Australian Regulatory Response to Genome Edited Plants

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Abstract

Genetic variation in plants is fundamental to food security. Biotechnology can speed up plant breeding and creation of that variation. Genome editing techniques, including CRISPR/Cas9, modify DNA more accurately and cheaply compared to older biotechnology techniques such as genetic modification. However, development and uptake of genome editing techniques requires clear regulatory pathways. Those pathways are contested in most jurisdictions and the regulation of the resulting plants is becoming an increasingly sensitive subject-matter. In particular, the techniques are challenging regulatory frameworks intended to respond to genetically modified plants. In Australia, regulatory reviews are being undertaken by Food Standards Australia New Zealand and the Gene Technology Regulator to determine the place of genome edited plants and their produce. These reviews may result in major shifts in Australia's regulatory approach to agricultural biotechnology, including improved consistency between the two frameworks and operation on an output basis (focusing on resulting products) rather than an input basis (focusing on the process used to create products). This paper examines Australian regulatory responses to genome edited plants and identifies challenges for regulators, the scientific community, and agricultural production and trade in light of them.

1 Introduction

The genetic material of plants has always been subject to change; some directed by humans and some not. Genetic change creates new varieties, which are fundamental for food security[1] and respond to society's calls for new and improved traits in agricultural plants.[2] Such traits include greater yields, resistance to pests and disease, and the need for less water or other resources.[3]

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1 Department of Agriculture, Fisheries and Forestry (Cth), *National Food Plan* (White Paper, 2013) 43. Australian government policy also recognises agricultural biotechnology is needed in part to produce that variation.

2 KPMG, National Farmers Federation and Telstra, 'Talking 2030' (Discussion Paper, March 2018) 33 ('Talking 2030').

3 Saminathan Subburaj et al, 'Targeted Genome Editing, an Alternative Tool for Trait Improvement in Horticultural Crops' (2016) 57(6) *Horticulture, Environment, and Biotechnology* 531, 531.

Although many genetic changes produced using genome editing could be achieved through older unregulated techniques, genome editing is quicker and allows more precise changes.[4] Its potential is such that it may 'revolutionise plant breeding and, by extension, farming'.[5]

Non-browning mushrooms were the first genome edited product approved for sale in 2016, and other products have since joined it on the American market.[6] As of 2018, no genome edited plants are cultivated or approved for sale in Australia, but Australian regulators are preparing for their introduction.[7] Genome editing is not clearly classified by regulations created for earlier biotechnologies such as genetic modification and mutagenesis. Regulatory uncertainty significantly impacts the entire innovation pipeline — delaying basic research through to the commercial availability of products and, in turn, impacting Australian agriculture's international competitiveness.[8]

Private governance is already responding to genome edited plants by limiting controversial uses of the technology.[9] Parthasarathy has noted that some organisations and researchers are using patent licenses for these techniques to reflect their own moral codes.[10] For plants, this has meant prohibitions on the use of gene drives to protect ecosystems,[11] on the creation of sterile terminator seeds to protect farmers, and on the commercialisation of tobacco products that may

4 Ibid.

5 'Talking 2030' (n 2) 15. For more on potential applications of genome editing in agriculture, see Council for Agricultural Science and Technology, 'Genome Editing in Agriculture: Methods, Applications, and Governance' (Issue Paper No 60, 2018) ('Genome Editing in Agriculture').

6 Stuart J Smyth, 'Canadian Regulatory Perspectives on Genome Engineered Crops' (2017) 8(1) *GM Crops & Food* 35, 37; Emily Waltz, 'Gene-Edited CRISPR Mushroom Escapes US Regulation' (2016) 532 *Nature* 293.

7 *Australia New Zealand Food Standards Code* (Cth) sch 26 ('*ANZFS Code*').

8 One Australian regulator has noted that regulatory ambiguity could inhibit the use and development of genome editing in Australia: see Office of the Gene Technology Regulator, *Updating Gene Technology Regulation in Australia* (Consultation Regulation Impact Statement, Department of Health (Cth), 30 Nov 2017) 5 ('*Updating Gene Technology Regulation in Australia*').

9 Christi J Guerrini et al, 'The Rise of the Ethical License' (2017) 35 *Nature Biotechnology* 22, 22. See also Ian Ayres and John Braithwaite, *Responsive Regulation: Transcending the Deregulation Debate* (Oxford University Press, 1992) for an introduction to the idea that regulation is more than legislation.

10 Shobita Parthasarathy, 'Use of the Patent System to Regulate Gene Editing' (2018) 562 *Nature* 486, 487.

11 Gene drives are 'genetic elements that are favoured for inheritance, and which can therefore spread through sexually reproducing populations at a greater rate than genes with standard Mendelian inheritance': Department of Health (Cth), *Third Review of the National Gene Technology Scheme* (Final Report, October 2018) 108 ('*Third Review of the National Gene Technology Scheme Final Report*').

increase public health burdens.[12] Turning to public governance, Parthasarathy suggests that governments could use the patent system to drive innovation in socially desirable ways.[13] Intellectual property systems are 'arguably one of the most important governance mechanisms influencing the evolution of technological trajectories or pathways in agricultural biotechnology'.[14] The granting of intellectual property rights (or not), licensing, enforcement and litigation also impact innovation adoption and regulation.

While Australia's intellectual property regime will have an important role in the regulation of genome edited plants, this paper focuses on two other Australian regulatory frameworks — food and gene technology. Two federal bodies, the Office of the Gene Technology Regulator ('OGTR') and Food Standards Australia New Zealand ('FSANZ'), are primarily responsible for the regulation of genetically modified ('GM') plants and their products in Australia through these frameworks.[15] Both have adopted interim approaches to genome edited plants, while completing reviews.[16] The scope of these frameworks is determined by a process trigger, where the use of a defined process requires compliance with the regulatory scheme.[17] The relevant process is the use of gene technology. Other jurisdictions, such as the European Union member states and New Zealand, also use process triggers in their regulatory schemes for genetically modified organisms ('GMOs'). But some jurisdictions, such as Canada and Argentina, use product-based triggers for GMO regulation. In these countries, regulatory obligations are determined by the final characteristics of the product or organism regardless of the process used to produce it.[18] For those jurisdictions, the fact that the same genetic changes can be produced using older techniques makes it likely

12 Guerrini et al (n 9) 22.

13 Parthasarathy (n 10) 488.

14 Derek Eaton and Gregory Graff, 'The Dynamic IP System in Crop Genetics and Biotechnology' in Stuart J Smyth, Peter WB Phillips and David Castle (eds), *Handbook on Agriculture, Biotechnology and Development* (Edward Elgar, 2014) 425, 425.

15 The OGTR was established pursuant to the *Gene Technology Act 2000* (Cth) ('*GT Act*'). Each Australian state and territory has mirroring legislation that refers powers to the national OGTR. FSANZ was created under the *Food Standards Australia New Zealand Act 1991* (Cth) ('*FSANZ Act*').

16 Both bodies are within the same federal government department, the Department of Health. However, a different ministerial forum is responsible for each. These forums, made up of ministers from federal and state/territory governments, provide broader policy guidance to the bodies.

17 *GT Act* (n 15) s 3, pt 4 div 2; *ANZFS Code* (n 7) standards 1.1.1–3, 1.1.1–10(5)(c), (6)(g), 1.5.2. See also Department of Health (Cth), *Third Review of the Gene Technology Scheme* (Preliminary Report, March 2018) 26.

18 Tetsuya Ishii and Motoko Araki, 'A Future Scenario of the Global Regulatory Landscape Regarding Genome-Edited Crops' (2017) 8(1) *GM Crops & Food* 44, 46.

that regulation will not trigger for genome edited plants. As discussed below, this fact is generally irrelevant where process triggers are used.

