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

Final report

Review of food derived using new breeding techniques

December 2019

Contents

Foreword

Since the food regulations for genetically modified (GM) food were established by FSANZ 20 years ago, there has been a steady emergence of new techniques for genetic modification. Given the continued emergence of such techniques is inevitable, it is important our regulatory systems are agile and able to support innovation, while at the same time continue to protect public health and safety now and into the future.

In June 2017, FSANZ commenced a review to consider the definitions for GM food and whether these are fit for purpose since the emergence of a range of new techniques for genetic modification – so called new breeding techniques or NBTs.

While this final report signals the conclusion of that review, it does not conclude FSANZ's work on this matter. FSANZ will shortly announce the commencement of a new process to consider how the definitions for GM foods should be amended.

The final report should be read in conjunction with the following documents:

- *Consultation paper: Food derived using new breeding techniques* (February, 2018)[1]
- *Preliminary report: Review of food derived using new breeding techniques – consultation outcomes* (August, 2018)[2]

Acknowledgements

FSANZ wishes to acknowledge and thank all those who contributed to this review. This includes:

- *Expert Advisory Group on New Breeding Techniques* whose advice and constructive feedback helped inform the development of the consultation paper;
- *Submitters* who contributed their valuable time to preparing submissions in response to the consultation paper; and
- *Reviewers* who provided helpful suggestions on the various review documents.

[1] Consultation paper: Food derived using new breeding techniques

[2] Preliminary report: Review of food derived using new breeding techniques – consultation outcomes

Glossary

Term	Description
Cell and tissue culture	A technique where plant or animal cells are grown in the laboratory.
Cisgenesis	Transferring genes between organisms of the same or a cross-compatible species.
Conventional breeding	A traditional method of developing new traits in plants or animals not involving gene technology.
Cross-breeding	The mating or cross hybridisation of different breeds or varieties within the same species.
DNA	DNA, or deoxyribonucleic acid, is the hereditary material for most living organisms. DNA is present in cells as two strands (double stranded) composed of a series of nucleotides.
Double-stranded break	When both strands of the double-stranded DNA molecule are severed.
Gene technology	A method that alters the DNA of living cells or organisms using recombinant DNA techniques. May also be called GM techniques.
Genetic modification	The process of altering the DNA of an organism.
Genetically modified organism (GMO)	An organism whose genome has been modified using gene technology.
Genome	The complete set of genetic material in a living cell or organism.
Genome editing	A technique which can be used to make specific changes at targeted locations in the genome of an organism.
GM food	Food derived from organisms that have been modified using gene technology.
Indel	An **in**sertion or **del**etion of nucleotides into or from the genome of an organism.
Intragenesis	Transferring a new combination of DNA into a related organism.
Mutagenesis	A way to induce changes to DNA.
New breeding techniques (NBTs)	A wide range of new techniques used to modify the genomes of plants, animals and microorganisms.
Nucleotide	The basic structural unit of DNA. For all living organisms, there are four types of nucleotides in DNA: adenine (A); guanine (G); cytosine (C) and thymine (T).
Null segregant	Progeny that have not inherited an introduced gene.
Point mutation	A change to a single nucleotide in DNA.
Recombinant DNA techniques	Recombining or joining DNA from two different sources.
GM rootstock grafting	Joining the vegetative (upper) part of a compatible plant variety to the rootstock of a GM plant.
Scion	The vegetative upper part of a plant that is joined to a rootstock.
Trait	A distinguishable characteristic belonging to an organism.
Transgenesis	Transferring DNA from unrelated organisms.

Executive summary

The *Australia New Zealand Food Standards Code* (the Code) contains definitions that determine what foods are food produced using gene technology and therefore subject to pre-market safety assessment and approval.

Over the last decade, a variety of new breeding techniques (NBTs) have emerged that are increasingly being applied to the production of food. The emergence of these techniques has generated uncertainty about the regulatory status of derived food products, specifically whether such foods would be considered food produced using gene technology and therefore require an application to FSANZ for pre-market approval.

In June 2017, FSANZ commenced a review of the Code to consider how it should apply to food derived using NBTs (NBT foods). The key questions the review was seeking to answer were:

- whether the definitions for '*food produced using gene technology*' and '*gene technology*' remain fit for purpose given the emergence of NBTs

- whether a pre-market safety assessment of NBT foods is justified based on risk.

A public consultation undertaken in February – April 2018 showed there are diverse and sometimes strongly polarised views about NBT foods. Following consideration of the submissions FSANZ identified seven key outcomes from the consultation.

While many submitters believe the definitions in the Code should be revised to improve clarity, views are divided on the type of definitional trigger that should be used and whether some foods could be excluded from pre-market scrutiny. A number of submitters expressed concern about the safety of NBT foods, and GM foods in general, as well as a strong preference for all NBT foods to be labelled as GM foods. A number of submitters were also in favour in greater alignment of definitions both domestically (i.e. those used in Australia for genetically modified organisms) as well as internationally. These outcomes and a summary of the submissions received were published in a preliminary report in August 2018.

Since the preliminary report was released, FSANZ has given further consideration to the two key questions above, taking into account the diverse views provided in submissions as well as the scientific evidence. FSANZ also undertook additional targeted consultation with key stakeholders in the government, public health, research and industry sectors.

In relation to the definitions themselves, FSANZ has found some of the wording to be ambiguous in the context of NBTs and it is this ambiguity that is responsible for the current uncertainty. Also, because the current definitions focus on a single technology and do not reflect the diversity of techniques now in use, they are now considered to be outdated.

FSANZ has also made a preliminary analysis of whether pre-market approval of NBT foods is justified based on risk. In considering this question, FSANZ has noted that NBTs may be used to produce a variety of different outcomes in terms of the food and that in some cases these outcomes may be similar if not identical to outcomes achieved using conventional breeding methods. There may therefore be a case for excluding some NBT foods from pre-market safety assessment if they are equivalent in terms of their characteristics to conventional food. The case for exclusion is strongest in relation to food derived from null segregant organisms but the equivalence argument may also be made for some foods derived through genome editing, GM rootstock grafting and cisgenesis.

FSANZ notes however that submitters were divided on whether or not foods should be excluded from pre-market scrutiny, with many expressing concern about the possibility that NBT foods could enter the food supply without any oversight by FSANZ. What constitutes an appropriate level of oversight is a question that will need to be further considered by FSANZ.

The key review findings are:

1. the definitions in the Code for '*food produced using gene technology*' and '*gene technology*' are no longer fit for purpose – they lack clarity, are outdated and do not reflect the diversity of techniques now in use

2. there may be a case, based on risk, for some NBT foods to be excluded from the requirement for pre-market safety assessment

3. divergent views exist among submitters about the acceptability and risk of NBT foods and how best to regulate them.

To determine the most appropriate way forward, and having regard to the prevailing uncertainty about the regulatory status of NBT foods under the Code and the need to future proof against further technology development, FSANZ considered three available options – maintain the *status quo* (do nothing), consider non-regulatory approaches, or amend the definitions in the Code.

