Disagreements and dissent:

The case of genetically modified organisms (GMOs) & New Genomic Techniques (NGTs)

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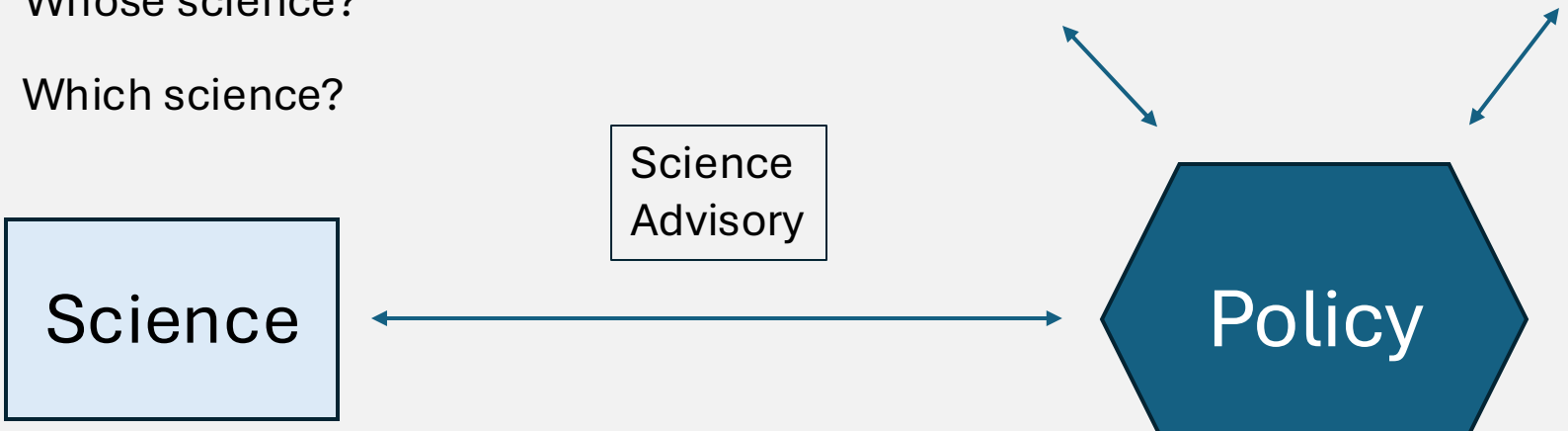
Athens - 16 May 2025

Overview

- Context
- Terms, concepts, definitions
- Systems, lego blocks, rabbits and elephants
- (and more assumptions)
- Precautionary principle
- Remits, CoI
- Topics at the Cartagena Protocol
- Topics at the CBD re Synthetic Biology

Context

- Whose science?
- Which science?



Cartagena Protocol | CBD | EU/EC | IUCN | FAO

Terms, Concepts, Definitions

These are essential components of scientific (and public) debate. They are shortcuts of meaning – and often subject of debate themselves (e.g. genes). Without clarity, debates and dialogue and understanding are being undermined.

e.g.

- Traditional breeding
- Precision
- Genetic engineering / modification
- Precautionary principle
- NGT redefined as equivalent to conventionally bred plants

Examples how scientific or general terms and concepts are being purposefully misused, redefined or degraded to obfuscate the picture, take away clarity and language necessary for meaningful debate, but importantly also, to confuse or mislead the public, who will no longer be able to distinguish and form an informed opinion.

Tower of Babel

מִגְדַּל בָּבֶל

Pieter Bruegel the Elder (1563)

https://en.wikipedia.org/wiki/Tower_of_Babel

Breeding

Traditional breeding

vs

Conventional breeding

vs

Mutational breeding

vs

“Precision breeding”

vs

“New breeding techniques” (NBTs)

Health Canada Santé Canada

Canada

Consultation Document:

Proposed Changes to Health Canada Guidance on the interpretation of Division 28 of Part B of the *Food and Drug Regulations* (the *Novel Food Regulations*):

When is a food that was derived from a plant developed through breeding a "novel food"?

March 2021

The goal of this public consultation is to obtain the views/perspectives of those for whom the new guidance is intended, including plant developers and the general public at large.

The final guidance will be published by the end of August 2021.

