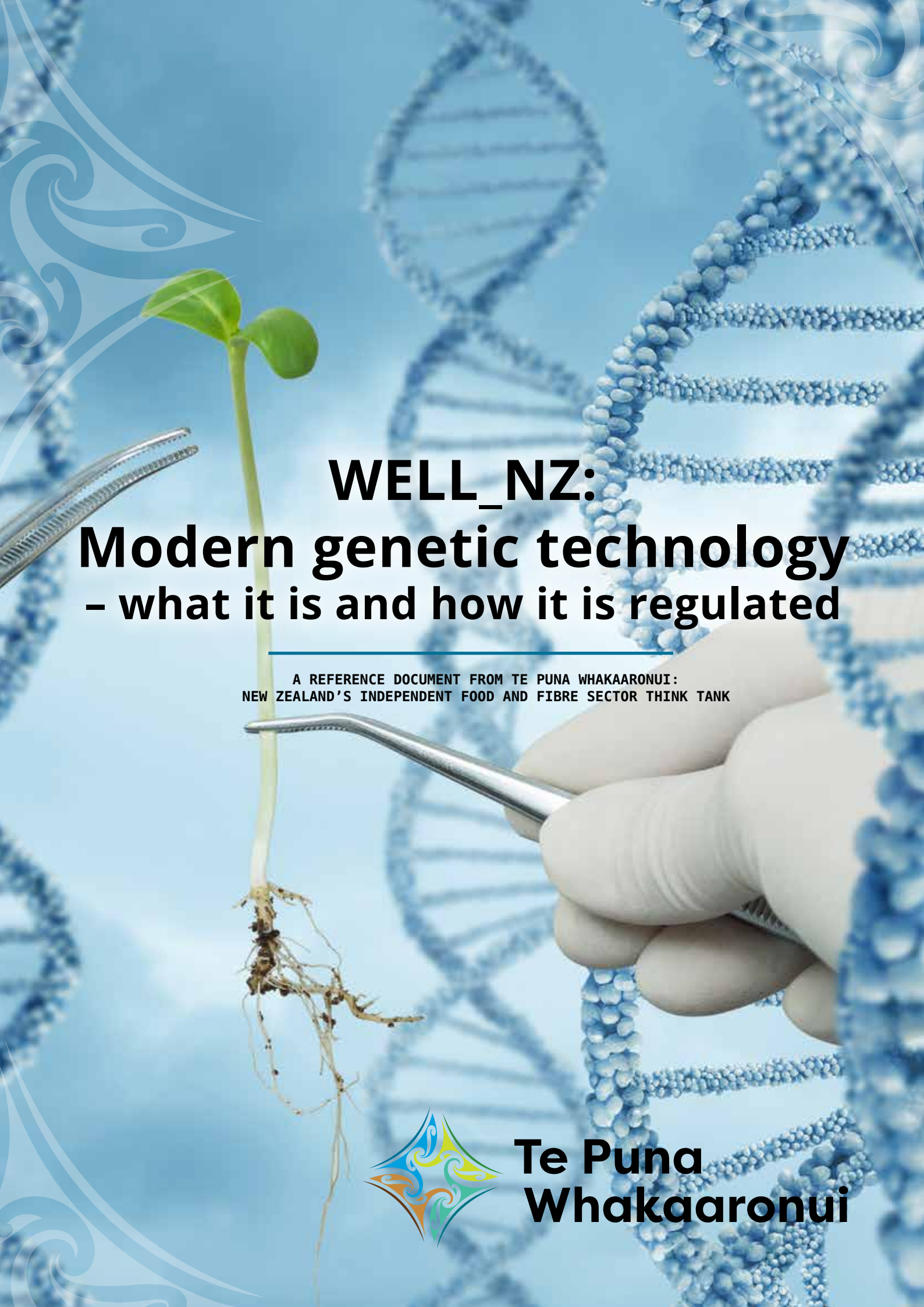

WELL_NZ:
Modern genetic technology
– what it is and how it is regulated

A REFERENCE DOCUMENT FROM TE PUNA WHAKAARONUI:
NEW ZEALAND'S INDEPENDENT FOOD AND FIBRE SECTOR THINK TANK

Te Puna Whakaaronui

Te Puna Whakaaronui is New Zealand's independent food and fibre sector think tank and was established as a key action under the *Fit for a Better World* Acceleration Roadmap, fulfilling the Primary Sector Council's recommendations for pan-sector thought leadership. *Fit for a Better World* will support New Zealand's food and fibre sector transformation over the next ten years.

Te Puna Whakaaronui's role is to help lead, co-ordinate and implement transformation through partnering with Māori and sector participants to provide thought leadership, strategic insights and advice.

The think tank has a voice independent of the Ministry for Primary Industries, its view does not represent Government policy.

ISBN: 978-1-99-106275-8 (print)
ISBN: 978-1-99-106276-5 (online)

February 2023

Te Puna Whakaaronui

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Foreword

Te Puna Whakaaronui was established to identify and address topical issues that could influence the future direction of the food and fibre sector globally and domestically. A core part of Te Puna Whakaaronui's work is to contribute to the knowledge base that informs understanding of significant trends and developments and thereby support meaningful conversation about issues that could impact New Zealand's food and fibre sector.

Global conversations about food – production, security, nutrition and climate change adaptation – are currently hot topics for governments, producers, consumers and agencies that are likely to remain live for several decades. For the last hundred years global food conversations have focused on production, availability and collective support for those facing food scarcity. Many longer-term issues, such as the environmental impact of intensive farming regimes and equitable food distribution, still form part of current discussions – but new, more acute, issues have come to the fore.

Pressure arising from pandemic, war, economic sanctions, increasingly frequent and severe climate change events, loss of core infrastructure, inflation, trade restrictions, technological change are adding urgency to the increasing number of calls for innovative solutions and new options to resolve food security and environmental sustainability issues. The need for fast solutions to acute pressures has brought genetic technology back into global food conversations.

Genetic technology has changed dramatically over the last twenty years and developed even more rapidly over the last ten to the extent that international jurisdictions are proactively reviewing their regulatory settings to recalibrate with the current state of genetic technology. Resilience to climate change as well as improved environmental and sustainability outcomes are key drivers behind several international regulatory reviews, including the current United Kingdom and European Union processes.

This document aims to provide an unbiased, fact-based resource for those seeking to better understand the current state of genetic technology and associated regulations around the world. By demystifying the science, Te Puna Whakaaronui intends that this document will inform conversations about genetic technology from a number of perspectives.

Terminology

Globally, several different and inter-changeable terms along the continuum of genetic technology are in use. For example, in the European Union (EU) what is referred to as New Genomic Techniques (NGTs) is referred to in the United Kingdom (UK) as Precision Breeding Techniques (PBTs). This variable terminology creates considerable confusion and gets in the way of a balanced conversation.

We have adopted the following convention throughout this document:

The umbrella term used for all techniques is **genetic technology.**

Cell fusion is the process by which two or more cells combine their plasma membranes (the 'wall' that separates the interior of the cell from the outside environment) to become a single, hybrid cell containing DNA from each original (parent) cell.

Deoxyribonucleic acid (DNA) is a molecule that contains the biological instructions that make each species unique. DNA, along with the instructions it contains, is passed from adult organisms to their offspring during reproduction.

GMO,GM and genetic engineering refer to all genetically modified organisms which cover both *transgenic* organisms and any organism that has been genetically modified through any genome editing technique.[1]

Gene refers to the basic unit of heredity passed from adult organism to offspring. A gene is made up of sequences of DNA, arranged one after another, at specific locations on chromosomes in the nucleus of cells.

Genome refers to the complete set of genetic material present in a cell or organism (i.e. includes RNA[2]).

In vitro (meaning in glass, or in the glass) studies are performed with microorganisms, cells, or biological molecules outside their normal biological context.

In vivo refers to research or work that is done within an entire living organism, for example studies in an animal or human clinical trials.

Trait refers to a characteristic or attribute of an organism that is expressed by genes and/or influenced by the environment and includes physical attributes such as hair colour.

Traditional Breeding Techniques refers to selective breeding, the controlled breeding of plants and animals by human intervention to selectively produce traits.

New Breeding Techniques (NBTs) are a diverse collection of new genetic techniques, many of which have emerged over the last decade and are still evolving.[3] For the purpose of this document, the term New Breeding Techniques encapuslates: New Genomic Techniques, Precision Breeding (PB), genome editing, gene editing, New Precision Breeding Techniques (NPBTs), Precision Breeding Techniques (PBTs) and New Plant Engineering Techniques, for more details see page 14.

Recombinant nucleic acid molecules are constructed outside living cells by joining DNA or Ribonucleic acid (RNA) segments (natural or synthetic) to DNA or RNA molecules (potentially from multiple source organisms) that can replicate within a living cell. DNA or RNA sequences can be created that would not naturally be found in the genome.

The Precautionary Principle is a default caution setting for decision-makers when, for example, scientific evidence about an environmental or human health hazard is limited or uncertain, and where the stakes are high. Typically the setting would be revised over time as more data and knowledge becomes available.

The Principle of Substantial Equivalence is used in food safety. This concept holds that the safety of a new food, particularly one that has been genetically modified, may be assessed by comparing it with a similar traditional food that has proven to be safe over time.

For more details about specific techniques refer to the *Introduction to genetic technology* section on page 9.

Table 1: Inter-changeable terms

Terminology used in this report	Inter-changeable terms
Selective breeding	• conventional breeding • traditional plant breeding • traditional breeding • artificial selection • random mutagenesis
Transgenic modification	• genetic modification (GM) • genetically modified (GM) • genetically modified organism (GMO) • genetic engineering (GE) • transgenic • transgenesis
New Breeding Techniques (NBTs)	• new genomic techniques (NGTs) • genome editing • gene editing • precision breeding (PB) • new precision breeding techniques (NPBTs) • precision breeding techniques (PBTs) • new plant engineering techniques

Executive Summary

Some pressing issues (pandemic, war, sanctions, impacts of climate change, loss of core infrastructure, inflation, trade restrictions, the progress of technology) are increasing the need to find solutions – or reconsider options to mitigate risk – at pace. These complex dynamics, coupled with major advances in biotechnology over the last decade, are raising the profile of genetic technology.

However, determining a common global starting point for a genetic technology conversation with governments and policy makers in the face of so many pressing priorities, is difficult.

This document, *WELL_NZ: Modern genetic technology – what it is and how it is regulated,* establishes an information base from a review of media, industry press releases, websites and academic literature, as well as industry, government, and multi-lateral organisation reports. In addition Te Puna Whakaaronui interviewed industry, food and fibre sector stakeholders and crown research institutes. Analysis of this material has informed our description of the regulatory status, the scientific processes and consumer perceptions of global and domestic genetic technology globally.

We have presented our findings in four sections:

- genetic technology;
- global regulations;
- consumer perceptions; and,
- New Zealand's regulation reviews.

The intention is that these information building blocks will support a better understanding of the current status of genetic technology internationally and highlight some.

1. Genetic technology

The description of global technology in this document is based on recent scientific research, publicly available information and examples to demonstrate: the continuum of the techniques, how they work, how they can and have been applied as well as any associated risks.

Key findings

The development of genetic techniques, applications and new products have continued to progress at pace over recent decades. These advances, plus an increasing number of gene edited products in-market, have led to more research and an increase in the number, and variety of applications for genetic technology. We found:

- genetic technology has evolved rapidly across a continuum of techniques with each new technique improving on the precision of the last;
- globally genetic technology has been applied across the food and fibre sector to improve yield, size, taste and nutritional content of produce as well as develop resistance to factors such as disease, pests, drought or salt tolerance;
- products developed through genetic techniques are being used more widely for health, animal feed, food and nutrition.

2. Global regulations

Twenty to thirty years ago, genetic technology was new, and not well understood. As a result, New Zealand and some other jurisdictions employed the precautionary principle to focus and guide the regulation of Genetically Modified Organisms (GMO) and techniques. In the intervening years, no instances of harm from the consumption of GM food (related to modification) has been documented.

The evolution of new genetic techniques over the last decade has made more precise genetic modifications possible without necessarily introducing foreign DNA into an organism. Gene technology developments have allowed for more precise genetic modifications in a way that is now judged by many countries as similar to – or

at least as safe as – traditional breeding techniques, including mutagenesis.[4]

At its core, regulation in every country aims to balance the benefits of new technologies (competitive, economic, health and environmental) with the need to keep humans, animals and the environment safe.

Since the 1990s most regulations have fallen under one of two broad approaches:

- a focus on the process; or
- a focus on the product.

Countries such as Australia, the United States of America (USA), China, Canada, Brazil, Argentina and Singapore are among several which regulate GMOs based on product traits, rather than process. They impose safety assessment processes and approvals on product characteristics, irrespective of whether the product has been produced using genetic technology. In contrast, the EU, UK and New Zealand have regulatory regimes that restrict all products which use any genetic engineering technique.

As expertise has developed, New Breeding Techniques (NBTs) have been at the forefront of innovation due to their potential to improve the resilience of plants and animals to climate change, produce greater yields and support domestic food security. Technological progress, coupled with pressing domestic need and a changing global environment and food system, has resulted in revised GMO regulation in most countries and trading blocs.

Among our main trading partners, the UK, EU and New Zealand are currently the only jurisdictions whose regulations remain purely process based. However, the UK has a Bill before Parliament, the *Genetic Technology (Precision Breeding) Bill 2022-23* [5], which, if passed would exempt certain gene editing techniques from broader GMO regulations. The EU is also well into a regulatory change process that is heading in the same direction.

Key drivers for global regulatory change are:

- economic, including keeping pace with technological progress to maintain trade competitiveness;
- ensuring regulation that is efficient, effective, consistent and practical to implement;
- the status of existing regulations and whether or not they are fit-for-purpose; and,
- how well existing regulations meet environmental, nutritional, health and economic objectives.

3. Consumer perceptions

A broad set of global studies and research reports have been produced to better understand consumers' perceptions of genetic technology and willingness to buy the resulting food product.

Responses vary depending on the country where the research was undertaken. The following findings are reflected across a number of international and New Zealand studies:

- **Would you buy GM foods?**
  a conditional 'yes', based on the perceived benefits the consumer receives, such as goods that are cheaper, healthier, have no spray residues, are more nutritious and contribute to positive biodiversity and environmental outcomes. Responses were less in favour if the benefits accrued solely to the grower, for example they were cheaper to grow or had a higher yield.
- **Is there a premium for non-GM product?**
  a conditional 'yes', there is a significant premium over GMO, but this declines based on other product characteristics, for example: product appearance, consumer perception about other benefits such as environmental and nutritional qualities, and the type of genetic technique used to produce the product. In addition, perceptions of value are very product specific – more caution should be used for commodity and ingredient-based products where production methods are less obvious to the consumer,
- **Does GM impact a country's brand?**
  a conditional 'no', when consumers are making purchasing decisions, country of origin (COO) is only one factor within a broader decision-making framework specific to that market's characteristics. The product's price, perceived benefits and cultural influences within that market, are weighed against the product's perceived risks. A survey of tourists entering New Zealand showed a significant "no" response to the question.

4. New Zealand's regulation reviews

In New Zealand there have been several studies, reviews, critiques and assessments of New Zealand's GMO regulatory regime over more than two decades, the most in-depth studies are these five formal reviews:

- Royal Commission on Genetic Modification, *Report and Recommendations,* 2001;
- The Royal Society Te Apārangi, *Gene Editing in Aotearoa*;
- Prime Minister's Chief Science Advisor briefing on the Royal Society Te Apārangi gene editing report, 2019;
- The Productivity Commission, *New Zealand firms: Reaching for the frontier*, 2021; and
- Food Standards Australia and New Zealand, Proposal P1055, *Definitions for gene technology and new breeding techniques* [6], 2021.

In 2001 the Royal Commission was grappling with emerging gene technologies and, like some other jurisdictions at the time, focused on applying the precautionary principle to New Zealand's regulation, to limit unknown risk. However, recommendations from its inquiry emphasised the need to ensure ongoing calibration between regulatory settings, technology and societal preferences, setting out guidelines and recommendations to ensure inclusive consultation would inform future policy and regulatory change.

Two decades on and genetic technology has advanced and developed in ways that could not be envisaged in 1996 when the Hazardous Substances and New Organisms Act (HSNO) was drafted, or in 2001 when the Royal Commission undertook its inquiry. Subsequent reviews by the Royal Society, the Productivity Commission and Food Standards Australia New Zealand (FSANZ) are unanimous in their recommendations for:

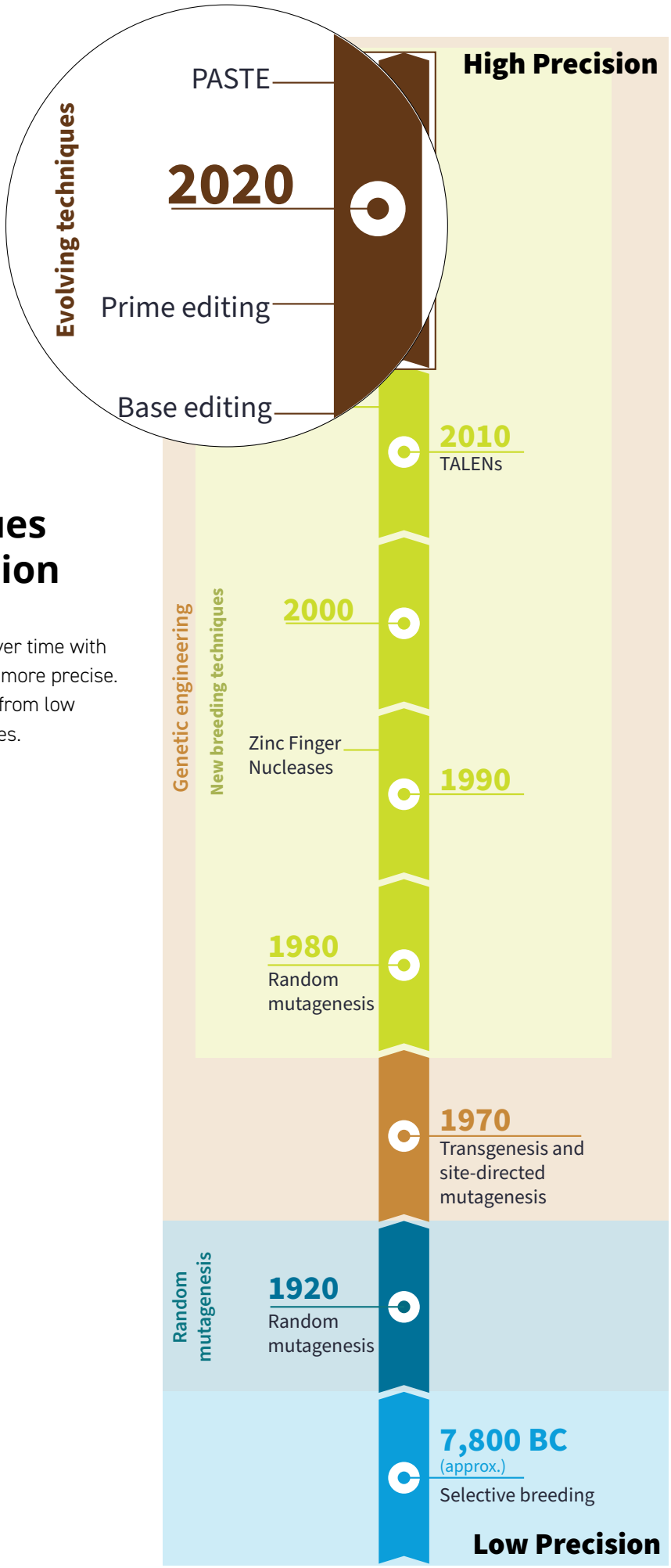
- re-calibration of regulatory settings with technology;
- an overhaul of the existing regulatory regime – it is no longer fit-for-purpose;
- the precautionary principle applied to regulation in the early 2000s to be replaced with a risk proportionate approach; and,
- regulation must include input from across society.

This document, *WELL_NZ: Modern gene technology – what is it and how it is regulated,* aims to provide a neutral information base to enable a shared, informed conversation across communities of interest in food and fibre production, science, iwi, catchment communities, industry and investors. It does not make recommendations or advise on a direction of travel, it is a presentation of baseline information.

Section 1: Introduction to genetic technology

Several techniques of varying precision

Genetic technology has advanced over time with techniques becoming progressively more precise. This diagram shows the continuum from low precision to high precision techniques.



Selective breeding

What is it?

Selective breeding is the oldest breeding technique and has been used by humans since at least 7,800 BC. The term *selective breeding* describes the human-controlled process of modifying species to enhance desirable traits, or to remove undesirable traits, through the selection of breeding pairs. This technique uses natural genetic variation to create an opportunity to introduce different genes into an organism (from the same or compatible species, such as the hybridisation of plants) which may or may not include the genes responsible for some specific, targeted trait.

Three methods are used for selective breeding to combine, enhance or remove specific traits:

1) Outcrossing involves the crossing of two plants or animals, unrelated over a potentially large number of generations, resulting in a wide genetic variation of traits. Outcrossing can bring diversified genetics and traits back together, or hide undesirable traits by keeping them recessive; this works best when the targeted trait is generated by dominant genes.

2) Linebreeding involves the mating of related plants or animals having a common ancestor; it shows more uniformity than outcrossing and has low incidence of genetic defects. The aim of this technique is generally to improve or maintain specific traits.

3) Inbreeding allows for the almost guaranteed selection of recessive traits that would not normally be observable in an unrelated breeding pair.

What does it do?