This report concludes that the only viable option to effectively address the current regulatory uncertainty, as well as future proof the Code, is to amend the definitions. Maintaining the *status quo* by not addressing the problem will only further exacerbate the regulatory uncertainty. Non-regulatory approaches, such as providing guidance on how to interpret the current definitions in the Code, are also not considered a viable option as they do not provide legal certainty and would not address new and emerging genetic technologies.

In terms of amending the current definitions, submitters were divided about whether to retain a process-based definition or adopt an outcomes-based approach that includes the use of more product-based definitions. FSANZ notes there are advantages and disadvantages to both approaches that will need to be further considered.

The primary objective in amending the definitions however should be to improve clarity, which could be achieved with either approach. Another important objective will be to ensure foods are regulated in a way that is commensurate with the risks they pose.

On this latter point, FSANZ acknowledges there are different views among stakeholders about the risks posed by NBT foods and therefore what level of regulation would be regarded as "commensurate with risk". In moving forward it will be important for FSANZ to engage in as wide a discussion as possible with stakeholders and the broader community to ensure any potential regulatory changes take into account the diverse range of views that exist. An important component of this will be to explore ways to raise awareness in the community about GM and NBT foods.

Recommendations

Recommendation 1: FSANZ prepare a proposal to revise and modernise the definitions in the Code to make them clearer and better able to accommodate existing and emerging genetic technologies.

Recommendation 2: As part of the proposal, FSANZ give consideration to 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.

Recommendation 3: Throughout the proposal process FSANZ will ensure there is open communication and active engagement with all interested parties and also explore ways to raise awareness about GM and NBT foods.

Next Steps

In line with Recommendation 1, FSANZ will prepare a proposal to amend the definitions in the Code for '*food produced using gene technology*' and '*gene technology*'. This work will commence as soon as practicable in 2020. FSANZ will continue to engage with stakeholders in the lead up to and throughout the proposal process and will communicate any relevant updates through the FSANZ webpage[3].

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

1. Introduction

The review was initiated to consider how the Code applies to food products derived using NBTs (NBT foods).

Definitions for '*food produced using gene technology*' and '*gene technology*' were considered and the review examined whether:

- the current definitions remain fit for purpose given the emergence of NBTs
- a pre-market safety assessment of NBT foods is justified based on risk.

The review did not consider issues related to labelling, i.e., it did not consider the current approach to GM food labelling, or the specific requirements in the Code that relate to GM food labelling.

The outcomes of this review have not changed any aspect of the Code that relate to food produced using gene technology, including mandatory labelling requirements.

The purpose of the review was to investigate whether there is a case for FSANZ to prepare a proposal to amend the Code. Any subsequent proposal to amend the Code will be conducted as a separate process according to requirements set out in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act) and will include further rounds of public consultation.

2. Review findings and recommendations

During the consultation FSANZ asked a number of questions (see Appendix 1) that relate to the following broad themes:

- the current definitions and whether they remain fit for purpose
- the safety of NBT foods and the need for pre-market safety assessment
- the definitional trigger that should be used for NBT foods.

Other themes also emerged through the consultation process, such as GM food labelling and international harmonisation. The submissions also showed there are many different views and perspectives that exist among stakeholders in relation to NBT foods and GM foods in general.

FSANZ's findings in relation to the above and subsequent recommendations are discussed below.

2.1 Current definitions

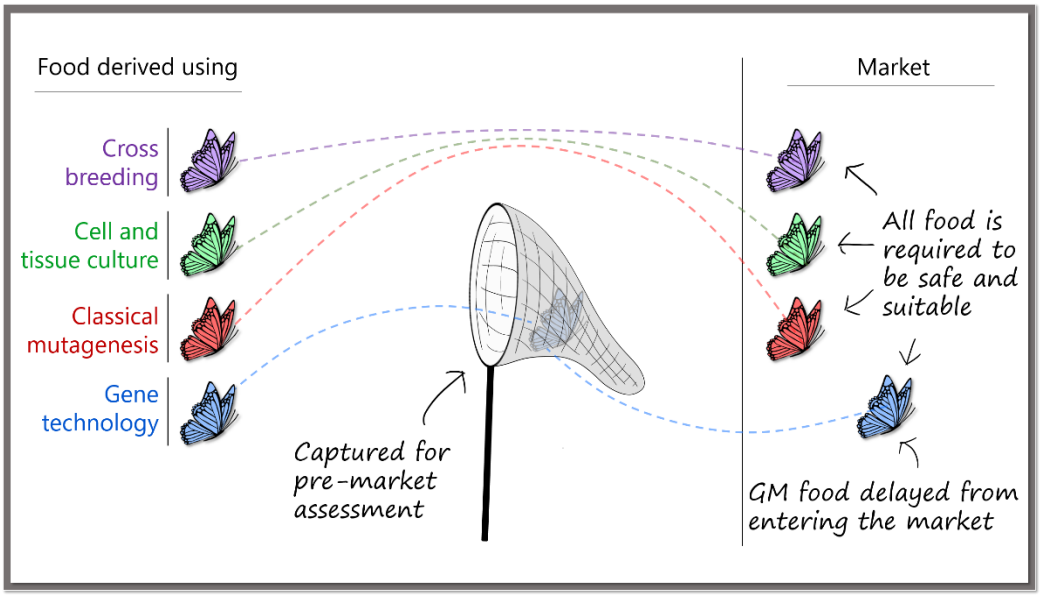
The need for clear definitions was the issue that generated the most agreement among submitters. Not all submitters agreed however that the definitions need to be changed. Some submitters consider an overly narrow interpretation of the current definitions has been applied and that NBT foods are clearly captured.

2.1.1 History and purpose of the definitions

The current definitions in the Code were put in place 20 years ago. They were intended to capture the types of GM food products that existed at the time. That is, food from transgenic organisms which had been developed using recombinant DNA techniques. The definitions were also intended to clearly exclude food derived using conventional breeding methods, such as traditional cross-breeding, cell and tissue culture techniques and classical mutagenesis. The definitions therefore created a clear dichotomy between GM foods and food derived through conventional breeding methods (Figure 1).

Since the transgenesis technique typically involves randomly inserting foreign DNA from unrelated organisms, it is easily distinguished from other types of genome modifications achieved using conventional breeding methods. Derived foods were perceived at the time to be a potentially greater source of risk compared to conventional foods, primarily because of concern about unintended effects arising from the random insertion of foreign DNA, as well as the potential for transfer of harmful characteristics, e.g. an allergen. For this reason it was considered appropriate to single out these types of foods for additional regulatory oversight in the form of pre-market assessment and approval, noting that under food law all food is required to be safe and suitable.

Figure 1: Effect of the current definitions in the code



2.1.2 Clarity and applicability of current definitions

The main reason for commencing the review was because of the uncertain regulatory status of NBT foods under Standard 1.5.2 – Food produced using gene technology of the Code. Food that comes within the scope of Standard 1.5.2 is required to undergo pre-market assessment and approval before it may be sold. To be subject to such requirements a food must meet the definitions for '*food produced using gene technology'* and '*gene technology*':

> *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.

FSANZ has considered the wording of these definitions and has identified two aspects that are a source of uncertainty in relation to NBTs. The first is the ambiguous nature of the wording "derived or developed from" in the definition of '*food produced using gene technology*', and the second is the absence of a definition for the term "recombinant DNA techniques" in the definition for '*gene technology*'.

