Public Health Association of Australia submission on the 2017 Review of the National Gene Technology Regulatory Scheme

Contact for recipient:
Gene Technology Secretariat
Department of Health
A: MDP 1060
GPO Box 9848, Canberra ACT 2601
E: gene.technology.review@health.gov.au
T: (02) 6289 2033

Contact for PHAA:
Michael Moore – Chief Executive Officer
A: 20 Napier Close, Deakin ACT 2600
E: phaa@phaa.net.au **T:** (02) 6285 2373

29 September 2017

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Introduction

The Public Health Association of Australia

The Public Health Association of Australia (PHAA) is recognised as the principal non-government organisation for public health in Australia working to promote the health and well-being of all Australians. It is the pre-eminent voice for the public's health in Australia. The Association seeks better population health outcomes based on prevention, the social determinants of health and equity principles. PHAA is a national organisation comprising around 1900 individual members and representing over 40 professional groups.

The PHAA has Branches in every State and Territory and a wide range of Special Interest Groups. The Branches work with the National Office in providing policy advice, in organising seminars and public events and in mentoring public health professionals. This work is based on the agreed policies of the PHAA. Our Special Interest Groups provide specific expertise, peer review and professionalism in assisting the National Organisation to respond to issues and challenges as well as a close involvement in the development of policies. In addition to these groups, the Association's journal, the Australian and New Zealand Journal of Public Health (ANZJPH), draws on individuals from within PHAA who provide editorial advice, and review and edit the Journal.

Health is a human right, a vital resource for everyday life, and key factor in sustainability. Health equity and inequity do not exist in isolation from the conditions that underpin people's health. The health status of all people is impacted by the social, cultural, political, environmental and economic determinants of health. Specific focus on these determinants is necessary to reduce the unfair and unjust effects of conditions of living that cause poor health and disease. These determinants underpin the strategic direction of the Association.

All members of the Association are committed to better health outcomes based on these principles.

In recent years, PHAA has further developed its role in advocacy to achieve the best possible health outcomes for the community, both through working with all levels of Government and agencies, and promoting key policies and advocacy goals through the media, public events and other means.

Vision for a healthy population

The PHAA has a vision for a healthy region, a healthy nation, healthy people: living in an equitable society underpinned by a well-functioning ecosystem and healthy environment, improving and promoting health for all.

Mission for the Public Health Association of Australia

As the leading national peak body for public health representation and advocacy, to drive better health outcomes through increased knowledge, better access and equity, evidence informed policy and effective population-based practice in public health.

PHAA Response to the 2017 Review of the National Gene Technology Regulatory Scheme Background Paper

PHAA's policy on Genetically Modified Foods

This submission is based on PHAA's policy on Genetically Modified Foods, which can be seen at https://www.phaa.net.au/documents/item/1700.

The PHAA develops policies via a lengthy and thorough process that involves review of a draft policy by the Vice President (Policy) of the PHAA, the placing of the draft policy on the Policy Forum in the Member Centre of the PHAA website, consideration of issues by the PHAA Policy team, liaison with the relevant Special Interest Group/proposer, and finally, approval by PHAA membership at the Annual General Meeting (AGM). The official policy is then published on the PHAA website. A Policy Statement is deemed to be current for three years after which it must be revised or archived[1]. PHAA's policies require evidence to support them, based on references from the peer-reviewed literature.

The PHAA has had a policy on GM foods since 1999. The policy has been revised and re-endorsed five times, most recently in 2016.

The policy has been informed by the training and experience of the members of the PHAA, which includes experts in food, nutrition, disease control, epidemiology, toxicology, medicine, and medical research. The PHAA has a Food and Nutrition Special Interest Group.

There are several items in the policy that are relevant to the topic of this submission.

First, the PHAA regards organisms developed using the new technologies described in the Background Paper of the 2017 Review of the National Gene Technology Regulatory Scheme as GMOs. Specifically, PHAA's policy on Genetically Modified Foods includes the following paragraph in its description of GMOs. "New techniques include crops designed to produce a new RNA molecule rather than a new protein,[2] and new gene editing techniques (e.g. CRISPR) that can also be used as a "gene drive" to spread altered DNA rapidly through a population and for developing synthetic biology.[3]"

Furthermore, the PHAA considers that GMOs should be regulated and that a GMO cannot be considered to be safe until there is independent, peer-reviewed evidence that it is safe. Assumptions of safety should never be used. It should be noted that various members of the PHAA have been, and continue to be, involved in investigations into claims of safety of e.g. tobacco, alcohol, pharmaceutical drugs, food-related substances, environmental toxins etc. and are aware that industry-related claims of safety are often overturned once independent laboratory, clinical and epidemiological research has been undertaken. As a result, members have learnt to be wary of claims of safety by vested interests and to require evidence to support such claims.

As a result of problems in the past when substances (e.g. pharmaceutical drugs) and procedures (e.g. surgical procedures) were claimed to be safe and efficacious, but were later found to cause harm, a process has been developed that now is regarded as the gold standard of how to assess safety. It is a step-by-step process where each step is concluded and assessed before the next step is undertaken. If a substance or procedure fails a step, the process stops. First, animal studies are conducted to determine benefits and harms. Then the four phases of human clinical trials are conducted, where Phase I looks at harm in a small number of volunteers, Phase II looks at benefits in a small number of volunteers, Phase III studies benefits and harms in a much larger number of people using a double-blind randomised controlled trial, and then the substance is monitored in the community (Phase IV). More conservative epidemiologists still do not

regard a substance or procedure to be safe and efficacious until several Phase III clinical evaluations have been conducted by different research groups and the results pooled using a Cochrane review meta-analysis. [4]

Even then, there are numerous examples of evidence of harm being found only during Phase IV of the process, i.e. after the substance or procedure had passed clinical trials, had obtained regulatory approval and was being monitored in the community. Vioxx (also known as rofecoxib), an anti-inflammatory drug, is one example. By the time independent researchers had concluded that it caused harm and the drug was withdrawn from sale against the wishes of the manufacturer, it was estimated to have caused 139,000 heart attacks and killed 26,000 people.[5]

Public health professionals have repeatedly seen this kind of outcome. Consequently, to a public health professional, because no organism made using these new techniques appears to have gone through Phases I, II and III of human clinical trials, these organisms cannot be considered to be safe for human health. For the same reason, neither can previous versions of GM foods. Moreover, the quality of animal studies used to support claims of safety of GM crops has been highly criticised as being poorly conducted, largely undertaken by vested interests, and lacking in endpoints that are relevant to human health.[6] There is therefore a dearth of evidence that organisms made using these new techniques are safe.

