



Induced genetic variation: innovation opportunities & challenges

Hennie Groenewald (PhD)



science
& technology

Department:
Science and Technology
REPUBLIC OF SOUTH AFRICA



'Panda Babies: Mission Critical'
August 28 at 8/7c
on the Nat Geo
WILD channel

GE

The
D
R E

SN

SCIENCE NEWS MAGAZINE
SOCIETY FOR SCIENCE & THE PUBLIC
SEPTEMBER 3, 2016



n

Trends
Biot



SEEK
PAM sequen
in CR

CHEMISTRY

TAKING
CHARGE

Energy storage beyond
the lithium-ion battery

PAGE 26

TAKING

Targeted

No
No
No

W I

And
of li
we
The
Eng



nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Dawn of the
gene-editing age

PAGE 155



EVERYWHERE

CONSERVATION

A WORLD OF
TWO HALVES

E. O. Wilson's vision for an
Earth shared with nature

PAGE 170

PLANT BIOLOGY

FLOWER
ARRANGEMENT

An attractant/receptor pair
driving pollen-tube growth

PAGES 178, 241 & 245

GROUP DYNAMICS

THE RIGHT
SIZE FOR A LAB

The skills mix and head
count needed for success

PAGE 263

NATURE.COM/NATURE

10 March 2016 £10

Vol. 531, No. 7590



SPEC

Eugen

Fraser Nelson on the race for designer babies

REFERENDUM RAGE
ALEX MASSIE

SEX, ORCHIDS AND MAPPLETHORPE
STEPHEN BAYLEY

THE RABBIT WHO MADE ME A TORY
MATTHEW PARRIS



The Economist

AUGUST 22ND - 28TH 2015

Editing

The prosp

No baldness

Sprinter
↓
Perf



Hum

Ed

NATION

SCIENCE

nature biote

THE SCIENCE AND BUS

CRISPR-Cas9 gene driv
Predicting drug effects
Optimal reporters for hi

Australasian Science

VOLUME 38 NUMBER 4
JULY/AUGUST 2017 | \$9.95

Gene Drives

A Fork in the Road for the GMO Debate

How Gene Drives Can Genetically Modify Populations

Could Gene Drives Stop Malaria in its Tracks?

How Gene Drives Could Benefit Biodiversity

Are Gene Drives the Future of Pest Control?

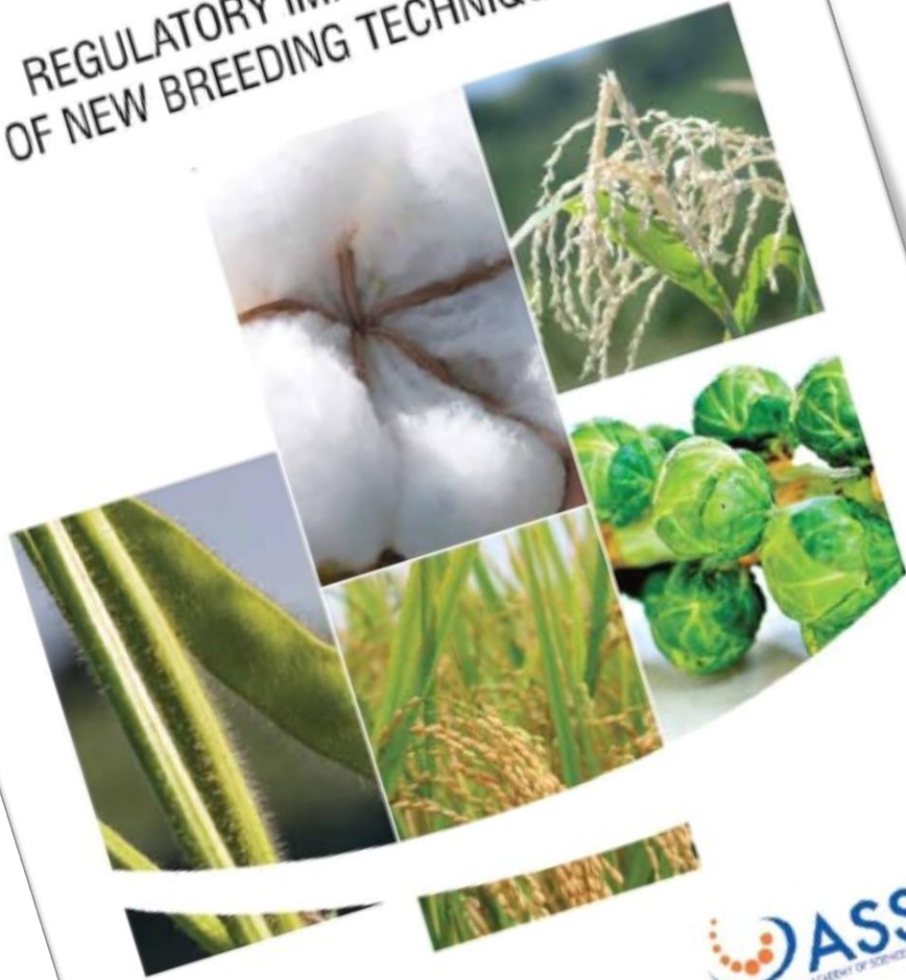
Practical and Ethical Concerns About Gene Drives