The ambiguity surrounding the meaning of "derived or developed from" is relevant to foods derived from genome editing, grafting and null segregant organisms (see Appendix 2). For example, it is unclear how "derived or developed' from should be interpreted in the case of a null segregant that has not itself inherited a genetic modification introduced using gene technology but is nonetheless descended from an organism that has been modified using gene technology.

The above wording could be interpreted as either including or excluding food derived from null segregant organisms but a broader interpretation, which would be consistent with the views of some submitters, is that food derived from null segregants is currently captured by the definition for '*food produced using gene technology*'.

The absence of a legal definition for “recombinant DNA techniques” makes it unclear whether certain NBTs are considered to be ‘*gene technology*’. A common scientific understanding of the term however is that it refers to the recombining or joining of DNA from two different sources. In practice, “recombinant DNA techniques” in the definition for ‘*gene technology*’ has resulted in foods derived primarily from transgenic organisms being captured for pre-market assessment and approval. The applicability of the term “recombinant DNA techniques” to some of the genetic modifications introduced using genome editing is unclear, particularly as there is no recombinant DNA that remains in the final food producing organism.

Finding 1: The definitions in the Code for ‘*food produced using gene technology*’ and ‘*gene technology*’ are no longer fit for purpose – they lack clarity, are outdated and do not reflect the diversity of techniques now in use.

2.1.3 Addressing the problem

Having determined that the current definitions are no longer fit for purpose, FSANZ considered different approaches that could be used to address the problem including whether there were any non-regulatory options that could be effective instead of amending the Code, as well as the potential impacts of doing nothing, i.e., maintaining the *status quo*.

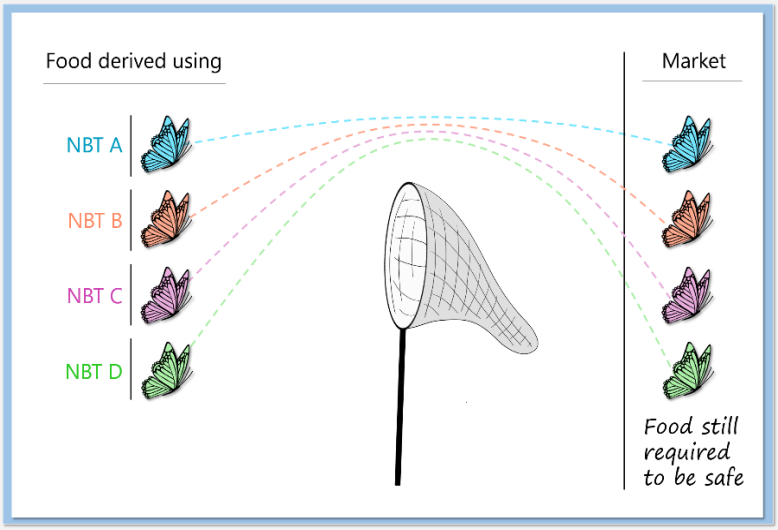
The non-regulatory options that FSANZ investigated as part of the review included the development of guidance or alternatively a code of practice to clarify the interpretation of the current definitions in the Code. It is unlikely that such approaches would be effective at addressing the problem because they would not provide any legal certainty. Legal certainty is important for product developers so they know the regulatory pathway to market for their product and is also important for enforcement agencies to enable them to determine if a food is compliant with the Code. Legal certainty also provides reassurance to the community that food law is being appropriately implemented and enforced.

The other disadvantage with non-regulatory options such as guidance is that it would only apply to the current definitions, which FSANZ has already determined are outdated and do not reflect the current diversity of techniques now in use. If FSANZ were to adopt an approach that maintained the current definitions, there is a risk that some foods will be deemed to be outside the scope of the current definitions even though a pre-market safety assessment may be justified.

In certain instances, particularly where viable non-regulatory options exist, maintaining the *status quo* and not introducing any amendments to the Code may be a reasonable option to consider, at least in the short term or as an interim measure. However in this case the continuing regulatory uncertainty may lead to a number of negative impacts (see Box 1).

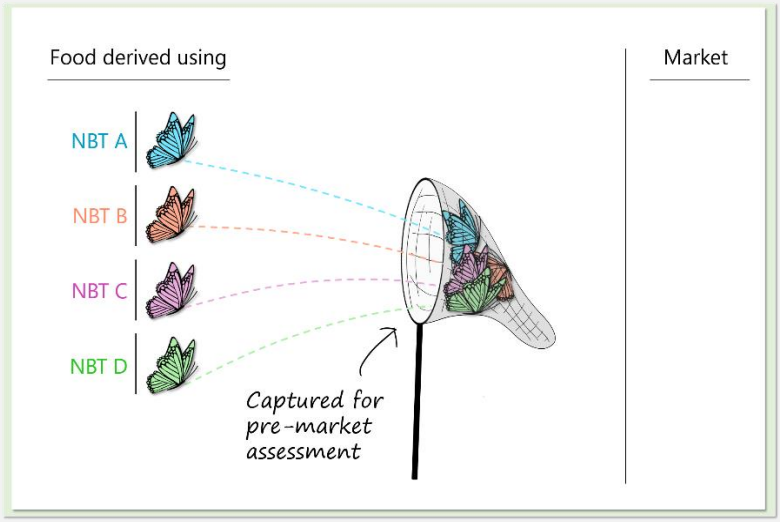
Box 1 | Possible scenarios if the current definitions remain unchanged

These scenarios are each associated with particular costs/disadvantages for consumers, food developers, regulatory authorities and society. These scenarios are non-mutually exclusive and for every given NBT each food developer could interpret the code differently. This could result in inconsistencies in the way such food is regulated.



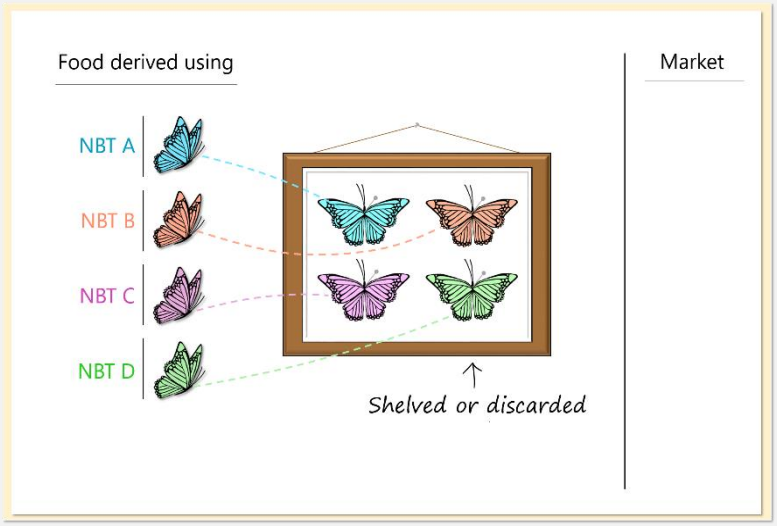
Scenario 1. *Non-compliant NBT foods might enter the market place.*

Food developers might incorrectly believe their product does not require pre-market scrutiny. Possible risks to public health and safety.



