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The Office of Gene Technology Regulator
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Re: Round 2 comments on Technical Review of the Gene Technology Regulations

A. Introduction

Thanks for the opportunity to comment on the Office of the Gene Technology Regulator's (OGTR) Regulatory Impact Statement, for proposals to amend the Gene Technology (GT) Regulations 2001. We also seek the opportunity to make further comments as the review progresses and to meet the reviewers again. Our whole submission is for publication.

The OGTR's Regulation Impact Statement (RIS) provides no credible or compelling rationale for the immediate deregulation of any or all of the new Genetic Manipulation (GM) techniques. Not all 'new' GM techniques are actually new, as the Australian Academy of Science publication, Recombinant DNA: An Australian Perspective, 1980,[1] refers to some techniques, such as ZFN (SDN). They predate the GT Act 2000, the Inter-government Agreement on GT, and the GT Regulations 2000. No one then questioned that they were GM techniques, though not exclusively transgenic, which shows the architects of the GT Scheme understood and intended that all new GM techniques, without exception, must be regulated.

Precaution, the GT Act 2000 and the GT Regulations 2001 dictate that dealings with all new GM techniques and their novel living products, wherever and whenever they are discovered or invented, must be notified, assessed, regulated, licensed and monitored by the OGTR, without exception. We expect that new GM techniques and processes will be constantly discovered, invented or adapted to new uses, so maintaining a robust regulatory scheme, with minimal exemptions, is the prudent course.

The new GM techniques are so generic that they can be used to manipulate the genetic makeup, traits and behaviour of any living organism on Earth. With such power at the disposal of so many people, and with no history of safe use and minimal evidence of harmlessness, regulating all of the new GM techniques is essential to serve the public interest.

The OGTR's RIS does not provide the impartial: "preliminary examination of the cost and benefits of various options for amending the GT Regulations," that it promises. Instead, OGTR advocates for the immediate deregulation of some CRISPR (SDN-1), RNAi and null segregants without providing any evidence of their safety or efficacy, that it has the responsibility to ensure.

The so-called Technical Review of the Gene Technology Regulations cannot be delinked from the Review of the National Gene Technology Scheme to which all Australian governments are party, as the scheme's policy settings and the GT Act 2000 would also require changing to enable the proposed amendments to the Regulations. All Australian Governments would need to agree. As the Phase 2 submissions to the scheme review remain unpublished and Phase 3 has not even begun, this Review of the Regulations is provisional and must not be characterized as final.

Assistant Professor Kevin Esvelt of Massachusetts Institute of Technology spoke to a University of Melbourne Science Convergence Network Forum on Tuesday February 13, 2018, with CRISPR co-inventor Jennifer Doudna. He asked the audience of 1500 scientists, students and the public:

> "Why is it that we scientists don't share what we're doing from the get go? Do we really think that science progresses more rapidly? I'm sceptical. Even brilliant and well-meaning scientists cannot

[1] Recombinant DNA : an Australian perspective, 1980, 129 Pp. https://catalogue.nla.gov.au/Record/2970636

> reliably anticipate the consequences of their work. The world is much too big. Because so much work is closeted, even if someone does see something wrong we can't possibly warn them because we don't know who they are or that they are doing it at all. Finally, 6 years ago, no-one imagined that we would have a tool that would work in so many different species, in terms of editing their genomes, and certainly no-one imagined that we might be able to edit entire wild populations."[2] [3]

A strong, comprehensive and precautionary GM regulatory regime is the best antidote our community has to the unacceptable scientific secrecy of which Esvelt speaks. It is also our most valuable insurance against unmitigated GM disasters. Public disclosure is not negotiable.

The OGTR's RIS does not make a compelling, evidence-based case for weakening the GT Regulations and exempting any of the new GM techniques, or their living products. Yet the RIS proposes this.

The RIS completely ignores the potential ecological impacts of the products of new GM techniques, which it is charged with minimizing or preventing. GTTAC does not include an ecologist[4] and this should be remedied. Gene drive (species extinction) techniques may be deployed to extinguish whole species of organisms yet the OGTR only recommends licensing gene drive R&D. Targets for elimination using gene drives include rodents, with Australian research funded by the US military[5], and mosquitoes which have a key role as plant pollinators.[6] Both organisms are food for birds.

B. Our critique of the OGTR's Regulation Impact Statement (RIS)

We agree, and the OGTR confirms, that:

> "the GT Regulations are fit for purpose, and appropriately support the object of the regulatory scheme."[7]

The GT Regulations do the tasks they were designed for and do not require most of the reforms that the OGTR proposes. The notification, assessment, regulation, licensing and monitoring of all dealings with Genetically Manipulated Organisms (GMOs) – humans, animals, plants and micro-organisms - are the linchpins and core strengths of the national GT regulatory system and must not be compromised. The proposed premature and permanent exclusion of several new GM techniques (SDN-1, RNAi and null segregants) from OGTR oversight would dramatically weaken the scheme, call its integrity into question, and undermine public confidence.