Genome Editing R&D

- Non-browning mushrooms*
- Herbicide tolerant canola*
- Waxy corn
- Disease resistant tomatoes, rice, wheat, bananas, etc.
- Slow growing cabbage
- Vitamin enriched oranges
- Drought tolerant maize, wheat, rice, etc.
- Hornless cattle
- Disease & pest resistant pigs, goats, chickens, etc.
- Female only chickens
- Double muscled pigs & cattle
- Hypoallergenic chickens
- Gene therapy in humans*

THE
REGULATORY IMPLICATIONS
OF NEW BREEDING TECHNIQUES



New opportunities, new challenges

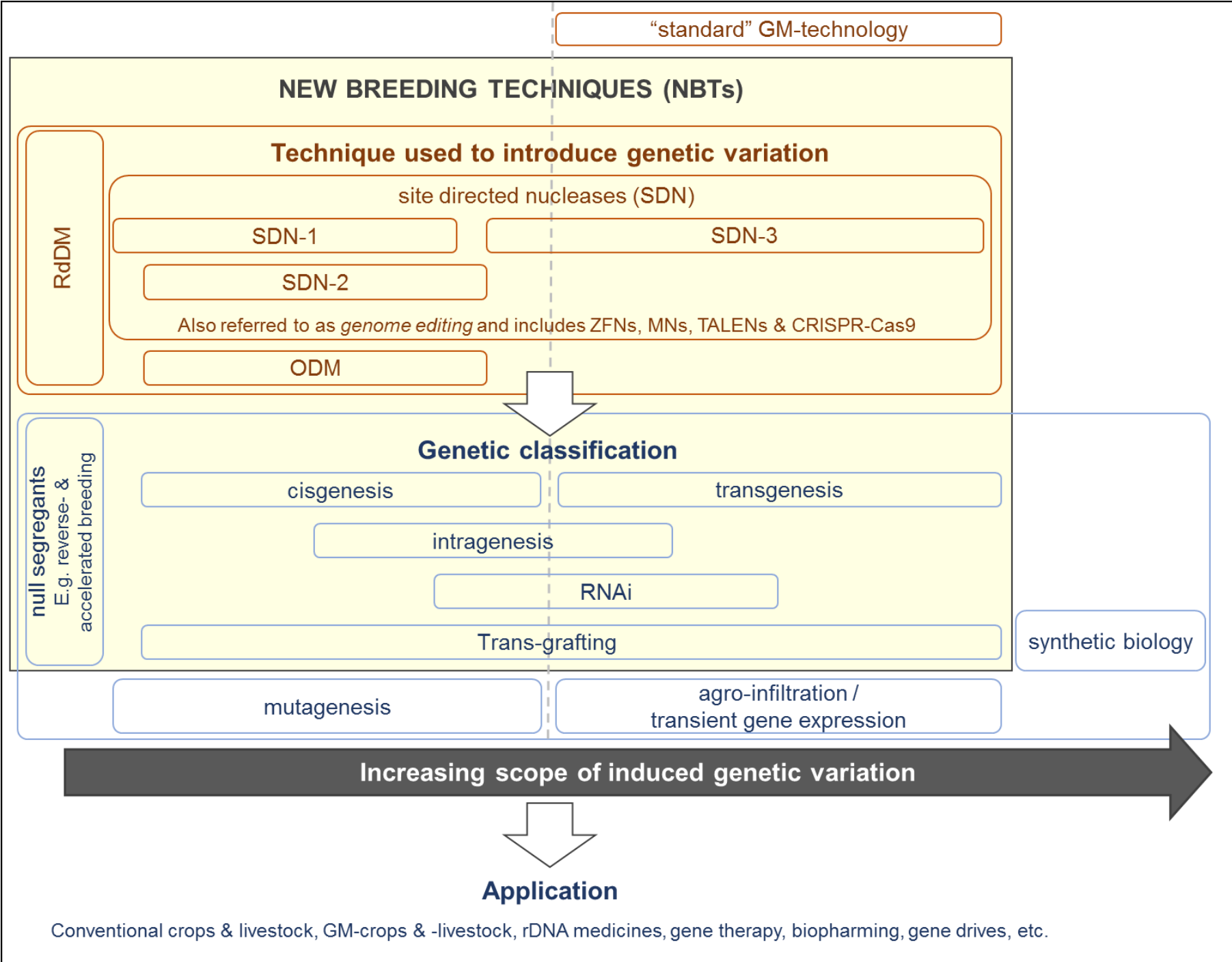
Key issues

1. Trigger - product vs process

2. Threshold

} Risk vs legal discussion

3. Managing risk vs managing risk perceptions



Findings

1.

NBTs hold great potential, in particular for developing biotech innovation systems, as they allow the relative quick, efficient, accurate and cost-effective modification of valuable genetic traits in crops, livestock and microorganisms.

2.

Only Argentina has published an official, national framework on how to regulate the products of NBTs.

In addition, countries such as Canada, which have a strong product-base regulatory trigger require no amendments.

[more recently also Israel, Chile - USDA, FDA “draft guidelines”]