Scenario 2. *An increase in applications to FSANZ.*

Food developers might incorrectly believe their product requires pre-market approval and submit an application to FSANZ. There are cost implications for both product developers as well as FSANZ.



Scenario 3. *The development of NBT products might be abandoned.*

Possible negative impacts on innovation because developers are uncertain about the regulatory pathway for a particular NBT food.

For example, there may be potential health and safety risks to the community if, as a result of the uncertainty, some developers incorrectly believed their product did not require pre-market approval. Conversely, developers may decide to err on the side of caution and submit products to FSANZ for assessment and approval that do not actually require pre-market approval under the current definitions, creating additional work for FSANZ. A third potential impact is that developers may refrain from investing in a product or abandon a product's development because of uncertainty about the regulatory requirements.

In this context FSANZ has also considered possible impacts of delaying further work on the definitions, given the work that is now being undertaken in Australia to implement the recommendations of the Gene Technology Scheme (GTS) review[4], including further consideration around definitions.

The risks of maintaining the *status quo* and doing nothing are the same as the risks of deferring further work until the GTS review recommendations are implemented. Neither are considered to be a viable option

Recommendation 1: FSANZ prepare a proposal to revise and modernise the definitions in the Code to make them clearer and better able to accommodate existing and emerging genetic technologies.

2.2 The need for pre-market safety assessment

2.2.1 The current approach to GM foods

Under Standard 1.5.2 – Food produced using gene technology, GM food must first be approved and listed in Schedule 26 of the Code before it may be sold in Australia and New Zealand. Approval is contingent on the outcome of a pre-market safety assessment.

Standard 1.5.2 came into effect in 1999 and was intended to capture all GM food for pre-market safety assessment irrespective of potential risk. This was considered justified because of the uncertainty that existed at the time regarding gene technology, i.e., it was a relatively new technology, few examples of GM foods existed, there was limited regulatory experience assessing such products as well as little empirical evidence of safety.

The main reasons for adopting Standard 1.5.2 were so that:

- the community could be assured about the safety for human consumption of food produced using gene technology and be confident in the food supply
- industry could have confidence that the regulatory framework will be clear and enable it to be innovative and internationally competitive
- consumers could have access to accurate information on the use of foods produced using gene technology including labelling where appropriate.

The approach fulfilled community expectations at the time that all products of gene technology be subject to regulatory scrutiny because of the perception of increased risk.

[4] More information is available on the Australian Government Department of Health website.

2.2.2 Food derived using NBTs

NBTs encompass a wide variety of new techniques for the modification of genomes. These techniques may result in a variety of different outcomes, both in terms of changes introduced to the genome as well as changes to the characteristics of a food. Therefore, the risk associated with NBT foods will vary according to the outcomes produced.

One of the key questions for the review was whether there is sufficient justification in terms of risk to subject all NBT foods to pre-market safety assessment or whether there are certain foods, or categories of foods, that could be excluded from such scrutiny.

Views among submitters were mixed in relation to this question. Some submitters argued that because the techniques are still relatively new there is insufficient evidence of safety of derived foods and also that there is no scientific basis for making a risk distinction between NBTs and older GM techniques.

Other submitters argued not only for the exclusion of certain categories of NBT foods but also for the exclusion of some existing GM foods, stating that such food poses the same or less risk as food derived using conventional breeding methods. A number of other submitters were comfortable with the current regulatory approach to older GM foods but considered there may be justification either for some categories of NBT foods to be excluded or for them to be subjected to a simplified safety assessment.

In the case of GM foods, FSANZ notes that safety is determined by comparison to a conventional counterpart food which is the benchmark for what is considered safe[5]. This type of comparison may also be applied to NBT foods.

The rationale for this approach is that if the characteristics of NBT foods are similar or the same as a conventional food, the NBT food can be considered to have the same benefits and risks as food already in the food supply. This would be a relevant consideration in determining whether a NBT food should be subject to additional regulatory scrutiny in the form of a pre-market safety assessment.

As a preliminary analysis, FSANZ considered the different types of NBT foods to determine if there was potential for some NBT foods to be similar to conventional foods in terms of their characteristics (see Appendix 2). The outcome of this analysis is that:

- food derived from null segregant organisms will be identical to conventional food
- food derived from cisgenic organisms may be similar to food derived through cross-breeding
- some food derived from GM rootstock grafting will be identical to conventional food
- some food derived using genome editing will be equivalent, if not identical, to conventional food, including that derived using classical mutagenesis methods.

More robust analysis and further consultation will be required before FSANZ makes any conclusions about the equivalence of some NBT foods to conventional food.

[5] *Foods derived from modern biotechnology* (Codex 2009), page 7.

FSANZ notes that submitters were divided on whether any foods should be excluded from pre-market scrutiny, with a number of submitters expressing concern about the possibility that NBT foods could enter the food supply without any oversight by FSANZ. What constitutes an appropriate level of oversight is a question that will need to be further considered by FSANZ and the broader food regulatory system.

Finding 2: There may be a case, based on risk, for some NBT foods to be excluded from the requirement for pre-market safety assessment.

Finding 3: Divergent views exist among submitters about the acceptability and risk of NBT foods and how best to regulate them.

Unintended changes

One of the prevailing concerns about GM foods, which flows through to NBT foods, is the potential for unintended changes to occur. A number of submitters consider that a pre-market safety assessment is essential for all GM and NBT foods to guard against the occurrence of unintended changes, which they consider to be the major source of risk.

FSANZ has been undertaking GM food safety assessments for the last 20 years and has examined a large amount of data and information as part of those assessments. While concern about unintended changes in GM foods persists, the accumulated evidence does not support the hypothesis they are inherently harmful or a major source of risk to the consumer.

The occurrence of unintended changes is not peculiar to gene technology but may also occur when conventional breeding methods are used[6]. The evidence to date indicates that gene technology is no more likely than conventional breeding to produce unintended changes[7]. It may also be argued that because techniques such as genome editing are more targeted or directed, the likelihood of unintended changes occurring is much less compared to other genetic modification methods including conventional breeding. FSANZ is aware of only very rare instances where unintended changes from conventional breeding has resulted in a potential food safety concern[8]. It is also important to emphasise that the fact a change is unintended does not make it any more likely to be harmful. An unintended change may be harmful, neutral or advantageous with respect to the final product and whether it is likely to be harmful is independent of the genetic modification method used.

2.3 Regulatory approach

2.3.1 Definitional trigger for pre-market assessment

In recommending that the definitions in the Code for '*food produced using gene technology*' and '*gene technology*' be amended, one of the key considerations will be to determine what type of definitional trigger would be appropriate. That is, whether to continue to rely on

[6] For more information see Schnell et al (2015) A comparative analysis of insertional effects in genetically engineered plants: considerations for pre-market assessments. *Transgenic research* 24:1-17.

[7] FSANZ Application Handbook (1 July 2019), page 36.

[8] For more information see page 12 of Channapatna S. Prakash (2001) The Genetically Modified Crop Debate in the Context of Agricultural Evolution. *American Society of Plant Physiologists* 126: 8–15.

process-based definitional triggers or change to more product-based definitions. To assist in the decision-making, it will first be important to identify what the key objectives should be for amending the definitions.