Once a substance is released into the food supply or the environment, epidemiological studies such as cohort or case-controlled studies are required to determine if they cause harm in the population. These studies compare the health outcomes of people exposed to a substance, to those who are not exposed. There are thousands of examples of where these studies have been used, including numerous examples investigating the effects of infectious diseases, tobacco, alcohol, asbestos and heavy metals such as lead (e.g. the Port Pirie study, leaded petrol) and mercury (e.g. Minamata disease) on health.

In order to do this type of study, it is important to be able to identify those who are exposed and those who are not exposed. If these new GM techniques are assumed to be safe and hence do not need to be regulated, then these GMOs will likely appear in the environment and in the food supply in a way that may make it almost impossible to determine who is exposed and who is not, thereby making it almost impossible to properly undertake epidemiological studies into their effects in the population. For example, the effects of eating these new GMOs couldn't be properly elucidated if it could not be determined who had been eating them because foods from these organisms were not labelled. If, as a result of the current Review, a decision is made that organisms made using these new techniques are not GMOs, then they will not be labelled. Given that these new techniques are very recent and their long-term effects are unknown, this would be a profoundly unwise step. That is, it would be profoundly unwise to, at this stage, through a lack of regulatory oversight, approve a process that would prevent later epidemiological studies into the health effects of these new organisms.

A view has often been expressed that we would know if a GM food caused harm to people because we would notice it, and because no-one has ever noticed anyone experiencing adverse effects from eating GM food, then the assumption is that GM food must be safe to eat. The Vioxx example shows that this belief is unfounded. Each year, millions of people go to hospital and millions die from a variety of ailments. Unless an epidemiological study is undertaken to determine if an exposure has contributed to a given illness or death, any link may not be found. With Vioxx, the red flag should have been raised with an extra 139,000 heart attacks and 26,000 deaths, but was not.

Not only does the PHAA have members who undertake these types of epidemiological studies, but it also has members who "pick-up the pieces", such as clinicians, once evidence of harm has been found. Consequently, the PHAA is well aware of the huge human and social costs that can accrue when things go

wrong because an incorrect assumption was made that something was safe; or incomplete, or insufficient information was given by vested interests to regulators and the public.

As a result, PHAA's policy on GM food states:

- Food regulation should aim to protect public health and provide information to consumers.
- The precautionary principle should be applied to GMOs.
- Most safety assessments on GM crops are done by people associated with the GM industry and there are relatively few independent assessments[7], particularly when a new GM crop is submitted to Food Standards Australia New Zealand (FSANZ). FSANZ does not require animal feeding studies to assess safety.[8] Industry animal studies usually involve short-term toxicology studies of a few days and do not measure allergic, reproductive or cancer outcomes. Any longer studies tend to use farm animals (e.g. chickens) that are not physiologically comparable to humans and measure outcomes that are not measures of human health (e.g. meat and milk production)[9]. Reviews of the latter studies tend to find little adverse effects, while some reviews of raw industry data[10] and independent toxicology studies have found adverse effects.[11]
- Regulators should use thorough, independent experimental evidence in assessments rather than assumptions. GM foods should not be considered safe until they have undergone long-term animal safety assessments utilizing endpoints relevant to human health and conducted by independent researchers.
- A comprehensive monitoring and surveillance system should be instigated to track the effects of GM foods.
- The labelling system should be improved to include all ingredients (including refined) originating from GM organisms (including micro-organisms), and from animals fed GM feed.
- Labelling laws should be policed.
- Australian governments should impose a freeze on importing GM foods, growing GM crops commercially and patenting genetic resources for food until thorough independent research into their effects is undertaken.
- The PHAA will advocate for publicly funded, independent research into the effects of GM crops, and for GMOs being made freely available to any researcher researching agronomic, environmental or health aspects of GM crops.
- The PHAA will advocate for a strong public health presence in the staff, advisory committees and Boards of the APVMA, OGTR and FSANZ to improve safety assessment procedures.

Object of the Gene Technology (GT) Act

The PHAA notes that the Object of the Gene Technology (GT) Act is:

> *"to protect the health and safety of people, and to protect the environment, by identifying risks posed by or as a result of gene technology, and by managing those risks through regulating certain dealings with GMOs."*

And that the recent OGTR Discussion Paper on options for regulating new technologies further states:

> *"The Explanatory Statement to the 2001 GT Regulations (the 2001 Explanatory Statement)[12] states that "The definition of 'genetically modified organism' in the GT Act was intentionally cast very broadly to ensure that the definition did not become outdated and ineffectual in response to rapidly*

> *changing technology." That is to say, as gene technology develops, the intended default setting of the scheme is to regulate new technology."*

It is therefore clear to the PHAA that these new technologies should be regulated according to the Gene Technology (GT) Act.