The paper begins with some necessary background and context. Section 2 describes the techniques for genetic change in plants: conventional breeding, mutagenesis, genetic modification (or gene technology as it is called in Australian regulation) and genome editing. Section 3 considers international responses to genome edited plants. The paper then focuses on the matters that Australian regulators must now decide. The regulatory frameworks and provisions responsible for uncertainty around the regulation of plant genome editing are identified in Section 4. Sections 5, 6 and 7 address the scope of the regulatory triggers and exclusions and Section 8 scrutinises proposed regulatory amendments. The paper concludes in Section 9 with discussion and suggestions for broader change to Australian regulation of innovation in agricultural biotechnology.

2 *Getting Genetic Variety in Plants*

Mixing parental DNA through sexual reproduction results in unique genetic combinations from which new varieties are developed. In conventional breeding, plant breeders select plants with the most useful traits and sexually cross them back with related plants to introduce that trait into future generations.[19] New varieties also arise following changes, called mutation, in a cell's DNA during growth.[20] These changes occur spontaneously or through human intervention by exposing plant cells to chemicals or radiation. Mutations can occur following breaks in a plant's DNA.[21] Whether such breaks are spontaneous or caused by human intervention, the cell recognises the break and 'repairs' it most commonly through a process known as nonhomologous end joining ('NHEJ').[22] Importantly for achieving genetic variation, errors (mutations) are often made by cells during this process.[23] Random deletions or more rarely, insertions, of nucleotides (which make up DNA) may occur. While such errors may have no effect, they can cause a gene (or gene-regulatory element, which controls when and how other genetic

[19] Agricultural Biotechnology Council of Australia, *The Official Australian Reference Guide to Agricultural Biotechnology and GM Crops* (Report No 3, 2017) 3.

[20] Joel L Carlin, 'Mutations Are the Raw Materials of Evolution' (2011) 3(10) *Nature Education Knowledge* 10.

[21] Wendy J Cannan and David S Pederson, 'Mechanisms and Consequences of Double-Stranded DNA Break Formation in Chromatin' (2016) 231(1) *Journal of Cellular Physiology* 3, 3.

[22] National Academies of Sciences, Engineering and Medicine (US), *Human Genome Editing: Science, Ethics, and Governance* (Report, 2017) 63 ('*Human Genome Editing*').

[23] For more on how changes occur, see Hisaji Maki, 'Origins of Spontaneous Mutations: Specificity and Directionality of Base-Substitution, Frameshift, and Sequence-Substitution Mutageneses' (2002) 36 *Annual Review of Genetics* 279.

sequences operate) to cease functioning, in turn causing a detectable change in the plant's traits.[24] Untargeted human directed mutagenesis has been used for over 80 years, with more than 3,220 mutant varieties in over 210 plant species having been officially released globally.[25] As explained below, plant varieties and their products produced by mutagenesis are excluded from Australian regulation because they are considered safe.[26] Therefore, they and their products enter the market without any pre-market safety review.[27]

But these techniques have limitations. Sexual reproduction requires the plants to be from the same or closely related species.[28] Possible genetic changes are therefore limited because the desired trait must be within the species for it to be heritable by successive generations.[29] Genetic change through conventional breeding and mutagenesis is also untargeted — the traits affected will not be known in advance.[30] Resulting individuals must be grown and promising ones selected and bred over multiple generations to assess the changes. In most cases, many generations of selective breeding with the most desirable plants must occur to remove unwanted genetic changes that accompany the desirable ones.[31] This means the techniques are slow. Time must be allowed for the plant to reach sexual maturity. Standard apple trees, for example, need 5–12 years before they will flower and fruit and therefore sexually reproduce.[32] Time is also needed for progeny to mature to assess the quality of the new variety and, if it has potential, to breed it on.

Innovation in plant breeding, such as genetic modification, address these problems. Genetic modification allows the genes responsible for a known trait to be deleted (if it is unwanted), enhanced or moved from one organism to another. Since sexual reproduction is not used, the plants do not need to be related —

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24 *Human Genome Editing* (n 22) 63, 218.

25 Souleymane Bado et al, 'Plant Mutation Breeding: Current Progress and Future Assessment' in Jules Janick (ed.), *Plant Breeding Reviews: Volume 39* (Wiley Online Library, 2015) 23, 23.

26 FSANZ, 'Food Derived Using New Breeding Techniques' (Consultation Paper, February 2018) 5 ('Food Derived Using New Breeding Techniques'). See also Natalie Weber et al, 'Crop Genome Plasticity and Its Relevance to Food and Feed Safety of Genetically Engineered Breeding Stacks' (2012) 160(4) *Plant Physiology* 1842, 1843.

27 This is not to say that the producer does not undertake safety testing of its own.

28 The Royal Society, *GM Plants: Questions and Answers* (Report, May 2016) 12.ß.

29 Ibid.

30 Office of the Chief Scientist (Cth), 'Gene Editing and CRISPR' (Occasional Paper No 14, September 2017) 2.

31 *Third Review of the National Gene Technology Scheme Final Report* (n 11) 24.

32 Noriko Yamagishi, Ryusuke Kishigami and Nobuyuki Yoshikawa, 'Reduced Generation Time of Apple Seedlings to within a Year by Means of a Plant Virus Vector: A New Plant-Breeding Technique with No Transmissions of Genetic Modification to the Next Generation' (2014) 12 *Plant Biotechnology Journal* 60, 60.

DNA can be moved between unrelated organisms. Genetic modification occurs by isolating and copying the gene intended to be transferred.[33] The gene of interest together with any necessary genetic controls are introduced into the cell to be modified using, for example, bacterium vectors (which carry the DNA into the cell) or particle bombardment (where minute particles of tungsten or gold coated with the relevant DNA are fired into plant cells). The inserted gene then integrates into the cell's genome, and the transformed cell is cultured and grown into plants that (all going well) express the desired change.[34] Genetic modification therefore allows changes that are not limited to the characteristics within the species concerned. It is also quicker than conventional breeding and mutagenesis and the trait of interest can be targeted for change.[35]

However, genetic modification has practical limitations. While it can focus on a trait and cut DNA in predictable and reproducible ways, it cannot control where the new genetic sequence is inserted in the receiving plant's genome.[36] Resulting plants must therefore be screened to identify those with successful genetic changes. It is also expensive, limiting the institutions that can afford to do it.[37]

Genome editing does not have the practical disadvantages of earlier plant breeding techniques. The underlying difference between genome editing and genetic modification is that instead of moving genes from one organism to another as commonly occurs in genetic modification, changes (mutations) are made to the plant's own DNA. But unlike conventional breeding and mutagenesis, the genetic changes are precise and targeted.

The predominant genome editing method is the use of site-directed (or targeted) nucleases ('SDN') to cut DNA. CRISPR/Cas is the best-known example of SDN.[38]

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33 For more information on genetic modification, see US National Academies of Sciences, Engineering, and Medicine, *Genetically Engineered Crops: Experiences and prospects* (Report, 2016) ('*Genetically Engineered Crops*').

34 International Service for the Acquisition of Agri-biotech Applications, *Agricultural Biotechnology (A Lot More Than Just GM Crops)* (Report, May 2014) 15–24.

35 *Human Genome Editing* (n 22) 65.

36 Ibid 63.

37 See also Phillips McDougall, *The Cost and Time Involved in the Discovery, Development and Authorisation of a New Plant Biotechnology Derived Trait* (Consultancy Study, CropLife International, September 2011) 14; Steven H Strauss and Joanna K Sax, 'Ending Event-Based Regulation of GMO Crops' (2016) 34(5) *Nature Biotechnology* 474, 475. Genetic modification to introduce just one trait costs as much as USD$250,000: see Smyth (n 6) 37.

38 For more on these techniques, see Maria Lusser et al, *New Plant Breeding Techniques: State-of-the-Art and Prospects for Commercial Development* (JRC Scientific and Technical Report No EUR 24760 EN, 2011); European Food Safety Authority Panel on GMOs, 'Scientific Opinion Addressing the Safety Assessment of Plants Developed Using Zinc Finger Nuclease 3 and Other Site-Directed Nucleases with Similar Function' (2012) 10(10) *European Food Safety Authority Journal* 2943; *Human Genome Editing* (n 22) 61–82.