OGTR claims the Regulations have three problems that require fixing. We disagree.

1. "ambiguity … so in some cases it is not clear whether organisms modified by certain techniques are 'GMOs' or not."

By excluding some new GM techniques and not others from regulation, ambiguity would increase not decrease. As further GM processes and methods are found, these arguments over including some while excluding other techniques, will become permanently confusing and ambiguous – to be debated and fought out every time a new GM innovation is made.

In the present proposal, for instance, the OGTR seeks to immediately deregulate some organisms manipulated using CRISPR (SDN-1 using no repair template), while requiring others (SDN1 using a repair template) to continue to be regulated. None of them have a history of safe use and the evidence of off-target impacts on the genomes and traits of the resulting GMOs is mounting. All should be regulated.

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[2] Kevin Esvelt, MIT. Assistant Professor of Media Arts and Sciences. https://www.media.mit.edu/people/esvelt/overview/

[3] Convergence Science Network, The Science and Ethics of Genome Editing - Assistant Professor Kevin Esvelt, Feb 15, 2018. https://www.youtube.com/watch?v=u6clZCLPr9c

[4] The Gene Technology Technical Advisory Committee (GTTAC), 2017-2020. http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/content/gttac-2

[5] Could WA be the genetic testing ground for 'synthetic mice' to end mice? Sydney Morning Herald, Saturday February 24, 2018. http://www.smh.com.au/environment/conservation/could-wa-be-the-genetic-testing-ground-for-synthetic-mice-to-end-mice-20180221-h0wev9.html

[6] *Zoe Statman-Weil, Aedes communis*: The Pollinating Mosquito. https://www.fs.fed.us/wildflowers/pollinators/pollinator-of-the-month/aedes_communis.shtml

[7] OGTR, Regulation Impact Statement for consultation, P4

The OGTR aligns its view with GM advocates who seek to confine the discussion to plant GM (New Plant Breeding Techniques). But inducing random mutations in humans, animals and microbes using SDN1 (with or without a template) raises many safety and health-related questions (as well as moral and ethical concerns) that the OGTR must play a key role in assessing and regulating. With the OGTR out of the picture there would be no clear path for new GM products through the regulatory system. Product regulators, without requisite genetic expertise, may evaluate and approve GM foods, pharmaceuticals, industrial materials, biocontrol agents, etc. without the OGTR playing any role.

2. "the techniques and organisms used in gene technology research have changed since the GT Regulations were last reviewed,"

This is true but irrelevant. The Gene Technology Act 2000 and the Gene technology Regulations 2001 were designed after very extensive public and expert consultation, to ensure that all dealings with all new GM techniques and their novel living products must be notified, assessed, regulated, licensed and monitored by the OGTR, in collaboration with end product regulators. Now the OGTR proposes to take down some of the goalposts and change the rules, with no knowledge of what game further new GM techniques may bring to the manipulation of life. Leave the Act alone and do not exempt any of the new GM techniques from the Regulations.

3. "improved clarity regarding the regulatory status of organisms that are not themselves categorised as GMOs but have been derived from GMOs."

This is fallacious as the OGTR then concedes that:

> "There is no problem with the current regulatory status of these organisms; rather, improved clarity would assist user understanding and compliance."

As the direct descendants of GMOs that possess their traits, null segregants must also be regulated as GMOs. User understanding and compliance will be optimized if all organisms derived from GMOs also remain categorized as GMOs. Such organisms only exist, and are of scientific or commercial interest, because they exhibit traits conferred on them using GM techniques, so there are logical and practical grounds for also continuing to class them as GMOs.

C. Our response to the OGTR's specific questions

1. What is your preferred option? Please explain why.

We advocate Option 3 in the OGTR's RIS (i.e. Option 2 in the first round). We are disappointed and annoyed that the RIS fails to fairly or fully expound any alternative to its preferred option 2 (formerly 3 in Round 1), to deregulate the research, development, commercial and clinical use of several new Genetic Manipulation (GM) techniques (CRISPR; RNAi; and null segregants).

It is unacceptable that the OGTR takes expert advice on these matters from people with professional[8] and possibly commercial conflicts of interest, when other experts with more critical and balanced views appear to have been excluded from the panels.

There is no record of any member of the OGTR's Gene Technology Technical Advisory Committee (GTTAC) abstaining from offering advice on the regulation of new GM techniques, though some have clear conflicts of interest. Yet GTTAC's influential advice may have affected how the OGTR framed its RIS. GTTAC's claim that "organisms altered by some site-directed nuclease techniques and oligo-directed mutagenesis are unlikely to pose risks that are different to natural mutations, conventional breeding or mutagenesis,"[9] contradicts the conclusions of overseas government agencies in Austria, Norway and elsewhere. Anyway, low risk does not imply or justify a failure to regulate.

