A submission on applications and proposals to change the *Australia New Zealand Food Standards Code* (the Code)

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Submission from Murdoch University, WA State Agricultural Biotechnology Centre

Summary

The following aspects are discussed in this submission:

- The current status of New Breeding Technologies (NBTs) in Australia and in a global context, with a focus on Gene Editing (GE) technology
- Particularly in relation to crop and food production, GE technology provides a powerful new set of opportunities for the Australian farming and food industries, which are needed to ensure Australia's competitiveness in the world marketplace in the future
- GE foods can democratise access to new breeding technologies
- In a regulatory context, Australia is falling behind major developed economies (for example, most countries in North and South America, Japan) in terms of reduced regulatory burden and certainty for progressing GE products
- There is a need to harmonise regulations and definitions as much as possible between OGTR and FSANZ
- **Murdoch University supports Option 3**, i.e. amending the definitions in the Code for 'food produced using gene technology' and 'gene technology' to accommodate existing and emerging genetic technologies and urges alignment with definitions adopted by OGTR.
- Updating these definitions and providing clarity to industry is needed as soon as possible, and FSANZ is lagging behind OGTR in that it has failed to address this important issue adequately before now
- A major drawback here is that the Gene Technology Act 2000 relates only to Australia, whereas FSANZ is a joint regulatory body between Australia and New Zealand. It is noted that, regarding GE products, Australia and New Zealand have diametrically opposing views and regulation
- New Zealand's approach (based on its domestic legislation – HSNO - and the Cartagena Protocol) leads to a very restrictive future for GE products being deregulated in New Zealand
- Given New Zealand's stance on GE crops, it is important that this does not drag Australia backwards so that the remarkable benefits GE technologies have to offer are not lost
- The question arises, what can be done to enable Australia to benefit from GE technologies and GE food products even if New Zealand is recalcitrant?
- Perhaps, for this aspect of food regulation, Australia and New Zealand should have separate regulations, rather than try to force two different national views or definitions into regulations which will not serve Australia's food production industries well in the future.

- As a general principle, any regulation should be commensurate with risk, and over-regulation and unnecessary red tape is to be avoided
- To truly modernise gene and food technology regulations in Australia, regulators need to consider risk-proportional regulation of NBTs
- Regulators must also seek to harmonise regulations with our trading partners, and to show leadership in this area, making use of science diplomacy to support future trade in our region

Background, the science and current status of New Breeding Technologies

Beneficial technologies ('New Breeding Techniques/Technologies') that can be used to improve both production and consumer attributes of foods are advancing rapidly. In this submission, we focus on horticultural and broadacre crops rather than food from domestic animals.

There is little doubt that these New Breeding Technologies (NBTs) will contribute to future food security, helping increase production per unit area, and the quality of the food in terms of human health. In turn, the application of NBTs will benefit the environment, by reducing the need to expand crop production into marginal lands, where most biodiversity resides.

Here we distinguish between the products of genetic manipulation (GMOs) which contain genetic sequences from unrelated organisms, and products of gene-editing (GE) using site-directed nucleases (SDNs).

Although comments will be restricted mainly GE technologies, it is important to note that GM food products have been produced widely over the last 25 years, and now contribute more than 10% of the world's foods. There have been NO VERIFIED INSTANCES of any adverse effects from the trillions of GM food meals eaten during this time, and this is supported by the many international studies by learned societies, national bodies including the EU, that foods derived from GM technologies are as safe or more safe than foods developed by conventional means.

It is well documented that the costs of regulatory compliance required for production of GM crops/foods has inhibited the wider application of GM technologies, and there is a need to prevent a similar limitation for Australia and the wider community for the production of GE crops/foods.