Furthermore, a recent review of CRISPR methods[13] states that for plant cells, "The Cas9 and gRNA expression cassettes are often put in one plasmid, which is then delivered into plant cells using conventional transformation methods." Then, after discussing how one can microinject or transfect in vitro–synthesized Cas9 mRNA (or protein) and gRNA(s) into animal embryos and plant protoplasts, the authors state that "however, because the regeneration capacity of protoplasts is very low for most plant species, the direct injection method only suits few plants." Consequently, the use of CRISPR/Cas9 to alter plants will in most cases result in a plant that has actually undergone a conventional genetic engineering process (which requires regulation) in order to introduce the CRISPR/Cas9 editing system into plant cells, in addition to any further editing of the genome that may occur by the CRISPR/Cas9 editing process. There is therefore a strong argument that these organisms should be regulated in the same way as previous GMOs.

Furthermore, inserting DNA into the genome in order for CRISPR-related molecules to be generated will result in those molecules being produced throughout the life of that plant and in future generations of that plant. As the CRISPR system is a means of using molecular "scissors" to cut DNA with the aim of then deleting or inserting genes, this means that the plant will be continually exposed to the molecular "scissors", which is likely to increase the probability of off-target effects over time.

ENSSER Statement

The statement was written by scientists associated with the European Network of Scientists for Social and Environmental Responsibility (ENSSER) in response to a push from the GM industry to have these new GM techniques deregulated in Europe. The statement can be found on-line at: https://ensser.org/wp-content/uploads/2017/09/ENSSER-NGMT-Statement-v27-9-2017.pdf and the list of scientists who have signed it can be found on-line at: https://ensser.org/wp-content/uploads/2017/09/SIGNATORIES-TO-NGMT-STATEMENT.pdf . Both the letter and the list of signatories have been attached to this document as Appendix 1 and Appendix 2 respectively. Please note that the statement was only released for scientists to sign a day or two before the deadline for this submission. It is therefore expected that the list of signatories is expected to grow considerably from the 60 who have already signed it.

The ENSSER statement contains important information about why these new techniques should be regulated. For example, advocates for deregulating the use of these new techniques in areas such as agriculture ignore the fact that it is well understood that when these new techniques are used in medicine, they can result in unexpected and unprecedented genetic modifications. Because of this, these new techniques are heavily regulated for medical applications. To regulate these new techniques in medicine but to deregulate them in areas such as agriculture would be policy double-speak. That is, apparently the techniques are so precise, predictable and safe that they do not need regulation, while at the same time being so imprecise, unpredictable and unsafe that they do require regulation.

The Statement also makes it clear that these new techniques are regulated for medical use for a good reason – these new techniques result in many unexpected changes at the place where genetic engineers are trying to alter DNA, as well as at other sites in the DNA where they are not trying to alter DNA.

In addition, advocates of deregulating these new techniques argue that some of the new techniques should be deregulated because they only cause a small change in the DNA or RNA of the organism. However, such small changes can be made repeatedly, which can result in an organism that can be substantially different to the starting organism. Moreover, even small changes to the DNA of an organism can have far-reaching

effects. There are many instances of small, point mutations in human DNA resulting in serious life-threatening illnesses.

The ENSSER statement is also in agreement with this submission, being, the new techniques can result in toxic products being unexpectedly produced, and therefore, all organisms made using these new techniques need to be fully regulated and fully safety assessed before they enter the environment or the food supply. It should also be noted that the organisms under consideration are usually organisms that have the ability to self-replicate and spread their modified genes far and wide, with far-reaching consequences.

The 60 scientists (and growing) who have signed the statement therefore call on these new techniques to be regulated at the strictest level of GMO regulation.

Risk

Public health professionals have considerable expertise in measuring and reducing risk. Amongst other things, epidemiology is about how to quantitatively measure risk. It is a cornerstone of public health. Drawing upon this knowledge, several things are made clear about these new techniques.

The first is that there seems to be uncertainty and debate about how these new techniques actually work, even amongst genetic engineers. Risks cannot be adequately determined without a full and proper understanding of the techniques. The second is that these new techniques are in their infancy and are constantly changing as techniques evolve, so that an understanding of the techniques used today may not provide an understanding of the techniques used tomorrow. Third, safety assessments of organisms made using these new techniques take time and therefore lag behind the development of the techniques themselves. For example, a review of histopathology studies of the gastro-intestinal tracts of rats where the rats were fed GM crops containing one or more of three commonly-used GM genes, found that there were no published histopathology studies for 81% of the 47 approved crop varieties. Furthermore, of the studies that were done, half were published at least nine years after approval[14]. As a result of this lag, there is little experimental evidence to be found in the peer-reviewed literature where the risks of these new techniques have actually been measured in animals or humans.

Consequently, any decision that is made now that these new techniques are safe are based on opinion and assumption rather than evidence. This includes the advice to the OGTR from the Gene Technology Technical Advisory Committee (GTTAC) of the OGTR, given in the previously-mentioned recent OGTR Discussion Paper, such as “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”, “the risks posed by organisms altered by SDN-1 are unlikely to be different to naturally mutated organisms”, and “SDN-1, SDN-2 and oligo-directed mutagenesis are unlikely to pose risks that are different to naturally mutated organisms. Without hard experimental evidence, such statements are conjecture.

Furthermore, while it is acknowledged that the GTTAC of the OGTR regulator contains members with considerable expertise, there are concerns that the expertise is heavily weighted towards those who do genetic engineering (some of whom are likely to have strong vested financial interests in deregulating the technology), and very underweighted towards people with qualifications or expertise in public health. Out of 19 members in 2016, only one was deemed to have expertise in public health. Therefore, there appears to be insufficient expertise in the GTTAC to undertake a robust public health risk assessment. As per PHAA’s policy, the PHAA is happy to assist the OGTR with such expertise.

As described more fully above, the risks of these new techniques are unknown until they are determined using experimental methods. Consequently, any decision now that they are safe would be scientifically unsound and deregulating something that is not known to be safe would be unwise. To conclude that

products of the new genetic techniques do not require regulation is to effectively decide, *ipso facto*, that every product of the new techniques is safe, before an adequate safety assessment is done on **any** product of the new techniques to determine if **any** product is safe. This could be considered to be a contravention of the Object of the GT Act.