[8] Could WA be the genetic testing ground for 'synthetic mice' to end mice? Sydney Morning Herald, Saturday February 24, 2018. http://www.smh.com.au/environment/conservation/could-wa-be-the-genetic-testing-ground-for-synthetic-mice-to-end-mice-20180221-h0wev9.html

[9] OGTR, Discussion paper: Options for regulating new technologies, 2016.

Most establishment science and the GM industry advocated total deregulation (Option 4) in Round 1. They want to proceed without a social licence, to fast track all the uses of new GM techniques and to deploy the various living GM products without public knowledge or debate. The GM industry seeks to neutralize the GT Act 2000 and GT Regulations 2001, to disempower the OGTR and marginalise the process-based approach embedded in the Act, which is used in most other countries.

Product focused regulation, like that in the USA and Canada, discounts the process of production as irrelevant. It would ignore the unique risks of using the new GM techniques; their moral and ethical ambiguity, particularly when used in humans and animals; and the unregulated GMOs which industry plans to create for a wide variety of purposes.

New GM Organisms (GMOs) have no history of safe use outside laboratories, in the environment, industrial production or clinical practice. Already much research evidence shows that the new GM techniques have many off-target impacts on the genetics, traits and behaviour of GMOs. They may also negatively impact the humans, animals or open environments into which they may be released. Without OGTR regulation of all GM techniques (past, present and future), no safety testing, regulation or labelling would be mandated for any of these production processes or their products. There will be no official means to enable public awareness, precaution or informed decisions.

Australia would be the first country to deregulate GM animals and anyone would be free to use new GM to genetically manipulate plants, animals or microbes - including humans, medical therapies and pharmaceuticals, insects, crop plants, trees, fish and animals.

If the new GM techniques are unregulated, startup companies and biohackers, most with minimal scientific training, skills or experience, may use the new GM techniques to experiment in dangerous, uncontained facilities. Public demonstrations of influential biohackers injecting themselves with new GM constructs on YouTube[10] are an invitation to copycat behaviour, though a repentant Zayner now says: "There's no doubt in my mind that somebody is going to end up hurt eventually."[11]

Such demonstrations and informal GM biohacking are incentives for others everywhere to create and misuse new GMOs, without any official regulation, monitoring or restraints on their activities. Yet OGTR Guidelines do not require such people to appoint Institutional Biosafety Committees (IBC) to oversee their research, nor to certify their facilities, as Accredited Organisations generally do.[12]

We recommend that the OGTR's Guidelines on Accredited Organisations be amended to require everyone using GM techniques to be accredited and to establish an IBC.

The GT Act 2000 rightly defines gene technology as, "any technique for the modification of genes or other genetic material". While this broad, robust and testable definition remains in the Act (as it should), all the new GM techniques and their GM products must be regulated, without exception.

Architects of the national GT Scheme envisaged the discovery or invention of new GM techniques and built in the flexibility to require their regulation. All parties to the GT Inter-government Agreement intended that the OGTR would, on their behalf, regulate dealings with all existing and future transgenic and new GM techniques (wherever and whenever invented and used), including all SDN-1 and RNAi processes.

This policy setting is explicitly enunciated in the Plain English Explanatory Statement to the Gene Technology Regulations 2001, which says:

> "The definition of 'genetically modified organism' in the Gene Technology Act was intentionally cast very broadly to ensure that the definition did not become outdated and ineffectual in response to rapidly changing technology."

The Scheme is therefore inherently disposed to regulate all new GM techniques and their products as they come on the scene, without exception. That is what we support.

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[10] Biohacker Injects Himself With An Untested DIY Herpes Cure https://www.youtube.com/watch?v=6_o6PWIAVVI

[11] Zhang, S. A Biohacker Regrets Publicly Injecting Himself With CRISPR, Feb 20, 2018 https://www.theatlantic.com/science/archive/2018/02/biohacking-stunts-crispr/553511/

[12] OGTR, Guidelines for Accreditation of Organisations. http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/accredguideorg-1 and the GT Act.

The OGTR's claim in the RIS that:

> "Australia's current gene technology legislation is not as effective as it could be in terms of providing clear and unambiguous regulatory requirements for those working with GMOs,"[13]

is merely a pretext for accommodating the goals and aspirations of those researchers and industries that do not want their GM work to be regulated, or to be brought to public attention.

We oppose deregulation of any site directed nucleases (SDN-1), RNA interference (RNAi) and null segregants as this would also ignore and undermine the Precautionary Principle which is the indispensible core of the Gene Technology Act 2000, that is integral to its spirit and intent.

2. Do the draft amendments clearly implement the measures described in Section 3 of the Consultation Regulation Impact Statement? If not, which areas of the draft amendments do you think require additional clarification, and what clarification is needed?

Nothing is very clear about Section 3, the 'Policy options under consideration'. For instance, the present Option 2, was Option 3 in the first round documents. But Option 3 in the present RIS is substantially the same as Option 2, in the first time around. Is this obfuscation deliberate or unintentional?

The OGTR's preferred Option 2 in the RIS is expounded and justified at considerable length, but other Options receive short and dismissive treatment, without explanation. This appears designed to mute debate and to make Option 2 a fait accompli. Recall that in the first round of submissions, with the exception of Option 1 (the status quo), Option 3 was least favoured of the 4 options.