The primary objective of any amendment to the definitions should be to provide greater clarity about what foods require pre-market assessment and approval and what foods do not. Clear definitions provide legal certainty which benefits all stakeholders.

To avoid further periods of uncertainty as new technologies continue to emerge, as well as frequent reviews of definitions, another important objective should be to adopt a definition that better accommodates current and future technology developments. Genetic technologies are in a constant state of evolution and the pace of change is also likely to increase over time. In the face of such technological advances, the Code needs to be flexible and forward thinking while remaining focussed on managing legitimate food-related health risks.

The other important objective will be to adopt a definition that results in NBT foods being regulated in a manner that is commensurate with the risks they pose. Regulation can have benefits by minimising risks to public health and safety but excessive regulation may stifle innovation and deter investment in the technology without providing any added public health protection. In the case of NBT foods, a case exists that pre-market approval should only be required where justified according to a reasonable expectation of greater risk compared to existing conventional foods.

FSANZ acknowledges there are different views among stakeholders about the risks posed by NBT foods and therefore what level of regulation would be regarded as “commensurate with risk”. In moving forward it will be important for FSANZ to engage in as wide a discussion as possible with stakeholders and the broader community to ensure any potential regulatory changes have regard to the diverse range of views that exist.

In summary, FSANZ proposes the objectives for revising and modernising the definitions in the Code should be to:

- improve clarity about what foods are captured for pre-market approval
- better accommodate new and emerging genetic technologies
- regulate NBT foods in a manner that is commensurate with the risks they pose.

Process-based and product-based definitions

One of the key questions for FSANZ to consider in contemplating an amendment to the current definitions in the Code is whether to continue with a process-based definitional trigger, or change to a more product-based approach. Product-based definitions are focussed on the outcome of the genetic modification, including the product characteristics, rather than the process or specific technique used to achieve the outcome.

In considering the responses from submitters on the relative merits of process-based and product-based definitions, FSANZ notes that views were divided.

A number of submitters were in favour of continuing to use process-based definitions as they see this as the most effective way to capture all NBT foods for pre-market safety assessment and approval. Some submitters also consider that a process-based definition would be more consistent with definitional triggers used elsewhere and that this would be better for trade.

Other submitters were more in favour of product-based definitions as they consider this type of definitional trigger is more likely to deliver risk-based outcomes in terms of what foods are captured and would also be more effective at future proofing the Code.

FSANZ notes that process-based definitions for triggering pre-market approval of GM foods have been widely adopted around the world. In terms of their advantages, such definitions can provide a simple and clear way to signal the regulatory status of certain products and make regulations more predictable in terms of outcome[9]. Capturing products on the basis of the process used can also provide an effective mechanism to prevent regulatory gaps in coverage and ensure comprehensive risk assessments are applied equally to all products derived using a specific technology.

The main disadvantage of process-based definitions is that they can quickly become outdated and therefore require periodic review and potentially need amendment as technology changes. Also, because some NBTs can result in foods that are identical or equivalent to conventional foods, a further disadvantage of process-based definitions is that they can result in identical products being regulated differently.

The advantage of product-based definitions is that they may be better able to accommodate a diverse range of technologies because of their focus on outcome, rather than process. It may also be argued that the use of product-based definitions allows regulations to be applied in a way that is commensurate with the level of risk. In terms of potential disadvantages, specific guidance may need to be developed to ensure implementation is effective, and such definitions may also have reduced compatibility with process-based regulatory systems.

In considering an amendment to the definitions in the Code, it will be important for FSANZ to weigh up the advantages and disadvantages of both types of definitional trigger, as well as consider which approach will best enable FSANZ to meet the three key objectives as outlined above.

Recommendation 2: As part of the proposal, FSANZ give consideration to 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.

2.3.2 Alignment of definitions with other regulatory schemes

The gene technology regulatory landscape in Australia and New Zealand is complex and the relevant legislation and regulations, including definitions, for genetically modified organisms (GMOs) and food produced using gene technology were developed independently from each other.

Many submitters to the consultation consider it is important for there to be alignment of definitions to avoid inconsistencies between what is regulated as a GMO and what is regulated as a GM food. Some submitters were also wary of FSANZ making any changes to definitions before the outcomes of other reviews addressing the *Gene Technology Act 2000* and its regulations are known.

In considering this issue, FSANZ believes it may be necessary to take a more pragmatic approach, and notes that despite the differences in current definitions in relevant legislation

[9] For more information see Eckerstorfer *et al* (2019) Plants Developed by New Genetic Modification Techniques-Comparison of Existing Regulatory Frameworks in the EU and Non-EU Countries. In *Frontiers in bioengineering and biotechnology* 7:26.

and regulations in both Australia and New Zealand, consistent regulatory outcomes have been achieved in terms of what is regulated as a GMO and what is regulated as a food produced using gene technology.

One of the important issues to consider in attempting to align definitions for example between the Code and the *Gene Technology Act 2000* (GT Act) and its regulations is their respective purposes. The objectives of the GT Act, and the risks to be managed, are significantly broader than those of the Code, and more specifically Standard 1.5.2, which was put in place specifically to manage risks associated with the consumption of food produced using gene technology.

Another important consideration is the lack of alignment in definitions between the GT Act and its regulations (as recently amended)[10] and in New Zealand, the *Hazardous Substances and New Organisms Act 1996* (HSNO Act). As the provisions in the Code for food produced using gene technology apply to food sold in New Zealand it would be difficult to develop a revised definition that would align with both the GT Act and the HSNO Act.

A final consideration is that the potential risks to human health and the environment of a GMO may be very different to that of derived food. Hence it may not be justified or appropriate for the Code to capture all foods derived from organisms captured as GMOs under either the GT Act or the HSNO Act.

It may be more practical to focus on the alignment of regulatory outcomes, rather than definitions, and to also consider the extent to which alignment of outcomes is appropriate given the different risks to be managed. This is something that will require further consideration during the next phase of the work.

2.3.3 International harmonisation of regulatory approaches

Many submitters stressed the importance of international harmonisation of regulations. If regulations are not harmonised there is concern about possible negative impacts on trade and market access.

FSANZ notes that internationally there is no single consensus on the regulatory approach to NBTs and derived foods with a number of different approaches being adopted around the world[9]. These approaches generally fall into three main types:

- countries that are revising existing definitions (e.g. Australia)
- countries that are applying existing regulatory frameworks to NBTs (e.g. New Zealand, Canada, European Union, United States, Japan)
- countries that are implementing supplementary legislation for NBTs to support existing regulatory frameworks (e.g. Argentina, Brazil).

Some of these countries continue to rely on process-based definitions, whereas others are applying more outcomes-based approaches.

The international situation in relation to the regulation of NBTs remains fluid, with little likelihood of harmonisation in the near future. Whether the absence of harmonisation will

[10] Information about the amendments to the *Gene Technology Regulations 2001* is available from the OGTR website.

impact trade is unknown at this stage as there are very few NBT food products that have been commercialised and traded between countries. FSANZ will continue to monitor international developments and will have regard to these during the next phase of the work.

2.4 Other relevant matters

2.4.1 GM food labelling

GM food labelling was not included in the scope of this review. Nevertheless, FSANZ recognises that the ability to exercise informed choice when purchasing foods containing GM ingredients is important to consumers. This was a dominant theme that came out of the consultation.

