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Genome Editing 'Rulemaking' in Australia – history, current status & observations

Dr Peter Thygesen

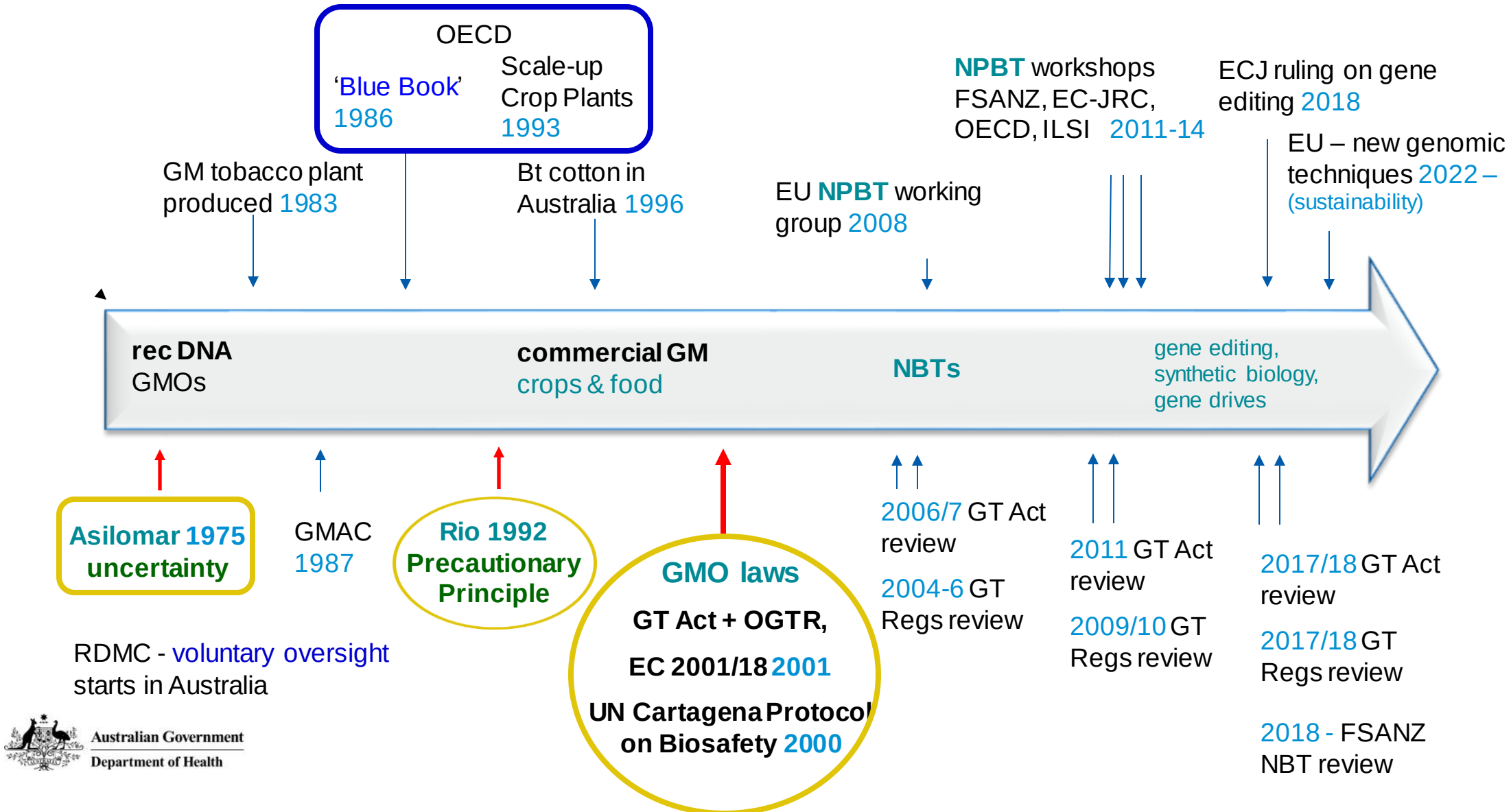
Sustainability in Agriculture & Food Systems – Innovation, Indicators & Implementation Conference ***24 May 2023***

Overview

- Where it all began ..
- Australian regulatory approach – GMOs – *www.ogtr.gov.au*
- Background to genome editing & regulation – what is the problem?
- Definitions & Principles
- Australian approach / experience
- Ongoing review work, including GM food

Disclaimer – my analysis, not legal advice

GMO history, or *'how did we get here?'*



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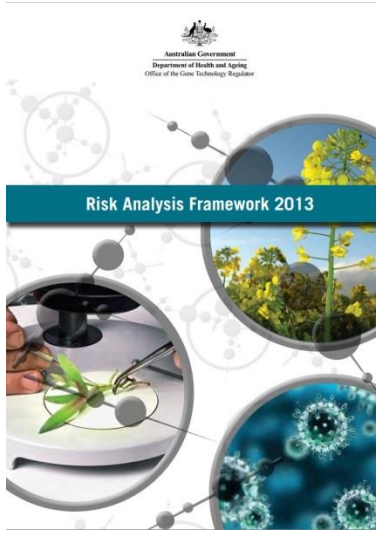
Australian approach to GMO regulation

- Adapt / adopt **existing guidance**

  eg Australian Standards, OECD
- **Focus on harm** and **plausible pathways** to harm
- Distinguish **events** vs **harm**
- Qualitative, comparative assessments
- **Differences** are **not *a priori* harmful**
- Regulatory science to support decisions
- **Management proportionate to risk**