The Office of the Gene Technology Regulator (OGTR) is ahead of FSANZ in considering definitions and regulations of GE technologies. The Gene Technology Act 2000, through OGTR, regulates living organisms developed through GM technologies. Our preferred definition of SDN technologies is shown in Figure 1:

Gene-editing definitions

SDN application	Targeting to specific genome location?	Use of repair template? Origin of the repair template	Type of targeted sequence change(s)
SDN-1	YES Defined by nuclease specificity	NO	**Mutation(s)** (Spontanious mutations: Deletions, replacements, additions of sequences)
SDN-2	YES Defined by nuclease specificity	YES Species own gene pool only	**Edit(s)** (Predefined mutations, sequence optimisation, allele replacement
SDN-3	YES Defined by nuclease specificity	YES Any source, including species own gene pool	**Insertion(s)** (Addition of sequence at the target genomics location)

Figure 1. Preferred gene-editing definitions used on this submission.

A pictorial representation of these technologies is shown in Figure 2:

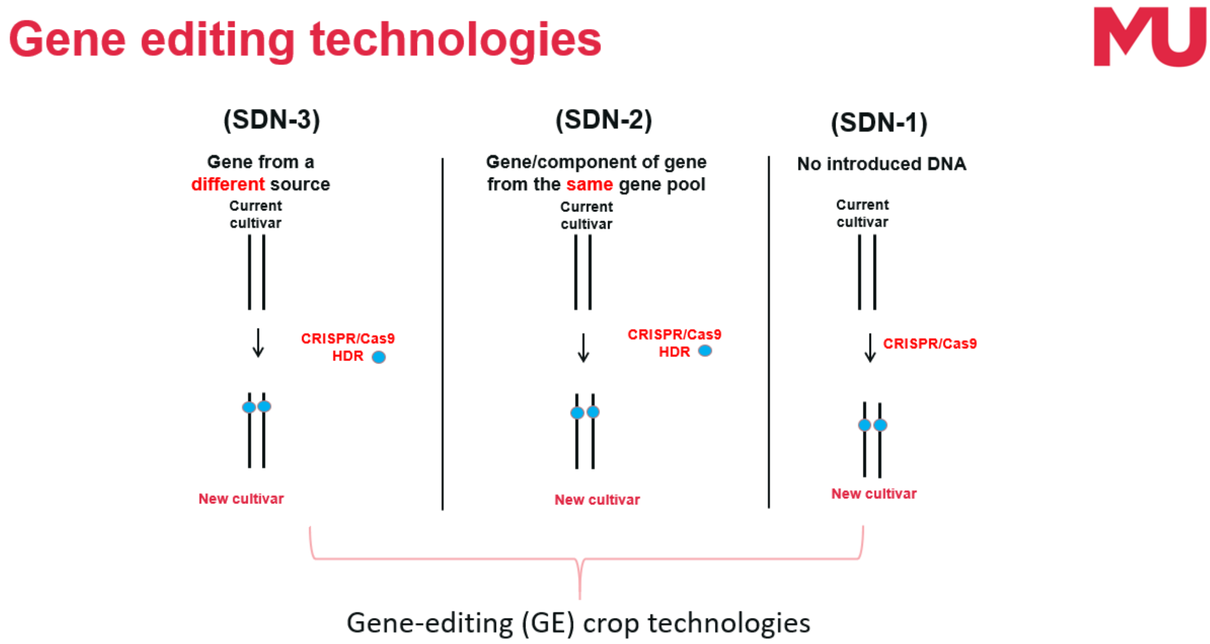


Figure 2. A pictorial representation of GE technologies under discussion, SDN – Site Directed Nucleases, the blue sphere represents a repair oligonucleotide used in Homology Directed Repair (HDR).

As defined above, SDN-1 products do not contain introduced DNA, and SDN-2 products *may contain genes of components of genes for the same gene pool* (via homology dependent repair, indicated as small blue spheres), that is, the products could have been generated by conventional breeding without regulation.

Following extensive consultations, products of Site-Directed Nuclease Technology (SDN-1), in which there is no repair template, have been deregulated in Australia by OGTR.