Other SDNs include zinc finger nucleases ('ZFN') and transcription activator-like effector nucleases ('TALENs'). In all of these, the SDN cuts both strands of the cell's DNA at the targeted site to initiate cellular repair of the DNA. The cell recognises there is a break in its DNA and repairs the break as described above.

Targeted changes are achieved because CRISPR/Cas, ZFN and TALENs allow molecular biologists to engineer recognition sequences. These find the DNA sequence to be changed in the cell's genome, much like a find-and-replace tool in word processing. Joining recognition sequences to the SDN causes the SDN to cut the targeted sequence located by the recognition sequence. The methods differ in the nature of the recognition sequence — ZFN and TALENs use protein segments and CRISPR uses RNA (a nucleic acid) sequences that recognise and bind to the targeted sequences in the DNA.[39] The attraction of CRISPR/Cas is that it is simpler, faster, and cheaper relative to ZFN and TALENs to synthesise the recognition sequence, and it is highly specific.[40] The SDN is degraded inside the cell once it has completed its task, but the fact that CRISPR introduces exogenous nucleic acid (that is, RNA originating from outside the cell) is, as discussed below, significant to the regulatory responses.

Whichever SDN technique is used, genome editing relies on errors being made during the DNA repair process in the same way as occurs in spontaneous or untargeted human induced mutagenesis — that when a cell repairs DNA, errors (mutations) are often made.[41] This simple form of SDN, known as SDN-1, produces deletions, insertions and rearrangements at repair sites indistinguishable at the DNA sequence level from those obtained using the earlier, and unregulated, mutagenesis techniques.[42]

The precision of genome editing can be improved by using additional tools with the SDN, which allow breeders to predict where the change will occur and the size and sequence of the change.[43] These tools take advantage of a second natural cellular repair mechanism called homology-directed repair ('HDR').[44] HDR occurs when the cell copies another piece of DNA sharing the same sequence with the cut DNA while rejoining the cut ends of the DNA.[45] Taking advantage of this, scientists introduce a short piece of DNA with the SDN. That DNA

39 *Human Genome Editing* (n 22) 64–5.

40 Ibid 65.

41 Ibid 218.

42 CropLife Australia, Submission to the OGTR, *Technical Review of the Gene Technology Regulations 2001* (16 December 2016) 5.

43 *Human Genome Editing* (n 22) 64.

44 Ibid.

45 This could be the equivalent site on the other chromosome of the relevant pair.

includes the desired change and acts as an alternative template.[46] Following this template causes the cell to make a mismatch repair based on the introduced DNA sequence rather than what the sequence was prior to the cut.[47] This is known as SDN-2 where the modification is to a single nucleotide or a small deletion or insertion.[48] Where large sequences of DNA, such as an entire gene,[49] are inserted, the technique is classed as SDN-3.50. From a regulatory perspective, SND-2 and SDN-3 introduce exogenous DNA, similar to genetic modification. However, unlike genetic modification, the inserted gene's location is controlled, meaning better precision and success than with the older science.[51] Nevertheless, off-target effects are still possible with SDN.[52] However, experts have assessed the ramifications of these effects as similar to those possible with older unregulated mutagenesis.[53]

Other new plant breeding techniques are also being developed. Some deliver new genes to the cell but do not intend that gene to be present in the final plant.[54] Accelerated breeding is an example of this. As noted above, apple trees take many years to reach sexual maturity. While it may be intended that conventional breeding or untargeted mutagenesis will be used to introduce a new trait into the plant, plant breeders may take advantage of genome editing to change the gene responsible for sexual maturity (flowering) so that the plant reaches maturity more quickly. Once mature, conventional techniques are used to introduce the desired attribute.[55] Progeny are then screened to determine which have been successfully altered.[56] From amongst that altered group, those that have not inherited the changed flowering gene are selected. These progeny have not

46 OGTR, 'Options for Regulating New Technologies' (Discussion Paper, October 2016) 26–7 ('Options for Regulating New Technologies'). See also European Food Safety Authority Panel on GMOs (n 38) 5–6.

47 'Genome Editing in Agriculture' (n 5) 4.

48 'Options for Regulating New Technologies' (n 46).

49 These DNA sequences can be naturally occurring or synthetically created. The line between small and large sequences is not entirely clear.

50 'Genome Editing in Agriculture' (n 5) 4.

51 Other new techniques can be used to stably insert new genes. See Lusser et al (n 38) for a detailed explanation of these techniques.

52 See, eg, Michael Kosicki, Kärt Tomberg and Allan Bradley, 'Repair of Double-Strand Breaks Induced by CRISPR: Cas9 Leads to Large Deletions and Complex Rearrangements' (2018) 36(8) *Nature Biotechnology* 765. See also Editorial, 'Keep Calm and Edit On' (2018) 36(8) *Nature Biotechnology* 667.

53 FSANZ, *New Plant Breeding Techniques* (Workshop Report, May 2012) 22 ('*New Plant Breeding Techniques 2012*').

54 Lusser et al (n 38) 9.

55 'Food Derived Using New Breeding Techniques' (n 26) 16.

56 Henryk Flachowsky et al, 'A Review on Transgenic Approaches to Accelerate Breeding of Woody Plants' (2009) 128(3) *Plant Breeding* 217, 222.

inherited the early maturity trait changed by genome editing and are referred to as null segregants.[57] Nevertheless, it is arguable that progeny are the result of genome editing, used to enable the conventional breeding or mutagenesis to take place much earlier than it otherwise would.

Grafting is another 'combination' of techniques, used in grape vines, apples and citrus particularly to improve fungal resistance and rooting ability.[58] Non-GM scions are grafted onto GM rootstock. The genome of the cells in the grafted scion do not carry the genetic modification nor does the fruit it produces.[59]

While genome editing and other new breeding techniques offer numerous practical advantages over older techniques, developing regulatory and trade responses raise concerns about the same cost, delay and market access issues arising for these plants as have arisen for GM plants.[60] The lack of an internationally accepted regulatory norm for GMOs and different national approaches add to the cost, delay and uncertainty of bringing GM plants to market.[61] Asynchronous approvals, when countries approve the same plant at different times, add to these problems.[62] That is why decisions on whether genome editing is genetic modification are so important.

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57 'Food Derived Using New Breeding Techniques' (n 26) 6.

58 Stuart J Smyth, Jillian McDonald and José Falck-Zepeda, 'Investment, Regulation and Uncertainty: Managing New Plant Breeding Techniques' (2014) 5(1) *GM Crops & Food* 44.

59 Lusser et al (n 38) 48.

60 While compliance with domestic regulatory frameworks is necessary, about two-thirds of Australia's agricultural output is exported: see Productivity Commission, *Regulation of Australian Agriculture* (Report No 79, 15 November 2016) 3.

61 *Third Review of the National Gene Technology Scheme Final Report* (n 11) 99.

62 On the costs of asynchronous approvals, see Richard D Smart, Matthias Blum and Justus Wesseler, 'Trends in Approval Times for Genetically Engineered Crops in the United States and the European Union' (2017) 68(1) *Journal of Agricultural Economics* 182; Hans De Steur et al, 'Status and Market Potential of Transgenic Biofortified Crops' (2015) 33 *Nature Biotechnology* 25; Rosane Nunes de Faria and Christine Wieck, 'Empirical Evidence on the Trade Impact of Asynchronous Regulatory Approval of New GMO Events' (2015) 53 *Food Policy* 22; Martin Henseler et al, 'On the Asynchronous Approvals of GM Crops: Potential Market Impacts of a Trade Disruption of EU Soy Imports' (2013) 41 *Food Policy* 166; Mauro Vigani, Valentina Raimondi and Alessandro Olper, 'International Trade and Endogenous Standards: The Case of GMO Regulations' (2012) 11(3) *World Trade Review* 415.

