THIRD REVIEW OF THE NATIONAL GENE TECHNOLOGY REGULATORY SCHEME

https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-gene-tech-consultation.htm

Submission on the Consultation Regulation Impact Statement (RIS) and Explanatory Paper

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Declaration of interests: Dr O'Sullivan and Prof Rasko are members of the Gene Technology Technical Advisory Committee (GTTAC). Prof Rasko is the Chair of GTTAC and Dr O'Sullivan is also a member of the Gene Technology Ethics and Community Consultative Committee (GTECCC).

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I. INTRODUCTION

The following information been abstracted from the Consultation Regulatory Impact Statement (RIS) for the purpose of providing readers of this submission the context in which the submission points in this document are made.

ABSTRACT FROM THE CONSULTATION RIS:

The Consultation Regulatory Impact Statement (RIS) describes three options:

- **Option A:** Status quo – no changes to the current scope or activities of the Gene Technology Regulator

- **Option B**: Risk-tiering model – dealings with GMOs would be categorised according to their indicative risk

- **Option C:** Matrix model – the nature of the dealing with the GMO would be the determinative factor for categorisation

Options B and C propose amendments to achieve the objectives of the reform. Option A is the base case, and is used to highlight the impacts of keeping the current regulatory system.

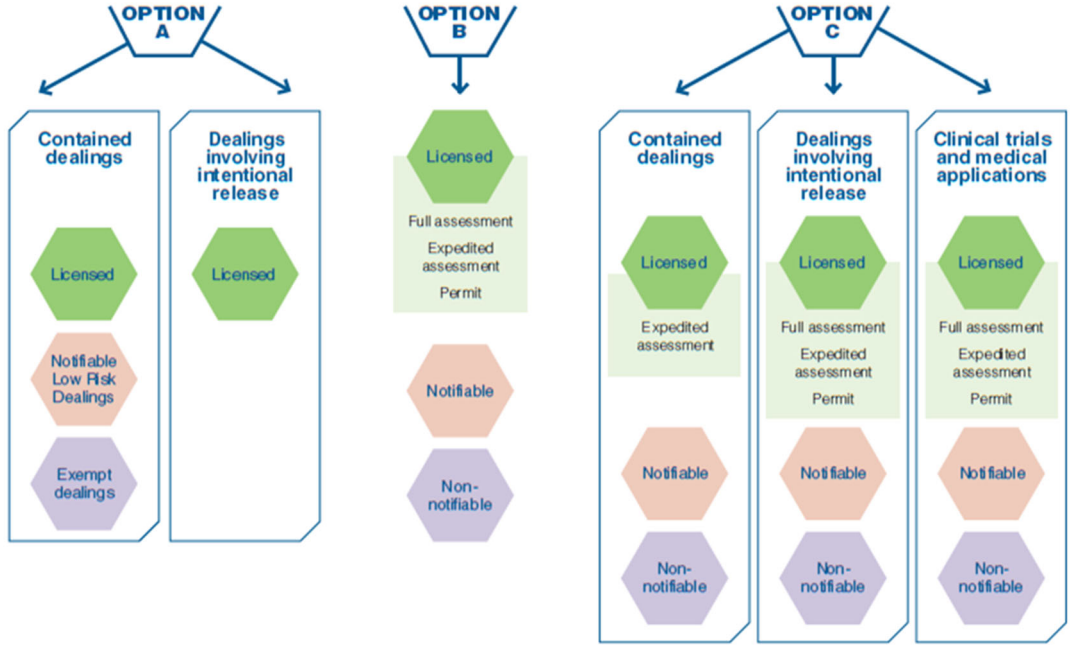
Note: A table comparing Options A, B and C in relation to whether the options address the policy problems identified in the Consultation RIS (section 4) and accomplish the objectives of government action (section 5) is provided in the Consultation RIS itself and from which it has been abstracted and placed in this document below.

II. THE OPTIONS AS PROVIDED IN THE CONSULTATION RIS

A. and B. below have been abstracted from the Consultation Regulatory Impact Statement (RIS) for the purpose of providing readers of this submission the context in which the submission points in this document are made.