During the GTS review, stakeholder dissatisfaction with GM food labelling was noted. Much of this dissatisfaction appears to be because many consumers had not encountered any foods that were labelled and had assumed (incorrectly) that GM food labelling was not mandatory. Market research undertaken in Australia recently indicates consumer knowledge about GM foods is limited, particularly in relation to the number and type of GM foods in the food supply[11]. At present there are no whole GM fruit or GM vegetables in the food supply. Most GM foods enter our food supply as ingredients (e.g. oil, flour, starch) in imported processed foods.

Current approach to GM food labelling

The policy approach and requirements for GM food, including its labelling, were developed 20 years ago and have not been changed. Under that approach food produced using gene technology is required to undergo pre-market safety assessment before being approved for sale. Approved food produced using gene technology is also subject to mandatory labelling requirements. Mandatory labelling was adopted not for safety reasons but rather to assist consumers to make an informed choice.

The approach to GM food labelling is product based[12]. That is, labelling is required based on the presence of novel DNA or novel protein in the final food or if the characteristics of the food have been changed in a meaningful way (an altered characteristic) (Figure 2). A number of exemptions to mandatory labelling apply that are either product based (e.g. the exemption for highly refined foods or ingredients) or based on other practical considerations (e.g. unintended presence).

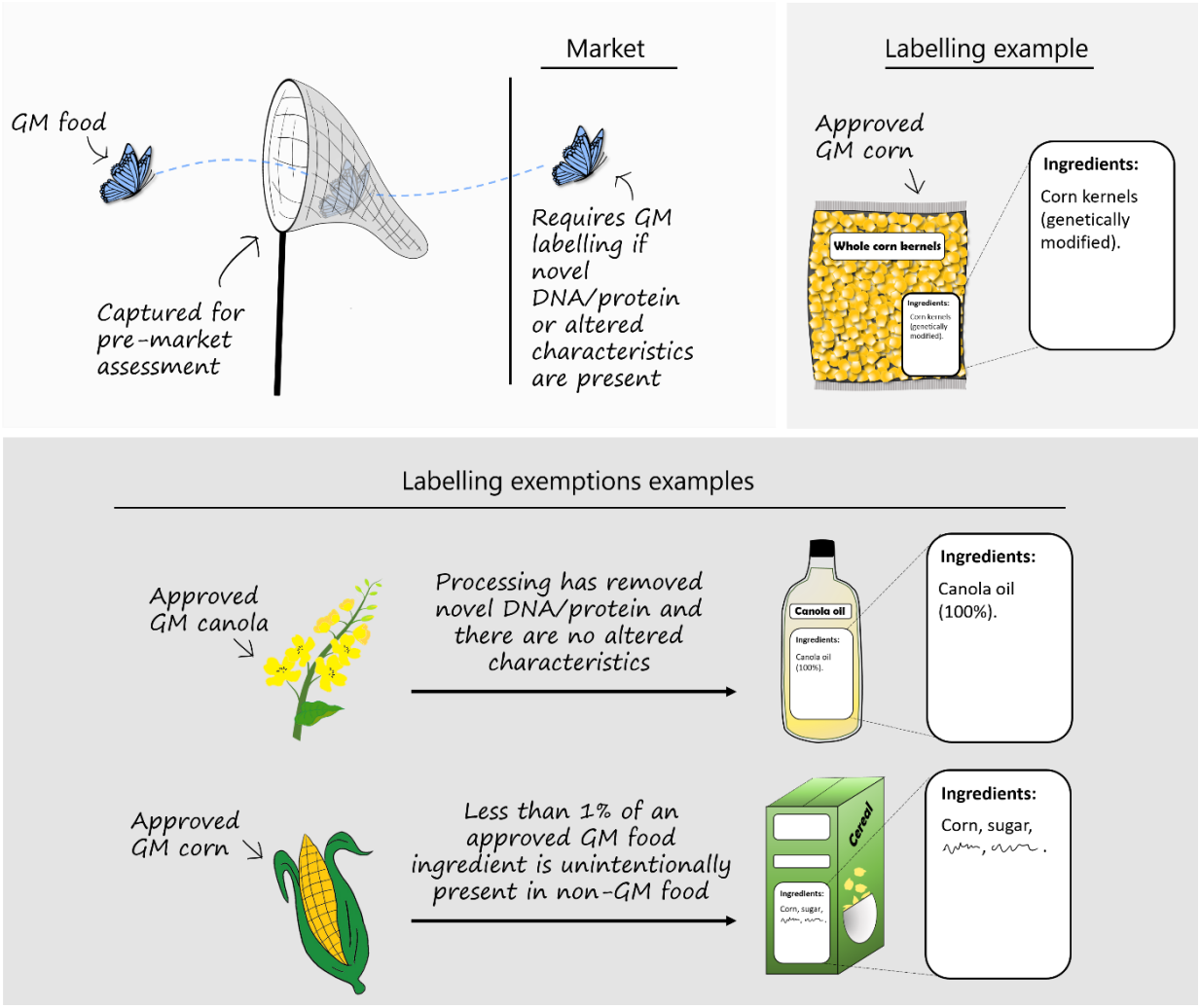
The labelling approach to GM foods was reviewed as part of *Labelling Logic: Review of Food Labelling Law and Policy* in 2011[13]. In response to that review, the Legislative and Governance Forum on Food Regulation considered the existing labelling provisions for GM food to be appropriate.

[11] More information is available on the Australian Government Department of Health website.

[12] More information is available on the FSANZ website.

[13] More information is available on the Food Regulation website.

Figure 2: Labelling requirements



Further consideration of definitions

In undertaking further work on NBT foods, including consideration of possible amendments to definitions, FSANZ does not intend to review the GM food labelling requirements. The GM food labelling requirements will therefore remain as they are and will continue to apply to approved food produced using gene technology.

FSANZ acknowledges the continued interest among stakeholders in GM food labelling and the importance of the definitions in determining what foods may be subject to those requirements.

As part of any future proposal, and consistent with the s18 objectives of the FSANZ Act, FSANZ will need to consider potential implications for consumer information arising from any amendments to definitions.

In addition, and having regard to the limited knowledge in the community about GM foods and their labelling, FSANZ will explore ways to raise awareness among consumers about GM foods and how labelling is applied.

2.4.2 Participation in the proposal process

In moving forward with a proposal to amend the Code, a key consideration will be to ensure the community is kept well informed about the process and opportunities for input and that FSANZ continues to engage in a transparent way.

FSANZ considers openness and transparency to be vital to this work given the diversity of views on gene technology, as well as the limited understanding in the community about NBTs[14]. FSANZ notes a multidisciplinary panel of experts, who carefully considered the implications of NBTs for New Zealand, has encouraged wide engagement with the community to help bridge this gap in understanding[15]. FSANZ acknowledges that feedback on public attitudes and ethical views are an important component of this engagement.

Such engagement will allow FSANZ to develop revised definitions that are informed by the science and consistent with community values and expectations. Engagement may not however always result in an outcome that is favourable to all members of the community but this is part of the democratic process of decision making.

