

# GENE EDITING IN AOTEAROA – LEGAL CONSIDERATIONS FOR POLICY MAKERS

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*Gene editing use in pest control, primary industries and human health care pose significant new challenges for regulation. Under current New Zealand legislation (the Hazardous Substances and New Organisms Act 1996) and a judicial ruling on interpretation of the legislation and regulations, the status of gene edited organisms in New Zealand are considered genetically modified and are regulated as new organisms employing a precautionary approach. This article has identified some of the complexities of the legislation inherent in regulating a rapidly developing technology, where such advances may be well ahead of current frameworks and public acceptance. Legal and policy issues have been considered. A future-proof framework to keep abreast rapidly advancing biotechnologies is required whereby new legislation for biotechnologies is developed and a single-entry point for biotechnology applications is implemented. Most importantly this article recommends valuing Treaty of Waitangi principles and have those principles lead us in all that we do.*

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## **I INTRODUCTION**

To explore the implications of gene editing technology for New Zealand, the Royal Society Te Apārangī convened a multidisciplinary panel of some of New Zealand's leading experts to consider the social, cultural, legal, ethical and economic implications of revolutionary gene editing technologies for New Zealand. This article is the opinion of the authors, Everett-Hincks and Henaghan, and it informs and is informed by the work of the Royal Society Te Apārangī Gene Editing Panel.<sup>1</sup>

Gene editing technologies use proteins, called enzymes, targeted to cut areas of DNA within an organism's genetic material. This process can modify genes, by enabling different repair information. In the past 10 years researchers have developed these technologies to manipulate specific genes with

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1 Royal Society Te Apārangī "Gene editing panel" <<https://royalsociety.org.nz>>.

growing precision, revolutionising biological science, accelerating research and offering an alternative tool in human healthcare, pest control and primary production. The bioeconomy is growing rapidly with the profusion of biotechnology products predicted to overwhelm regulatory systems.<sup>2</sup>

Advancement of gene editing technologies provide an opportunity to review current regulatory frameworks and devise a future-proof framework to keep abreast of rapidly advancing biotechnologies. The Hazardous Substances and New Organisms Act 1996 (HSNO Act) is the core legislation in a regulatory framework for gene editing technologies. Two decades have passed with minor amendments to the HSNO Act. The HSNO Act never contemplated CRISPR-Cas gene editing technology and might have, if a Commission on Biotechnology had been established to provide a horizon scanning function, as recommended by the Royal Commission on Genetic Modification in 2001. Open, honest and inclusive debate is required on whether "gene editing" is "genetic modification".

The HSNO Act defines what a genetically modified organism is and provides regulations for when organisms are not genetically modified.<sup>3</sup> Organisms are not genetically modified when they result solely from: selection;<sup>4</sup> mutagenesis using chemical or radiation treatments that were in use prior to July 1998;<sup>5</sup> by the movement of nucleic acids using physiological processes;<sup>6</sup> or spontaneous deletions, rearrangements and amplifications within a single genome.<sup>7</sup> With the discovery of CRISPR-Cas gene editing technology and its ability to manipulate genetic material using "in vivo" and "ex vivo" techniques, the scientific definition of genetic modification is evolving and thus the legislative definition, relying on in vitro manipulation along with exceptions in regulations, requires review. Currently in New Zealand the use of gene editing technologies, including CRISPR-Cas, is likely deemed genetic modification and the organisms for which CRISPR-Cas is used, are deemed "new organisms" according to the HSNO Act. It is an offence to develop or field test or knowingly import or release, a new organism without prior regulatory approval.<sup>8</sup>

Scientific evidence provides a tool for policy makers to decide how it is to be used. However, Donnelly stated in *Nature* (2018) that: "[a]n accurate, concise and unbiased synthesis of the available evidence is arguably one of the most valuable contributions a research community can offer decision

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2 National Academies of Sciences, Engineering and Medicine *Preparing for Future Products of Biotechnology* (The National Academies Press, Washington DC, 2017).

3 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998.

4 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(a).

5 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(ba).

6 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(d).

7 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(e).

8 Hazardous Substances and New Organisms Act 1996 Act [HSNO Act], s 109.

makers."<sup>9</sup> Donnelly suggests that the common question "[w]hat is the evidence?" could be rephrased to "[h]as sufficient synthesis of all the evidence been done in relation to that [gene editing]?"<sup>10</sup> Four principles are necessary for good evidence synthesis for policy makers and researchers: inclusive, rigorous, transparent and accessible.<sup>11</sup> Policy makers require multiple lenses and a clear synthesis of the best available evidence. This will go some way to engaging public debate and decision-making.

Aotearoa is unique and the Treaty of Waitangi is part of our constitution.<sup>12</sup> The HSNO Act contains provisions designed to ensure Māori views are taken into account when decisions are made about genetically modified organisms.<sup>13</sup> However, the Waitangi Tribunal concluded in the 2011 Wai 262 report:<sup>14</sup>

... that the law and policy in respect of GMOs does not protect the interests of kaitiaki in mātauranga Māori or in the genetic and biological resources of taonga species.

Better implementation of Treaty of Waitangi principles and protection of kaitiaki in mātauranga Māori interests are central to inclusive decision-making about gene editing in Aotearoa. Valuing the Treaty of Waitangi in legislation ensures that Treaty of Waitangi principles will underpin and guide all policy and decision-making.

New Zealand's regulatory framework warrants review in light of advanced genetic technologies and evolving societal, cultural and ethical views. This article provides an analysis of New Zealand's regulatory framework, primarily focussing on the HSNO Act and other statutes as they apply to gene editing technologies (in particular CRISPR-Cas9) in human healthcare, pest control and primary industries.

The content of the article is presented in the following order: firstly, overriding principles of the Treaty of Waitangi and indigenous intellectual property are highlighted. Secondly an overview of New Zealand's regulatory framework including the findings of the Royal Commission on Genetic Modification are provided. Thirdly and primarily, an analysis of the legal and policy implications of gene editing application in human health care, pest control and primary industries in New Zealand are provided. The legal analysis is based on a series of scenarios, produced by the Royal Society Te Apārangi Gene Editing Panel. More information on the scenarios analysed in this article can be found

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9 Christl A Donnelly and others "Four principles for synthesizing evidence" (2018) 558 Nature 361 at 361.

10 At 361.

11 At 362.

12 BV Harris "The Treaty of Waitangi and the Constitutional Future of New Zealand" [2005] NZ L Rev 189.

13 Sections 4, 6(d) and 8.

14 Waitangi Tribunal *Ko Aotearoa Tenei: A Report into the Claims Concerning New Zealand Law and Policy Affecting Māori Culture and Identity* (Wai 262, 2011) vol 1 at 191 [Wai 262 vol 1].

by visiting the Royal Society Te Apārangi website.<sup>15</sup> Fourthly, a brief review of international regulation is provided, exploring process and product-based regulation. International agreements are discussed focussing primarily on the Cartagena Protocol. Latterly and for entirety, a brief review and comment of domestic liability for loss resulting from this technology is provided. Finally, the authors recommend a new integrated regulatory framework for emerging biotechnologies and a single entry point for biotechnology applications and identify further work required.

Throughout the article the authors' conclusions are expressed as *considerations*, for review by government, regulators, policy makers, stakeholders and the public.

While emphasis has been on the science and technical aspects of the law, Treaty of Waitangi principles should be the overriding consideration in a quest for policies that generate ora – intergenerational wellbeing for all of Aotearoa.

The Royal Commission of Genetic Modification recommended in 2001 that New Zealand should preserve its opportunities by allowing the development of genetic modification whilst minimising and managing the risks involved.<sup>16</sup> This is the underlying principle of this article, reporting on the legal and policy implications of gene editing on New Zealand's current regulatory framework.

## **II BACKGROUND**

The gene editing revolution is here with the discovery of CRISPR-Cas9. Doudna and Charpentier developed the CRISPR-Cas9 gene expression system that when introduced into living cells, makes site specific changes to genomes.<sup>17</sup>

Gene editing technologies use proteins, called enzymes, targeted to cut areas of DNA within an organism's genetic material. This process can modify genes, by enabling slightly different repair information from what was there before. This tool enables us to advance our biological knowledge, alter genomes of microbes, plants and animals and treat human genetic diseases. It raises many ethical questions, in particular, whether people should be able to alter their own DNA and the DNA of their future children. The CRISPR-Cas tool is improving rapidly with further research, however, there remains concerns as to its safety resulting primarily from genome wide off-target effects.<sup>18</sup>

CRISPR-Cas has the potential to be more precise, more efficient and less expensive than other genome editing tools and has facilitated a wide range of studies that were previously unachievable.

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15 Royal Society Te Apārangi "Gene editing in Aotearoa" <<https://royalsociety.org.nz>>.

16 Ministry for the Environment *Report of the Royal Commission on Genetic Modification* (July 2001) at 2.

17 Jennifer A Doudna and Emmanuelle Charpentier "The new frontier of genome engineering with CRISPR-Cas9" (2014) 346 *Science* 1077.

18 Michael Kosicki, Kart Tömberg and Allan Bradley "Repair of double-strand breaks induced by CRISPR-Cas9 leads to large deletions and complex rearrangements" (2018) 36 *Nature Biotechnology* 765.

CRISPR-Cas is being researched for use in human healthcare, agriculture, animal welfare and conservation. It is already being used in the United States to produce polled dairy cows (hornless) to minimise animal welfare harms,<sup>19</sup> reduce browning in mushrooms for the restaurant trade<sup>20</sup> and reduce populations of malaria carrying mosquitos.<sup>21</sup>

Gene editing is being considered for treating people with genetic disorders such as Huntington disease. Huntington disease is an inherited brain disorder that causes cells in specific parts of the brain to die which results in impairment of both mental capability and physical control. The Huntington disease gene is dominant, which means that each child born to a parent with Huntington disease has a 50 per cent chance of sharing the same fate and is thus a target for gene therapy.<sup>22</sup> The benefits in human healthcare from gene editing are difficult to deny when other treatments are not available. However, at the extreme end, bioterrorism experts are concerned with biohackers practicing gene editing and creating viruses and new strains of bacteria from mail order DNA kits.<sup>23</sup> More recently a Chinese Scientist has been condemned for gene editing babies.<sup>24</sup>

In 2015 Doudna and other scientists called for a moratorium on the clinical use of gene editing at an International Summit on Human Gene Editing held in Washington DC. Scientists were concerned that the science was getting ahead of considerations about ethics, societal implications and random people in various parts of the world using it for nefarious purposes.<sup>25</sup>

### **III THE TREATY OF WAITANGI AND INDIGENOUS INTELLECTUAL PROPERTY**

The principles of the Treaty of Waitangi were discussed in *New Zealand Maori Council v Attorney-General*.<sup>26</sup> The Court found that the agreement between Māori and the Crown gave rise to

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19 Alison Van Eenennaam and Maci Mueller "Use Of Gene Editing To Introduce The Polled Trait Into Elite Germplasm" (12 June 2018) Dairy Herd Management <[www.dairyherd.com](http://www.dairyherd.com)>.

