CropLife AUSTRALIA

*Representing **the best** of the plant science industry*

CropLife submission to Updating Gene Technology Regulation in Australia | Consultation Regulatory Impact Statement

21 February 2018

1 INTRODUCTION

CropLife Australia is the national peak industry organisation representing the agricultural chemical and plant biotechnology sector in Australia. CropLife represents the innovators, developers, manufacturers and formulators of crop protection and agricultural biotechnology products. CropLife's membership is made up of both patent holding and generic Australian and international and small and large companies and accordingly, advocates for policy positions that deliver whole of industry benefit. The plant science industry provides products to protect crops against pests, weeds and diseases, as well as developing crop biotechnologies that are key to the nation's agricultural productivity, sustainability and food security. The plant science industry is worth more than $17.6 billion a year to the Australian economy and directly employs thousands of people across the country. CropLife Australia is a member of CropLife Asia and part of the CropLife International Federation of 91 CropLife national associations globally.

CropLife welcomes the opportunity to provide feedback on draft amendments to the Gene Technology Regulations as detailed in the Consultation Regulatory Impact Statement (RIS) 'Updating Gene Technology Regulation in Australia', released for public comment in November 2017.

CropLife supports the overarching objective of the Technical Review to keep the Gene Technology Regulations up to date with advances in technology and increased scientific understanding. It was with this objective in mind that CropLife strongly supported 'Option 4' in the 2016 Discussion Paper.

The option supported by CropLife reflected its views that *plant varieties developed through the latest breeding methods should not be differentially regulated based on the techniques employed during their development if they are similar to, or indistinguishable from varieties that could have been produced through earlier breeding methods.*

The focus of this submission is to provide comment on the Exposure Draft Regulations as detailed in the Consultation RIS that aim to implement 'Option 3' from the 2016 Discussion Paper in addition to improving clarity regarding the regulatory status of RNAi and of organisms that are not themselves GMOs but have been derived from GMOs (null-segregants).

CropLife **strongly recommends** that the Exposure Draft Regulations be viewed only as an interim solution until the completion of the 2017 Review of the National Gene Technology Regulatory Scheme, in which CropLife has advocated for changes to policy settings that will enable the Gene Technology Regulator to implement 'Option 4' from the 2016 Discussion Paper.

2 SUPPORTED OPTION

Option 3

CropLife supports **Option 3** in the Consultation RIS – *amend the GT Regulations with some but not all draft amendment proposals*.

CropLife is generally supportive of all the proposed elements of the Exposure Draft Regulations (Option 2), however, we do believe there are some elements that need further consideration to achieve the desired outcome of providing legal clarity.

Elements in Draft Gene Technology Amendment (2017 Measures No. 1) Regulations 2017 that require further consideration

Schedule 1 Clause 30

Add: *Introduction of RNA into an organism, if:*

a) the RNA cannot be translated into a polypeptide; and
b) the introduction of the RNA cannot result in an alteration of the organism's genome sequence; and
c) the introduction of the RNA cannot give rise to an infectious agent.

CropLife is unsure why the Regulator is saying that topical (exogenously applied, *ex planta*) RNA would involve "introduction of RNA into an organism"? The term 'introduction' is often used to describe the insertion of a gene into the genome, so it may be confusing to use that term for topical applications. CropLife's position has always been that topical application of RNA is a biological treatment that is not passed to the next generation.

Schedule 1 Clause 31

Insert: *Schedule 1B – Organisms that are genetically modified organisms*

Organisms that are genetically modified organisms	
Item	**Description of organism**
1	An organism that has had its genome modified by oligonucleotide-directed mutagenesis
2	An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was added to guide homology-directed repair

The proposal to regulate SDN-2 and ODM as GMOs in the new Schedule 1B remains a fundamental point of disagreement between CropLife and the Regulator. Induced mutagenesis, and transfer of DNA between compatible species, whether these processes are facilitated by a repair template, or are achieved otherwise, by methods with established history of safe use, should not form the basis for regulatory differentiation.

A discriminatory application of regulation would result in a situation where certain methods of gene technology are excluded from the scope of regulation on the basis of their history of safe use, while regulation would be applied to methods that result in even more precise and more predictable outcomes than ever achievable with earlier excluded methods.

In CropLife's view, this is inconsistent with the principles of proportionate and science-based regulation. Furthermore, such discrimination between various induced mutagenesis tools and genetic transfer methods, does not help in addressing the potential risks associated with the resulting organisms. In our understanding, identical outcomes could be achieved with the application of different methods, some of which are more recent and more efficient than earlier ones. It is not scientifically justified to regulate the process on the basis of it being more recent while not considering the outcome of the method – the resulting product.

CropLife's view is that the use of a template as part of a genome editing technique should not be used as a distinguishing factor for deciding whether or not a product of plant breeding innovation should be included in Schedule 1. The decision as to whether or not an organism is regulated as a GMO should reflect what changes have been made in the final product and whether it is likely to present new or increased risk for adverse effects to human health and the environment.

Changes introduced using SDN-2 and ODM are in principle comparable to the outcomes of techniques listed in Schedule 1A, Items 1, 2, 3, 4 and 10.