OGTR deregulated SDN-1 products for a number of logical reasons, not the least that there are about 3,500 varieties of food products generated by imprecise chemical or irradiation mutagenesis available for purchase without regulation. These contain many off-target double-stranded (ds) break and other unknown chromosomal changes, because classical mutagenesis is simply a crude way of generating ds breaks in DNA, a small minority of which may yield beneficial changes (eg seedless oranges, ruby-red grapefruit). In comparison GE SDN-1 processes generate ds breaks at precise locations (e.g. using CRISPR/Cas9), and have been described as *targeted mutagenesis* because of this precision. Also, conventional cross-breeding can lead to uncharacterised mutations, chromosomal breaks and rearrangements. Both of these forms of breeding are not regulated.

Industry regards the decision not to deregulate GE products of SDN-2 changes (as defined above), to be 'highly conservative', and that Australia has gone from a regulatory leader to lagging behind other countries.

A map depicted the current regulatory status of GE crops is shown Figure 3:

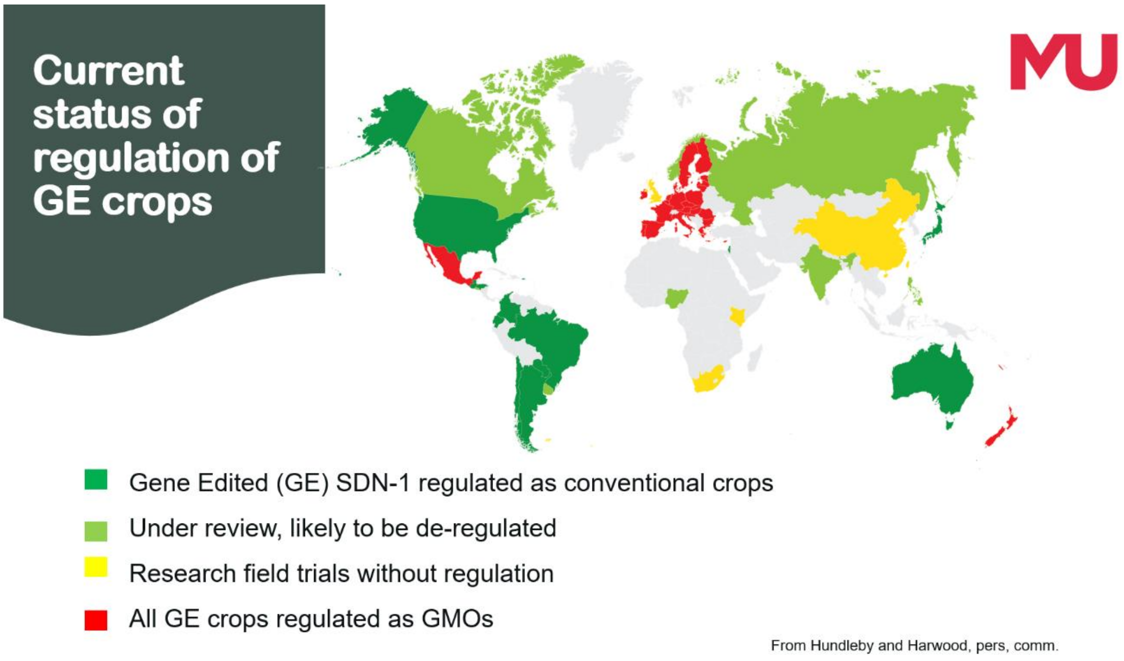


Figure 3. The current status f regulation of GE crops worldwide.

An important detail is that New Zealand, coloured in red in this map, is out of step with the majority of advanced countries, in that it regulates the products of GE technology, including SDN-1, as GMOs.

On a global scale, OGTR's decision to deregulate only SDN-1 products is clearly conservative, because an increasing number of countries in North and South America, and Japan, have also deregulated products of SDN-2 (as defined above). For example, this would deregulate allele replacement, which is a major aim and activity of conventional breeding, but which takes a long time to achieve by conventional means.

