European Network of Scientists for Social and Environmental Responsibility

Getting EU risk assessment protecting environment and health to achieve its legal objectives.

Escaping reductionist fallacies

CASE EXAMPLE GMOs (& pesticides)

Based on this paper

Hilbeck *et al. Environ Sci Eur* (2020) 32:54
https://doi.org/10.1186/s12302-020-00325-6

Environmental Sciences Europe

REVIEW Open Access

GMO regulations and their interpretation: how EFSA's guidance on risk assessments of GMOs is bound to fail

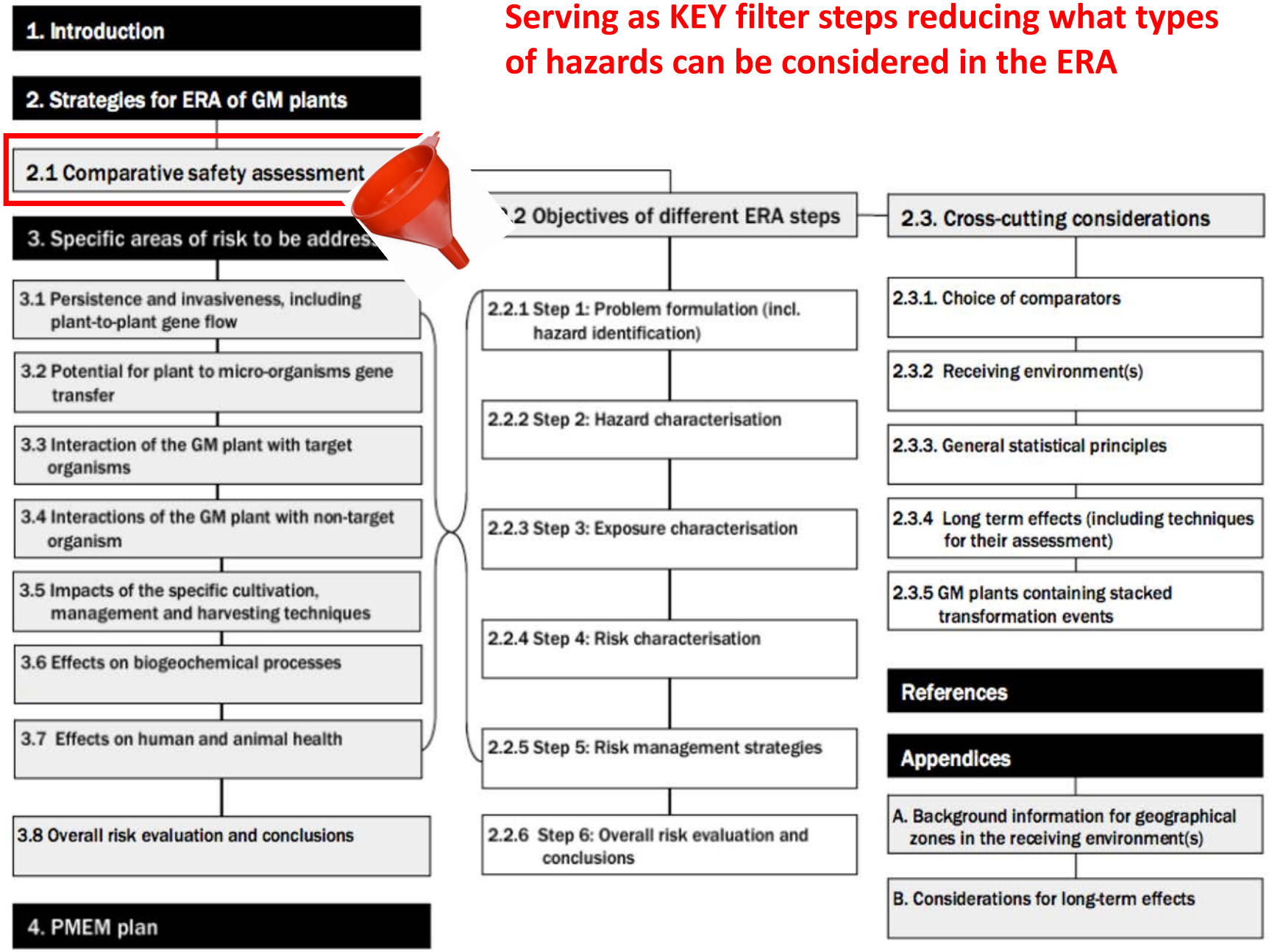
Angelika Hilbeck[1,2*], Hartmut Meyer[2], Brian Wynne[2,3] and Erik Millstone[2,4]

European Network of Scientists for Social and Environmental Responsibility

KEY ISSUE: Reductionism

Begins with the FRAMING of Environmental Risk Assessment (ERA) from the start

Serving as KEY filter steps reducing what types of hazards can be considered in the ERA



‘Comparative Safety Assessment’ is in essence …

The concept of substantial equivalence has never been properly defined; the degree of difference between a natural food and its GM alternative before its ‘substance’ ceases to be acceptably ‘equivalent’ is not defined anywhere, nor has an exact definition been agreed by legislators.

Millstone et al. 1999, p. 525

Concept of Familiarity
- No Recognition in GMO ERA

European Network of Scientists for Social and Environmental Responsibility

Cartagena Protocol on Biosafety:

Concept of Familiarity was introduced in 1996 (BSWG-1), discussed in BSWG-2 and BSWG-3, finally rejected in 1998 (BSWG-4)

Directive 2001/18/EC:

no mentioning of the Concept of Familiarity

European Network of Scientists for Social and Environmental Responsibility

Problems of this FRAMING:

