

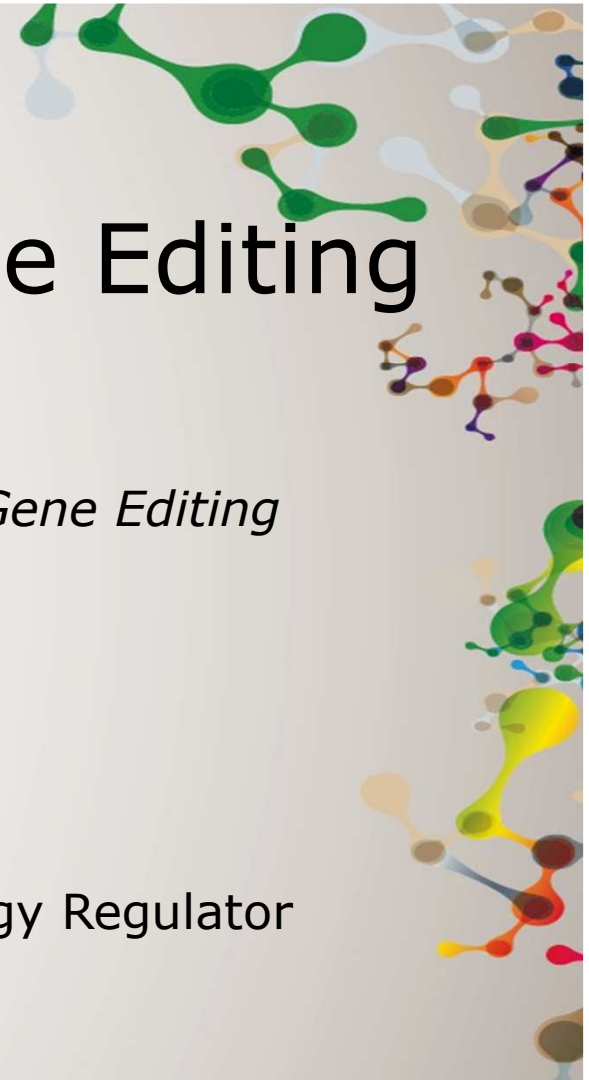


Australian Government
Department of Health
Office of the Gene Technology Regulator

OGTR Perspective on Gene Editing

Presentation at the *CSIRO Gene Editing
of Crops Workshop*
28-30 November 2017

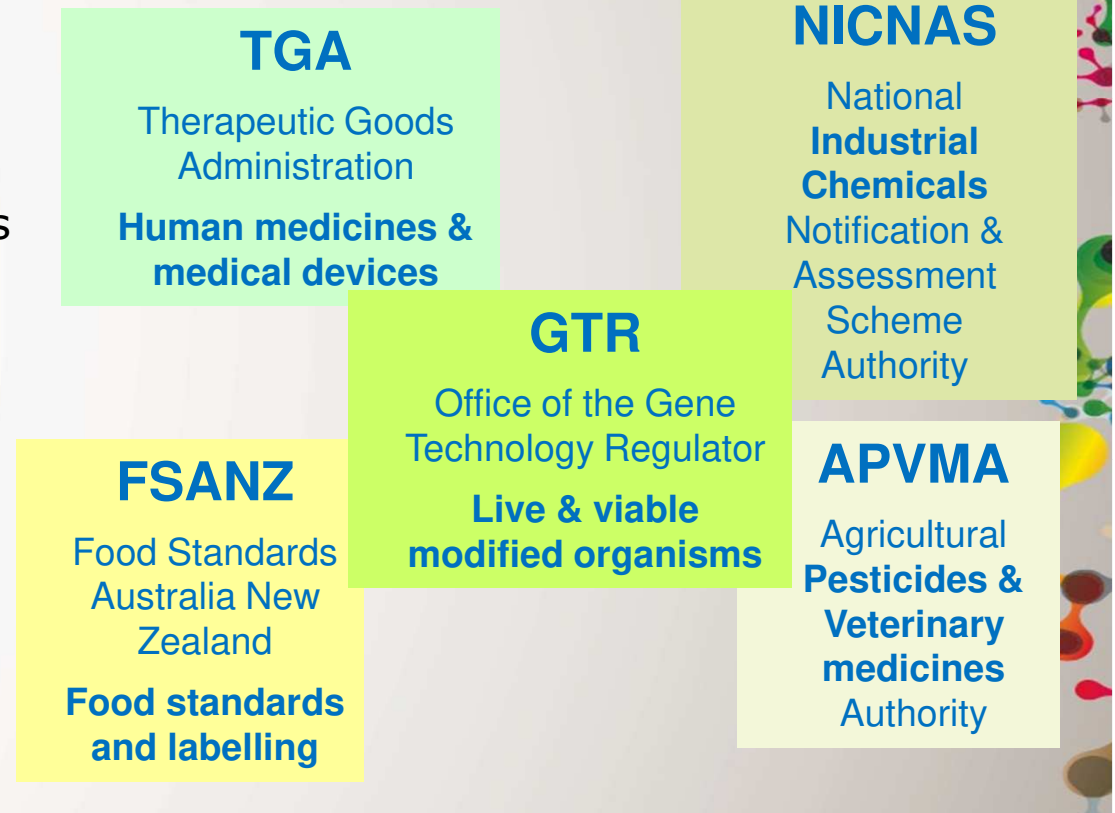
Dr Andrea Robold
Regulatory Practice Section
Office of the Gene Technology Regulator





