

The question for this category is whether there is sufficient justification (based on risk) to require pre-market assessment and approval for food obtained from null segregants. By definition, null segregant organisms would not contain any new DNA from the initial GM organism and also no longer exhibit the GM trait. It has been common practice for a number of years for FSANZ to allow the use of null segregants as non-GM comparators for compositional analysis as part of a GM food safety assessment (FSANZ 2016)[18]. FSANZ also notes the OGTR has stated that, under the Gene Technology Regulations, null segregants are not GMOs[19].

3.1.2 Questions

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

Yes. I believe food from null segregant organisms should be excluded from pre-assessment and approval.

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

Multilayer screening strategies must be in place that ensure GM variants do not reach consumers. This is vital for maintaining public and political trust in GM and NB technologies.

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

[18] Page 32 of FSANZ *Application Handbook*.

[19] Page 18 of the *Discussion Paper: Options for regulating new technologies*, released by the OGTR in October 2016 as part of the Technical Review of the Gene Technology Regulations 2001. The discussion paper is available from the OGTR website (http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/reviewdiscussionpaper-htm) .

3.1.3 Genome changed but no new DNA

The NBTs producing this outcome are the genome editing techniques. In some cases, introducing the edit can involve the insertion of new DNA coding for a protein that facilitates the editing process. If this is the case, progeny will be selected that do not contain the new DNA once the edit has been made. Some genome edited organisms may therefore also be null segregants.

Changes are made to the existing genome but no new DNA is present in the organism from which food for sale is obtained

The issue to be considered for this category is the nature of the genome changes that may be introduced (both targeted and off-target) and the extent to which they may be similar to changes introduced using conventional techniques such as chemical or radiation mutagenesis (which introduce similar changes to genome editing except at random sites in the genome), or that occur spontaneously in nature (and are representative of natural variation).

This is a relatively complex category because the techniques can be used to introduce a variety of genome changes of different complexity and scale. The changes introduced include deletions of pieces of DNA, insertion and/or deletion of one or a few nucleotides (indels) or re-writing the existing DNA sequence (typically involving only a small number of nucleotides although could be more extensive). DNA deletions as well as indels are typically associated with the loss of function or "knock-out" of a gene or genes, whereas a change to the DNA sequence would typically be done to modify the function or characteristics of an existing protein.

Genome editing may be used to produce organisms with novel traits (e.g. herbicide tolerant plants, hornless dairy cows) but this may not necessarily result in food with novel or altered characteristics. Also, the size of the genome change (e.g. a large deletion versus a single nucleotide change) is not a predictor of whether there is likely to be any impact on the food.

In addition to targeted changes, some degree of off-targeting may be associated with genome editing which means genome changes may also be introduced at other than the intended site. The likelihood of an off-target change occurring at a given site in the genome can be predicted to some extent because generally off-target sites are similar in sequence to the intended target site. A number of strategies have been developed to reduce or, in some cases, prevent the occurrence of off-target changes, and several approaches are also available for the detection of off-target changes[20].

[20] For a review, see Zischewski et al (2017) Detection of on-target and off-target mutations generated by CRISPR/Cas9 and other sequence-specific nucleases. *Biotechnology Advances* **35**: 95-104. (https://www.sciencedirect.com/science/article/pii/S0734975016301586?via%3Dihub)

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?

No. Foods from site-specific gene editing technologies are likely to be of less risks than those from chemical or radiation mutagenesis. Previous mutagenesis techniques act in a random manner, whilst gene editing technologies (e.g. ZFNs, TALENs and CRISPR) can make precise edits to the genome, giving scientist much greater control over the outcome.

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?

3.2 Other techniques

In undertaking this review the focus has been on those techniques considered most likely to be used in food production and which were the subject of technical workshops hosted by FSANZ in 2012 and 2013 (see Section 1.2).

It will be important however to also have regard to other types of techniques which may not currently have food applications but could do so in the future as the technology develops.

An example would be DNA methylation techniques which may be used to alter the methylation status of the genome without changing the DNA sequence itself. Changes to the methylation pattern of a genome can change the characteristics of an organism (and potentially derived food products) by altering how genes are expressed. In some cases these methylation changes can be inherited by the next generation.

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?

No.

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

At present, I think DNA methylation should be subject to pre-market safety assessment and approval. More research needs to be undertaken on this front.