Genuine public consultation would offer all information in plain English and a national public consultation would be held. Secret closed-door, technical conversations among 'experts' from a narrow range of disciplines is undemocratic and imperils the integrity of the GT regulatory system, especially as some advisors have obvious conflicts of interest with their scientific and commercial aspirations. Experts from diverse disciplines, civil society advocates, policy specialists, and the interested public, with a broad range of expertise and perspectives, should now be deliberatively and actively engaged in this Regulatory Review. The legitimacy of any changes depends on broad agreement and the integrity of the processes used to reach conclusions.

The justifications given for proposed deregulation are weak and unconvincing. For instance:

> "Organisms modified using SDN-1 would be excluded from regulation, as organisms that are not GMOs, on the basis of risk, compliance enforceability and consideration of the policy settings of the regulatory scheme."

These measures are irrelevant to the definitions of GMOs and GM dealings in the GT Act.

Risk is a consideration in the national GM Regulatory Scheme and it is open to the OGTR to classify some dealings as 'low risk'. But risk level in no way justifies completely deregulating particular techniques. The RIS does not convincingly question that SDN-1 without a template is still a "technique for the modification of genes or other genetic material" as defined in the GT Act.

Compliance enforceability and clarity will not be enhanced as the OGTR claims, if these techniques are deregulated. Once exempt, compliance will become a non-issue. At least one major pharmaceutical company says it wants the present policy settings maintained and all the GM techniques regulated, in the interests of maintaining its customers' safety and its high reputation.[14] The RIS just ignores such perspectives. Will the OGTR tell the live vaccine industry to self-regulate instead?

If an unregulated product that harmed customers had entered the market through a technical loophole or a lack of regulation, disaster would strike that company and likely a whole industry. But would the OGTR, and the regulatory and political systems get off scot-free? We hope not, since regulating GM dealings is their job and they should not shirk it. The National Regulatory Scheme must continue to be precautionary

[13] Ibid. P4
[14] Pers. comm. 2018.

and broad in scope, with those responsible for protecting the public interest diligently doing so.

Recall, for instance, the 1989 L-Tryptophan (LT) case which confirmed that even small genetic changes in microorganisms may have very serious and unforeseen health consequences. In 1988 and 1989:

> "Showa Denko produced L-Tryptophan through a fermentation process (and) began to use a new, genetically-altered strain of bacillus amyloiquefaciens (and also) reduced the amount of activated carbon in the purification process by one-half."
>
> By 1994, there were 1,500 cases of the permanently disabling disease eosinophilia-myalgia syndrome (EMS) in the USA, including 38 fatalities and an unknown number of EMS cases in other countries where L-Tryptophan was sold. A US National Institutes of Health review concluded in 1996 that, "Evidence from an array of scientific studies strongly supports the conclusion that ingestion of products containing L-Tryptophan (LT) produced by Showa Denko KK caused the 1989 epidemic of eosinophilia-myalgia syndrome (EMS) in the United States."[15]

Locally, Garibaldi mettwurst claimed one life and 23 permanently disabled victims in the 1990s. The coroner found that the South Australian Health Commission (SAHC) had multiple warnings several years in advance of the disaster but did nothing, and was also complacent in responding to the final outbreak.[16] The recent regulatory response to imported frozen berries harbouring Hepatitis A appears to have been more proactive and apparently satisfactory, though the number of people infected is not disclosed.[17]

We also expect full preparedness, vigilance and responsiveness from the OGTR and its collaborators in the national GT Scheme – other regulators, state and territory governments and local councils. But this cannot be assured if new GM techniques are immediately exempt from regulation. Deregulation would also undermine the capacity of State and Territory Governments to exercise their powers, to establish GM and GM-free Zones on marketing grounds, under a Policy Principle made under S 21 of the GT Act.

The RIS suggests that SDN-1 GMOs, without template repairs, would not be detectable. Though the issue of detection was raised as a concern when the scheme was established it has never created intractable GM regulatory problems. As the RIS concedes:

> "All GMOs currently licenced for commercial release in Australia can be unambiguously identified by their introduced DNA sequence."

Despite the problem failing to materialise up till now, the RIS persists in claiming:

> "This would not be possible for organisms modified using SDN-1."[18]

It is spurious to claim they could not be distinguished from natural organisms, making regulations unenforceable. There has never been any ambiguity or confusion over No-Gall[19] and Ice-Minus,[20] GM microorganisms produced in the 1980s with gene deletions, that are not dissimilar in effect to SDN-1 proposals. Both mimicked organisms that occasionally occur in nature and were proposed for general release.

By deleting a single gene, in Adelaide Professor Kerr created No-Gall (a disarmed and therefore non-pathogenic strain of agro-bacterium tumefaciens, occasionally found in nature) that went on to be widely accepted as an inoculant in orchard trees and rose bushes, for the prevention of crown gall disease.