Recommendation 3: Throughout the proposal process FSANZ will ensure there is open communication and active engagement with all interested parties and also explore ways to raise awareness about GM and NBT foods.

3. Next steps

The review was undertaken in accordance with section 113 (s.113) of the FSANZ Act. The publication of this report signals the conclusion of the review.

As soon as practicable after the conclusion of the review, FSANZ intends to prepare a proposal to amend the Code. Proposals to amend the Code are undertaken in accordance with specific provisions in the FSANZ Act, including various statutory criteria that FSANZ must have regard to in its assessment of proposed amendments to the Code.

For the next phase of the work, FSANZ will therefore need to consider how best to progress the recommendations, the scope and timing of any proposal, and the regulatory options for amending the definitions in the Code. Throughout this next phase FSANZ will continue to engage with stakeholders (through public consultation as well as other means) and communicate any relevant matters.

[14] More information is available on the OGTR website.

[15] More information is available on the Royal Society Te Apārangi website.

4. Background

4.1 How we conducted the review

The review was conducted over a two and a half year period and included a number of stages as outlined below in Figure 3. A key part of the review was the public consultation undertaken in February – April 2018. The consultation paper was developed with the assistance of an Expert Advisory Group on New Breeding Techniques[16] and a preliminary report was released in August 2018. Further consideration of submissions and the key consultation outcomes, as well as additional targeted consultation undertaken over the last 12 months, were used to inform the key findings and recommendations.

Figure 3: Steps taken in the review

[16] More information on the Expert Advisory Group on New Breeding Techniques is available on the FSANZ website.

4.2 Relationships to other reviews

Two other reviews conducted in Australia have coincided with the FSANZ review of food derived using NBTs. Those reviews are:

- the Technical Review of the *Gene Technology Regulations 2001*, conducted by the Office of the Gene Technology Regulator (OGTR), which was concluded in April 2019 and resulted in amendments to the *Gene Technology Regulations 2001*[17]

- the Third Review of the National Gene Technology Scheme, conducted by a collaboration of Commonwealth, state and territory officials on behalf of all Australian governments, which was concluded in October 2018[18].

While these reviews have also considered new technologies, they are separate and independent of the FSANZ review. The outcomes of these reviews have not changed any parts of the Code that relate to food produced using gene technology.

4.3 Terminology

The term new breeding techniques or NBTs has been used throughout the course of the review and associated documents.

NBTs refers to a wide range of new techniques used to modify the genomes of plants, animals and microorganisms and includes such techniques as genome editing, GM rootstock grafting, cisgenesis, intragenesis and techniques producing null segregants (see Appendix 2). The term NBT has been widely adopted around the world and is used to distinguish the newer techniques from older methods of genetic modification. FSANZ acknowledges that not all stakeholders agree with this distinction and the use of such terminology.

[17] Information about the OGTR's Technical Review of the *Gene Technology Regulations 2001* is available from the OGTR website.

[18] Information about the Third Review of the National Gene Technology Scheme is available from the Australian Government Department of Health website.

Appendix 1: Consultation questions

Question 3.1.1: 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?

Question 3.1.2: 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?

Question 3.1.3: 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?

Question 3.2: 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? Should food derived from other techniques, such as DNA methylation, be subject to pre-market safety assessment and approval?

Question 3.3: 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?

Question 3.4: 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?

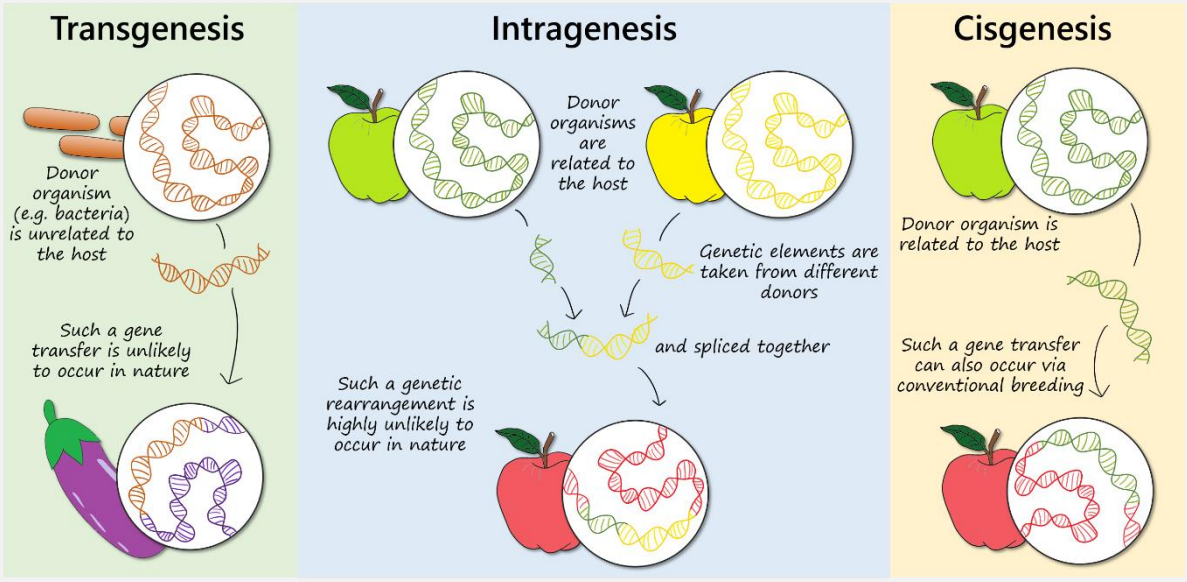
Appendix 2: Equivalence assessment

Appendix 2 outlines some of the NBTs used to produce food and the potential for these products to be equivalent to food derived using conventional breeding methods.

Genome contains new DNA

This category includes transgenesis, intragenesis and cisgenesis (Box 2).

Box 2 | Genome contains new DNA

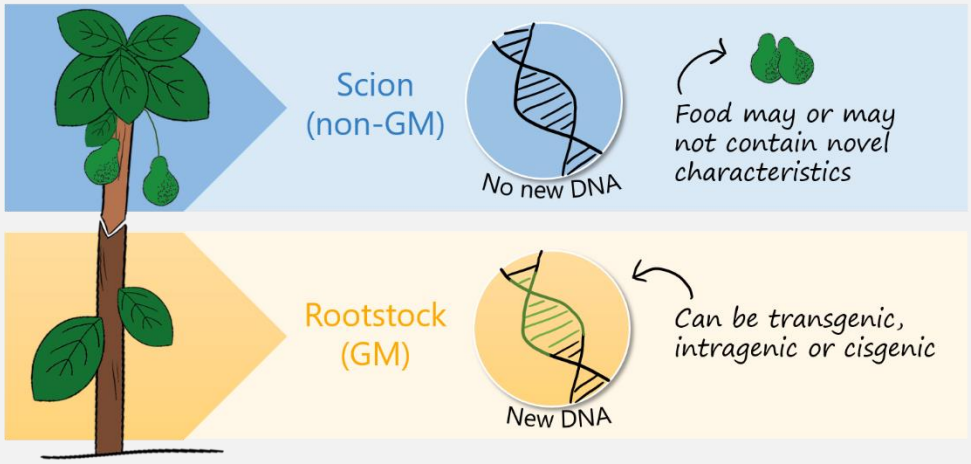


While all three techniques involve introducing new DNA into the genome, cisgenesis may be distinguished from intragenesis and transgenesis because it typically involves transferring traits between related varieties or breeds and may therefore reproduce outcomes that could be achieved using cross-breeding. Food derived from cisgenic organisms may therefore be similar in terms of its characteristics to food derived through cross-breeding.