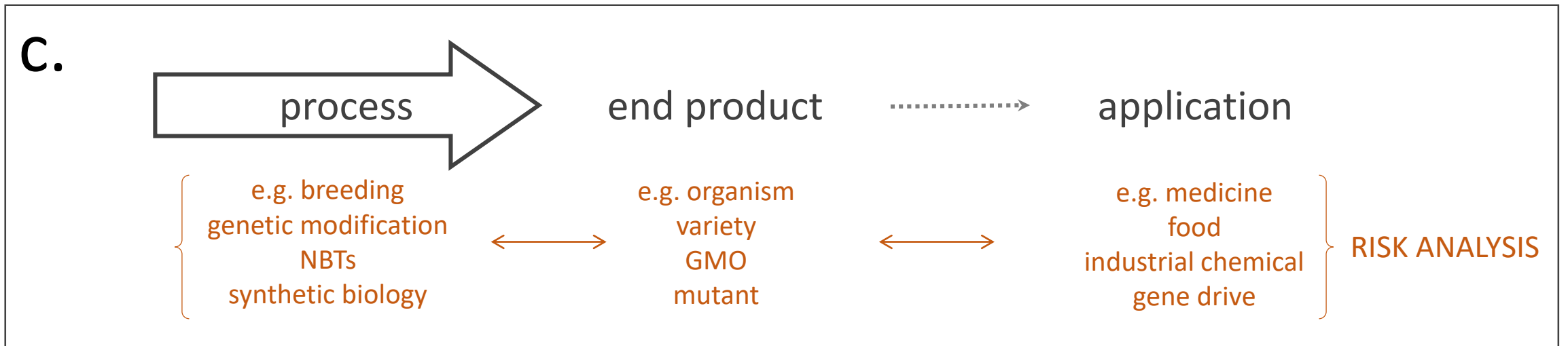
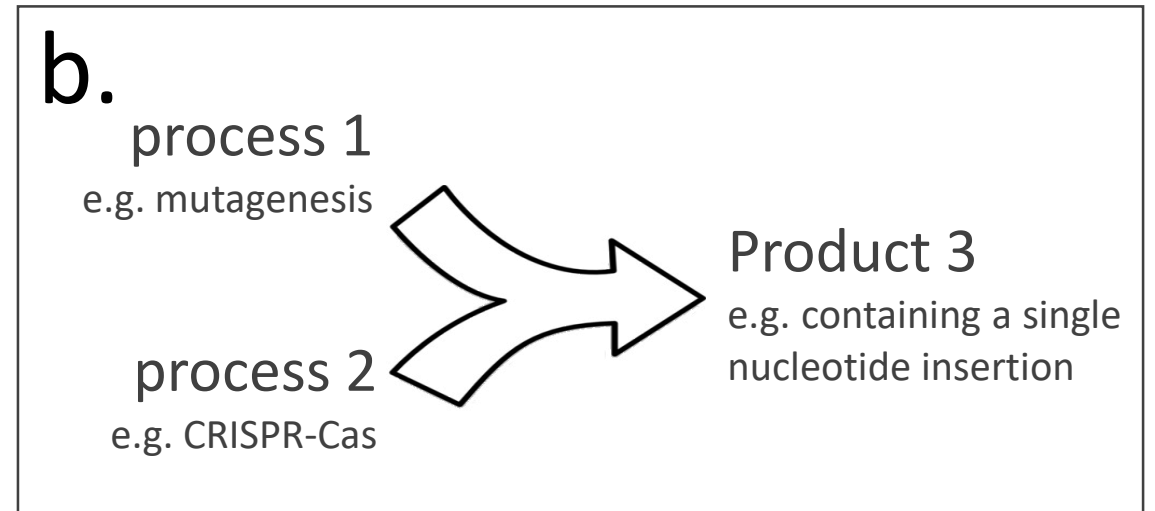