In contrast, Ice-Minus (a natural variant, pitched as prevention for frost damage to strawberries and other frost-susceptible plants) research and deployment were promptly discontinued as the GMO appeared to pose a potential hazard to global weather patterns by interfering with ice nucleation in clouds.

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[15] Kilbourne E.M. et al. (1996) Tryptophan produced by Showa Denko and epidemic eosinophilia-myalgia syndrome, J Rheumatol Suppl. 46:81-8; discussion 89-91. https://www.ncbi.nlm.nih.gov/pubmed/8895184

[16] Doherty, F. A look back at Garibaldi: A preventable epidemic, October 13, 2014. http://www.ontherecord-unisa.com.au/?p=7223

[17] Dr Brett Sutton, Deputy Chief Health Officer (Communicable Disease), Health alert: 170004, Hepatitis A outbreak associated with frozen berries, 02 Jun 2017. https://www2.health.vic.gov.au/about/news-and-events/healthalerts/alert-hepatitis-a-berries-2-june-2017

[18] Regulation Impact Statement, P10

[19] NOGALL™ http://www.newbioproducts.net/nogall-.html

[20] Ice-minus bacteria. https://en.wikipedia.org/wiki/Ice-minus_bacteria

Incidentally, its natural non-GM relative is Ice-Plus that nucleates ice crystals and snow flakes. It is marketed as SnoMax and is widely used in snow making machines.

No one questioned that both are GMOs, yet similar to some organisms created with SDN-1. They were both assessed and 'regulated' as GMOs, though formal regulatory systems were not then established. When the national GT Scheme was set up, No-Gall was again acknowledged to be a GM product, now included in its own exempt category in the GT regulations.

Existing SDN-1 GMOs, such as non-browning mushrooms, are tagged for patent enforcement and therefore are identifiable. Full molecular characterisation should be required to enable traceability.

There are already techniques to identify organisms produced using SDN-1. Cheaper and more reliable methods to detect even single base pair changes in new GMOs could and should be encouraged and, then, required. Likewise for RNAi and also null segregants, as they retain GM traits of their ancestors.

The OGTR should require a detection test with each application to use a GMO made with the new GM techniques. Exempting GMOs from regulation on the slippery pretext that they may not be detectable anyway is just unacceptable. All SDN-1 events should be regulated.

Fully regulated, new SDN-1, RNAi and null segregant constructs may eventually accumulate a body of safety evidence and a history of safe use, suitable for review. Perhaps they may then be considered, on a case-by-case basis, for entry in the Regulations as exempt dealings (like No-Gall). This prudent and precautionary approach, with a path through the regulatory system, deserves consideration.

3. If your preferred option is Option 3, please indicate which amendments (or parts thereof) you support being progressed and why.

The GT Act 2000 and the GT Regulations 2001 were clearly not designed exclusively to regulate transgenesis. So we strongly favour the regulation of all GM techniques for the production of GMOs, including all SDN-1, RNAi and null segregants. Deregulating any of them with insufficient evidence of safety and no history of safe use would be foolhardy. It would also set a dangerous and unacceptable precedent for the evaluation and regulation of future GM innovations.

4. What are the costs and benefits to you or your organisation from the proposed amendments? Please describe these compared to current arrangements, for each area of amendment:

The OGTR appears to have a clear agenda to respond to and encourage industry and establishment science to support deregulation, as the RIS declares that:

> "Broader impacts of the proposed changes may include increased innovation and increased commercialisation of products (such as food crops or human or animal therapeutics), because of reduced regulatory costs and anticipated increased consumer acceptance of product that are not GMOs."

This is a clear example of the OGTR's special pleading and advocacy for science and industry. Massaging public opinion to promote the acceptance of GM products is not the business of the OGTR, which we expect to operate as an expert arbiter and impartial referee on GM. Likewise, exempting GMOs to weaken regulation, so that innovation and commercialization of GM products may increase, is a totally unacceptable role for the OGTR and other public servants.

The RIS's Executive Summary makes these special pleadings more egregious as it also asserts:

> "Review is limited to the existing policy settings of the regulatory scheme, and cannot extend to topics outside of the current scope of the GT regulations, for example, the safety assessment and labelling of genetically modified food."

So shoppers will, by redefining GMO, be systematically deprived of reliable and honest information. Their ability to make informed decisions about foods, pharmaceuticals or other products made using GM techniques, and on living GMOs such as seeds, animals, vaccines, etc., will be made impossible if the