Note – benefits cannot be considered



AS/NZS HB294
Post-border Weed
Risk Management

Australian GMO regulatory scheme

intergovernmental Gene Technology Agreement 2001

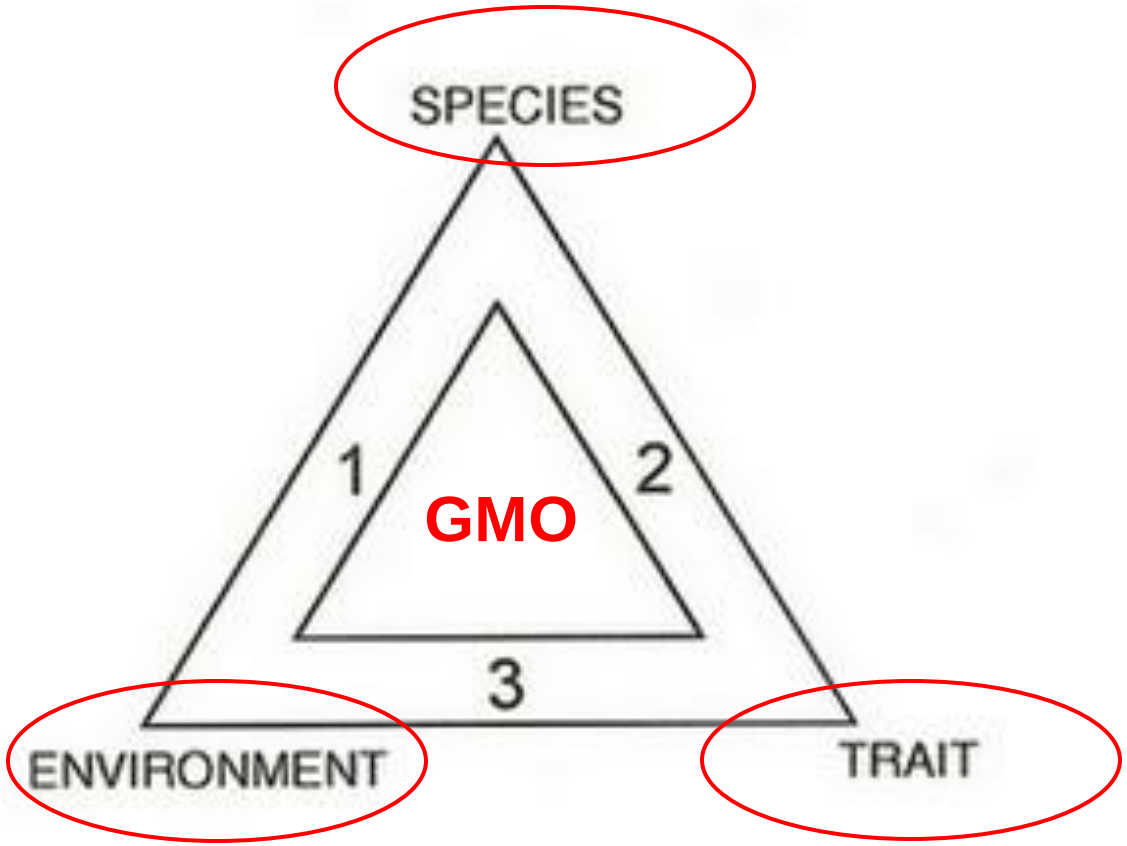
Gene Technology Ministers Meeting

The [Australian] Regulatory scheme:

- be based on a **scientific assessment of risks** undertaken by an independent Regulator
- regulatory burden commensurate with risks
- be able to be amended to respond to the development of gene technologies
- be characterised by transparent decision-making and extensive stakeholder and community involvement

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 (experience)

case by case assessment

step by step development

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Harms from GMOs – basis in biology

genetic modification

WEED ?

PEST ?

PATHOGEN ?

in comparison / relative to the unmodified parent organism

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GMOs – uncertainty & familiarity

c. 1975 – recombinant DNA ➡ uncertainty (Asilomar Conference)

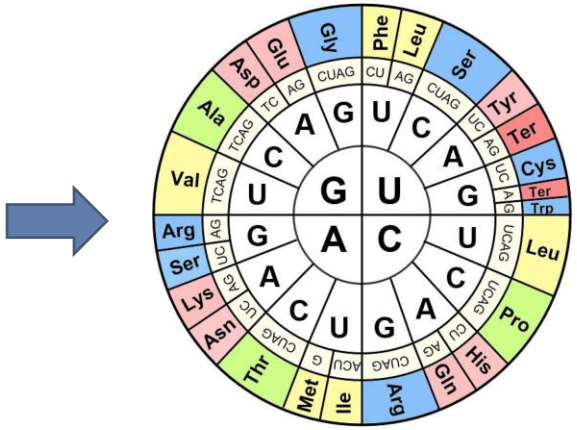
1992 – Precautionary Principle (Rio Declaration)

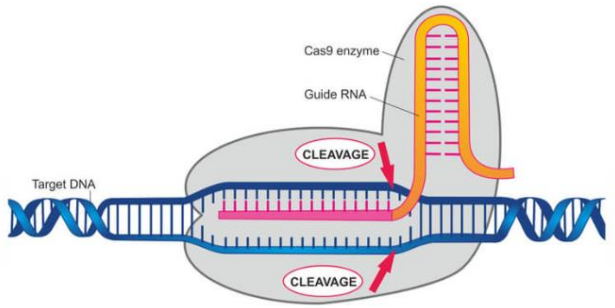
c. 2000 – GMO regulation ➡ unintended [harmful] effects??

… but …

GMOs are (still) **organisms** … **rDNA is** (still) **DNA** …

Biological systems behave in predictable ways





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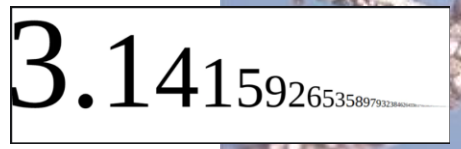
Data requirements – OGTR approach

Regulatory science & risk analysis to: **support decision making:**

- '**need to know**' vs 'nice to know' – answer **meaningful risk Qs**
- **predictive value** of information?

  eg molecular/genotypic vs **phenotypic data**
- evidence to satisfy the Regulator vs prescriptive data

  risk assessment focus in **OGTR application forms**
- **'weight of evidence approach'**



Why spend a day in the library when you can learn the same thing by working in the laboratory for a month?
Frank Westheimer

Context – rDNA, GMO & GM food laws

circa 2000 - concepts for rDNA laws

- new technology – precautionary, 'pre-market assessment'
- *exclude* 'traditional' breeding, mutagenesis techniques

Regulatory approaches
GMO-specific laws – **process 'trigger'**
technology, ~rDNA

e.g.
EU, Australia, Argentina,
Korea, Japan *et alia* …

Novelty – **product 'trigger'**
**process may be considered*

Canada*,
New Zealand*

Adapt **existing laws**
**product &/or process*

USA
(e.g. pest sequences)

Context – expert committees to LAWS

e.g. Australia

1975 to 2000 – voluntary regulation by Expert Committee (RDMC, GMAC) & local Institutional Biosafety Committees (IBCs)

- expert scientific judgement about categorisation of organisms as GMOs and appropriate assessment & management – **flexibility**

➡ ***GMOs coming 'to market', public concerns …***

post-2000 – mandatory regulation under legislation (still with IBCs)

- categorisation (definitions), decision making processes – **set in law**
- laws can be amended (of course) – but this is then **BIG-P Policy**

Process triggers – *e.g.* Australia's *GT Act*

2000 - Broad definitions with exclusions

GMO = an organism modified by gene technology

= organism declared a GMO*

≠ organism declared not a GMO*

gene technology = any technique for modification of genes or other genetic material, *but not*

≠ sexual reproduction, homologous recombination

≠ any technique declared not gene technology*

* GT Regulations

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2001 - Gene Technology Regulations

Exclusions

e.g.