Annex 3: Examples of Conventional Methods of Plant Breeding

Techniques for overcoming reproductive barriers
• Bridge cross • Pollination through use of sub- or supra-optimal stigma age, or suboptimal conditions • Chemical-facilitated pollination • Pollination using pollen mixture treatments • Pollination through treatment and/or manipulation of the style • *In vitro* pollination • *In vitro* culture of excised ovaries • *In vitro* culture of excised ovules • *In vitro* culture of excised embryos (embryo rescue) • *In vitro* fertilization
Techniques for chromosome and genome manipulation
• Haploidization • Genome doubling, polyploidization • Production of alien addition or substitution lines • Chromosome translocation breeding • Manipulation of chromosome pairing in meiosis • Mutagenesis (via chemical mutagens or ionizing radiation) • Cell fusion (i.e., somatic hybridization) • Partial genome transfer
Other plant-breeding techniques
• Interspecific grafting • Hybrid variety production • *In vitro* tissue culture • Sex expression in monoecious or dioecious species • Apomixis • Marker-assisted breeding (MAB) • TILLING • Cell sorting

* Detailed descriptions and examples of the listed techniques can be found in van de Wiel et al., 2010. Traditional plant breeding methods. Wageningen UR Plant Breeding, Wageningen. Report 338.

** This table represents a list of methods which were, at the minimum, researched as potential tools for plant breeding. The majority of these methods were adopted by plant breeders and are used in current breeding programs.

WAGENINGEN UR
For quality of life

Traditional plant breeding methods

Clemens van de Wiel, Jan Schaart, Rients Niks & Richard Visser

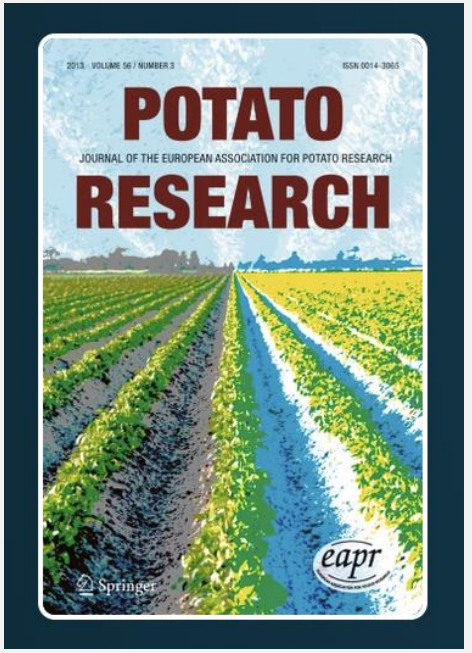
Report 338

The aim of this report is to present an overview of 'traditional' plant breeding techniques, that is, 'traditional' in the sense that they do not lead to plants/varieties covered by the EU directive 2001/18/EC on the deliberate release of GMOs into the environment. Therefore, the term 'traditional' as used here is not implying the absence of modern developments or any lack in sophistication in some of the techniques described. The following categories of techniques are discussed:

https://edepot.wur.nl/141713

van de Wiel et al., 2010. Traditional plant breeding methods. Wageningen UR Plant Breeding, Wageningen. Report 338.

Traditional breeding
&
Cisgenesis



Cisgenesis, a New Tool for Traditional Plant Breeding, Should be Exempted from the Regulation on Genetically Modified Organisms in a Step by Step Approach

Published: 26 June 2008

Volume 51, pages 75–88, (2008) Cite this article

Jacobsen, E., Schouten, H.J. *Potato Res.* **51**, 75–88 (2008).
https://doi.org/10.1007/s11540-008-9097-y

Council of the European Union

Brussels, 7 March 2025
(OR. en)

6426/25

LIMITE

AGRI 67
AGRILEG 25
ENV 96
CODEC 162
PI 32
IA 11

Interinstitutional File:
2023/0226(COD)

Cisgenesis & Breeders' gene pool

(5) 'cisgenesis' means techniques of genetic modification resulting in the insertion, in the genome of an organism, of genetic material already present in the breeders' gene pool. The genetic material may be incorporated as a continuous (exact) copy (cisgenesis in the strict sense) or a re-arranged copy of sequences already present in the breeder´s gene pool (intragenesis, also considered a subset of cisgenesis in a broader sense);

(6) 'breeders' gene pool' means the total genetic information available in one species and other taxonomic species with which it can be cross-bred, including by using advanced techniques such as embryo rescue, induced polyploidy and bridge crosses;

Precision

- of what ?
- at which level ?
- to which purpose ?