The Austrian Government is one of the few governments worldwide to consider the biosafety risks of these new techniques. They concluded that there is insufficient knowledge about the risks posed by these new techniques and that they should be regulated in the same way as earlier methods, and on a case-by-case basis[15].

DIY genome editing

The accessibility of some of the new techniques to the general public through "do it yourself" projects leads to particular risks that need addressing. Two examples of many are provided here. In the first example, there are credible reports[16] that kits that allow the general public to do this are already on sale. Specifically, "at an event for synthetic biology start-up firms in San Francisco" in February of 2016, "Amino Labs showed off the Amino One", a briefcase-sized "table-top lab for the consumer market", where "beginners will be able to modify bacterial cells to create medicinal chemicals, scents and even foodstuffs such as yogurt, beer and bread." In addition, "Amino Labs wants people to improvise, hacking together different scents and materials". The article makes it clear that these kits will by now have been shipped to people who backed its crowdfunding campaign and that "the price is expected to fall to a few hundred dollars once the company begins mass-producing the devices in 2017."

In a second example, Indiegogo hosted a crowd-funding project[17] that promised "Everything you need to make precision genome edits in bacteria at home including Cas9, gRNA and Donor DNA template for an example experiment" for as little as $130. And for $3000, "We will set you up with everything you need to start your own extensive home lab doing molecular biology and genetic engineering. We will guide you through setting it up and we will also provide you with a CRISPR kit and other kits to get you started!" and that "everyone will be able to use these kits (they contain everything you need, no extra equipment is required), even if you have had zero experience with Biotechnology (there will be extensive written protocols and videos available)".
Given that other companies are likely to follow suit and that the capacity of the biotechnology achievable by such kits is only likely to increase, it is important that the OGTR maintains its ability to regulate the importation and development of such kits, given that the kits will be used in uncontained environments (e.g. the home) and are likely to result in living modified organisms being flushed down the sink to enter the environment, and therefore potentially eventually the food and water supplies.

Detection

A view is often expressed by proponents of GMOs that organisms developed using new GM techniques should not be regulated because they cannot be detected. Three things should be noted about this view.

The first is that detection techniques for these new organisms are currently available using omics techniques such as transcriptomics, proteomics and metabolomics[18]. And, as these techniques improve over time, their ability to detect these new organisms will improve. The current and potential future uses of these techniques for detection is discussed at length in Chapter 7 of the National Academies of Science report of 2016[20]. That report concluded that these techniques could play an important role in the regulation of crops developed using these new techniques.

It should also not be assumed that omics methods will be the only methods of detection available in the future.

The second is that it is highly unlikely that a patented organism would be released by a company or organisation for sale without some means of protecting their intellectual property (IP) rights over that organism. After all, there is little point in spending large amounts of time and money on developing a new GMO if developers cannot recoup their investment money and make a profit from the sale of their product. It is therefore logical that the developer will have a means of genetically ”branding” a GMO to ensure that it is not used without a licence, i.e. so that it can be legally proven that a particular GM organism belongs to a particular company so that payment can be enforced for any use of that GMO.

The third is that difficulty with compliance has not prevented Commonwealth and State Governments and the judiciary from enacting compliance procedures elsewhere. In one of many examples, it is legal to take opioids as long as they are prescribed by a doctor. It is illegal to take them otherwise and illegal use can result in a jail sentence. Codeine is exempt and is easily available. The usual detection test for taking opioids is to detect certain opioid breakdown products in the urine. However, this test will also test positive for codeine consumption. Yet these difficulties in enforcing compliance have not stopped courts imposing court orders upon people to abstain from illegal opioid use and for that abstinence to be monitored.

Burden

The proponents of deregulating these new GM techniques often argue that regulation constitutes a burden to the industry, that it is a form of “red tape” that incurs a cost to the industry and impedes innovation. However, whenever burden is discussed, only the regulatory burden to those who are developing and commercialising organisms using these new techniques is discussed. There is no mention of another, more important burden. If organisms developed using these new techniques are not regulated, then they will be released into the environment and food supply without any safety assessments. However, if in reality some of these organisms are not safe, then these organisms may cause a huge health and financial burden for Australia. And while the regulatory burden is largely carried by a few entities that wish to profit from these organisms (i.e. privatising the profits), a health burden can be a much higher cost that is carried by potentially thousands of individuals, including primary health care providers, hospitals, State and Federal governments, taxpayers and those who get ill and their families (i.e. socialising the losses).

It should be noted that the health and financial burden will be high even if only a small proportion of the population is affected by ill-health. Based on the current population of Australia being 24 million, if a GMO made using one of these new techniques caused only 1 in 1,000 people to get ill, then 24,000 people would be ill in Australia, with the cost being picked-up by Australian State and Commonwealth governments. Consequently, of these two burdens, it is clearly preferable to err on the side of a regulatory burden rather than a health burden.

The discipline of Public Health Economics informs us that the latter burden can be huge. Consequently, it is suggested that a Health Impact Assessment (HIA) of any deregulation of these new techniques should be conducted to determine the latter cost. According to the CDC (Centres for Disease Control and Prevention) of the USA, a HIA “brings together scientific data, public health expertise, and stakeholder input to identify the potential health effects of a proposed policy, plan, program, or project. An HIA offers practical recommendations for ways to minimize risks and capitalize on opportunities to improve health.”[19]

Australia’s repeated experience with organisms that have been released into the environment (e.g. lantana, rabbits, cane toads) is that once they are released, they cannot be controlled or recalled. It is also Australia’s repeated experience that such organisms can cause enormous environmental and financial damage. It would therefore be prudent to ensure that any GMOs have been assessed for their environmental and health impacts using a regulatory system before they are released into the environment.