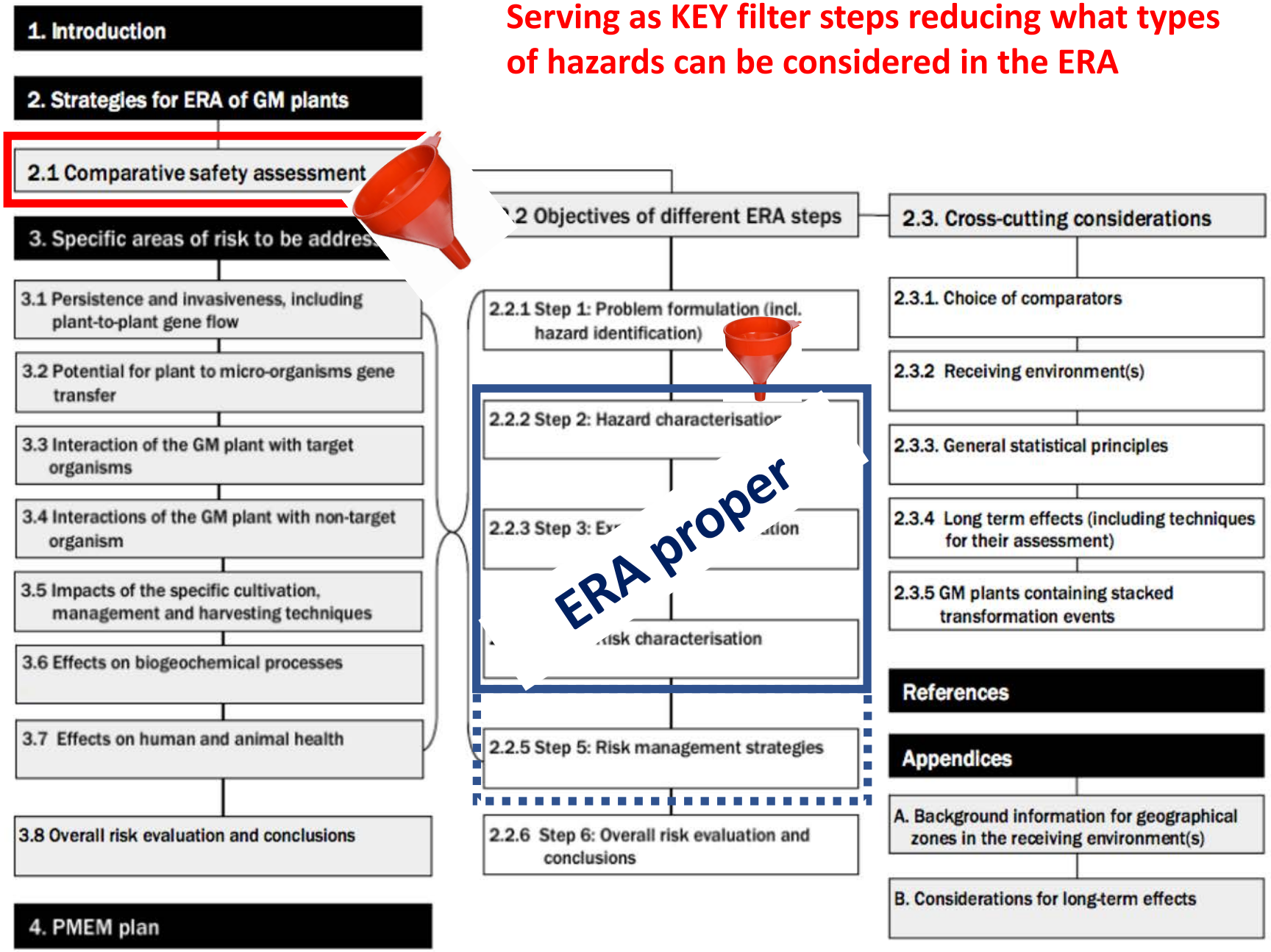
In the '**comparative assessment**' (aka **substantial equivalence**) step, the GM plant (=organism) is reduced to its chemical components:

Instead of assessing the GMO within its complex network of ecological interactions in the real world, EFSA:

- limits the **focus on the 'added' chemical substances 'coded' for by the transgene**, i.e. Bt-toxins

- arrives at its conclusions regarding risks based on data produced with **Bt toxins isolated from an artificial bacterial surrogate syste**m – not the GM Bt plant.

Serving as KEY filter steps reducing what types of hazards can be considered in the ERA



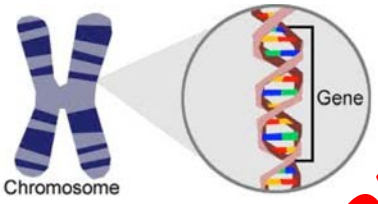
European Network of Scientists for Social and Environmental Responsibility

CASE EXAMPLE 1:

GM Bt plants

All-exclusive Risks

Declared SAFE through substantial equivalence!



Bt transgene construct

PATENTED

Bt and other transgenic proteins

Bt transgenic proteins

Other transgenic proteins

Declared SAFE!

Tested as isolated, microbial CHEMICAL like a pesticide

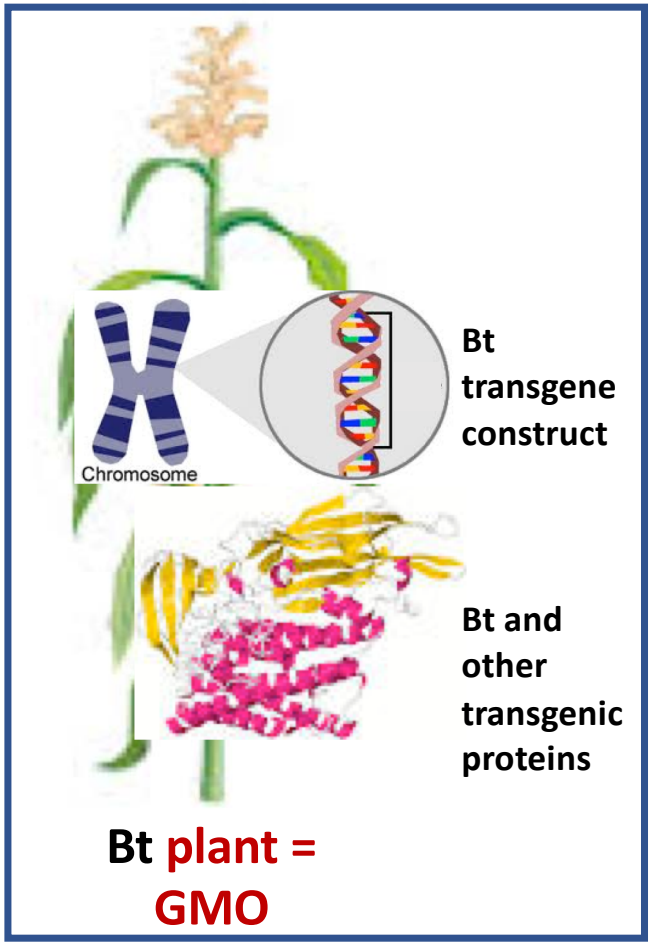
or

Not tested

~~GM Bt~~

Plant

All-inclusive Benefits



Bt plant = GMO

STRESSOR?