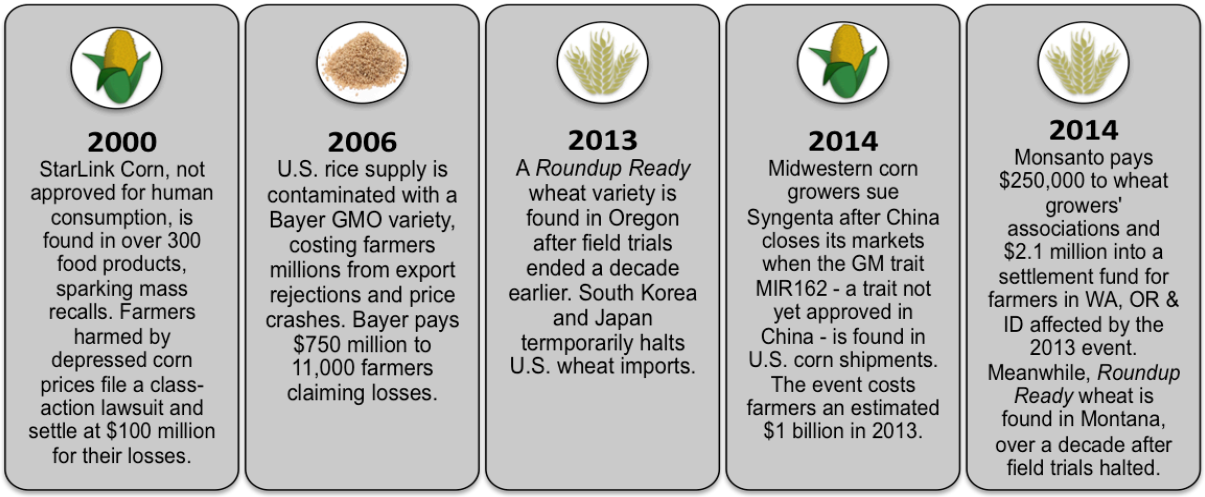
OGTR chooses not to regulate and not to disclose. Esvelt rightly calls out the negative impacts of scientific secrecy but his remarks apply equally to our regulators, who are charged with serving the public, not sectional interests. The RIS is a shameful example of partiality and bias.

The proposal to exempt several new GM techniques and their products from the Regulations would likely have knock on effects, for instance, in the food standards. FSANZ is now deciding how to treat the products of the new GM, also with the advice of some experts who have conflicts of interest. The OGTR's position is likely to erode the FSANZ stance on GM food regulation and labeling even further.

Though the OGTR is not responsible for end product assessment and labeling in the gap fill scheme, other regulators are consulted on proposed GMO dealings. If the Legislative and Governance Forum on Gene Technology (LFGT) changes the policy settings in the scheme, permitting the OGTR to deregulate generic CRISPR, RNAi and null segregant techniques, we fully expect the end product regulators to follow the OGTR's lead and also deregulate dealings with GM end products.

Consistency and uniformity with the OGTR's regulations would lead the Environment Minister, Therapeutic Goods Administration (TGA), Food Standards Australia New Zealand (FSANZ), Australian Pesticides and Veterinary Medicines Authority (APVMA), National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Department of Agriculture Forestry and Fisheries (DAFF) Biosecurity and Local Councils to also deregulate and exempt from assessment all dealings with the living products of the new GM techniques – vaccines, human and animal therapeutics, biologics, pharmaceuticals, food, crop plants, insects, fish, trees, micro-organisms – any GMO. This is not what the national scheme or the law intends, and nor does the public.

The RIS chooses to downplay and trivialise legitimate local industry concerns over trade, including that Australia could be out of step with trading partners that have not yet decided their regulatory positions on the new GM techniques and their products. Yet the rejection of unapproved GM commodities has been a major cost burden to farmers and food industry. Some examples of the biggest impacts are:



These five contamination incidents caused huge economic losses, for which farmers, supply chain managers and others will never be fully compensated.

The OGTR's first round discussion document asked for our views on trade and other issues, outside its remit to protect public health, safety and the environment. Yet the RIS asserts that:

> "… no changes will be recommended that relate to topics outside of the current scope of the GT regulations. For example, any issues raised through the consultation process which relate to the regulation of genetically modified food, marketing and trade issues, or the application of new technologies to humans or embryos cannot be considered further through this process."[21]

Then inconsistently, at P5 of the RIS says, for instance:

> "Possible consequences of this (ambiguity) are that the progress of basic research may be held

[21] OGTR, Regulation Impact Statement for consultation, P8

back, and that products (such as food crops or human or animal therapeutics) may not be commercialised. Alternatively there may be delays in bringing new products to market, meaning that the benefits from these products may not be made available in Australia. In the longer term, if uptake of these technologies continues to be inhibited this could hamper industry development and affect the international competitiveness of Australian businesses."

Thus, placing these "topics outside of the current scope of the GT regulations" is a mere device for narrowing discussion, enabling the OGTR to advance its view on trade in support of deregulation without rebuttal. Key export markets such as the European Union and China have yet to make a decision on how they will regulate new GM techniques but already have zero tolerance policies for unapproved GMOs. In contrast, our key agricultural export rival New Zealand will regulate all organisms derived from the new GM techniques as GMOs[22] to reassure trading partners and meet their requirements.

Trade pretexts aside, we are not aware that the OGTR has ever stalled or rejected any GM proposal, or failed to approve a licence application. Nor do FSANZ, APVMA or other GM product regulators appear to reject any GM product applications, following the OGTR's lead on genetics and approving such products.