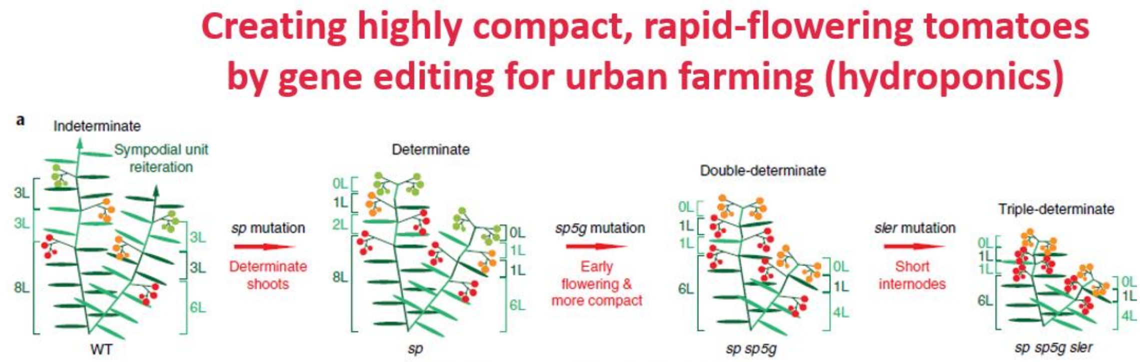
Examples of existing GE foods in the marketplace

It is useful to note that there are already food products from gene-edited organisms in the marketplace overseas, and these demonstrate the importance for Australia of not being left behind, or preventing the Australian crop and food industry, and consumers, from benefitting from new breeding technologies. The following examples show two commercialised gene-edited products and two examples of SDN-1 gene-edited wheat in the pipeline.

Example 1. GE tomatoes that reduce blood pressure - Japan

Tomatoes edited to over-express GABA γ-Aminobutyric acid (GABA), a non-protein amino acid that has hypotensive effects - enhanced GABA reduces blood pressure. (Nonaka et al (2021) Sci Rep &,7,7057, DOI:10.1038/s41598-017-06400. Efficient increase of ɣ-aminobutyric acid (GABA) content in tomato fruits by targeted mutagenesis).

Example 2. GE dwarf, rapidly growing tomato plants for urban hydroponic farming

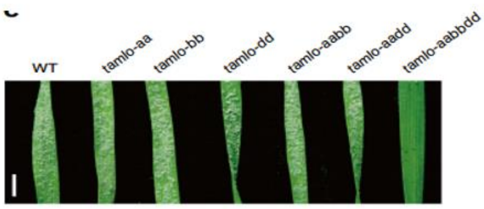


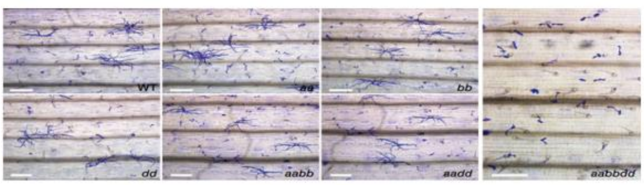
Rapid customisation of Solanaceae fruit crops for urban agriculture - one-step CRISPR–Cas9 gene editing restructured vinelike tomato plants into compact, early yielding plants suitable for vertical farming. Kwon et al (2020). Rapid customisation of Solanaceae fruit crops for urban agriculture. Nature Biotech https://doi.org/10.1038/s41587-019-0361-2.

Examples of wheat crop improvement by gene-editing

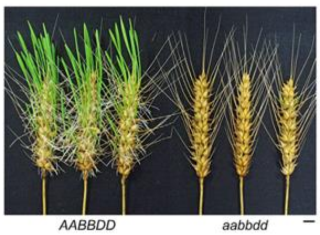
Gene-edited wheat for resistance to powdery mildew and reduced pre-harvest sprouting:

- *Gene-editing of all six MLO alleles in hexaploid bread wheat confers heritable, broad-spectrum resistance to powdery mildew (TaMLO-A1)(Wang et al, 2016, Nature Biotech)*





- *Gene-Edited Triple-Recessive Mutation Alters Seed Dormancy in Wheat* (Abe at al Cell Reports 2019).