3 *Lack of International Consensus*

Jurisdictions are adopting different regulatory responses to genome edited plants in the same way as was the case with GM plants.[63] Some jurisdictions, such the European Union and New Zealand, regulate genome edited plants as GMOs, whilst others have deregulated at least some genome edited plants.[64]

The Court of Justice of the European Union ('CJEU') recently ruled that plants created using genome editing are within the scope of the European Union's GMO Directive.[65] This was despite the EU Advocate General recommending the techniques be exempt from such regulation like older mutagenesis techniques, provided the plants did not contain DNA from other species or synthetic DNA.[66] GMO regulation within the European Union requires a lengthy and expensive approval process with additional regulations depending upon which EU country is involved — some countries prohibiting GMO cultivation and others allowing it subject to conditions.[67] Genome editing techniques may eventually be exempted from GMO regulation, but experts have suggested that in the meantime European research will move elsewhere or cease as a result of the CJEU's approach.[68] New Zealand has taken a similar approach to that of the CJEU.[69] In 2016, regulations on the introduction of GMOs into New Zealand were amended to clarify that genome editing techniques are regulated as genetic

63 Tetsuya Ishii, 'Crop Gene-Editing: Should We Bypass or Apply Existing GMO Policy?' (2018) 23(11) *Trends in Plant Science* 947.

64 Ishii and Araki (n 18) 44.

65 *Confédération paysanne v Premier ministre and Ministre de l'agriculture, de l'Agroalimentaire et de la Forêt* (Court of Justice of the European Union, C-528/16, ECLI:EU:C:2018:20, 25 July 2018). The full title of the GMO Directive is *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* [2001] OJ L 106/1.

66 *Confédération paysanne v Premier ministre and Ministre de l'agriculture, de l'agroalimentaire et de la forê*t (Court of Justice of the Eurpoean Union, C-528/16, ECLI:EU:C:2018:20, 18 January 2018) (Advocate General Bobek).

67 *Genetically Engineered Crops* (n 33) 480.

68 Ewen Callaway, 'EU Law Deals Blow to CRISPR Crops' (2018) 560 *Nature* 16, 16. See also Frank Hartung and Joachim Schiemann, 'Precise Plant Breeding Using New Genome Editing Techniques: Opportunities, Safety and Regulation in the EU' (2014) 78(5) *The Plant Journal* 742.

69 *Sustainability Council of New Zealand v Environmental Protection Authority* [2014] NZHC 1067.

modification.[70] Only organisms resulting from mutagenesis using chemical or radiation treatments in use on or before 29 July 1998 are exempted.[71]

The departure of the United Kingdom ('UK') from the European Union may allow a change in its approach to the regulation of GMOs and genome edited plants. Following the CJEU decision, a group of UK research institutions, universities, crop agronomy and biotech companies, and farmer and land owner organisations wrote to the UK Department for Environment, Food and Rural Affairs ('DEFRA'). The group asked DEFRA to address the implications of the decision 'if the UK is to retain its strength in plant genetics, to use innovation to boost productivity and competitiveness, and to meet the challenges of nutritional health and environmental protection'.[72] DEFRA has since stated that 'gene-edited organisms should not be regulated as GMOs if the changes to their DNA could have occurred naturally or through traditional breeding methods'.[73]

Other jurisdictions, such as the United States ('US') and Canada, have taken the opposite approach. The US Department of Agriculture announced in March 2018 that it 'does not regulate or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques'.[74] Canada's decision to regulate genome edited plants in the same way as it regulates GMOs means only plant varieties with a novel trait are regulated 'regardless of how they were developed, meaning that the variety could be developed by gene editing, genetic modification, mutagenesis or even conventional breeding.'[75] There is no regulatory definition of novel for these purposes, but the rule of thumb is 'that if the specific trait they are selecting for expresses at 20% to 30% higher or lower than conventional varieties' the regulator should be consulted.[76]

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70 *Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998* (NZ) SR 1998/219, as amended by *Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Amendment Regulations 2016* (NZ) SR 2016/196.

71 *Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998* (NZ) SR 1998/219, reg 3(1)(ba).

72 John Innes Centre, 'Call for Clarity After EU Ruling on Gene-Edited Crops' (Press Release, 13 September 2018) <https://www.jic.ac.uk/press-release/call-for-clarity-after-eu-ruling-on-gene-edited-crops/>.

73 Ibid.

74 US Department of Agriculture, 'Secretary Perdue Issues USDA Statement on Plant Breeding Innovation' (Press Release No 0070.18, 28 March 2018) <https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation>.

75 Smyth (n 6) 38.

76 Ibid.

4 Questions for Australian Regulators

Australian regulators must now decide whether genome edited plants and their products should be regulated as a development of genetic modification. This involves decisions around the breadth of regulatory triggers based on the definition of gene technology and the exclusions from regulation for mutagenesis.

For FSANZ, this process began with two scientific workshops in 2012 and 2013.[77] The expert scientific panel continues to advise FSANZ on the science and potential food safety risks, if any, associated with new breeding techniques, although is not involved in decisions around the regulatory classification of the techniques. However, FSANZ has indicated that the panel's conclusions will be relevant in considering applications for food produced using these techniques.[78] The formal review commenced in June 2017, with a Consultation Paper released in February 2018, on which the public were invited to comment.[79] The review's scope includes food products of genome editing,[80] and its objectives are to consider what foods require pre-market assessment and approval and whether relevant definitions need amendment.[81] The Preliminary Report summarising public comments on the Consultation Paper was released in August 2018.[82] A Final Report was originally due early 2019,[83] but has been delayed. While no final determinations have been made, FSANZ's approach is foreshadowed in these documents.

The gene technology regime has undergone two parallel reviews in preparation for genome editing. The Technical Review of the Gene Technology Regulations commenced in October 2016, with a Discussion Paper.[84] The purpose of the Technical Review was to provide clarity on whether organisms developed using

77 *New Plant Breeding Techniques 2012* (n 53); FSANZ, *New Plant Breeding Techniques* (Workshop Report, August 2013) ('*New Plant Breeding Techniques 2013*').

78 'Food Derived Using New Breeding Techniques' (n 26) 4; Michael Jones, Horticulture Innovation Australia, *New Breeding Technologies and Opportunities for the Australian Vegetable Industry* (Final Report, 2016) 52.

79 'Food Derived Using New Breeding Techniques' (n 26). The review is being undertaken pursuant to *FSANZ Act* (n 15) s 113.

80 These include genome editing, as well as oligonucleotide-directed mutagenesis ('ODM'), grafting, agro-infiltration, RNA-dependent DNA methylation ('RdDM'), and reverse breeding.

81 'Food Derived Using New Breeding Techniques' (n 26).

82 Food Standards Australia New Zealand, *Review of Food Derived Using New Breeding Techniques: Consultation Outcomes* (Preliminary Report, August 2018).

83 Ibid 4.

84 'Options for Regulating New Technologies' (n 46). This review considered the regulation of organisms produced using a slightly different group of technologies compared with the food regulatory review, but also included genome editing.

new technologies are subject to regulation and are 'regulated in a manner commensurate with the risks they pose'.[85] This review could only address possible amendments to the *Gene Technology Regulations 2001* (Cth) ('*GT Regulations'*) and not to the *GT Act*. For the interim period until the *GT Regulations* were amended, general advice from the OGTR on coverage of new technologies was released in 2016.[86] Following public comment on the Discussion Paper and an exposure draft, amendments to the *GT Regulations* were passed in April 2019.[87]

In parallel with the Technical Review, a third periodic review of the broader gene technology framework ('GT framework') has been completed. This review, called the Gene Technology Regulatory Scheme Review, commenced in July 2017 with the release of a Background Paper calling for public input.[88] This was followed by a Consultation Paper in December 2017,[89] Preliminary Report in March 2018,[90] and Final Report in October 2018.[91] Unlike the Technical Review, this review can recommend broader policy and legislative changes to the Ministerial Forum responsible for policy setting, the Gene Technology Legislative and Governance Forum.[92]

Both the food and GT frameworks rely on a process trigger to attract the operation of the regulations. That trigger is the use of gene technology. Both regulators are tasked with protecting human health and safety from risks posed

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85 Legislative and Governance Forum on Gene Technology, '2017 Review of the National Gene Technology Regulatory Scheme' (Background Paper, July 2017) 4 ('2017 Review of the National Gene Technology Regulatory Scheme Background Paper').

