SCRA virtual Workshop: “Nuts & Bolts of U.S. Regulatory Dossiers for Genetically Engineered Products”, 19 – 21 September 2023

National and regional regulatory frameworks for biosafety outside the US

19 September 2023

Prof. Piet van der Meer

1986 – 2000: In charge of biosafety/GMO regulation in the Netherlands
2000 – 2002: Supporting EU accession countries with biosafety/GMO regulation
2002 – 2004: Leading the UNEP-GEF National Biosafety Framework Implementation Project
2004 – today: Supporting public research institutes, international organisations and governments
2006 – today: Faculty of Sciences, Ghent University, Belgium
2011 – today: Faculty of Law, Ghent University, Belgium
2014 – today: Faculty of Science, Vrije Universiteit Brussel (VUB), Belgium
2020 – today: Multidisciplinary Program on Sustainable Food and Biomass Systems, Office of the Vice Rector, VUB, Belgium

Topics

- The ‘regulatory cycle’
- Structure and scope of regulatory frameworks for biosafety
- EU regulatory framework for biosafety
- The regulatory status of gene edited organisms

Regulatory frameworks for biosafety

The ‘Regulatory cycle’:

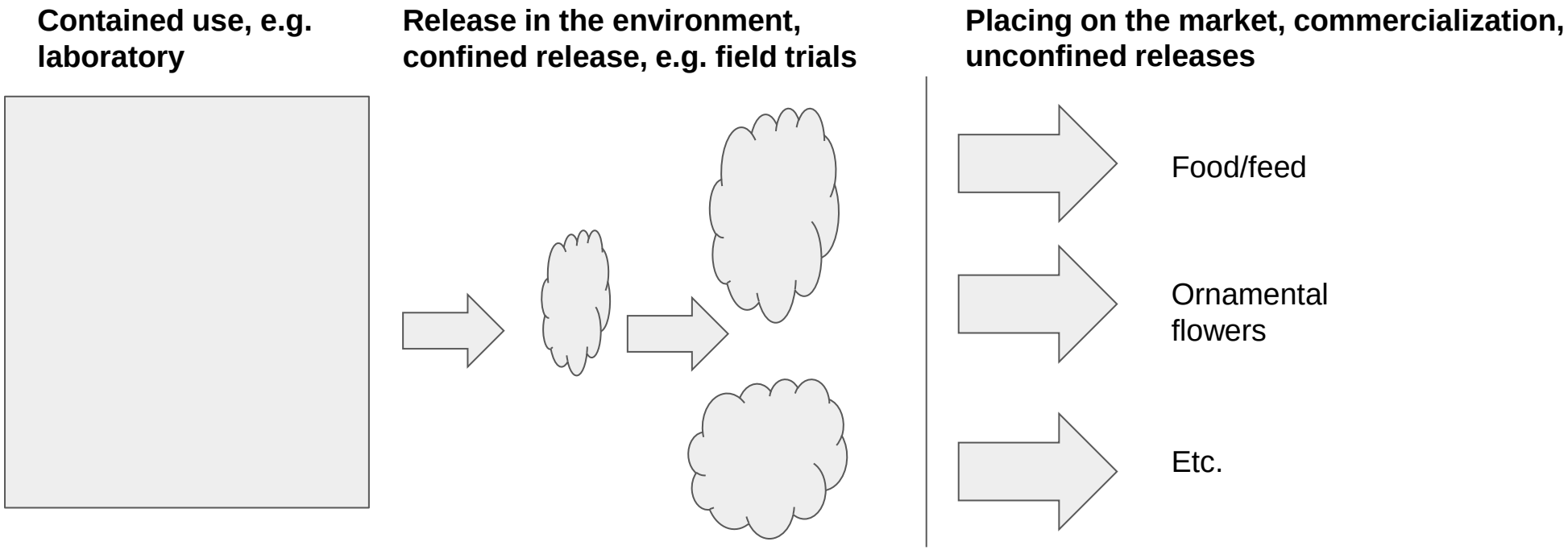
- Development
- Implementation/Compliance
- Review and assessment