Left – pre-harvest sprouting, Right – edited to prevent pre-harvest sprouting (heads equally treated with water). Pre-harvest sprouting reduces grain quality and value.

Other examples from SDN-1 R&D in Australia include: reducing the browning of potato crisps on frying after cold storage, reducing the presence of carcinogenic acrylamide in fried potatoes, reducing the glycemic index of potato cultivars to help reduce Type II diabetes (Crop Biotechnology Research Group, Murdoch University). Other GE modified attributes include high oleic, low linolenic soybean oil, reduced polyunsaturated fatty acids.

These are but a few examples of the beneficial power GE technology.

GE foods can democratise access to new breeding technologies

Taking Argentina, which is five years ahead of Australia in deregulating GE crops and food, as an example, which uses is a product-based approach to GE to organisms and their products (FSANZ P1055 Supplementary Data 3, Table 1), it is clear that a simplified regulatory approach has been game-changing. In the five years in which GE products have been commercialised, the landscape has changed completely from large multinationals to local SMEs (Figure 4):

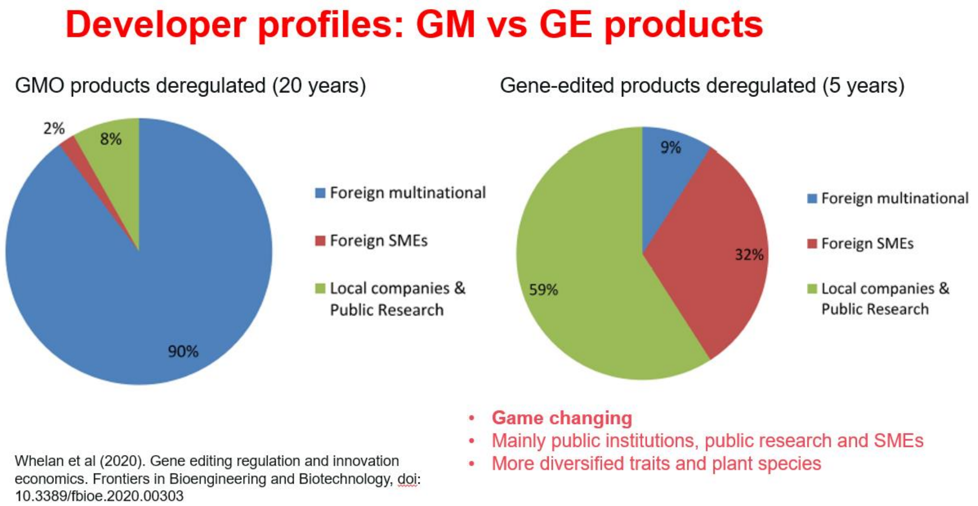


Figure 4. The remarkable change in the landscape over the last 25 years in Argentina. GE has democratised and enabled small companies, universities and public bodies to develop GE foods, and expanded the traits and plant species developed.

The need for harmonisation of regulations between OGTR and FSANZ

Returning to FSANZ, which regulates food, not living organisms. To streamline regulations in Australia there is a clear need to avoid inconsistencies between what is regulated as a GMO by OGTR and what is regulated as GM food by FSANZ. That is a need to harmonise definitions and regulations, which otherwise become red tape and barriers to applying beneficial technologies.

A major drawback here is that the Gene Technology Act 2000 relates only to Australia, whereas FSANZ is a joint regulatory body between Australia and New Zealand. ***As is evident from the map above (Figure 3), regarding GE products, Australia and New Zealand have diametrically opposing views and regulations.***

New Zealand's approach (as shown in FSANZ P1055 Supporting Document 3, Table 2) to use both its domestic legislation (HSNO) and the Cartagena Protocol, leads to a very restrictive future for gene-edited products being deregulated in New Zealand.