Schedule 1A – Techniques that are not gene technology

- radiation & chemical mutagenesis
- somatic cell nuclear transfer, protoplast fusion
- a natural process* not involving genetically modified material

  *eg conjugation, transduction, transformation, transposon mutagenesis

[Rationale - Pre-rDNA techniques, concept of 'natural processes', 'occurs in nature']

Context – genome editing rapid advances

‘classical’ GMOs – relatively small number of:

- species – maize, soy, cotton, canola *(global bulk commodities)*
- traits – herbicide tolerance, insect resistance *(transgenes)*
- technology developers / providers – *‘multinationals’*

Gene edited – *more tractable technology*, many:

- species – local crops, small/niche commodities
- traits – wide variety, including *small genome changes*
- new technology developers – incl. *local SMEs, institutes*

Context – international 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'

transgenics

cisgenesis, intragenesis

2023

'genome editing'

oligo-directed mutagenesis (ODM),

NPBTs, CRISPR, ZFN (SDNs), base editors …

= 'GMO' ✓

= 'GMO' ?

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GMOs vs Genome editing

GMOs

aka transgenics, LMOs

Random site of insertion

Incorporation of (whole) gene constructs, normally from another species

Takes a long time

Genome editing

aka - new plant breeding techniques, new genomic techniques, precision breeding

Targeted changes to genome

Changes may be small

Changes may be similar to conventional mutagenesis

Relatively fast

The 'problem' - transgenics to genome editing

2000

- 35S-transgene-nos

Different definitions

⇨ **same** regulatory outcomes

GMO 'everywhere'

= harmonised (practically)

2023

- NPBT, genome edited

Different definitions ***may result in***

Different regulatory outcomes

⇨ ***asymetry*** – **not GMO** in **economy A**

and **GMO** in **economy B**

uncertainty in definitions = **GMO ??**

compliance? - potential identity with naturally occurring mutants (e.g. waxy corn)

risk proportionate regulation ?

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Genome editing 'regulatory problem' (not unique)

over time, knowledge, technology, practices, circumstances change …

Protection goals, Values, Policy

Governments make laws

define what is to be regulated

What should be regulated? Why? How?

Regulators administer laws

regulate

Science

Risk analysis

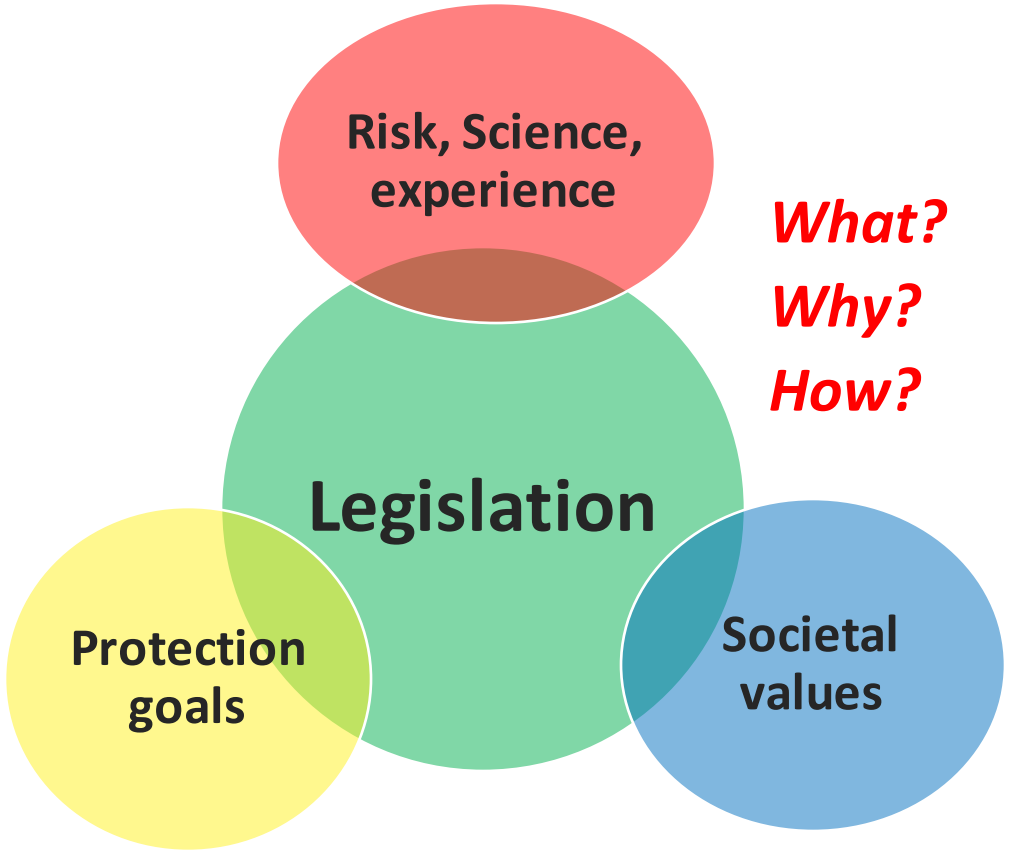
Courts adjudicate laws

decide what is, and is not, regulated

Δ Time, Δ changes

Designing/amending regulation - principles

Broad consultation and discussion,
regulatory impact analysis, proportionality



What?
Why?
How?

