Regulation of GM and gene edited animals – Australian situation and other reflections

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Overview

• Key message – legal vs scientific definitions
• Background to genome editing & regulation
• Definitions & Principles
• Global state of play & implications
• Australia & genome editing – GMOs

No GM animals approved in Australia for field trial or commercial production

Disclaimer – my analysis, not legal advice
History – rDNA to genome editing

- **OECD ‘blue book’** 1986
- **GM tobacco plant produced** 1983
- **Asilomar 1975 uncertainty precaution**
- **OECD ‘Scale up of crop plants’** 1993
- **Bt cotton in Australia 1996**
- **OECD, ILSI 2011-14**
- **NPBT workshops FSANZ, EC-JRC, OECD, ILSI 2011-14**
- **EU NPBT working group 2008**
- **OECD ‘Scale up of crop plants’** 2018
- **European Court of Justice ruling on gene editing 2018**
- **1996**
- **2000**
- **2001**
- **2011**
- **2018**
- **2017**
- **2018 OECD Conference on Genome Editing in Agriculture**
- **2018-2021 “Am I regulated?” regulatory reviews & initiatives:**
  - Argentina, Brazil
  - USA, Canada
  - Australia, Japan
  - European Commission

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**Progression of Genetic Engineering**

1. **Asilomar 1975 uncertainty precaution**
2. **GM tobacco plant produced 1983**
3. **OECD ‘blue book’ 1986**
4. **Asilomar 1975 uncertainty precaution**
5. **OECD ‘Scale up of crop plants’ 1993**
6. **Bt cotton in Australia 1996**
7. **OECD, ILSI 2011-14**
8. **EU NPBT working group 2008**
9. **OECD ‘Scale up of crop plants’ 2018**
10. **European Court of Justice ruling on gene editing 2018**
11. **1996**
12. **2000**
13. **2001**
14. **2011**
15. **2018**
16. **2017**
17. **2018 OECD Conference on Genome Editing in Agriculture**
18. **2018-2021 “Am I regulated?” regulatory reviews & initiatives:**
   - Argentina, Brazil
   - USA, Canada
   - Australia, Japan
   - European Commission
Context – rDNA, GMO (& GM food) laws

Concepts for rDNA laws c. 2000

- new technology – precautionary, ‘pre-market assessment’
- exclude ‘traditional’ breeding, mutagenesis techniques

Regulatory approaches

GMO-specific laws – process ‘trigger’ technology, ~rDNA

Novelty – product ‘trigger’
*process may be considered

Adapt existing laws
*process &/or product

E.g.
EU, Australia, Argentina, Korea, et al.
Canada*, New Zealand*
USA (e.g. pest sequences)
Context – GMO production internationally & rapid application of new genome editing techniques
Context – international agreements & GMOs

Parties to **Cartagena Protocol on Biosafety**

Mariotti (2016)
www.researchgate.net/publication/311965379_La_biodiversita_e_i_suoi_hotspot_in_Italia_e_altrove
Context – international regulatory landscape

• Different countries
• Different laws & legal systems
• Different definitions
• Different approaches, policies, publics

... can lead to different regulatory outcomes:

• what is regulated and how?
The ‘problem’ - transgenics to genome editing

2000
‘recombinant DNA, genetic modification’

2021
‘genome editing’

transgenics

cisgenesis, intragenesis

= ‘GMO’ ✔

oligo-directed mutagenesis (ODM), NPBTs, CRISPR, ZFN (SDNs)

= ‘GMO’ ?
The ‘problem’ - transgenics to genome editing

2000

• 35S-transgene-nos

*Different* definitions resulted in

*same* regulatory outcomes

= GMO ‘everywhere’

= harmonised (practically)

2021

• NPBT, genome edited

*Different* definitions

*may* result in

*different* regulatory outcomes

= *asymmetry* – GMO in country A

but not GMO in country B

uncertainty in definitions = GMO ??

potential identity with naturally occurring mutants

risk proportionate regulation ?
Regulation – roles & responsibilities

Governments make laws
- define what is to be regulated

Regulators administer laws
- regulate

Courts adjudicate laws
- decide what is, and is not, regulated

Protection goals, Values, Policy
- what should be regulated?