86 'General Advice from the Regulator on Coverage of New Technologies', *OGTR* (Web Page, 10 April 2019) <www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/newtechnologies-htm>.

87 *Gene Technology Amendment (2019 Measures No 1) Regulations 2019* (Cth), which will commence from 8 October 2019; Office of the Gene Technology Regulator, *Draft Future Law Compilation of Gene Technology Regulations 2001* (30 November 2017). This was accompanied by a Regulation Impact Statement: see *Updating Gene Technology Regulation in Australia* (n 8). See also OGTR, *Updating Gene Technology Regulation in Australia* (Consultation Quick Guide, 30 Nov 2017) ('*Consultation Quick Guide*').

88 '2017 Review of the National Gene Technology Regulatory Scheme Background Paper' (n 85).

89 Department of Health (Cth), 'Review of the National Gene Technology Scheme 2017' (Consultation Paper, November 2017) ('Review of the National Gene Technology Scheme Consultation Paper 2017').

90 Department of Health (Cth), *Third Review of the Gene Technology Scheme* (Preliminary Report, March 2018).

91 *Third Review of the National Gene Technology Scheme Final Report* (n 11).

92 This is required pursuant to Clause 44 of the *Gene Technology Agreement* between national, state and territory governments. The agreement can be downloaded at: <https://www1.health.gov.au/internet/main/publishing.nsf/Content/gene-tech-agreement>.

by particular products of gene technology (food for FSANZ and GMOs for the OGTR), and each assesses such risk in the context of risks posed by the non-modified parental organisms.[93] Decisions are based on currently available science and each regulator can undertake independent research.[94] Nevertheless, as will be discussed, the two regulatory schemes are responding to genome edited plants differently to each other. Using the results of the reviews described above, this paper now turns to those responses.

5 *Defining Gene Technology*

In 1999, a new standard — Standard 1.5.2 – Food Produced Using Gene Technology — was added to the *Australia New Zealand Food Standards Code* ('*ANZFS Code*') to specifically regulate food produced using gene technology.[95] The *ANZFS Code* is adopted by the relevant Food or Health Acts in each Australian jurisdiction to create a national standard and to require compliance with the Code.[96] The *ANZFS Code* prohibits the sale of food produced using gene technology unless expressly permitted by, and listed in, the Code.[97] The enactment of the *Gene Technology Act 2000* (Cth) ('*GT Act*') and its accompanying regulations created a regulatory framework specifically for gene technology.[98] That legislation is mirrored in each state and territory to create a national scheme.[99] The *GT Act* prohibits all dealings with organisms produced using gene technology in Australia unless authorised under the legislation.[100] Where gene

[93] *GT Act* (n 15) s 3; *FSANZ Act* (n 15) s 18. See also *Third Review of the National Gene Technology Scheme Final Report* (n 11) 24. The OGTR is also been tasked with protecting the environment, as that term is defined in the legislation: *GT Act* (n 15) ss 3, 10(1). FSANZ also has other objectives, namely, the provision of adequate information relating to food to enable consumers to make informed choices and the prevention of misleading or deceptive conduct: *FSANZ Act* (n 15) s 18(1). For more on the risk assessment process see OGTR, *Risk Analysis Framework 2013* (Report, May 2013); FSANZ, *Application Handbook* (1 March 2016).

[94] *GT Act* (n 15) s 27(h); *FSANZ Act* (n 15) s 18.

[95] *ANZFS Code* (n 7) standard 1.5.2. This standard was revised in 2016.

[96] *Food Act 1992* (ACT); *Food Act 1989* (NSW); *Food Act 1986* (NT); *Food Act 1981* (Qld); *Food Act 1985* (SA); *Public Health Act 1962* (Tas); *Food Act 1984* (Vic); *Health Act 1911* (WA).

[97] *ANZFS Code* (n 7) standard 1.5.2—3. It is an offence not to comply with the *ANZFS Code*: see standard 1.1.1—10.

[98] *Gene Technology Regulations 2001* (Cth) ('*GT Regulations*').

[99] *Gene Technology Act 2003* (ACT); *Gene Technology (New South Wales) Act 2003* (NSW); *Gene Technology (Northern Territory) Act 2004* (NT); *Gene Technology (Queensland) Act 2016* (Qld); *Gene Technology Act 2001* (SA); *Gene Technology (Tasmania) Act 2012* (Tas); *Gene Technology Act 2001* (Vic); *Gene Technology Act 2006* (WA).

[100] *GT Act* (n 15) ss 32(1), 33(1). For the meaning of dealings, see s 10(1) (definition of 'deal with').

technology is used to produce food (in the case of FSANZ) or create an organism (in the case of the OGTR) the regulatory scheme triggers and must be complied with. As Table 1 summarises, each regulatory framework uses its own definition of gene technology, potentially causing consumer and industry confusion. Decisions made nearly 20 years ago to define the same science in different ways is not due to needs of the regimes themselves — the regimes up to now have regulated essentially the same science. But scrutiny in preparation for genome edited plants has revealed ambiguities and important differences in those definitions.

Table 1: Trigger definitions relevant to genome edited plants

	Gene Technology Regime	**Food Regulation Regime**
Regulated entity	Genetically modified organisms	Food produced using gene technology
Definition of Regulated entity	An organism modified by gene technology	Food which has been derived or developed from an organism which has been modified by gene technology
Definition of gene technology	Any technique for the modification of genes or other genetic material	Recombinant DNA techniques that alter the heritable genetic material of living cells or organisms

5.1 Gene Technology Regulatory Framework

Two definitions are central to the GT framework: GMO and gene technology. Gene technology for the purposes of the GT framework means 'any technique for the modification of genes or other genetic material'.[101] However, the GT framework does not regulate gene technology per se. Instead, it regulates dealings with GMOs, a GMO being 'an organism *modified* by gene technology'.[102] Although these definitions had been the subject of two previous reviews, only since the practical development of genome editing have ambiguities been identified.[103] In particular, it was unclear whether the phrase 'an organism

[101] Ibid s 10(1) (definition of 'gene technology').

[102] Ibid (definition of 'GMO' and 'genetically modified organism') (emphasis added). The definition allows for the regulations to declare organisms not to be a GMO: see s 10(1) (definition of 'genetically modified organism': para (e)). These exclusions are, pursuant to reg 5, listed in the *GT Regulations* (n 98) sch 1. 'Mutant' is excluded as sch 1, item 1.

[103] The first review, in 2006, predated practical development of genome editing: see Department of Health and Ageing (Cth), *Statutory review of the Gene Technology Act 2000*

modified by gene technology' in the definition of GMO requires that modification to be permanent. As discussed below, this has been addressed in recent amendments.

The definition of gene technology on the other hand, is unambiguous. Difficulties arise though, because its broad scope makes the ambit of the regulatory exceptions important. Subject to those exceptions, discussed below in section 6, all genome editing techniques are gene technology for the purposes of the GT regulatory framework because they 'modify' an organism's genetic material. Under the Australian regulations, the use of human directed modification is sufficient to attract regulation. The process trigger means that it is irrelevant whether that modification produces a novel combination of DNA. [104] Interestingly, while the novelty of the resulting DNA is irrelevant to the process trigger, the OGTR has used the possibility of a natural counterpart to justify excluding organisms modified using the most simple class of genome editing, SDN-1, from the scope of regulation.[105] The OGTR has concluded that no unique biosafety risks are created by these organisms when compared with 'natural mutations' because the break is repaired through the same mechanisms that repair naturally occurring DNA breaks, and the same range of changes to the DNA nucleotide sequence can occur as for natural mutations. The possible changes to the characteristics of the organism are therefore the same, and pose the same risk.[106]

5.2 Food Regulatory Framework

The definition of gene technology is much narrower in the *ANZFS Code* than the *GT Act*. The *ANZFS Code* defines gene technology as 'recombinant DNA techniques that alter the heritable genetic material of living cells or organisms'.[107] 'Recombinant DNA techniques' is not itself defined. FSANZ has advised that recombinant DNA techniques generally means the recombining or joining of DNA from two or more sources and inserting it into an organism. [108] The organism's genome must contain new pieces of DNA, which can be derived from any source including the same species.[109] As noted in section 2 SDN-1 methods

see Allen Consulting Group, *Review of the Gene Technology Act 2000* (Report, August 2011).