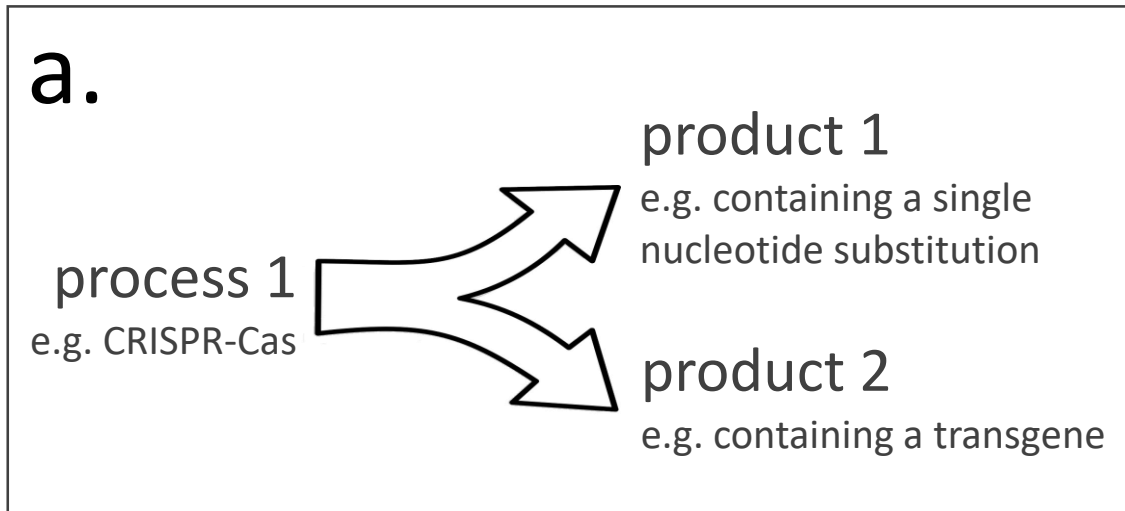
[Brazil, China, Sweden, UK, EU, Japan, Korea, ... updates]

3.