Harmonisation of regulation regarding new technologies

The recent OGTR Discussion Paper on options for regulating new technologies discussed possible deregulation of these new GM techniques and described how some countries have determined that organisms made using these new techniques are GM and other countries have decided that they are not. Many countries have yet to make a determination, but as reviews commissioned by the Austrian and Norwegian governments have concluded that there is insufficient knowledge about the risks of these new techniques, and that products derived from them should undergo a comprehensive case-by-case risk assessment, [20] it is likely that the EU will regulate these new techniques. Therefore, it is likely that there will be a patchwork of different regulatory requirements globally, with some of Australia's trading partners having regulatory requirements and not others.

Therefore, while some commentators have suggested that regulating these new organisms in Australia could lead to trade restrictions for Australia, it is also true that exempting these organisms from regulation could also lead to trade restrictions when Australia exports to countries that require these organisms to be regulated and labelled.

Of greater importance, however, as the OGTR Discussion Document has noted, "New Zealand has recently amended its legislation to clarify that techniques developed after 1998, including genome editing, are within the scope of regulation as GMOs". Consequently, the New Zealand Government has, by definition, determined that these new techniques are GM.

This occurred after New Zealand's Environmental Protection Authority (EPA) decided that two new breeding techniques did not produce GMOs and could go into New Zealand fields without any formal consultation or assessment. In a similar process suggested for Australia in the current OGTR Discussion Paper, certain traditional plant breeding techniques had been excluded from New Zealand's laws and the EPA decision effectively added to the exemption list. In a warning for any Australian process, the Sustainability Council of New Zealand appealed that decision in the New Zealand High Court and won[21]. The Court quashed the EPA's decision, agreeing with the Sustainability Council that only the Cabinet or Parliament can decide which techniques are exempt, and that the EPA had misinterpreted the law and failed to exercise proper caution.[23]

As Food Standards Australia New Zealand (FSANZ) sets food standards for New Zealand as well as Australia, it is unlikely that FSANZ could make a determination that organisms made using these new techniques are not GMOs, now that one of the governments it serves has decided that they **are** GMOs. Hence, it is highly likely that FSANZ will require these organisms to undergo a food safety assessment and be labelled. If the Review decides that these organisms are not GMOs, then one regulator of GMOs in Australia could contradict another regulator, leading to great uncertainty and confusion, and a possibly unworkable GMO regulatory system in Australia.

If there is a determination that these new organisms are not GMOs, then they will enter our food supply without any regulatory requirements, safety assessment or testing. They will also enter the Australian food supply without labelling so that consumers will have no choice as to whether they eat them or not, and it will be very difficult to be able to conduct epidemiological assessments into their long-term impacts. As described more fully above and in PHAA's policy on GM food, the PHAA finds this unacceptable.

In the PHAA's recent submission to the Technical Review of the Gene Technology Regulations 2001, the PHAA stated that it agreed with Option 2 (to regulate new gene technologies) in the recent OGTR Discussion Paper, and the OGTR's reasons for that option which are, in the OGTR's words:

> *"This option would give legal clarity as to which technologies are subject to regulation, and so provide certainty for researchers and industry. Some of the general arguments that could be made to support option 2 are:*

- *These techniques were developed very recently and, because there is not enough scientific understanding of how they work or possible unintentional effects, full regulatory oversight is needed to protect human health and safety and the environment.*
- *These techniques might unintentionally interfere with the functioning of an organism's genome, for example through unforeseen interactions between altered genes and native genes, or through the altered genes having unexpected effects on biochemical pathways. Because such effects might pose risks, the techniques should be regulated as gene technology.*
- *The precision of oligo-directed mutagenesis and site-directed nucleases is not established. The processes involved can give rise to unintended changes to the genome. Because such effects might pose risks, the techniques should be regulated as gene technology."*

In addition, this option will most closely align Australia with New Zealand, thereby preventing any conflict between the OGTR and FSANZ as to which GMOs to regulate.

It is important to reiterate that, due to the lack of experimental safety data on these new techniques, the risks of these new techniques, including gene drives, are unknown. Only once the risks have been measured can methods to manage the risks be determined. Consequently, it is premature to decide which techniques require regulation and which could be de-regulated. Such a decision should be deferred until the risks have actually been measured. In the meantime, they should be regulated in case they are later found to have adverse effects.

The risks of gene-drive organisms are particularly worrying, because these organisms are designed to push a genetic change throughout the "natural", non-GM population of those organisms, thereby potentially extinguishing the "wild-type" organism. Consequently, extra care should be taken with these organisms, particularly as Australia has many examples of organisms spreading widely, regardless as to whether they were intentionally released (e.g. lantana, cane toads, rabbits) or unintentionally released (e.g. fire ants).

Care is also needed because an organism that may be a pest in one country may be indigenous to another and an important contributor to the ecosystem there. For example, rabbits are a pest in Australia and cause considerable damage to farms and ecosystems here, but they are indigenous to much of Europe. If a gene drive to kill rabbits escaped from a laboratory in Australia to infect rabbits here and was then accidentally or purposely introduced into Europe, it could cause major ecological damage there.

In support of this, detailed evidence is given about what happened when a new virus accidentally escaped from confinement in Australia. Rabbit calicivirus (RCV) was imported into Australia to control rabbits. While it was undergoing contained field tests where rabbits were housed in confinement in cages on Wardang Island, several kilometres off the coast of South Australia, it escaped and infected rabbits on the mainland. Emergency containment procedures were then enacted to try to rid the mainland of the virus, but these failed. The virus subsequently spread across the entire country, showing how difficult it can be to contain new organisms and how quickly they can spread.

However, of even greater importance is the role that people can play in the spread of an organism once it has escaped. Consequently, any suggestions that gene-drive organisms could be easily contained, particularly once released into the environment in any way, should be regarded with considerable caution.

It is therefore recommended that gene-drive organisms be fully regulated.