Regulatory frameworks for biosafety

Main types of provisions

- General provisions, e.g. objective, scope and definitions
- Operational provisions for described activities
- Final/Other provisions, e.g. review and assessment

Regulatory frameworks for biosafety – scope, operational provisions



EU Regulatory framework for GMOs since 2003

Objectives:

- Protect human and animal health and the environment by introducing a safety assessment of the highest possible standards at EU level before any GMO is placed on the market.
- Put in place harmonised procedures for risk assessment and authorisation of GMOs that are efficient, time-limited and transparent.
- Ensure clear labelling of GMOs placed on the market to enable consumers as well as professionals to make an informed choice.
- Ensure the traceability of GMOs placed on the market

EU Regulatory framework since 2003

Secondary law, e.g:

- Directive 2009/41/EC on contained use of GM micro-organisms.
- Directive 2001/18/EC on the deliberate release of GMOs.
- Directive 2015/412 - the possibility of ‘Opt out’ of cultivation
- Regulation 1829/2003 on GM food and feed
- Regulation 1830/2003 on traceability and labelling.
- Regulation 1946/2003 on transboundary movements of GMOs
- Regulation (EU) 2019/1381 on transparency in risk assessment

EU Regulatory framework since 2003

Tertiary law, implementing rules and decisions, e.g.:

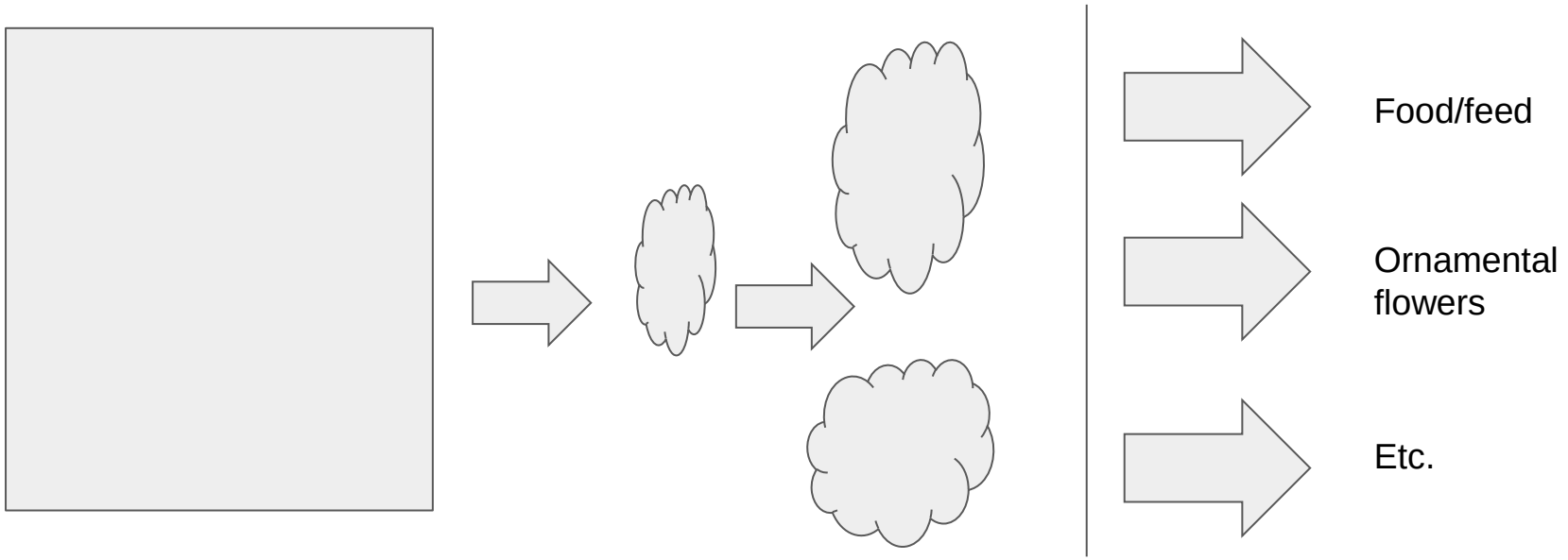
- Commission Directive 2018/350 amending Directive 2001/18/EC, concerning the environmental risk assessment (ERA) of GMOs.
- Commission Implementing Decision 2018/1790 on guidance notes on the environmental risk assessment of GMOs.
- Commission Implementing Regulation 503/2013 on applications for authorisation of GM food conform Regulation 1829/2003
- Decision 2009/770/EC establishing standard reporting formats for presenting monitoring results