Science

Risk analysis
Designing/amending regulation - principles

Broad consultation and discussion

Risk, Science

Legislation

Protection goals

Societal values
Administering regulation - principles

**Legislation**

- **Risk**
- **Protection goals**
- **Societal values**

**Fair and equitable application of laws**

**Compliance**

*cannot interpret laws:*

“this is what it *meant to say*”

“this is what it *should have said*”
Definitions – e.g. Australia’s Gene Technology Act

GMO = organism modified by gene technology (broad capture)
= organism declared a GMO*
≠ organism declared not a GMO*

gene technology = any technique for modification of genes
or other genetic material (broad capture)
≠ sexual reproduction, homologous recombination
≠ any technique declared not gene technology*

* GT Regulations – inclusions & exclusions
Regulatory status – pitfalls of overviews

“Words matter ...”

Schmidt et al 2020 *Evolving landscape* around genome editing in agriculture. EMBO Rep, DOI: (10.15252/embr.202050680)
Regulatory status – pitfalls of overviews

Some genome edited crops are not regulated as GMOs in Australia, some are regulated.

Schmidt et al 2020 *Evolving landscape* around genome editing in agriculture. EMBO Rep, DOI: (10.15252/embr.202050680)
Definitions

International definitions - Cartagena Protocol & CODEX

(g) “Living modified organism” means any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology;

(h) “Living organism” means any biological entity capable of transferring or replicating genetic material, including sterile organisms, viruses and viroids;

(i) “Modern biotechnology” means the application of:

a. In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or

b. Fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection;
Regulatory reactions to genome editing

Legal Decisions / clarifications

- European Court of Justice, 2018
- New Zealand High Court, 2014

geno editing = GMO

Regulatory reviews, changes, approaches

- Argentina & Brazil – pre-assessment viz. GMO or not GMO
- Australia, Japan – reviews, regulatory changes / clarifications
- Canada – May 2021 – consultation on guidance
- USA – “am I regulated”, new exclusions

International – Convention on Biological Diversity

- ‘synthetic biology’ (ongoing debates)
Australia & genome editing – GMOs – definitions & exclusions

Process features

- targeted changes: unguided repair
- template guided repair

2019 changes to GT Regulations: SDN-1 exclusions

Product features

- Extent of sequence changes:
  - point mutations, deletions
  - long sequences inserted

not gene technology (thus not GMOs)
gene technology, not GMOs
gene technology, GMOs

inserting transgenes

SDN-1
SDN-2 ODM
SDN-3
oligonucleotide long template

natural mutations
mutagenesis

+ template
no template
Australia and genome editing regulation

GMOs

2019 – GT Regulations amended to clarify regulation of SDN-1, SDN-2 (following a technical review 2017-18)

2018 – Policy review GT Act

“... recommends updating, where required, the existing definitions in GT Act to clarify the scope of regulation in light of ongoing technical advances. ... take into account ... ongoing work internationally.”

More info – 2020 Consultation Regulatory Impact Statement & Explanatory Paper

(definitions)

Australian GMO risk assessment

- Adapt / adopt existing guidance
  *eg* Australian Standards, OECD
- Define terms and concepts
- Qualitative, comparative assessments
- Focus on harm and plausible pathways to harm
- Distinguish events vs harm
- Regulatory science to support decision making on risk – need to know vs nice to know
OECD Guidance & Principles

www.oecd.org/science/biotrack/

Environmental risk assessment of GMOs:

*interaction* of
• biology of parent organism
• GM trait
• receiving environment
• intended use

• familiarity
• case by case
• step by step
OECD & genome editing – risk assessment

Working Party for the Harmonisation of Regulatory Oversight in Biotechnology

2014 – Workshop Environmental Risk Assessment (ERA) of products derived from New Plant Breeding Techniques

“Current guidance and tools for ERA of transgenic plants are applicable to plants developed by NPBTs, where such ERA is required.”

2014 – present – ongoing information sharing on experiences with risk assessment / regulation of NPBT / genome editing

https://www.oecd.org/chemicalsafety/biotrack/ - Recent Developments in Delegations on Biosafety (2021)
GMO environmental risk assessment considerations

• is the parent organism a weed / pest / pathogen?
• phenotype of the GMO, receiving environment
• will the modification increase weed/pest potential / pathogenicity?
• will the GMO be toxic / harmful – species specificity?
• will the modification confer a selective advantage?
• spread in space and time? (GMO vs parent)
• gene transfer (occurrence vs harm)?
• can the parent / GMO be controlled?
Recap – regulatory landscape genome editing

• Genome editing & regulation – rapid scientific advances
• Definitions, policy approaches
• Principles – precautionary legislation,
• Global state of play & implications
• Ongoing scientific & regulatory policy debate: risks gene edited vs conventional, rDNA

Key messages:
• legal vs scientific definitions
• regulatory landscape is still evolving