  (e.g. to avoid regulation & assessment?)
- how precise is “precise” ?

JBC REVIEWS

Applying gene editing to tailor precise genetic modifications in plants

Received for publication, April 10, 2020, and in revised form, July 27, 2020 Published, Papers in Press, July 28, 2020, DOI 10.1074/jbc.REV120.010850

Joyce Van Eck*

From the Boyce Thompson Institute, Plant Breeding and Genetics Section, School of Integrative Plant Science, Cornell University, Ithaca, New York, USA

Edited by Joseph M. Jez

The ability to tailor alterations in genomes, including plant genomes, in a site-specific manner has been greatly advanced

lian cell lines and in organisms such as bacteria and zebra fish; however, as methods became available in these systems, they

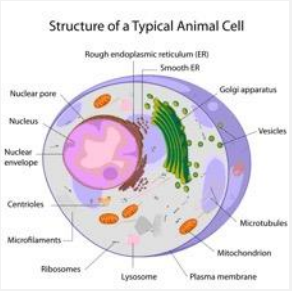
“….. in a site-specific manner ….. “

Levels & interactions relevant for risk understanding

Complexity, uncertainty (limited knowledge):

Plant / animal

1. **Genome:** Nucleotides and DNA (molecules)
2. **Epigenome:** gene regulation
3. **Cells:** function and communication
4. **Organism:** incl. action and interaction



5. **Populations:** behaviour, genetic diversity
6. **Ecosystems:** interdependence; function (and services)
7. **Landscapes**
8. **Biosphere:** climate change, water cycles, nutrient cycles
9. **Socio-economic circumstances** (differ across the globe)

Across time and space

Council of the European Union – as above

Criteria of equivalence of NGT plants to conventional plants

A NGT plant is considered equivalent to conventional plants when it differs from the recipient/parental plant by no more than 20 genetic modifications per monoploid genome of the types referred to in points 1 to ~~5~~4, in any DNA sequence sharing sequence similarity with the targeted site that can be predicted by bioinformatic tools.

Criteria specific to the use of targeted mutagenesis:

(1) substitution or insertion of no more than 20 nucleotides;

(2) deletion of any number of nucleotides;

Criteria specific to the use of cisgenesis:

(3) on the condition that the genetic modification does not interrupt an endogenous gene or that the resulting combination of DNA sequences in the recipient plant already occurs in a species from the breeders' gene pool:

(a) ~~targeted~~ insertion of a ~~contiguous~~ continuous DNA sequence existing in the breeders~~'s~~ gene pool;

(b) ~~targeted~~ substitution of an endogenous DNA sequence with a ~~contiguous~~ continuous DNA sequence existing in the breeders~~'s~~ gene pool;

(4) targeted inversion of a sequence of any number of nucleotides ;

Unintended modifications due to GM process

= process induced random mutations

ARTICLE Open Access

Whole-genome sequencing reveals rare off-target mutations in CRISPR/Cas9-edited grapevine

Grapevine (*Vinis vinifera*)

Insertion of a CRISPR/Cas gene via standard GM processes so as to enable genome editing.

Upon genome sequencing, they found that the GM processes (here the use of tissue culture and *Agrobacterium*) caused between

9,325 and 12,959 point mutations, with

230-377 of these in the coding region of genes,

Wang X, Tu M, Wang Y, et al. (2021). Whole-genome sequencing reveals rare off-target mutations in CRISPR/Cas9-edited grapevine. *Hortic Res*. 8(1):114. doi:10.1038/s41438-021-00549-4

Genetic Engineering

vs

Genetic Modification

"In Europe genetic modification is synonymous with genetic engineering while within the United States of America and Canada genetic modification can also be used to refer to more conventional breeding methods"

- Wikipedia (Genetic Engineering"

Is that correct? How far does the meaning of genetic modification stretch?

• The headline on this article was amended on 13 May 2025. An earlier version said the beans were genetically engineered; however, this is not the case.

Beans are being genetically engineered to grow in the UK – but how do they...