ABSTRACT FROM THE CONSULTATION RIS:

A. Pictorial representation of the authorisation pathways under the three options presented in the Consultation RIS.



B. Table summarising whether the presented options in the Consultation RIS address the policy problems and achieve the objectives of government action

	Policy problem – The Scheme responds slowly to advances in the field of gene technology (Review recommendation 4)	**Policy problem –** Authorisation pathways in the GT Act are no longer suitable for new GMO applications (Review recommendation 9)	**Policy problem –** The Scheme is no longer risk proportionate (Review recommendations 9 and 10)	**Objectives of government action achieved**
Option A (status quo)	**Not addressed**	**Not addressed**	**Not addressed**	**Objective 1 achieved –** protection of safety of humans and the environment
Option B (Risk tiering model)	**Fully addressed –** Both Options B and C introduce the same amendments to the definitions in the GT Act	**Fully addressed –** the new authorisation pathways classify GMO dealings based on their indicative risk	**Fully addressed –** both Options B and C introduce streamlined authorisation pathways for dealings that ' are low risk and/or regulated by other product regulators	**All objectives achieved**
Option C (Matrix model)		**Partially addressed –** the introduction of a new overarching category for clinical trials and medical applications improves the categorisation of GMO dealings for medical purposes. However keeping the overarching categories of contained dealings and dealings involving the intentional release of a GMO into the environment makes the classification of certain GMOs dealings ambiguous	Both Options allow for the prompt reclassification of a GMO dealing into a new authorisation category in response to new information about risk	**All objectives achieved with the exception of objective 5** as the regulatory framework would not be simplified by would increase in complexity

III. ANSWERS TO THE QUESTIONS POSED IN THE CONSULTATION RIS

1. Key consultation questions – Option A

- ***Q1. Are there additional impacts of Option A that need to be taken into account?***

  A. No comments to add.

- ***Q2. Please provide further information, including quantitative data, on the costs associated with maintaining the status quo.***

  A. Examples of just some of the costs of maintaining the status quo would be the savings (outlined in the answer to Q7 below) that would be lost by not implementing Option B. Another example, would be the reduction in workflow and opportunity for exercising science innovation (outlined in the answer to Q8 below).

- ***Q3. To what extent would maintaining the status quo stifle innovation?***

  A. Greatly compared to Options B or C. See also the answers to Q2, Q7 and Q8.

- ***Q4. What are the benefits of maintaining the status quo?***

  A. There are no benefits.

2. Key consultation questions – Option B

- ***Q5. Would Option B address the identified policy problems?***

  A. Yes

- ***Q6. Please outline any additional impacts of Option B that have not been identified in the current impact analysis.***

  A. None

- ***Q7. Please provide further information, including quantitative data, on any costs and benefits to your organization associated with Option B.***

  A. Under Option B, licence applicants would not need to consult internally and externally (as is currently required under the status quo Option A) to make a decision about which kind of application to make: DNIR or DIR. For each licence application where this is not clear, Option B would save at least one round of organizational consultation prior to the application being commenced.

  To estimate the potential benefits of this we need to consider that IBCs and the OGTR are often consulted in pre-application decision-making processes. If, at a minimum, two persons from the IBC and one person from the OGTR contribute one hour of their time to this, there would be a conservative minimum time and money saving of 3 person hours.

  Consultations such as these involve staff with different levels of expertise, responsibility, authority and remuneration. At an unlikely minimum of $60/hour, 3

person hours would amount to $180. If we add in the necessary steps involved in documenting (3 person hours) and communicating (3 person hours) the details, this process will cost an unlikely minimum of $540 and 12 person hours. If this process is discussed for 10 minutes by an IBC which has 6 members for the purpose of noting or ratifying it (which may be an organizational requirement automatically triggered by the fact that a decision is being made regardless of its utility) it will consume a minimum of $60 (=6 x $10/member) and 1 person hour (=6 x 10 minutes) of the collective IBC members' salaried time (noting that most IBC members fulfil their IBC duties from within their own working time and are not paid extra for this, although they do gain other career related benefits). This will bring the unlikely minimum cost to $600 (=$540+$60) and 13 (=12+1) person hours for making a decision regarding what is not a very useful delineation under the current regulatory system (as the review alludes to in providing Option B).

The estimates above are very conservatively low. They do not take any account of at least three related additional activities that would be necessary to any pre-application decisions: (a) '*to and fro'* communications, (b) '*re-work'* in finalizing a decision, and (c) '*lost productivity*' in other areas due to time taken out to address pre-application '*which-kind-of-application-to-make'* decisions.