All-exclusive Risks

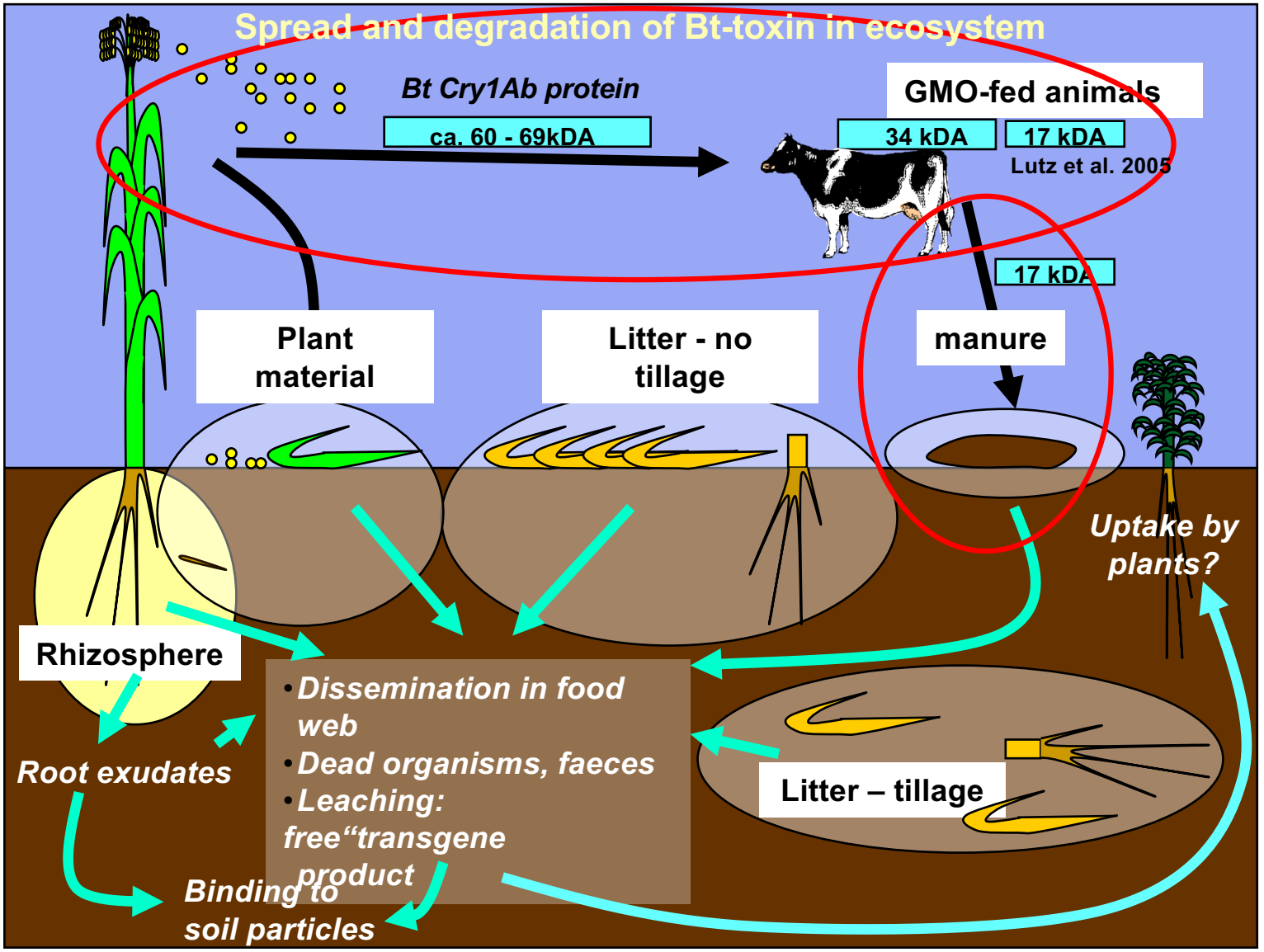

Bacillus thuringiensis; bacterial spore, mother cell and parasporal crystals

Tested as isolated, microbial CHEMICAL like a pesticide

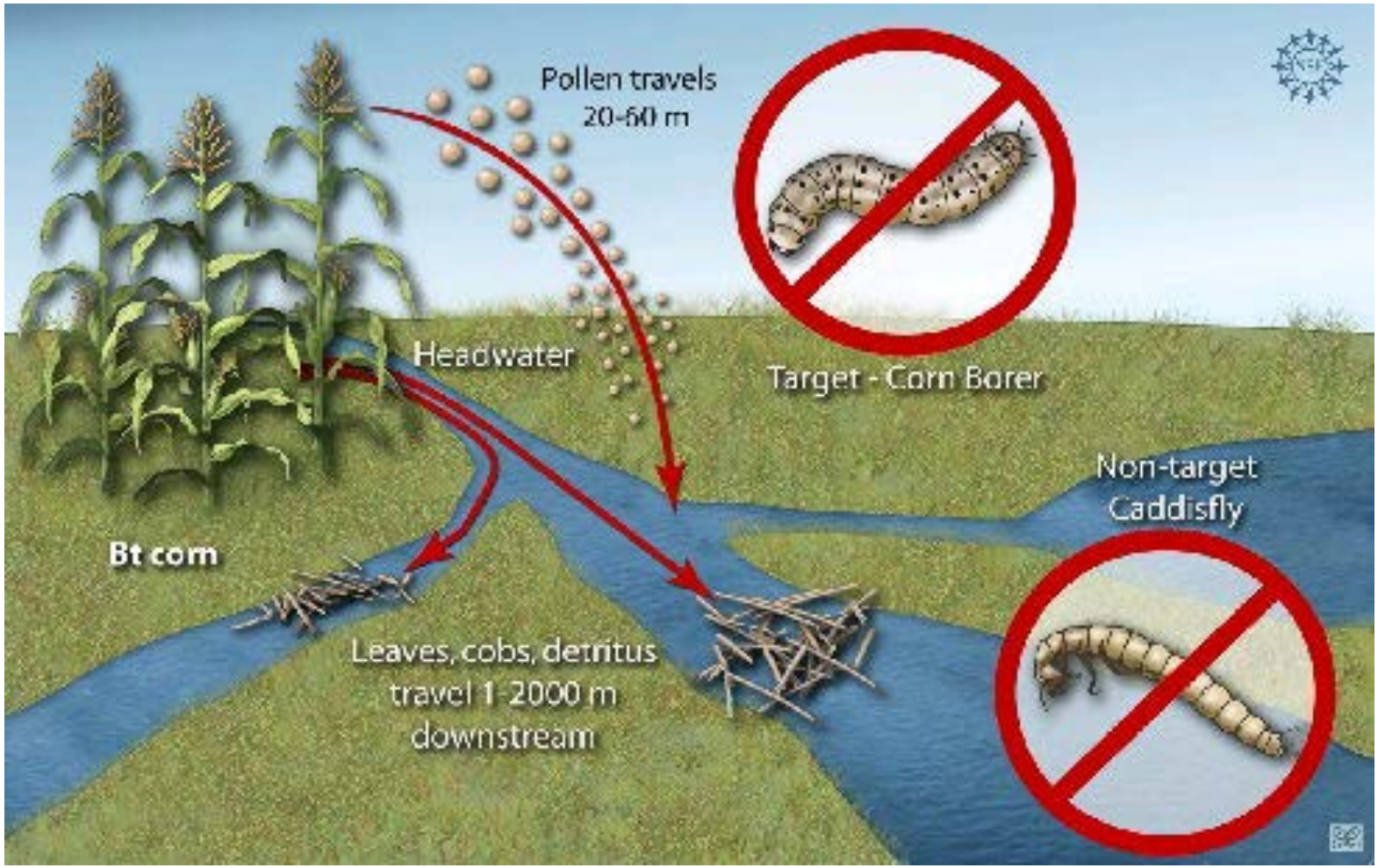
THE REALITY

THE REALITY

POSSIBLE SPREAD & EXPOSURE ROUTES



AQUATIC ECOSYSTEMS



EFSA Hazard ID builds on narrow narratives that are undocumented and outdated:

Mode of action ⟶ Specificity ⟶ efficacy (target effects) ⟶ nontarget effects

Paradigm	Outdated	Updated
GM plant- vs microbe-produced toxin	Identical	Different
Mode of action	Single	Multiple
Specificity	High (few insect taxa)	Broader (many taxa)
Nontarget effects	Few if any	Many

BIOTECHNOLOGY AND GENETIC ENGINEERING REVIEWS, 2017
https://doi.org/10.1080/02648725.2017.1357295

Taylor & Francis
Taylor & Francis Group

OPEN ACCESS Check for updates

The distinct properties of natural and GM cry insecticidal proteins

Jonathan R. Latham[a], Madeleine Love[b] and Angelika Hilbeck[c]

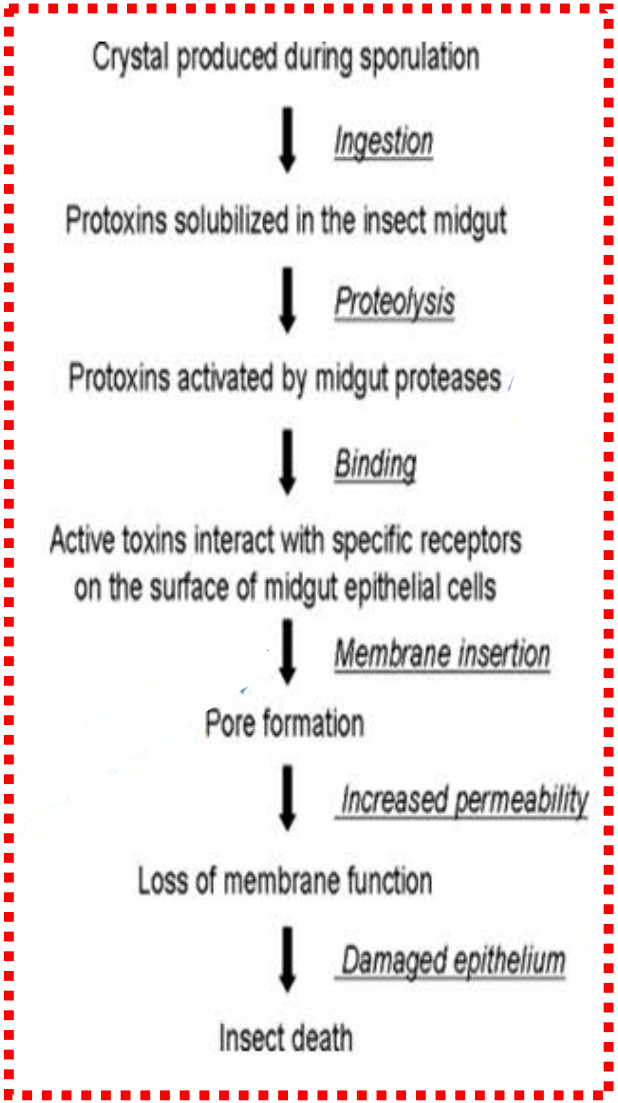
GM plant- vs microbe-produced Bt toxin – significantly different

Truncations, mutations, additions create novel toxins unknown in nature

Goal: Impact new target pests, increase toxicity to target pests, new patents

"*… common industry and regulator narrative maintains that none of these alterations matter much when it comes to environmental and human and animal health safety issues, while they do induce significant novelties and changes with regard to patents and efficacy*." RAGES Report 2019

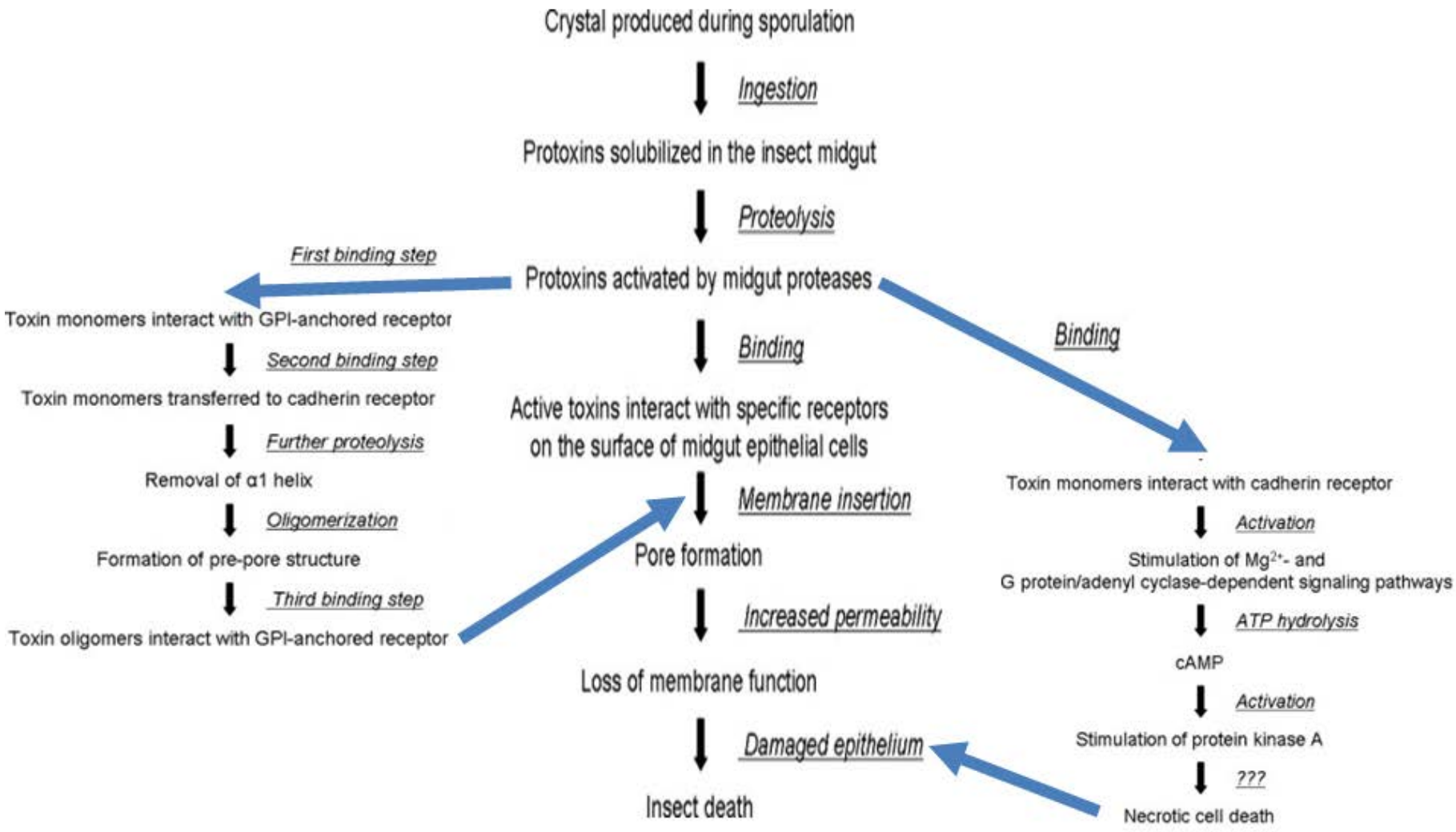
In EFSA ERA: 1 concept of mode of action