Given NZ's stance on GE crops, it is important that this does not drag Australia backwards, so that the remarkable benefits GE technologies have to offer are not lost.

The question arises, what can be done to enable Australia to benefit from GE technologies and GE food products even if New Zealand is recalcitrant?

Perhaps, for this aspect of food regulation, Australia and New Zealand should have separate regulations, rather than try to force two different national views or definitions into regulations which may well not serve Australia's food production industries well in the future.

What is also needed is to future-proof regulatory policies, so that as new technologies emerge, regulatory approaches are flexible enough that breeders and food producers can make full use of beneficial new advances, in particular those which allow effective use of genetic variation naturally present in crop plant gene pools. This means a greater emphasis on the product itself, and less on the process by which it was developed. This includes consideration of proportional risk, history of safe use and the avoidance of undue regulatory burden when there is no risk to human health or the environment.

Given this issue, FSANZ's response is encapsulated in the three possible Options proposed.

Possible regulatory and non-regulatory options

Option 1 – Status quo

Murdoch University agrees completely with FSANZ that Option 1 is not viable. It does not address new technologies and is outdated, and would contribute to regulatory uncertainty and prevent the application of valuable and beneficial new breeding technologies to underpin both production and improved food quality for consumers.

Option 2 – Status quo combined with non-regulatory approaches

Murdoch University agrees completely with FSANZ that Option 2 is not viable, and would not create clarity and certainty regarding products of new breeding technologies. This is because non-regulatory approaches are subject to interpretation.

Option 3 – Amend the definitions in the Code

Again, *from the limited Options provided, in our view, Option 3 is the preferred Option.*

This Option involves amending the definitions in the Code for 'food produced using gene technology' and 'gene technology' to accommodate existing and emerging genetic technologies.

FSANZ P1055 proposes that the current definitions should be amended as follows:

- revise and expand the process-based definition for 'gene technology' to capture all methods for genetic modification other than conventional breeding; and
- revise the definition for 'food produced using gene technology' to include specific product-based criteria for excluding certain foods from pre-market safety assessment and approval as GM food. Foods not meeting all relevant exclusion criteria would require an application to FSANZ.

It is noted that these proposed changes to definitions do not align well with OGTR definitions relating to gene editing, and that an opportunity to attain the desirable goal of harmonising OGTR and FSANZ definitions may well be/have been missed.

Of course, the primary aim of FSANZ, is to protect public health and safety by taking into account possible unknowns in relation to future technology development and future products.

However, as a general principle, any regulation should be commensurate with risk, and over-regulation and unnecessary red tape is to be avoided. Given the raft of unjustified claims and untruths of many current foods on supermarket shelves which go unregulated and unchecked, GE food should not be over-regulated to the point where the great promise for genuine community benefit is stifled.

Nevertheless, expanding a process-base definition would be an improvement, as would a clear statement of product-based criteria for excluding certain foods from pre-market safety assessment and approval as GM food. If an application is required from FSANZ, this should be undertaken in a timely and efficient manner.

If a GE plant is deregulated by OGTR, there should be parallel deregulation by FSANZ, unless there is good reason not to do so. Gene-editing of crop plants so far is always based on improving the properties of existing, un-regulated advanced breeding germplasm or existing varieties, and the changes made are usually much less (ie more targeted) than occur after conventional cross-breeding.

It follows that exclusions should apply to NBT foods that have the same product characteristics as conventional food with a history of safe use. Similarly, exclusions should apply to processed food from SDN-1 and SDN-2 treatments.

In formulating a revised definition of gene technology, keep it simple and clear.

A definition of conventional breeding is needed, as there are many opportunities or manipulative steps, from tissue culture and possible somaclonal variation (used routinely to produce doubled haplid cereals), to whole genome selection using e.g. 90k SNP chips and classical mutagenesis. These can generate many more genetic changes than GM or GE processes, but are not regulated or captured as gene technology. Rather than over-regulate conventional cross-breeding, there should be parity in risk assessments of *all* foods.