Simply, at the biological level, selective breeding involves the mixing and matching of DNA.[7] Through selective breeding, the DNA of two organisms (the parents) are combined to produce a new organism (the offspring) whose DNA will be some combination of the parents. Selective breeding aims to combine two desirable traits to produce a targeted trait in the offspring, or to ensure the presence of a targeted trait in the offspring within breeding stock.

How has it been used?

Over thousands of years farmers have been able to refine the breeding stock of plants and animals for the traits they value. Selective breeding has been used in all commercially produced plants and animals globally; some benefits include:

- **plants:** new varieties; crops with increased resistance to diseases and pests, larger seeds, shortened growing seasons, improved nutritional content or shelf life; adaptation to diverse ecological conditions under which they can be grown; and,

The evolution of common vegetables

Over the last few thousand years, farmers have bred *Brassica ol*eracea, or wild mustard plant, to create dozens of wildly different vegetables. By selecting and breeding plants with bigger leaves, altered flowers or larger buds, various cultivars were created including: Brussel sprouts, cabbage, kohlrabi, broccoli, cauliflower, Chinese broccoli and kale.

Brassica oleracea is a biennial coastal plant native to the Mediterranean and British Isles. Scientists believe the wide range of the plant is a key factor in the vast genetic diversity of the species. *Brassica oleracea* uses food reserves stored over the winter in its rosette of leaves to produce a spike of yellow flowers at the end of its second summer, it then dies. These nutritious leaves make its domesticated derivatives important food crops in much of the world today. For example:

- kale and collard greens, part of the same sub-species, were created by making the ancestor plant's leaves bigger; they were domesticated in Europe sometime before 300 BC;
- red, green and Savoy cabbages were created from a kale cultivar (likely the European collard greens) in the 1200s;
- kohlrabi was created by selecting for a thicker stalk in a kale plant around the 1400s; and,
- Chinese broccoli, another sub-species, was selectively bred in China from a kale predecessor in the 1500s.

The selective breeding of *Brassica oleracea* into a range of nutritionally valuable cultivars from an almost indistinguishable shared ancestry shows that humans have been successful in modifying the genetics of our food for a very long time.

- **livestock:** increased milk production; improved docile nature, reproductive performance, feed efficiency, reduced methane production, longevity, quality and structure of fibres.

Over time the repetitive application of this technique over many generations can produce dramatic results at a species level, for example breeding wild wolves into corgi dogs. The long history and familiarity with selective breeding methods means that they are widely used and accepted.

Risks or limitations of this breeding technique

Results generated through selective breeding are uncertain and often don't produce the targeted trait as selective breeding:

- targets the physical traits rather than the underlying gene(s);
- often does not account for singular physical traits being produced by a variety of genes; and,
- acts upon the entire genome of the organism, including all its natural mutations, both good and bad.

Multiple, unwanted offspring may be produced through selective breeding. The random nature of the technique often leads to very long timeframes to produce the desired result. It can often take years to achieve the intended result in complex organisms such as plants or animals, but is faster for less complex organisms such as bacteria for cheese production, for example.

The concentration of undesired traits within a species creates additional risk, leading to vulnerability and resulting in birth defects or susceptibility to pests and diseases. A good example of this is the *Gros Michel* bananas, grown commercially in Central America from the 1830s, and once the dominant export banana for Europe and North America. Selective breeding created a plant variety that was especially susceptible to disease; it was largely wiped out in the 1950s because of this[8].

From simple grass to high yielding commodity

The selective breeding of corn has produced a dramatic alteration. Corn, or maize, began as a wild grass called teosinte that had tiny ears with only five to twelve kernels. Modern plans can produce ears of corn with up to twelve hundred kernels.

Historians believe the people who lived in central Mexico were the first to develop corn about 5-7000 years ago. Teosinte kernels had a hard coating[9] that was unpalatable to humans and it was selectively bred to reduce this. By purposefully propagating and growing only those teosinte plants with softer kernel coatings and the largest number of kernels, teosinte was selectively bred into modern corn[10] over hundreds of years.

Teosinte

Modern Corn

It is also possible that selective cross breeding within species will not always result in a positive or safe outcome. For example, the Lenape potato cultivar was first released in 1967. A wild potato was crossed with another potato known for its resistance to the insect pest 'blight', as well as its low sugar content, making it particularly good for potato chips. It was removed from the market in 1970 after it was found to cause nausea due to high levels of naturally occurring toxins (solanine).

Random mutagenesis

What is it?

Mutagenesis is a process by which an organism's DNA is altered by an induced mutation through chromosomes being broken apart.

Mutations are the primary source of all genetic variation in any organism, including humans. It is a natural process, which occurs spontaneously and slowly – over generations – in people, plants, animals, and all other living beings. The natural process is driven by mistakes in the replication of DNA in cell division, through such things as radiation from the sun, and infections by viruses. In the 1920s researchers figured out how to induce mutagenesis via the application of mutagens such as chemicals and radiation for example, which breaks apart DNA, causing changes to the genome that result in random mutations.

Whilst random mutagenesis can produce a change in a single DNA base that is, a single point along the DNA, it does not offer much control over which DNA base is being changed, how it will be changed, or if one or many DNA bases are impacted.

What does it do?

The application of a mutagen breaks apart the DNA strands – creating double-stranded breaks (DSB), often in multiple locations, or removes sections of DNA altogether. When the DNA is repaired by the cell, the way in which it repairs itself creates changes that manifest in the organism as new traits. Whether the targeted trait is achieved or not is largely up to chance. This is because mutagenesis makes many changes across the genome increasing the frequency of change above that of the rare spontaneous mutations that occur naturally. Extensive screening is required to identify a desired mutation which requires the assessment of a large number of individual organisms to find a mutation at a particular place on the DNA. Once located, further repetitions are required to remove the other (unwanted) mutations present.

How has it been used?

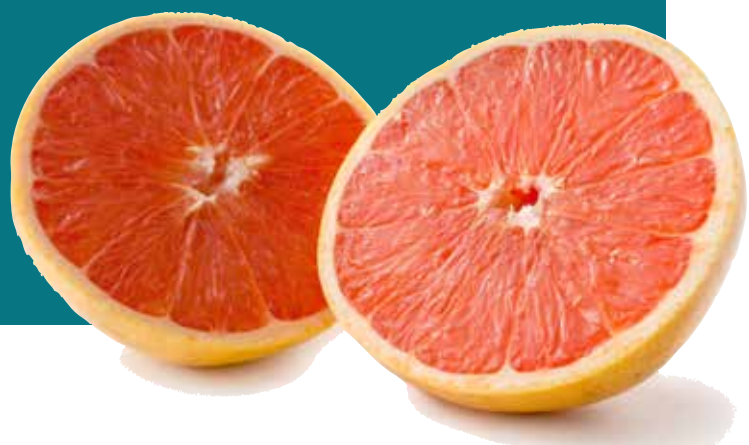
Since the 1920s, around three thousand plant varieties have been created world-wide using random mutagenesis and early site-directed mutagenesis techniques. Ruby Red grapefruit (see below), commodity crops, fruits and vegetables have been registered and brought to market. The artificially generated mutations

Ruby Red grapefruit

In 1929, farmers stumbled on the Ruby Red grapefruit, a natural mutation, with a comparatively sweet flesh. Its flesh faded to pink through the growing season, however, and scientists used radiation to produce mutants of deeper colour — Star Ruby™, released in 1971, and Rio Red™, released in 1985.

Star Ruby™ became a highly valued commodity in South Africa, Australia, Israel, Turkey, Spain, and Cyprus (Da Graça et al., 2004). It accounts for 75% of all grapefruit grown in Texas, and is available to gardeners and for commercial sale in New Zealand.

The ruby red grapefruit now on the market have inherited traits created by random mutagenesis in the parent fruit. The offspring themselves have not been subject to modification and can be marketed as conventional or organic foods.



have improved yield, quality, taste, size, resistance to disease and have helped plants adapt to diverse climates and conditions[11].

Risks or limitations of this breeding technique

Random mutagenesis cannot target specific regions or sequences of the genome. While the early site-directed mutagenesis methods could be used to produce a change in a single nucleotide, they did not offer much control as to which nucleotide is being changed. Because of the relatively random nature of results, this method can be particularly uncertain in terms of both timing and outcome.

New Breeding techniques

Genetic technology has advanced significantly since the early techniques of the 1970s. The New Breeding Techniques (NBTs) are a group of methods that allow for the gene editing of plants and animals by creating specific changes to their DNA, and target traits more precisely and more quickly. There is no definitive 'set' of techniques that have emerged from recent advances in biotechnology that fit under the umbrella term NBTs.

NBT terminology

Understanding the difference between NBT techniques is important because different regulations apply to different techniques and can vary by country. *Transgenesis* falls under Genetically Modified Organism (GMO) regulations or food safety protocols in most countries. However, *cisgenesis* and *intragenesis* techniques are exempt from GMO regulations in several jurisdictions where the outcomes of these techniques are judged to be the same, or at least as safe as, traditional selective breeding techniques.

Transgenesis, cisgenesis and intragenesis

Transgenesis describes the process of introducing a transgene, or foreign gene, from a different species with the aim of the resulting organism exhibiting some new characteristic that could not be achieved through selective breeding due to a reproductive barrier.

Cisgenesis describes a process where DNA from the same, or a closely related species, is inserted into the organisms genetic information without changing the inserted DNA sequence or arrangement.

Intragenesis is similar to cisgenesis, except the DNA to be inserted is changed from its original form, often to include additional pieces of DNA from the same or a closely related species[12], and/or rearranged in some way before being inserted in the genome.

Transfer of a gene (cisgenesis) or combination of genes (intragenesis) between organisms of the same species, or from a cross-compatible species, is different from transgenesis in that it uses no foreign DNA. Cisgenesis may lead to a new organism that is indistinguishable from its wild relative and could feasibly be produced via selective breeding, intragenesis, on the other hand, may produce an organism that is not obtainable by selective breeding alone.

Increased eggplant resilience reduces insecticide use

Known as eggplant, brinjal or aubergine this widely consumed plant has a number of variations and is widely grown in tropical and sub-tropical regions. It is prone to a 30-60% yield loss from the Eggplant Fruit and Shoot Borer (EFSB) even if the crop is repeatedly sprayed with insecticides. In the major growing areas of Bangladesh this can be up to eighty times in a 4-5 month growing season, leaving high levels of pesticide residue on the fruit which, in turn, kills beneficial insects, exposes farm workers to hazardous chemicals and contributes to local environmental pollution. However, it is an important cash crop for small, resource-poor Bangladeshi farmers – a genetically modified cultivar was developed and is now grown on nearly 50,000 hectares (2022).

The genetically modified *Bt Brinjal* eggplant was created through a public-private partnership between Indian seed company Mahyco and the Agricultural Biotechnology Support Project II, funded by the USA Agency for International Development. The Bangladesh Agricultural Research Institute (BARI) was provided with the transgene to create four further GM insect-resistant varieties that were approved for cultivation by the National Committee on Biosafety (NCB) of Bangladesh in October 2013.

The *Bt Brinjal* varieties are open-pollinated, allowing farmers to save seed for re-use, although farmers are discouraged from doing so across multiple seasons because of the potential for outcrossing to other varieties, especially to non-*Bt Brinjal* plants grown in bordering 'refuge' rows as part of a resistance management strategy.

Several studies have documented the performance of *Bt Brinjal*, finding that there are significant yield and revenue benefits (average yield increase of 19.6% and revenue increase of 21.7%) and reduced expenditure (61%) for farmers that grow *Bt Brinjal* (2016-17)[13]. In a two-year study ending in 2018, researchers found that all four *Bt Brinjal* varieties provided virtually complete control of EFSB without the use of insecticides for EFSB control[14].

A government impact assessment in 2018 found that *Bt Brinjal* leads to:

- 95% reduction in EFSB infestation;
- 56% reduction in the environmental toxicity of pesticides used;
- 10% reduction in self-reported symptoms associated with pesticide exposure among individuals in households growing *Bt Brinjal*;
- 42% increase in yields; and,
- US$400 increase in profit per hectare[15].

Site-directed mutagenesis

In the 1970s scientists discovered a way to make mutagenesis more targeted – a process called site-directed mutagenesis[16]. Early methods of site-directed mutagenesis enabled scientists to determine where on the DNA a change would be made, but exactly what that change was could not be controlled.

Longer lasting potatoes

The Ranger Russet potato is a good example of site-directed mutagenesis.

A non-GMO but gene-edited potato variety was created by USA plant geneticist Dan Voytas of Cellectis Plant Sciences, and released to market in 1991. He used TALENs techniques to remove the vacuolar invertase gene (VInv), believing that without it the potatoes' storage time could increase without any quality impairment.

This potato doesn't accumulate sweet sugars at typical cold storage temperatures, meaning that it will last longer. An added advantage of Ranger Russet is that, when it is fried, it does not produce as much acrylamide, a suspected carcinogen.

Voytas's gene-editing technique left behind no trace other than a few deleted letters of DNA.

Site-directed nucleases

The site-directed nucleases (SDN) are a suite of techniques for modern site-directed mutagenesis that have been created since the 1990s. They fall under the category of NBTs in many policy-related conversations because of their ability to be tailored for a range of uses.

This sub-group includes:

- Zinc-Finger Nucleases (ZFNs);
- Transcription Activator-Like Effector Nucleases (TALENs);
- Clustered Regularly Interspaced Short Palindromic Repeats CRISPR-associated protein 9 (CRISPR-Cas9); and,
- evolving technologies using elements of the CRISPR-Cas system.

These techniques are all artificially generated but are based on naturally occurring components, such as proteins occurring in animals, plants, fungi and algae[17].They represent advances in targeting that improves significantly through ZFN and TALENs, and then by an even larger increment with CRISPR.

What do they do?

Each SDN is used to create a double-stranded break (DSB) at a targeted site that is responsible for a particular characteristic. Three results are possible:

- the break is repaired by the host organism without further intervention. This can result in mutations that change the function of the gene, normally disabling it (Type 1);
- a DNA template is provided to convert the gene to another version from the same or a different species (Type 2); and,
- a DNA template is provided, and a new (trans)gene is inserted at the DSB site (Type 3).

SDNs make it possible to modify a range of agriculturally important plants and animals relatively easily and cheaply, and without permanently introducing foreign DNA sequences[18].

How have they been used?

ZFNs, TALENs, and CRISPR-Cas9 have been used to achieve similar goals in both plants and animals: productivity, resilience, lower inputs and lower greenhouse gas emissions. A key feature of these techniques is their ability to produce new organisms at speed, meaning commercialisation can be completed in a relatively short time.

A literature review of two hundred and thirty one studies by Menz et al. (2020) found that globally, between 1996 to 2020[19]:

- 41 plants for commercial purposes were developed using ZFNs, TALENS and CRISPR-Cas9 and,
- 140 different applications of the techniques were identified; most for soil management and crop production purposes[20] as well as food and feed quality, and organism stress tolerance.

Specific SDN applications include:

ZFN has been used to genetically modify kale, cress, tobacco, maize, petunia, soy bean, rapeseed, rice, apple and fig. Some applications of the technique include the development of:

- herbicide tolerant maize). This maize cultivar also reduces the amount of phytate which naturally accumulates in the plant. Phytate is a component of seeds which impairs the absorption of iron, zinc, and calcium in humans; and
- transgenic cows which produce milk containing lysostaphin, which helps relieve mastitis. Due to different laws and regulations affecting GMO, these animals are only commercially available in a few regions.

TALENs has been applied across a variety of crops, for example, to create:

- blight resistant rice – a bacterial disease that causes yield loss, in some cases up to 70% losses in environments favourable to the disease (the earlier the disease occurs, the higher the yield loss);
- powdery mildew resistant wheat – a fungal infection that impact the health of plants and reduces their yields;
- improved nutritional profile and shelf-life of crops (soy beans, tomatoes and potatoes); and,
- disease resistance in pigs (African Swine Fever) and cattle (*Mycoplasma bovis*).

CRISPR-Cas9 has become the most common tool for crop improvement due to its versatility. Some examples of CRISPR-Cas-9 uses are:

- crop quality improvement: physical appearance, edible quality, shelf-life, fruit texture and nutritional value of key crops such as tomato, rice, wheat and soy bean;
- development of nutrient-enriched fruit and vegetables such as:
  - increased carotenoid content in banana, rice, and tomatoes;
  - increased y-Aminobutryic acid[21] content in tomatoes and rice;
  - increased micronutrients such as selenium, zinc, iron, and iodine in rice; and,
  - improved fatty acid composition in soy bean, rapeseed and camelina; and
  - reduced concentration of unwanted substances in rapeseed (phytic acid), wheat (gluten proteins), and rice (cadmium).

Globally, research activities employing genetic technology are continuing to increase, raising the number of plants, animals and micro-organisms created by genetic engineering to meet market and environmental demands.

Risks or limitations of this breeding technique

While it is possible to affect a gene, other than the one targeted, using SDNs, evidence to date suggests these techniques have less unintended outcomes than traditional breeding and certainly no more.

There are public perceptions of risk associated with plant, animal and human health, however, there is no evidence that producing new organisms using gene editing is more likely to have unintended consequences than using selective breeding. While gene editing is much less likely to introduce unforeseen outcomes than the less precise mutagenesis technique, it is possible for cuts to occur in unexpected places. Even though off-target impacts happen much less than they do with non-direct mutagenesis, it is still an issue that needs to be monitored.

Healthier soya bean oil

Oils with low polyunsaturated fats are considered to be a healthier alternative to those high in polyunsaturated fats which can hydrogenate and produce unhealthy trans-fatty acids. Soy bean varieties with low levels of polyunsaturated fats have been developed via TALENS, using foreign DNA, by US company Calyxt. The resulting product, Calyno™ oil, comprises approximately 80% oleic acid and up to 20% less saturated fatty acids than conventional commodity soy bean oil, and contains no naturally occurring or added trans fats.

Calyno was released in the USA in 2019, making it the first commercialised product from a gene-edited plant sold to the foodservice industry – a non-transgenic, premium feed ingredient with enhanced nutritional benefits for livestock.[22]

Slick gene makes cool cows

Heat stress is a challenge for dairy farmers around the world, with many using different cooling systems to help tackle hot and humid seasons. In some regions and operations the solution isn't straightforward, especially as climate change related heat wave events are increasing in frequency.

Enter, Slick genetics. 'Slick', or short-haired, cattle were bred on the Caribbean island of St. Croix from Senepol cattle stock. The slick-hair coat is caused by a natural gene mutation which gives cattle the ability to better regulate their internal body temperature with an increased capacity for sweating. The Slick 'allele' (or one of the pair of genes determining a characteristic) is dominant and therefore the slick-hair characteristic is observed in the cattle. The characteristic is passed on to off-spring.

Scientific studies have shown that cattle with this extremely short, slick-hair coat are better able to withstand hot weather. Cattle that are not stressed by heat and comfortable in their environment are less likely to experience temperature-related stress, resulting in improved body weight and more efficient food production. The characteristic can improve animal welfare in warmer climates.

Gene editing has been used to include the 'Slick' mutation into beef cattle. Slick cattle were approved for sale and consumption in January 2022 by Brazil's Ministry of Science, Technology and Innovations, which declared that the cattle are not genetically modified and hence not subject to GM laws. In March 2022, the US Food and Drug Administration declared that products from the CRISPR-edited cattle pose no risk "to people, animals, the food supply, and the environment."

The New Zealand Livestock Improvement Company (LIC) identified the Slick gene in 2014 and began a breeding programme to incorporate the mutation into elite New Zealand dairy animals. "Over the past seven years we've been crossing Senepol beef sires with New Zealand dairy cows to breed Slick bulls that could potentially produce a more heat tolerant dairy herd in the future," LIC Chief Scientist, Richard Spelman, February 2022.

Overseas CRISPR-Cas9 is being used to modify the slick-hair coat gene. Natural mutations can be selectively bred into dairy herds from beef cattle. In New Zealand the same result has been achieved by selective breeding over several generations of livestock.[23]

Evolving techniques

What are they?

Researchers continue to investigate new gene editing techniques that use a modified CRISPR-Cas9 system that do not create double-stranded breaks (DSBs) as older techniques do. These evolving techniques include:

- base editing;
- prime editing; and,
- programmable addition via site-specific targeting elements, or PASTE.

These emerging techniques have not yet been widely applied in a food and fibre sector setting. However, they offer an opportunity to further improve the precision of current applications genetic technology applications.

What do they do?

Improving on CRISPR-Cas9, these new and evolving methods allow targeted gene manipulation without the creation of double standard breaks in DNA.

Base editing

Developed in 2016 Base Editing is a CRISPR-Cas9-based gene editing method that efficiently converts one base pair to a different base pair without inducing a DSB. Two major classes of base editor have been developed:

- cytosine base editor (CBEs) which allows the conversion of a C:G to a T:A base pair; and,
- adenine base editor (ABEs) which allows the conversion of an A:T to a G:C base pair[24].

Although it hasn't been used to develop a food product, a medical trial using base editing to correct a gene involved in hypercholesteremia (a human cholesterol disorder) is currently under way in New Zealand[25].

Prime editing

Developed in 2019, prime editing differs from the CRISPR-Cas9 system by employing a DNA mismatch repair rather than relying on NHEJ or HDR26 to fix the DNA break . What sets prime editing apart from base editing is that it expands the number of potential new combinations of bases in pairings.

There are currently four prime editor (PE) iterations**:**

- PE1, the first version developed that demonstrated insertions, deletions, and base transversions at modest editing efficiencies;
- PE2, contains further modifications that led to improved binding and thermostability;
- PE3 and PE3b, which include the ability to mend the mismatch sequences that occur with prime editing; and
- twin prime editing (twinPE), enables the editing of large DNA sequences, potentially of the whole gene rather than just a portion of it.