Classical model

adapted from Vachon et al., 2012.

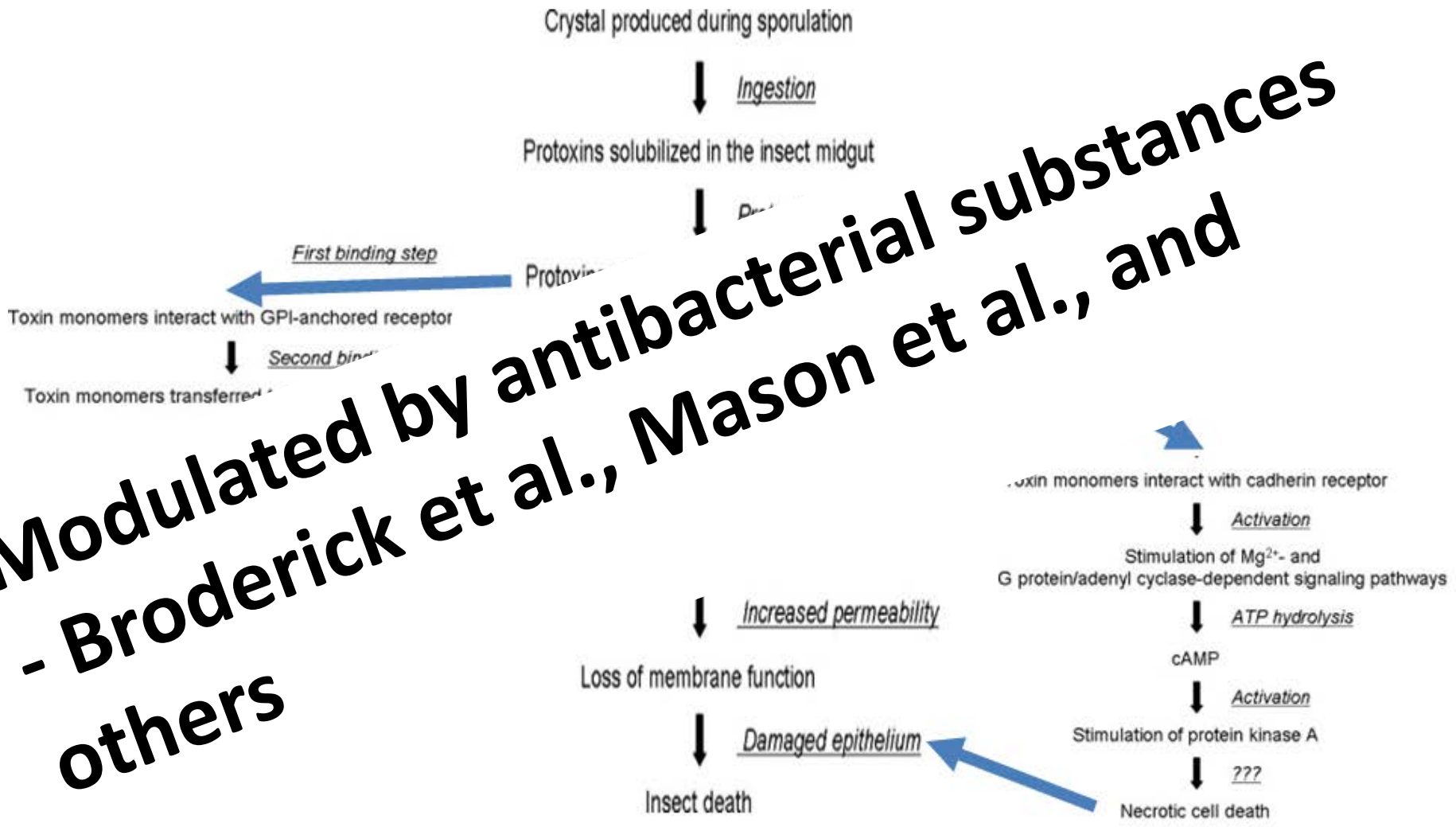
Published: Many different concepts for modes of action



Sequential binding model **Classical model** **Signaling pathway model**

adapted from Vachon et al., 2012.

Published: Many different concepts for modes of action



Modulated by antibacterial substances
- Broderick et al., Mason et al., and others

Sequential binding model **Classical model** **Signaling pathway model**

adapted from Vachon et al., 2012.

Exposure of NTOs in food webs is clearly underestimated

Bt toxins:

a) persist longer in the food web than commonly declared which increases the likelihood of exposure of NTOs,

b) occur in different biochemical forms than in microbes

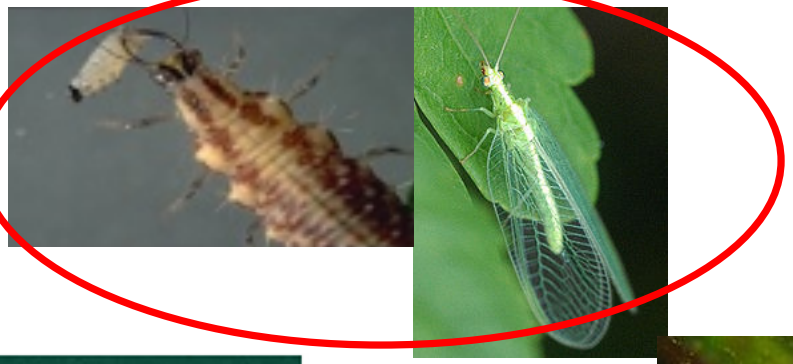
c) their presence can extend beyond the presence of the Bt toxin source, i.e. through pollen and plant residues it can reach both other terrestrial and aquatic ecosystems

d) they can further spread through as of now unrecognized processes like intergenerational transfer (as published by Paula/Andow team)

We found 39 peer-reviewed publications that report significant, diverse, UNPREDICTABLE (adverse) effects of Bt toxins on many 'out-of-range' species, including representatives from non-arthropod taxa, like snails or crayfish or bacteria.