RNA interference techniques

The risks of dsRNA techniques to human health and the environment have been thoroughly reviewed by Heinemann et al (2013).[22] These authors reviewed 100 publications and concluded that there was sufficient evidence that these techniques posed risks to human health and the environment. Evidence was presented that gene silencing may be inherited by the offspring of some organisms that eat the dsRNA, and

that dsRNA produced by these new GM crops could survive digestion in people and change how those people's genes are expressed. A review of how three government safety regulators (for either food or the environment) regulated the technology found that the safety of dsRNA molecules was usually not considered at all, and if it was considered in any way, these regulators, including the OGTR and FSANZ, simply assumed that any dsRNA molecules were safe, rather than requiring proof that they were safe. The authors found many scientific studies showing that these assumptions were incorrect.

The authors developed and provided a safety testing procedure for all GM plants that may produce new dsRNA molecules, as well as for products where the active ingredient is dsRNA. This is summarised in the following figure, and this submission supports that suggested process.

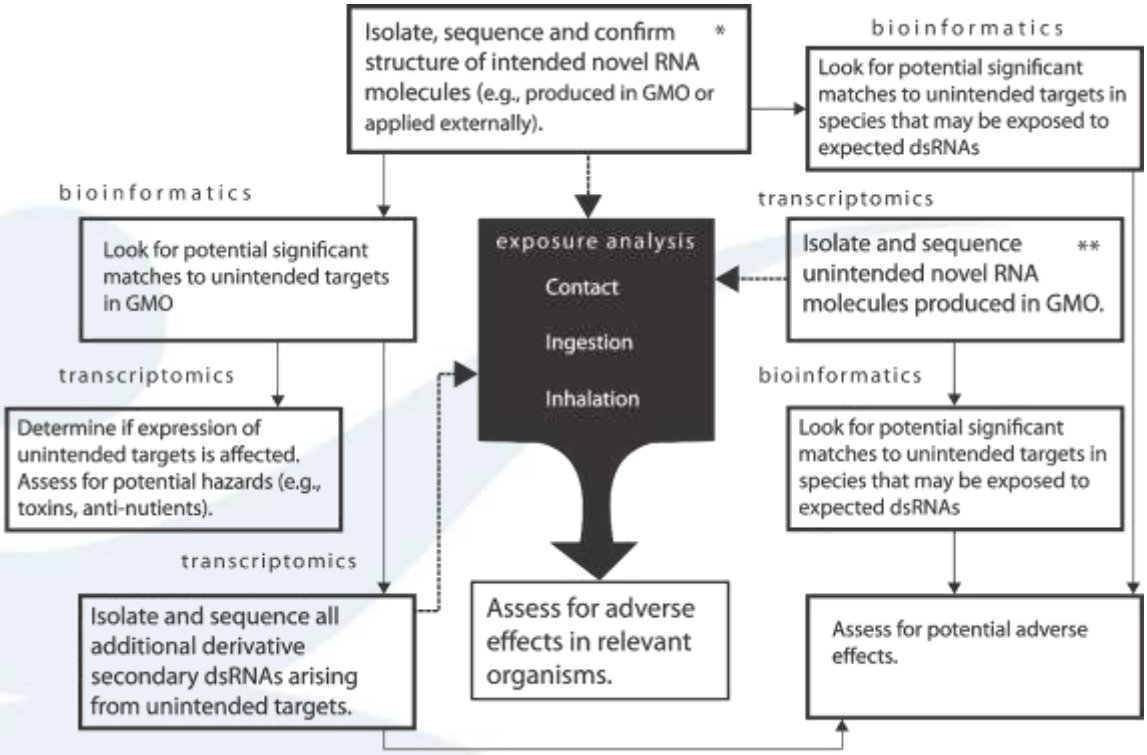

Figure 3. Sequential approach to assessing the potential for adverse effects arising from dsRNA-initiated modifications to organisms. Bioinformatics is used to capture known hypothetical targets of both intended and unintended dsRNAs so that potential adverse effects can be assessed. Transcriptomics is used to verify and characterise all relevant changes at the transcriptome level. Exposure analysis is used to design the appropriate kinds of organism-level tests for adverse effects. (*) Starting point for intentional introduction of dsRNAs; (**) starting point for unintended changes to the transcriptome. Bioinformatics assessments are inferences or judgments made based on predictions. Assessments made following exposure are based on data from experiments.

1. Current developments and techniques, as well as extensions and advancements in gene technology to ensure the Scheme can accommodate continued technological development

Current developments and techniques, as well as extensions and advancements in gene technology are extensively reviewed, above. As a result, this submission echoes the views of the 60+ scientist signatories to the ENSSER Statement (above), that these new techniques should be regulated at the strictest level of GMO regulation. While some argue that this would impede development, there is no evidence for that view.

2. Existing and potential mechanisms to facilitate an agile and effective Scheme, which will ensure continued protection of health and safety of people and the environment

The PHAA has long been concerned about the regulatory environment around GMOs. The following points from PHAA's policy on GM food are pertinent to this Review:

- The precautionary principle should be applied to GMOs.
- Thorough, independent experimental evidence should be used in safety assessments rather than assumptions. GM foods should not be considered safe until they have undergone long-term animal safety assessments utilising endpoints relevant to human health and conducted by independent researchers.
- A comprehensive monitoring and surveillance system should be instigated to track the effects of GM foods.
- Australian governments should impose a freeze on importing GM foods, growing GM crops commercially and patenting genetic resources for food until thorough independent research into their effects is undertaken.
- Publicly funded, independent research into the effects of GM crops should be undertaken, and GMOs should be made freely available to any researcher researching agronomic, environmental or health aspects of GM crops.
- There should be a stronger public health presence in the staff, advisory committees and Boards of the OGTR to improve safety assessment procedures.

In addition, "null segregants (offspring of GMOs that have not inherited the genetic modification or a trait from genetic modification) should be regarded as GMOs because it cannot be assumed that there have been no changes in genetic material or genetic expression elsewhere in the organism unless both matters are thoroughly checked. Therefore, these organisms should be regulated as GMOs.