Programmable addition via site-specific targeting elements (PASTE)

Developed in 2022 PASTE, can be described as a 'drag and drop' technique for gene editing. The technique incorporates prime editing and it enables the targeted insertion of large DNA sequences (up to 36,000 bases), without creating DSBs. Scientists can now simultaneously, and precisely, insert three different genes at three different points on a chromosome, and with fewer off-target effects. This is important for traits that are controlled by multiple genes. Previous genetic techniques have not been able to alter these traits. PASTE allows for large-scale precision gene editing enabling new applications in basic research, cell engineering and gene therapy.

Risks or limitations from these techniques

These techniques are so new and evolving so rapidly that there is minimal data on potential risks and limitations. Base editing applications are limited by their ability to make only four out of the twelve possible base combination changes. However, prime editing is capable of making all twelve combination changes. The extent to which these advanced techniques create off-target effects is believed to be minimal compared to the New Breeding Techniques.

Summary

The use of any of the genetic technology outlined here, can only be employed subject to the rules, laws and regulations of the countries in which they occur, and in some cases, where the goods are traded if they are produced elsewhere.

The emergence of genetic technologies in the 1970s generated an immediate international response with communities seeking guidelines on how to balance potential benefits with potential risks. Each nation and jurisdiction put in place legal and regulatory frameworks aimed at balancing risks and benefits in a way that is safe for people, animals, and the environment.

In the 1990s concerns about the release of organisms altered with foreign DNA (transgenic), led to many countries adopting a cautious approach to genetic technology in general. Over the last decade progress in achieving greater precision through NBTs has seen the global regulatory trend move to a more trait-based and proportionate risk approach, the product is assessed for safety not the process which has produced it.

The next section presents some illustrative examples of how genetic technology regulations have evolved over more than two decades, and how jurisdictions are now approaching legal and regulatory frameworks to ensure that technology, regulation, and social licence are harmonised.

For a deeper understanding of this topic Te Puna Whakaaronui highly recommends taking the time to read the New Zealand Royal Society Te Apārangi's, *Gene Editing for the Primary Industries* (2019), available on their website.

Section 2: Global regulations

Regulatory systems provide the rules for all participants within a market, they provide even opportunity between participants, promote positive outcomes, and manage perceived risks to ensure the safety of all participants in the market from producers and providers through to consumers. As with all new technologies sufficient 'checks and balances' and 'minimisation of risk' is a primary consideration – especially when only limited data is available. However, as markets mature, and more information becomes available regulations are reviewed and amended. These cycles are normal practice and an ongoing process within and across regulatory systems around the globe.

Early regulation

A game changing biotechnology breakthrough occurred in 1973 when scientists Herbert Boyer and Stanley Cohen engineered the first successful genetically modified organism by very specifically cutting out a gene from one organism and pasting it into another (transgenesis)[27]. This discovery led to the first synthetic production of human insulin, now a US$18 billion industry.

Suddenly a world of possibilities for the new technology presented itself. Alongside the positives came the potential negative ramifications for human health and the earth's ecosystems, generating many scientific, economic, political, and ethical questions. So significant and universal were these 'unknowns' that in 1974 a worldwide moratorium on genetic engineering projects was observed until experts, scientist, lawyers and government officials could get together to debate the issues and decide on next steps. This took place at the Asilomar Conference on Recombinant DNA in 1975, where the safety of genetic modification experiments was debated for three days.

The eventual conclusion from the Asilomar Conference was that GMO projects should be allowed to continue with certain guidelines in place. Safety and containment regulations were defined to mitigate the risks of each experiment, and accountability protocols were also put in place. A key outcome from the conference was the expectation that the guidelines would be fluid over time, so that changes would emerge, based on the growing knowledge and understanding of the technology[28].

This is the context from which GMO regulations were first developed and which, in the 1990s, were embedded into policy settings around the world, under a variety of approaches. Most approaches were underpinned by varying degrees of caution or the *precautionary principle* (New Zealand and the European Union), with the single universal thread guiding all regulations being the aim of each country to balance the benefits of new technologies (including competitive, economic, health and environmental benefits) with the need to keep humans, animals, and the environment safe. The EU's legal framework articulates the key objectives well:

1. protect human and animal health and the environment by introducing a safety assessment of the highest possible standards at EU level before any GMO is placed on the market;
2. put in place consistent procedures for risk assessment and authorisation of GMOs that are efficient, time-limited, and transparent;
3. ensure clear labelling of GMOs placed on the market in order to enable consumers as well as professionals (e.g. farmers, and food feed chain operators) to make informed choices; and,
4. ensure the traceability of GMOs placed on the market[29].

The resulting regulations were designed to manage the risks associated with the use of the technology and to manage the potential impact from GMOs that were either consumed or released into the open environment.

The evolution of regulatory regimes

The 1980s and 1990s were a formative time for GMO regulatory regimes and from then to the present day, everywhere in the world where there is the regulatory infrastructure to support it, the use and release of GMOs continues to be treated with caution and subject to rigorous safety assessment before being approved for release. However the legal and regulatory frameworks implemented by different jurisdictions vary and have become less consistent over time, especially as the technology has developed in the areas of intragenesis and cisgenesis[30] for which there is a growing trend of a lighter touch in regulation, similar to those that apply to traditional breeding techniques.

When New Genomic Techniques (NGTs) are not GMO

There is no international consensus on mandatory regulation or labelling of GM food, and food that contains GM ingredients. Neither is there an internationally agreed threshold level of genetic material in a food product that would make labelling compulsory[31].

Individual national priorities, coupled with the pace of technological change, have resulted in differences in regulatory settings around the world. What varies most are the regulatory approaches governing NBTs. There are now a growing number of jurisdictions judging that the precision NBTs enables produces outcomes that are the same as, or at least as safe as, traditional breeding techniques.

The resulting regulatory regimes in many cases (such as the USA, Australia, Canada, Japan, India, and Argentina) have excluded NBTs from the more restrictive regulatory mechanisms that apply to *transgenic* GMOs. This is consistent with the very early safety considerations around GMOs and the expectation that regulations and guidelines would be influenced by developments in genetic technology and the growing body of knowledge and understanding of the risks.

Original approaches

The two original approaches to regulation were:

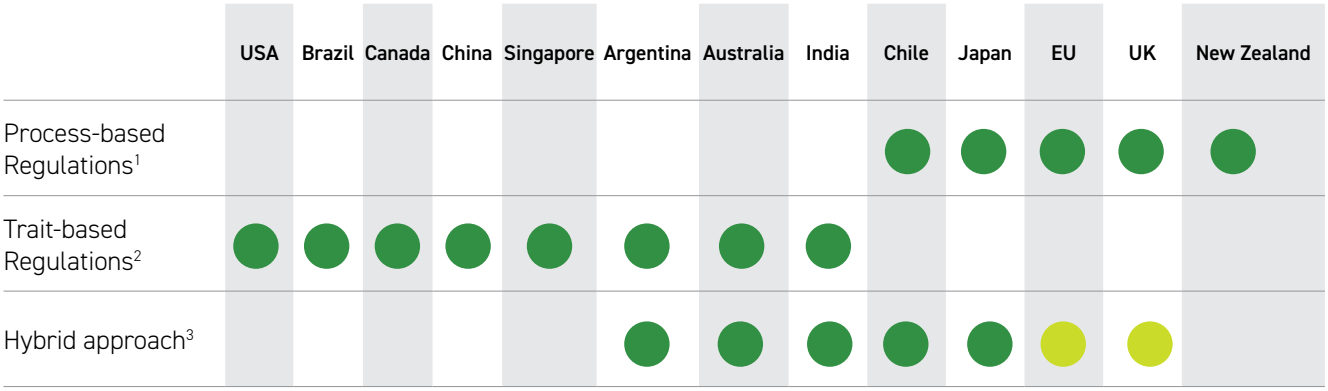
- a focus on the process; and,
- a focus on the product (trait).

Recent international trends in regulating genetic technology have evolved into a third approach – essentially a hybrid approach[32] – where GMO regulatory regimes and the associated strict safety protocols remain in place, but NBTs are excluded from GMO definitions in those jurisdictions that judge NBTs to be sufficiently similar to, or as safe as, products of traditional breeding techniques.

Regulations have evolved into three approaches overtime:

1. **focus on the process:** regulatory restrictions apply to GMO products *and* products produced using GMO at any stage of the production **process** (except for cheese);
2. **focus on the product:** regulatory restrictions apply to products with GM and/or novel **traits** and require safety assessments on GM foods before being approved for release in market; and,
3. **hybrid systems have exemptions:** products produced via NBTs are exempt from GMO regulatory restrictions that continue to apply GMOs (i.e. the presence of *transgenic* material).

Figure 1: International approaches to GMO regulation



Notes:
1. Includes GMO products and those produced using GMOs in the process.
2. Regulates based on novel traits.
3. Transgenic GMOs regulated but products of NBTs exempt.

International trends

Among our main trading partners, the UK, EU and New Zealand are currently the only remaining jurisdictions whose regulations remain purely process based, described on the following page, part (a), of the EU definition. However, the UK has a bill before Parliament, ***the*** *Genetic Technology (Precision Breeding) Bill 2022-23* [33] which, if passed would exempt NBTs from its broader GMO regulations, and the EU is also well into a regulatory change process that is heading in the same direction.

The Figure 1 on page 23 illustrates which countries (relevant to New Zealand as either, important export markets, or that produce competing products), have which regulatory approach, and those considering exemptions from GMO regulations for NBTs.

The following sections describe some of the evolution and implementation issues of the EU's GMO regulation over the last three decades.

European Union

Establishing EU regulation

In the mid-1980s a lack of harmonised national GMO regulations, and a lack of regulation in some Member States, was found to be detrimental to the achievement of the EU's internal market. The European Commission pushed for a coherent regulatory approach across the European Union's Member States with two major objectives at the forefront:

- protecting health and the environment; and,
- guaranteeing the free circulation within the European Union of products originating from genetic engineering.

The excerpt below is from the EU GMO Directive which governs how the EU regulates GMOs and illustrates how the regulation is *process* focused. It reflects the state of biotechnology in 1990s and early 2000s.

Qualitative and precautionary basis

The EU directives are qualitative in scope, they have no value limit or quantitative threshold. They provide a notification and authorisation system for activities involving Genetically Modified Micro-organisms (GMMs) or GMOs with the main objective being preventative risk management for both human health and the natural environment. The GMO Directives were developed to be consistent with the precautionary principle prevailing in the EU and reflect the general principle that 'risks from any contained use or deliberate release of GMOs should be assessed on a case-by-case basis before an activity could be authorised'.

A genetically modified organism (GMO) is defined under 2001/18/EC, Part A as being:

"... an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination; and within the terms of this definition as set out in Part I A, (a) and (7) of the directive:

(a) Genetic modification occurs at least through the use of techniques listed in Annex I A, part 1, these are stated as being:

- Recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not naturally occur but in which they are capable of continued propagation.
- Techniques involving the direct introduction into an organism of heritable material prepared outside the organism including micro-injection, macro-injection, and micro-encapsulation.
- Cell fusion (including protoplast fusion) or hybridisation techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally.

(7) "Product" means a preparation consisting of, or containing, a GMO or a combination of GMOs, which is placed on the market[34]."

European environmental regulation is based on the precautionary principle in the case of scientific uncertainties, it adopts preventive measures against damage and takes into account the worst-case scenario and the highest risk. In practice, a scientific risk assessment is required before a GMO product can be placed on the market. The European Food Safety Authority (EFSA)[35] implements the risk assessment process and closely co-ordinates its activities with Member States.

Assessment process

The EFSA has a GMO Panel which publishes guidance documents for food or feed product GMM risk assessment[36]. The assessment consists of two parts:

- the characterisation of the GMM; and,
- the possible effects that the modification might have on the safety of the product itself.

Higher crop yield through GMM improved soil microbes

The development of next-generation genetic technologies, coupled with recent advances in understanding the role of the plant-soil microbiome, has led to the development of new GMMs for improved crop productivity.

Soil microbes naturally have a mutually beneficial synergistic relationship with plants, including a capacity to fix nitrogen. By tailoring such micro-organisms, the dependence on synthetic fertilisers can be reduced. In the USA, Pivot Bio has employed this concept to develop a biological fertiliser. Their product, ProveN™, exploits a corn-root-based bacterium, activating once dormant nitrogen-fixing genes by turning on a genetic switch.

Their latest product, ProveN-40, replaces up to forty pounds per acre of synthetic nitrogen and is utilised on over 1.4 million acres of farmland growing corn in the USA. In the majority of instances (93%), ProveN-40 performed similarly or better than standard practices, with an average increase in biomass of 12%. The environmental benefits of this solution are substantial, as synthetic nitrogen fertilisers are estimated to contribute to approximately 10.6% of agricultural emissions and 2.1% of global GHG emissions.

Such benefits are observed both in production and efficiency. Synthetic nitrogen fertilisers are synthesised through a chemical-based and energy-intensive Haber-Bosch process. When applied, approximately half of the reactive nitrogen is lost to the environment through either leaching leading to nitrates in waterways or volatilisation, leading to nitrous oxide emissions. By contrast, GMM produced by Pivot Bio are produced through a low-energy fermentation process, the GMM adheres to the roots of plants (making it less subject to rainfall and preventing it from volatising into the air).

Pivot Bio GMM microbes have been commercially available since 2019 and approved in thirty three states within the USA. In 2022 they expanded into Canada, where product trials are underway on corn, wheat and canola.

Source: SCION

It also establishes that the characteristics of the GMM consist of different parts, that are individually evaluated, such as:

- the parental organism;
- the donor of the genetic material used;
- the type of genetic modification;
- the final GMM and its traits;
- the composition, nutritional value, potential toxicity/ allergenicity; and
- the impact of the product on the environment.

After the risk assessment is complete, the outcome goes through scientific evaluation to declare whether it raises safety issues. This evaluation is used by different European regulatory authorities to decide whether the product should be authorised for commercial use.[37]

Increasing regulatory complexity

Some specific genetic modification techniques are identified and excluded under a section of the Directive on the condition that they do not involve the use of recombinant nucleic acid molecules or genetically modified organisms made by techniques other than those specifically excluded,[38] these are:

- mutagenesis (definition page 4); and,
- cell fusion (definition page 4).

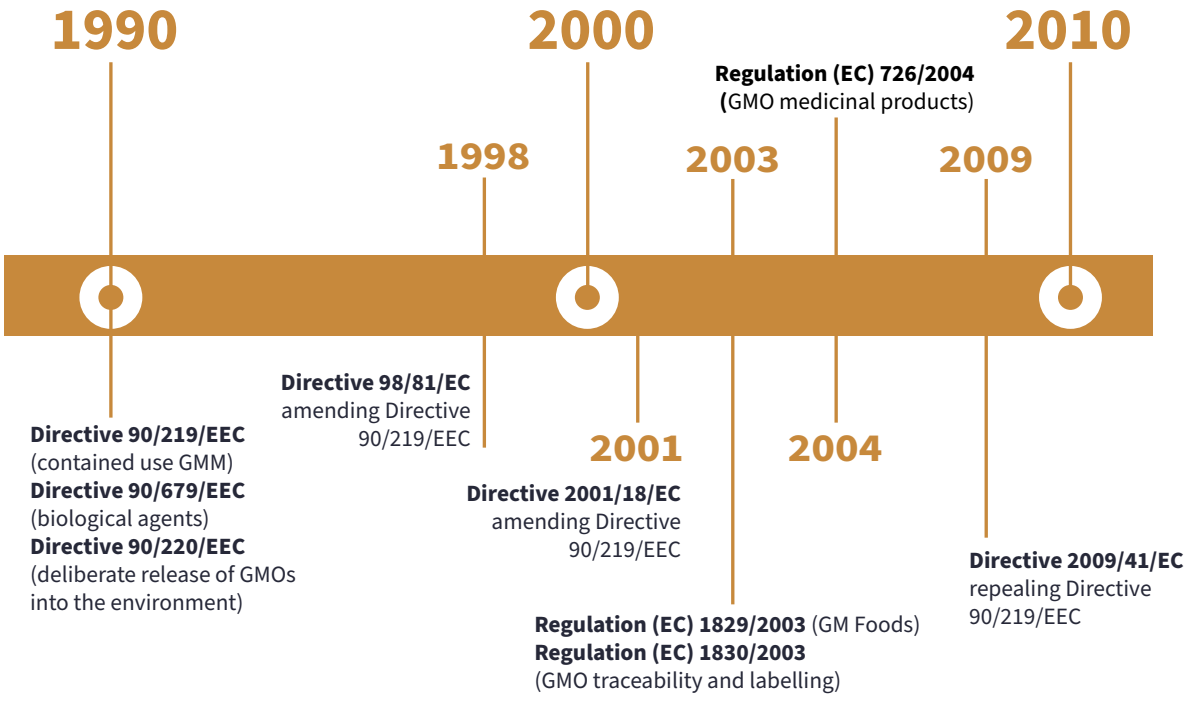
Drivers of regulatory amendment and change

Over the last three decades the main issues that have prompted review and re-consideration of the EU's regulatory settings can be summarised as:

- economic considerations focused on ensuring that advances in international biotechnology do not adversely affect the EU's ability to be competitive in the global market;
- the efficiency and effectiveness of the regulatory regime and its application across EU Member States; and,
- the extent to which the GMO Directives, and their amendments, remain fit-for-purpose in the context of the EU's broader environmental, health and economic objectives as set out in the European Green Deal and the Farm to Fork Strategy[39].

The EU has recognised that several layers of amendments over the years (illustrated in Figure 2 below) have increased regulatory complexity and ambiguity.

Figure 2: Historical amendments to the EU's GMO Directive[40]



Source: Belgian Biosafety Server

European Commission study on the status of new genomic techniques under European Union law

Key findings

In 2019 the European Council, having regard to biotechnology advances, the suite of tools available to help Europe achieve its broader aspirations and a 2018 European Court ruling on GMOs[41], requested the European Commission[42] provide a study on new genomic techniques.

The Council also asked the Commission to "submit a proposal, if appropriate, and in view of the outcomes of the study, or otherwise to inform the Council on further measures required as a follow-up to the study"[43]. This was to be accompanied by an impact assessment. The study was published in April 2021.

For the study, the European Commission defined "new genomic techniques" (NGTs) as techniques that are capable of altering the genetic material of an organism and that have emerged or have been developed since 2001, when the current legislation on GMOs was adopted.

The study confirms that organisms produced through NGTs fall under existing GMO legislation but that developments in biotechnology, combined with poor definitions of key terms, give rise to ambiguity of interpretation, and contribute to regulatory uncertainty.

The EC study explains that NGTs constitute a diverse group of techniques, each of which can be used in a number of ways to achieve different results and products. For this reason, says the study, safety considerations should be determined according to the technique, how it is used and the characteristics or traits in the resulting product, and cannot be made on all techniques as though they were all the same.[44]

The study explains that for certain NGTs[45], EFSA found no new hazards compared to both conventional breeding and established genomic techniques. EFSA also made the point that random changes to the genome occur independently of the breeding methodology. That is, insertions, deletions or rearrangements of genetic material arise in conventional breeding, genome editing, *cisgenesis and intragenesis*. In addition, EFSA has concluded that off-target mutations potentially induced by site-directed nuclease (SDN) techniques are of the same type as, and fewer than, those mutations in conventional breeding. Therefore, in certain cases, targeted *mutagenesis* and *cisgenesis* carry the same level of risk as conventional breeding techniques.

Implementation and enforcement challenges

Implementation and enforcement challenges also arise in relation to detection as several NGT products contain no foreign genetic material. On the other hand, where detection methods can detect small alterations in the genome, these might also have occurred as a result of conventional breeding. So in that case, even though the genome alteration is detected, the fact that it is has occurred through conventional breeding means that it would not be subject to the GMO legislation. Hence compliance with the legal requirements to submit a reliable detection method might be impossible in certain cases.

Commercial and economic considerations

The study also cites reports of negative commercial and economic impact following the 2018 European Court[46] ruling and confirmed that even though there is considerable interest in research on NGTs in the EU, most of the development is taking place outside the EU. Further negative impacts were reported regarding public and private research on NGTs and have been attributed to the current regulatory framework.

Delivering on food security, environmental, sustainability, and resilience objectives

Another primary consideration is the potential for NGTs to contribute to the objectives of the EU's Green Deal, especially the Farm to Fork, biodiversity strategies, and including the UN's Sustainable Development Goals for a more resilient and sustainable agri-food system. Examples cited in the study include plants that are more resistant to diseases and environmental conditions or climate change effects in general, improved agronomy and nutritional traits, reduced use of agricultural input (including plant protection products) and faster plant breeding.

Public responses to EU consultation

Consultation shows a wide range of views on GMOs across society and stakeholders. Concerns from some stakeholders over any sort of genetic modification prevail and there are opposing views on the need to label NGTs as GMOs and on the effectiveness of such labelling in providing useful information for consumers.

Respondents to consultation undertaken for the EC study expressed diverse, sometimes opposing views regarding the level of perceived safety of NGTs and their products, and on the need and requirements for risk assessment. Case-by-case risk assessment was widely recognised as the appropriate approach[47].

The pace of technological change and harmonising regulatory settings

Evaluations made in the course of the study also conclude that the rate of innovation in the global biotechnology sector is unlikely to slow down and keeping the legislation relevant is likely to be an ongoing challenge. This is especially so if the focus remains on the techniques used, rather than the characteristics of the final products and the traits they express. These innovative technologies continue to create new challenges for the existing regulatory system.