A selection of reportedly adversely affected nontarget beneficial organisms to illustrate diversity of taxa – often only when using plant material

CASE EXAMPLES



highly publicized cases disputed by EFSA

ADVERSE EFFECTS

Growing diversity of affected species reported, most of which cannot be detected in short-term acute direct toxicity tests that follow first tier OECD toxicity protocols.

Continued Bias and Double Standards in EFSA assessment

ALL studies reporting unexpected adverse effects on NTOs are dismissed

While almost all studies confirming no effects are accepted – with rare recent exceptions

Arguments for dismissal continue to be:

- **out-of-range paradigm/not meeting expectations**
- **double standards – bridging data to show safety but not risks**

Notorious double standards

… the GMO panel argued that the findings reported by Paula et al. 2015 and Paula and Andow 2016 '*have no direct relevance for the environmental risk assessment of maize MON810 because none of the Cry proteins evaluated … correspond to the protein expressed in maize MON810, i.e. Cry1Ab*.'

No RISK conclusions can be drawn from studies using Cry1Ac or any other Cry toxin for Cry1Ab (i.e. MON810)

Notorious double standards

'*Based on the known spectrum of activity of **Cry1Ac and Cry1F proteins** and its selectivity to lepidopteran species and the phylogenetic distance between ladybird beetles and target species (pests of the order Lepidoptera), susceptibility of H. axyridis to **Cry1Ac and CryF** proteins is **not expected at field concentrations***'

'*Similar findings (no adverse effects) have been reported in the scientific literature for **Cry1F** and other Bt-proteins on this ladybeetle. In direct feeding assays, ingestion of biologically-active purified **Cry1Ac, Cry2Ab, Cry1Ca, Cry1F or Vip3A** proteins by H. axyridis larvae did not negatively affect their development, survival or weight (Ali et al. 2016).' EFSA GMO Panel 2019*

No Cry1Ab (i.e. MON 810) tested!

SAFETY conclusions can be drawn from studies using any other toxin from the Cry1 class – Bridging ok!

Notorious double standards

'Based on the known spectrum of activity of Cry1Ac and Cry1F proteins and its selectivity to lepidopteran species and the phylogenetic distance between ladybird beetles and target species (pests of the order Lepidoptera), susceptibility of H. axyridis to Cry1Ac and CryF proteins is not expected at field concentrations'

'*Similar findings (no adverse effects) have been reported* ***in the scientific literature for Cry1F and other Bt-proteins on this ladybeetle. In direct feeding assays, ingestion of biologically-active purified Cry1Ac, Cry2Ab, Cry1Ca, Cry1F or Vip3A proteins by H. axyridis larvae did not negatively affect their development, survival or weight (Ali et al. 2016).'*** *EFSA GMO Panel 2019*

Additionally, lack of scrutiny in studies that confirm safety:
EFSA did not critically assess this study by Ali et al. 2016 because no adverse effect
Ali et al. used flawed protocols with unexplained excessive amounts of antibiotics known to significantly alter (=MASK) the impact of Bt toxins!

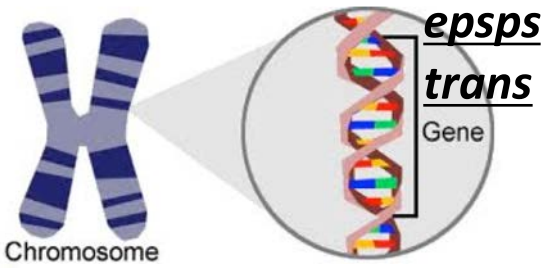
European Network of Scientists for Social and Environmental Responsibility

CASE EXAMPLE 1:

GM HT plants

REDUCTIONISM

Transgene products: <u>EPSPS enzyme</u>



<u>epsps trans</u>

GMO regulations = known enzyme, no testing

PATENTED

Formulation ingredients: Tallowamine, etc.

Regulations for ingredients – less stringent than those for active ingredients

Active (formula) ingredients: Glyphosate

Regulations for active ingredients

REDUCTIONISM

Transgene products: <u>EPSPS enzyme</u>

GMO regulations = known enzyme, **no testing**

= product-based risk assessment

European Network of Scientists for Social and Environmental Responsibility

CONCLUSIONS and CORE PROBLEMS

Narrow ERA model
effectively denies relevant biological complexity and contingency, such as interactions between Bt-toxins, GM plants and ecological communities in the environment.

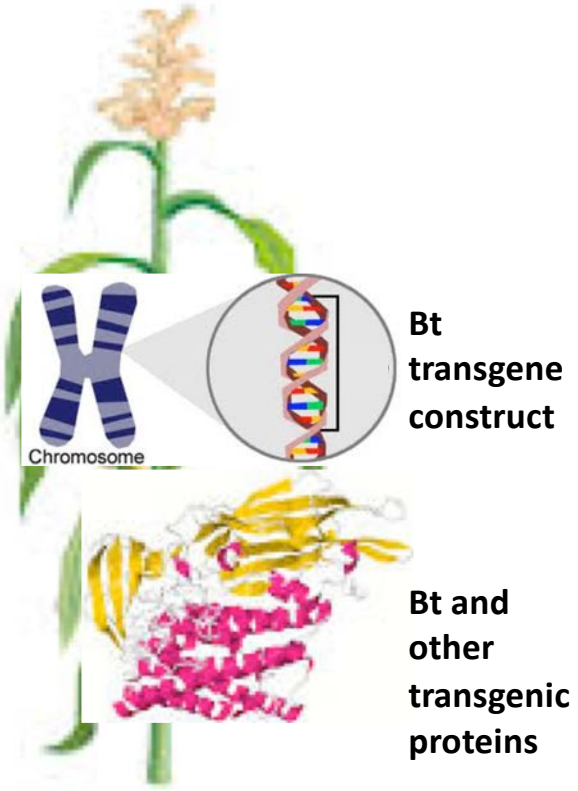
Consequences
EFSA is relieving the applicants from their obligation to prove the safety of their products based on new data and the most recent science and is placing the burden of proof on independent scientists with extremely limited funding.

Reversal of the Precautionary Principle

What we want!