If we add a conservative factor of 10% ($60) for each of the three related activities (a-c above), the cost becomes $780 (=$600+$180) and 14.3 (=13+1.3) person hours. If only 20% (i.e., 126) of the 632 licences for Dealings Not Involving Intentional Release (DNIRs) currently listed on the GMO record (as of 11 March 2021) require such pre-application-commencement consultations, the cost becomes $98,280 (=$780 x 126) and 1,802 (=14.3 x 126) person hours before an application has even commenced.

The figures above are very conservative and likely to be higher. Although most likely to arise in the context of DNIR applications, they do not take account of pre-application-commencement decision making processes in relation to licences for Dealings Involving Intentional Release (DIRs).

For the reasons above, it is clear that Option B would provide benefits in not having to engage in these processes. Option B would not result in any reduction in risk management as the OGTR could assign the appropriate licence under it.

- ***Q8. How might Option B promote science innovation?***

A. The answers to Q7 show how Option B can reduce wasteful activities and costs that detract from efforts put into science innovation. There are other ways in which Option B will promote science innovation. For example, it will better enable the Gene Technology Regulator to exercise efficiencies and risk proportional regulation based on accumulating experience and knowledge regarding particular types of GMO dealings. This will enable better communication between the Regulator and the regulated community which will promote better workflow and science innovation.

3. Key consultation questions – Option C

- ***Q9. Does Option C address the policy problems identified in the Consultation RIS?***

A. Option C does not address the policy problems as well as Option B.

- ***Q10. Please outline any additional impacts of Option C that have not been identified in the current impact analysis.***

  A. The impacts of Option C have been identified.

- ***Q11. Please provide further information, including quantitative data, on the costs and benefits to your organisation associated with Option C.***

  A. Option C has some similar problems to maintaining the status quo (Option A). It would require similar decision making processes with additional complexities as outlined in the Consultation RIS. Therefore the costs of Option C would be similar (and possibly greater than) the costs of not implementing Option B (as outlined in the answer to Q2 in relation to Option A). Please see the answer to Q7 for an example of potential cost-savings of Option B.

- **Q12. Please outline any risks or additional considerations that need to be taken into account with regard to this option.**

  A. No comments to add.

- ***Q13. Does Option C promote science innovation? If so, how?***

  A. Not as well as Option B.

4. Key consultation questions - Overall

- ***Q14. In your opinion, what Option offers the greatest net benefit? Please provide reasons supporting your choice.***

  A. 1. Option B will provide the greatest net benefit. Provided its implementation is structured properly to meet needs specific to different types of gene technology applications (e.g., agricultural, medical), it will provide a simpler, more flexible, responsive and risk proportionate regulatory system without compromising risk management. It will enable the regulatory system to respond better to advances in science, technology and development. This will have greater net benefits across all parts of society.

  The reasons for supporting Option B are:

  - (i) It does not require licence applicants to decide what kind of application to make based on whether the dealing is 'contained', 'released', a 'clinical' or 'non-clinical' application, all of which can be difficult to decide when work does not fit neatly into one of those categories.
  - (ii) Within the licenced category, Option B does not prevent the OGTR from using sub-categories it considers relevant to stratifying risk management (such as 'contained', 'released', 'clinical' or 'non-clinical'). However, the vast majority of applications will likely be able to be stratified by the OGTR into whether they are clinical or nonclinical with a potentially very small grey zone.
  - (iii) It allows the Regulator to adjust licence requirements based on growing knowledge and experience with each type of GMO and the situation it is used in.

- (iv) It allows, where appropriate, one licence to be issued that covers a number of development and application processes that can be updated as the work progresses.
- (v) This means there will be more opportunity for researchers and developers to conceive at the beginning of their work one whole work plan from development to application in the field.
- (vi) It will not prevent multiple licence applications where there are such different types and levels of risks at different stages that would warrant a separate licence. For example, work with a GM pathogenic organism to elucidate its mechanism of infection and isolate and conduct preclinical studies on pathogenic materials from it could be conducted under one licence whereas clinical studies of therapeutic potential could be conducted under another licence.

2. Overall, the proposed changes to the gene technology regulatory system and definitions should be designed to be sufficiently able to satisfactorily address complex issues and questions as they arise, such as issues related to mitochondrial donation and potential for inheritable genetic modification; as well as possibilities for the production of sperm or ova from induced Pluripotent Stem Cells (iPSCs).

IV. ANSWERS TO QUESTIONS POSED IN THE EXPLANATORY PAPER

5. Key consultation questions - Definition of gene technology

- ***Q15. Does the proposed definition of gene technology address the issues identified?***

A. The issues identified in the Explanatory Paper are that the current definition of gene technology may not cover the creation of new genetic materials or new organisms or the application of new epigenetic marks.