Similarly, GM rootstock grafting may, in some circumstances, result in foods that are similar to conventional foods (Box 3). Some genetic modifications to the rootstock may influence the characteristics of the upper part of the plant (scion) and potentially also the food, while others may not. In the latter case, the final food, such as a fruit, will be identical in its characteristics to conventionally bred fruit already in the food supply.

Box 3 | GM rootstock grafting

Involves joining the vegetative (upper) part of a compatible plant variety to the rootstock of a GM plant.



Genome unchanged by gene technology

The techniques in this category are those producing null segregants. Such techniques are highly diverse but the end result is that the final food producing line will not contain any new DNA as a result of the use of gene technology because it will be segregated away (see example in Box 4).

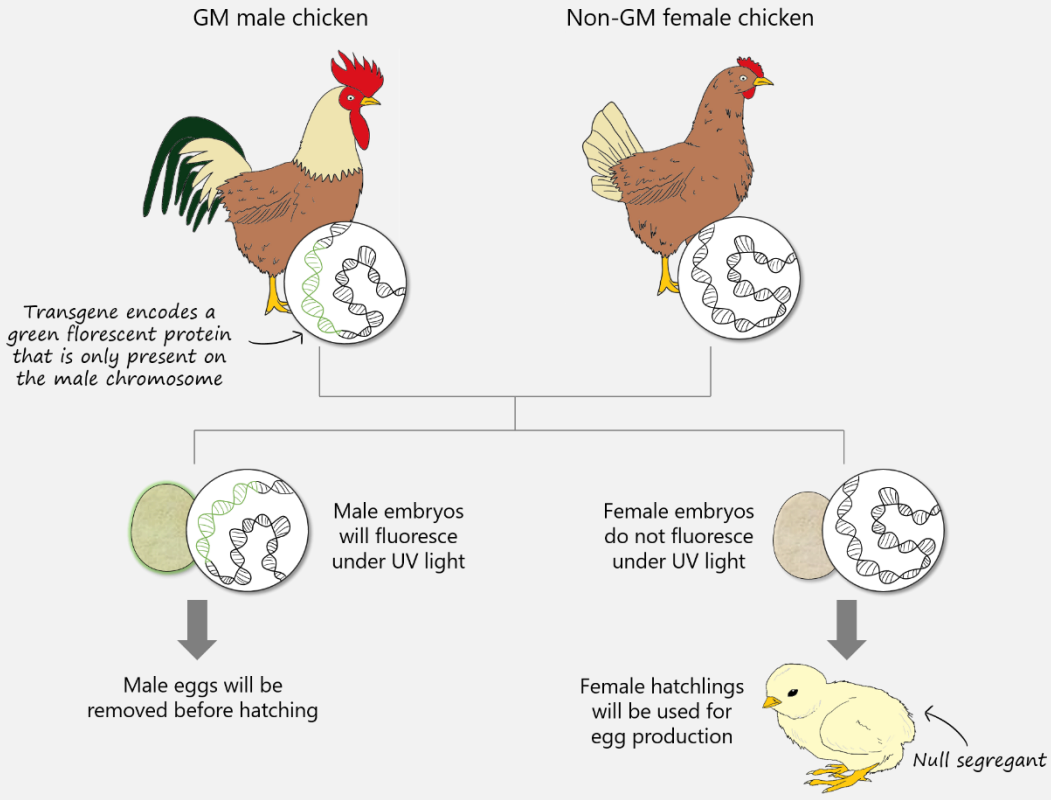
Once any introduced DNA has been segregated away, any changes associated with that DNA should no longer be present in the final food producing lines or derived foods. The food will therefore be equivalent to food derived using conventional methods approaches.

There is a clear case for excluding food derived from null segregants from pre-market assessment and approval as it would be indistinguishable from conventional food and be equivalent in terms of risk. FSANZ also notes that under the 2019 amendments to the *Gene Technology Regulations 2001*, the OGTR has clarified that null segregant organisms are not GMOs and do not pose risks as a result of gene technology because they do not possess traits introduced using gene technology. For a number of years it has also been common practice for FSANZ to allow the use of null segregants as non-GM comparators for the purpose of GM food safety assessment[19].

[19] FSANZ *Application Handbook (1 July 2019)*, page 35.

Box 4 | Sex selection in layer chickens

Male hatchlings of layer chickens are normally culled after hatching. A NBT could allow the detection and removal of male eggs before hatching. This technique will result in null segregant female hatchlings.



Genome changed but no new DNA

This category refers specifically to the genome editing techniques. The edits to the genome typically include point mutations, small insertions/deletions (indels) and larger deletions. These types of genome changes are not particular to genome editing. They also occur spontaneously in nature and are the basis of natural variation used in conventional breeding[20]. Similar changes can also be randomly induced using classical mutagenesis methods. Some of the foods produced using genome editing techniques may therefore be equivalent, if not identical, in their characteristics to foods that have been produced using classical mutagenesis methods, or that exist in nature.

One of the most frequently raised concerns in relation to genome editing is the potential for off-target changes to be introduced as a result of a double-stranded break being introduced at other than the intended site, or other changes that may occur during repair of the double-stranded DNA break.

[20] For more information see Custers et al (2018) Genetic Alterations That Do or Do Not Occur Naturally; Consequences for Genome Edited Organisms in the Context of Regulatory Oversight. In *Frontiers in Bioengineering and Biotechnology* 6:213.

FSANZ notes that both genome editing and classical mutagenesis can produce double-stranded breaks as well as errors during the repair process. In the case of genome editing, off-target changes may also occur. The frequency of such off-target changes is typically much lower than the frequency of non-targeted random changes that occur with classical mutagenesis methods[21]. Irrespective of whether the double-stranded DNA break is a result of genome editing or classical mutagenesis, the process of double-stranded DNA break repair is the same[22]. Errors during repair is a normal part of this process and occur irrespective of whether the double-stranded break has occurred as a result of classical mutagenesis methods or through genome editing.

The most significant difference between genome editing and classical mutagenesis is that the site of DNA breakage is pre-determined in the design of the genome editing tool, while the DNA breakage is random in classical mutagenesis. Since the genetic change is much more predictable and directed than classical mutagenesis, genome editing tools are much less prone to off-target changes[20] (Box 5).

The sequence specificity of genome editing tools means that any off-target sites are generally similar in sequence to the intended target site therefore the potential for an off-target event can be predicted to some extent. Importantly, an off-target change does not necessarily equate to a harmful consequence in the final food produced.

[21] For more information see Zhao, H. & , Wolt, J. D. (2017) Risk associated with off-target plant genome editing and methods for its limitation. *Emerging Topics in Life Sciences* 1:231–240

[22] More information is available from Current Biology

Box 5 | Mutagenesis – off-target and unintended changes