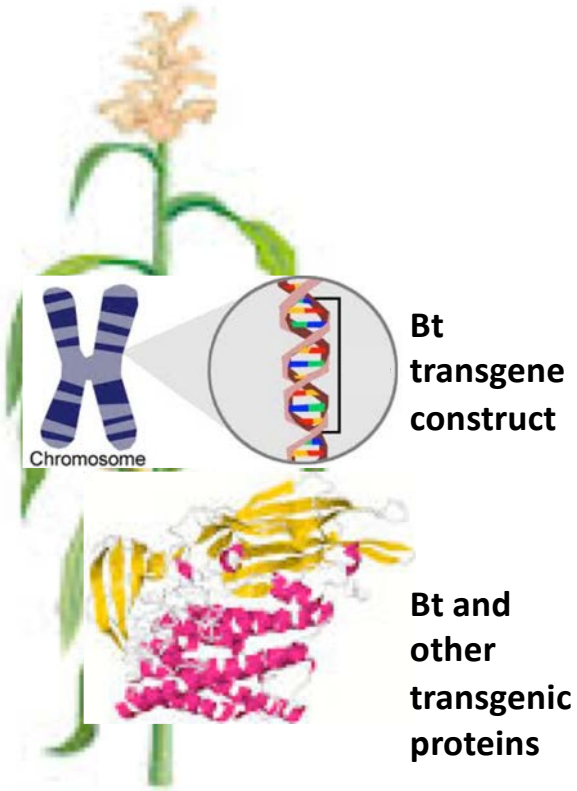
European Network of Scientists for Social and Environmental Responsibility

All-inclusive Benefits



GM Bt plant

All-inclusive Risks



GM Bt plant = Stressor

European Network of Scientists for Social and Environmental Responsibility

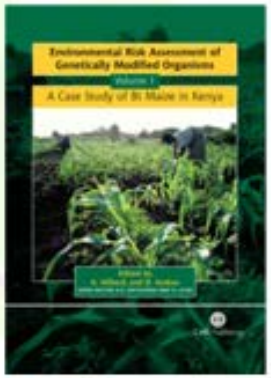
Better ERA model available –
New Species selection procedure embedded in ERA components

Improved alternative concept needed, designed for a GM**O** rather than a **pesticide**

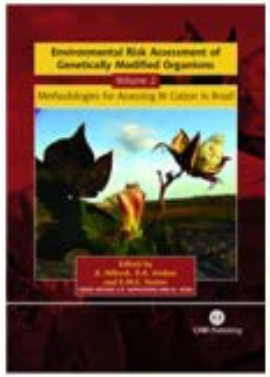
In a 6-year project funded by SDC and local partners, public sector scientists developed an improved concept, tested it in 4 GM crop cases in 3 countries: Kenya (maize), Brazil (cotton) Vietnam (cotton). Published in a CABI book series....

Major Publications

CABI Book Series: 'Environmental Risk Assessment of Genetically Modified Plants'



Kenya
Vol I 2004



Brazil
Vol II 2006

Vietnam
Vol IV 2008

GEF-STAP sponsored publication

HANDBOOK on Problem formulation & Options Assessment

http://www.gmoera.umn.edu/public/publications/index.html

While the ecotox model is

prescriptive with regard to species and protocols – starts narrow and considers other (e.g. long-term, cumulative) effects only if acute, short-term effects of a plant-produced novel protein occur.

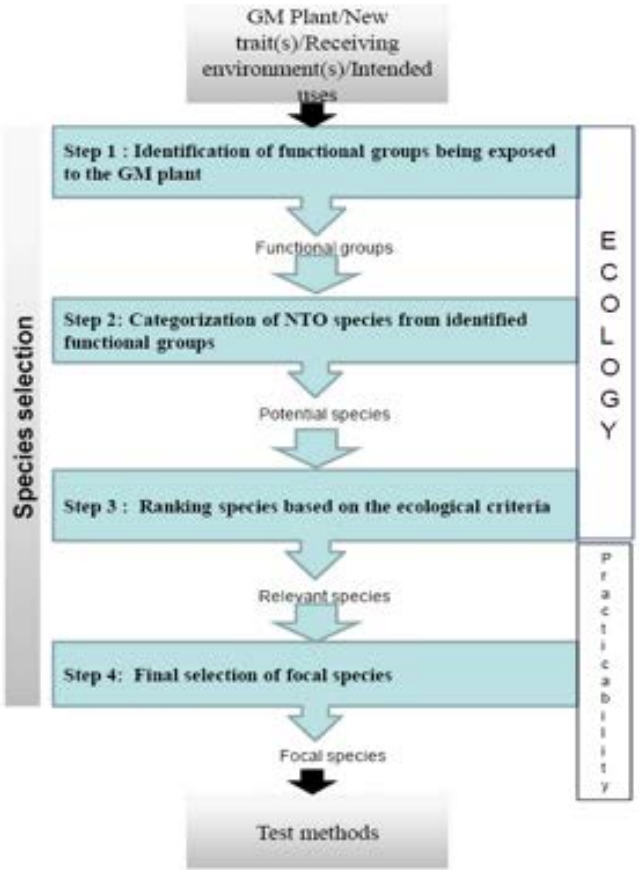
The GMO ERA Model is

prescriptive with regard to the selection procedure for testing species from the receiving environment ....

Whole Plant - GMO ERA Model

- Based on a biodiversity function approach
- Starts broad – reducing species number through a transparent process based on ecological criteria like: abundance, phenology, ecological significance, exposure
- Aim: Filtering out those that are associated with highest potential risk (= exposure x ecol. significance)
- Selection process informs: potential adverse effect scenarios → formulation of risk hypotheses → design of proper experiments and protocols

2010 Final Draft



2009 Draft

Selection of "focal species"