Requiring regulation of all the new GM techniques, GMOs, products and the people who use them - biohackers and startups included - would unequivocally dispel any ambiguity. Prematurely deregulating some techniques and not others will compound ambiguity and uncertainty.

The OGTR's stance should be fair to everyone but is irrational, inequitable and indifferent to the public interest. Genetic manipulation industries and establishment scientists will be the major financial and professional beneficiaries if the new GM techniques SDN-1, RNAi and null segregants are deregulated. Yet some of their people are insiders in the review process.

In contrast, our whole society will bear the costs of environmental damage, harm to human and animal health, and lost export markets from unregulated GMOs created with these new techniques.

5. Are the proposals to change the classification of certain NLRDs and exempt dealings (identified in Appendix B of the Consultation RIS) commensurate with any risks to the health and safety of people and the environment posed by the dealings?

Deregulating some SDN-1, RNAi, and null segregants removes the checks and balances required to minimize the risks to the health and safety of people and the environment posed by these dealings. All uses of these techniques, to manipulate the genetic makeup of any living organism, pose risks that require notification, assessment, regulation, licensing, monitoring and surveillance. Deregulation would set the new techniques and their products outside this precautionary regime where they would not be subject to any official oversight.

Our governments owe us even stronger regulation of new and untried GM techniques, as CRISPR kits are for sale on the web, informal biohacking labs such as Biofoundry in Sydney[23] are popping up (without the Institutional Biosafety Committee' supervision which legitimate GM R&D organisations have), and security services warning of potential bioterror and military uses.[24]

As Esvelt confirms, new GM techniques can be used to manipulate the DNA of any organism. With the new GM techniques and materials accessible to anyone, regardless of their training and experience, we can expect that some unexpected, unforeseen and unpredictable mutations may be readily induced in some organisms with which they choose to work.

Pathogens, toxins or allergens may be produced. GM-made L-Tryptophan was one product in which a minor change to microbial DNA resulted in a tiny amount of an extremely potent toxin being produced. It was not filtered out, went undetected, caused many deaths and thousands of permanent disabilities. Deregulating use of new GM techniques, especially in microbes, poses major biosafety risks.

[22] Smith, N. GMO regulations clarified, 5/4/16, https://www.beehive.govt.nz/release/gmo-regulationsclarified-0
[23] Biofoundry Hacking Days. http://foundry.bio/hack-days/
[24] Regalado, A. (2016) Top U.S. Intelligence Official Calls Gene Editing a WMD Threat, MIT Technology Review, 9/2/16, https://www.technologyreview.com/s/600774/top-us-intelligence-official-calls-gene-editing-a-wmd-threat/

The deregulation of the new techniques in animals may also greatly increase animal experimentation, raising major ethical and safety issues. An expert advisor to the OGTR's Regulation Review and the GT Scheme Review appears to have serious conflicts of interest as a result of his engagement in gene drive research in Australia to control invasive species, which the US's military research arm is funding.[25]

Recall that Australian researchers inadvertently developed a lethal mousepox virus using standard GM techniques to insert the gene for interleukin-4 (IL-4). They hoped to induce infertility in mice but instead found the altered virus could kill both mice that were naturally resistant to, and mice that had been vaccinated against, ordinary mousepox. When they published their findings, materials and methods, critics alleged they alerted would-be terrorists to new ways of making biological weapons.[26]

Given the risks that gene drives pose, we seek a total moratorium on all gene drive R&D.

6. Are there any features in the options presented that you have concerns with? Or, are there any particular features that you believe should be included? Please explain why and give substantiating evidence where possible.

The proposed deregulation of some SDN-1 techniques is unacceptable. The OGTR's claims that new GM techniques such as CRISPR "do not give rise to any different risks to natural mutations" are indefensible and reflect the OGTR's over-reliance on advice from scientists with their own commercial and scientific barrows to push.

For the reasons already enumerated above we consider that techniques such as CRISPR (SDN-1), which is likely to be widely used, must be subject to the GT regulatory scheme. We refute claims that SDN-1 without template repair can be deregulated because its products may be nature identical. The GM processes by which the deletions are achieved cannot be ignored or discounted and clearly fall within the definition of GM dealings in the GT Act 2000.

Evidence on the mechanisms of SDN repair is sparse. New CRISPR techniques were only invented five years ago. Austrian and Norwegian government reviews conclude that insufficient is known about their risks so recommend comprehensive case-by-case risk assessments.

How double stranded DNA breaks are repaired, and the potential results of faulty repair, are not well understood.[27] A Norwegian government-commissioned review found repair mechanisms are poorly understood and pointed out that most experiments used mammalian cells, not plant, microbial or animal cells, which may confound results.[28] They also conclude that off-target mutations, impossible to predict in advance, occur with the use of all SDN techniques. Such changes may also be inherited.