Integrated regulation of GMOs & GM Products

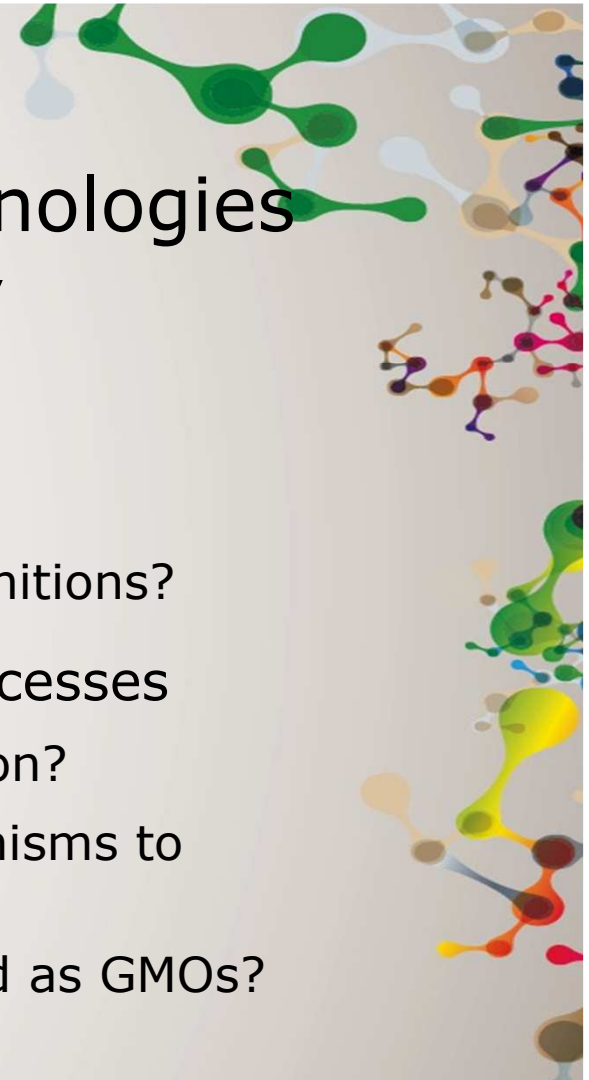
- GTR regulates GMOs
- avoid duplicating regulation
- align decision making as far as possible.





What challenges do new technologies pose for the Gene Technology Regulator?

- New methodologies and applications
 - How do these fit with legislative definitions?
- New techniques that utilise natural processes
 - Are there risks that warrant regulation?
 - How different are the resulting organisms to natural mutants?
 - Should these organisms be regulated as GMOs?





What is a GMO?

Section 10 of the *Gene Technology Act 2000*:

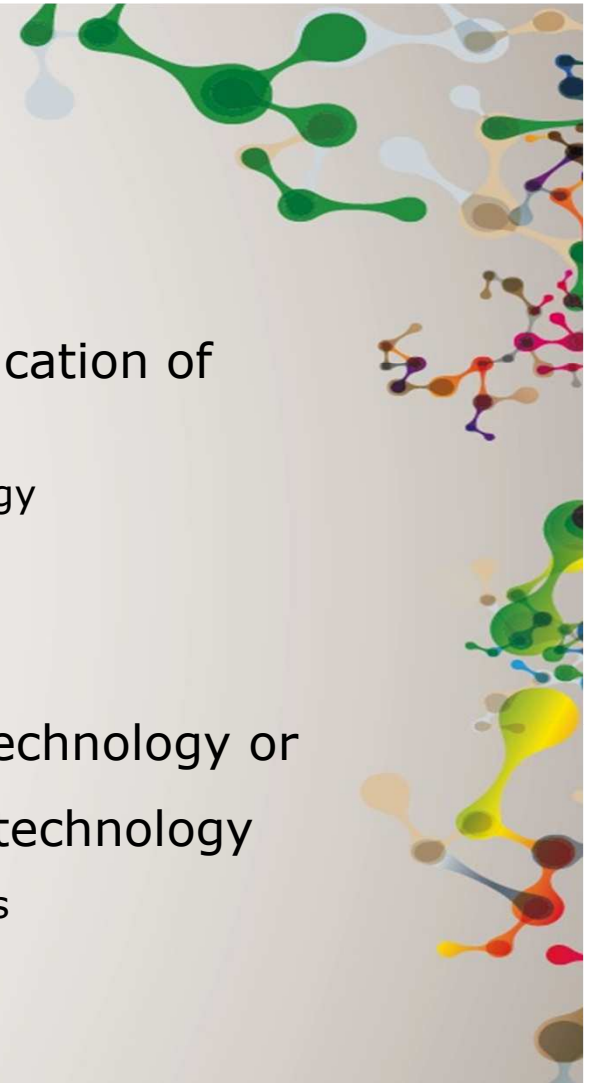
Gene technology is any technique for the modification of genes or genetic material

the Regulations can declare techniques not to be gene technology

A **GMO** is

- a) an organism that has been modified by gene technology or
- b) inherited traits that occurred because of gene technology