An over-emphasis on unintended changes in GE or GM products is greatly overstated, since we routinely eat hundreds of thousands of genes and proteins every day, and eat totally new genes/protein/metabolites when travelling overseas (e.g. sea urchins gonads in Japan!). A greater range of unintended changes occur in conventional breeding than with GM or GE foods, and yet that food is accepted without question. Changes themselves are very rarely of biological significance, especially after processing, cooking and digestion

Equivalence to conventional food is therefore a legitimate basis for excluding certain foods from pre-market assessment, as are foods from null segregants if an initially product is GM. The OGTR Schedule 1 definition of null segregants is good.

One aim of GE technology is to reduce levels of natural antinutritional compounds and allergens, so 4.3.2 (ii) and (v) need modifying to allow such beneficial traits to be excluded.

To truly modernise gene technology regulation in Australia, regulators need to consider risk-proportionate regulation of NBTs: GM foods have now been eaten for more than 25 years, and so there is ample evidence of their safety, and there is also no evidence of unsafe properties of GE produce.

Regulators need to develop enough flexibility to assess future technologies, and should avoid undue regulatory burdens when there is no evidential basis for risks to human health and safety, or the environment.

Trade potential, international harmonisation, and the importance of regulatory support

The regulations that FSANZ develops for GE products have much broader implications than just in Australia or NZ. Australia is an exporting country, with 71% of horticultural produce exported to SE Asia/APAC, and the majority of grains exported to SE Asia/APAC and the Middle East. It is vital that Australia harmonises regulations (OGTR and FSANZ) with our trading partners, or this will stifle the applications of new technologies in Australia: Australia as a country will fall further behind and be less competitive internationally.

This is because products of GE and new breeding technologies can make the transition from lab to market in a very short timespan, regulatory approaches permitting. Lack of harmonisation is the most significant cause of trade-related asynchronisation in the biotech crop market. By virtue of their evidence-driven deregulation, countries in the Americas have taken market advantage by adapting legislation to support the use of GE.

As Australia looks to expand its trading opportunities in the changing geopolitical and geoeconomics environment in the Asia-Pacific region with a rising ongoing tech decoupling between USA and China, there is a need to leverage NBTs. New market opportunities in NBTs are emerging, as reflected by the United Kingdom pursuing a revision to its regulations following Brexit. Australia can only benefit from these changing dynamics if its regulations are 'in sync' with conventional and emerging trading partners.

Australia's academic prowess and technical expertise in the area is on par with the best globally, but industry outcomes and commercial benefits are underperforming.

This is highlighted in the Commonwealth Government DESE University Research Commercialisation Consultation paper (2021), which emphasises 'that excellence in research does not necessarily lead to excellence in research commercialisation. The 2020 WIPO Global Innovation Index ranks Australia as the 23rd most innovative country overall, *but we are 40th when it comes to knowledge and technology outputs*. Australia performs well in knowledge creation but *poor in translating this knowledge into new products* or other innovations'.

Pursuit of Option 3 is also in line with the Australia 2030 Strategy of the Government which aspires to ensure Australia's ongoing prosperity by stimulating high-growth firms and raising productivity. It also underlines the role of the Government as a catalyst for innovation and to be a global leader in innovative service delivery.

The objective of commercialisation and translational research can also be achieved by unlocking the potential of GE products.

International / Science Diplomacy Impact

Australia conventionally enjoys a favourable position in international affairs, in part due to its innovation driven approach to socio-economic development. An opening-up of the NBT market will allow us create new leverage to extend our global profile. Furthermore, as countries are now increasingly deploying science diplomacy to foster international scientific collaboration and increasing share in the global knowledge economy, Australia can also contribute to this cause. The achievement of the UN Sustainable Development Goals is also linked to how countries can effectively make use of science for solving global problems such as climate change and food security.

Pursuit of Option 3 also allows DFAT a new avenue to their diplomatic outreach and extending support to developing countries.