3.3 Regulatory trigger

The current process-based definitions for '*food produced using gene technology*' and '*gene technology*' were developed nearly 20 years ago. They were a simple way of making a clear distinction between foods from organisms with new pieces of DNA inserted and conventionally derived foods. At the time, DNA insertions were generally expected to be a complete gene or genes sourced from an unrelated organism. Derived food was therefore thought to be a potentially greater source of risk in contrast to conventional foods.

As a mechanism for capturing foods with new DNA inserted, the process-based approach has generally worked well, in that it achieved its intended purpose. However, the issue to be considered in relation to NBTs is whether the use of a process-based trigger for pre-market approval is an approach that remains fit for purpose given the rapid pace of technological change and also whether such an approach is likely to deliver appropriate risk-based outcomes in terms of what foods are captured for pre-market safety assessment.

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?

No. For NBT we require a product-based trigger for pre-market approval.

My main apprehension with NBT is the number of unique loci targeted in an individual organism. With current gene editing technologies, increasing the number of unique loci targeted, increases the likelihood of off-target effects and the potential for chromosomal rearrangements.

I believe gene edits performed at more than one locus (1000 bp region) in any individual organism should require pre-market approval. The obvious way around this would be to crossbred two edited lines or perform multiple rounds of editing in the same line – both acceptable approaches as it reduces the likelihood of chromosomal rearrangements.

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?

Finally, I would like to praise FSANZ for their work on this front as the current regulatory framework is stagnating public research and private investments.

3.4 Other relevant issues

This paper is focussed on the Code and whether foods produced using NBTs should be the subject of a pre-market safety assessment before being permitted for sale.

Should FSANZ proceed with a proposal to change the Code, there are a number of other issues that FSANZ would need to consider including maintaining confidence in the food supply, ensuring regulation is proportionate to the risk and provides a net benefit, and the enforceability of the proposed changes. The FSANZ Act also includes specific criteria that FSANZ **must** have regard to when assessing proposed amendments to the Code (see Appendix 2).

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?

Appendix 1

New DNA

For the purposes of this paper, 'new DNA' means a fragment of DNA that is introduced to a host organism, irrespective of its source. That is, the DNA may be derived from an unrelated organism, the same species, or the host organism itself.

Examples where DNA may be considered new include:

- the DNA sequence was not previously present in the host organism;
- the DNA sequence is present in the host organism but has been reintroduced at a different location in the genome;
- the DNA sequence is present in the host organism but has been rearranged or introduced into the host organism in a different orientation.

Genome editing[21,22]

Genome editing refers to a set of techniques which can be used to introduce targeted changes into the genome. Currently the predominant approach involves the use of site-directed nuclease techniques. Other methods such as oligo-directed mutagenesis and the more recently developed base-editing are also being used. These approaches can be used in both animal and plant cells.

Site-directed nuclease (SDN) techniques

Engineered SDNs are used to cut both strands of the DNA at a precise location in the genome, introducing what is called a double-stranded DNA break. The cell's own enzyme machinery can repair the break in the DNA using one of two mechanisms – non-homologous end joining (NHEJ) or homology directed repair (HDR). It's during the repair process that changes to the DNA sequence at the break site can occur.

In the case of NHEJ-based repair, the cell's enzymes repair the DNA break by directly joining the two ends back together. Usually the repair is faithful to the original DNA sequence but occasionally errors may be introduced, typically small deletions or small insertions (called indels). When these small errors occur the DNA sequence change is entirely random. Deletions of pieces of DNA are made by introducing two DNA breaks, rather than one. The piece of DNA between the two breaks is lost.

HDR involves the use of a DNA template which has a DNA sequence that complements the DNA sequence at the break site. The template can be one that already exists within the cell (a homologous chromosome or a sister chromatid) or it can be supplied externally. Externally

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[21] Songstad, D.D., Petolino, J.F., Voytas, D.F., Reichert, N.A. (2017) Genome editing of plants. *Critical Reviews in Plant Sciences* **36**: 1-23 https://doi.org/10.1080/07352689.2017.1281663

[22] http://www.sciencemag.org/news/2017/10/novel-crispr-derived-base-editors-surgically-alter-dna-or-rna-offering-new-ways-fix

supplied templates can be designed to introduce precise modifications to the DNA sequence during the repair process. These modifications can range from single nucleotide changes, indels up to the insertion of new pieces of DNA such as whole genes. The use of SDNs to introduce new genes is a form of transgenesis, the only difference is that the DNA is inserted at a precise location, rather than randomly.