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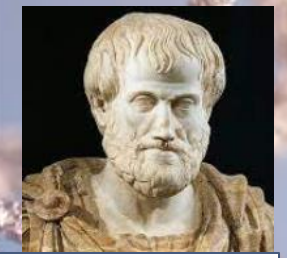
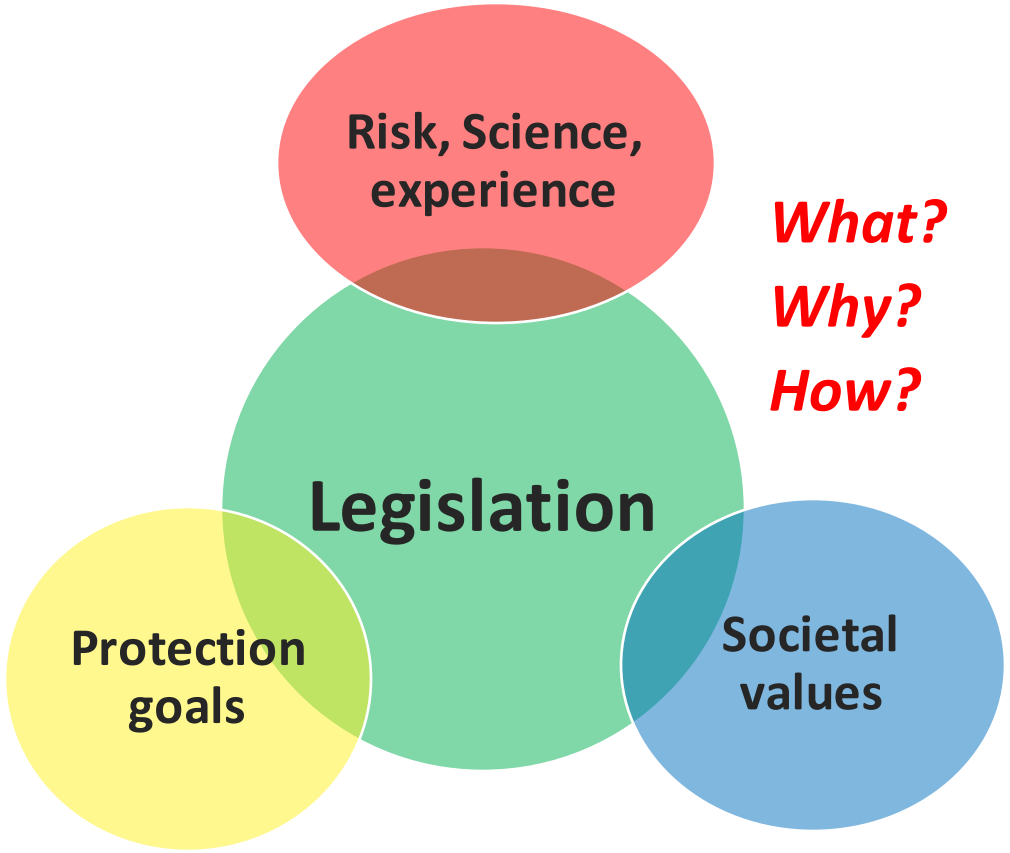
Designing/amending regulation - principles



Broad consultation and discussion, regulatory impact analysis, proportionality

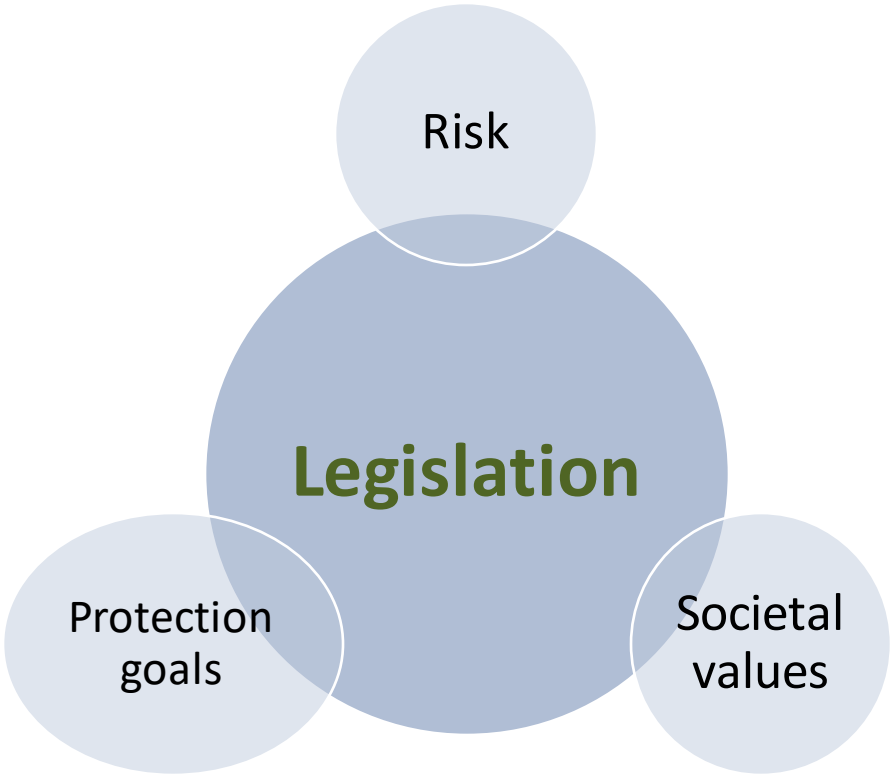
Regulate like things alike

cf. Aristotle & Principle of Proportionality



What?
Why?
How?

Administering regulation - principles



Fair and equitable application of laws

Compliance

cannot interpret laws: "this is what it *meant to say*"
"this is what it *should have said*"

Regulatory reactions to genome editing

Legal Decisions / clarifications – legal defniitions

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

➡ genome editing = GMO

Regulatory reviews, changes, approaches

- Argentina & Brazil – pre-assessment viz. GMO or not GMO
- Australia – reviews, some regulatory changes
- Japan –notification but not regulated as GMO
- Canada – May 2023 – novelty remains key
- USA – SECURE rule, “am I regulated”, new exclusions

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Australian laws & genome editing

GMOs:

- Gene Technology Act, Regulations
- Gene Technology Regulator and OGTR

Science-based, case by case assessments & approvals

Food:

- Australia NZ Food Standards Code
- Standard 1.5.2 - Food produced using gene technology *(aka 'GM food')*
- Food Standards Australia New Zealand