20 Emily Waltz "Gene-edited CRISPR mushroom escapes US regulation" (2016) 532 Nature 293.

21 Jose Mendez "Cutting Down Malaria with CRISPR: Mosquito gene editing as a new form of transmission prevention" (12 March 2018) PLOS Research News <<https://researchnews.plos.org>>.

22 Michael Eisenstein "To cut is to cure" (2018) 557 Nature S42.

23 Sarah Zhang "A Biohacker Regrets Publicly Injecting Himself With CRISPR" (20 February 2018) The Atlantic <[www.theatlantic.com](http://www.theatlantic.com)>.

24 "China scientist condemned for gene editing babies, loses job" (22 January 2019) Aljazeera <[www.aljazeera.com](http://www.aljazeera.com)>.

25 International Summit on Human Gene Editing "A Global Discussion" (3 December 2015) The National Academies Press <[nationalacademies.org](http://nationalacademies.org)>.

26 *New Zealand Maori Council v Attorney-General* [1987] 1 NZLR 641 (CA).

a partnership, to act in good faith, fairly and reasonably.<sup>27</sup> The Crown's duty extended to active protection of Māori in the use of their lands and other interests to the fullest extent practicable.<sup>28</sup>

The Waitangi Tribunal released *Ko Aotearoa Tēnei: A Report into Claims Concerning New Zealand Law and Policy Affecting Māori Culture and Identity* on the Wai 262 claim.<sup>29</sup> Wai 262 was a claim to Māori cultural and intellectual property and to indigenous flora and fauna. The report encompasses the role of Māori culture, Māori traditional knowledge and Māori identity within Aotearoa. The Waitangi Tribunal emphasised the necessity for the government and Māori to work in partnership, that "protecting and transmitting mātauranga Māori is a responsibility to be shared between Māori and the Crown: neither party can succeed without the help of the other".<sup>30</sup>

The HSNO Act contains provisions designed to ensure that Māori views are considered when decisions are made about genetically modified organisms.<sup>31</sup> However, the Waitangi Tribunal concluded in the Wai 262 report:<sup>32</sup>

... 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.

*Consideration 1: History – Part 4A was repealed from the HSNO Act by s 10 of the HSNO Amendment Act 2011 regarding the establishment, function, appointment and terms of reference for Ngā Kaihautū Tikanga Taiao. Under the Environmental Protection Authority Act 2011, Ngā Kaihautū Tikanga Taiao was disestablished under s 28 and a Māori Advisory Committee was established under s 18. Review and enhance the statutory power and functions of the current Māori Advisory Group.*

New Zealand's native and taonga species are a matter of national importance to be preserved, sustainably managed and protected.<sup>33</sup>

In *Bleakley v Environmental Risk Management Authority*, Justice Goddard noted that the words "culture and traditions" were included in the HSNO Act<sup>34</sup> both to underscore the special nature of the relationship of Māori (as opposed to any other group) to the matters listed in the provision and to

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27 At 683 per Richardson J.

28 At 664 per Cooke P.

29 Wai 262 vol 1, above n 14.

30 Waitangi Tribunal *Ko Aotearoa Tenei: A Report into the Claims Concerning New Zealand Law and Policy Affecting Māori Culture and Identity* (Wai 262, 2011) vol 2 at 584 [Wai 262 vol 2].

31 HSNO Act, ss 4, 6(d) and 8

32 Wai 262 vol 1, above n 14, at 114.

33 Resource Management Act 1991, ss 5 and 6; National Parks Act 1980, s 5; and Biosecurity Act 1993, s 54.

34 Section 6(d).

"ensure that the relationship of Maori with taonga is not read down, dissipated or minimised by those charged with exercising functions, powers and duties under the Act".<sup>35</sup> In Goddard J's view:<sup>36</sup>

... this relationship is to be interpreted holistically, in light of the purpose of the Act (to protect from and prevent and manage adverse effects) and in recognition of and with provision for all the relevant principles.

The Waitangi Tribunal in the Wai 262 report commented that they did not think the Environmental Risk Management Authority (the Authority at the time) had yet reached the point where its systems, policies, and modes of operation achieve the standard articulated by Justice Goddard.<sup>37</sup>

*Consideration 2: Valuing the Treaty of Waitangi in legislation ensures that Treaty of Waitangi principles are incorporated into New Zealand law and Aotearoa's native and taonga species are preserved, sustainably managed and protected. Importantly, Treaty of Waitangi principles will underpin and guide all policy and decision-making. Treaty of Waitangi principles are incorporated into s 8 of the HSNO Act. Incorporate Treaty of Waitangi principles into the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act), Animal Welfare Act 1999, Biosecurity Act 1993, National Parks Act 1980 and Reserves Act 1977.*

The Waitangi Tribunal in the Wai 262 report surmised: "[a]s both the courts and Tribunal have said, Treaty principles are not set in stone. They can and must evolve to meet new circumstances."<sup>38</sup>

Whilst this article provides an analysis of the science and technical aspects of the law, Treaty of Waitangi principles should be the overriding consideration in a quest for policies that generate ora – intergenerational wellbeing for all of Aotearoa.

#### **IV NEW ZEALAND'S CURRENT REGULATORY FRAMEWORK**

Genetically modified organisms are regulated primarily by the HSNO Act. This is the primary code for genetically modified organisms,<sup>39</sup> limited to new organisms identified post 1998 and new organisms developed using in vitro methods. In simplified terms, genetically modified organisms are new organisms, however not all new organisms are genetically modified (Figure 1).

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35 *Bleakley v Environmental Risk Management Authority* [2001] 3 NZLR 213 (HC) at [353].

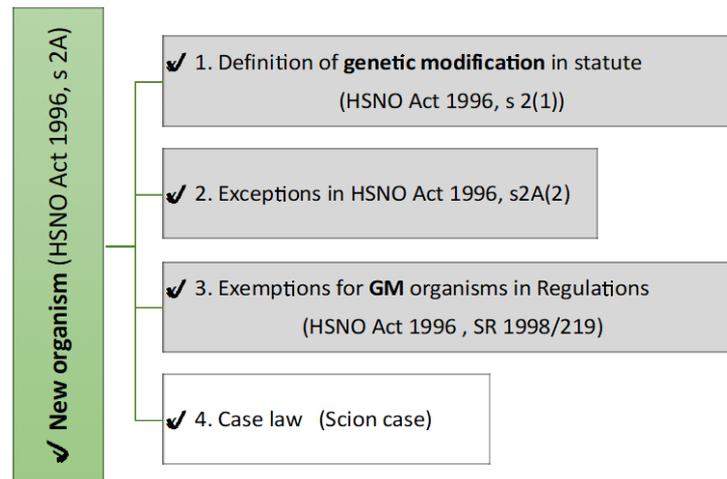
36 At [353].

37 Wai 262 vol 1, above n 14, at 191.

38 At 324.

39 *Federated Farmers of New Zealand v Northland Regional Council* [2015] NZEnvC 89, [2015] NZRMA 217 at [47].

**Figure 1.** Simplified diagram of classification of a new organism according to the HSNO Act.



The HSNO Act defines genetic modification<sup>40</sup> and provides regulations for when organisms are not genetically modified.<sup>41</sup> Organisms are not genetically modified when they result solely from: selection;<sup>42</sup> mutagenesis using chemical or radiation treatments that were in use prior to July 1998;<sup>43</sup> by the movement of nucleic acids using physiological processes;<sup>44</sup> or spontaneous deletions, rearrangements and amplifications within a single genome.<sup>45</sup> Currently in New Zealand, the use of gene editing technologies, including CRISPR-Cas, is likely deemed genetic modification and the organisms for which CRISPR-Cas is used, are deemed new organisms according to the HSNO Act.

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40 Section 2(1) defines "genetically modified organism" as:

... unless expressly provided otherwise by regulations, any organism in which any of the genes or other genetic material— (a) have been modified by *in vitro* techniques; or (b) 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.

41 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations.

42 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(a).

43 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(ba).

44 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(d).

45 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, r 3(e).

New organisms are regulated by the Environmental Protection Authority (EPA). The EPA was established by s 7 of the Environmental Protection Authority Act and has a number of functions, powers and duties pertaining to new organisms.<sup>46</sup>

According to s 25(1) of the HSNO Act, no new organism shall be imported, developed, field tested or released otherwise than in accordance with an approval under the HSNO Act. The EPA may, on application of any person, determine whether or not any organism is a new organism and the determination must be issued in the *New Zealand Gazette*.<sup>47</sup> The EPA may revoke or reissue a determination issued by it under s 26(6) if it receives further information.

The Royal Commission of Genetic Modification released its report on 27 July 2001.<sup>48</sup> The Royal Commission concluded that New Zealand should preserve its opportunities by allowing the development of genetic modification whilst minimising and managing the risks involved.<sup>49</sup> Following the Royal Commission's report, the Government extended its voluntary moratorium on genetic modification until October 2003. This was to allow for changes to be made to legislation and to implement the Royal Commission's recommendations. The Government agreed with the Royal Commission's "precautionary approach" to genetic modification that preserved options for the future.

The New Organisms and Other Matters Bill 2003 (Bill) aimed to amend the HSNO Act before the moratorium was lifted in October 2003.<sup>50</sup> At the time, the HSNO Act was said to have provided for controls on the development of genetically modified organisms (GMOs) in contained conditions and for the release of new organisms into the environment, but was deficient in that it could approve release of new organisms without conditions. The Government at the time noted that there was no intermediate level of control and believed "[t]his reduces the opportunities for proceeding with caution with genetic modification because new organisms with potential benefits can not be released outside containment with conditions attached to that release."<sup>51</sup>

The aim of the Bill was to amend the HSNO Act, the Medicines Act 1981 and the ACVM Act for the management of new organisms, including genetically modified organisms.<sup>52</sup>

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46 HSNO Act, s 11.