Three types of beans have been more than a decade in the making and hit shelves amid booming interest in legumes

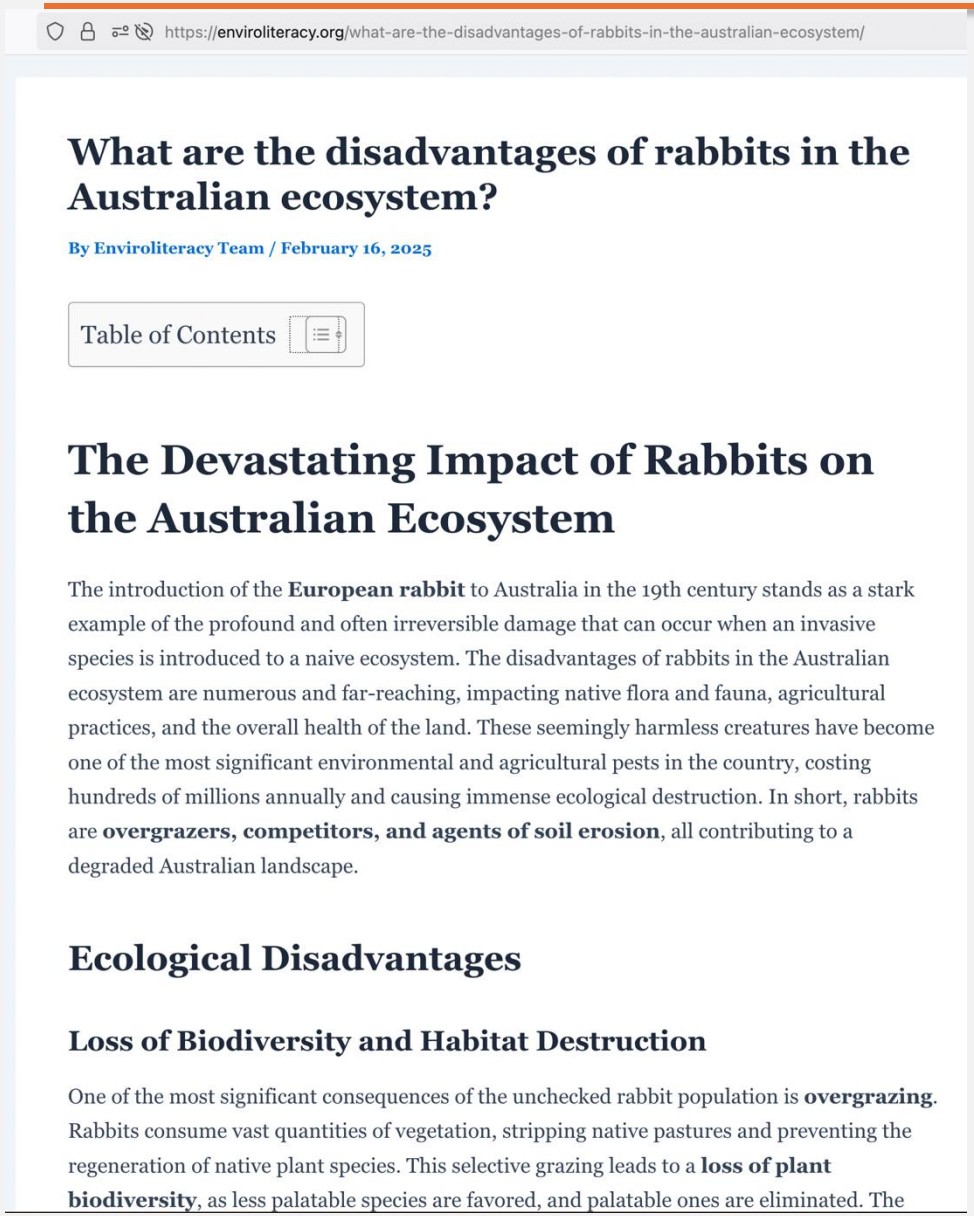
www.theguardian.com · 10 May

‘Beans are cool now’: we taste test a new variety developed especially for the UK

Three types of beans have been more than a decade in the making and hit shelves amid booming interest in legumes

https://www.theguardian.com/food/2025/may/10/beans-are-being-genetically-engineered-to-grow-in-the-uk-but-how-do-they-taste

Rabbits and elephants & more assumptions



https://enviroliteracy.org/what-are-the-disadvantages-of-rabbits-in-the-australian-ecosystem/

What are the disadvantages of rabbits in the Australian ecosystem?