Summary of EU 2021-2022 regulatory change process

Overall, the EC study found NGTs have significant potential to contribute to a more sustainable food system which would contribute to the objectives of the European Green Deal[48] and the Farm to Fork Strategy[49], and that the EU's current GMO legislation, adopted in 2001, is not-fit-for purpose.

The EC 2021 study concluded that, the EU's GMO regulations have become extremely complex, have not kept pace with technology and are no longer fit-for-purpose. It found that regulating solely for safety will not help the EU meet its overarching objectives for practical safety procedures, competitiveness, delivering on the European Green Deal, its Farm to Fork strategy, sustainability, and resilience goals.

The EC, appreciating the need for societal points of view and social licence for regulatory change, undertook a twelve-week public consultation process from 29 April-22 July 2022 and published responses in September 2022.

If the study's findings translate into regulatory change, the result will be a trait-based risk appropriate regulatory regime.

EC study's main conclusion

The study's concluding finding on regulation is that a purely safety-based risk assessment is unlikely to be enough to promote sustainability, and contribute to the EU's broader objectives, and that the benefits of the techniques need to be weighed against the risks.

Next steps are for the development of detailed regulatory change proposals with European Commission adoption planned for quarter three, 2023. Details are not yet available on precisely how the EU will change its GMO regulatory system at that time.

Source: EC study on new genomic techniques.

United Kingdom

The United Kingdom's current GMO regulations are the same as the European Union's, due to the UK having historically been an EU member until it officially withdrew on 31 January 2020 ('Brexit'). In May 2022 the UK submitted a bill for GMO regulation change which reached its final stage of consideration in the House of Lords in December 2022.

Considerations for the 2020s

The Government's motivation in submitting the bill includes the potential for:

- precision breeding to allow a range of foods with health, environmental or commercial benefits to be developed more quickly than traditional breeding methods; and,
- greater use of these techniques to help address global food security, climate change and human health challenges.

Implementation and enforcement challenges

The UK Government has recognised the regime that currently applies to all GMOs is complex and that leaving the EU provided the UK an opportunity to adopt a '*more science based and proportionate approach to the regulation*' of precision bred organisms which has led to the *Genetic Technology (Precision Breeding) Bill 2022-23*[50] being tabled before Parliament. The UK Government says the primary policy objective of the bill is to ensure plants, animals, food and feed products developed using precision breeding technologies are "*regulated proportionately to risk*" and that this will "*introduce simpler regulatory measures to enable these products to be authorised and brought to market more easily.*"[51]

Most notably, from a regulatory perspective, is that the legislation would remove gene edited organisms from the regulatory system that governs genetically modified organisms. In other words, GMO regulatory settings continue to apply to *GMOs*, but there are exemptions for *precision breeding techniques* (NBTs) .

The UK drivers to exclude precision breeding techniques from the more restrictive GMO regulations, reflect those that underpin the EU's considerations for legislative change, and begin to move closer to regulatory approaches already applied in several other countries, including Japan, USA, Canada and Australia. For example in the USA, GMOs and GM products are evaluated on the basis of risk analysis and science principles. Risk analysis on GM products in the USA follows the principle of *substantial equivalence* and is made on a case-by-case basis which means that GM products are evaluated on their risk to human health and the eco-environment with the same criteria used in evaluation of conventional (non-GMO) products.

Commercial and economic considerations

The overarching aim of the *Genetic Technology (Precision Breeding) Bill 2022-23* is to encourage agricultural and scientific innovation in the UK and for the legislation to unlock the potential for new technologies to promote sustainable and efficient farming and food production. The bill will apply to precision bred plant and vertebrate animals (excluding humans) and establish that these are gene edited[52].

The four key policy changes proposed in the bill are to:

- remove plants and animals produced through precision breeding techniques from regulatory requirements applicable to the environmental release and marketing of GMOs;
- introduce two notification systems; one for precision bred organisms used for research purposes and the other for marketing purposes. The information collected will be published on a public register on website: www.gov.uk;
- establish a proportionate regulatory system for precision bred animals to ensure animal welfare is safeguarded. Changes to the regulations for animals will not be introduced until this system is in place; and,
- establish a new science-based authorisation process

for food and feed products developed using precision bred organisms[53].

Public consultation

As in other jurisdictions, varied and often opposing views on GMO prevail across UK society. To ensure that legislative and policy change decisions consider the perspectives of the society affected by them, the Department for Environment, Food and Rural Affairs (DEFRA) conducted a consultation process encouraging respondents to share their views.

Consultation ran from 7 January 2021 to 17 March 2021 and received 6,440 responses, a summary of which was published in July 2021. It consisted of two parts:

Part 1 focused on the regulation of gene edited organisms (GEO) possessing genetic changes which could have been introduced by traditional breeding; and,

Part 2 aimed at gathering views on the wider regulatory framework governing genetically modified organisms (GMOs).

Most individuals (88%) and businesses (64%) supported continuing to regulate GEOs as GMOs. Although, when asked about criteria to distinguish GEOs from traditionally bred organisms, the most common view expressed was that scientific criteria should be established to assess risk and to test for the presence of genetic material from a different species. This suggests widespread lack of understanding that *transgenesis*, (the introduction of foreign DNA into an organism) need not occur in several NBTs[54].

Key themes highlighted in consultation responses were:

- those in favour of keeping the current regulations felt that traditional methods have a history of being safe, but that the scientific understanding of gene editing was currently incomplete;
- concerns were raised around consumer choice and public trust (including ownership and intellectual property relating to GEOs, with many individuals in support of labelling;
- those in favour of changing the regulations acknowledged the potential role of gene editing technologies in responding to sustainability and climate change issues and the benefits of gene editing technologies for farmers; and
- many businesses and NGOs called for improving awareness and understanding of gene editing through public campaigns and better education.

A key point raised by several businesses and NGOs is the need to improve awareness and understanding of gene editing through public campaigns and better education. The variable levels of understanding evident from respondents participating in the consultation suggests that understanding will be a salient issue for other jurisdictions to address when considering appropriate GMO regulations and the social licence to support them.

New Zealand

Alongside the UK and EU, New Zealand also regulates GMOs based on process rather than trait and operates an authorisation process that involves several statutory and regulatory regimes. These settings were first implemented in the late 1990s.

New Zealand's primary GMO legislation

In order to be considered a GMO, an organism must first be captured by the broad definition of a GMO under the Hazardous Substances and New Organisms Act 1996 (HSNO). If captured by this definition, the second step is to determine whether the organism is identified in the Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998 (the Regulations).

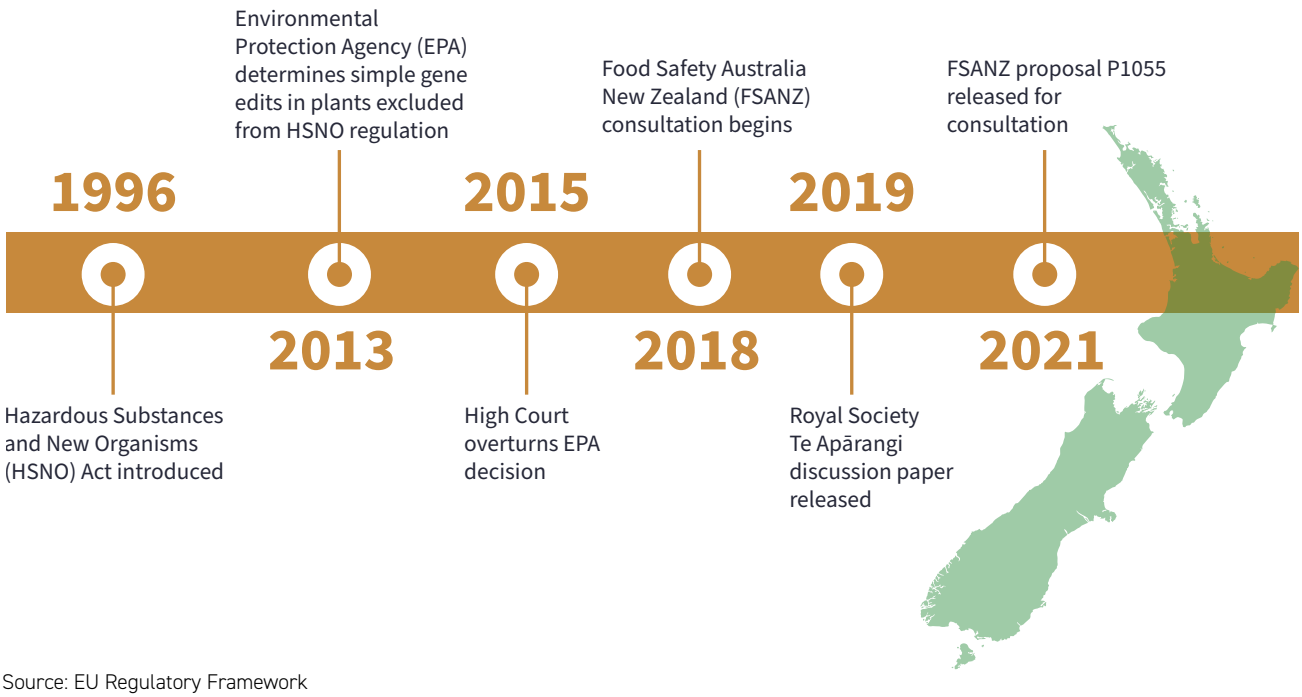
Hazardous Substances and New Organisms Act 1996 (HSNO)

"genetically modified organism means, unless expressly provided otherwise by regulations, any organism in which any of the genes or other genetic material:

- have been modified by in vitro[55] techniques; or
- are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by *in vitro* techniques".

Similar to the EU regime, regulations under the New Zealand HSNO Act explicitly prescribe organisms to be excluded from the act and not to be regarded as genetically modified for the purposes of the act. The regulations contain a list of techniques, some of which can be used to alter an organism's genome. If an organism was developed using any of those techniques, it is not considered a GMO[56]. This list constitutes the techniques in use at the time the HSNO Act was deemed to have come into effect (29 July 1998).

Figure 3: Gene editing in New Zealand



Source: EU Regulatory Framework

Process and regulatory authorities

The Environmental Protection Authority (EPA) is the New Zealand regulator for new organisms, including GMOs, through the HSNO Act. The EPA assesses applications for field trials or GMO release based on risks and benefits, on a case-by-case basis. A number of field trials have been approved to date but so far only one genetically modified organism has been approved for release[57] in New Zealand for use in the agricultural sector – a modified vaccine to protect horses against equine influenza.

The Ministry for the Environment (MfE) is the policy lead on genetic modification issues in New Zealand. MfE administers the Environmental Protection Authority Act 2011 (which established the EPA), and is responsible for monitoring the EPA's activity. EPA regulates under the HSNO Act. In New Zealand gene editing is considered genetic modification and is subject to regulation under the HSNO Act.

The Ministry for Primary Industries (MPI) has a role as the compliance and enforcement agency for new organism containment or conditional release approvals and is also responsible for enforcing compliance with genetic modification requirements at New Zealand's borders.

MPI also has an interest in agricultural biotechnology due to the potential benefits and risks it can bring to the food and fibre sector. Foods and organisms are regulated separately in New Zealand. Genetically modified foods are not regulated under the HSNO Act unless the food is a viable seed, as foods are not considered organisms.

New Zealand and Australian legislation require food produced using gene technology to be assessed and listed in Schedule 26 of the Australia New Zealand Food Standards Code, referred to as pre-market assessment and approval. Approved foods are also subject to labelling provisions to assist consumers to make informed choices.

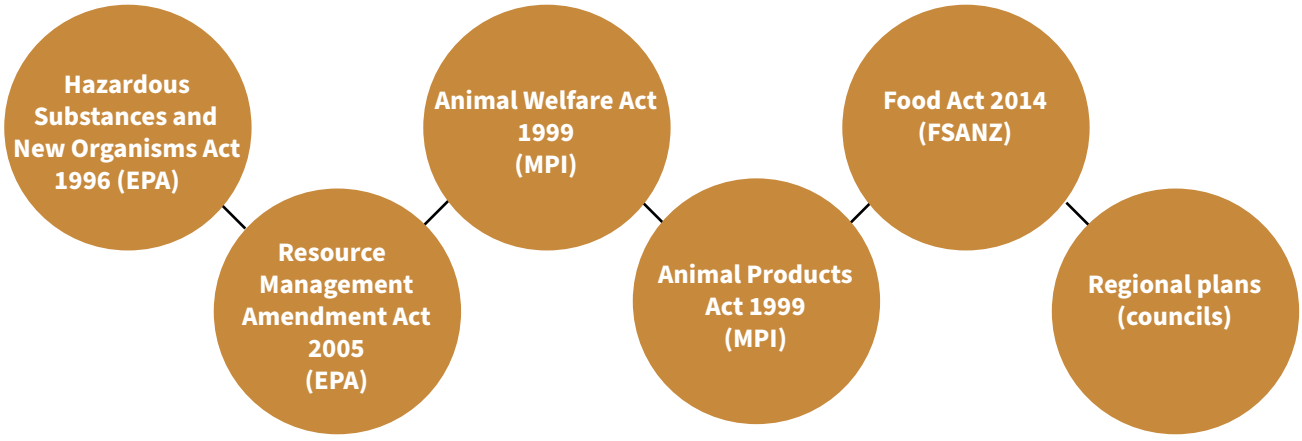
Food Standards Australia New Zealand (FSANZ) was established under the Food Standards Australia New Act 1991. The responsibilities of FSANZ include developing, varying and reviewing standards for food available in Australia and New Zealand – these are set out in the Australia New Zealand Food Standards Code.

However, while the composition and labelling requirement for foods for sale in New Zealand are regulated under the Food Standards code for which FSANZ is responsible[58], and while the definition of GMO under the HSNO Act also captures NBTs, food is not an organism under the act which means NBT produced food will be available in New Zealand under FSANZ standards but not produced domestically unless regulatory processes are met, and specific approvals are given.

Food producers must apply to FSANZ for new GM foods to be assessed and approved. The safety assessment follows the United Nations Food and Agriculture Organisations' Codex[59] scientific principles and guidelines; and includes public consultation. The goal of the safety assessment is to consider whether the GM food is comparable to the conventional counterpart food (e.g. GM corn versus non-GM corn) and to identify new or altered hazards.

Under New Zealand regulation, a GM food may be assessed as safe and approved for sale as food – however the same food product may not be grown or produced in New Zealand. To date there have been no approvals granted for full release of GM crops of any species and there are no GM crops in commercial production in New Zealand.

Figure 4: The statutory and regulatory settings governing GMO in New Zealand



Source: Resource Management Amendment Act 2005 (EPA)

The United States of America

Trait-based regulations and the principle of substantial equivalence

The United States of America's regulation differs from the approach taken by the EU, UK and New Zealand in two fundamental ways, the USA follows:

- a *trait-based* rather than a *process-based* system; and,
- the principle of "*substantial equivalence*" and risk-based analysis, rather than a strictly "*precautionary*" principle.

The USA considers there is no essential difference between GM technology and conventional breeding technology but takes into account that some genes used in GM technology might pose certain risks.

In the United States, all genetically modified products are evaluated on the basis of risk analysis and scientific principle. Risk analysis on GM products follow the principle of substantial equivalence and case-by-case study, that is, GM products must be evaluated on their risks to human health and the eco-environment according to the same criteria used in evaluating conventional products.

In the USA products that contain genetically modified material, or that are the product of genetic techniques, are not regulated by special laws and regulations, but are categorised by their specific use, and accordingly, subject to existing laws and regulations. Canada, Brazil and Argentina are also big growers and exporters of GM products and have similar approaches to the USA on GMO administration.

Process and accountability

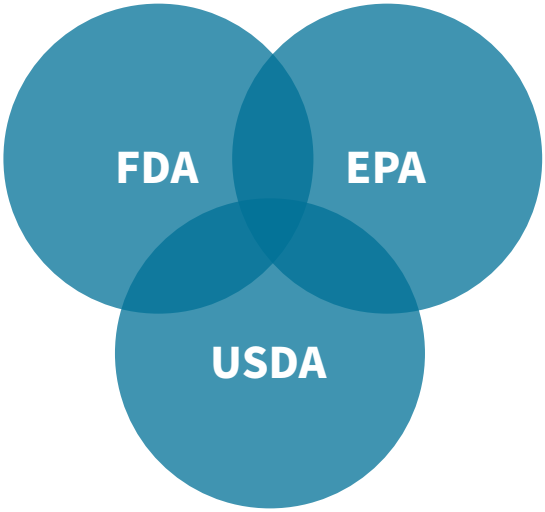
The overarching objective of USA GMO regulations is the same as in other jurisdictions, and the USA Federal Government's co-ordinated, risk-based system is tasked with ensuring that new biotechnology products are safe for the environment and human and animal health. Established as a formal policy in 1986, the Co-ordinated Framework for Regulation of Biotechnology sets out the USA Federal Government's system for evaluating products developed using modern biotechnology.

The co-ordinated framework is based on existing laws that are designed to protect public health and the environment. The USA government has written new regulations, policies, and guidance to apply these laws to biotechnology-derived products. Government agencies responsible for oversight of the products of agricultural modern biotechnology are, the FDA, EPA and USDA (see figure 5).

Depending on its *characteristics* a product may be subject to the jurisdiction of one or more of these agencies. Regulatory officials from the three agencies regularly communicate and exchange information to ensure that any safety or regulatory issues that may arise are appropriately resolved.

Figure 5: US GMO regulatory regime

The Department of Health and Human Services' Food and Drug Administration (FDA): regulates most human and animal food, including GMO foods. In doing so the FDA aims to ensure the foods that are GMOs, or have GMO ingredients, meet the same strict safety standards that apply to producers, processors and those who store, ship or sell food, must follow – no matter how the foods were created.



The US Environmental Protection Agency (EPA): is responsible for protecting human health and the environment, which includes regulating pesticides. EPA regulates the safety of the substances that protect GMO plants, referred to as plant-incorporated protectants (PIPS), that are in some GMO plants to make them resistant to insects and disease. EPA also monitors all other types of pesticides that are used on crops. Including on GMO and non-GMO crops.

The USA's Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS): protects agriculture in the USA against pests and disease. APHIS set regulations to make sure GMO plants are not harmful to other plants, and USDA's Biotechnology Regulatory Services implements these regulations.

Source: US Food and Drug Administration

Global regulations summary

Across jurisdictions, the primary objectives for regulating GMOs are both universal and stable over time. They aim to balance the benefits of new technologies (including competitive, economic, health and environmental benefits) with the need to keep humans, animals and the environment safe. However, the emergence of new, more precise, and evidently, safer genetic techniques have in recent years influenced most countries to review their regulations to keep pace with technological change, ensure regulations are fit-for-purpose and now also to mitigate the effects of climate change and to support domestic food security.

With these objectives in mind, governments and policy makers endeavour to take into account public perspectives on genetic technology and to understand the balance of opinion across society. The following section summaries some studies into consumer perceptions and behaviour to illustrate the diversity of views and the complex web of underlying influences on purchasing behaviour.

All regulatory systems must evolve to remain effective in their operating environments. The genetic technology industry has both internal changes (e.g. technological) and external changes (e.g. political, climate, food shortages) that necessitate calibration with the regulatory system.

Both the EU and UK have found that their genetic technology regulations require review and recalibration with technological development and broader health, economic and environmental objectives. If both jurisdictions implement the changes proposed, their systems will move closer to other large food producing and importing jurisdictions.

Section 3: Consumer perceptions

The prospect of growing, selling and consuming GM food products raises a different set of questions, including country of origin brand and reputation. These issues are entangled within a myriad of factors: cultural beliefs, cost v benefit, product categorisation, import country constraints, impact on the environment and on human and animal health. None of these factors are easily understood nor can they be resolved in isolation from one another.

From our review of a wide range of research papers, literature reviews, and previous studies we have identified a few common threads and some distinct differences that are worth noting, and which have been grouped below.

Would you buy GM foods?

Based on the studies reviewed, we found that consumers generally took a position that maximised personal benefits to them. The Eurobarometer report[60] found that although consumers were generally strongly opposed to the concept of GM foods, when additional attributes with perceived personal benefit were identified, some respondents shifted their perspective:

- if it contained less pesticide residues than other food – 18% of respondents indicated a "yes, definitely", with 33% indicating "yes, probably"; and,
- asked whether they would buy GM food if it were cheaper than other foods – 12% indicated "yes, definitely", and 24% indicated "yes, probably".

Knight et al[61] also found, in their six-country study, that price had a bearing on consumers' willingness to purchase GM foods where there was some additional benefit to the consumer, such as lower price for spray-free fruit (this study included New Zealand respondents).

Another study by Knight et al.[62] sought to understand views within the food distribution system, with a study of the Chinese system. It concluded, similarly, that Chinese consumers were likely to accept GM foods if they felt that there were additional benefits over non-GM products such as lower price, more health benefits or environmental benefits.

The study went further and noted that China is actively progressing research and development of GM crops able to be grown in China. The expectation is that, when markets more readily accept GM foods, China would develop the full potential of its GM capability for export. If correct, and if these markets do change, food producers should expect the Chinese market to rapidly open to GM foods too.

Premium or no premium?

While there are several inter-woven factors that influence consumers' purchasing decisions – price is a key determinant for many consumers. Many of the research studies use 'willingness to pay' valuations to explore the full influence of price on purchasing decisions.

A Lusk et al.[63] meta-analysis found, from their assessment of twenty-five studies, that non-GM food products attracted a 29% premium. This compares to Dannenberg's[64] meta-analysis, which found on average a 45% price premium for non-GM products. These studies found:

- variations from country to country are significant: USA consumers are more accepting of GM foods than Europeans who are willing to pay premiums for non-GMO products; and,
- the size of the premium depends on the type of genetic modification, the type of food and how the modification alters the final product, consumers were also found to:
  - be less accepting of genetic modification of animals compared to plants;
  - be more accepting of GM foods when the product had direct benefits – to the consumer (e.g. improved nutrition, spray free);
  - distinguish between GM foods developed using genes within the same species compared with foods developed using genes from different species (Colson, Huffman, and Rousu[65]).