The current definition is:
*'**gene technology** means any technique for the modification of genes or other genetic material, but does not include:*
a. sexual reproduction; or
b. homologous recombination; or
c. any other technique specified in the regulations for the purposes of this paragraph.'

The example proposed definition in the Explanatory Paper is:
*'**gene technology** means any technique:*
*a. for the **creation** or modification of genes or other genetic material; or*
*b. **specified in the regulations** for the purpose of this paragraph but does not include:*
c. sexual reproduction; or
d. homologous recombination; or
e. any other technique specified in the regulations for the purposes of this paragraph.'

The Explanatory Paper also notes that the '*inclusion of any technique in the regulations would continue to require consultation, the agreement of the Forum and Parliamentary oversight. This process would ensure regulatory creep is avoided*.'

The example proposed definition in the Explanatory Paper along with having in place the ability for the Regulator to make determinations and for techniques to be included in the regulations would address the issues identified.

There should also be capacity to support international harmonisation of definitions where possible even though this may be challenging where the Australian system differs from other international regulatory systems.

Please note also the answer A2 to Q14 above regarding ensuring ability to address complex issues.

- ***Q16. Does the proposed definition of gene technology introduce any new issues?***

A. Under the current scheme the proposed definition (along with having in place the ability for the Regulator to make determinations) does not seem likely to introduce new issues for some time. The Regulations have the capacity to be used to include and exclude new techniques and organisms as they arise (e.g., RNA interference is excluded under Schedule 1A of the GT Regulations).

- ***Q17. Are there any other desirable changes to the definition of gene technology that would address the issues identified in the Third Review and the objectives agreed by the Forum (e.g., to increase flexibility, future-proof the legislation, etc.)?***

A. Please note the answer A2 to Q14 above regarding ensuring ability to address complex issues.

- ***Q18. Would interpretative guidance on the definition of gene technology issued by the Regulator be adequate, or should the Regulator have the capacity to make binding determinations that something is or is not a technique for the modification of genes or genetic material?***

A. The Regulator should have capacity to make binding determinations. The definitions in the Regulations need regular updating as technology and applications advance.

6. Key consultation questions - Definition of GMO

- ***Q19. Does the proposed definition of GMO address the issues identified?***

A. The issues identified are that the current definition of GMO does not cover the creation of new organisms using gene technology such as organisms created by the use of synthetic biology. The example proposed definition simply adds the words '**or created**' to the current definition. This would (along with having in place the ability for the Regulator to make determinations and for techniques and organisms to be included in the regulations) address the issues identified.

- ***Q20. Does the proposed definition of GMO introduce any new issues?***

A. The same answer as given under considerations of the definition of gene technology (see the answers to Q15 and Q16) also apply here, which is that under the current scheme the proposed definition (along with having in place the ability for the Regulator to make determinations) does not seem likely to introduce new issues or some time. The Regulations have the capacity to be used to include and exclude new techniques and organisms as they arise (e.g., RNA interference is excluded under Schedule 1A of the GT Regulations).

- ***Q21. Are there any other desirable changes to the definition of GMO which would address the issues identified in the Third Review and the objectives agreed by the Forum (e.g. to increase flexibility, future-proof the legislation etc.) noting that the Review also recommended that a process-based trigger be maintained as the entry point for the Scheme at the present, to allow for any potential risks associated with new technologies to be initially considered within the scope of the Scheme (refer recommendation 8)?***

A. There are no other changes to suggest at this time. The process trigger continues to be effective and is supported by findings in the earlier stages of the review of the Scheme. Please note also the answer A2 to Q14 above regarding ensuring ability to address complex issues and the answer to Q15 above regarding supporting international harmonisation.

7. Key consultation questions - Definition of 'deal with'

- ***Q22. Does consolidating the definition of deal with into the concepts of make, supply and use address the issues identified?***

A. The issues identified are that the current definition of 'deal with' is geared towards agriculture and is not so relevant to therapeutic goods, animals and microorganisms and it does not align well with concepts of use used by like regulators. The proposed definition includes the current concepts used to manage risks of GMOs to people and the environment as well as the concepts of 'supply' and 'use' as understood by other regulators such as the TGA for example. The proposed definition is therefore better than the current definition.