By Enviroliteracy Team / February 16, 2025

Table of Contents

The Devastating Impact of Rabbits on the Australian Ecosystem

The introduction of the **European rabbit** to Australia in the 19th century stands as a stark example of the profound and often irreversible damage that can occur when an invasive species is introduced to a naive ecosystem. The disadvantages of rabbits in the Australian ecosystem are numerous and far-reaching, impacting native flora and fauna, agricultural practices, and the overall health of the land. These seemingly harmless creatures have become one of the most significant environmental and agricultural pests in the country, costing hundreds of millions annually and causing immense ecological destruction. In short, rabbits are **overgrazers, competitors, and agents of soil erosion**, all contributing to a degraded Australian landscape.

Ecological Disadvantages

Loss of Biodiversity and Habitat Destruction

One of the most significant consequences of the unchecked rabbit population is **overgrazing**. Rabbits consume vast quantities of vegetation, stripping native pastures and preventing the regeneration of native plant species. This selective grazing leads to a **loss of plant biodiversity**, as less palatable species are favored, and palatable ones are eliminated. The

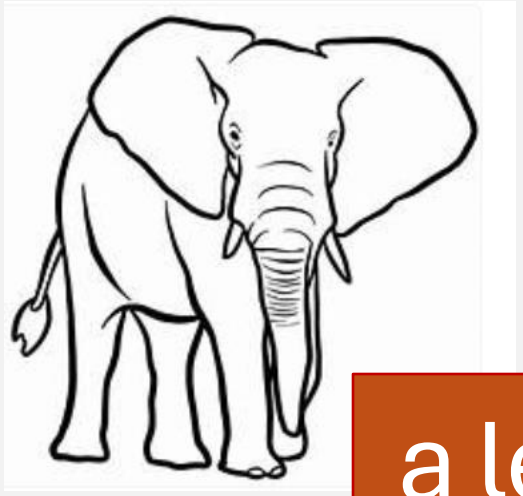
A rabbit is a rabbit is a rabbit

Transferability

enviroliteracy.org

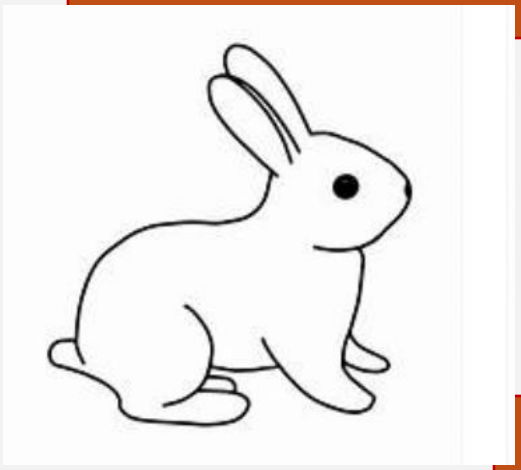
Rabbits and elephants & more assumptions

Transferability



a gene

a lego block



gene ecosystems

systems

a rabbit

Assumptions & outdated knowledge (1)

OLD: "~~Mutations are random as to where they occur in the genome~~"

Multiple research shows: Random mutations do NOT occur everywhere or just anywhere across the whole genome! e.g.

2018

DNA mismatch repair preferentially protects genes from mutation

Eric J. Belfield,[1,5] Zhong Jie Ding,[2,5] Fiona J.C. Jamieson,[1] Anne M. Visscher,[1,3] Shao Jian Zheng,[2] Aziz Mithani,[4] and Nicholas P. Harberd[1]

[1]*Department of Plant Sciences, University of Oxford, Oxford OX1 3RB, United Kingdom;* [2]*State Key Laboratory of Plant Physiology*

- Certain DNA regions and genes are specifically protected against random mutations due to
  - special 'packaging', epigenetic markers, eu/hetero-chromatin, histone modification, DNA sequence,
  - specific and different repair mechanisms and processes, etc.