EU Regulatory framework for biosafety

Directive 2009/41

Directive 2001/18

Directive 2001/18
Regulation 1829/2003
Regulation 1830/2003
Regulation 1946/2003



Contained use, e.g. laboratory

Introduction into the environment, e.g. field trials

Placing on the market

Regulatory discussion on New Breeding Techniques (NBTs)

There is a worldwide regulatory discussion about NBTs/NGTs, because they can result in

- genetic alterations, without insertion of foreign DNA, that can also be obtained with conventional breeding, or
- a genetic make up that at the end is the same as before the use of the NBT,

This raises the question whether those organisms fall under the regulatory definitions.

New Breeding Techniques (NBTs)

NBTs is an umbrella term under which a large variety of techniques are discussed:

- Genome/gene editing
- RNA-directed DNA methylation
- Grafting on GM rootstock
- Reverse breeding
- Agro-infiltration/Transient expression
- Cis genesis

Genome/gene editing

Genome editing is the targeted modification of the genome of the genome.

There are different types of genome editing, e.g.:

1. Oligo-directed mutagenesis (ODM) type of genome editing

2. Site-Directed Nuclease (SDN) genome editing, e.g.:
   - ✓ Zinc Finger Nucleases (ZFN)
   - ✓ TAL Effector Nuclease (TALEN)
   - ✓ CRISPR/Cas9

Results of genome/gene editing

The result of CRISPR engineering depends on what happens after DNA cleavage, e.g.:

1. Short, NHEJ random deletions and/or insertions (indels) (‘SDN1’), e.g. resulting in loss of function of the target gene (‘knock out’)

2. HDR base pair editing of a target gene sequence (‘SDN2’), e.g. correcting genetic diseases

3. HDR Removal or adding entire genes into the target site (‘SDN3’)

The possibilities are continuously expanding as new CAs systems are discovered, RNA editing, prime editing, combo editing, et cetera. See COST Action PlantEd webinar series.

Regulatory discussion on NBTs (continued)

In most jurisdictions where the discussions about the regulatory status of NBT derived organisms has been finalized, the result is a differentiated picture, e.g.:

- all/most SDN1 and SDN2 not covered by the regulatory definitions or the rules and
- all/most SDN3 covered by the regulatory definitions and the rules.

These conclusions have been reflected in various ways:

- a clarification of the scope of the regulatory definitions
- clarification plus an additional rule to submit organisms developed with NBTs to assess whether those organisms fall under the definitions
- a change of the rules, e.g.:
  - exempting certain categories of genome edited organisms
  - adjusting the definitions, (e.g. aligning with the Biosafety Protocol).

Regulatory status of NBT developed organisms in the EU

- 2007: EC established the New Techniques Working Group on (NTWG)
- 2012: report NTWG finalised, but not officially published. No legal opinion EC
- 2018: CJEU ruling on the mutagenesis exemption – EC states that the CJEU ruling means all organisms developed with NGTs are GMOs -> much debate
- 2019: Council asks EC, in light of CJEU ruling, for a study regarding the status of NGTs
- 2021, April: EC study: current legislation not fit for purpose and in need of adaptation.
- 2021, September: Inception Impact Assessment (IIA):
- 2022, July: public consultation on plants produced by SDN and cis genesis
- 2023: European Commission published a proposed regulation on plants obtained by certain new genomic techniques and their food and feed

Thank You

Questions and indications of interest in the proposed doctoral network can be sent to:
Pieter.Jan.Van.der.Meer@vub.be