However, the findings above are at odds with those from a more recent review by Kym Anderson, 'The Independent Review of the South Australian GM Food Crop Moratorium'[66]. This report found:

- very few market benefits in being GM-free[67] and that the main benefits related to marketing attributes such as being perceived to be "clean and green";
- that on a cross-state comparison of different GM regulations "segregation and identity preservation protocols, and codes of practice, can and do ensure the successful coexistence of GM and non-GM crops in Australia"; and,
- that cumulatively, South Australian farmers had incurred an estimated cost of AUS$11-33 million between 2004-18, and foregone profits of a further AUS$5 million by 2025. These were attributed to weed control costs and loss of yield[68].

These mixed findings illustrate that perceptions about GM foods, and their impact on consumer behaviour, are not straight forward and should be interpreted with care.

Does GM status impact a country's brand?

The value of New Zealand's image as 'clean and green' is a theme often raised in the context of GM discussions and is frequently cited as a reason not to explore genetic technology in New Zealand.

The studies reviewed, demonstrate that the importance of country of origin (COO) GM status varies by product, market, the level of socio-economic constraints and cultural perspectives of consumers in the importing market and consumer access to information. In addition COO credentials for quality, reliability and food safety history have the potential to mitigate negative perceptions at a product specific level. While there are numerous studies in this area, this report, *WELL_NZ: Understanding modern genetic technology* focuses on two examples that specifically relate to New Zealand as well as one on dairy products in China, a major export destination for New Zealand.

A study on perceptions of dairy products in China conducted by Rongbin et al. showed that the Chinese market is influenced by perceptions of a country's attributes (economic, technological, environmental) or 'image'. They found consumers prioritise Chinese products overall, however consumer animosity will influence purchasing decisions. For example the baby formula scandal of 2008 destroyed Chinese consumer confidence in domestic dairy products.

Rongbin et al. found that Chinese consumers are a 'risk adverse and collectivised group'. This means that food safety is a critical factor for the Chinese consumer whose purchasing decisions are heavily influenced by positive word of mouth recommendations and influencer reviews, and for whom in-direct product experience can outweigh COO attributes. In summary, COO status is an important factor in dairy product purchases in China, but safety and trust in the product remain priority factors in purchasing decisions.

A New Zealand study, *GM Crops and damage to country image: much ado about nothing?* undertaken by John Knight[69], Otago University, 2016, considered how international tourists perceive New Zealand via a series of interviews taken on arrival at Auckland Airport. The findings describe travellers' perceptions of New Zealand's desirability as a destination under hypothetical scenarios of in-country genetic technology use.

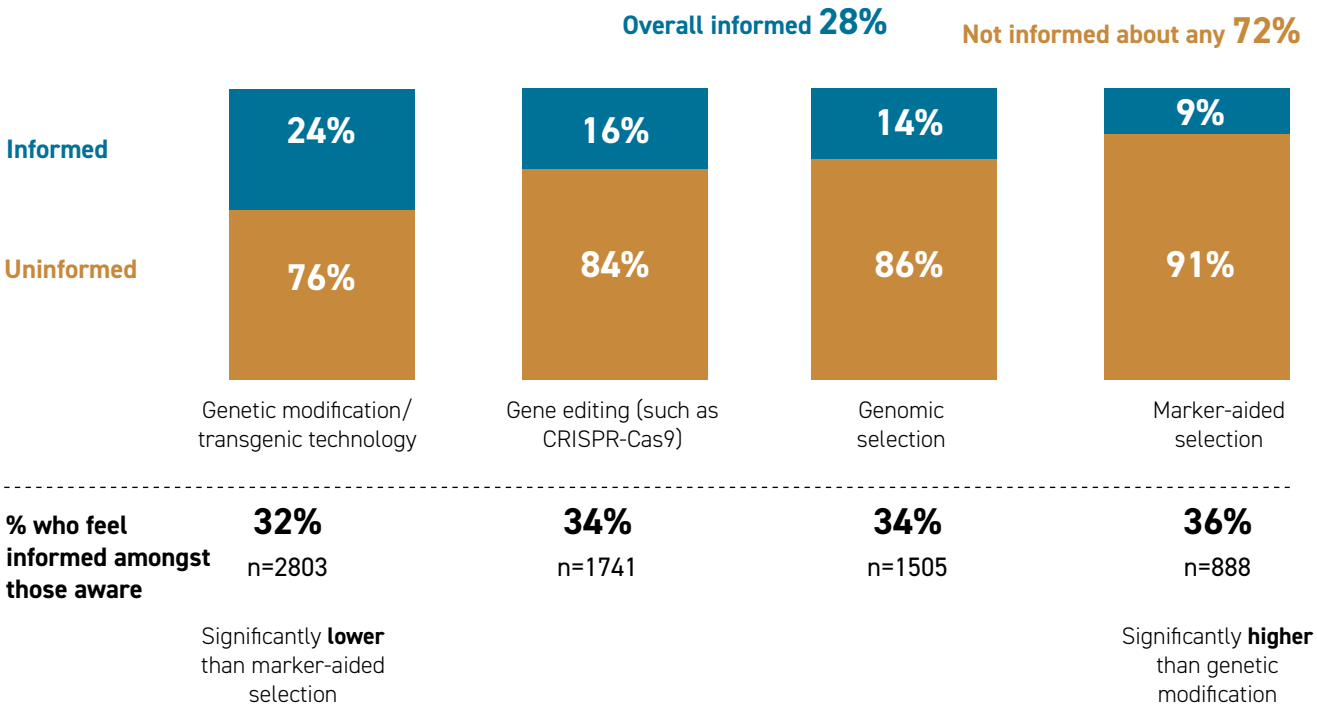
The results showed:

- disease resistant GM-pines: 92.8% would definitely somewhat or slightly agree to still visit New Zealand;
- GM rye grass grown for animal welfare: 91.4% would definitely, somewhat or slightly agree to still visit New Zealand;
- GM rye grass: 92.9% would definitely, somewhat or slightly agree to still visit New Zealand;
- GM bacterium used to clean up DDT: 90.3% would definitely, somewhat, slightly agree to still visit New Zealand;
- GM bacteria used to reduce methane: 89.4% would definitely, somewhat or slightly agree to still visit New Zealand;
- and in response to the statement: "*GM is an acceptable form of technology for food production and environmental protection*": 49.2% definitely, somewhat or slightly, agreed that it is acceptable.

The report concludes that "the data in this paper provide evidence from which it can be inferred that the introduction of GM crops into New Zealand is highly unlikely to do lasting damage to perceptions in overseas markets of the image of New Zealand as a source of high-quality food products or as a highly desirable scenic and 'clean, green tourist destination'". In addition the report found that "results from in-bound tourist surveys provide clear evidence that tourist destination choice is scarcely affected at all by controversial technologies that are in use in a particular country, even if the individual tourist may hold very negative views of that type of technology".

Also in New Zealand, Scion[70] commissioned Colmar Brunton to undertake a survey[71] of New Zealanders' current opinions and understanding of genetic technologies. It surveyed over 4,000 New Zealanders between the ages of 18-69 years[72]. It found that more people are aware of GMO (*transgenic*) gene modification technologies, 68%, than of gene editing (New Breeding Techniques), 41%. However the study also found that although the majority of the population is aware, this does not translate to knowledge, with less than a third of the population overall saying they feel informed about some type of genetic technology and only a third of those who are actually aware of each technology feeling informed.

Figure 6: How informed are New Zealanders about genetic technologies?

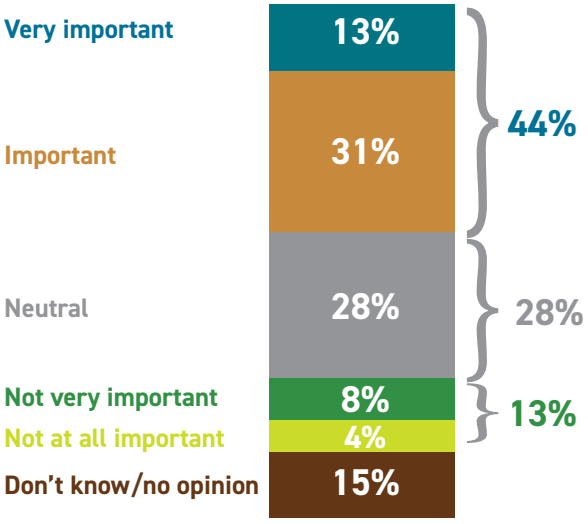


Source: SCION 2019

Consistent with these and several other studies which investigate the acceptance of genetic technologies, the level of acceptance goes up the more important the outcome is to the respondent. In the Scion study 44% of all respondents believed that genetic technologies are important for New Zealand's future.

The survey also canvased questions like how important conservation was to them personally, with 78% responding that it was either important or very important. A subsequent question asking about how accepting respondents would be of using genetic technology to save the Kauri tree, only 3% considered it not at all acceptable.

Figure 7: Importance of genetic technologies for New Zealand's future



Importance significantly higher among:

- Males (49%)
- 55-69 years old (48%)
- NZ European (48%)
- University educated (55%)
- Aware of genetic technologies (51%)
- Informed about genetic technologies (60%)

Neutral significantly higher among:

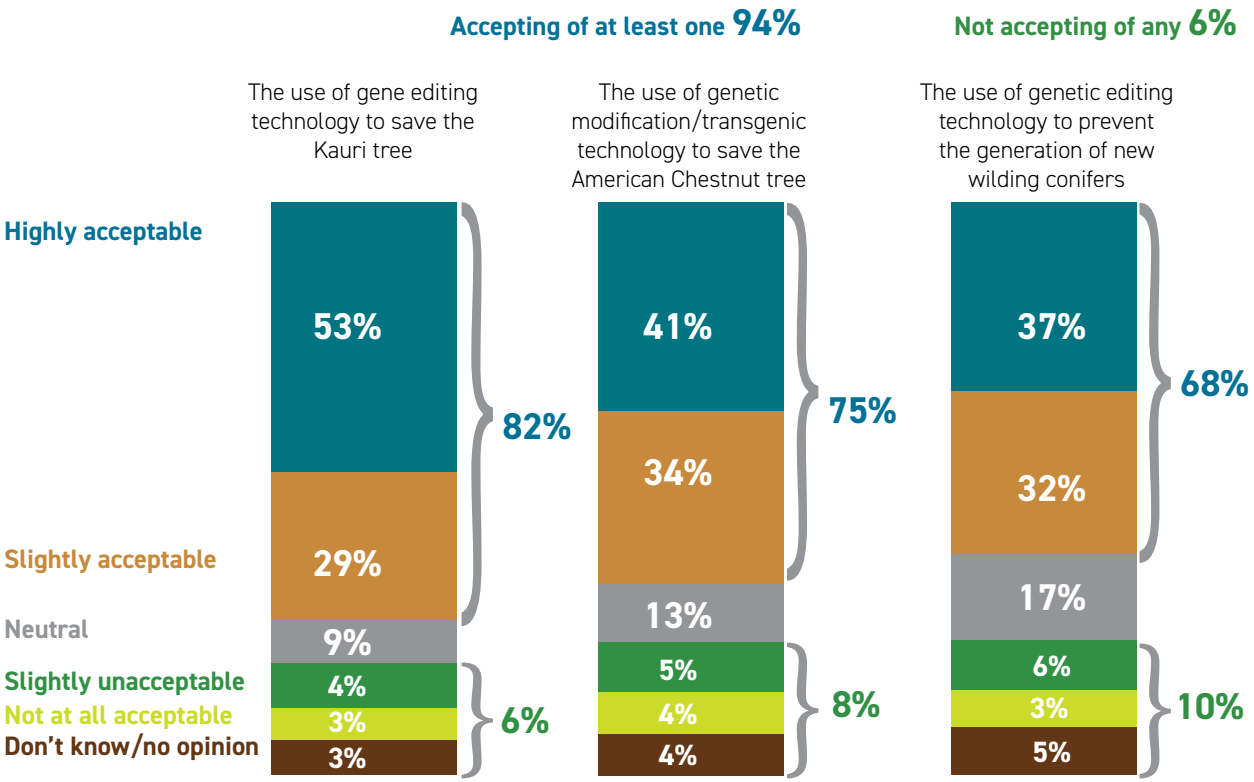
- 18-39 years old (31%)
- Other South Island (32%)
- High School Educated (31%)
- Earning and income of less than $50k (31%)
- New Zealanders of Maori descent (33%)

Unimportance significantly higher among:

- 55-69 years old (15%)
- Living in a rural area (15%)
- Earning an income of less than $100k (14%)

Source: SCION 2019

Figure 8: Acceptance of genetic technology use for conservation



Source: SCION 2019

Summary

Study results and responses are heavily nuanced and sensitive to, among other things, the approach and methodology of the study. However the following summary of common questions asked are reflected in varying degrees across a number of the studies:

- **Would you buy GM foods or agree to the use of GM technologies?**
  A conditional 'yes', based on the perceived benefits the consumer receives, foods that are: cheaper, healthier, no spray residues, more nutritious, and with positive biodiversity and environmental outcomes. However, responses were less in favour if benefits accrued solely to the grower, for example they were cheaper to grow or had a higher yield.

- **Is there a premium for non-GM product?**
  A conditional 'yes', a significant premium over GMO, but this declines in the presence of other product characteristics (e.g. product appearance, consumer benefits such as environmental and nutritional qualities and the GM approach used to produce the product). In addition, perceptions of value are very product specific – more caution should be used for commodity and ingredient-based products, as seen in the South Australia canola example where it found farmers incurred an opportunity cost by foregoing productivity benefits of growing GM canola crops allowed in other Australian States.

- **Does GM impact a country's brand?**
  A conditional 'no', when consumers are making purchasing decisions country of origin is only one factor within a broader decision-making framework specific to that market's characteristics: the product's price, perceived benefits and cultural influences within that market, weighed against the product's perceived risks. A survey of tourists entering New Zealand gave a clear 'no' response to the question.

Section 4: New Zealand's regulation reviews

The rapid advancement of biotechnology, and genetic technology in particular, over the last thirty years has prompted many nations to re-assess their GMO regulations head-on. We have seen how governments in the UK and EU are proactively considering existing regulatory regimes to bring them up to date. Both are proposing alternative settings to better balance perceived risks and benefits of modern gene editing techniques, and to improve the effectiveness and efficiency of implementation in achieving broader objectives.

Over the last two decades New Zealand has, from time to time, also conducted formal reviews and investigations into how its own regulatory settings should be managed. There have been several studies, reviews and critiques on New Zealand's GMO regulatory regime but the most in-depth and broad-based studies at a national level over the period are:

- The Royal Commission on Genetic Modification, *Report and Recommendations*, 2001;
- The Royal Society Te Apārangi, *Gene Editing in Aotearoa*, 2019;
- Prime Minister's Chief Science Advisor briefing on the Royal Society Te Apārangi gene editing report, 2019;
- The Productivity Commission, *New Zealand firms: Reaching for the frontier*, 2021; and
- Food Standards Australia and New Zealand, Proposal P1055 – *Definitions for gene technology and new breeding techniques*[73], 2021.

This section sets out the key findings from each of these reports to illustrate emerging themes on the regulation of gene technology in New Zealand.

The Royal Commission on Genetic Modification

The Royal Commission on Genetic Modification's Report and Recommendations[74] was published in 2001. Its aim was to: "...stimulate a broad-ranging discussion on genetic modification and to report on the strategic options available to enable New Zealand to address genetic modification now (2000) and in the future... for the concerns of New Zealanders to be heard and evaluated... and [provide] advice as a result of hearings and research as to how we should act in this new environment." Hon. Marian Hobbs, Minister for the Environment (2001)

Preserving opportunities and identifying national values

On the whole, the major theme of the report was to preserve opportunities, with the Royal Commission explicitly rejecting the idea of New Zealand being totally free of all genetically modified material at one extreme, and the option of unrestricted use of genetic modification at the other. None of the recommendations conflicted with government policy or strategic direction of the time and there was strong endorsement for the existing regulatory structure and frameworks.

In compiling the report, the views of New Zealanders were gathered through submissions, hearings, and public opinion survey work. This led to the identification of seven shared values to be used as a framework for reaching conclusions about genetic modification:

- the uniqueness of New Zealand;
- the uniqueness of our cultural heritage;
- sustainability;
- being part of a global family;
- the well-being of all;
- freedom of choice;
- participation.

Among the report's forty-nine recommendations a number aimed to address its major theme – to preserve opportunities. These included:

- mechanisms to manage the co-existence of different kinds of agriculture (organic, GM, conventional and integrated pest management);
- a new category of 'conditional release' of GM organisms (currently the only option is to release without controls); and,
- a provision that would see the first application for release of any genetically modified crop decided by the Minister for the Environment.

For the ongoing oversight of biotechnical developments the Government (based on the commission's recommendation), established Toi te Taiao, the Bioethics Council, in 2002[75] to:

- act as an advisory body on ethical, social, and cultural matters in the use of biotechnology in New Zealand;
- assess and provide guidelines on biotechnological issues involving significant social, ethical, and cultural dimensions; and,
- provide an open and transparent consultation process to enable public participation in the council's activities.

Synchronising regulatory settings with emerging technology and social values

The comprehensive report was clear that, while it endorsed the legislative and regulatory frameworks as appropriate for the technology of the time, the Royal Commission recognised that a medium and long-term strategy was needed to ensure that the settings remain appropriate for New Zealand, and the people of New Zealand, as technology and social-milieu continue to evolve.

The Royal Society Te Apārangi

The section of the Royal Society Te Apārangi report on *Gene Editing – legal and regulatory implications,* had six key findings that related to definitional issues:

- defining genetic modification;
- regulatory complexity and consistency;
- international regulation and enforcement;
- risk-proportionate regulation;
- community engagement; and,
- capacity and capability to support effective decision making.

Evidence of regulatory inconsistency

The report found that currently, legal, and scientific definitions are not harmonised across legislation and regulatory frameworks, meaning that there is no shared or commonly agreed language with which to engage with communities. Debates are likely to be confused by this lack of shared understanding. For example:

- the use of human versus human cell (or embryo);
- animal, excluding and including invertebrates (such as the honeybee);
- pest versus unwanted organism; and
- biological product versus biological compound.

Inconsistencies also arise, says the Royal Society, in relation to organisms which may have the same or similar characteristics, but which are the result of different processes. For example, they identify "the use of gene editing technologies, including CRISPR-Cas9, are deemed genetic modification under current legislation, and the resulting organisms are, therefore, classed as new organisms. By contrast those generated by random mutagenesis, which results in many more gene alterations in addition to the targeted change, do not count as new organisms. It does not make scientific sense for organisms with genetic changes that are already found in their population to be considered new organisms under the HSNO Act." [76]

Regulations should reflect modern reality

The Royal Society Te Apārangi also found that statutory provisions and regulations should account for an increasingly nuanced view and reflect the modern reality that organisms cannot be simply categorised as 'genetically modified' or 'not-genetically modified'.

There is a need to ensure coherence across the regulatory regime and its implementation. A key question is: how best to achieve this in a way that is appropriately nuanced, technically sound, and culturally inclusive?

Ensuring Treaty of Waitangi obligations

The Royal Society Te Apārangi New Zealand also highlighted the need to take Treaty of Waitangi obligations and cultural considerations into account. The HSNO Act requires that all persons exercising powers and functions under HSNO consider the relationship of Māori, their culture and traditions with their ancestral lands, water, sites, waahi tapu, valued flora and fauna, and other taonga.

The Ko Aotearoa Tēnei: Report on the Wai 262 Claim, released by the Waitangi Tribunal in 2011,[77] recognises that Māori have a strong interest in genetic modification, particularly from the perspective of being kaitiaki. This special relationship would need to be considered in any review of the HSNO Act and related legal and regulatory instruments.

Trade and the economic value of 'GMO Free'

New Zealand continues to focus on achieving premium status and value for its primary industry products. The Royal Society Te Apārangi report recognised that export markets might vary in response to genetic modification, and since products are often marketed as brand 'New Zealand', the GM status of only a proportion of NZ products could potentially impact the entire brand.

The Royal Society Te Apārangi report noted that to be in New Zealand's interests, a market premium is required for "GM-Free" produce, and that this premium must be weighed against other potential benefits of gene editing.

The report found that the potential trade and regulatory enforcement impacts, from the different treatment of gene editing technologies in different countries, needs to

be investigated to ensure that New Zealand's regulations continue to be fit-for-purpose, both domestically and internationally.

Chief Science Advisor's Prime Ministerial briefing

The Prime Minister's Chief Science Advisor, Dame Juliet Gerard, in her 2019 briefing to the Prime Minister on the Royal Society Te Apārangi report[78], raised a number of issues of particular interest to policy makers.

The briefing notes that, while there was some public consultation undertaken in the course of compiling the report, more substantive input is required, especially from Māori. The briefing cites Hudson, Mead et al's review of contemporary te āo Māori views on genetic technologies, noting how key Māori values (whakapapa, mauri, mana, kaitiakitanga) speak to the use of this technology, with one conclusion being that, ".. a widespread social license for the use of gene-based technology is unlikely in the short term. Generally, Māori do not oppose new and emerging gene technologies a priori, but instead raise concerns about how the technologies should be used and the rationale, objectives and consequences of choosing them."[79]

This framing, Gerard says, aligns with the over-riding consideration of a quest for policies that create ora and inter-generational wellbeing for all New Zealanders, in the overarching context of the Treaty of Waitangi.[80]

The briefing further noted agreement with the Royal Society Te Apārangi's finding that:

- New Zealand's current legal and regulatory frameworks are not fit-for-purpose due to, scientific and legal definitions being at odds with one another;
- definitions of key concepts being inconsistent across different pieces of legislation; and
- these anomalies need to be addressed.