104 This is in contrast to the approach taken by the only international agreement dealing exclusively with trade in GMOs, the *Cartagena Protocol on Biosafety to the Convention on Biological Diversity*, opened for signature 15 May 2000, 2226 UNTS 208 (entered into force 11 September 2003). Australia is not a party to the Protocol.

105 *Consultation Quick Guide* (n 87) 3.

106 Ibid.

107 *ANZFS Code* (n 7) standard 1.1.2—2.

108 'Food Derived Using New Breeding Techniques' (n 26) 7 n 8.

109 Ibid 7, 10.

described above do not use DNA (ZFN and TALENS using protein and CRISPR/Cas using RNA) and therefore fall outside the scope of regulation. However, where a DNA template is used to direct cellular repair it is possible, although unclear, that application of the regulatory scheme will be triggered.

FSANZ is proposing to use its own classifications to address the regulation of genome editing, in light of the unique definition of gene technology in the *ANZFS Code*.[110] Those classifications and the impact on regulation are:

i) Where the genome of the organism from which food for sale is obtained remains unchanged, food produced by the organism will not be regulated.

ii) Where the genome is changed but no new DNA is present in the organism from which food for sale is obtained, such food will not be regulated.

iii) Where the genome contains new DNA, food produced by the organism will be regulated.

New DNA in this context is a 'piece of DNA' that is new to the host organism in terms of its nucleotide sequence, genome location or orientation of insertion.[111] It seems that a change to a single or few nucleotides is not new DNA for these purposes because the Consultation Paper groups such changes into category (ii) above.[112] Food from plants which have undergone accelerated breeding but which no longer contain the genome edit (null segregants) will also be classified in category (ii) and not regulated under the standard.[113] However, as part of the review, FSANZ is addressing whether risks from targeted or off-target changes mean that pre-market assessment and approval should nevertheless be required for food in category (ii).[114] The scientific panel advising FSANZ has previously concluded that changes introduced using simple forms of genome editing, would be similar to those made by classical mutagenic techniques and do not present significantly greater food safety concerns than those from other forms of mutagenesis.[115]

Food within category (iii) will be regulated as having been produced using gene technology. SDN-3 is not referred to in the Consultation Paper but because SDN-

[110] Ibid 10–12. The paper describes genome editing as being SDN-1, SDN-2, SDN-3, ODM and base editing (app 1).

[111] 'Food Derived Using New Breeding Techniques' (n 26) 4.

[112] Ibid 12.

[113] Ibid 4.

[114] Ibid 12.

[115] Ibid 11.

3 introduces a new gene it is likely that food from plants modified using SDN-3 will be regulated as food produced using gene technology.[116]

5.3 Grafting

For the GT regulatory framework, it seems likely that the whole plant produced when a non-GM scion is grafted onto GM rootstock will be a GMO. The Act does not allow for parts of an organism to be treated apart from the remainder.[117] Similarly, FSANZ has concluded that such plants will be treated as a single organism and therefore food produced by such plants will be classified as food produced using gene technology, needing pre-market safety assessment. The safety concern is that novel gene products may travel to the non-GM scion or its products or the scion or its products may have altered characteristics. However, the scientific panel advising FSANZ has recommended a simplified safety assessment be used and this matter is being considered further in FSANZ's formal review.[118] The panel has also proposed that particular GM rootstock could be assessed and approved for use with any non-GM scion without the need for individual assessment of the resulting plant.[119]

5.4 Summary

The broader scope of the definition of gene technology in the GT framework means that all of the genome editing techniques discussed in this paper (SDN-1, SDN-2, SDN-3, accelerated breeding and grafting) are classified as gene technology. In contrast, only SDN-3 and grafting are classified as gene technology by the food regulatory framework. This difference may be appropriate given the regimes regulate different things but it is likely to cause public confusion. The GM labelling obligations in the *ANZFS Code* are intended to inform consumers about the agricultural production method used to produce the food (namely gene technology), that food having been assessed as safe to consume.[120] But the differences mean that the GT framework, which regulates agricultural production of GMOs, classifies a broader group of genome editing techniques as being gene technology.

116 *New Plant Breeding Techniques 2012* (n 53) 22; *New Plant Breeding Techniques 2013* (n 77) 11.

117 A similar conclusion was reached by Jones (n 78).

118 *New Plant Breeding Techniques 2012* (n 53) 4.

119 Ibid 17.

120 *ANZFS Code* (n 7) standard 1.2.1—8(1)(k).

6 *Excluding Mutants from Regulation*

When the GT framework was created, it was recognised that genetic mutants spontaneously occur in nature and had been deliberately created for more than 80 years. These mutants are generally considered 'safe'.[121] Mutants and classical techniques used to produce them were therefore excluded from the scope of the GT regulatory framework. However, there are ambiguities in those exclusions when genome edited plants are considered. The *ANZFS Code* does not have exceptions to the definition of gene technology or food produced using gene technology. Instead, the relevant standard does not apply to food from organisms produced using conventional breeding. Conventional breeding means 'all methods used to produce plants, excluding techniques that use gene technology'.[122] Whether food from mutant plants is regulated under the gene technology food standard therefore depends on whether it was produced using gene technology, as discussed above.

The definition of gene technology in the *GT Act* allows for techniques to be excluded from its scope by being specified in the Regulations.[123] Relevantly, the Regulations exclude natural mutagenesis and mutagenesis induced by particular named methods: electromagnetic radiation, particle radiation and chemical. Genome editing uses molecular biology tools to trigger mutations in pre-determined specific sites in plants' DNA.[124] Given these tools are themselves chemicals — DNA, RNA or protein — it could be argued that genome editing is a form of chemical mutagenesis and therefore excluded from being gene technology. That would mean plants modified by genome editing would be outside the scope of regulation. However, it is unlikely genome editing will be treated as a form of chemical-induced mutagenesis. The OGTR has advised that the use of ZFN is not chemical mutagenesis for the purposes of the *GT Act*.[125] This means the undertaking of genome editing must be authorised under the *GT Act* if the plant under development is a GMO, even though the final plant may not be a GMO and commercial release of that final plant would not need authorisation. However, plants under development will not be regulated as

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121 Senate Committee on Community Affairs, *A Cautionary Tale: Fish Don't Lay Tomatoes* (Report, 1 November 2000) 23–5.

122 *ANZFS Code* (n 7) sch 26—2(2) (definition of 'conventional breeding').

123 *GT Act* (n 15) s 10(1) (definition of 'gene technology' para (c)). See also *GT Regulations* (n 98) reg 4, sch 1A. While the definitions in the legislation have not been amended since their introduction in 2000, the *GT Regulations* (and the schedules that list the exclusions from those definitions) were amended in 2006 and will be again effective from 8 October 2019.

124 Smyth, McDonald and Falck-Zepeda (n 58).

125 Letter from the Office of the Gene Technology Regulator to Dow AgroSciences Australia, 7 May 2012 <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/content/C2FFDD165F9AE9AECA257E56007F4B20/$File/Dow%20Exzact%20advice%20letter%20of%20May%202012.PDF>.

GMOs if they are an excluded mutant. Whether they are mutants is considered in the next section.

7 What is a Mutant?

The definition of GMO in the GT regulatory framework provides for organisms to be excluded from the scope of the definition by being listed in the Regulations.[126] Mutants are listed as such an exclusion.[127] If organisms created using genome editing techniques are mutants they will not be regulated as GMOs even though they are created using gene technology. Mutants are defined as organisms 'in which the mutational event did not involve the introduction of any foreign nucleic acid (that is, non-homologous DNA, usually from another species)'.