Oligo-directed mutagenesis (ODM)

ODM does not require a DNA break at the target site but is DNA template based. Short pieces of DNA (called oligonucleotides) are made that complement the DNA sequence of the target site, except for one or a few differences. Once the oligonucleotide binds to the target site the small mismatch in DNA sequence will trigger the cell's repair mechanism. The cell uses the oligonucleotide as a template to guide the repair, resulting in the DNA sequence at the target site being changed to match that of the oligonucleotide. The oligonucleotides are synthesised to contain chemically modified nucleotides to prevent them being incorporated into the host genome. The oligonucleotide is eventually degraded by the cell.

Base editing

Base editing is a relatively new form of genome editing that involves the chemical modification of nucleotides at a specific target site in the genome. This chemical modification results in their conversion to a different nucleotide, thus changing the DNA sequence. This can be achieved without introducing a DNA break or relying on an externally provided DNA template. These types of nucleotide changes are called transitions. It's possible to chemically convert all four nucleotides (A, C, T, G) that make up the genetic code – A to G, C to T, T to C and G to A.

Examples of techniques producing null segregants

Accelerated breeding following induction of early flowering[23]

This aim of this technique is to shorten the time it takes for a plant to flower. Some tree species can have long flowering times (10 years or more) which means the breeding process can be both time consuming and costly. Shortening flowering time is therefore a very important breeding objective for some species.

While early flowering can be induced using conventional approaches, more significant reductions in flowering time have been achieved using transgenic approaches. The transgenic approach involves over-expressing genes involved in the flowering pathway. These transgenic lines (with a shortened flowering time) can then be used to accelerate subsequent conventional breeding steps, e.g. to introduce a disease resistance gene from a related variety using traditional cross-breeding. In the final stages of breeding, null segregant lines are selected that have not inherited the early flowering transgene. These lines (now having a normal flowering time) would then be used to obtain the final commercial lines.

[23] Flachowsky, H., Hanke, M.-V., Piel, A., Strauss, S.H., Fladung, M. (2009) A review of transgenic approaches to accelerate breeding of woody plants. *Plant Breeding* **128**: 217-226 http://onlinelibrary.wiley.com/doi/10.1111/j.1439-0523.2008.01591.x/pdf

Sex selection in layer chickens[24]

Male hatchlings of layer chickens have no economic value – they can't lay eggs, and are not considered suitable for meat production – and are culled after hatching.

Current research is looking for a way to detect and remove eggs with male embryos prior to hatching. Recent advancements could allow marking of the male chromosome by inserting a gene coding for green fluorescent protein. Developing male embryos will fluoresce when the egg is exposed to UV light enabling them to be identified and removed well before hatching. Female embryos do not inherit the marked chromosome and are thus considered null segregants – their genome does not contain any new DNA. Null segregant female chicks would be used for egg production.

[24] Doran T. (2016) Sex selection in layer chickens. Animal Production Conference, Adelaide. http://www.asap.asn.au/wp-content/uploads/abstract-2015/332/attach_brief.pdf

Appendix 2

Statutory criteria for assessment of proposed amendments to the Code

Is each amendment required in order to:

(a) protect public health and safety;

(b) enable consumers to make informed choices by providing them with adequate information relating to food; and/or

(c) prevent misleading or deceptive conduct?

Would the costs that arise from the amendments outweigh the direct and indirect benefits to the community, Government or industry?

Are there other measures (available to FSANZ or not) that would be more cost-effective than the amendments? If so, what are they and how and why are they more cost effective?

Are there any relevant New Zealand standards? How are they affected by the amendments? How would they relate to the amendments?

Is each amendments based on or justified by a risk analysis that used the best available scientific evidence?

Will the amendments promote consistency between domestic and international food standards? If so, how?

Will the amendments contribute to an efficient and internationally competitive food industry? If so, how?

Will the amendments promote fair trading in food (i.e. in the consumer protection sense)? If so, how?

Is each amendment consistent with any relevant policy guidelines formulated by the Forum on Food Regulation?

Are there any other relevant matters that need to be considered?