For all genome modified organisms the principle source of risk, i.e. the hazard, is the organism itself and not the technique/process used to generate it.

This resulting **product** should therefore be the **trigger** and subject of regulation and the regulatory requirements should be **proportionate** to the possible risks it poses.

[also consider scope, science-basis & administrative coherence]



Findings

4.

South Africa's robust and experienced regulatory system for GMOs can be used to effectively regulate the products of NBTs and possible new techniques developed in future, where appropriate.

To allow this accept that -

- the GMO Act has a product-based **trigger**, and
- the **threshold** is genetic variation beyond that which may occur naturally.

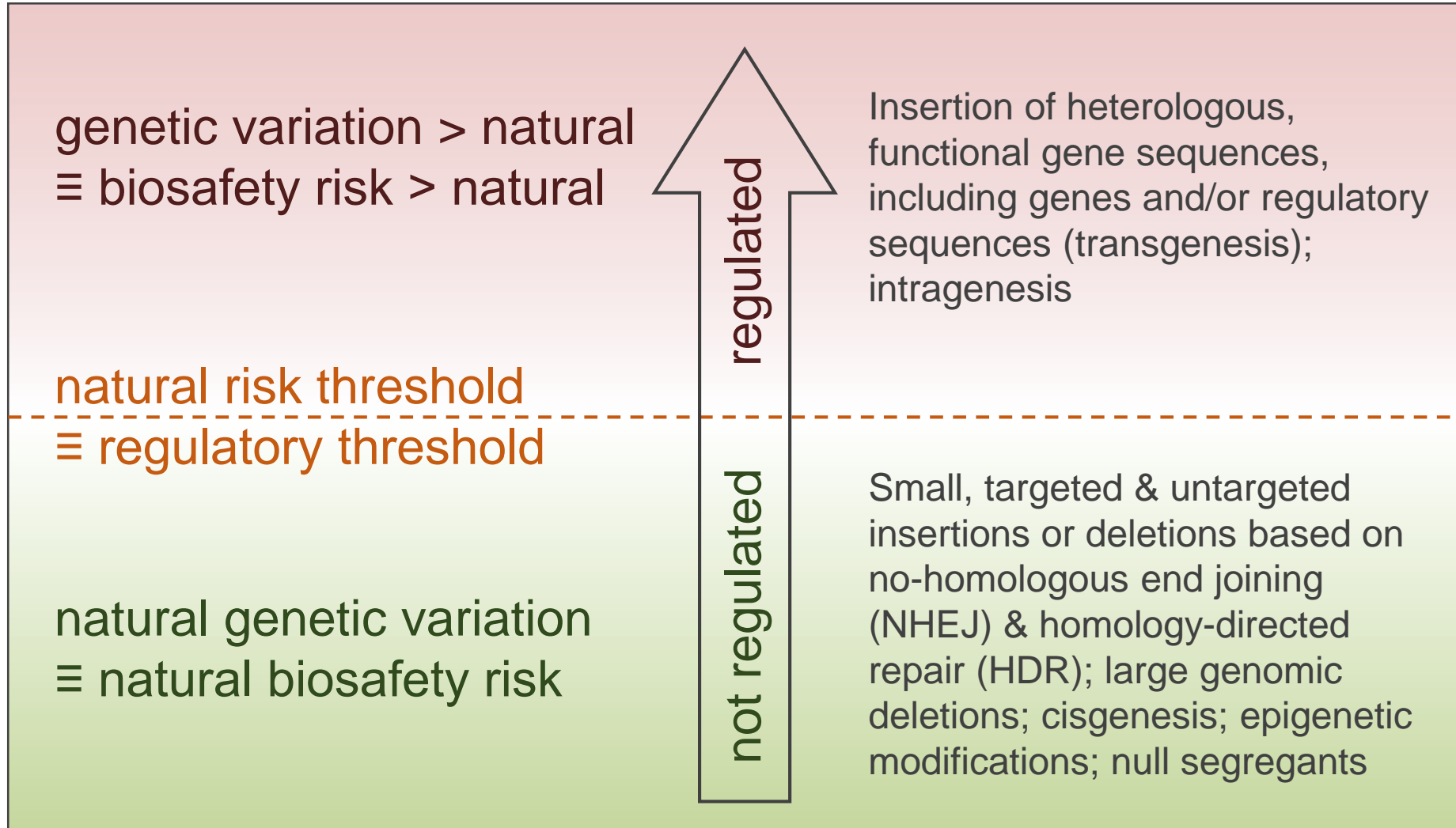
GMO Act's definition:

“GMO means an organism the genes or genetic material of which have been modified in a way that does not occur naturally through mating or natural recombination or both, and 'genetic modification' has a corresponding meaning.”

PLUS exclusions:

mutagenesis, ploidy manipulations and somatic hybridisation

[all excluded techniques are limited to harnessing endogenous genetic potential & human intervention / process is not considered an absolute trigger for regulation]

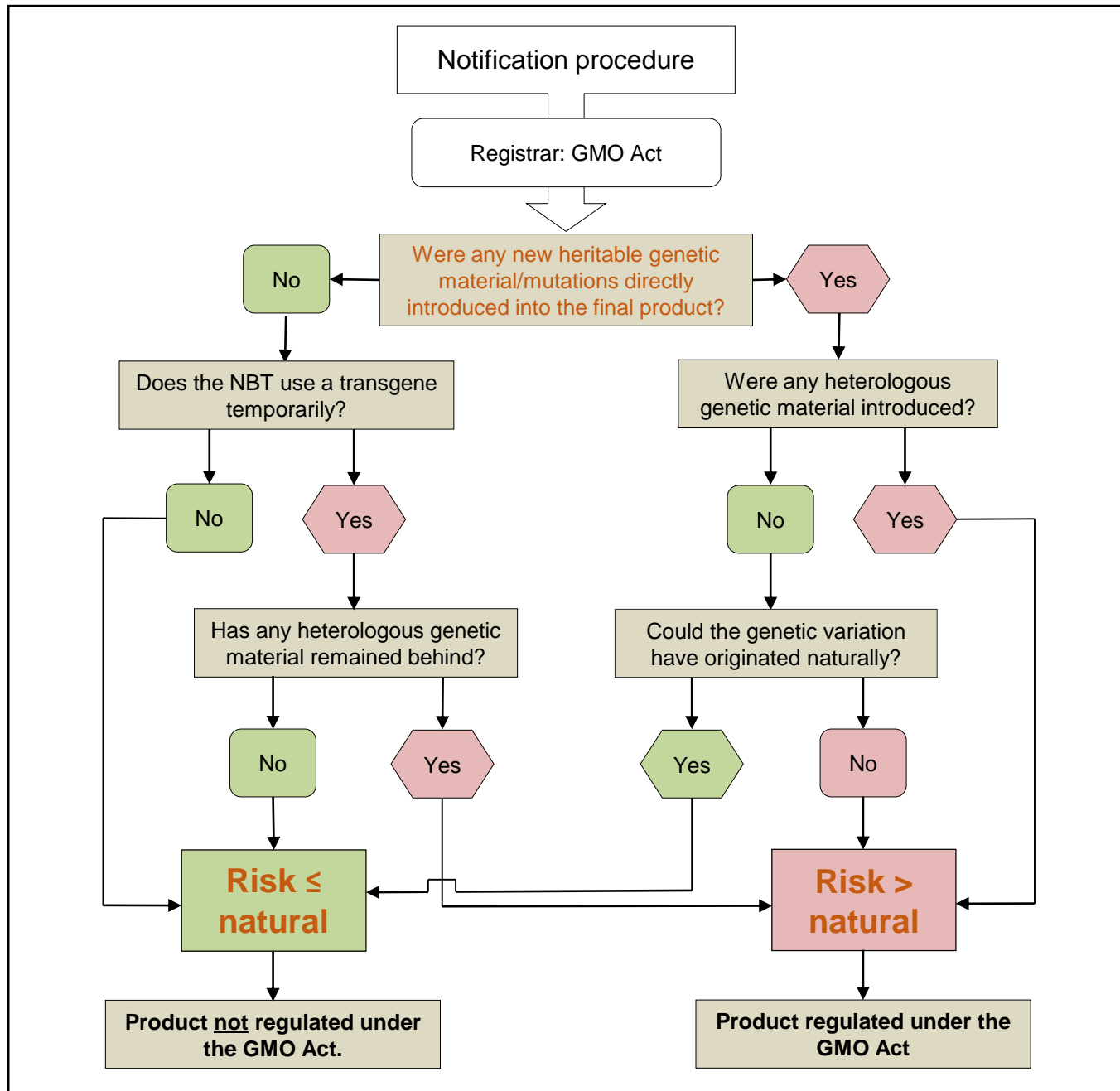


[figure 7.1, p79]

5.

The products of NBTs can simply be classified as those that may have genetic variation / risks greater than what may occur naturally, which will be subject to regulation under the GMO Act, or those having genetic variation risks similar to those that may occur naturally, which will not be regulated under this Act.

A succinct “notification procedure” could ensure a mechanism for making case-by-case decisions and appropriate oversight.



“Oversight”


Regulation

6.

Likely regulatory outcomes of the suggested framework aligns well with the currently available consensus discussions.

Its implementation will ensure effective and appropriate oversight to **ensure the safety and sustainability** of all relevant products, **without unduly impacting on innovation.**

Table 7.1. The likely regulatory outcome for specific products of various NBTs based on the proposed product-based regulatory trigger and unnatural genetic variation threshold.

Nr	Genetic change 	Technique used	Regulated as a GMO?
1	Small, targeted & untargeted inserts or deletions based on no-homologous end joining (NHEJ)	Site-directed nucleases (SDNs) ¹ , mutagenesis	No
2	Small, targeted inserts or deletions based on homology-directed repair (HDR)	SDNs, oligonucleotide-directed mutation (ODM)	No
3	Large, targeted genomic deletions	SDN pairs	No