Also noted is the fact that, the HSNO Act's list of genetic tools that do not attract regulation, dating from 1998, create further anomalies. *For example, "mutagenesis by radiation or chemicals, which creates multiple uncontrolled changes to DNA, is much less regulated than a single controlled change at a specific point. It is analogous to saying that electric cars should attract a greater penalty than petrol cars, because electric cars were not invented in 1998."*[81]

In contemplating a way forward, the briefing suggests that more nuanced thinking is required now than has been applied the past. A number of key points are raised including that:

- the argument that 'gene editing is not GM', that 'gene editing is safe', or 'gene editing is not safe' are not helpful;
- there is a spectrum of GM technology and regulatory frameworks should focus on the hazards and benefits of the case at hand;
- gene editing is a tool which, like other tools, for example hazardous substances, must include safety measures that protect society from rogue actors – rather than from the potential benefits inherent in the technology itself; and
- the legal and regulatory framework must facilitate, not hinder, asking and answering key ethical questions through an honest discussion of the hazards and benefits of the myriad of possible applications of genetic tools.

The briefing's closing comment is that *"a fresh, open-minded look at the legal, regulatory and policy framework is needed."* [82]

New Zealand Productivity Commission

The New Zealand Productivity Commission's 2021 report: *New Zealand firms: Reaching for the Frontier*[83], focuses on New Zealand's 'frontier firms' – those at the global productivity frontier characterised as being typically larger, more profitable, younger with a high propensity to patent – because of their critical contribution to New Zealand's overall economic performance. The purpose of the inquiry was to identify policies and interventions that could maximise the performance and economic contribution of these firms by focusing specifically on:

- improving the performance of the frontier firms themselves; and,
- helping innovations diffuse more effectively from frontier firms to other New Zealand firms.

In addition to providing advice on opportunities and potential new initiatives, the Productivity Commission identifies existing barriers and constraints to productivity and innovation.

Analysis for the 'Reaching for the frontier' report identifies constraints to primary sector innovation finding that: "the current regulation of genetic modification (GM) does not reflect technological advances."[84]

The report finds this to be a constraint on innovation

and productivity, broader than just food in the context of the Productivity Commission report, and calls for a full regulatory review.

The Productivity Commission notes in its report that the New Zealand regulatory regime was last reviewed in 2001 by the Royal Commission on Genetic Modification with subsequent amendments being incorporated into the HSNO Act.[85]

Technologies have advanced in ways not envisaged in 2001

The report highlights that: "technologies have moved on significantly over the last twenty years. In particular, advances in gene editing have produced technologies such as CRISPR, which enable much faster and more precise modification than earlier tools."

The Productivity Commission also notes that there have been substantial technological developments that could not have been contemplated at the time regulations were last reviewed. For example: "*Modern gene-editing techniques enable changes to made in vivo (directly inside an organism) – a technique that was not envisaged at the time the current regulations were made. These techniques can also produce changes that do not involve inserting foreign DNA. This is in stark contrast to earlier techniques, which sparked consumer fears of "Frankenfoods" created from mixed genetic sources. The precision of gene editing means these changes can be indistinguishable from naturally occurring organisms, and indistinguishable from changes made by techniques that are exempt from regulation.*"[86]

Outdated regulatory settings

The report cites Ministry for the Environment advice from 2018 which raised concern over regulations quickly becoming out-dated and hard to enforce. It also notes that a 2014 High Court decision to adopt a strict definition of gene editing technologies means that modern genetic techniques are more highly regulated than those created using exempt techniques – that is, those allowed by exception under the HSNO Act.

> Organisms developed using new and more precise technologies receive the same level of scrutiny as earlier GM techniques that are not listed in the 'not-GM regulations'… This may result in organisms being regulated at a level not proportionate to the risk they pose and New Zealand missing out on the benefits they could provide (such as medical treatments, crops, trees, or forage with beneficial properties).
>
> Anecdotal evidence suggests the high level of regulation is discouraging potential applicants from submitting an application to the Environmental Protection Authority (EPA) for field trials in containment, or a release of a GMO, as the perception is, they are unlikely to be successful or it will take too much time, effort and financial backing."
>
> (Ministry for the Environment, 2018)

A comprehensive approach

The Productivity Commission report finds that current regulatory and legislative systems can work against each other, leading to unintended consequences. It therefore recommends a comprehensive approach to a regulatory review, including consideration of emerging regulatory approaches in other jurisdictions, especially in key product destination and competitor markets.

An inclusive, informed national conversation about GM is recommended

Examples of views across the spectrum include the risk of falling behind our international competitors and missing much needed opportunities while New Zealand plays technology catch-up (MfE 2018), to the belief that there is so much consumer resistance to GMO products that allowing them in New Zealand would wipe out any productivity benefits (Sustainability Council of New Zealand submission on the Productivity Commission's 2021 report New Zealand firms: ***Reaching for the Frontier***)[87].

The Productivity Commission consider that this sample of opposing views illustrates that a national conversation about GM will be challenging but considers that it is important, and further emphasises the need for a society wide, inclusive conversation that engages industry interests, Māori interests, and assesses public attitudes to new genetic technology and their application.

In summary, the Productivity Commission recommended the Government undertake a full review of GM regulation to ensure it is fit-for-purpose and supports domestic innovation, which should:

- consider emerging regulatory approaches in other jurisdictions, particularly New Zealand's key product destination and competitor markets;
- consider the trade and regulatory enforcement impacts from different treatment of GM technologies in different markets;
- assess consumer attitudes in New Zealand and internationally;
- consider the potential impacts on New Zealand firms that wish to retain GM-free status, and on New Zealand's reputation and brand more generally;
- recognise Māori views on GM and the rights and interests of iwi in taonga species (indigenous flora and fauna);
- co-ordinate with the whole-of-government work that is considering the recommendations of the Waitangi Tribunal's Ko Aotearoa Tēnei: Report *on the Wai 262 Claim*, in particular those relating to GM legislation;
- look beyond the Hazardous Substances and New Organisms Act 1996, across all relevant acts and regulations, to ensure consistency of definitions and approach;
- assess the fitness for purpose of the current regulatory oversight and enforcement arrangements;
- consider the merits of separate legislation and/or a standalone regulator for genetic technology; and,
- undertake wide public engagement, including with Māori and industry, and backed by information resources to support public understanding of modern GM technologies.

Food Standards Australia and New Zealand

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

Emergence of new technology prompts standards review

In 2017 FSANZ considered the variety of new breeding techniques (NBTs) that have emerged over the last decade and which are increasingly being applied to the production of food. FSANZ found that the emergence of these techniques generated uncertainty about the regulatory status of derived food products (foods produced using NBTs) and specifically, whether such foods would be considered *food produced using gene technology* and would 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). 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; and,
- whether a pre-market safety assessment of NBT foods is justified based on risk[88].

Consultation

In early 2018 FSANZ began consulting with the key stakeholders and the community to look at how food derived from NBTs should be captured for pre-market approval under the standard relating to food produced using gene technology (Standard 1.5.289) and

whether the definitions for 'food produced using gene technology' and FSANZ (Standard 1.1.2–2~~–~~90) should be changed to improve clarity about which foods require pre-market approval.

Feedback on the consultation showed there are diverse views in the community about the safety and regulation of food derived from NBTs, but most agreed the current definitions are no longer fit for purpose and lack clarity.

In December 2019 FSANZ made three recommendations:

1. FSANZ to draft a proposal to revise and modernise the definitions in the Code to make them clearer and better able to accommodate existing and emerging genetic techniques;
2. as part of the proposal, FSANZ to 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; and,
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.

FSANZ proposes to update definitions

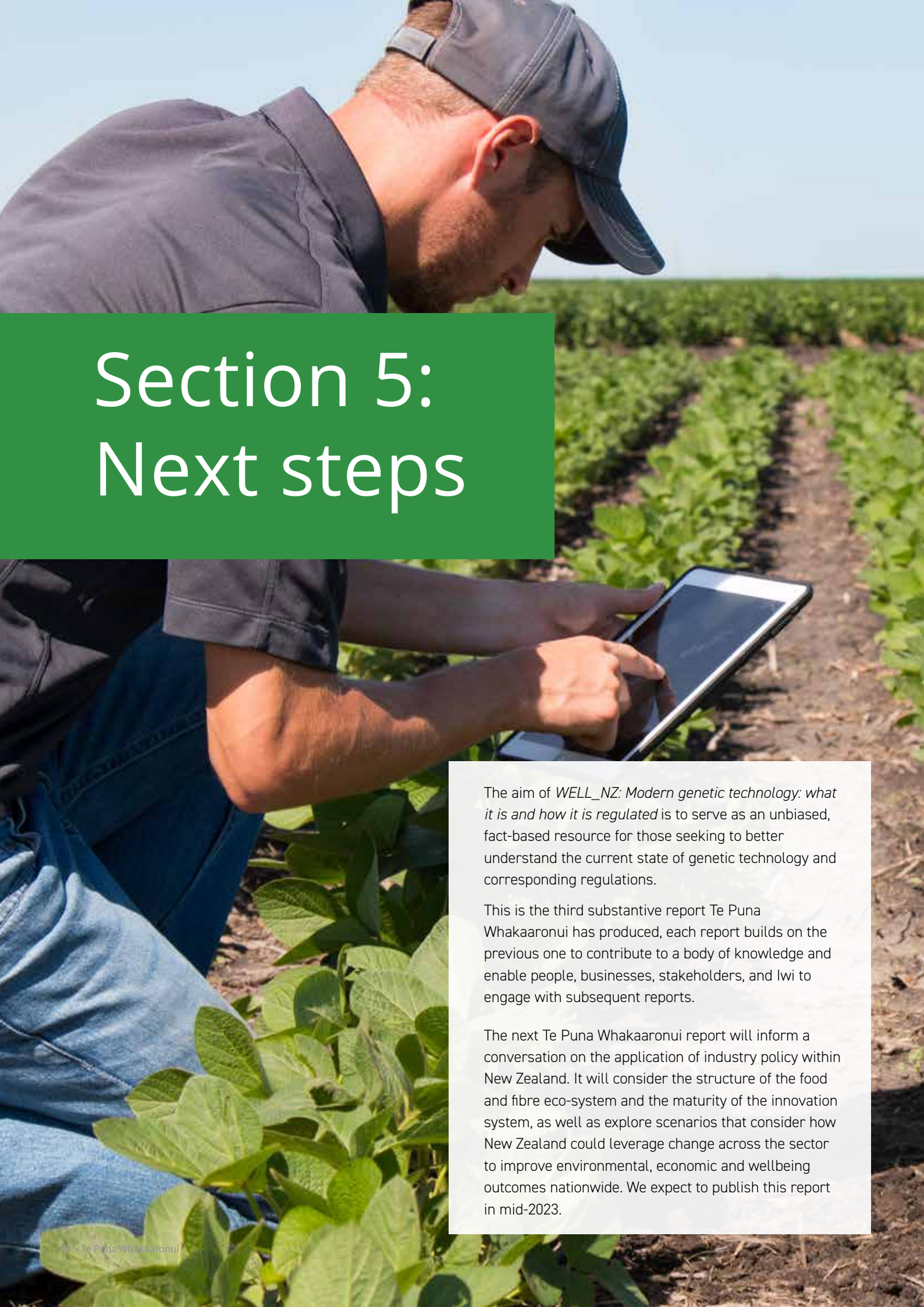
FSANZ's proposal P1055 (March 2022) aims to amend the definitions for 'food produced using gene technology' and 'gene technology' in the Australia New Zealand Food Standards Code (the Code).

These definitions determine which foods are classed as genetically modified (GM) food under the Code. Currently, all GM food available for sale in Australia and New Zealand must have been assessed for safety by FSANZ and be expressly permitted and listed in relevant Code schedules. FSANZ is proposing to update the definitions to make them clearer and better able to accommodate food produced by existing, emerging, and future genetic technologies [91]

Summary

In 2001 the Royal Commission was grappling with new technology and, like other jurisdictions at the time, was guided by the precautionary principle to limit risk from a technology that was not yet well understood. In doing so it emphasised the need to ensure ongoing calibration between regulatory settings, technology, and society's preferences. The Royal Commission set out guidelines and recommendations to ensure inclusive consultation would inform settings in the future.

Two decades on and technology has advanced and developed in ways that could not have been envisaged in 1996 when the HSNO Act was drafted, or in 2001 when the Royal Commission undertook its inquiry. Recent reviews by the Royal Society Te Apārangi, the Prime Minister's Science Advisor, the Productivity Commission and FSANZ are unanimous in their view that there is a need to recalibrate regulatory settings with technology and that existing regulations are no longer fit-for-purpose. They suggest a more risk proportionate approach over the current precautionary approach.



Section 5: Next steps

The aim of *WELL_NZ: Modern genetic technology: what it is and how it is regulated* is to serve as an unbiased, fact-based resource for those seeking to better understand the current state of genetic technology and corresponding regulations.

This is the third substantive report Te Puna Whakaaronui has produced, each report builds on the previous one to contribute to a body of knowledge and enable people, businesses, stakeholders, and Iwi to engage with subsequent reports.

The next Te Puna Whakaaronui report will inform a conversation on the application of industry policy within New Zealand. It will consider the structure of the food and fibre eco-system and the maturity of the innovation system, as well as explore scenarios that consider how New Zealand could leverage change across the sector to improve environmental, economic and wellbeing outcomes nationwide. We expect to publish this report in mid-2023.

Endnotes

1 This section aims to simplify the broad use of terminology and excludes international or domestic regulatory definitions which are addressed in Section [3] of this document "Genetic technology regulations around the world".

2 Ribonucleic acid (RNA), a nucleic acid present in all living cells. Its principal role is to act as a messenger carrying instructions from DNA to control the synthesis of proteins. In some viruses, RNA rather than DNA, carries the genetic information.

3 Food Safety Australia New Zealand (FSANZ) makes a distinction between NBTs and older GM techniques because NBTs can be used to make a wider variety of genetic changes, many of which are the same as those introduced using traditional breeding or that occur naturally. NBTs can also be used to make the same genetic changes as some of the older GM techniques.

Approaches adopted elsewhere were cautious but did not explicitly invoke the precautionary principle as a basis to significantly restrict or prevent GMO authorisations.

4 It is the lack of a transgene in the final product that is the basis for them not being regulated as GMOs, i.e. foreign DNA will have been introduced (the gene editing machinery) and then been crossed so that there is no foreign DNA in the final organism. Under a trait based – not process based -regulatory regime such a product will avoid the legislative or regulatory trigger for GMOs.

5 The UK's process is progressing ahead of the EU's, with the UK Government's Genetic Technology (Precision Breeding) Bill, introduced in May 2022 having completed its passage through the House of Commons and is in the final stages of review by the House of Lords.

6 WG Hill. 2001. Selective Breeding. *Encyclopaedia of Genetics,* Academic Press, 1796-1799

7 While not technically a review of New Zealand's GMO regulations, FSANZ does set food product standards for New Zealand and therefore its recent review of definitions for gene technology and new breeding techniques is relevant to this discourse.

8 Ploetz, Randy C. 2000. Panama Disease: A Classic and Destructive Disease of Banana, *Plant Health Progress, 1.1: 10*

9 B Katz. 2018. Rethinking the Corny History of Maize. *Smithsonian Magazine*

10 NSF Organization List. [n.d.]. "Scientists Trace Corn Ancestry from Ancient Grass to Modern Crop," Nsf.gov <https://www.nsf.gov/news/news_summ.jsp?cntn_id=104207>

11 www.nytimes.com/2007/08/28/science/28crop.html

12 A key point is that this other species can breed naturally in the wild but rarely produce new progeny, or it may cross and produce many progeny. This is relevant for both cisgenesis and intragenesis.

13 Rashid, M. A., M. K. Hasan, and M. A. Matin. 2018. Socio-Economic Performance of Bt Eggplant Cultivation in Bangladesh, *Bangladesh Journal of Agricultural Research*, *43.2: 187–203*

14 Prodhan, M. Z. H., M. T. Hasan, M. M. I. Chowdhury, M. S. Alam, M. L. Rahman, and others. 2018. "Bt Eggplant (Solanum Melongena L.) in Bangladesh: Fruit Production and Control of Eggplant Fruit and Shoot Borer (Leucinodes Orbonalis Guenee), Effects on Non-Target Arthropods and Economic Returns," *PloS One, 13.11: e0205713*

15 Ahmed, Akhter U., John F. Hoddinott, Kazi Shaiful Islam, A. S. M. Mahbubur, Rahman Khan, and others. 2019.*Impacts of Bt Brinjal (Eggplant) Technology in Bangladesh*

16 This technique includes vector-based, PCR-based and programmable site-directed nuclease-based methods of genetic engineering. For the purposes of this report, the site-directed nucleases are factored under the category of New Breeding Techniques and will be touched on later.

17 For example, ZFN is made by combining a zinc finger protein with a FokI endonuclease, both of which are found in nature, (proteins in animals, plants fungi and algae) but would not naturally form a functional ZFN.

18 While SDN techniques can be used to create GMO organisms by introducing DNA from another species, for the purposes of the report the following section will focus only on non-GMO applications.

19 Menz, Jochen, Dominik Modrzejewski, Frank Hartung, Ralf Wilhelm, and Thorben Sprink. 2020. "Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment," *Frontiers in Plant Science, 11: 586027*

20 Agronomy traits relate to plant growth and include, amongst other traits: plant height, growth habit, uniformity in flowering, crop water requirement.

21 y-Aminobutryic acid is an amino acid that functions as a primary inhibitory neurotransmitter for the central nervous system. Consumption of foods or supplements with y-Aminobutryic acid is thought by some to be helpful in reducing stress or anxiety and in lowering blood pressure.

22 https://geneticliteracyproject.org/2022/10/05/growing-rice-in-the-ocean-crispr-might-be-utilized-to-tweak-ancient-genes-could-be-a-future-super-food/

23 Lamerton, Michelle. 2022. Meet New Zealand's Coolest Dairy Cows, *LIC International*

24 CBEs and ABEs create point mutations, as occur with earlier genetic techniques. The difference, however, is that CBEs and ABEs have the ability to determine what the mutation will be. For example, converting a C:G base pair to a T:A base pair to create a change to a specific trait.

25 https://www.nature.com/articles/s41587-022-01445-5

26 There are two ways in which the non-homologous end joining (NHEJ), and homology-directed repair (HDR) are two ways in which DNA repairs itself after the creation of a double-stranded break. NHEJ involves sealing of the two ends of the DNA back together (leading to the deletion of a gene), wherein a DNA template is used to repair the DSB.

27 They transferred a gene that encodes antibiotic resistance from one strain of bacteria into another giving antibiotic resistant to the recipient. A year later Jaenishch and Beatrice Mintz used a similar procedure in animals, introducing foreign DNA into mouse embryos. – Harvard University, 2015.

28 From Corgis to Corn: A Brief Look at the Long History of GMO Technology. 2015. *Science in the News*

29 "GMO Legislation." 2011. *Food Safety*

30 refer p.14 *New Breeding Techniques* section in this document.

31 Labelling on Genetically Modified Food. 2022. *Singapore Government, Singapore Food Agency*

32 Noting that many products might be transgenic/GMOs during their production (and regulated as such) but when the transgene is crossed out they are regulated based on the product (*trait)* and not the process that produced them.

33 The UK's regulatory amendment process is progressing ahead of the European Union's. The UK Parliament's *Genetic Technology (Precision Breeding) Bill (England only)* provides for gene-edited food crops to be developed, grown and sold in England. The Bill was introduced in May 2022 and has moved quickly through to its final report stage in the House of Lords, December 2022.

34 "Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the Deliberate Release into the Environment of Genetically Modified Organisms and Repealing Council Directive 90/220/EEC – Commission Declaration." 2001. *Access to European Law*

35 In 2002, when the European Food Safety System was revised, the European Food Safety Authority (EFSA) was established as a new independent institution was created to deal with risk assessment and communication.

36 EFSA. 2011. "Guidance on the Risk Assessment of Genetically Modified Microorganisms and their Products Intended for Food and Feed Use." *EFSA Journal* 9(6): 2193.

37 Wesseler, J, Kleter, G, Meulenbroek, M, Purnhagen, KP. 2022. "EU Regulation of Genetically Modified Microorganisms in Light of New Policy Developments: Possible Implications for EU Bioeconomy Investments," *Applied Economic Perspectives and Policy: 1–21*

38 *In vitro* fertilisation, natural processes such as: conjugation, transduction, transformation, and polyploidy induction.

39 Includes competition, innovation, health, wellbeing, management of environmental limits, combating climate change and enhancing sustainability and resilience.

40 EU Regulatory Framework on biosafety

41 European Court of Justice decided that under the EU regulation on genetically modified organisms, modern techniques and methods of directed alteration of genetic material (genome editing) constitute a genetic modification and do not fall under the mutagenesis exemption. As a consequence of the judgment, trial releases of plants and animals obtained by genome editing will be subject to the requirements of risk assessment and authorisation.

42 The European Council is the body that represents the governments of the individual member countries. The Presidency of the Council is shared by the member states on a rotating basis. The European Commission represents the interests of the union as a whole.