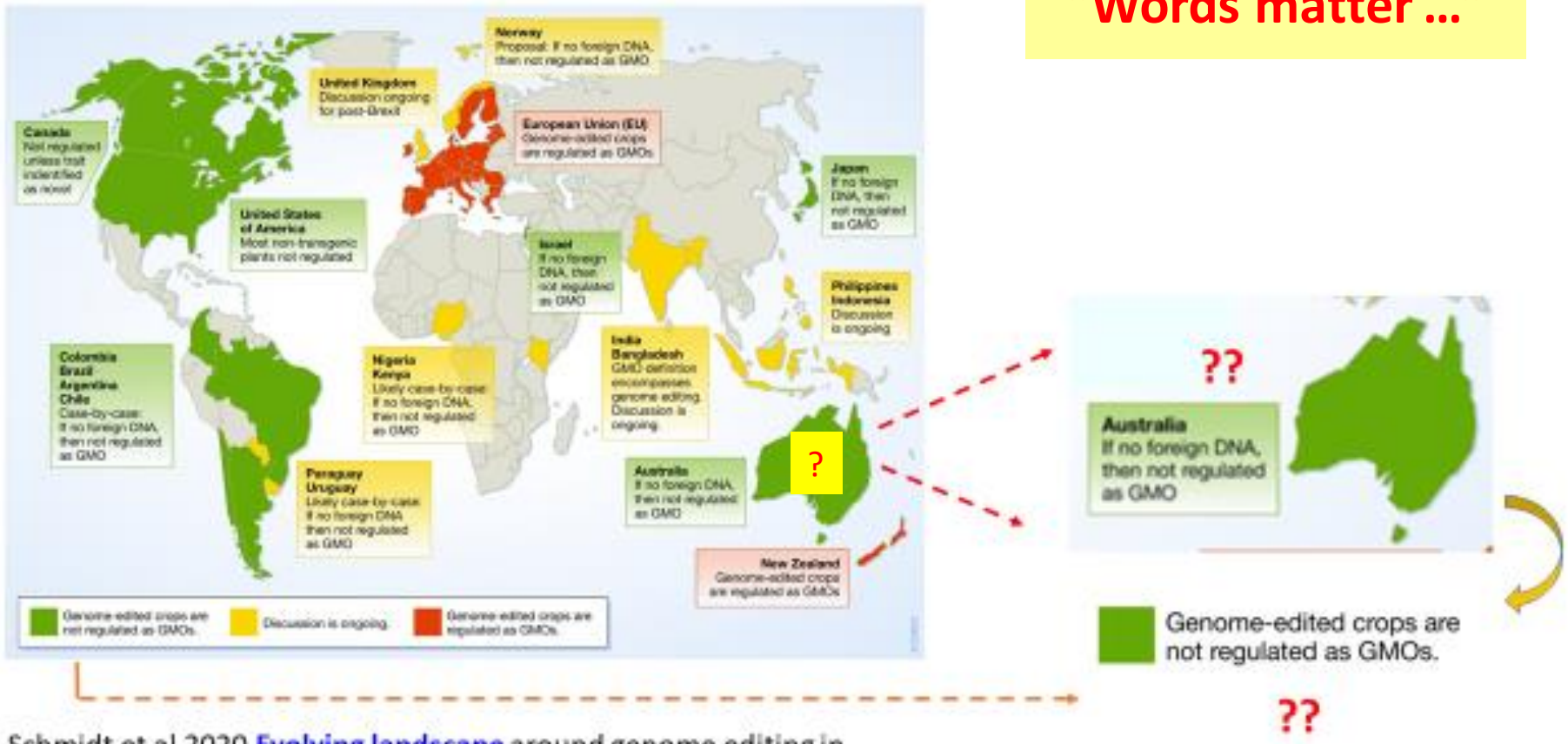
→ legal definitions

'process trigger'

→ legal definitions

Regulatory status – pitfalls of overviews

"Words matter …"

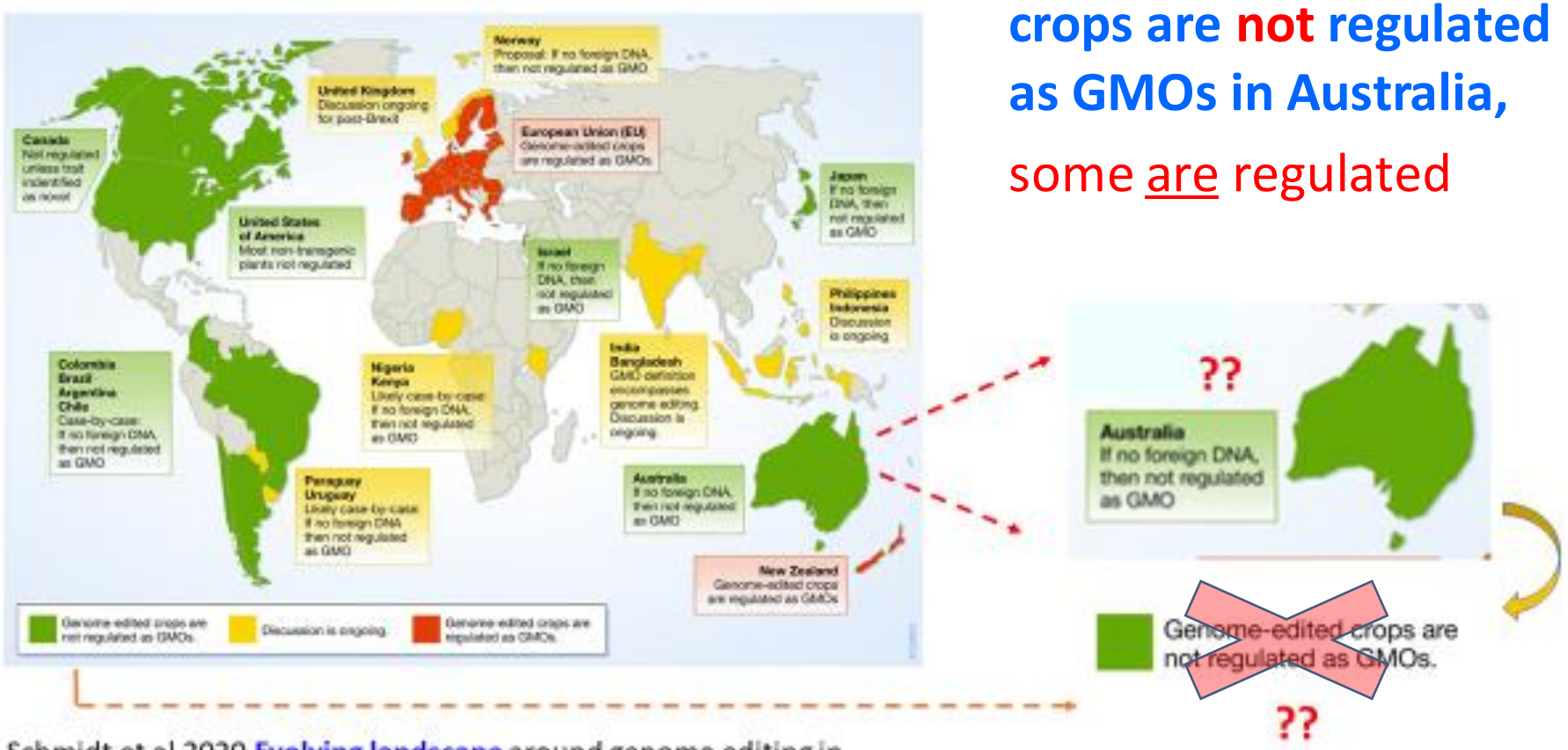


Schmidt et al 2020 **Evolving landscape** around genome editing in agriculture. EMBO Rep, DOI: (10.15252/embr.202050680)

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)

Rise of genome editing – "is this regulated?"