47 HSNO Act, s 26.

48 *Report of the Royal Commission on Genetic Modification*, above n 16.

49 At 2; and Ministry for the Environment "Royal Commission on Genetic Modification" (29 August 2016) <[www.mfe.govt.nz](http://www.mfe.govt.nz)>.

50 New Organisms and Other Matters Bill 2003 (47-2).

51 New Organisms and Other Matters Bill *Bills Digest* No 964 at 4.

52 New Organisms and Other Matters Bill *Bills Digest* No 964.

The Government supported the Royal Commission's promotion of a precautionary approach.<sup>53</sup> However the Government was concerned that the HSNO Act was not sufficiently precautionary and proposed in the Bill that research practices should adhere to strict safety guidelines, including secure containment, thereby limiting the regulatory authority's discretion when determining conditions of research. The Royal Commission's recommendations pertaining to evaluation of the regulatory framework are summarised in the following table along with comment on their current status.

**Table 1.** Status of Royal Commission biotechnology recommendations.

<b>Royal Commission of Genetic Modification</b> Chapter 14: The biotechnology century <sup>54</sup>	<b>Comment on Status</b>
<b>Recommendation 14.1:</b> HSNO Act, s 68 be extended to include significant cultural, ethical and spiritual issues as grounds for the Minister's call in powers.	Completed: refer to HSNO Act, s 68(1) Minister's call in powers.
<b>Recommendation 14.2:</b> that the Government establish Toi te Taiao, the Bioethics Council 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.	Established in 2002 and disestablished in 2009.
<b>Recommendation 14.3:</b> Government establish the office of Parliamentary Commissioner on Biotechnology to undertake future watch, audit and educational functions with regard to the development and use of biotechnology in New Zealand.	A separate dedicated Commissioner was not supported by Cabinet. Parliamentary Commissioner for the Environment established (Environment Act 1986).
<b>Recommendation 14.4:</b> Ministry of Research, Science and Technology develop on a consultative	Refer to the Ministry of Business Innovation and Employment's <i>Strategic Science</i>

<sup>53</sup> *Report of the Royal Commission on Genetic Modification*, above n 16, at [95]. The Royal Commission reached the following conclusion with regard to the precautionary principle:

... there is more merit in hearing and responding to the message contained in the words than in seeking to define the meaning or determine how the [precautionary] principle should be applied. In any event, we were not convinced that a single principle could be applied across the board to the use of genetic modification in New Zealand. Decisions on the use of technology must rest on a range of factors, including the risks and acceptability to the public of the proposed use. They are factors that should inform the process of managing genetic modification.

<sup>54</sup> At 341.

basis, a medium and long-term biotechnology strategy for New Zealand.	<i>Investment Fund Investment Plan 2017-2024</i> . <sup>55</sup>
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The HSNO Act has been described as a comprehensive, strict and rigorous code, regulating the effects of the technique on the organism and not the product or outcome.<sup>56</sup> Recent amendments have sought to increase control following release of the organism, including reassessment,<sup>57</sup> conditional release<sup>58</sup> and clarification of the meaning of genetically modified organism.<sup>59</sup>

The HSNO Act and its regulating authority, the EPA, have undergone judicial analysis. Most notable was *Sustainability Council of New Zealand Trust v Environmental Protection Authority (Scion case)*; that case concerned wilding pine),<sup>60</sup> which resulted in limiting the discretionary power of the EPA to assess editing techniques, emphasising the precautionary approach and clarifying the classification of gene edited organisms as new organisms for the purposes of the Act.<sup>61</sup> Additionally, the New Zealand Environment Court in *Federated Farmers of New Zealand v Northland Regional Council* (that case concerned crops) enabled Regional Councils to control the use of genetic modification under the Resource Management Act 1991 through regional policy statements and

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55 Ministry of Business, Innovation and Employment *Strategic Science Investment Fund Investment Plan 2017–2024: 2017 Update*.

56 Drew L Kershen "Sustainability Council of New Zealand Trust v The Environmental Protection Authority: Gene editing technologies and the law" (2016) 6 GM Crops & Food 216.

57 Section 63.

58 Section 38.

59 Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, reg 3(ba).

60 *Sustainability Council of New Zealand Trust v Environmental Protection Authority* [2014] NZHC 1067, (2014) 18 ELRNZ 331 [*Scion case*].

61 HSNO Act, ss 63 and 38. The EPA has the power, upon receipt of an application, to determine whether an organism is a new organism for the purposes of the HSNO Act. In October 2012, Scion, the Crown Research Institute for forest resources, applied to the EPA for a determination of whether forest plants created by using Zinc-Finger Nuclease Type 1 (ZFN-1) and Transcription Activator-Like Effectors (TALENs) techniques were new organisms. In its application, Scion argued that ZFN-1 and TALENs techniques were equivalent to genetic changes made in plants through chemical mutagenesis and therefore were within the EPA's exemptions. EPA staff concluded that plants created with ZFN-1 and TALENs would be considered genetically modified organisms. But the Authority decided that these plants would be exempt under the regulations because ZFN-1 and TALENs techniques are more similar to chemical mutagenesis than genetic modification. The High Court Judge ruled that the exemption list is a closed list. The conclusion was based on an interpretation of the language of the regulation and that the regulations did not prescribe factors for the EPA to add other techniques to the list. The Judge interpreted the HSNO Act and the regulations as not implicitly giving the EPA discretionary power to add to the exemption list and ruled that the EPA could not expand the exemption list to include techniques similar to chemical mutagenesis and adding to the exemption list was a political decision, not an administrative decision.

plans.<sup>62</sup> These cases have wide ranging implications for New Zealand and are not generally limited to genetically modified wilding pines and crops, and by analogy apply to other genetically modified plants and possibly animals.

Two decades have passed since the HSNO Act's promulgation, with minor amendments to the HSNO Act. Importantly the HSNO Act never contemplated CRISPR-Cas genome editing technology and perhaps could have if a Parliamentary Commissioner on Biotechnology had been established to provide a horizon scanning function (see Recommendation 14.3 of the Royal Commission report). With the discovery of CRISPR-Cas gene editing technology and its ability to manipulate genetic material using *in vivo* and *ex vivo* techniques, the scientific definition of genetic modification is evolving and thus the legislative definition, relying on *in vitro* manipulation along with exceptions in regulations, requires review.

New Zealand's current regulatory framework and liability system warrant review in light of advanced genetic technologies and evolving societal, cultural and ethical views. This report will now provide an analysis of New Zealand's regulatory framework as it applies to gene editing technologies (in particular CRISPR-Cas) in human healthcare, pest control and primary industries.

## **V REGULATION OF HUMAN GENE EDITING**

In New Zealand treatment that is aimed at altering the genomic constitution of a person or introducing genetic material from another organism for therapeutic purposes is regulated by the HSNO Act and the Medicines Act. An added level of regulation is imposed when the modification is made in the reproductive context (for example pre-implantation genetic modification of embryos), which is governed by the Human Assisted Reproductive Technology Act 2004 (HART Act). Implantation of a genetically modified gamete or human embryo is prohibited.<sup>63</sup> Restrictions on specified biotechnical procedures, referring primarily to xenotransplantation, are regulated by the Medicines Act.<sup>64</sup>

The network of legal instruments that require consideration alongside the HSNO and Medicines Acts are presented in Figure 2.

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62 *Federated Farmers of New Zealand*, above n 39.

63 Human Assisted Reproductive Technology Act 2004 [HART Act], sch 1, cl 8.

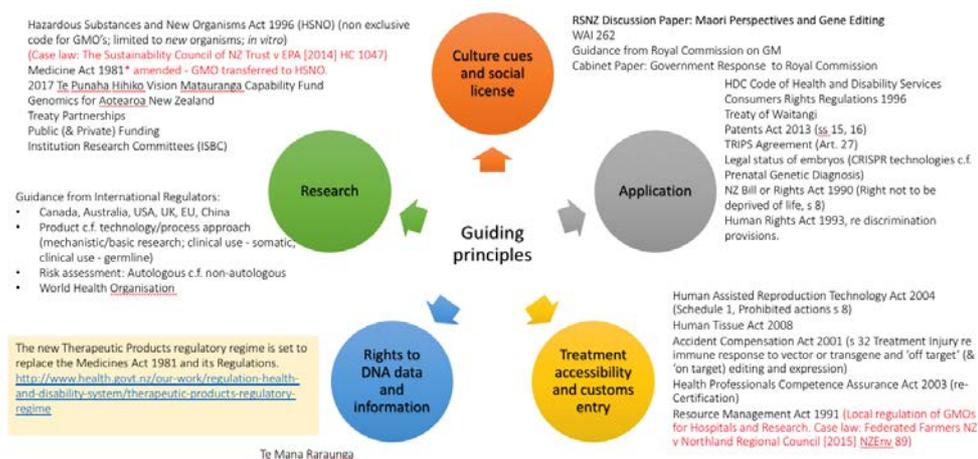
64 Section 96A defines "xenotransplantation" as:

(a) ... a medical procedure that involves the insertion or injection into a human being of any matter that consists of, or includes, living biological material of an animal, whether or not that biological material also includes biological material of a human being; and (b) includes the transfusion into a human being of any human blood or any human body fluid if the blood or the fluid has, as part of a biotechnical procedure, been in contact with living biological material of an animal.

The HSNO Act's primary role is regulating the development, importation and containment of new organisms as per its purpose, in contrast to the Medicines Act, which is to regulate human medicines for therapeutic purposes.

## A Hazardous Substances and New Organisms Act 1996

**Figure 2.** Human gene editing regulation in New Zealand (Source: Everett-Hincks).<sup>65</sup>



The purpose of the HSNO Act is to protect the environment and health and safety of people and communities by preventing or managing the adverse effects of hazardous substances and new organisms. The HSNO Act never intended for new organisms to include human beings.<sup>66</sup>

The New Organisms and Other Matters Bill 2003 inserted the definition of "human cells" into the interpretation section and an amendment was made to the definition of "organism" to include human cells. Genetic modification of human cells (outside a human being) was unregulated prior to 2001. As a consequence, a transitional provision, s 50(A) was inserted to enable regulation of research involving genetic modification of human cells in registered containment facilities. The transitional provision ceased to apply one year after commencement.<sup>67</sup> However, reference to human cells remained within the interpretation section of the HSNO Act.

<sup>65</sup> Julie Everett-Hincks (one of the authors) created this diagram and compiled these figures.