Genome editing has crystallised ambiguities in the definition of mutant. In particular, *introduction* and *foreign nucleic acid* create uncertainties. As explained in section 2, CRISPR/Cas uses a RNA sequence as its site recognition sequence for targeting its SDN. This could be considered foreign nucleic acid. However, it is arguable that the nucleic acid concerned must be DNA, given the bracketed text following that term in the definition. This interpretation would mean the SDN techniques which rely on NHEJ would be excluded from the scope of regulation because DNA is not used.

But where a DNA template is used with the SDN to direct cellular repair by HDR at least three ambiguities arise in deciding whether the resulting plant is a mutant: must the foreign DNA be included in the plant's genome? Must that inclusion be permanent? And must the DNA come from a different species? The OGTR has acknowledged these ambiguities in the definition.[128] The OGTR's approach is that the presence of a DNA template and its interaction with the cell's genome introduces DNA even though the template does not become part of the plant's genome.[129] The resulting plant will therefore not be an excluded mutant, and will continue to be regulated as a GMO.

However, it is only while the genome edited trait is present that plants will be regulated. Recent amendments discussed in the next section mean that the fact that a plant contained a template during its development, is not sufficient to cause the final organism to be a GMO if the template and genome edited sequence are no longer present in the plant. This is significant for plants developed using accelerated breeding, provided the early maturity trait is removed or progeny are

126 *GT Act* (n 15) s 10(1) (definition of 'genetically modified organism': para e).

127 *GT Regulations* (n 98) reg 5, sch 1 item 1. This exclusion will be deleted from 8 October 2020.

128 *Consultation Quick Guide* (n 87) 3.

129 Ibid.

selected without the genome edited trait and also for other null segregants. These will not be regulated under the GT regulatory framework.[130]

The third identified ambiguity is significant because genome editing is sometimes used to introduce genes (or control elements) from the same species or species that are sexually compatible.[131] These forms of genome editing are known as cisgenesis and intragenesis and it is arguable, like with the exclusion of plants created using SDN-1, that the possibility of a natural counterpart should justify the exclusion of these organisms from the scope of regulation. As noted above, the OGTR has used this reasoning to justify the exclusion of plants created using SDN-1.[132] However, the word 'usually' in the definition of mutant arguably indicates that the introduced DNA does not have to be from another species. That approach means plants resulting from cisgenesis and intragenesis are not mutants and will be regulated as GMOs even though the same plant could result from conventional breeding and untargeted mutagenesis. This is the OGTR's approach.

8 Where to from Here?

Table 2 summarises the interim approach to genome editing techniques by the food and gene technology regulators. In summary, genome editing is always gene technology for the purposes of the GT framework but not for the food regulatory framework. However, genome edited plants are not necessarily within the scope of the gene technology scheme. The OGTR's approach is that whether the resulting plant is a mutant (and therefore excluded from the scope of regulation) or not (and remains a regulated GMO) depends upon whether a repair template was used. Genetic changes caused during cellular repair using NHEJ are treated in the same way as spontaneous or untargeted mutations, and the resulting plant is not regulated. However, if genome editing involves a template DNA the resulting plant will be regulated as a GMO. This is the case even where cisgenesis or intragenesis is used to introduce a gene from the same species. FSANZ's approach can be summarised as regulating only food from plants created using genome editing involving a repair template that causes the introduction of new DNA, where that DNA is still present in the plant when the food is produced.

130 Ibid 4.

131 Lusser (n 38) 24–5.

132 *Consultation Quick Guide* (n 87) 3.

Table 2: Interim regulatory conclusions on genome edited plants

	Gene Technology Regime	**Food Regulation Regime**
Whether SDN-1 is gene technology	Yes	No
Whether plant / product produced using SDN-1 is regulated	No — because is excepted, as a mutant / specifically excluded after October 2019	No — because gene technology not used
Whether SDN-2 is gene technology	Yes	No
Whether plant / product produced using SDN-2 is regulated	Yes — because does not come within definition of mutant / specifically included after October 2019	No — because gene technology not used
Whether SDN-3 is gene technology	Yes	Yes
Whether plant / product produced using SDN-3 is regulated	Yes — because does not come within definition of mutant / specifically included after October 2019	Yes
Whether null segregant produced using accelerated breeding is regulated	No — provided doesn't inherit GM trait / specifically excluded after October 2019	No — but considering whether to nevertheless regulate
Whether grafted plants / products are regulated	Yes	Yes — but considering whether to apply simplified safety assessment

However, while the above conclusions can be drawn using the regulators' responses so far, uncertainty remained over their legality.

To clarify the scope of regulation, amendments to the definitions of both GMO and mutant were recently passed. The current definition of mutant will be deleted.[133] Further items will be added to the list of exceptions to the definition of GMO. The first of these is:

[133] *Gene Technology Amendment (2019 Measures No 1) Regulations 2019* (Cth) reg 4 sch 3 item 1.

> An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was not added to guide homology-directed repair.[134]

This will exclude a narrower group of organisms than the current definition of mutant. The OGTR considers that the exclusion of chemical and radiation-induced mutagenesis from being gene technology, means that organisms that would otherwise have been outside the scope of regulation will remain outside regulatory scope even following the deletion of the 'mutant exception'.[135] The alternative approach to reform, of adding SDN-1 to the list of excluded techniques, was not adopted because the OGTR wants to retain regulatory authority over the intermediate GMOs produced in the course of SDN-1. For example, plants stably expressing a SDN.[136]

Nevertheless, the proposed exclusion could be improved by using more flexible and technology neutral language. By naming the particular molecular tool (SDN), the exclusion may quickly become outdated. SDNs may be replaced in future, by recombinases or other DNA modifying enzymes to get the same effect.[137]

Other exclusions from the definition of GMO include:

- An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was not added to guide homology-directed repair.[138]

- An organism that was modified by gene technology but in which the modification, and any traits that occurred because of the gene technology, are no longer present.[139]

These exclusions are intended to make clear that null segregant progeny from accelerated breeding are not within the scope of the GT regulatory framework. However, the term 'occurred … because of gene technology' was ambiguous because, as explained in section 2 above, it is arguable that the introduction of traits using conventional breeding or untargeted mutagenesis was facilitated by

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134 Ibid reg 4 sch 1 items 8 and 26 (new item 4).

135 *Updating Gene Technology Regulation in Australia* (n 8) 11. The OGTR notes that there are two organisms excluded pursuant to item 1 that cannot take advantage of the proposed approach and will therefore be unintentionally reclassified as GMOs if item 1 is deleted. It is proposed that they will be specifically listed in sch 1 items 10 and 11 to ensure they continue to be excluded from regulation.

136 *Updating Gene Technology Regulation in Australia* (n 8) 11.

137 Future alternatives include DNA methylases and deaminases.

138 *Gene Technology Amendment (2019 Measures No 1) Regulations 2019* (Cth) reg 4 sch 1 items 8 and 26 (new item 4).

139 Ibid reg 4 sch 1, items 8 and 27.

the genome edited trait of early maturity. A further exclusion from the definition of GMO has therefore been added to clarify that such organisms are not GMOs.[140]

In contrast, FSANZ's Consultation Paper raises for consideration whether food from null segregant organisms should continue to be excluded from pre-market assessment and approval. FSANZ's practice has been to allow the use of null segregants as non-GM comparators as part of its safety assessment and not to regulate null segregants.[141] The scientific panel advising FSANZ considered the risks arising with such food to be similar to those from food produced using untargeted mutagenic techniques.[142] However, unlike the *GT Act* which makes it clear that before progeny are regulated as GMOs they must inherit the relevant GM trait,[143] the *ANZFS Code* does not make this clear.[144] It is possible that in responding to genome editing, FSANZ may broaden the scope of existing regulated practices to now impose regulation on null segregants.