Innovation & regulation – **terms of art** vs **definitions**

- *ante*-NBT - 'cisgenics'? – not in Australian legislation – not relevant
- *c.* 2011-2016 - NBTs to genome editing – increasing enquires about regulatory status
- *post*-NBT – 'synthetic biology'? – *cf.* 'cisgenic' – not relevant

Rise of genome editing – "is this regulated?"

2016-2018 - **Technical Review of the Gene Technology Regulations**

- Narrow focus – '**within current** [big P] **policy settings**' (Regs vs Act)
- Proposed amendments to clarify regulatory status of some organisms produced with genome editing techniques

… another (standard) principle – **'Policy – Regulatory split'**

… metaphors – tails & dogs; who is in charge of the blood bank? …

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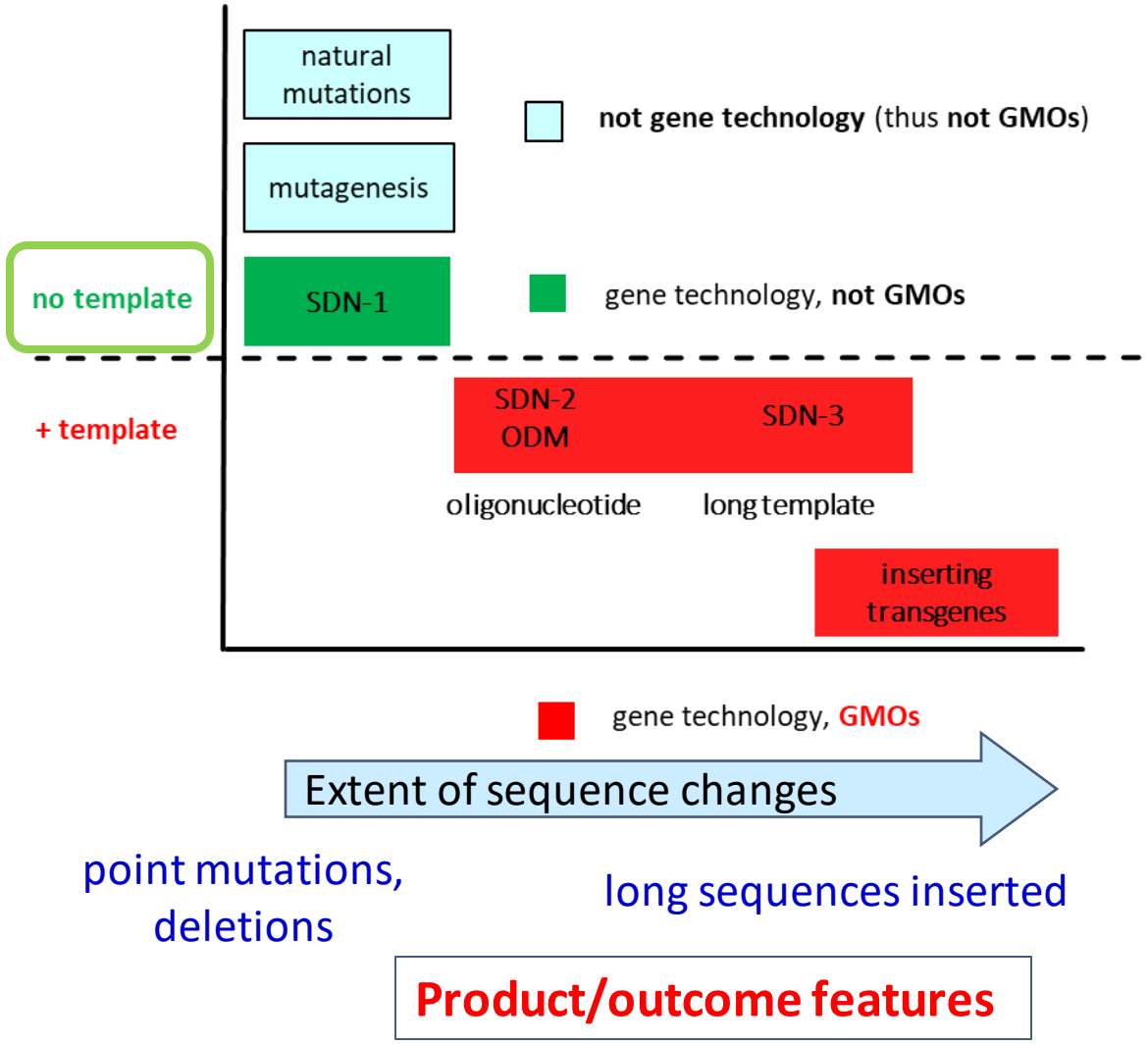
Australia & genome editing – May 2023

GMOs – exclusions in Regulations under unchanged Act definitions

Process features

targeted changes: unguided repair

template guided repair



Product/outcome features

2019 changes to **GT Regulations**:

SDN-1 exclusions

GT Regulations & genome editing - at May 2023

Schedule 1 – Organisms that are *not* GMOs

Genome editing

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.

SDN-1

Schedule 1B – Organisms that are GMOs

Genome editing

An organism that has had its genome modified by oligonucleotide-directed mutagenesis

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

SDN-2
SDN-3

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General OGTR advice re gene editing

‘Gene technology is a rapidly developing field of science, and future developments may pose challenges in **applying the current definitions**.

If you have queries about **regulatory coverage** please **discuss these with OGTR**.

The Regulator can only provide advice on a case-by-case basis and on an **understanding** of the technology as presented and the **legislation in its form at the time**.

the Regulator must take a conservative approach, consistent with … the **broad scope of the definition of GMO** contained in Section 10.’

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2017 Review of GT Act – Big-P-Policy

- July 2017 – Terms of Reference set by GT Ministers Meeting
- July 2017 – Invitation for public submissions
- Nov 2017 – Consultation Paper
- Mar 2017 – Preliminary Report
- Oct 2018 – Final Report
- Nov 2018 – Action Plan 2018-2023
- Jun 2019 – Implementation Strategy
- Dec 2020 – Consultation Regulatory Impact Statement
- July 2021 – Decision Regulatory Impact Statement

www.genetechnology.gov.au

Drafting of amendment legislation

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2017 Review of GT Act – Big-P-Policy

October 2018 – **Final Report**

Recommendation 8: The Review recommends 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.