<sup>66</sup> New Organisms and Other Matters Bill 2003 (47-2) *Bills Digest* No 964 at 3.

<sup>67</sup> HSNO Act, s 50A(2).

Human cells, outside of the human body, are deemed "human tissue" and are regulated by s 7(1)(b) of the Human Tissue Act 2008. Human embryo or human gamete is not human tissue for the purposes of any provision of the Human Tissue Act and are regulated by the (HART Act).<sup>68</sup>

The Hazardous Substances and New Organisms Amendment Act 2003 includes the term human cell. Subsequently organism is defined in the HSNO Act as including a human cell (grown or maintained outside the human body).<sup>69</sup>

*Consideration 3: Currently, human gene edited tissue is classified as genetically modified and thus a new organism according to the HSNO Act. This is an oversight following the removal of the transitional provision in 2004. The term "human cell" should be deleted from the definition of organism.*<sup>70</sup>

## ***B Medicines Act 1981***

The Medicines Act refers to the HSNO Act for the definition of new organism and for determining and assessing a "qualifying new medicine".<sup>71</sup> It is through these terms, defined in s 2, that the Medicines Act and the HSNO Act interact when gene editing technology is used to produce a medicine. In particular, a qualifying new medicine is defined in s 2 of the Medicines Act as a new medicine that is or contains a new organism and meets the criteria set out in s 38I(3) of the HSNO Act. That is, it is highly improbable that administration of the medicine would have significant adverse effects on the public and form a self-sustaining population and would have significant adverse effects on: the health and safety of the public; or any valued species; or natural habitats; or the environment.<sup>72</sup> However, the EPA's assessment of whether a "qualifying organism" is or is contained in a qualifying medicine does not consider the effect of the medicine or qualifying organism on the person who is being treated with the medicine.<sup>73</sup>

The Medicines Act was amended in 2005, with the following biotechnical procedures repealed and subsequently provided for in the HART Act as prohibited actions in sch 1: cloned human organism; cloning procedure; genetically modified embryo; genetically modified gamete and germ cell genetic procedure. However, it is unclear whether all gene editing procedures in human meet the

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68 Human Tissue Act 2008, s 7(2).

69 Section 2(1).

70 HSNO Act, s 2(1).

71 Medicines Act 1981, s 2

72 Section 38I(3).

73 Section 38I(4)(a).

definition of genetic modification in the HSNO as genetic material may be modified by in vivo or ex vivo techniques, and not in vitro techniques as required by the Act.<sup>74</sup>

A purpose of the HART Act is to prohibit "unacceptable" assisted reproductive procedures and unacceptable human reproductive research.<sup>75</sup>

*Consideration 4: The HART Act currently prohibits genetic modification of gametes and embryos. Should the HART Act distinguish between gene editing and genetic modification? Should gene editing gametes and embryos be permitted as "acceptable" in some contexts? These decisions are best left for the Advisory Committee on Assisted Reproduction and the policy makers working with the HART Act, to be assessed on a case-by-case basis.*

*Consideration 5: Regulatory definitions – "genetically modified" is not defined in the HART Act and does not refer to the HSNO Act for definition. The HART Act should be amended to refer to the HSNO Act for the legal definition of genetic modification.<sup>76</sup>*

### **C Dual Legislative Process**

Determination of a qualifying new medicine is a dual legislative process. Gene editing human cells, tissue or organs, that are not gametes or embryos, follows the legislative steps in Figure 3 before it is approved for use. In brief, it has to meet the definition of "medicine"; medicine for a "therapeutic purpose" likely to achieve its principal intended action and meet the definition of qualifying new medicine; containing a new organism and meeting the HSNO Act's assessment criteria.

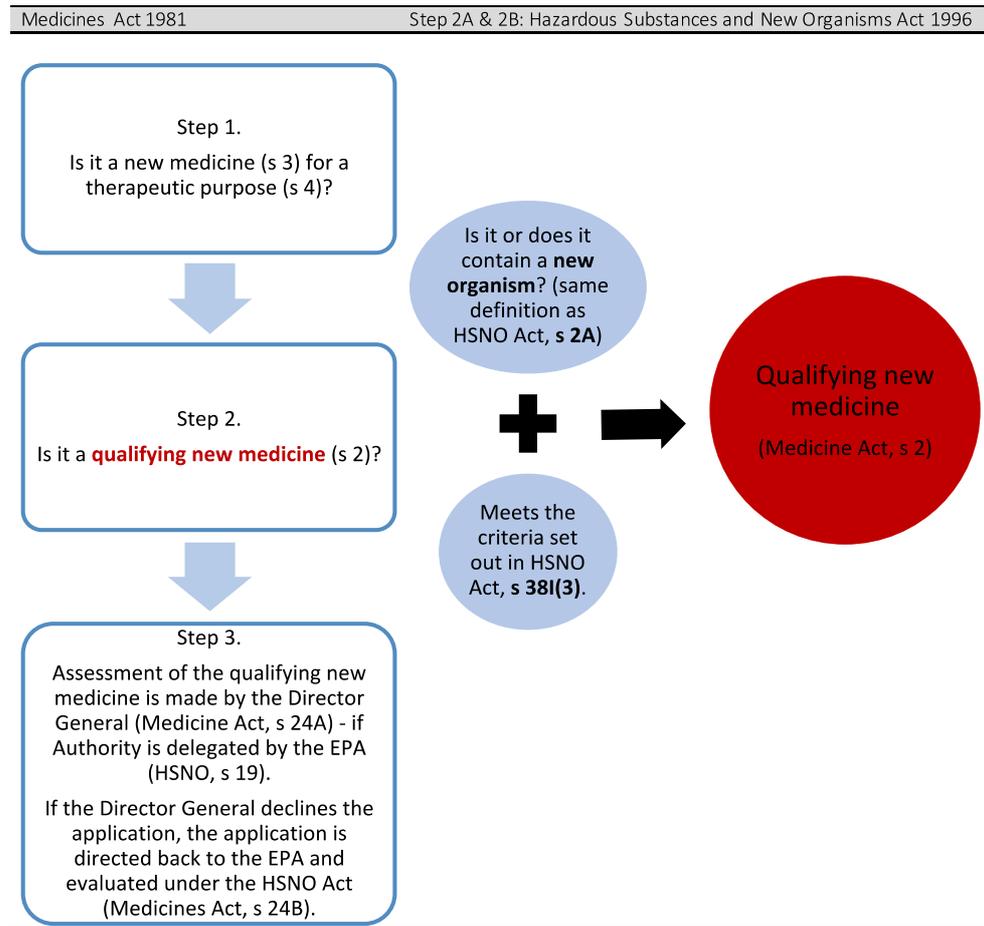
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74 HSNO Act, s 2(1).

75 HART Act, s 3(c).

76 The s 2(1) definition of "genetically modified organism" is given at n 40.

**Figure 3.** Dual legislative process summarised for determining and assessing a qualifying new medicine.



*Consideration 6: The EPA does not assess the effect of the qualifying organism on the person (individual) being treated with a qualifying medicine.<sup>77</sup> The EPA's purpose is to assess the effect of the qualifying new medicine on people, communities and the environment.<sup>78</sup> In practice, MEDSAFE has delegated assessment of qualifying new medicines to the EPA, even though this is a dual*

<sup>77</sup> HSNO Act, s 38I(4)(a).

<sup>78</sup> HSNO Act, s 4.

legislative process. The requirements of the Medicines Act are additional to the HSNO Act.<sup>79</sup> Therefore, a review is required to determine if the EPA's assessment of qualifying organisms for release meets the requirements of the Medicine Act.

*Consideration 7: GMOs are "new organisms" under the HSNO Act.<sup>80</sup> A new organism includes an "organism" that has been "genetically modified"<sup>81</sup> "by in vitro techniques".<sup>82</sup> The CRISPR-Cas genome editing system is developed by in-vitro methods, thereby classifying it as an "in vitro technique" for the purposes of meeting the definition of a GMO. However, some advanced gene editing therapies use in vivo and ex vivo treatment methods. Therefore, the definition of genetic modification should be extended to include organisms that have been genetically modified by in vivo and ex vivo methods.*

The CRISPR-Cas machinery needs a "vehicle" to get to its target cells. Human studies utilise adenoviral vectors as delivery vectors for CRISPR-Cas9. However, these have shown gene disruption in the host genome of various human cells.<sup>83</sup>

*Consideration 8: The delivery vector for the CRISPR-Cas machinery, warrants independent risk assessment, as concerns have been raised regarding its safety and this could be provided for by controls imposed by the EPA. New Zealand's current process based regulatory approach assesses the safety of the delivery vector whereas a product based regulatory system may not. EPA's risk assessment policy and procedures require review to ensure delivery vectors for administering gene edited products are assessed and would be assessed if New Zealand adopted a product based regulatory system.*

*Consideration 9: The Therapeutic Products and Medicines Bill 2006 (set to replace the Medicines Act and in its second reading), does not address the use of advanced genetic technologies in medicine, therapeutic products, and reproductive treatments and thus requires review to determine the implications of advanced gene editing technologies used in human medicine.*

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79 Medicines Act, s 5A.

80 Section 2A.

81 HSNO Act, s 2A(1)(d).

82 HSNO Act, s 2(1).

83 Ignazio Maggio and others "Adenoviral vector delivery of RNA-guided CRISPR/Cas9 nuclease complexes induces targeted mutagenesis in a diverse array of human cells" (2014) 4 Scientific Reports 1.

## ***VI REGULATION OF THE USE OF GENE EDITING AND GENE DRIVES FOR PEST CONTROL***

Next generation and novel pest control tools are being considered for use in New Zealand.<sup>84</sup> In particular, gene drives using advanced gene editing technology have been investigated as a potential tool to assist the government in achieving New Zealand predator free status by 2050.<sup>85</sup>

Gene editing tools have not been used to date in conservation of wildlife, but their use in the control of non-native invasive organisms is being explored with the use of "gene drives".