43 European Commission, *New techniques in biotechnology*

44 For example, some NGTs (site-directed nuclease techniques, oligonucleotide-directed mutagenesis) in plant applications are widely addressed in expert opinions from the European Food Safety Authority and Member State authorities, and in Member States' and stakeholders' views on safety and risk assessment. Less information is available on other NGTs and micro-organism or animal applications.

45 Site-directed nuclease type 1 and type 2 (SDN-1, SDN-2), , oligonucleotide-directed mutagenesis, cisgenesis.

46 "European Court of Justice Ruling on Genome Editing." 2018. *IUCN*

47 This is currently the case for GMOs under the current regulation.

48 The European Green Deal is a package of policy initiatives, which aim to set the EU on a path to green transition, with the ultimate goal of reaching climate neutrality by 2050. It supports the transformation for the EU into a fair and prosperous society with a modern competitive economy.

49 The Farm to Fork Strategy aims to accelerate the EU's transition to a sustainable food system that will: have a neutral or positive environmental impact, help to mitigate climate change and adapt to its impacts, reverse the loss of biodiversity.

50 Gene Technology (Precision Breeding) Bill 2022-23.

51 European Court of Justice Ruling on Genome Editing. 2018. *IUCN*

52 The term "gene edited" in the UK, is analogous to the term :"new genome technology" used in the EU.

53 "Genetic Technology (Precision Breeding) Bill Factsheet 1 – Overview." 2022. *Department for Environment, Food and Rural Affairs.*

54 As defined for the Gene Technology (Precision Breeding) Bill 2022-23.

55 Performed or taking place in a test tube, culture dish, or elsewhere outside a living organism.

56 In 2013, the EPA determined that use of the gene editing techniques ZFN-1 (zinc finger nuclease-1s) and TALEs (Transcription Activator-Like Effectors), neither of which incorporate foreign DNA into the genome, do not give rise to organisms classed as GMOs under the HSNO Act. The basis for this determination was that the EPA considered that these two techniques were 'comparable and sufficiently similar' to techniques listed as exempt in the Regulations. This determination was legally challenged by the Sustainability Council, and in 2014, the High Court determined that the Regulations set out an exhaustive list of exempt techniques, and thus that EPA had erred in its interpretation of the Regulation. Therefore gene-edited organisms are regulated as GMOs (regardless of the presence or absence of foreign DNA).

57 "HSNO Application Register: GMR07001", 2008. *Environmental Protection Agency*

58 The composition and labelling of GMO foods are regulated under Standard 1.5.2. There are approximately seventy GM foods currently approved, all are derived from plants including soybeans, canola, corn, potato, sugar beet, cotton, lucerne and rice.

59 Codex Alimentarius role in biotechnology is primarily concerned with the risk assessment aspect of food safety and in countries where GM labelling is mandatory it enable consumers to make an informed choice.

60 Gaskell, George, Agnes Allansdottir, Nick Allum, Cristina Corchero, Claude Fischler, and others. 2005. "Europeans and Biotechnology in 2005: Patterns and Trends,"*Goldenrice.org something missing?*

61 Knight, John, Damien Mather, David Holdsworth, and David Ermen. 2007. "Acceptance of GM Food – An Experiment in Six Countries," *Nature Biotechnology*, 25: 507–8.

62 Knight, John, and Hongzhi Gao. 2009. "Chinese Gatekeeper Perceptions of Genetically Modified Food," *British Food Journal*, 111: 56–69.

63 Lusk, Jayson L., Mustafa Jamal, Lauren Kurlander, Maud Roucan, and Lesley Taulman. 2005. "A Meta-Analysis of Genetically Modified Food Valuation Studies," *Journal of Agricultural and Resource Economics*, 30.1: 28–44.

64 Dannenberg, Astrid. 2009. "The Dispersion and Development of Consumer Preferences for Genetically Modified Food — A Meta-Analysis," *Ecological Economics: The Journal of the International Society for Ecological Economics*, 68.8–9: 2182–92.

65 Colson, Gregory J., Wallace E. Huffman, and Matthew C. Rousu. 2011. "Improving the Nutrient Content of Food through Genetic Modification: Evidence from Experimental Auctions on Consumer Acceptance," *Journal of Agricultural and Resource Economics*, 36.2: 343–64.

66 Anderson, Kym. 2019. *Independent Review of the South Australian GM Food Crop Moratorium.*

67 Other than for Kangaroo Island canola where the importer believed it beneficial to be able to claim GM-free status.

68 The South Australian Parliament has since passed changes that will allow GM food crops to be cultivated in South Australia, except on Kangaroo Island.

69 Knight, John. 2016. "GM Crops and Damage to Country Image: Much Ado about Nothing?," *Acta Horticulturae*: 23–32.

70 Scion™ is an NZ crown research institute that specialises in research, science and technology development for the forestry, wood product, wood-derived materials and other biomaterial sectors.

71 Undertaken as a 10 minute online survey using the Colmar Brunton Flybuys panel.

72 "*A look at New Zealanders' current opinions and understanding of genetic technologies*", SCION™ 2019.

73 While not technically a review of New Zealand's GMO regulations, FSANZ does set food safety standards for New Zealand and therefore its recent review of definitions for Gene Technology and new breeding techniques is relevant to this discourse.

74 At the time of publishing in 2001, copies could be purchased from the government printer for $45 or on CD-Rom for $5.

75 Toi te Taiao, the Bioethics Council was disestablished in 2009

76 Royal Society Te Apārangi *Gene Editing Legal and Regulatory Implications* p.5

77 Commonly known as the "flora and fauna" claim, the *Ko Aotearoa Tēnei: Report on the Wai 262 Claim*, released by the Waitangi Tribunal in 2011, considers the ownership and use of Māori knowledge, cultural expressions, indigenous species of flora and fauna, all known as taonga (treasures), and inventions and products derived from indigenous flora and fauna and/or utilising Māori knowledge.

78 "Briefing to the Prime Minister on the Report on Gene Editing from Royal Society Te Apārangi", 2019. *Office of the Prime Minister's Chief Science Advisor*

79 Hudson, Maui, Aroha Te Pareake Mead, David Chagné, Nick Roskruge, Sandy Morrison, and others. 2019. "Indigenous Perspectives and Gene Editing in Aotearoa New Zealand," *Frontiers in Bioengineering and Biotechnology*, 7: 70.

80 Of specific relevance here is that the Waitangi Tribunal noted that 'the law and policy in respect of genetically modified organisms does not sufficiently protect the interests of kaitiaki in mātauranga Māori or in the genetic and biological resources of taonga species. Waitangi Tribunal Ko Aotearoa Tenei: A report into the claims concerning New Zealand Law and Policy Affecting Māori Culture and Identity (2011).

81 Office of the Prime Minister's Chief Science Advisor, 2019. "Briefing to the Prime Minister on the Report on Gene Editing from Royal Society Te Apārangi," p.3

82 Office of the Prime Minister's Chief Science Advisor, 2019. "Briefing to the Prime Minister on the Report on Gene Editing from Royal Society Te Apārangi," p.5

83 The New Zealand Productivity Commission is an independent crown entity focused on providing advice to the government of the day on improving New Zealand in a way that supports the overall wellbeing of New Zealanders and that has regard to a wide range of communities of interest and population groups in New Zealand society.

84 New Zealand Productivity Commission, 2021. *New Zealand Firms: Reaching for the Frontier 2021* 10.4, p.178

85 The Hazardous Substances and New Organisms Act 1996.

86 New Zealand Productivity Commission, 2021. *New Zealand Firms: Reaching for the Frontier 2021* p. 178-179

87 Hill, WG, , S, Miller, JH. 2001. Selective Breeding. *Encyclopaedia of Genetics*, 1796-1799

88 This is likely to become a higher profile issue with the growth of plant based and alternative protein foods, (cellular agriculture).

89 FSANZ Standard 1.5. 2 provides definitions of the terms 'conventional breeding', 'line' and 'transformation event', and lists approved foods produced using gene technology and any conditions for use of the food.

90 FSANZ (Standard 1.1.2-2) prescribes definitions used throughout the code.

91 NB: While FSANZ food safety standards apply in New Zealand, under the HSNO Act food is not an organism meaning that GMO food can be bought and sold in New Zealand but not produced.

Bibliography

Global Regulations

1st Call for Submissions – Proposal P1055. 2021. *Food Standards Australia New Zealand*

About Codex Alimentarius. 2022. *Codex Alimentarius International Food Standards*

Applying for a GMO Permit. 2011. *Business.gov.Nl*

Beal, J, Goñi-Moreno, A, Myers, C, Hecht, Ariel, Del Carmen de Vicente, M, Parco, M, Schmidt, M, Timmis, K, Baldwin, G, Friedrichs, S, Freemont, P, Kiga, D, Ordozgoiti, E, Rennig, M, Rios, L, Tanner, K, de Lorenzo, V, Porcar, M. 2020. The Long Journey towards Standards for Engineering Biosystems: Are the Molecular Biology and the Biotech Communities Ready to Standardise? *EMBO Reports, 21.5: e50521*

Berg, Paul. 2008. Meetings That Changed the World: Asilomar 1975: DNA Modification Secured. *Nature, 455.7211: 290–91*

Biosafety Regulations in Japan: Act on the Conservation and Sustainable Use of Biological Diversity Through Regulations on the Use of Living Modified Organisms. [no date].*Ministry of the Environment, New Zealand*

Biosafety Worldwide – Historical Background. 2015. *Belgian Biosafety Server*

Biotechnology. 2022. *Codex Alimentarius International Food Standards*

Bugnosen, Zabrina J. 2022. Introducing Genome-Edited Foods to the Public – Lessons from Japan. *Science Speaks*

Chronology of Genetic Engineering Regulation in Australia: 1953-1999. 2008.*Parliament of Australia*

Dan, Sujan M. 2019. How Interface Formats Gain Market Acceptance: The Role of Developers and Format Characteristics in the Development of de Facto Standards. *Technovation*, 88.102054: 102054

Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the Deliberate Release into the Environment of Genetically Modified Organisms and Repealing Council Directive 90/220/EEC – Commission Declaration. 1990. *Publications Office of the European Union*

European Commission Study on New Genomic Techniques. 2021. *European Commission*

European Court of Justice Ruling on Genome Editing. 2018. *International Union for Conservation of Nature*

Food Produced by Recombinant DNA Techniques. [no date]. *Ministry of Health, Labour and Welfare, Japan*

Garcia-Alonso, Monica, Jacobs, Erik, Raybould, Alan, Nickson, Thomas E., Sowig, Peter, Willekens, Hilde, Van Der Kouwe, Pier, Layton, Raymond, Amijee, Firoz, Fuentes, Angel, M, Tencalla, Francesca. 2007. A Tiered System for Assessing the Risk of Genetically Modified Plants to Non-Target Organisms. *Environmental Biosafety Research, Cambridge University Press, 5.2: 57–65*

Genetic Technology (Precision Breeding) Bill 2022-23. 2022. *UK Parliament*

Genetic Technology (Precision Breeding) Bill Factsheet 1 – Overview. 2022. *Department for Environment, Food and Rural Affairs, UK Governmet*

Genetically Modified Organisms. 2019. *Ministry of Health Singapore*

GMO Legislation. 2011. *European Commission*

Heinemann, Jack A., Paull. Deborah J., Walker, Sophie, Kurenbach, Brigitta. 2021. Differentiated Impacts of Human Interventions on Nature. *Elementa (Washington, D.C.), 9.1: 00086*

How GMOs Are Regulated in the United States. 2022. *U.S. Food and Drug Administration*

In Boost for Agriculture India Exempts Gene Edited Crops from Biosafety Assessment. 2022. *Alliance for Science, Cornell University*

ISAAA Brief 55: Global Status of Commercialized Biotech/GM Crops for 2019. 2019. *ISAAA*

Kato-Nitta, N, Maeda, T, Inagaki, Y, Tachikawa, M. 2019. Expert and Public Perceptions of Gene-Edited Crops: Attitude Changes in Relation to Scientific Knowledge. *Palgrave Communications, 5.1: 1–14*

Labelling of Foods and Products Containing GMOs. 2011. *Government of the Netherlands*

Labelling on Genetically Modified Food. 2022. *Singapore Food Agency*

Ladenheim, Andrew. 2022. Pressure Mounts on EU and NZ to Review Their Strict Anti-GMO Policies. *Genetic Literacy Project*

Lau, Jessica. 2015. Same Science, Different Policies: Regulating Genetically Modified Foods in the U.S. and Europe. *Science in the News*

Ledford, Heidi. 2019. CRISPR Conundrum: Strict European Court Ruling Leaves Food-Testing Labs without a Plan. *Nature*, *572.7767: 15*

Macnaghten, P, Habets, Michelle G. J. L. 2020. Breaking the Impasse: Towards a Forward-looking Governance Framework for Gene Editing with Plants. *Plants, People, Planet, 2.4: 353–65*

Neo, Pearly. 2021. Japan GM Food Safety Update: Transgenic Soy, Rapeseed Have No Impact on Biodiversity Even after 15 Years – Government Study. *FoodNavigator Asia*

Neo, Pearly. 2022. Japan GM Food: New Data 'Further Supports' the Case for Genetically Modified Ingredients – Government Study. *FoodNavigator Asia*

Paull, J,. Hennig, B. 2019. New World Map of Genetically Modified Organism (GMO) Agriculture: North and South America = 85%. *Acres Australia*: 59–60

Pavone, V, Goven, J, Guarino, R. 2011. From Risk Assessment to In-Context Trajectory Evaluation – GMOs and Their Social Implications. *Environmental Sciences Europe*, *23.1.3*

Position Statement – Gene Technology and Gene Modification. 2018. *Australian Academy of Science*

Proposal P1055 – Definitions for Gene Technology and New Breeding Techniques. 2022. *Food Standards Australia New Zealand*

Questionnaire for Risk Assessment of Genetically Modified Organisms (GMOs) Related to Agriculture. 2022. *Genetic Modification Advisory Committee Singapore*

Rajan, S.R., Letourneau, D.K. 2012. What Risk Assessments of Genetically Modified Organisms Can Learn from Institutional Analyses of Public Health Risks. *Journal of Biomedicine & Biotechnology*, *2012: 203093*

Ramsay, T, Robinson, B, Coche, I, Hackett, K, Emerson, C. 2022. Ethical Aspects of GMO Regulation in the EU: Regulating New Plant Breeding Techniques as GM Has Negative Effects on Sustainability, Diversity and Inclusion. *EMBO Reports*, *23.9: e55583*

Regulation of Biotech Plants. 2022. *US Department of Agriculture*

Rennie, Richard. 2022. Take GE Decision to the People, Urges Sir Peter. *Farmers Weekly*

Roberts, P, Herkert, J, Kuzma J. 2020. Responsible Innovation in Biotechnology: Stakeholder Attitudes and Implications for Research Policy. *Elementa (Washington, D.C.), 8.1: 47*

Royal Commission on Genetic Modification: Government Response. 2001. *Office of the Minister for the Environment, New Zealand*

Royal Commission on Genetic Modification. 2001. Report Back of the Royal Commission On Genetic Modification, *Ministry for the Environment, New Zealand*

Several European Countries Move to Rule out GMOs. 2015. *European Commission*

Singapore Guidelines on the Release of Agriculture-Related GMOs. 2020. *Genetic Modification Advisory Committee, Singapore*

Spök, A, Sprink, T, Allan, AC, Yamaguchi, T, Dayé, C. 2022. Towards Social Acceptability of Genome-Edited Plants in Industrialised Countries? Emerging Evidence from Europe, United States, Canada, Australia, New Zealand, and Japan. *Frontiers in Genome Editing, 4: 899331*

Stilgoe, J, Owen, R, Phil Macnaghten. 2013. Developing a Framework for Responsible Innovation. *Research Policy*.

The Japanese Policy for Genetically Modified Foods. 2017.*Food and Fertiliser Technology Agricultural Policy Platform*

Towards Integrity in Public Dialogue on Issues That Matter. 2019. *The Centre for Informed Futures*

Rodríguez, AV, Rodríguez-Oramas, C, Sanjuán Velázquez, Hardisson de la Torre, A, Rubio Armendáriz, C, Iruzubieta, C. 2022. Myths and Realities about Genetically Modified Food: A Risk-Benefit Analysis. *MDPI Applied Sciences Journal, 12.6: 2861*

Vesprini, F, Whelan, AI, Goberna, MF, Murrone ML, Barros, GE, Frankow, A, Godoy, P, Lewi, DM. 2021. Update of Argentina's Regulatory Policies on the Environmental Risk Assessment. *Frontiers in Bioengineering and Biotechnology*, *9: 834589*

Wesseler, J, Kleter, G, Meulenbroek, M, Purnhagen, KP. 2022. EU Regulation of Genetically Modified Microorganisms in Light of New Policy Developments: Possible Implications for EU Bioeconomy Investments. *Applied Economic Perspectives and Policy*

Consumer Perceptions

Anderson, Kym. 2019. *Independent Review of the South Australian GM Food Crop Moratorium*

Colson, GJ., Huffman, WE, Rousu, MC. 2011. Improving the Nutrient Content of Food through Genetic Modification: Evidence from Experimental Auctions on Consumer Acceptance. *Journal of Agricultural and Resource Economics*, *36.2: 343–64*

Dannenberg, Astrid. 2009. The Dispersion and Development of Consumer Preferences for Genetically Modified Food — A Meta-Analysis. *Ecological Economics: The Journal of the International Society for Ecological Economics*, *68.8–9: 2182–92*

Proposal P1055 – Stakeholder feedback summary report. 2022. Food Standards Australia New Zealand.

Gaskell,G, Allansdottir, A, Allum, N, Corchero, C, Fischler, Hampel, J, Jackson, J, Kronberger, N, Mejlgaard, N, Revuelta, G, Schreiner, C, Stares, S, Torgersen H, Wagner, W. 2005. Europeans and Biotechnology in 2005: Patterns and Trends. *European Commission*

Knight, J, Mather, D, Holdsworth, D, Ermen, D. 2007. Acceptance of GM Food-An Experiment in Six Countries. *Nature Biotechnology, 25: 507–8*

Knight, J, Gao, H. 2009. Chinese Gatekeeper Perceptions of Genetically Modified Food. *British Food Journal*, *111: 56–69*

Knight, J., Clark, A, Mather, DW. 2013. Potential Damage of GM Crops to the Country Image of the Producing Country. *GM Crops & Food, 4.3: 151–57*

Knight, John. 2016. GM Crops and Damage to Country Image: Much Ado about Nothing? *Acta Horticulturae*: 23–32

Kuzma, J, Grieger, K. 2020. Community-Led Governance for Gene-Edited Crops. *Science, American Association for the Advancement of Science, 370.6519: 916–18*

Lusk, JL., Jamal, M, Kurlander, L, Roucan, M, Taulman, L 2005. A Meta-Analysis of Genetically Modified Food Valuation Studies. *Journal of Agricultural and Resource Economics*, *30.1: 28–44*

Rongbin, Y, Ramsaran, R, Wibowo, S. 2018. An Investigation into the Perceptions of Chinese Consumers towards the Country-of-Origin of Dairy Products. *International Journal of Consumer Studies, 42.2: 205–16*

New Zealand Reviews

Caradus, John. 2022. Impacts of Growing and Utilising Genetically Modified Crops and Forages – a New Zealand Perspective. *New Zealand Journal of Agricultural Research, 1–30*

Consumer Responses to the Use of NBTs in the Production of Food: A Systematic Literature Review. 2021. *Australian National University*

Final Report – Review of Food Derived Using New Breeding Techniques. 2021. *Food Standards Australia New Zealand*

Food Derived Using New Breeding Techniques – Review. 2021. *Food Standards Australia New Zealand*

Fritsche, S, Poovaiah, C, MacRae, E, Thorlby, G. 2018. A New Zealand Perspective on the Application and Regulation of Gene Editing. *Frontiers in Plant Science*, *9: 1323*

Gene Editing in Aotearoa. 2019. *Royal Society Te Apārangi, New Zealand*

Gene Editing for the Primary Industries. 2019. *Royal Society Te Apārangi, New Zealand*

Gene Editing in Healthcare. 2019. *Royal Society Te Apārangi, New Zealand*

Gene Editing: Legal and Regulatory Implications. 2019. *Royal Society Te Apārangi, New Zealand*

Gene Editing Technologies. 2019. *Royal Society Te Apārangi, New Zealand*

Genetic Engineering Review. 2009. *Whangarei District Council*

GMO Regulation – Absence of a Sound Case for Review. 2021. *Sustainability Council of New Zealand*

Ha, M, Schleiger, R. 2020. Selective Breeding and Genetic Engineering. *Biology LibreTexts*

Hudson, M, Beaton, A, Milne, M, Port, W, Russell, K, Smith, B, Toki, V, Uerata, L, Wilcox, PL. 2016. Te Mata Ira Guidelines for Genomic Research with Māori. *University of Waikato*

Hudson, M, Mead, ATP, Chagné, D, Roskruge, N, Morrison, S, Wilcox, PL, Allan, AC. 2019. Indigenous Perspectives and Gene Editing in Aotearoa New Zealand. *Frontiers in Bioengineering and Biotechnology, 7: 70*

HSNO Application Register: GMR07001. 2008. *Environmental Protection Agency, New Zealand*

Krinke, Charlotte. 2022. A Minority of States Support Deregulation of New GMOs. *Infogm.org*

New Zealand Firms: Reaching for the Frontier. 2021. *New Zealand Productivity Commission*

New Zealand Must Support Global Regulation of Synthetic Biology 'Pandora's Box'. 2022. *GE-Free New Zealand*

Norman, Cushla. 2022. Genetic Modification Review Being Called for, Reigniting Debate. *TVNZ, 1News*

OPMCSA. 2019. Briefing to the Prime Minister on the Report on Gene Editing from Royal Society Te Apārangi. *Office of the Prime Minister's Chief Science Advisor*