Process Trigger retained:

- definitions of ‘gene technology’ & ‘GMO’ might be amended

www.genetechnology.gov.au

2017 Review of GT Act – Big-P-Policy

December 2020 – **Consultation Regulatory Impact Statement**

- *Recommendations 4 and 6* – Update existing definitions in the GT Act to clarify the scope of regulation in light of on-going technological advances.
- *Recommendation 9* – Introduce a new risk tiering framework that ensures regulation remains commensurate with the level of risk and there is flexibility to move GMOs between authorisation categories based on identification of new risks, a history of safe use and other additional factors.
- *Recommendation 10* – Reduce regulatory burden through streamlining processes and current regulatory requirements where appropriate.

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2017 Review of GT Act – Big-P-Policy

July 2021 – **Decision Regulatory Impact Statement**

Modernising and future-proofing the National Gene Technology Scheme

Drafting of amendment legislation

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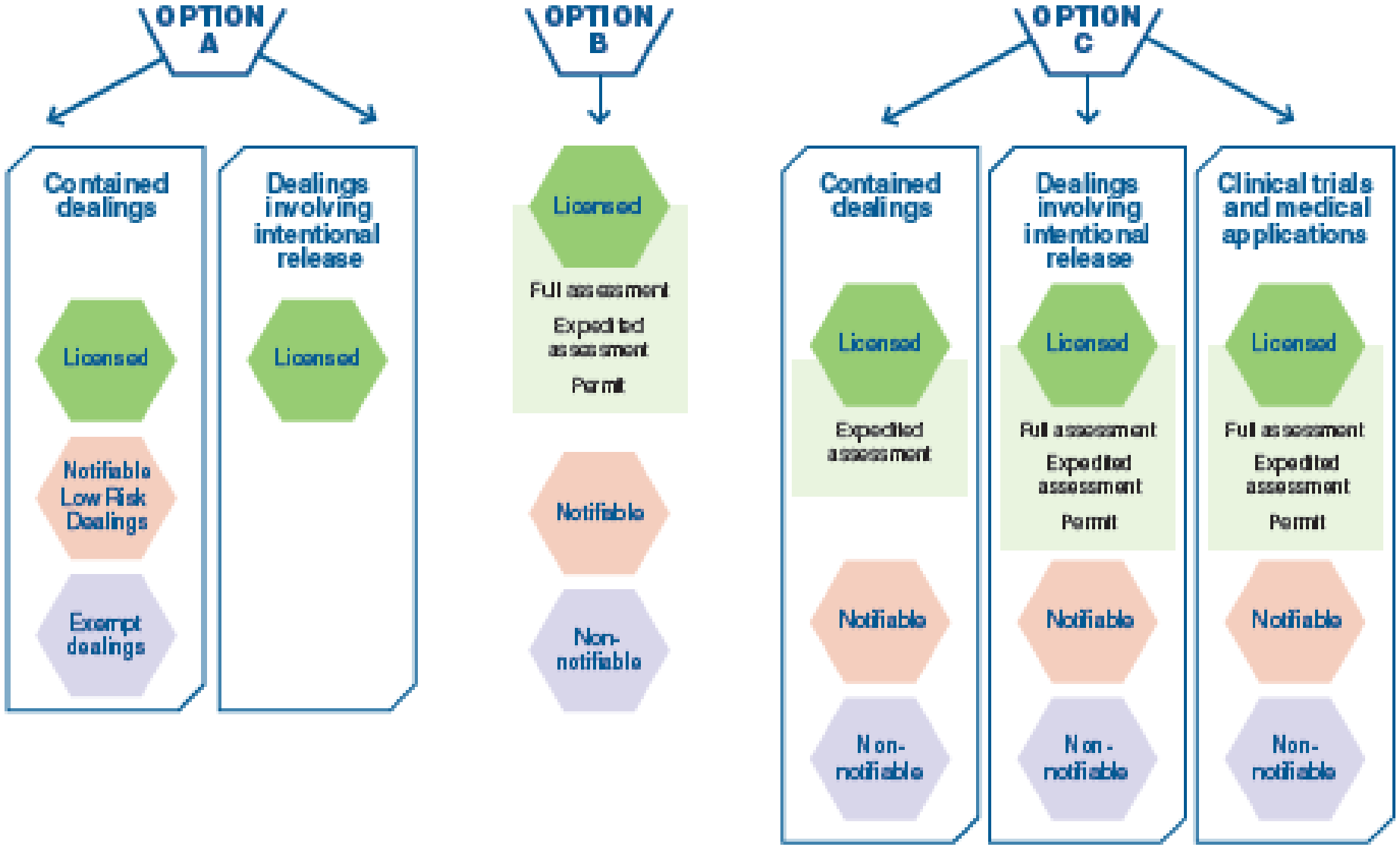
Risk Tiering options for GMO Regulation



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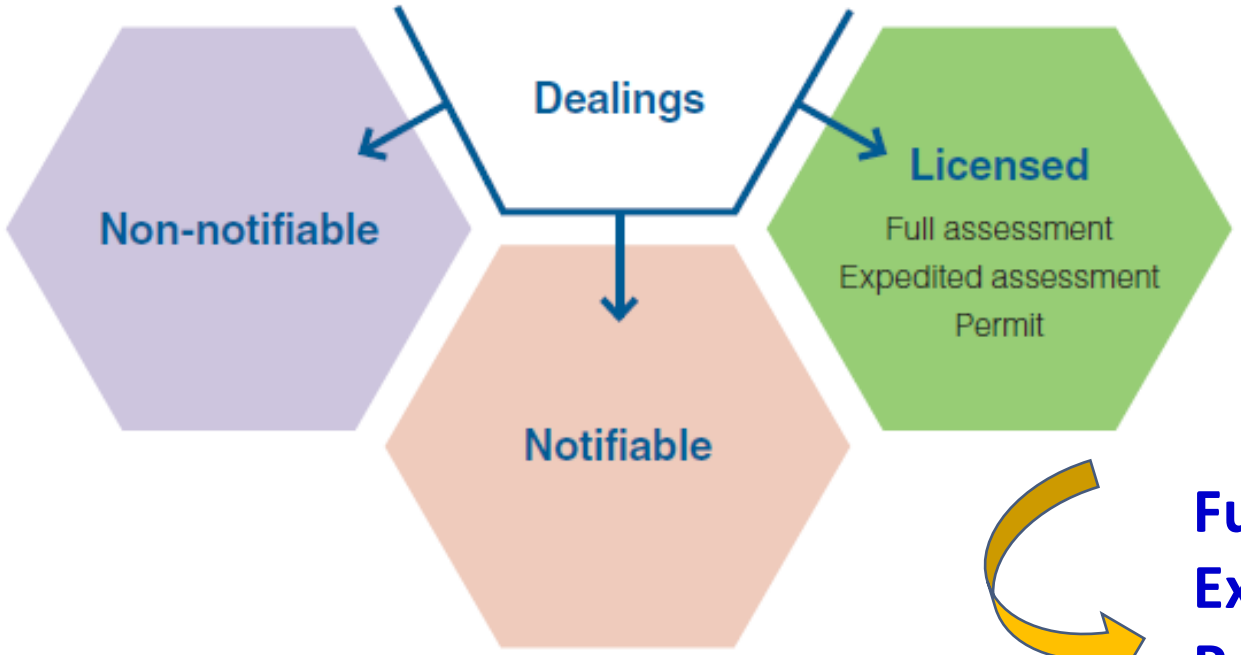
Risk Tiering model for updating GT Act