the Regulations can also declare things to be GMOs or not GMOs





GT Regulation in the year 2000

not gene
technology

natural
mutations

mutagenesis

inserting
transgenes



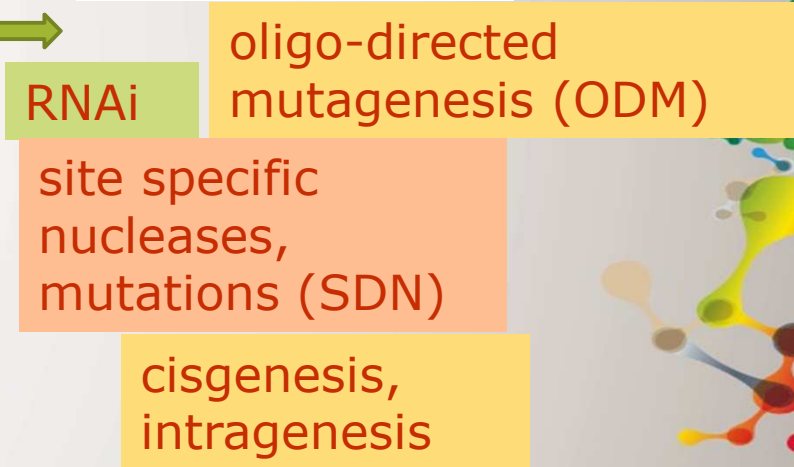


Science – technical advances

2000



2015

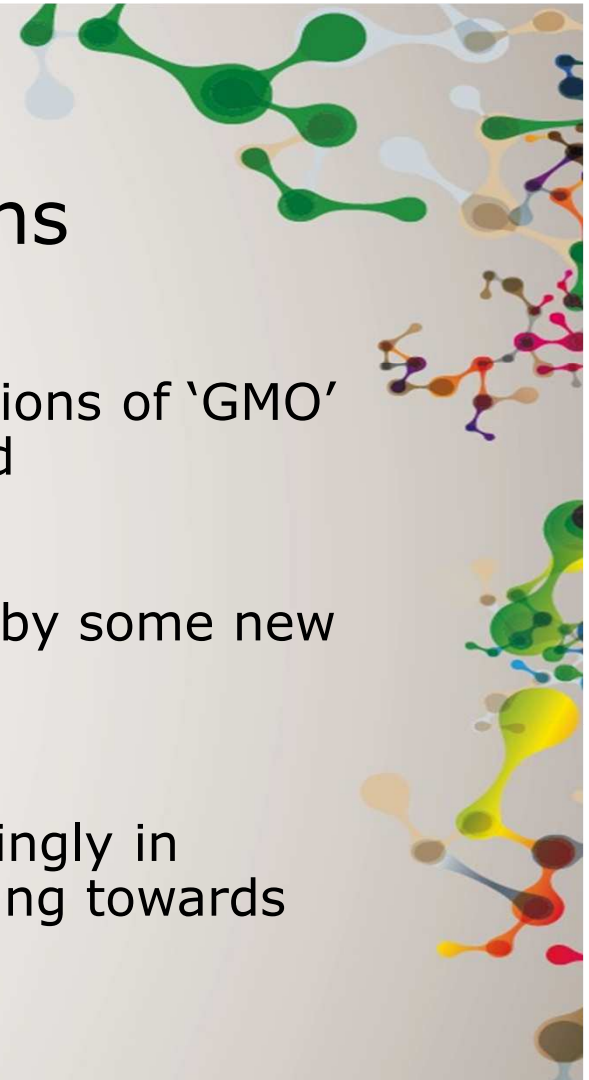




Technical review of the Regulations

What is the problem?

- Technology has changed since the definitions of 'GMO' and 'gene technology' were last amended
- It's unclear whether organisms modified by some new technologies are GMOs
- New technologies are being used increasingly in research and development, and are moving towards commercialisation





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Review of the Regulations

Primary aim:

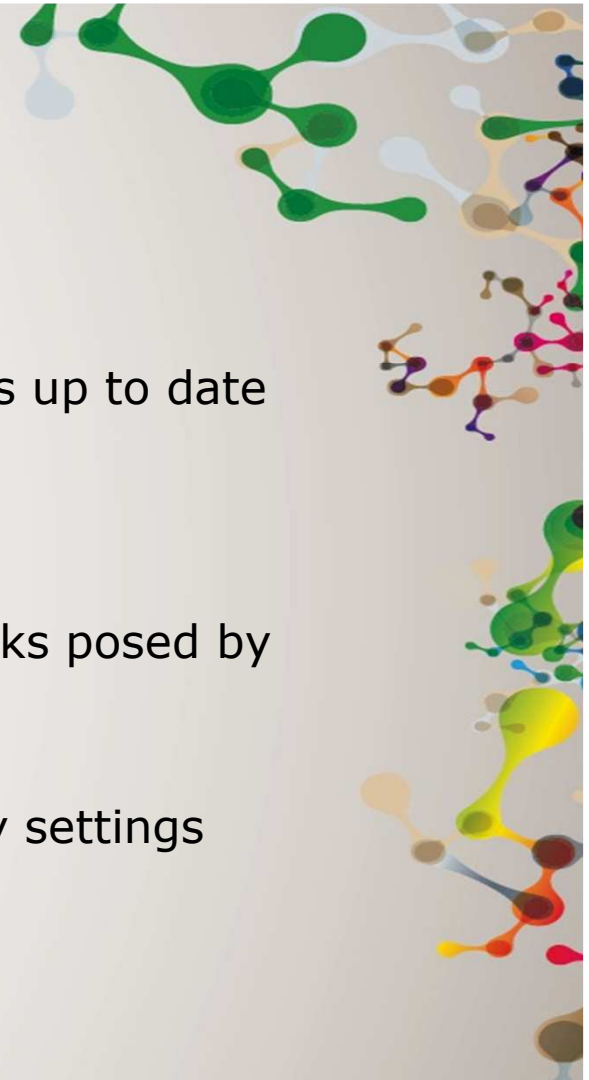
Bringing the lists of exclusions in the Regulations up to date with current science to provide clarity

Main consideration:

Regulation should be commensurate with the risks posed by gene technology

An important constraint: can't alter the policy settings

- E.g. process trigger





Review progress to date

First round of consultation was in 2016

- 4 options for how new technologies could be regulated
- options paper and submissions are on the OGTR website