4	Targeted insertion of homologous, functional gene sequences, including genes and/or regulatory sequences (cisgenes)	cisgenesis using SDNs	No
5	Targeted insertion of reorganised, homologous, functional gene sequences, including genes and/or regulatory sequences (intragenes)	intragenesis using SDNs	Yes
6	Targeted & untargeted insertion of heterologous, functional gene sequences, including genes and/or regulatory sequences	transgenesis, using "conventional GM technology" or SDNs	Yes
7	Epigenetic modifications	RNA-dependent DNA Methylation	No
8	Null segregants	Reverse breeding	No
9	GMO / non-GMO grafting (transgrafting)	GMO rootstock or scion and products	Yes
		Non-GMO rootstock or scion and products	No

¹e.g. ZFNs, MNs, TALENs & CRISPR/Cas.

CHALLENGES

- Defining “*genetic variation beyond that which may also occur naturally*” → i.e. defining an acceptable threshold. [≡ “novel combination” in other systems]
- International harmonization [& leadership].
- [Arguing] Alignment with Cartagena Protocol on Biosafety.

“...any living modified organism resulting from modern biotechnology that may...”

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

Need to better distinguish between...

Terms - techniques, genetic impact and use.

Better communicate...

1. Variability
2. Risk analysis vs. risk perception
3. Value (particularly in public innovation systems)

And avoid...

Increasing uncertainty and confusion (especially in unexperienced systems)

STATUS

National

- Recommendations accepted in principle.
 - DAFF initiated broad consultation process to facilitate implementation.
-

International

- Legal discussion rather than a technical/risk one.
- Now time for formal international alignment discussions.



*Applying scientific thinking
in the service of society*



THANK YOU!

Dr Hennie Groenewald hennie@biosafety.org.za