Trafford, Guy. 2022. Is the GMO Ban Solving Any Real Issues? Interest.co.nz

What GM Crops Are Being Grown and Where? 2016. *Royal Society Te Apārangi*

The Waitangi Tribunal. 2011. *Ko Aotearoa Tēnei: A Report Into Claims Concerning New Zealand Law and Policy Affecting Māori Culture and Identity, Volume 1*

The Waitangi Tribunal. 2011. *Ko Aotearoa Tēnei: A Report Into Claims Concerning New Zealand Law and Policy Affecting Māori Culture and Identity, Volume 2*

Genetic Modification: Current Controls in New Zealand and the Royal Commission's Recommendations. 2001. *Ministry for the Environment, New Zealand*

Genetic Modification The New Zealand Approach. 2004. *Ministry for the Environment, New Zealand*

Novel Food Regulations around the World. 2022. *The Global Food Institute Asia Pacific*

Restrictions on Genetically Modified Organisms. 2014. *Law Library of Congress*

Uncertain but Inevitable : The Expert-Policy-Political Nexus and High-Impact Risks. 2021. *Koi Tū: The Centre for Informed Futures*

Technology

A Brief Guide to Genomics. 2019. *National Human Genome Research Institute*

Abbas, Mohamed Samir Tawfik. 2018. Genetically Engineered (Modified) Crops (Bacillus Thuringiensis Crops) and the World Controversy on Their Safety. *Egyptian Journal of Biological Pest Control*, *28.1*

Akst, Jef. 2022. CRISPR Patent Ruling Favors Broad Institute. *The Scientist Magazine*

Ania, Wieczorek. 2012. History of Agricultural Biotechnology: How Crop Development Has Evolved. *Nature Education Knowledge*, *3.3:9*

Antoniou, P, Miccio, A, Brusson, M. 2021. Base and Prime Editing Technologies for Blood Disorders. *Frontiers in Genome Editing*, *3: 618406*

Anzalone, AV, Randolph, PB, Davis, JR, Sousa, AA, Koblan, LW, Levy, JM, Chen, PJ, Wilson, C, Newby, GA, Raguram, A, Liu, DR. 2019. Search-and-Replace Genome Editing without Double-Strand Breaks or Donor DNA. *Nature, 576.7785: 149–57*

Azadi, H, Taheri, F, Ghazali, S, Moghaddam, SM, Siamian, N, Goli, I, Choobchian, S, Pour, M, Özgüven, AI, Janečková, K, Sklenička, P, Witlox. F. 2022. Genetically Modified Crops in Developing Countries: Savior or Traitor? *Journal of Cleaner Production*, *371.133296: 133296*

Becker, S, Boch, J. 2021. TALE and TALEN Genome Editing Technologies. *Gene and Genome Editing*, *2.100007: 100007*

Bezie, Y, Tilahun, T,Atnaf, M, Taye, M. 2020. The Potential Applications of Site-Directed Mutagenesis for Crop Improvement: A Review. *Journal of Crop Science and Technology, Springer, 10.01.321984*

BMC Biotechnology. 2022. *BioMed Central*

Bovine Genome Sequencing and Analysis Consortium. 2009. The Genome Sequence of Taurine Cattle: A Window to

Ruminant Biology and Evolution. Science, American Association for the Advancement of Science, *324.5926: 522–28*

Broad, William J. 2007. Useful Mutants, Bred with Radiation. *The New York Times*

Bt Cotton. [no date]. *UT Crop News, Institute of Agriculture, University of Tennessee*

Calderon, Ignacio. 2021. Graphic: Nearly All Cash Crops Are Genetically Engineered Now. *The Counter*

Carey, Bjorn. 2010. Enviropig: A Bioengineered Pig That Excretes Fewer Pollutants. *Popular Science*

Cellectis, Thermo Fisher Make TALEN Pacts. 2014. *GEN – Genetic Engineering and Biotechnology News*

Change in Rules for Some Gene-Edited Plants and Organisms. 2022. *Chronicle India*

Crabbe, John C. 2018. Using Signatures of Directional Selection to Guide Discovery in Molecular-Genetic and Statistical Techniques for Behavioural and Neural Research, ed. by Robert T. Gerlai. *Elsevier, pp. 243–63*

Da Graca, JV, Louzada, E, Sauls, JW. 2004. The Origins of Red Pigmented Grapefruits and the Development of New Varieties, *International Society of Citriculture*

Derks, MFL., Steensma, M. 2021. Review: Balancing Selection for Deleterious Alleles in Livestock. *Frontiers in Genetics*, *12: 761728*

Disruptive CRISPR Gene Therapy Is 150 Times Cheaper than Zinc Fingers and CRISPR Is Faster and More Precise. 2015. *Gene Therapy Net*

Dubock, Adrian. 2017. Golden Rice: Instructions for Use. *Agriculture & Food Security*, *6.1*

Dudde, A, Krause, ET, Matthews, LR, Schrader, L. 2018. More than Eggs – Relationship between Productivity and Learning in Laying Hens. *Frontiers in Psychology*, *9: 2000*

Edelheit, O, Hanukoglu, A, Hanukoglu, I. 2009. Simple and Efficient Site-Directed Mutagenesis Using Two Single-Primer 9.1:61 Reactions in Parallel to Generate Mutants for Protein Structure-Function Studies. *BMC Biotechnology*, *9.1: 61*

Enroth, C, Johnson, K, Swihart, E. 2015. We've Been Genetically Altering Plants for Thousands of Years. *University of Illinois Extension*

Fuller, Hannah. 2020. Bananas: A Story of Clones and Colonization. *Grounded Grub*

García-Bastidas, FA., Van der Veen, AJT, Nakasato-Tagami, G, Meijer, HJG, Arango-Isaza, RE, Kema GHJ. 2019. An Improved Phenotyping Protocol for Panama Disease in Banana. *Frontiers in Plant Science*, *10: 1006*

Gene Editing Is a Key to Environmental Sustainability. 2020. *Innovature*

Genetic Editing Eliminates Dairy Cattle Horns. 2019. *International Milk Genomics Consortium*

Genetically Modified Medicines and Food. 2004. *Ministry for the Environment, New Zealand*

Genetically Modified (GM) crops in Australia, 2021. *Office of the gene technology regulator*

Genetically Modified Organisms: The Golden Rice Debate. [no date].*NYU Langone Health*

Genome. 2014. *Scitable by Nature Education*

Golden Rice. 2018. *International Rice Research Institute*

Gould, Skye. 2017. These 6 Common Vegetables Are Actually All the Same Plant Species, *Business Insider*

Greeff, Johan. 2020. Genetic Selection and Using Australian Sheep Breeding Values. *Department of Primary Industries and Regional Development*

de Haas, Y., Veerkamp, RF, de Jong, G, Aldridge, MN. 2021. Selective Breeding as a Mitigation Tool for Methane Emissions from Dairy Cattle. *Animal: An International Journal of Animal Bioscience*, *15 Suppl 1.100294: 100294*

Hillary, VE, Ceasar, SA. 2022. Prime Editing in Plants and Mammalian Cells: Mechanism, Achievements, Limitations, and Future Prospects. *BioEssays: News and Reviews in Molecular, Cellular and Developmental Biology*, *44.9: e2200032*

Himme, Ben. Transgenesis. [no date]. *Pathwayz*

History of Sheep. 2020. *International Wool Textile Organisation*

Ioannidi, EI,Yarnall MTN, Schmitt-Ulms,C, Krajeski, RN, Lim, J, Villiger, L, Zhou, W, Jiang, K, Garushyants, SK, Roberts, N, Zhang, L, Vakulkskas, A, Walker, JA, Kadina, AP, Zepeda, AE, Holden, K, Ma, H, Xie, J, Goa, G,Foquet, L, Bial, G, Donnelley, SK, Miyata, Y, Radilof, DR, Henderson, JM, Ukita, A, Abudayyeh, OO, Gootenberg, JS. 2021. Drag-and-Drop Genome Insertion without DNA Cleavage with CRISPR-Directed Integrases. *Nature Biotechnology, p. 2021.11.01.466786*

Jackson, N, Maddocks, IG, Watts, JE, Scobie, D, Mason, RS, Gordon-Tomson, C, Stockwell, S, Moore, GPM. . 2020. Evolution of the Sheep Coat: The Impact of Domestication on Its Structure and Development. *Genetics Research*, *Cambridge University Press, 102.e4: e4*

Johnson, Charlotte. 2022. Genetically Modified Salmon: Changing the Future. *thefishsite.com*

Joung, JK, Sander, JD. 2013. TALENs: A Widely Applicable Technology for Targeted Genome Editing. *Nature Reviews. Molecular Cell Biology, 14.1: 49–55*

Kawall, Katharina. 2021. The Generic Risks and the Potential of SDN-1 Applications in Crop Plants, *Plants*, *10.11: 2259*

Khan, Sikandar Hayat. 2019. Genome-Editing Technologies: Concept, Pros, and Cons of Various Genome-Editing Techniques and Bioethical Concerns for Clinical Application. *Molecular Therapy. Nucleic Acids*, *16: 326–34*

Klug, Aaron. 2010. The Discovery of Zinc Fingers and Their Development for Practical Applications in Gene Regulation and Genome Manipulation. *Quarterly Reviews of Biophysics*, 43.1: 1–21

Kou, J, Tang, Q, Zhang, X. 2015. Agricultural GMO Safety Administration in China. *Journal of Integrative Agriculture*, *14.11: 2157–65*

Kranthi, KR, Stone, GD. 2020. Long-Term Impacts of Bt Cotton in India. *Nature Plants*, *6.3: 188–96*

Labrou, Nikolaos E. 2010. Random Mutagenesis Methods for in Vitro Directed Enzyme Evolution. *Current Protein & Peptide Science*, *11.1: 91–100*

Lamas-Toranzo, I., Galiano-Cogolludo, B, Cornudella-Ardiaca, J. Cobos-Figueroa, O, Ousinde, Bermejo-Alvarez, P. 2019. Strategies to Reduce Genetic Mosaicism Following CRISPR-Mediated Genome Edition in Bovine Embryos. *Scientific Reports*, *9.1: 14900*

Laursen, Kristian. 2016. Site Directed Mutagenesis by PCR. *Addgene Blog*

Lenape Potato. 2021.*Wikipedia, The Free Encyclopaedia*

Li, Y, Lu, Y, Hallerman, EM, Peng,Y, Wu, K. 2017. Commercial Use and Governance of Bt Cotton in China in *Genetically Modified Organisms in Developing Countries*, ed. by Adenle, AA. Morris, EJ, Murphy, DJ. *Cambridge University Press, pp. 225–35*

Lillico, SG, Proudfoot, C, King, TJ, Tan, W, Lei Zhang, Mardjuki, R, Paschon, DE, Rebar, EJ, Urnov, FD, Mileham, AJ, McLaren, DG, Whitelaw, CBA. 2016. Mammalian Interspecies Substitution of Immune Modulatory Alleles by Genome Editing. *Scientific Reports*, *6.1: 21645*

Liu, L, Guo, R, Qin, Q, Fu, F. Liu, B. 2020. Expression of Bt Protein in Transgenic Bt Cotton Plants and Ecological Fitness of These Plants in Different Habitats. *Frontiers in Plant Science*, *11: 1209*

Liu, Paul P. 2022. Transgenic. *National Human Genome Research Institute*

Liu, Q, Yang, F, Zhang, J, Liu, H, Rahman, S, Islam, S, Ma, W, She, M. 2021. Application of CRISPR/Cas9 in Crop Quality Improvement. *International Journal of Molecular Sciences*, *22.8: 4206*

Liu, X, Wang, Y, Guo, W, Chang, B, Liu, J, Guo, Z, Quan, F, Zhang, Y. 2013. Zinc-Finger Nickase-Mediated Insertion of the Lysostaphin Gene into the Beta-Casein Locus in Cloned Cows. *Nature Communications*, *4.1: 2565*

Lu, Y, Mbakam, CH, Song, B, Bendavid, E, Tremblay JP. 2022. Improvements of Nuclease and Nickase Gene Modification Techniques for the Treatment of Genetic Diseases. *Frontiers in Genome Editing, 4: 892769*

Madre, Y, Agostino, VD. 2017. New Plant-Breeding Techniques: What Are We Talking About? *Farm Europe*

Mao, Z, Bozzella, M, Seluanov, A, Gorbunova, V. 2008. Comparison of Nonhomologous End Joining and Homologous Recombination in Human Cells. *DNA Repair*, *7.10: 1765–71*

Mark, Joshua J. 2022. Near East. *World History Encyclopaedia*

van Marle-Köster, E, Visser, C. 2021. Unintended Consequences of Selection for Increased Production on the Health and Welfare of Livestock. *Archives Animal Breeding*, *64.1: 177–85*

Matheson, N, Schahczenski, J, Adam, K. 2018. Genetically Modified Crops: Transgenics and Cisgenics. *The National Centre for Appropriate Technology*

Matika, O, Riggio, V, Anselme-Moizan, M, Law, AS, Pong-Wong, R, Archibald, A. Bishop, SC. 2016. Genome-Wide Association Reveals QTL for Growth, Bone and in Vivo Carcass Traits as Assessed by Computed Tomography in Scottish Blackface Lambs. *Genetics, Selection, Evolution*, *48.1: 11*

Matsoukas, Ianis G. 2020. Prime Editing: Genome Editing for Rare Genetic Diseases without Double-Strand Breaks or Donor DNA. *Frontiers in Genetics*, *11: 528*

Menz, J, Modrzejewski, D, Hartung, F, Wilhelm, R, Sprink, T. 2020. Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment. *Frontiers in Plant Science*, *11: 586027*

Minard, Anne. 2010. Gene-Altered 'Enviropig' to Reduce Dead Zones? *National Geographic*

Modrzejewski, D, Hartung, F, Lehnert, H, Sprink, T, Kohl, C, Kielwagen, J, Wilhelm, R. 2020. Which Factors Affect the Occurrence of Off-Target Effects Caused by the Use of CRISPR/Cas: A Systematic Review in Plants. *Frontiers in Plant Science*, *11: 574959*

Morange, Michel. 2017. What History Tells Us XLIV: The Construction of the Zinc Finger Nucleases. *Journal of Biosciences*, *42.4: 527–30*

Mushtaq, M, Sakina, A, Wani, SH, Shikari, AB, Tripathi, P, Zaid, A, Galla, A. Abdelrahmen, M, Sharma, M, Singh, AK, Salgotra, RK. 2019. Harnessing Genome Editing Techniques to Engineer Disease Resistance in Plants. *Frontiers in Plant Science*, *10: 550*

Mutagenesis (Molecular Biology Technique). 2022. *Wikipedia, The Free Encyclopaedia*

National Science Foundation. Scientists Trace Corn Ancestry from Ancient Grass to Modern Crop. 2005.

NCI Dictionary of Genetics Terms. 2012. *National Cancer Institute*

Nemudryi, AA, Valetdinova, KR, Medvedev, SP, Zakian, SM. 2014. "TALEN and CRISPR/Cas Genome Editing Systems: Tools of Discovery. *Acta Naturae*, *6.3: 19–40*

New Kid On The Block: Prime Editing as a Precision Gene Editing Tool. 2022. *Synthego Corporation*

Scientists Trace Corn Ancestry from Ancient Grass to Modern Crop. 2005. *National Science Foundation*

Genetically Modified (GM) Crops in Australia. 2021. *Office of the Gene Technology Regulator*

Oladosu, Y, Rafii, MY, Abdullah, N, Hussin, G, Ramli, A. 2016. Principle and Application of Plant Mutagenesis in Crop Improvement: A Review. *Biotechnology, Biotechnological Equipment*, *30.1: 1–16*

Transgenesis. 2019. *Biology Online*

Ordonez, N, Seidl, MF, Waalwijk, C, Drenth, A, Kilian, A, Thomma, BP, Ploetz, RC, Kema, GH. 2015. Worse Comes to Worst: Bananas and Panama Disease: When Plant and Pathogen Clones Meet. *PLoS Pathogens, 11.11: e1005197*

Overview of Genome Editing Applications Using SDN-1 and SDN-2 in Regard to EU Regulatory Issues. 2020. *Testbiotech*

Palgrave, CJ., Gilmour, L, Lowden, CS, Lillico, SG, Mellencamp MA, Whitelaw, CBA. 2011. Species-Specific Variation in RELA Underlies Differences in NF-~~B~~ Activity: A Potential Role in African Swine Fever Pathogenesis. *Journal of Virology*, *85.12: 6008–14*

Philippines Becomes First Country to Approve Nutrient-Enriched 'Golden Rice' for Planting. 2021. *International Rice Research Institute*

Ploetz, Randy C. 2000. Panama Disease: A Classic and Destructive Disease of Banana. *Plant Health Progress*, *1.1: 10*

Podevin, N, Davies, HV, Hartung, F, Nogué, F, Casacuberta, JM. 2013. Site-Directed Nucleases: A Paradigm Shift in Predictable, Knowledge-Based Plant Breeding. *Trends in Biotechnology*, *31.6: 375–83*

Potrykus, Ingo. 2001. The 'Golden Rice' Tale. *In Vitro Cellular & Developmental Biology. Plant: Journal of the Tissue Culture Association*, *Society for In Vitro Biology*, *37.2: 93–100*

Queremel, M, Daniel, A, Chauhan, PR. 2022. Genetics, Mosaicism. *StatPearls Publishing*

Ranger Russet. 2015.*Institute of Agriculture and Natural Resources*

Recombination. 2014. *Scitable by Nature Education*

van Rijssen, WJ, Morris, EJ. 2018. Safety and Risk Assessment of Food from Genetically Engineered Crops and Animals: The Challenges in Genetically Engineered Foods, ed. Holban AM, Grumezescu AM. *Science Direct, Elsevier, pp. 335–68*

Rodgers, K, McVey, M. 2016. Error-Prone Repair of DNA Double-Strand Breaks. *Journal of Cellular Physiology, 231.1: 15–24*

Rose, Ian James. 2014. Breeding Strategies to Make Sheep Farms Resilient to Uncertainty. *Wageningen University, The Nederlands.*

SCION. A look at New Zealanders' current opinions and understanding of genetic technologies. 2019.

Science Daily, University of California – Berkeley. *Simple Technology Makes CRISPR Gene Editing Cheaper: Inexpensive Technique Can Quickly Turn Entire Genomes into Thousands of Guide RNAs.* 2015.

Scott, Christopher Thomas. 2005. The Zinc Finger Nuclease Monopoly. *Nature Biotechnology, 23.8: 915–18*

SDN: Site-Directed Nuclease Technology. 2014. *NBT Platform*

van Seters, John. 1992. Prologue to History: The Yahwist as Historian in Genesis. *Louisville, KY: Westminster/John Knox Press*

Shahbandeh, M. 2021. Genetically Modified Crops – Statistics & Facts. *Statista*

Silva, G, Poirot, L, Galetto, R, Smith, J, Montoya, G, Duchateau, P, Paques, F. 2011. Meganucleases and Other Tools for Targeted Genome Engineering: Perspectives and Challenges for Gene Therapy. *Current Gene Therapy, 11.1: 11–27*

Sonesson, Anna K. 2022. Advancing Selective Breeding in Sea Bass and Sea Bream. *thefishsite.com*

Sticklen, Mariam. 2015. Transgenic, Cisgenic, Intragenic and Subgenic Crops. *Advances in Crop Science and Technology, 03.02: 1–2*

Sutipatanasomboon, Arpaporn. 2021. Site-Directed Mutagenesis: Methods and Applications. *Conduct Science*

Tachioka, M, Sugimoto, N, Nakamura, A, Sunagawa, N, Ishida, T, Uchiyama, T, Igarashi, K, Samejima, M. 2016. Development of Simple Random Mutagenesis Protocol for the Protein Expression System in Pichia Pastoris. *Biotechnology for Biofuels, 9.1: 199*

Taylor, Güneş. 2019. Green Editing: The Environmental Benefits of Gene-Tweaking. *Nesta*

Thompson, Stuart. 2019. The Quest to Save the Banana from Extinction. *The Conversation*

Transgenesis. 2019.Biology Online

Vidyasagar, A, Lanese, N. 2021. What Is CRISPR? *Live Science*

Viljoen, A, Ma, L, Molina, AB. 2020. Fusarium Wilt (Panama Disease) and Monoculture in Banana Production: Resurgence of a Century-Old Disease in *Emerging Plant Diseases and Global Food Security. The American Phytopathological Society, pp. 159–84*

West, Brian R. 2018. Selective Breeding. *Encyclopedia.com*

What Is Nutritionally Enhanced Golden Rice and Why Is It Controversial? 2019. *Genetic Literacy Project*

What Is Selective Breeding? Wellcome, 2021.*Your Genome*

Wray-Cahen, D, Bodnar, A, Rexroad III, C, Siewerdt, F, Kovich, D. 2022. Advancing Genome Editing to Improve the Sustainability and Resiliency of Animal Agriculture. *Centre for Agriculture and Bioscience International Agriculture and Bioscience, 3.1*

Zhang, Y, Butelli, E, De Stefano, R, Schoonbeek, H, Magusin, A, Pagliarani C, Wellner N, Hill L, Orzaez D, Granell A, Jones JD, Martin C. 2013. Anthocyanins Double the Shelf Life of Tomatoes by Delaying Overripening and Reducing Susceptibility to Gray Mold. *Current Biology: CB, 23.12: 1094–1100*

Zhang, Y, Massel, K, Godwin, ID, Gao, C. 2018. Applications and Potential of Genome Editing in Crop Improvement. *Genome Biology, 19.1: 210*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