Option B:

Risk-tiering model – dealings with GMOs would be classified into three authorisation pathways according to their indicative risk



Risk-based categorisation

www.genetechnology.gov.au

Full assessment
Expedited Assessment
Permit

Watch this space …

Figure 1: New authorisation pathways to achieve risk tiering under Option B.

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Reviews – NBTs & Food

FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

2019

Final report

Review of food derived using new breeding techniques

In the first of two rounds of public consultation, FSANZ invited interested parties to comment on its proposed approach to:

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

revise definitions

- 'gene technology' to capture all methods for genetic modification other than conventional breeding
- 'food produced using gene technology' – product-based criteria to exclude certain foods from assessment as GM food

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Reviews – NBTs & Food

Proposal P1055 – Definitions for gene technology and new breeding techniques

Last updated: January 2022

P1055 is a proposal to amend the definitions for 'food produced using gene technology' and 'gene technology' in the Australia New Zealand Food Standards Code (the Code).

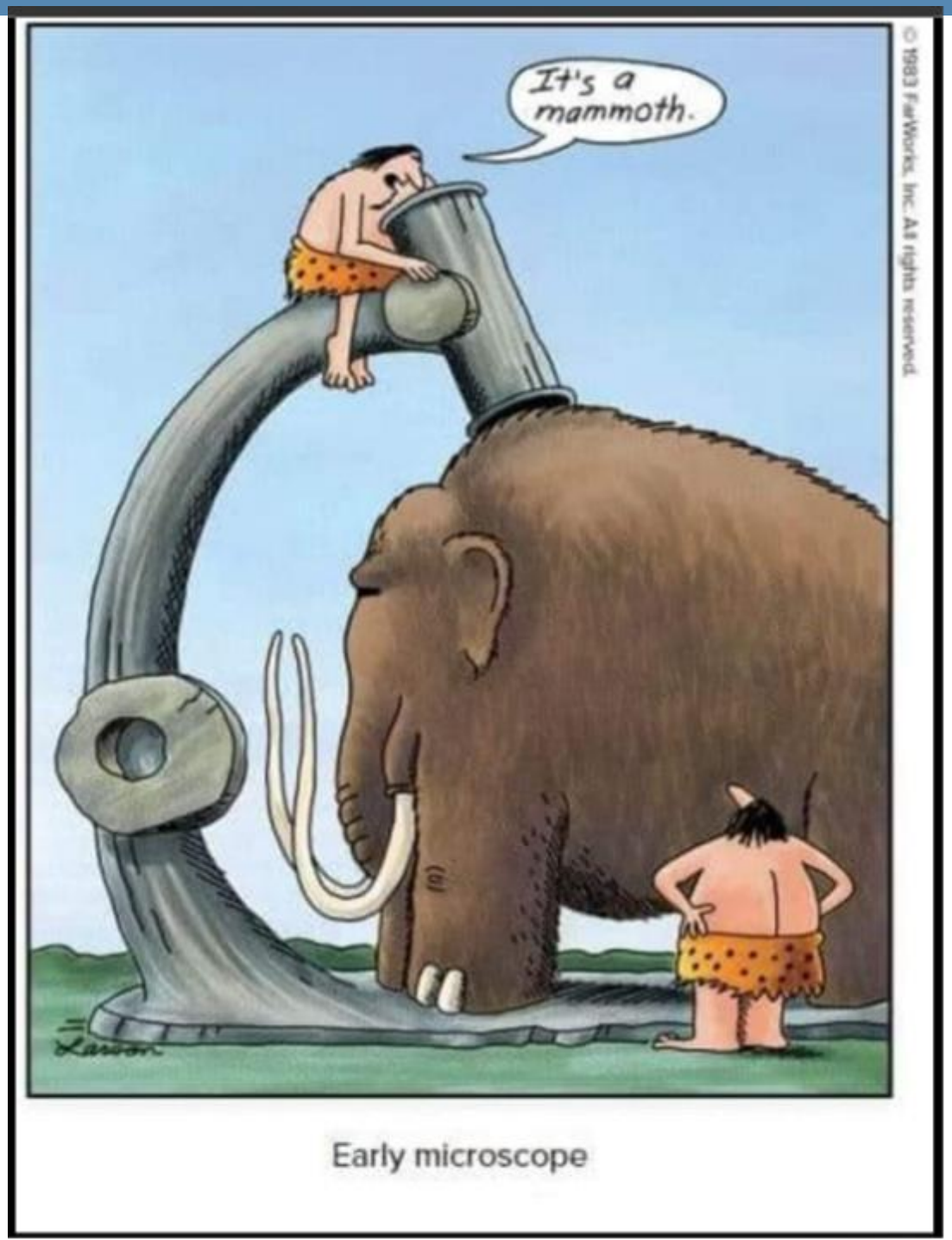
These definitions determine what foods are classed as genetically modified (GM) food under the Code. Currently, all GM food available for sale in Australia and New Zealand must have been assessed for safety by FSANZ and be expressly permitted and listed in relevant Code schedules.

FSANZ is proposing to update the definitions to make them clearer and better able to accommodate food produced by existing, emerging and future genetic technologies.

www.foodstandards.gov.au – Proposal P1055

… Watch this space …

Questions ?


It's a mammoth.
© 1983 FarWorks, Inc. All rights reserved.
Larson
Early microscope

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