Kawall, K. (2019) New possibilities on the horizon: genome editing makes the whole genome accessible for changes. *Frontiers in Plant Sciences*, 10: 525. https://doi.org/10.3389/fpls.2019.00525

Monroe, J.G., Srikant, T., Carbonell-Bejerano, P. *et al.* **(2022).** Mutation bias reflects natural selection in *Arabidopsis thaliana*. *Nature,* https://doi.org/10.1038/s41586-021-04269-6

Assumptions & outdated knowledge (2)

OLD: ~~"Silent / synonymous mutations are largely (near) neutral".~~ ?

Article Published online: 08 June 2022 nature research

Synonymous mutations in representative yeast genes are mostly strongly non-neutral

https://doi.org/10.1038/s41586-022-04823-w
Xukang Shen[1], Siliang Song[1], Chuan Li[2,3] & Jianzhi Zhang[1]✉

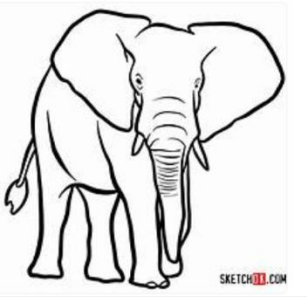
- Quantifying mutational fitness effects of 1000s of coding mutations in 21 different genes.
- "The cracking of the genetic code in the 1960s revealed that between one-quarter and one-third of single nucleotide mutations in protein-coding genes do not alter protein sequences."
- "The strong non-neutrality of most synonymous mutations, if it holds true for other genes and in other organisms, would require re-examination of numerous biological conclusions about mutation, selection, …."

Possibly due to impacts on gene regulation, 3-D effects, …

Assumptions & Combinatorial uncertainties

Re GM Eucalyptus (USA – field trials)

(cold tolerance, male sterility, reduced lignin)



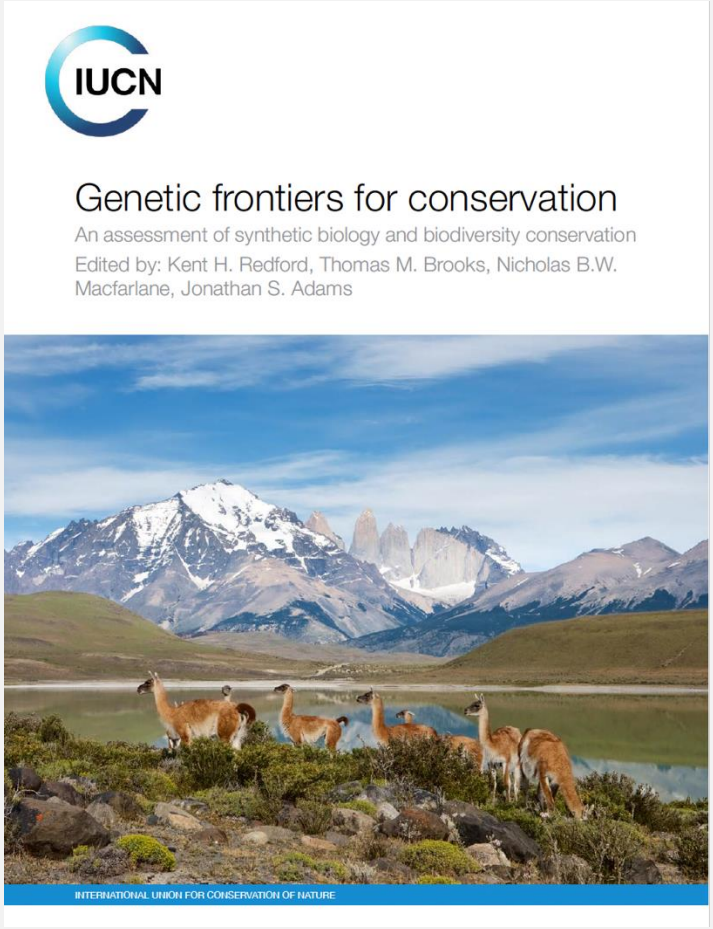
Because clone EH1 is a hybrid, the EA concludes a number of times that since neither of the parental lines is known to be a problem, the combined hybrid is not expected to cause any problems.

YET: "…the soil samples from *E. grandis* X E. *urophylla* plantations had an inhibitory effect on germination of maize, bean and watermelon **but had a stimulatory effect on squash**. The soil from *E. grandis* plantations had an **inhibitory effect** on squash."