In 2015, researchers demonstrated the use of CRISPR-Cas9 to develop gene drives, a genetic system named for the ability to "drive" itself and nearby genes through populations of organisms over many generations. In normal sexual reproduction, offspring inherit two versions of every gene, one from each parent. Each parent carries two versions of the gene, having a 50 per cent chance that a particular variant of the gene will be passed on. However, gene drives ensure that the genetic modification will almost always be passed on, allowing that variant to spread rapidly through a population. Dearden and others offer a list of potential target species in New Zealand for genetic modification with technologies developed and required to implement a gene drive system. Potential target species include vespine wasps, pasture damaging weevils, Australian blowfly, possum, stoat, rats and mice.<sup>86</sup>

Gene editing a pest to include a gene drive would be regulated primarily by the HSNO Act. However, many statutes require referral, proving a complex regulatory framework for evaluating advanced genetic technologies as a method for controlling, managing and eradicating pests. It is seldom that one path would be taken. For example, administering a gene drive to rid New Zealand's conservation estate of possums will likely require at a minimum: animal ethics approval (Animal Welfare Act), a Pest Management Plan (Resource Management Act and Biosecurity Act), a conservation management plan (Conservation Act 1987), risk assessment for the agricultural industry and trade (ACVM Act), wild animal controls (Wild Animal Control Act 1977), along with approval from the Director General of Conservation (Conservation Act), in addition to EPA approval for the new organism (HSNO Act, s 27). Figure 4 provides a diagram of the legislation that requires consideration alongside the HSNO Act, for pest control using gene editing technologies.

Gene drives are a disruptive technology, having the potential to lead transformational change in conservation, agriculture and in areas that we have not yet considered. Dearden and others recommend that regulation of gene drives in all contexts is required, as they risk reducing population genetic

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84 Peter K Dearden and others "The potential for the use of gene drives for pest control in New Zealand: A perspective" (2017) 48 *Journal of the Royal Society of New Zealand* 225.

85 Department of Conservation "Predator Free 2050" <[www.doc.govt.nz](http://www.doc.govt.nz)>.

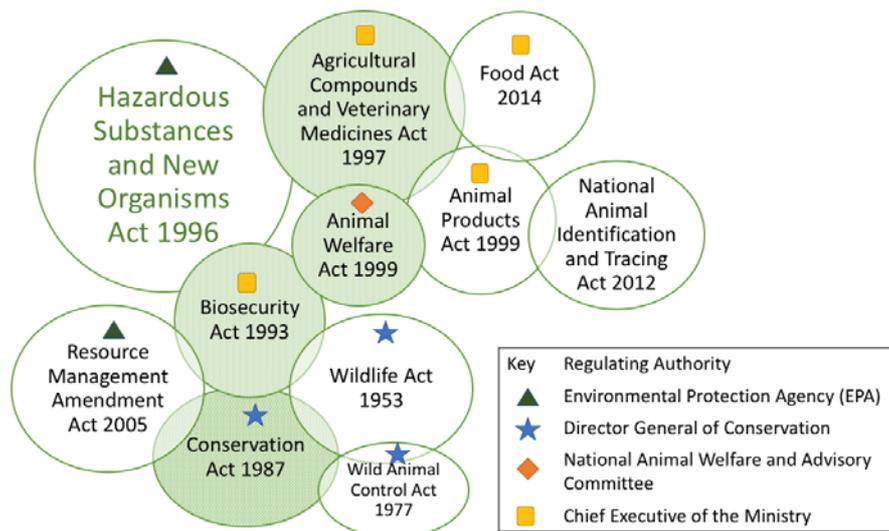
86 Dearden and others, above n 84.

diversity along with potential development of resistant populations or strains.<sup>87</sup> For production animals and plants, these effects render the affected population more susceptible to management, disease and environmental challenge in the future.

No one organism should be evaluated in isolation of its ecosystem. A risk assessment method incorporating a long-term time scale view, over a number of breeding cycles, is required to: reduce resistance to gene drives in pests and unwanted organisms; assess the impact on an ecosystem over time; investigate unintended consequences; and for production animals and plants (non pests), retain genetic diversity, essential for adaptation to changing environmental and management conditions.

*Consideration 10: Risk assessment undertaken by the EPA balances beneficial effects against adverse effects.<sup>88</sup> Adverse effects will still be realised. An environmental bottom lines approach is more supportive of the precautionary approach and should be deployed for disruptive technologies.*

**Figure 4.** New Zealand legislation influencing genome editing technologies in animals and other organisms. The HSNO Act is the primary statute. Overlapping statutes have interacting provisions. Please note that the Animal Welfare Act and the HSNO Act are not joining, as the Animal Welfare Act's genetic modification term does not refer to the HSNO Act for meaning. Regulating authorities for each of the statutes are presented in the key provided.



87 Dearden and others, above n 84.

88 HSNO Act, s 38.

*Consideration 11: Regulatory complexity limits our ability to provide a coordinated and timely response. Regulation of gene editing technologies and their products comprises multiple pieces of legislation with different regulatory authorities. Biotechnologies (including gene editing technologies) would benefit from a single statute and a single entry point for applications.*

### **A Proposed use of CRISPR-Cas**

The purpose for which CRISPR-Cas and other advanced genetic technologies are proposed to be used will direct the regulation pathway. Pest management is legislated under the Biosecurity Act, where "pest" and unwanted organism are defined.<sup>89</sup> Pest is also defined in the ACVM Act in relation to agricultural security. Agricultural security is defined as the exclusion, eradication and effective management of pests or "unwanted organisms" under s 2(1) of the Biosecurity Act.

*Consideration 12: Regulatory definition of "pests" and "unwanted organism" differs between multiple statutes. Legislative overlap for pests and unwanted organisms leads to regulatory complexity causing confusion for policy makers. Differing definitions in legislation and science will cause confusion for everyone. The following terms need to be defined consistently across legislation: animal; pest; unwanted organism; management of animals; biological product/compound; and genetic modification.<sup>90</sup>*

*Consideration 13: Once genetically modified and deemed a new organism, is the new organism still deemed a pest or unwanted organism? For example, wilding pine species, lodgepole pine (*Pinus contorta*) are deemed unwanted organisms according to the MPI unwanted organism database (UOR).<sup>91</sup> Would a genetically modified wilding pine species rendering it sterile and thus a new organism still be deemed a pest or unwanted organism? Reclassification of new organisms will be required, as they may no longer be deemed unwanted organisms or pests.*

*Consideration 14: Should EPA's assessment of risk differ for applications to genetically modify and release unwanted organisms and/or pests? These organisms are already causing harm to the*

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<sup>89</sup> Section 2(1).

<sup>90</sup> "Animal" is defined differently in both the Animal Welfare Act 1999 and the Agricultural Compounds and Veterinary Medicines Act 1997 [ACVM]. "Pest" is defined differently in the Animal Welfare, Biosecurity and ACVM Acts. "Organism" and "unwanted organism" have the same meaning in both the Biosecurity and HSNO Acts. The Animal Welfare Act refers to "biological product". Does this have the same meaning as "biological compound" in the ACVM Act? The Animal Welfare Act includes "genetic modification" of breeding animals, but does not define genetic modification and does not refer to the HSNO Act for definition. "Management" of animals is not defined in legislation and therefore could be interpreted to mean the control and eradication of agricultural pests.

<sup>91</sup> Biosecurity New Zealand "Registers and lists for pests and diseases: Unwanted Organisms Database" (27 June 2019) <[www.mpi.govt.nz](http://www.mpi.govt.nz)>.

*environment in their natural, non-genetically modified and wild type state. Review risk assessment provisions in the HSNO Act for genetically modifying pest and unwanted organisms.*

### ***B Conservation, National Park and Reserves Legislation***

The Reserves Act and the National Parks Act refer to the term genetic modification in provisions authorising the Minister to introduce any biological control organism to control wild animals or animal pests or plant pests in any reserve, or National Park invested in the Crown.<sup>92</sup>

*Consideration 15: Genetic modification is not defined in the Reserves and National Parks Acts and these Acts do not refer to the HSNO Act for definition. Regulatory definition of genetic modification is required. Provisions in the Reserves and National Parks Acts require review in the context of advanced genetic technologies and gene drives being considered for pest control and conservation.*

## ***VII REGULATION OF GENE EDITING IN PRIMARY PRODUCTION***

Gene editing for primary production such as reducing environmental impact of wilding pines, responding to insect pests, speeding up apple breeding, protecting taonga species such as mānuka and providing new human health benefits from cow milk, requires evaluation of a vast network of regulatory instruments alongside the HSNO Act.<sup>93</sup> Primarily, the ACVM Act; Animal Welfare Act; Biosecurity Act; Resource Management Act; and the Cartagena Protocol to the Convention on Biological Diversity require referral.<sup>94</sup>

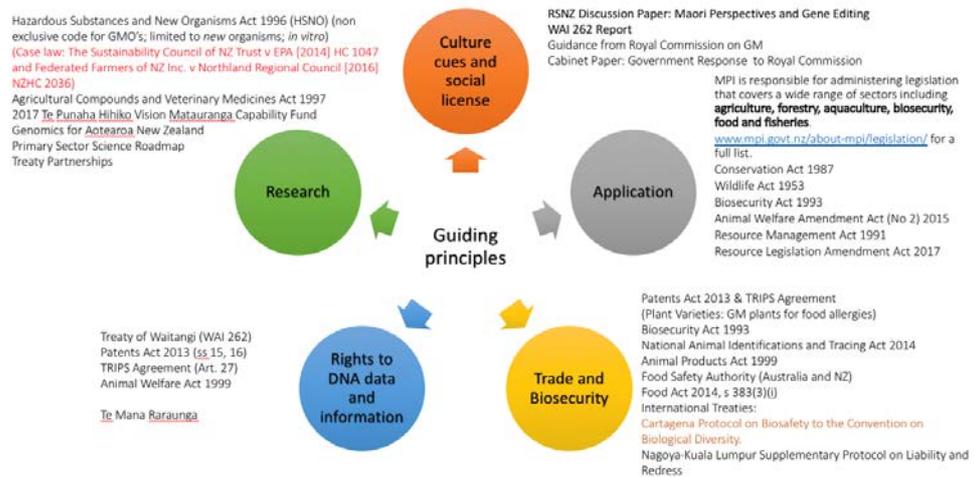
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92 Reserves Act 1977, s 51A; and National Parks Act, s 5A.

93 Royal Society Te Apārangi *The use of gene editing in the primary industries: Discussion paper* (October 2018).

94 Cartagena Protocol on Biosafety to the Convention on Biological Diversity 2226 UNTS 208 (opened for signature 15 May 2000, entered into force 11 September 2003).