Finally, as noted above, the use of a repair template is considered by the OGTR to cause the resulting organism not to come within the group of excluded mutant organisms. However, the deletion of the mutant exception and possible uncertainty around that conclusion have led to amendments to clarify that such organisms are GMOs.[145] The legislative definition of GMO provides for the regulations to *include* organisms as GMOs beyond those named in the legislation but this has not previously been done.[146] Such a list has now been created and includes:

> An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was added to guide homology-directed repair.[147]

This approach is consistent with the OGTR's focus on the 'process' used to modify the organism to decide whether to regulate. But it means that resulting organisms will be regulated even though they may be of no greater risk (and may be of less risk) than plants produced through untargeted (and unregulated) mutagenesis techniques which are considered safe. This is an unnecessary cost for the taxpayer, particularly given the OGTR's conclusions that the current

140 Ibid reg 4 sch 1, items 8 and 26 (new item 9).

141 In particular, null segregants are used for compositional analysis comparisons.

142 *New Plant Breeding Techniques 2013* (n 77) 3–4.

143 *GT Act* (n 15) s 10(1) (definition of 'GMO' para (b)).

144 *ANZFS Code* (n 7) sch 26—2(2) (definition of 'line' para (b)).

145 *Gene Technology Amendment (2019 Measures No 1) Regulations 2019* (Cth) reg 4 sch 1 items 7 and 25.

146 *GT Act* (n 15) s 10(1) (definition of 'GMO' para (c)).

147 *Gene Technology Amendment (2019 Measures No 1) Regulations 2019* (Cth) reg 4 sch 1 items 7 and 25. This will be sch 1B of the *GT Regulations* from 8 October 2019. Organisms modified by ODM will also be included.

funding arrangements for the scheme may not be sustainable long-term and that there are strong arguments against a full cost recovery funding model.[148]

9 Discussion and Conclusions

This paper has examined Australian regulatory responses to plant genome editing. Australian regulators are aware that regulatory uncertainty arises because 'new technologies for altering genetic sequence and gene expression are not specifically addressed in the legislation'.[149] They are also aware of the possible adverse impacts if that uncertainty continues. For some time though, these regulators had not publicly acknowledged that differences between Australian regulatory frameworks could pose similar risks. FSANZ has however, recently acknowledged calls for the definition of gene technology to be consistent across regulatory frameworks, both domestic and international, and is now waiting for the results of the GT regulatory reviews before finalising its review.[150]

More broadly, examination of the regulatory responses to genome edited plants has led Australian regulators to publicly question decisions made over 20 years ago to adopt process triggers. Both FSANZ and the OGTR have acknowledged that process triggers may no longer be suitable.[151] Critics have long identified that process triggers create a binary approach tied to a particular definition of a science, and inevitably cause difficulties as science develops.[152] As Marchant and Stevens have observed, 'process-based regulatory systems … will become increasingly stretched and scientifically undermined by trying to force the new technologies into their already outdated binary process-based regulatory frameworks'.[153] Regulatory regimes using product triggers that instead focus on the potential risks of the resulting product is one alternative. However, this is not the first time it has been recommended to government that these process triggers

148 *Third Review of the National Gene Technology Scheme Final Report* (n 11) 72.

149 *Updating Gene Technology Regulation in Australia* (n 8) 4.

150 'Food Derived Using New Breeding Techniques' (n 26) 15. After the review, FSANZ will consider whether to amend the *ANZFS Code*. This will be a separate process to the review and involves further public consultation.

151 'Review of the National Gene Technology Scheme Consultation Paper 2017' (n 89) 16, 19; Lisa Kelly, 'Food Regulatory Perspective on Gene Editing' (Presentation, CSIRO Gene Editing of Crops Workshop, 28–30 November 2017). Ms Kelly said the 'focus is on characteristics of food itself' and that it 'no longer makes sense to make distinctions based on process, or use of a specific technique'.

152 For an alternative approach to responding to developing technologies, see ACIL Tasman, *Biotechnology and Australian Agriculture: Towards the Development of a Vision and Strategy for the Application of Biotechnology to Australian Agriculture* (Report, July 2008) 59.

153 Gary E Marchant and Yvonne A Stevens, 'A New Window of Opportunity to Reject Process-Based Biotechnology Regulation' (2015) 6(4) *GM Crops & Food* 233, 240. See also ACIL Tasman (n 152) 57.

be removed[154] and it seems unlikely they will be changed within the short to medium term in the GT regulatory framework at least.[155] The recently released Final Report by the OGTR confirms that such change is unlikely.[156] The OGTR's explanation includes the observation that a change of trigger would require the process trigger used by other Australian regulatory schemes, including food, to also be changed.[157] However, given that the schemes already use different definitions of the process and are likely to regulate genome edited plants differently, it is unclear why that conclusion was reached.

The policy behind the frameworks is fundamental in assessing the appropriateness of regulatory responses to genome edited plants. Both frameworks are intended to protect human health and safety (and also, in the case of the GT framework, the environment). It is not asserted here that the regimes do not achieve that but regulation comes at a public and private cost and impacts innovation. Decades of research has shown that no risks are posed by genetic modification itself, but rather with the resulting products and numerous studies have shown that 'these risks were no greater or lesser than the risks posed by products of traditional technologies'.[158] Commercial GM plants and their products are as safe to eat as conventionally created counterparts.[159] Nevertheless, past policy decisions on using process triggers mean that the use of the defined process renders the actual risks posed by plants and their products largely irrelevant to the scope of regulation. The OGTR's recommendations to introduce risk tiering and streamline procedures are a good start to addressing these problems.[160]

Turning to the future, decisions must be made as to whether it is appropriate and efficient to regulate genome edited plants and their products as if they involve genetic modification. The OGTR has acknowledged that current regulations ignore the reality that plants produced using genome editing techniques may be indistinguishable from conventionally bred plants.[161] This causes problems for

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154 ACIL Tasman (n 152) 59. See also Advisory Committee on Releases to the Environment, *Towards an Evidence Based System for Regulation of GMOs* (Report No 1, 2013); *Genetically Engineered Crops* (n 33).

155 Department of Health (Cth), *The Third Review of the National Gene Technology Scheme* (Preliminary Report, March 2018), 26–7.

156 *Third Review of the National Gene Technology Scheme Final Report* (n 11) 6.

157 Ibid.

158 Alan McHughen, 'A Critical Assessment of Regulatory Triggers for Products of Biotechnology: Product vs Process' (2016) 7(3–4) *GM Crops & Food* 125, 154.

159 Organisation for Economic Cooperation and Development, *Recombinant DNA Safety Considerations* (Report, 1986) <https://www.oecd.org/sti/biotech/40986855.pdf>.

160 *Third Review of the National Gene Technology Scheme Final Report* (n 11) recommendations 9 and 10.

161 'Updating Gene Technology Regulation in Australia' (n 8) 9.

compliance and monitoring. If they are regulated as GMOs, the regulatory frameworks will need to develop to allow for certification, blockchain technology or other measures to establish whether particular breeding techniques have been used.[162] It is submitted that the involvement of human directed and targeted mutagenesis should not attract specific regulation through frameworks created for gene technology where the changes are those that can occur through conventional breeding or untargeted mutagenesis. The danger of shoe horning genome edited plants and their products into regimes designed for genetically modified plants and products is that it distorts the development and uptake of potentially valuable new techniques. That is the concern behind the responses of the EU Advocate General and UK DEFRA to the issue. It is also the concern of those who have investigated the economic survival of Australian agriculture.[163] As with all innovations, it must be determined whether the products of genome editing are in fact 'risky'. But the food regulatory regime will apply to food produced by genome edited plants even without the application of the GM standard and will still require food to be safe. With respect to the GT framework, the regulation of plants simply because of human intervention, where the outcome is one that could occur using older techniques is an unnecessary overreach. There are still many regulatory uncertainties around genome edited plants but what is certain is that genetic change will continue.

[162] Gema Albújar and Bernd van der Meulen, 'The Legal GMO Concept' (Working Paper No 3/2017, European Institute for Food Law, December 2017) 11.

[163] 'Talking 2030' (n 2) 22; Productivity Commission (n 60) 286–8.