3. The appropriate legislative arrangements to meet the needs of the Scheme, now and into the future, including the Gene Technology Agreement

3.1 Scientists' access to materials to test

GMOs are currently not freely available to researchers to be able to conduct independent safety assessments or environmental impact assessments. For example, if researchers try to buy seeds for GM crops from a seed merchant to conduct a health and safety assessment, they are required to sign a legal agreement stating that they will not undertake research on the seeds or give them to anyone else to do research on. This severely impedes research into the safety of GMOs by restricting safety assessments to only those researchers who have been approved by the GM company, leading to a potential bias towards reporting findings that are favourable to the industry and avoiding the reporting of adverse findings. Note that there are numerous scientific papers describing how research conducted by pharmaceutical companies and their affiliated researchers tends to report positive outcomes while independent researchers tend to find adverse effects. Often, adverse effects of a new pharmaceutical drug only become apparent once this independent research is done. It is therefore recommended that legislation be enacted to make it a condition that the GMO to be made freely available to any researcher researching agronomic, environmental or health aspects of GMOs before any commercial release of a GMO. This should apply for GMOs developed under existing or new techniques. If required, the OGTR can have oversight over such research.

3.2 Safety data

There are numerous examples where safety issues of various pharmaceutical drugs only came to light when the company's raw data were re-analysed by independent researchers. The case of Vioxx, described above, is one example. Despite numerous clear examples of adverse effects lying hidden in plain sight in company data, there is no requirement for any safety or environmental data, used to justify the company's position that a GMO is safe, being released for independent scientists to look at. While some argue that such data are given to government regulators for scrutiny.

As a result of numerous examples from other areas of research, it is recommended that it be mandated that all safety data generated by a GM company about a GMO be given to government regulators, that those regulators be required to analyse the data, and that the data be made freely available on-line to all interested independent researchers at the time that an application is made to a government regulator.

3.3 Oversight of FSANZ and the OGTR

FSANZ and the OGTR are the principle agencies that regulate GMOs in Australia. Under the Act governing FSANZ, the main role of FSANZ is to protect public health and safety. However, its other roles include promoting fair trade, trade and commerce and consistency between domestic and international concerns. These conflicting roles could be regarded as generating a conflict of interest within FSANZ and diluting its role to protect public health and safety. Support for this view comes from FSANZ's own safety assessment documents for GMOs, where trade concerns are frequently considered in what is supposed to be a safety assessment document. It is therefore recommended that FSANZ's role in protecting health and safety be made real and effective by removing the requirement of FSANZ to promote fair trade, trade and commerce and consistency between domestic and international concerns.

In addition, oversight of FSANZ is provided by its Board. The Board has been criticised in the past for being weighted towards those with strong past or present affiliations with the food industry[23], which could be considered to be a bias towards industry input and away from independent advice from public health experts. It is therefore recommended that it be compulsory for every Board member to disclose any potential conflict of interest (COI) on the FSANZ website. It is also recommended that it be mandated that the Board of FSANZ contain representatives from several public health bodies in order to obtain free and unfettered advice from independent experts. For example, from a State Government Communicable Disease Control branch (for advice on food-borne disease), the Public Health Association of Australia, the Dietetics Association (for advice on nutritional matters), a University-employed toxicologist, a member of the Australian Faculty of Public Health Medicine (AFAPHM, for advice on public health medicine), and the Australian Epidemiological Association. A medical representative from e.g. the Australian Medical Association (AMA) and a consumer representative should also be included. It is further recommended that such independent advisors constitute the majority of the Board of FSANZ.

Meanwhile, the OGTR obtains advice mainly from its committee, the GTTAC. While the role of the OGTR is to assess the potential effects of GMOs on health and the environment, this Committee tends to be heavily weighted towards those who do genetic engineering (some of whom are likely to have strong vested financial interests in deregulating the technology), and very underweighted towards people with qualifications or expertise in public health or environmental health. For example, out of 19 members in 2016, only one was deemed to have expertise in public health. Therefore, there appears to be insufficient expertise in the GTTAC to undertake a robust public health risk or environmental health assessment. It is therefore recommended that it be compulsory for every member of GTTAC to disclose any potential COI on the OGTR website. It is also recommended that it be mandated that the GTTAC contain representatives from several public health bodies in order to obtain free and unfettered advice from independent experts. For example, from a State Government Communicable Disease Control branch (for advice on the

communicable disease potential of GMOs), the Public Health Association of Australia (PHAA), a University-employed toxicologist, and a member of the Australian Faculty of Public Health Medicine (AFAPHM, for advice on public health medicine). A medical representative from e.g. the AMA, as well as University-employed environmental scientists should also be included. It is further recommended that such independent advisors constitute the majority of the GTTAC.

3.4 Better safety assessments of GMOs

Currently, FSANZ requires no animal or human studies in order to make a determination that a GMO is safe for release into the environment or to enter the Australian food supply. Moreover, as described above, the quality of any animal studies used to support claims of safety of GM crops has been highly criticised as being poorly conducted, largely undertaken by vested interests, and lacking in endpoints that are relevant to human health. There is therefore a lack of evidence that GMOs are safe, particularly compared to the standards required of pharmaceutical drugs. It is therefore recommended that regulation of GMOs to enter the food supply be aligned with the much better standards of the European Union, which now requires 90 day sub-chronic rat toxicology studies to be undertaken for GMOs that are to enter their food supply. We further recommend longer, chronic studies to better reflect the Australian population's exposure to GMOs. It is further recommended that those rat studies actually meet OECD guidelines and that animal testing be required to assess all four major areas of concern, being allergies, reproductive outcomes, toxicology and cancer. If the GMO passes these tests, it should be further tested in basic human trials before release. This is particularly the case for GMOs that will enter the Australian food supply, because 24 million Australians would then likely be exposed to the GMO and to any adverse effects from that GMO.