**Figure 5.** Gene editing regulation in New Zealand's primary industries.



*Consideration 16: Regulatory complexity. Primary industries regulation of gene editing technologies and their products comprises multiple pieces of legislation with different regulatory authorities. Biotechnologies (including gene editing technologies) would benefit from a single statute and a single entry point for application (see Figure 4, Consideration 11).*

Gene edited plants and animals pose significant new challenges for regulation. Under current legislation, such as the HSNO Act, and a judicial ruling in the *Scion case* on the interpretation of that legislation, gene edited crops and animals are deemed genetically modified.<sup>95</sup> However, in many cases gene edited crops and animals will have genetic modifications that in theory could be induced by non-regulated methods, such as radiation or chemical-induced mutagenesis prior to 1998, or simply occurring naturally from spontaneous mutation.<sup>96</sup> This calls into question the robustness of a risk management approach that focuses on how the modification is produced rather than the risks posed by the organism/product developed.

For importers, in the absence of a declaration process, it will be difficult to distinguish gene edited organisms and products from non-modified contemporaries. The export of living modified organisms is prohibited, except as provided by the Imports and Exports (Living Modified Organisms) Prohibition Order 2005. Exporters require authorisation from the Minister for the Environment to export "living

<sup>95</sup> *Scion Case*, above n 60.

<sup>96</sup> HSNO Act; and Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, reg 3(ba).

modified organisms" (LMO's) intended for: contained use;<sup>97</sup> food or feed or for processing;<sup>98</sup> or intentional introduction into the environment.<sup>99</sup> International trade agreements and the Cartagena Protocol are discussed further below.

*Consideration 17: Regulatory oversight – challenge of recognising imported gene edited products, with international agreements on what is being regulated, varying between countries. The definition of genetic modification differs between countries and jurisdictions. Gene editing cannot be detected in some situations. A review of international regulation is required along with an assessment of the implications for New Zealand's international trade agreements.*

## **A Agricultural Compounds and Veterinary Medicines Act 1997**

In addition to the HSNO and Biosecurity Acts, the ACVM Act has possibly the greatest effect on this technology. The purpose of the ACVM Act is to prevent or manage the risks associated with "agricultural compounds", ensure the use of agricultural compounds does not breach domestic food residue standards and that consumers receive sufficient information about agricultural compounds.<sup>100</sup> The ACVM Act aims to achieve its purpose by providing that no agricultural compound may be used, including those imported, manufactured or sold in New Zealand, unless its use is authorised under the Act.<sup>101</sup>

Gene editing use in New Zealand's primary industries can meet the definition of a "biological compound" and subsequently an agricultural compound for managing plants and animals.<sup>102</sup> The purpose of the Act is to prevent and manage risks associated with agricultural compounds to public health; trade in primary produce; animal welfare; and agricultural security.<sup>103</sup>

Gene edited products used to "manage" animals will undergo risk assessment according to the ACVM Act. A "veterinary medicine", according to s 2(1) of the ACVM Act, means any substance, mixture of substances, or biological compound used or intended for use in the "direct management"

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97 Imports and Exports (Living Modified Organisms) Prohibition Order 2005, cl 6.

98 Imports and Exports (Living Modified Organisms) Prohibition Order, cl 7.

99 Imports and Exports (Living Modified Organisms) Prohibition Order, cl 8.

100 Section 4.

101 Section 4A(1)

102 Section 2(1).

103 Section 4.

of an animal. A "qualifying veterinary medicine" is defined in the HSNO Act as a veterinary medicine that is or contains a new organism<sup>104</sup> and meets the criteria set out in s 38I(3) of the HSNO Act.<sup>105</sup>

*Consideration 18: There is potential for imported gene edited animals and plants (and other organisms) to bypass containment provisions in the HSNO Act and to be released without controls.<sup>106</sup> This is legally possible when advanced genetic technology is deemed a "qualifying organism" in a "veterinary medicine" used in the "direct management of the animal". This consideration would also apply to the management of pests. An assessment of potential implications is required should containment be bypassed, for a qualifying organism in a veterinary medicine. Should legislation be amended to ensure imported veterinary medicines are imported into containment?*

## **B Animal Welfare Act 1999**

The Animal Welfare Act determines whether animals can be manipulated in s 3. The CRISPR-Cas genetic technique and the reproductive technique used to genetically modify animals is deemed a "manipulation".<sup>107</sup> Manipulation includes the breeding or production of an animal using any breeding technique (including genetic modification) that may result in the birth or production of an animal that is more susceptible to, or at greater risk of pain or distress during its life as a result of breeding or production.<sup>108</sup> This provision considers the effect of genetic modification on the animal's production performance and on its progeny.

*Consideration 19: The associated effect of an edited gene on other genes in the animal may not be known and is required to determine the risk of adverse effects on resulting progeny under s 3(1B) of the Animal Welfare Act. Ensure animal genetic association analyses and findings are incorporated in risk assessment methods.*

*Consideration 20: Regulatory definition – genetic modification is not defined in the Animal Welfare Act and this Act does not refer to the HSNO Act for interpretation. Amend the Animal Welfare Act to refer to the HSNO Act for definition of genetic modification.*

Manipulation of an animal means to deliberately interfere with the normal physiological, behavioural, or anatomical integrity of the animal by deliberately subjecting it to a procedure which is unusual or abnormal when compared with that to which animals of that type would be subjected

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104 Section 2(1).

105 ACVM Act, s 2(1).

106 Section 38I(1).

107 Sections 3(1)(a)(i) and 3(1B).

108 Section 3(1B).

under "normal management or practice".<sup>109</sup> The procedure involves exposing the animal to any "microorganism" or "biological product".<sup>110</sup>

*Consideration 21: Lack of regulatory definitions and inconsistent regulatory definitions leads to stakeholder uncertainty for proposed use of advanced genetic technologies. The following terms are not defined by the Animal Welfare Act and do not refer to other legislation for definition: "normal management or practice", "biological product" and "microorganism". Amend the Animal Welfare Act to include definition for these terms.*

## **VIII INTERNATIONAL REGULATION OF GENE EDITING**

A summit held in 2015 identified that many countries, including Canada, the United States, Australia, the United Kingdom and Europe, are grappling with how to define and regulate gene edited plants and animals, given many gene edited organisms will be indistinguishable from those generated by traditional plant and animal breeding processes.<sup>111</sup>

The New Zealand High Court judgment in the *Scion case* has possibly the greatest implications for the regulation of gene editing tools, highlighting to international observers New Zealand's steadfast precautionary approach to gene editing technology.<sup>112</sup> According to Kershen, the *Scion case* has potentially influenced the European Union (EU) to remain committed to the precautionary approach as it investigates how to regulate gene editing techniques.<sup>113</sup>

Advancement of genome editing technologies have been advocated by some, as a time and opportunity to review current regulatory frameworks and devise a future-proof framework to keep abreast of rapidly advancing technologies.<sup>114</sup> A potential solution is product directed legislation in contrast to process directed legislation (for example evaluating agri-food products based on an examination of the actual characteristics of the new food on our health, and not on the processes or techniques used to obtain the food). The question of whether biotechnology regulation should be based on the product or the process is currently being debated, with different jurisdictions adopting different approaches. New Zealand has implemented a process-based approach, along with the EU,

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109 Animal Welfare Act, s 3(1)(a).

110 Animal Welfare Act, s 3(1)(a)(ii).

111 International Summit on Human Gene Editing "A Global Discussion" (3 December 2015) The National Academies Press <nationalacademies.org>.

112 *Scion case*, above n 60.

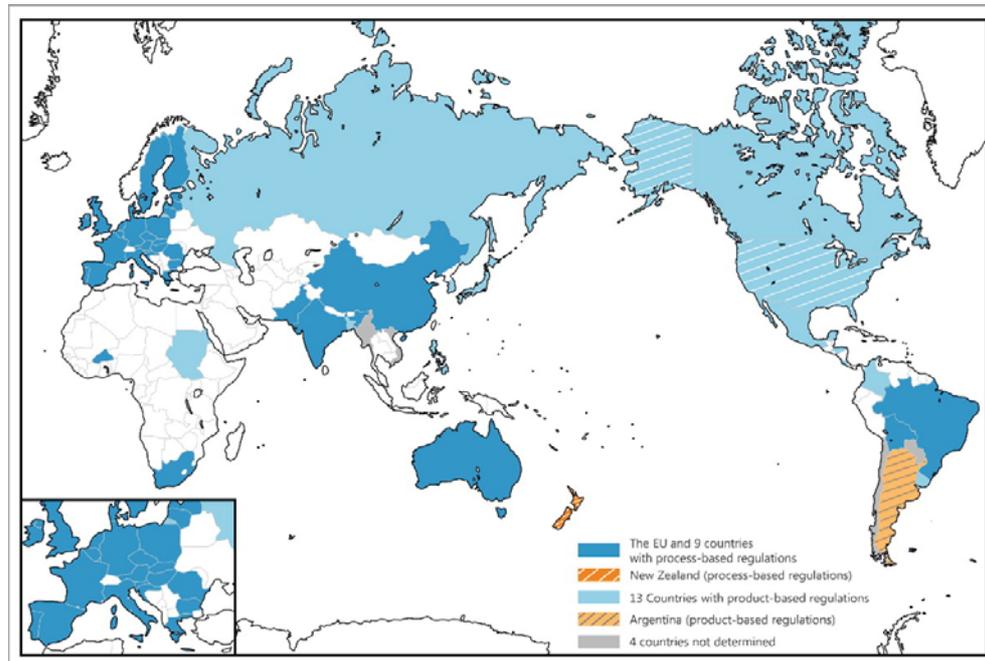
113 Kershen, above at 56.

114 Gary E Marchant and Yvonne A Stevens "A new window of opportunity to reject process based biotechnology regulation" (2015) 6 GM Crops & Food 233.

whereas Canada has adopted a "novel product" based approach and the United States has implemented a product-based regulation system (see Figure 6).<sup>115</sup>

*Consideration 22: Differing product directed and process directed regulation systems provide challenges for international trade resulting in uncertainty for our primary industries. Determine if the risk is commensurate with the regulatory burden. Compare and evaluate product directed and process directed regulation systems.*

**Figure 6.** The international regulatory landscape regarding GMOs. The Countries (n=29) are coloured according to the survey on the regulatory concepts that they employ regarding GMOs. The darker blue countries have adopted process-based regulations. The light blue countries have employed product-based regulations. Note that the United States (product-based GMO regulations), Argentina (product-based GMO regulations) and New Zealand (process-based GMO regulations) are highlighted with stripes because their regulations have responded to genome edited crops.<sup>116</sup>



<sup>115</sup> Tetsua Ishii and Motoko Araki "A future scenario of the global regulatory landscape regarding genome-edited crops" (2017) 8 GM Crops & Food 44.