Public consultation

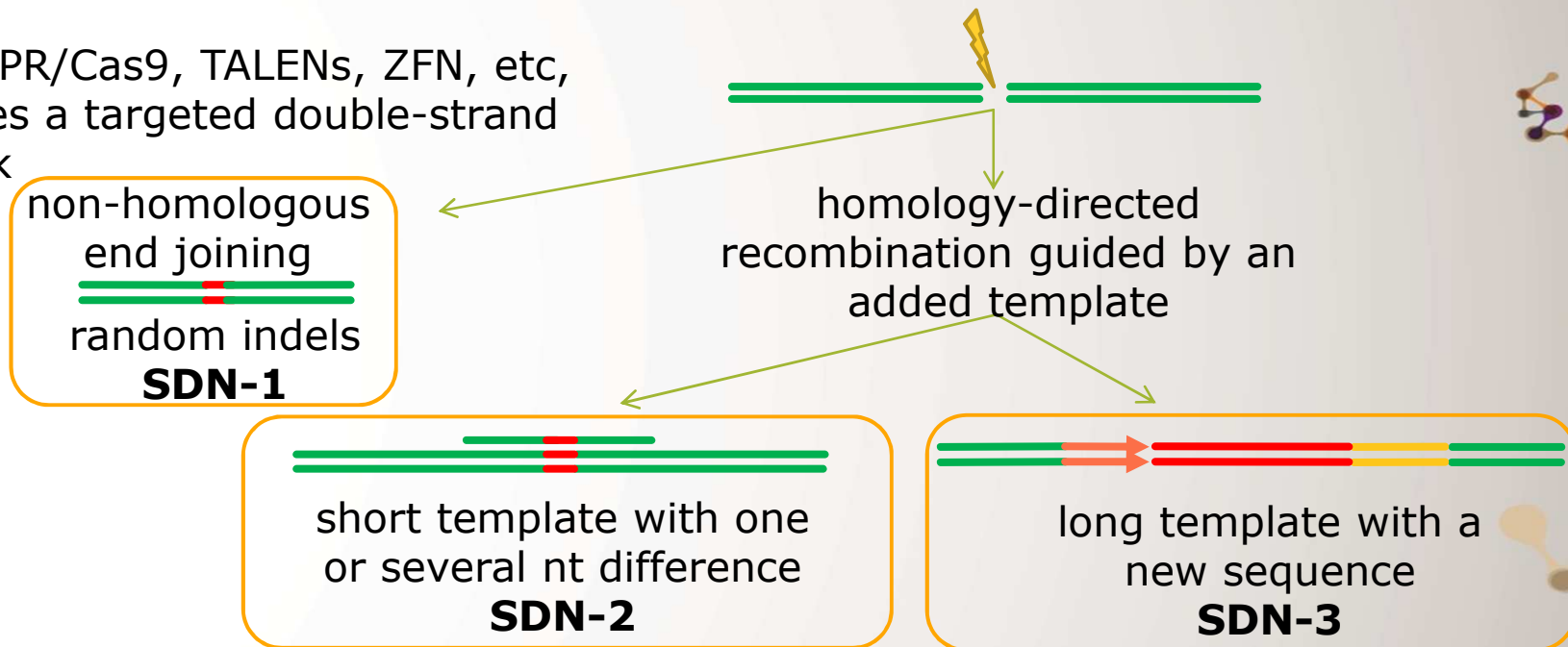
- on draft amendments to the Regulations
- open until February 2018





Site-directed nucleases

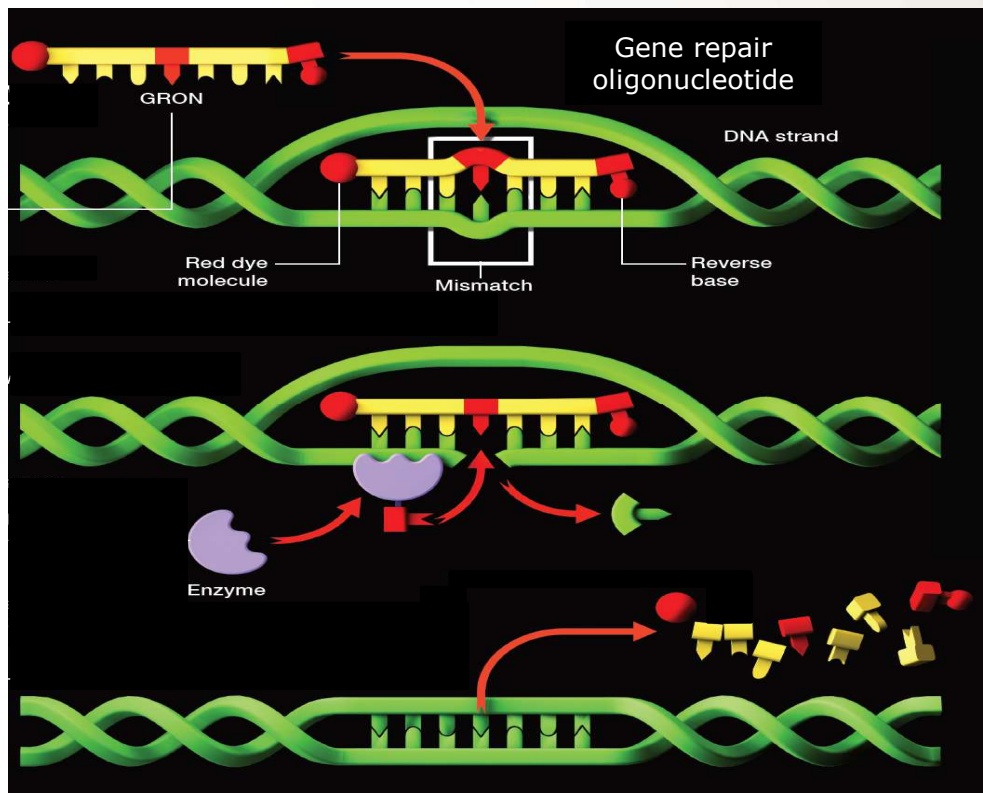
CRISPR/Cas9, TALENs, ZFN, etc,
makes a targeted double-strand
break