An Austrian Environment Agency review[29] found SDNs may have unexpected impacts. Off-target effects from SDN use – CRISPR, ZFN and TALEN – appear to include cutting DNA beyond the target site, creating unforeseen and unpredictable mutations. CRISPR/Cas9 can result in hundreds of unexpected mutations.[30]

Deregulating techniques such as CRISPR, given the knowledge gaps that exist around the risks they pose and their off-target impacts,[31] scraps the Precautionary Principle embedded in the GT Act.

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[25] Could WA be the genetic testing ground for 'synthetic mice' to end mice? Sydney Morning Herald, Saturday February 24, 2018. http://www.smh.com.au/environment/conservation/could-wa-be-the-genetic-testing-ground-for-synthetic-mice-to-end-mice-20180221-h0wev9.html

[26] Jackson *et al*, *Journal of Virology*, 2001 and EMBO reports (2010) 11, 18-24 DOI 10.1038/embor.2009.270, 11.12.2009 http://embor.embopress.org/content/11/1/18#B4

[27] Vu, G. T. H., et al., Endogenous sequence patterns predispose the repair modes of CRISPR/Cas9-induced DNA double-stranded breaks in Arabidopsis thaliana. Plant J, 92: 57–67, 2017. doi:10.1111/tpj.13634

[28] Agapito-Tenfen, S.G. & Wikmark, O-G (2015) Biosafety and knowledge gaps of site directed nucleases and oligonucleotide-directed mutagenesis, P5. http://genok.no/wp-content/uploads/2015/06/250615_Emerging_technologies_final.pdf

[29] Eckerstorfer, M. et al. New plant breeding techniques: risks associated with their application, Austrian Environment Agency, 2014. http://www.ekah.admin.ch/fileadmin/ekahdateien/New_Plant_Breeding_Techniques_UBA_Vienna_2014_2.pdf

[30] Han, A.P. New Sequencing Methods Reveal Off-Target Effects of CRISPR/Cas9, 2015. https://www.genomeweb.com/sequencing-technology/new-sequencing-methods-reveal-target-effectscrisprcas9

[31] Howden, J. CRISPR gene editing causes hundreds of unintended, off-target mutations. **https://cosmosmagazine.com/biology/crispr-gene-editing-causes-hundreds-of-unintended-off-target-mutations**

D. Our comments on proposed technical amendments

We agree with the OGTR's proposal to repeal Item 1 of Schedule 1 as it "contains many undefined terms" with no clear meaning, creating "a problem because organisations or individuals undertaking work in this area are not able to confidently determine the regulatory requirements to which they must comply when using these new technologies."[32] Regardless of whether or not any 'foreign nucleic acid' is introduced, dealings with organisms altered using all GM techniques (past, present and future) must be regulated as GMOs,

We disagree with the proposed additions of Section 13(3A), and Section 2.2(2) to Schedule 3, as the safety of a GM microorganism cannot be assumed or predicted from whether its non-manipulated parent is pathogenic or safe.

We also oppose the proposed S13(3)(b) which would permit written authorisation of transport and/or disposal of GMOs beyond present S13(3)(a) requirements.

New reporting requirements for NLRDs (S13C) propose to permit an annual, instead of a prompt, report to the OGTR after an IBC's assessment is received. We disagree, as delayed reporting compromises the OGTR's capacity to monitor, audit and enforce Regulations.

The proposed S39 change would lessen NLRD reporting requirements and remove the requirement to submit a GM product description and other information, so we do not agree.

In Schedule 1A, we oppose inclusion of RNA techniques as they are GM.

We strongly oppose anything that would weaken or compromise the present definitions of GM, GMO and GMO dealings in the GT Act 2000, GT Regulations, the GT Inter-government Agreement and all associated documentation. We therefore reject the proposed inclusion of Schedule 1B (and regulation 4A) for reasons FoE advances in its submission. We also seek answers to the questions FoE poses.

We oppose the proposed addition of items 4, 8, 9, 10 and 11 to Schedule 1 as the organisms are all GM and their status must not be compromised.

E. Conclusions and recommendations

We conclude that, on all the evidence we have presented, the OGTR must stringently regulate all new GM techniques (past, present and future), including SDN-1, RNAi, null segregants and gene drives. No proposed exemptions can be made under the GT Regulations or by changes to the GT Act.

We also recommend that:

- the OGTR's Guidelines on Accredited Organisations be amended, to require:
    - any group of persons using any GM techniques to be accredited;
    - all accredited organisations to establish IBCs;
    - to have their laboratories inspected and certified; and
    - only appropriately trained and experienced people be permitted to perform Genetic Manipulation R&D;
- all new GM techniques and their products be regulated as GMOs;
- full molecular characterisation be required to enable traceability;
- encourage development of cheaper and more reliable detection methods for even single base pair changes in all GMOs;
- a moratorium on all gene drive R&D;
- GTTAC[33] be required to include an ecologist.

also supports this submission and agrees to its publication.

[32] Ibid. P5.
[33] The Gene Technology Technical Advisory Committee (GTTAC), 2017-2020. http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/content/gttac-2