<sup>116</sup> Ishii and Araki, above n 115.

There appears to be a fundamental divide in how biotechnology should be regulated. According to Alta Charo, speaking at the International Summit on Human Gene Editing:<sup>117</sup>

It is whether or not we think of biotechnology as a thing unto itself, or if we think of it as simply one more tool that goes into making various products. If you regulate the technology, you regulate everything about the technology in a comprehensive way ... It also has the problem of needing much more specific legislation to focus in on the individual products, because as is noted in a contrasting system where you regulate the product and not the technology, as is the case in the United States, the technology itself is neither inherently dangerous or safe.

Alta Charo went on to say that:<sup>118</sup>

Regulating by product gives you the advantage of being able to be much more specific about the degree of risk that you fear or anticipate, and the degree of caution you need.

It has been predicted that process-based regulatory systems, which are premised on a binary system of transgenic and conventional approaches, will become increasingly obsolete and unsustainable with the advancement of genome editing tools. Marchant and Stevens conclude that countries that have adopted process-based approaches will need to migrate to a product-based approach that considers the novelty and risks of the individual trait, rather than the process by which that trait was produced.<sup>119</sup>

An example of product directed legislation is Canada's Food and Drug Act<sup>120</sup> and its subordinate regulations, where Canada regulates products derived from biotechnology processes as part of its existing regulatory framework for novel products. The focus is on the traits expressed in the products and not on the method used to introduce those traits. Australia's regulatory system is process-directed and thus similar to New Zealand's. However, New Zealand's regulatory framework differs from Australia's as Australia has a dedicated Gene Technology Act 2000. Australia's Gene Technology Act applies to genetically modified organisms other than humans.<sup>121</sup> Australia's Office of the Gene Technology Regulator (OGTR) is currently reviewing the operation of the Gene Technology Act, as legislated four years after the commencement of the Act.<sup>122</sup> The OGTR review will be discussed further below.

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117 Alta Charo "The Governance of Human Gene Editing" (speech to the International Summit on Human Gene Editing: A Global Discussion, Washington DC, 1–3 December 2015).

118 Charo, above n 117.

119 Marchant and Stevens, above n 114.

120 Canada's Food and Drug Act RSC 1985 c F-27.

121 Section 10.

122 Gene Technology Act 2000 (Cth), s 194.

### ***A Product-directed Regulation***

In 2016 the United States Department of Agriculture (USDA) approved the cultivation and sale of a waxy corn<sup>123</sup> and gene edited mushroom,<sup>124</sup> without regulation. Under its biotechnology regulations, the USDA does not currently regulate, or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques, as long as the plant is developed without the use of a plant pest as the donor or vector and they are not themselves a plant pest.<sup>125</sup>

Canada regulates on a case-by-case basis focusing on the risks associated with the outcome of the modification (new traits) rather than the process used to generate the trait change.<sup>126</sup> Canada has created a regulatory framework that regulates novel products produced through biotechnology, under existing regulations for traditional products.<sup>127</sup>

### ***B Process-based Regulation***

On July 25, 2018, the Court of Justice of the European Union provided its judgment that organisms created through many newer genome editing techniques are to be regulated as GMOs in the EU. Taken from the judgment:<sup>128</sup>

Article 2(2) of Directive 2001/18 must be interpreted as meaning that organisms obtained by means of techniques/methods of mutagenesis constitute GMOs within the meaning of that provision, and Article 3(1) of Directive 2001/18 ... must be interpreted as meaning that only organisms obtained by means of techniques/methods of mutagenesis which have conventionally been used in a number of applications and have a long safety record are excluded from the scope of that directive.

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123 Letter from Michael J Firko (APHIS Deputy Administrator, Biotechnology Regulatory Services, Animal and Plant Health Inspection Service, USDA) to Daria H Schmidt (Director, Registration and Regulatory Affairs – North America, DuPont Pioneer) regarding the Confirmation of Regulatory Status of Waxy Corn Developed by CRISPR-Cas Technology (18 April 2016).

124 Waltz, above n 20, at 293.

125 "A CRISPR definition of genetic modification" (2018) 4 Nature Plants 233 <www.nature.com>.

126 Stuart J Smyth "Canadian regulatory perspectives on genome engineered crops" (2017) 8 GM Crops & Food 35.

127 Library of Congress "Restriction on Genetically Modified Organisms: Canada" (9 June 2015) <www.loc.gov>.

128 Case C-528/16 *Confédération paysanne v Premier ministre, Ministre de l'agriculture, de l'agroalimentaire et de la forêt* ECLI:EU:C:2018:583 at [54]. Mutagenesis is a process by which the genetic information of an organism is changed, resulting in a mutation. It may occur spontaneously in nature, or as a result of exposure to physical or chemical agents that change the genetic material. It can also be achieved experimentally using laboratory procedures.

An opinion issued by the Court in March 2018, prior to the judgment above, suggested that EU regulations should be relaxed for "gene edited plants" and that they should not be subject to risk assessment and review requirements as are applied to the cultivation and import of "transgenic" varieties (incorporating foreign genes into the organism).<sup>129</sup> However, as mentioned, the Court subsequently ruled that new genome editing methods are not covered by the Directive's "mutagenesis exemption" and are thereby subject to a precautionary approach and the same rigorous risk assessment, product development and trade requirements as transgenic plant varieties.<sup>130</sup>

In Australia, a scientific and technical review of the Australian Gene Technology Act 2000 was initiated in October 2016, by the Australian OGTR.<sup>131</sup> Human and food products are outside the scope of the review. Under OGTR's proposed changes, gene editing using site directed nucleases (SDN-1) without introduced templates to guide genome repair would not be regulated as GMOs, as the repairs would be guided by the cell's normal repair processes. Similarly, organisms modified by introduced RNA that blocks gene expression (RNAi) will not be deemed to be GMOs provided the RNA does not give rise to any change in the genome sequence. Currently, if a template is used to guide genome repair (for example SDN-2 and SDN-3), the resulting organisms are GMOs, as are organisms modified using site specific mutagenesis. These would continue to be regulated under the proposed option (Figure 7).

*Consideration 23: Practically, it is not possible to distinguish products of SDN-1 from naturally occurring mutation. Certainty for stakeholders is improved by deeming SDN-1 as non-GMO. New Zealand consider adopting the Australian OGTR recommendation.*

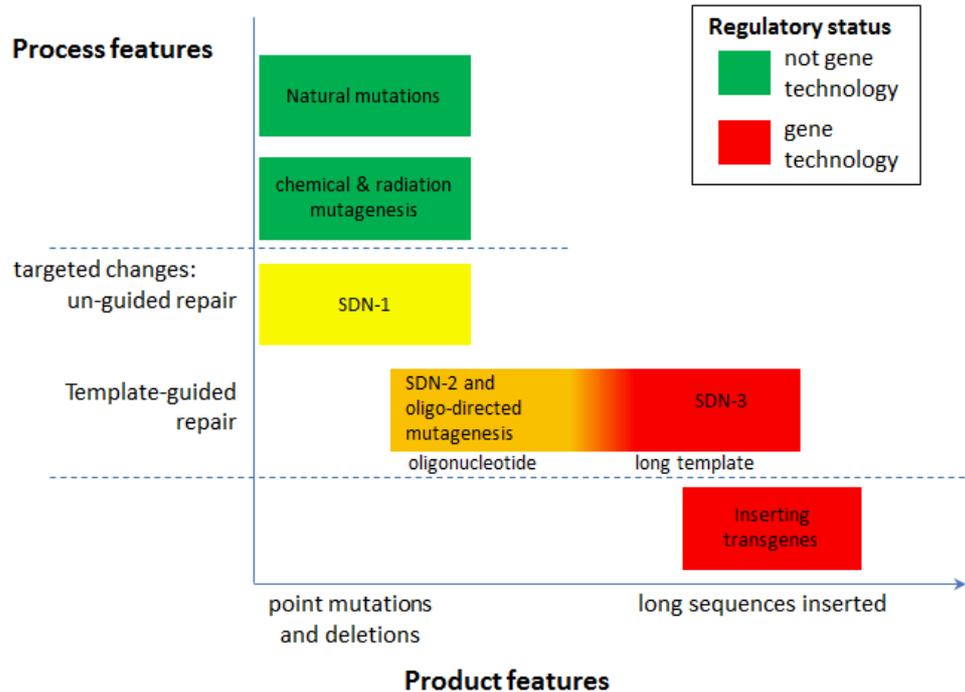
**Figure 7.** Site-directed nuclease (SDN) techniques and site specific mutagenesis are represented according to their process and product features, relative to unregulated techniques (natural mutations, chemical mutagenesis and radiation mutagenesis) and regulated techniques (inserting transgenes). SDN-1 involves the unguided repair of a targeted double strand break, producing sequence changes similar to natural mutations and mutagenesis. SDN-2 and SDN-3 involve template-guided repair of a targeted double-strand break. SDN-2 and oligo-directed (site specific) mutagenesis use an oligonucleotide to guide small sequence changes that may be identical to the outcomes of SDN-1.

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129 Alison Abbott "European court suggests relaxed gene-editing rules" (19 January 2018) Nature International Journal of Science <[www.nature.com](http://www.nature.com)>.

130 Court of Justice of the European Union "Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive" (press release, 25 July 2018).

131 Australian Government Department of Health Office of the Gene Technology Regulator *Technical Review of the Gene Technology Regulations 2001: Discussion paper – Options for regulating new technologies* (October 2016).



SDN-3 uses a long template to insert new sequences, with similar outcomes to inserting transgenes by other gene technology techniques.<sup>132</sup>

### ***IX INTERNATIONAL TREATIES – CARTAGENA PROTOCOL***

The Cartagena Protocol to the Convention on Biological Diversity in accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, is an international agreement that aims to ensure an adequate level of protection in the field of safe transfer handling and use of "living modified organisms" (LMOs).<sup>133</sup> Particular attention is given to LMOs resulting from biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, considering risks to human health and specifically focusing on transboundary movements.<sup>134</sup>

Gene editing many of our species would likely meet the definition of an LMO resulting from modern biotechnology as long as the modified organism possessed a novel combination of genetic

<sup>132</sup> At 12.