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Oligo-directed mutagenesis



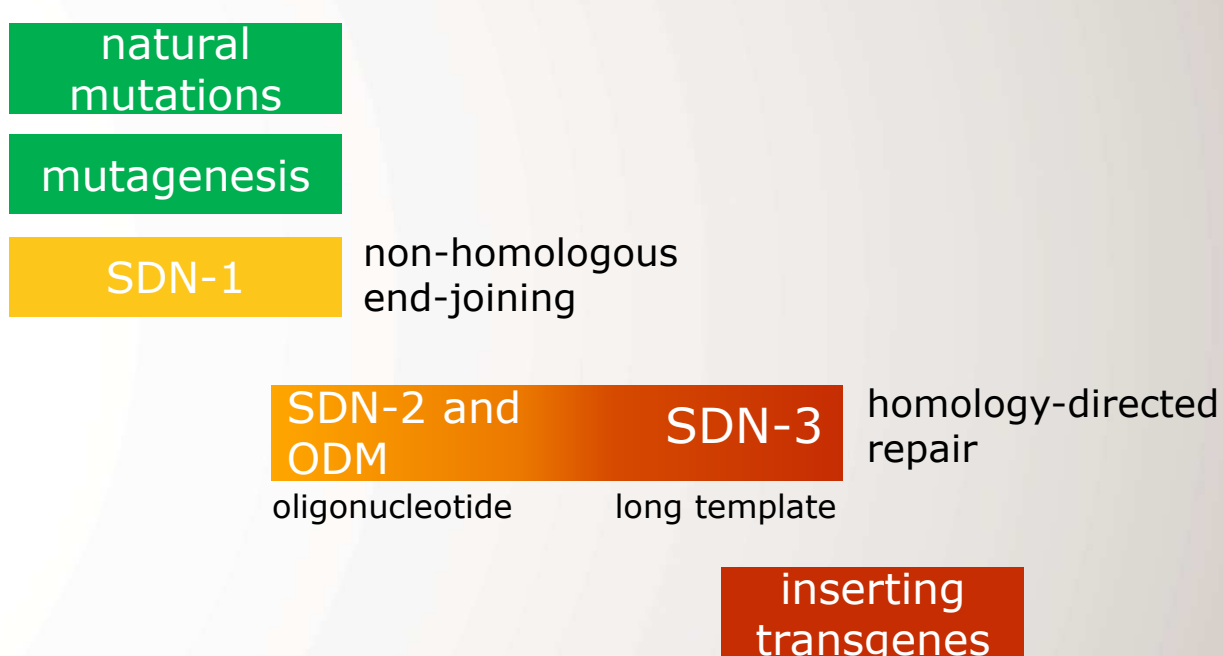
Cibus' Rapid Trait
Development System





Some new technologies fit 'in-between'

not gene
technology





New technologies proposal

Amendment proposal for public consultation – subject to change

natural
mutations

mutagenesis

SDN-1

Regulate template-guided changes

Any organism with its genome modified by SDN-2, ODM and SDN-3 will be regulated, whether or not it also contains other genetic modifications, such as a DNA insert for delivery of the technology.

Exclude SDN-1 from regulation

SDN-2 and
ODM

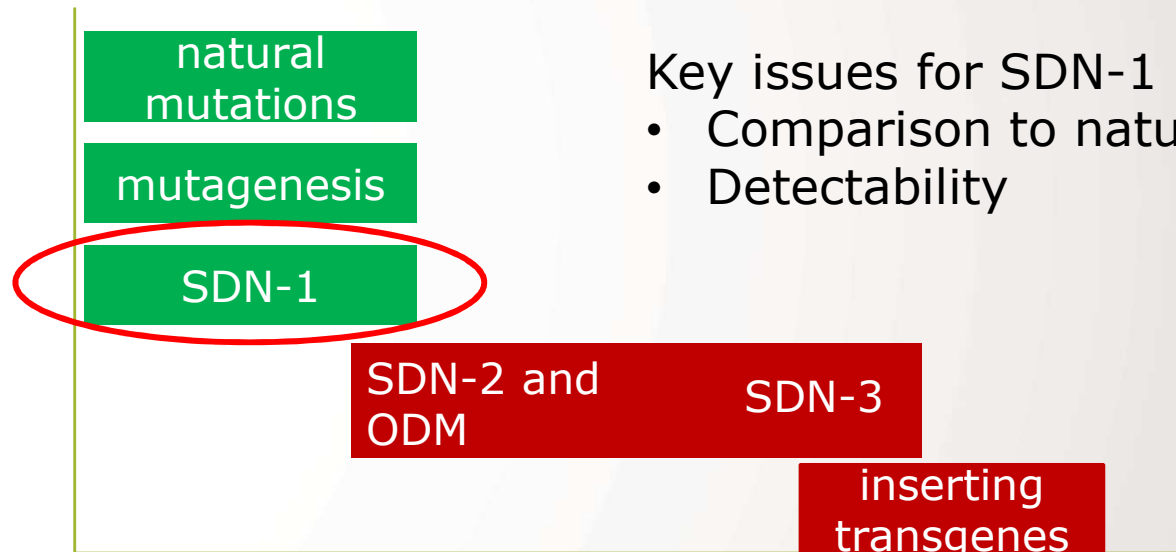
SDN-3

inserting
transgenes



New technologies proposal

Amendment proposal for public consultation – subject to change





New technologies proposal

Amendment proposal for public consultation – subject to change

natural
mutations

mutagenesis

SDN-1

SDN-2 and
ODM

SDN-3

inserting
transgenes

Key issues for SDN-2 & ODM:

- Submitter concerns depending on parent organism, or repeated use of technique



New technologies proposal

Amendment proposal for public consultation – subject to change

natural
mutations

Consistent with current policy settings

mutagenesis

Provides clarity until policy is reviewed

SDN-1

SDN-2 and
ODM

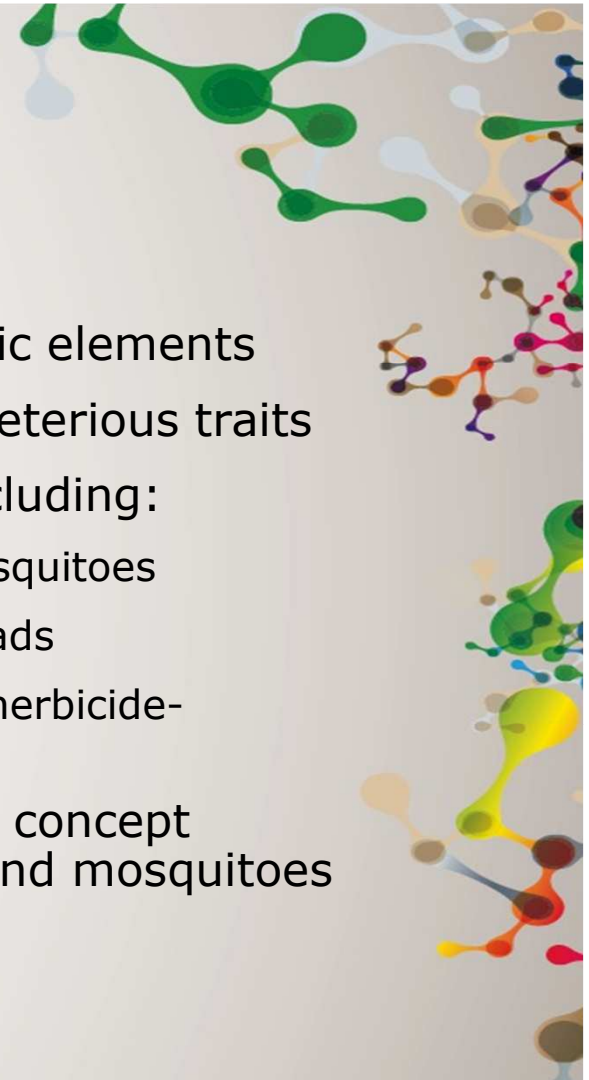
SDN-3

inserting
transgenes



Gene drives

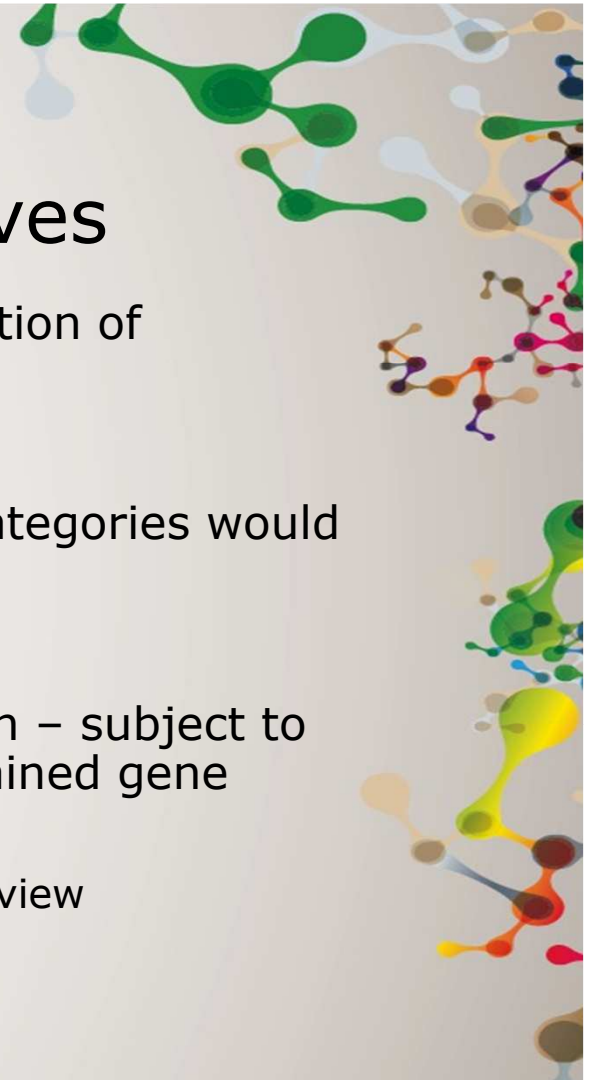
- Gene drives are preferentially inherited genetic elements
- 'drive' a trait into a population – including deleterious traits
- Many possible uses have been speculated, including:
 - Disease control, eg virus transmission by mosquitoes
 - Invasive species control, eg rodents, cane toads
 - Agricultural applications, eg fruit fly control, herbicide-resistant weeds, pesticide-resistant insects
- Research is in an early phase: recent proof of concept laboratory experiments in yeast, *Drosophila* and mosquitoes