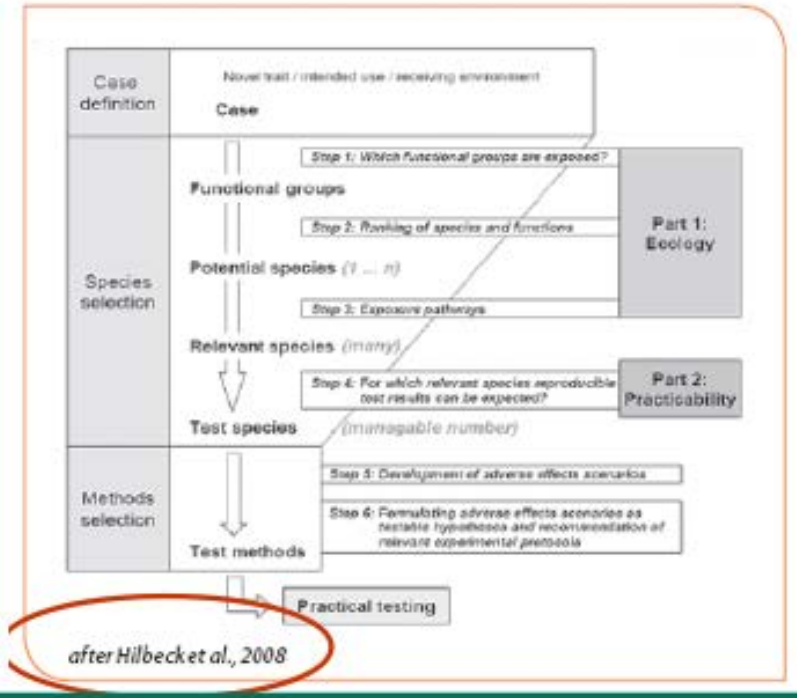
Preserving the functional biodiversity

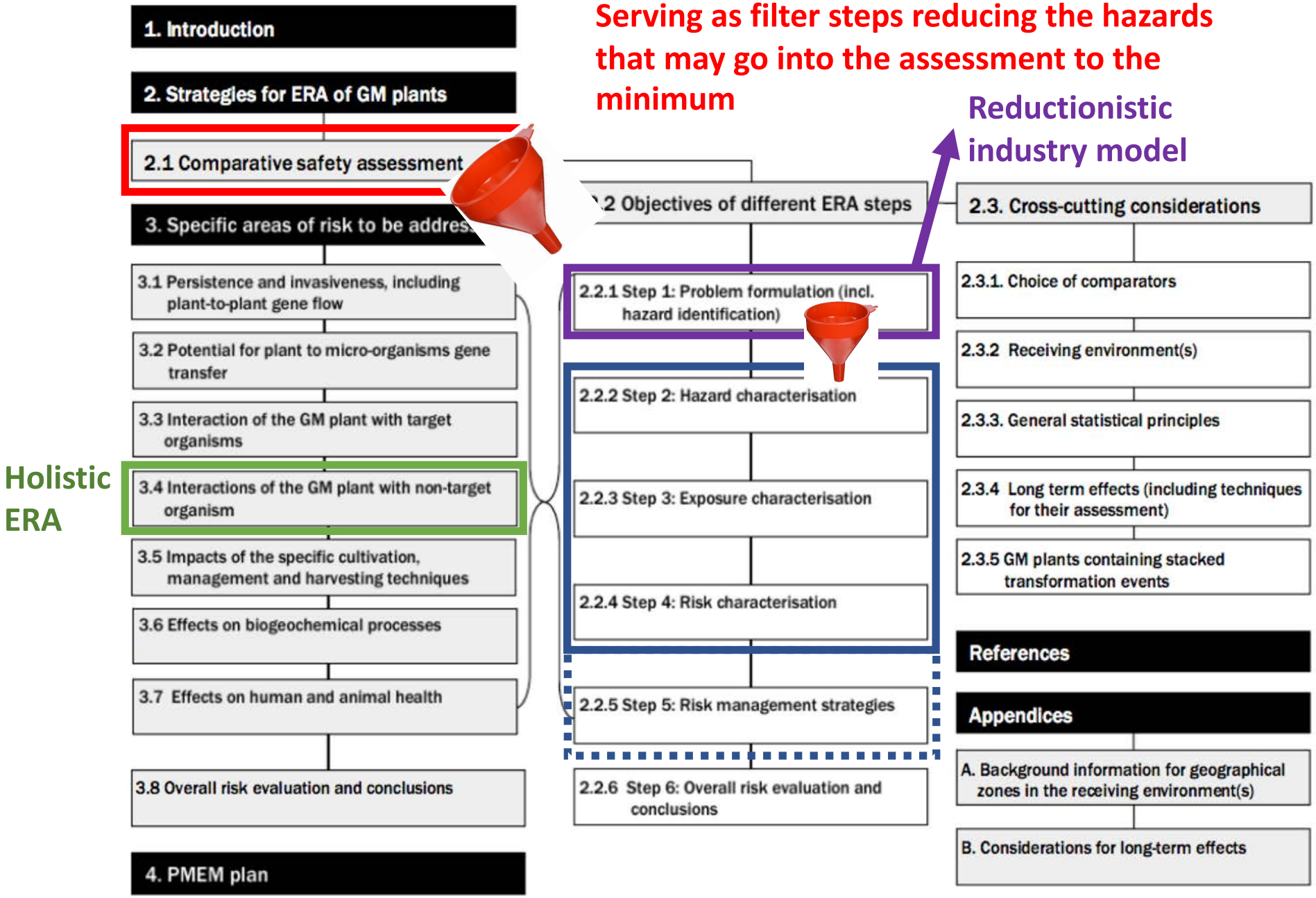
- Herbivores
- Predators
- Parasitoids
- Pollinators, pollen feeders
- Decomposers
- **Species of conservation/cultural conc**

EFSA meeting summary report 4

EFSA AND GMO RISK ASSESSMENT FOR HUMAN AND ANIMAL HEALTH AND THE ENVIRONMENT

Self-tasking Working Group on environmental impacts of GM plants on Non-Target Organisms




Serving as filter steps reducing the hazards that may go into the assessment to the minimum
Reductionistic industry model
Holistic ERA
1. Introduction
2. Strategies for ERA of GM plants
2.1 Comparative safety assessment
3. Specific areas of risk to be addres
3.1 Persistence and invasiveness, including plant-to-plant gene flow
3.2 Potential for plant to micro-organisms gene transfer
3.3 Interaction of the GM plant with target organisms
3.4 Interactions of the GM plant with non-target organism
3.5 Impacts of the specific cultivation, management and harvesting techniques
3.6 Effects on biogeochemical processes
3.7 Effects on human and animal health
3.8 Overall risk evaluation and conclusions
4. PMEM plan
2 Objectives of different ERA steps
2.2.1 Step 1: Problem formulation (incl. hazard identification)
2.2.2 Step 2: Hazard characterisation
2.2.3 Step 3: Exposure characterisation
2.2.4 Step 4: Risk characterisation
2.2.5 Step 5: Risk management strategies
2.2.6 Step 6: Overall risk evaluation and conclusions
2.3. Cross-cutting considerations
2.3.1. Choice of comparators
2.3.2 Receiving environment(s)
2.3.3. General statistical principles
2.3.4 Long term effects (including techniques for their assessment)
2.3.5 GM plants containing stacked transformation events
References
Appendices
A. Background information for geographical zones in the receiving environment(s)
B. Considerations for long-term effects

“The problems highlighted … indicate that substantial changes are required both at EFSA and in the European Commission, and in their interactions.

At a minimum, the Commission should properly research, understand, and then deliver on the commitments concerning explicitly articulating risk assessment policies, in advance of risk assessments, and in accordance with the inclusive and accountable procedure stipulated in the Codex provisions on risk assessment policy-making.

It should have done this some years ago.

(Hilbeck et al. 2020)

“Then we might … discover two major all-round benefits: that EFSA’s science is able to support and comply with EU democratic legislative and regulatory objectives, rather than to undermine them; and that EFSA’s repeated failure to achieve European public and Parliamentary respect [83 , 84] might begin to reverse itself.”

(Hilbeck et al. 2020**)**

THANK YOU

More information and details:
https://www.testbiotech.org/en/content/research-project-rages