<sup>133</sup> Cartagena Protocol on Biosafety to the Convention on Biological Diversity, above n 94.

<sup>134</sup> Cartagena Protocol on Biosafety to the Convention on Biological Diversity, above n 94, art 1.

material. However, "novel combination" is not defined in the Cartagena Protocol. A novel combination of genetic material may not be likely using CRISPR-Cas9 where CRISPR-Cas9 is used to delete a nucleotide using a sequence that is already present in the species population. However, it may be deemed an LMO when applying the precautionary approach of the Cartagena Protocol.

*Consideration 24: LMO definition – the gene editing technique may not produce a novel combination of genetic material as it may only be used to delete or add a nucleotide that is already present in the species population. Research is required to determine whether SDN-1 would be deemed a "novel combination of genetic material" in some situations.*

The EU, New Zealand, China and Japan have ratified the Cartagena Protocol. The United States is not a party to the Cartagena Protocol. Australia and Canada are parties but have not ratified the agreement.<sup>135</sup> Each party is obligated to take necessary and appropriate legal, administrative and other measures to implement its obligations under the Protocol. The Cartagena Protocol has emerged as a blueprint for an international regulatory regime that has the potential to minimise the risks to environmental biodiversity from the transboundary movement of biotechnology products, as well as guide and standardise risk assessment principles globally.

The Cartagena Protocol imposes strict requirements on both exporters and importing countries with respect to agriculture biotechnology products, such as seeds, trees, plants and live fish that are intended to be introduced into the environment. Agricultural and other products that fall within the scope of the Cartagena Protocol are divided into three classes: 1) those intended for release into the environment; 2) those for food, feed, and processing; and 3) those in transit and for contained use. Human pharmaceutical products produced using biotechnology methods are excluded from the Cartagena Protocol if they are addressed by other international agreements.

Parties may enter into bilateral, regional and multilateral agreements and arrangements regarding intentional transboundary movements of LMOs consistent with the objective of the Cartagena Protocol, provided that such agreements and arrangements do not result in a lower level of protection. Each party has to adopt appropriate domestic measures aimed at preventing and, if appropriate, penalising transboundary movements of LMOs carried out in contravention of its domestic measures. The parties are encouraged to cooperate on research and information exchange on any socio-economic impacts of living modified organisms, especially on indigenous and local communities.

The issue of liability and redress for damage resulting from the transboundary movements of LMOs was one of the themes on the agenda during the negotiation of the Cartagena Protocol. In 2010 a new international treaty, the Nagoya – Kuala Lumpur Supplementary Protocol on Liability and

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<sup>135</sup> Convention on Biological Diversity "Parties to the Cartagena Protocol and its Supplementary Protocol on Liability and Redress" (3 May 2018) Biosafety Clearing-House <<https://bch.cbd.int>>.

Redress to the Cartagena Protocol on Biosafety, was adopted.<sup>136</sup> New Zealand is a party, but has not ratified the supplementary protocol on liability, neither have China, Australia or Canada. The EU and Japan have ratified the Nagoya – Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety.<sup>137</sup>

## **X LIABILITY AND REDRESS**

The Law Commission considered and reported on issues surrounding domestic liability for loss resulting from development, supply, or use of genetically modified organisms in its 2002 Study Paper 14.<sup>138</sup> The Law Commission investigated the adequacy of statute and common law with issues of liability for loss from genetically modified organisms.

The Royal Commission on Genetic Modification considered liability, that is who is and who should be liable for damage caused by genetic modification.<sup>139</sup> The report concluded that the existing liability regime of tort and statute at the time was sufficient and:<sup>140</sup>

... the common law...[is] well able to mould new remedies for novel situations ... From a legal perspective we have not been persuaded there is anything so radically different in genetic modification as to require new or special remedies.

As noted by the Law Commission a key problem with liability for damage caused by genetic modification is that it is difficult to assess the level of risk posed or the size of the potential damage. Given these uncertainties, the increasing use of genetic modification in New Zealand may cause damage that cannot be covered under any liability regime. If damage is extreme (either in quantity or because it is not compensable for example, loss of biodiversity) the losses will either lie where they fall, that is the party suffering the loss has no remedy, or the government will have to cover the shortfall.

The Law Commission summarised that a liability regime for GMOs will need to address the following difficulties: unknown level of risk; unknown magnitude of potential damage; the possibility of catastrophic, irreversible and/or in-compensable damage; the possible time lapse before damage is covered; and the need to prove causation.

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136 Nagoya – Kuala Lumpur Supplementary Protocol on Liability and Redress on the Cartagena Protocol on Biosafety (opened for signature on 7 March 2011, entered into force 5 March 2018).

137 "Parties to the Cartagena Protocol and its Supplementary Protocol on Liability and Redress", above n 135.

138 Law Commission *Liability for Loss Resulting from the Development, Supply or Use of Genetically Modified Organisms* (NZLC SP14, 2002).

139 *Report of the Royal Commission on Genetic Modification*, above n 16.

140 At [80].

*Consideration 25: A liability regime specific to GMOs will only cover those activities encompassed by the definition of genetic modification used. It will not address techniques falling outside the definition even if such techniques also carry with them unpredictable risks similar to those of GMOs.*

The Law Commission suggested that any new liability regime should treat human activities or technologies that pose similar risks in the same way, rather than treating them differently on the basis of the particular technology used.<sup>141</sup> This approach has been adopted by Canada under its regulations for novel food where the focus is on the properties of the final product rather than the process by which it is made. In New Zealand, the existing relevant statutes tend to treat GMOs as only one type of new organism,<sup>142</sup> new food,<sup>143</sup> or new medicine<sup>144</sup> with no exclusive legal requirements for genetic modification.

The Law Commission concluded in 2002 that legislation and common law will not ensure compensation for all damage caused by GMOs. Few remedies will be available for liability claims that may take decades to surface and it is thus a policy decision as to the appropriate limitation period for actions based on GMO damage.

## **XI SUMMARY**

At the International Summit of Gene Editing in 2015, Alta Charo reported that "the regulatory framework is going to determine the speed at which biotechnology moves from laboratory to research to marketed product".<sup>145</sup>

This article has raised a number of legal and policy considerations deserving review and has not discussed the most challenging – public engagement. Royal Society Te Apārangi is encouraging New Zealanders to consider and share their views on some potential uses of gene editing in New Zealand. To assist public discussion, three papers have been produced outlining scenarios for the use of gene editing for pest control, human healthcare and primary industries.<sup>146</sup>

Existing regulation for a platform technology, such as advanced gene editing, with broad use is complex. Immediately, consistent interpretation of terms between statutes and international

141 Law Commission, above n 138, at [33].

142 HSNO Act, s 2A; and Biosecurity Act, s 2.

143 Food Act 1981; and A18 of the Food Standards Code 1987.

144 Medicines Act, s 3.

145 Charo, above n 117.

146 Royal Society Te Apārangi *Gene Editing Scenarios in the Primary Industries* (August 2019); Royal Society Te Apārangi *Gene Editing Scenarios in Pest Control* (August 2019); and Royal Society Te Apārangi *Gene Editing Scenarios in Healthcare* (August 2019).

agreements is required as "statutory borrowing" of terms is rarely used.<sup>147</sup> The *Scion Case* has emphasised the importance of correctly interpreting new organism and genetic modification, concluding that the relevant regulation provides an exhaustive list that can only be modified by Parliament.<sup>148</sup> This decision has implications for CRISPR-Cas technologies, potentially classifying all organisms for which CRISPR-Cas complexes are used as genetically modified when the nucleotide alteration may be no different than mutagenesis or a modification to "wild type".

In summary, regulation of gene editing technologies has come to a crossroads and provides an opportunity to review current regulatory frameworks and devise a future-proof framework to keep abreast rapidly advancing biotechnologies.<sup>149</sup>

In brief, this article's authors purport New Zealand would benefit from an integrated regulatory system for biotechnologies:

- (a) Led by Treaty of Waitangi principles.
- (b) Governed by shared values for Aotearoa New Zealand, such as: uniqueness of Aotearoa; our indigenous and cultural heritage; sustainability; being part of a global family; well-being of all; and freedom of choice and participation (as recommended by the Royal Commission on Genetic Modification).
- (c) Having a single entry point for applications, to promote efficiency and minimise costs for researchers and stakeholders.
- (d) Regulated by one authority (for conservation, biosecurity, primary industries and human health), with capability to horizon scan.
- (e) Incorporating the Wai 262 recommendations, to enhance the statutory power of Maori.
- (f) Incorporating sub-tiers of multidisciplinary expertise in conservation, biosecurity, primary industries and human health; containing scientific, advisory and ethics committees which strive to keep abreast of global biotechnology developments and aim to preserve opportunities for Aotearoa.
- (g) Regularly reviewed and consistent interpretation of key statutory terms.

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147 Statutory borrowing of definitions: except in cases where one statute expressly adopts the definition of another, "statutory borrowing" seldom occurs as each statute is a separate entity and the meaning of the words in that statute do not depend on other statutes. There have been occasional instances of judicial borrowing of definitions in New Zealand. This practice may be adopted where two statutes are *in pari materia* (on the same subject), but this cannot be relied upon. Relevant case law suggests a number of factors when definitions may be borrowed and include: the statutes having a similar purpose; administered by the same officers; and passed into law about the same time. A comparison of the purpose and context of the Acts is critical. Borrowing of definitions is only to take place with great caution: see Ross Carter *Burrows and Carter Statute Law in New Zealand* (5th ed, LexisNexis, Wellington, 2015).

148 *Scion case*, above n 60; and Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations, reg 3.

149 Marchant and Stevens, above n 114.

- (h) That uses systems-based risk analysis processes, incorporating an environmental bottom lines approach for disruptive technologies such as gene drives.
- (i) That compares the new biotechnology against alternative tools and technologies.
- (j) That utilises modelling to assist the prediction of future genetic diversity and resistance in populations.

Differing product directed and process directed regulation systems provide challenges for international trade resulting in uncertainty for our primary industries. A study is necessary to compare and evaluate product directed and process directed regulation systems and assess whether the risk is commensurate with the regulatory burden.

This article has identified some of the complexities of the legislation inherent in regulating a rapidly developing technology where such advances may be well ahead of current frameworks and public acceptance. A resilient legislative and regulatory approach is required whereby new legislation for biotechnologies is developed and a single entry point for biotechnology applications is implemented.

Most importantly this article recommends valuing Treaty of Waitangi principles and have those principles lead us in all that we do.