3.5 Regulation of dsRNA technologies

It is recommended not only that dsRNA technology be regulated by the OGTR and FSANZ, but that the technology be regulated according to the evidence-based methods described by Heinemann et al (2013), above.

3.6 Regulation of DIY kits

It is recommended that the development of GMO DIY kits within Australia be regulated by the OGTR. It is further recommended that the importation of GMO DIY kits into Australia be regulated by the OGTR and AQIS.

3.7 Labelling

GMOs made using existing and future techniques should be labelled for three reasons. First, as described above, labelling allows GMOs to be traced and monitored in the environment and in the food supply, thereby allowing epidemiological studies to be undertaken. This allows early detection of any adverse effects of a GMO which in turn allows for the speedy withdrawal of that GMO from the environment and/or food supply, which will minimise harm to the population and costs to the State and Commonwealth governments of Australia. Second, it permits regulatory oversight of GMOs. Third, labelling allows for consumer choice. Allowing choice is important to maintain trust in the Australian food supply. Furthermore, labelling should be improved to match the standards of the European Union, where oil from GM crops is also labelled. In fact, as PHAA's policy states, all ingredients (including refined), originating from GMOs (including micro-organisms) should be labelled, as should products such as milk, meat and eggs from animals fed GM fed.

3.8 A surveillance system

It is recommended that a surveillance system be established in Australia to monitor the effects of GMOs in the environment and in the food supply. In this way, early detection of any adverse effects of a GMO can be

made, which in turn allows for the speedy withdrawal of that GMO from the environment and/or food supply, in order to minimise harm to the population and the financial burden to Australian State and Commonwealth governments.

3.9 Heath Impact Assessment (HIA)

A Health Impact Assessment (HIA) by a health economist into the consequences of any deregulation of these new GM techniques should be conducted to determine the true costs of any deregulation.

3.10 States' rights

Currently, individual States in Australia are able to place a moratorium on the commercial planting of a GM crop for economic reasons. This should be allowed to continue and be expanded to allow a State to conduct its own risk-based assessment as to whether a given GMO should be released in the State for whatever reason the State thinks suitable, such as particular local environmental conditions that the OGTR may not have considered.

4. Funding arrangements to ensure sustainable funding levels and mechanisms are aligned with the level of depth of activity to support the Scheme

While the Commonwealth government has allocated money to the research and development of GMOs, e.g. through the CSIRO, we are not aware of any money that the Commonwealth Government has allocated towards researching the health and environmental impacts of GMOs. We believe that the Commonwealth Government should, through NHMRC and ARC grants at least, allocate specific funds for independent research into the health and environmental impacts of GMOs. For health research, all four major areas of concern, should be researched, being allergies, reproductive outcomes, toxicology and cancer.

Conclusion

The PHAA welcomes the opportunity to provide input to the 2017 Review of the National Gene Technology Regulatory Scheme. The PHAA is the principal non-government organisation for public health in Australia with approx. 1900 members representing over 40 professional groups and an evidence-based policy on GM foods. The PHAA has drawn heavily upon that policy to write this submission.

The PHAA would like to particularly highlight the following points:

- Food regulation should aim to protect public health and provide information to consumers.
- It is more important to protect public health than promote commercialisation.
- The precautionary principle should be applied to GMOs.
- These new techniques are in their infancy and are constantly evolving. There is uncertainty and debate about how these new techniques actually work. Consequently, any decision that is made now about the safety of these new techniques is based on opinion, assumption and conjecture, rather than evidence. The new techniques are imprecise, can cause unpredictable outcomes and need thorough safety assessments. They result in organisms that are GMOs. For all these reasons, the techniques and the GMOs that they produce should be regulated. DIY kits should also be regulated. dsRNA techniques should be regulated according to recommendations made in Heinemann et al (2013).
- GMOs should be made freely-available to any researcher researching agronomic, environmental or health aspects of a GMO.

- All safety data generated by a GM company should be given to government regulators, those regulators should be required to analyse it, and the data should be made freely available on-line to all interested independent.
- FSANZ's role in protecting health and safety should be made real and effective by removing FSANZ's conflicting requirement to also promote fair trade, trade and commerce and consistency between domestic and international concerns. The majority of the Board of FSANZ should consist of experts who are independent of vested interests.
- The majority of the members of the GTTAC of the OGTR should consist of people who are experts in determining the effects of a GMO on health and the environment, and independent of vested interests.
- Government regulators should use thorough, independent experimental evidence in assessments rather than assumptions. These new organisms should not be considered safe until they have undergone long-term animal safety assessments that follow OECD Guidelines, utilizing endpoints relevant to human health and conducted by independent researchers. These studies should be followed by limited testing on people if the GMO is destined for human consumption.
- A monitoring and surveillance system should be instigated to track the effects of GMOs.
- A Health Impact Assessment (HIA) by a health economist into the consequences of any deregulation of these new GM techniques should be conducted to determine the true costs of any deregulation.
- GMOs made using existing and future techniques should be labelled in order for them to be traced, monitored and to allow for epidemiological studies into them. Labelling also allows for regulatory oversight and allows for consumer choice which maintains trust in the food supply.
- States' rights to place a moratorium on the commercial release of GMO into the environment should remain and be strengthened.
- Regulating the technology does not mean that Australia will suffer from trade disruptions. Rather, Australia will then be in general agreement with the laws of New Zealand. FSANZ regulates food for both Australia and New Zealand and different definitions of what constitutes a GMO between those two countries would put it in a difficult position.
- The Commonwealth Government should allocate funding for independent research into the health and environmental impacts of GMOs.

Please do not hesitate to contact me should you require additional information or have any queries in relation to this submission.

Michael Moore BA, Dip Ed, MPH
Chief Executive Officer
Public Health Association of Australia

29 September 2017

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