Espinosa-Garcia FJ, Martinez-Hernandez, Quiroz-Flores A (2008) Allelopathic potential of *Eucalyptus* spp. plantations on the germination and early growth of annual crops. Allelopathy J 21:25–38

Bias material as basis for policy making

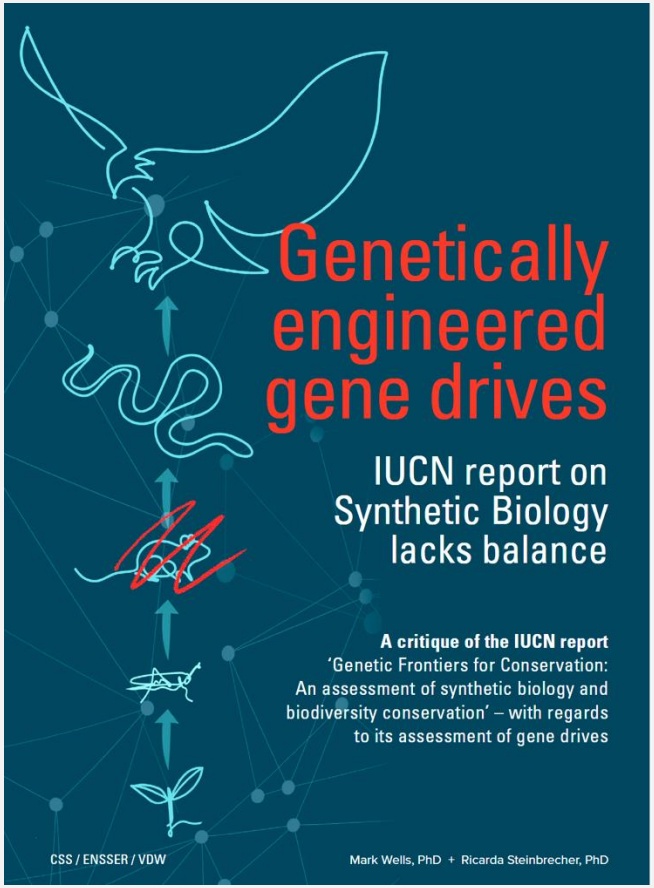
IUCN



*An assessment of **synthetic biology** and biodiversity conservation. Technical assessment.*

> *"In the context of using synthetic biology for conservation **the precautionary principle can, however, be utilised to support different positions**. These dual interpretations of the precautionary principle are particularly important to surface and discuss given ongoing global biodiversity loss (Butchart et al., 2010) and the insufficiency of existing efforts and methods to prevent it (Maxwell et al., 2016).* – p. 123

Redford, K.H., Brooks, T.M., Macfarlane, N.B.W. and Adams, J.S. (eds.) (2019). Genetic frontiers for conservation: An assessment of synthetic biology and biodiversity conservation. Technical assessment. Gland, Switzerland: IUCN. xiv + 166pp. www.iucn.org/resources/publications



This critique identifies eight major areas of concern

These need to be properly addressed before the IUCN make policy decisions on the use or release of gene drive organisms.

…

6. Assumption that any risk can be managed or predicted

7. Bias or conflict of interest of the authors

…

the report proposes a 180-degree flip in terms of how to interpret the precautionary principle, to be specifically applied to the technologies and substances of synthetic biology.

Precautionary principle

some other points

- Precautionary principle
- “Innovation principle”
- Progress
- Remits
- CoI
- Data as new commodity

Horizon scanning & monitoting of synthetic biology trends and developments (under CBD)

CPB: Parties requests for RA guidance materials

- Living modified **algae**
- Living modified animals
- Living modified **fish**
- Living modified **microorganisms**
- LMOs containing stacked events
- **Genome-edited mammals for agriculture**
- LMOs produced through new biotechnologies
- LMOs expressing **genome editing machinery for pest or pathogen control**
- **Long term and cumulative effects** of genetic constructs and LMOs
- LMOs for food, feed and processing
- Detection and monitoring of LMOs
- Operationalizing protection goals into relevant assessment endpoints
- **Simplified procedures** related to Article 13 and Agreements and arrangements as per Article 14
- **Transportability** of data for risk assessment of living modified organisms
- Use of LMOs in centres of origin and in traditional agricultural systems

Thank you !

Looking forward to our discussion