Schedule 1 Clause 32

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

CropLife submits that in addition to site-directed nucleases, product developers may use recombinases or other DNA modifying enzymes such as DNA methylases or deaminases (used for base editing) where the intended effect may be the same as an SDN-1 based mutation.[1]

CropLife supports the intent of this amendment, but **recommends** the Regulator focus on more flexible and futureproof language, rather than on the name of the tool as this may lead to the ability to better deal with future developments that affect double-stranded DNA breaks, which are repaired by non-homologous end-joining.

Alternatively, the objective of this Clause could be implemented by specifically listing site-directed mutagenesis as a technique that is not gene technology in Schedule 1A. This Clause could then be amended to remove the specific reference to site-directed nuclease and focus on the intent of the modification to the product.

[1] See, for example: Bevan, M. W., et al (2017). Genomic innovation for crop improvement. *Nature*, *543*(7645), 346; Kuscu, C., et al (2017). CRISPR-STOP: gene silencing through base-editing-induced nonsense mutations. *Nature methods*, *14*(7), 710; and Bernardo, R. (2017). Prospective targeted recombination and genetic gains for quantitative traits in maize. *The plant genome*, *10*(2).

Schedule 1 Clause 33

Add: *Schedule 1 (at the end of the table)*

8	*An organism that is descended from a genetically modified organism (the initial organism), but which has not inherited any traits that occurred in the initial organism because of gene technology.*
9	*An organism that was modified by gene technology but in which the modification, and any traits that occurred because of gene technology, are no longer present.*
10	*Agrobacterium radiobacter strain K1026 (known as NoGall).*
11	*Pasteurella multocida strain PMP1 (known as Vaxsafe PM).*

New Items 8 and 9 to Schedule 1 ('Organisms that are not genetically modified organisms') raise questions for CropLife concerning the definition used for 'null-segregants' involving the removal of the GM trait from the final organism. The language 'occurred because of gene technology' may be open to interpretation. For example, a targeted genome modification achieved via application of SDN-1, might be argued as being a trait that occurred because of gene technology. This is particularly problematic because site-directed mutagenesis is not included in the list under Schedule 1A - Techniques that are not gene technology. Language that calls out the absence of genetic material developed using gene technology might be better and less easy to misinterpret.

CropLife suggests that null-segregants in the context of genome editing are plants that contain targeted genome modification but do not contain a SDN insert[2]. Generation of such plants occurs through the same inherent biological mechanisms (genetic segregation and genetic recombination) as used to obtain null-segregants in breeding with transgenes or breeding with native (endogenous) genes.

CropLife further believes that the amendments to the Regulations regarding null-segregants may lead to confusion as currently drafted as they could be interpreted to apply only to null segregants derived from older 'traditional' techniques for creating transgenic crops, and may not capture null-segregants derived from newer plant breeding innovations.

Use of trade names in regulations

CropLife suggests that the use of trade names, such as 'NoGall' and 'Vaxsafe PM' in Regulations sets a bad precedent. In particular, if these organisms are marketed under different trade names by different companies, it may lead to confusion concerning their regulatory status. It is unusual for Regulations to specifically list the trade names of products.

[2] An 'SDN insert' is defined as a stably integrated DNA sequence derived from the plasmids or linear DNA fragments used to deliver genetic elements necessary to trigger targeted DNA single or double-strand breaks or used otherwise during the transformation process.

Schedule 2 Clause 1

Repeal *Schedule 1 (table item 1)*

CropLife would have preferred the Regulator maintain Schedule 1 Item 1 of the Gene Technology Regulations 2001 as it appears to be consistent with the direction that other countries, such as Argentina, are heading towards for regulation of genome edited crops.

CropLife submits the repeal of this Item may prove problematic as it could lead to broader confusion and lack of legal certainty of whether certain mutagenic techniques are properly excluded from regulation under Schedule 1A.

CropLife submits that site-directed mutagenesis could be specifically included in Schedule 1A as a technique that is not gene technology.

3 ADDITIONAL COMMENTARY

The assumptions used to differentiate between different categories of site-directed nucleases are worth exploring further as the draft Regulations appear to be relying on the use of 'template-guided repair' to distinguish between SDN-1, SDN-2, and SDN-3.

SDN-2 and SDN-3 applications utilise a DNA repair template to facilitate targeted edits or targeted insertions, respectively, through homology-directed repair mechanisms. SDN-2 and SDN-3 repair template driven applications are facilitating a broad range of potential outcomes, from precise targeted mutations, to integration of sequences (partial or complete regulatory and/or coding sequences, or combinations thereof) from same or cross compatible species to transgenes.

This broad range of outcomes is defined by the nature of the repair template used but not by the category of site-directed nuclease. Furthermore, we note the overlap between the potential outcomes achievable by induced mutagenesis techniques (as currently listed in Schedule 1A), the outcomes resulting from application of SDN-1 (proposed for inclusion in Schedule 1) and certain SDN-2 applications depending on the repair DNA template used.

We also note the potential overlap between outcomes currently included in Schedule 1, Item 6 and certain applications of SDN-2 and SDN-3 depending on the choice of the repair DNA template used. Because of the noted overlaps between the outcomes of different SDN applications, CropLife believes that an alternative grouping for inclusion and exclusion from regulation based on the outcomes of the repair template used rather than the currently proposed differentiation based on the use of repair template would achieve to a greater extent the stated objective of the Regulator and ensure the proportionate and coherent application of the regulations.