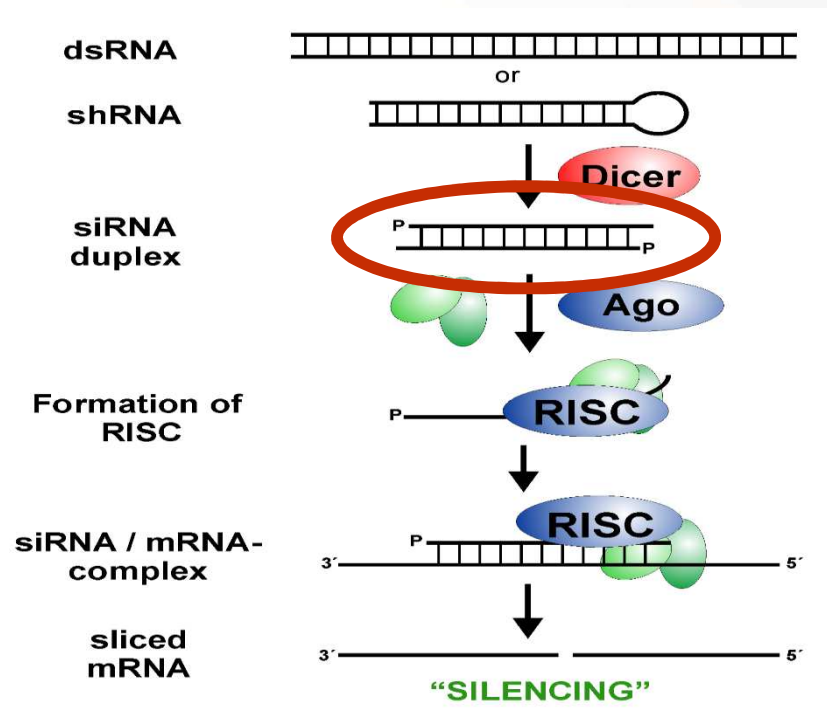
Regulatory status of gene drives

- Engineered gene drives involve stable integration of modified genes – these organisms are GMOs
- **Currently:** general plant and animal NLRD categories would include most contained gene drive work
- **Amendment proposal** for public consultation – subject to change: case-by-case assessment of all contained gene drive work (DNIR licence)
 - to be reassessed at the next Regulations Review



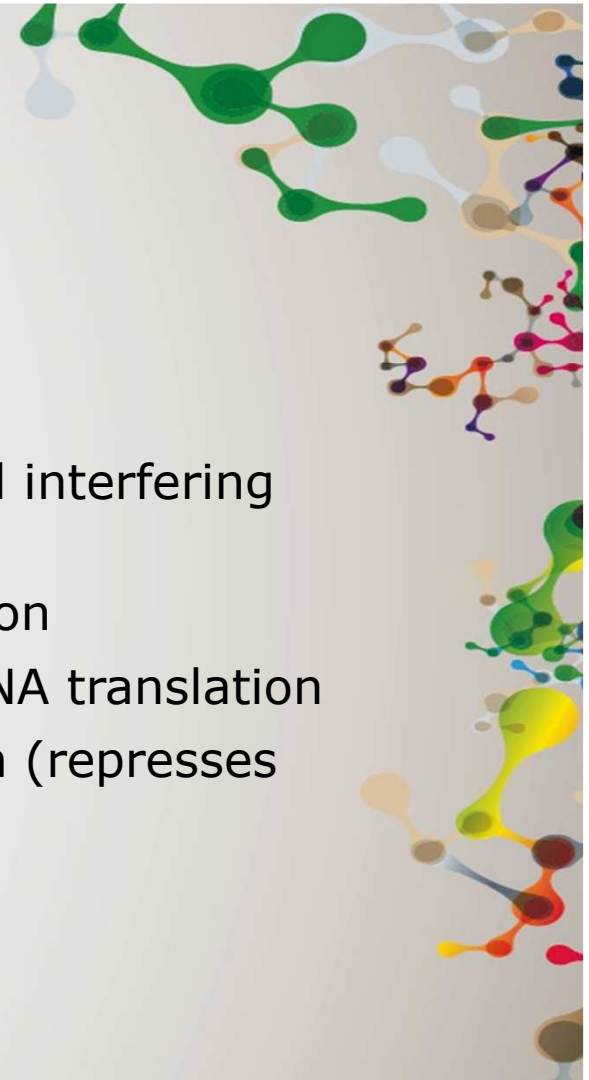


RNA interference



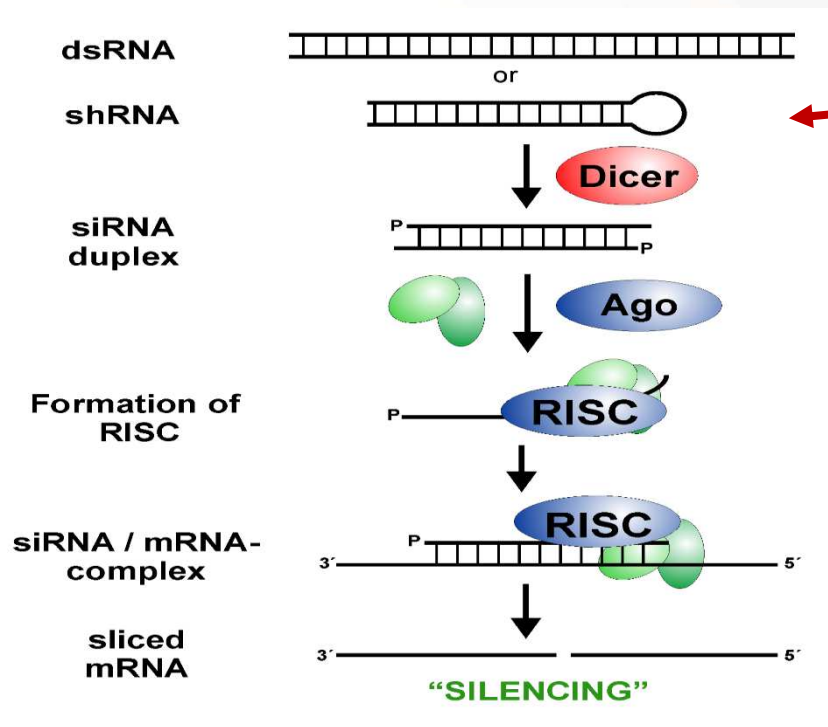
Gene-specific small interfering RNAs may lead to:

- mRNA degradation
- inhibition of mRNA translation
- DNA methylation (represses transcription)





RNA interference



Permanent effects:
integrated transgene

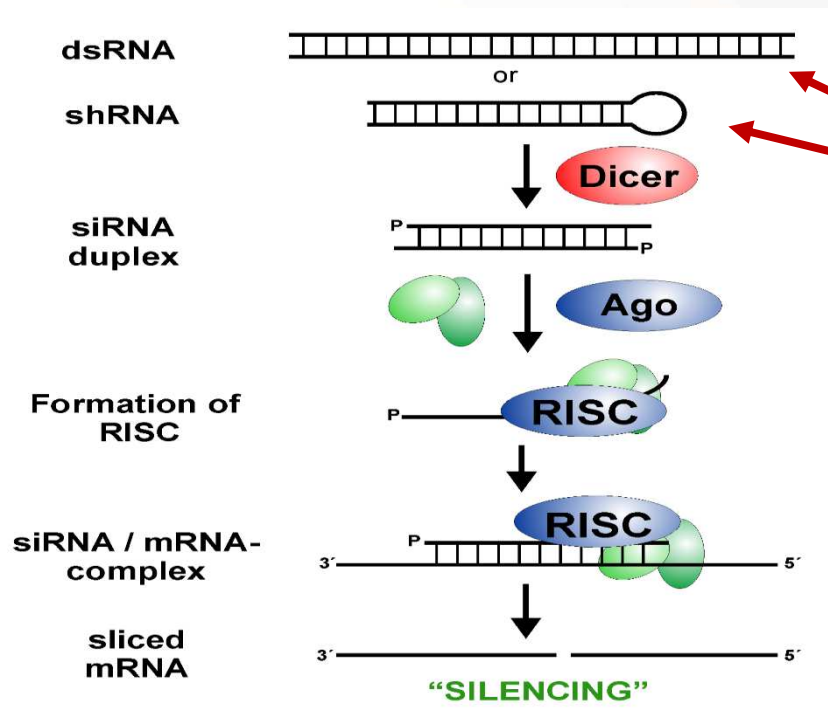
Short-term effects:
Viral vector

Applied as RNA





RNA interference



Permanent effect:
integrated transgene

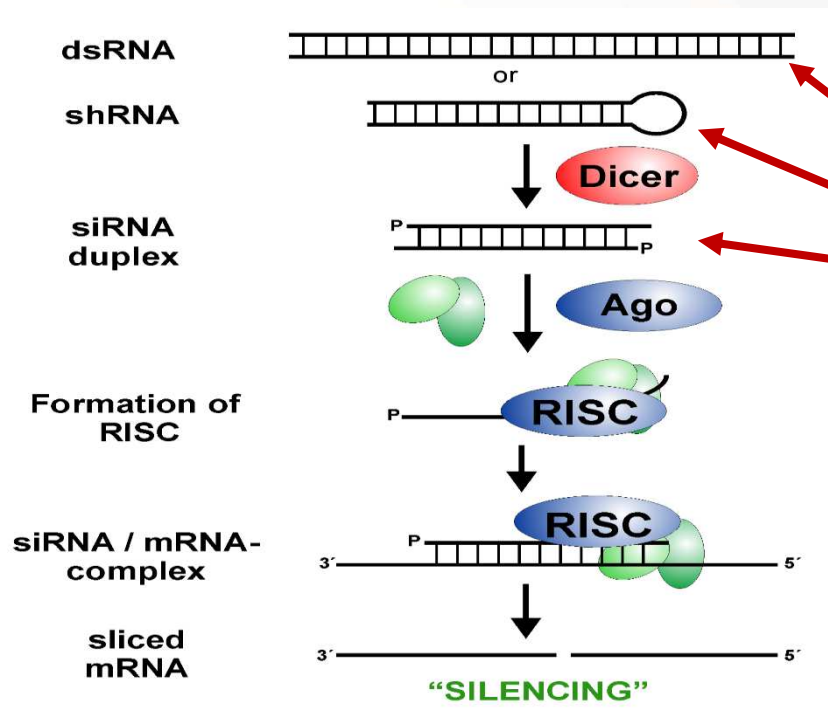
Short-term effect:
Viral vector

Applied as RNA





RNA interference



Permanent effect:
integrated transgene

Short-term effect:
Viral vector

Applied as RNA





RNA interference proposal

Amendment proposal for public consultation – subject to change

RNAi techniques involving direct application of RNA will **not** be gene technology if they

- do not cause changes to genomic sequence
- do not allow translation of novel proteins
- do not cause formation of an infectious agent

e.g. directly applying siRNAs and dsRNA

RNAi techniques that will remain gene technology involve:

- inserting sequences into the genome and
- vector delivery.



What's next?

- Public consultation until February 2018 on
 - drafted amendments
 - paper outlining the directions
- Finalise amendments, taking submissions into account
 - **proposals may be modified**
- State and Territory approvals, Australian Government Regulation-making process
 - **amendments would not commence before 2019**

**Do not act on any of these proposals now.
Always apply the current legislation!!!**



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How can you contribute?

Technical review consultation aims to:

- fine-tune the amendment wording for best clarity and
- help us understand the impacts of these proposals.

Get involved in the Review of the National Gene Technology Scheme at

<https://consultations.health.gov.au/health-systems-policy-division/genetechreview2017/>





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