For readers' reference the proposed definition is:

> ***'deal with**, in relation to a GMO, means the following:*
>
> *a. make the GMO, including to develop the GMO, produce the GMO, breed the GMO, propagate the GMO, manufacture the GMO and grow, raise or culture the GMO*
>
> *b. supply the GMO, including to import the GMO, store the GMO and transport of the GMO*
>
> *c. use the GMO, including to conduct experiments with the GMO, use the GMO in the course of manufacture of a thing that is not the GMO, release the GMO into the environment and dispose of the GMO*
>
> *and includes possession of the GMO for the purposes of, or in the course of, a dealing mentioned in any of paragraphs (a) to (c).'*

- ***Q23. Does consolidating the definition of deal with introduce any new issues?***

  A. No

- ***Q24. Is it preferable to consider the role of other regulators through the consideration of risk in the new pathways described in Chapter 4, or should the intersection be addressed through a revised definition of deal with?***

  A. The revised definition of deal with does not prevent considerations of the role of other regulators. Changes to the Scheme can be designed to accommodate both.

8. Key consultation questions - Non-notifiable dealings

- ***Q25. What types of dealings would be appropriate to include in the non-notifiable pathway for Option B?***

  A. No comments at this time.

- ***Q26. For each of the three categories for Option C, what types of dealings would be appropriate to include in the non-notifiable pathway?***

  A. No comment. Option B is preferred.

- ***Q27. What are the relevant risk indicators (to be established in the GT Act) that could guide the Regulator's determination of what is a very low risk dealing?***

  A. No comments at this time.

- ***Q28. What are the advantages and disadvantages of categorising dealings using existing concepts (e.g., contained dealings and intentional release) that do not account for risk or modern technology?***

  A. No further comments at this time.

- ***Q29. Under Option C, what are the advantages and disadvantages of first categorising the dealing in the context of the non-notifiable dealing authorisation pathway?***

  A. No comment. Option B is preferred

9. Key consultation questions - Notifiable dealings

- ***Q30. What types of dealings would be appropriate to include in the notifiable pathway for Option B?***

  A. Similar dealings to those included at present.

- ***Q31. For each of the three categories for Option C, what types of dealings would be appropriate to include in the notifiable pathway?***

  A. No comment. Option B is preferred.

- ***Q32. What are the relevant risk indicators (principles) that could be considered in determining what a low-risk dealing is for the purposes of categorisation as a notifiable dealing?***

A. Similar to exempt dealings at present.

- ***Q33. Under Option C, what are the advantages and disadvantages of first categorising the dealing in the context of the notifiable dealing authorisation pathway?***

A. No comment. Option B is preferred.

10. Key consultation questions - Licensed dealings

- ***Q34. What risk indicators would inform the split between a permit, an expedited assessment or a full assessment for Option B?***

A. (i) Whether or not there is previous knowledge and experience with the GMO to enable standard licence conditions to apply.
(ii) The circumstances under which the GMO is used (e.g., clinical setting, home setting, clinical trial setting or commercial therapeutic release under the ARTG).
(iii) Whether or not a replication defective vector or a replication competent virus is proposed for use.
(iv) Whether or not patients or the general population is proposed to be treated.
(v) Other indicators will become apparent in future consultations once the preferred Option is chosen.

It will be important for whichever type of authorisation is given (a permit, an expedited assessment or a full assessment) that it incorporate appropriate risk management. For example, although cell therapy is an exempt dealing under the Gene technology Regulations 2001, it still requires significant clinical risk management to ensure risks to patients are managed appropriately. Although this may fall under the TGA, it will be important to ensure that any kind of licence or permit issued by the OGTR does not inadvertently undermine the ability of organisations to implement these therapies in a safe way. Institutional requirements will always be very important to safe implementation. A permit or licence should not undermine that by not including requirements to ensure that, in addition to ethics requirements, institutional requirements are followed.

- ***Q35. For Option C, what risk indicators would inform the split between a permit, an expedited assessment or a full assessment for the categories 'dealings involving intentional release' and 'clinical trials and medical applications'?***

A. No comment. Option B is preferred.

- ***Q36. Under Option C, what are the advantages and disadvantages of first categorising the dealing before using risk indicators to determine the relevant licence type?***

A. No comment. Option B is preferred.

11. Key consultation questions - Essential enablers

- **Q37. What current processes (that are unnecessarily burdensome) could be resolved by an improved IT system?**

A. Unsure - flexibility for different users will be important.

- **Q38. What other advantages could be gained from the implementation of an automatic data management system?**

A. As above