Key types of environmental risks for the risk assessment of GMOs

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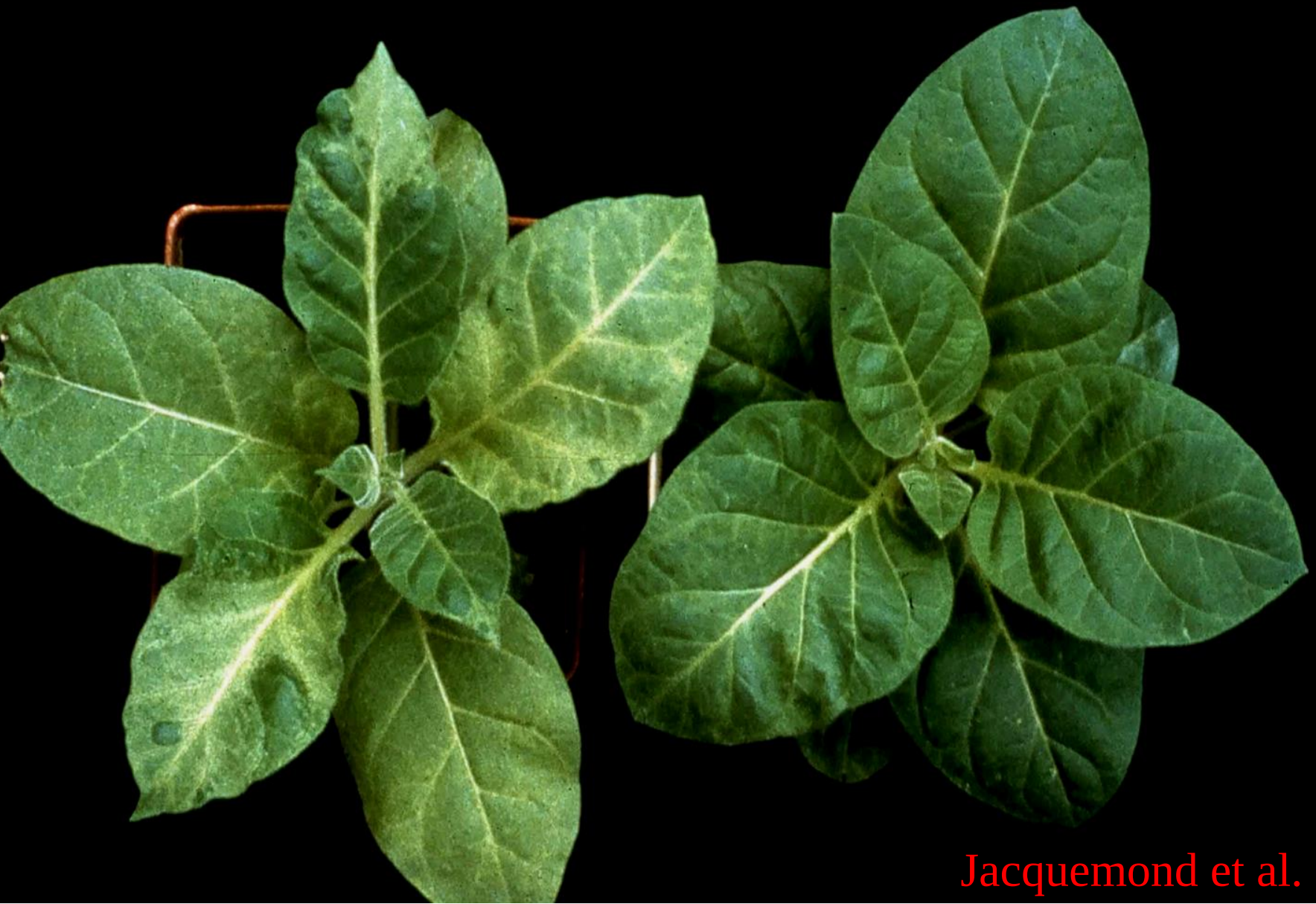
Lima, Peru, 20-22 January 2014

Special thanks to Monica Garcià-Alonso, Estel, UK and Patrick Rudelsheim, Perseus, Belgium

Expression of a *Cucumber mosaic virus* (CMV) satellite RNA in tobacco confers tolerance to CMV



Jacquemond et al. 1988

Expression of the LMV coat protein in oilseed rape confers resistance to TuMV

Expression of the PFBV coat protein in geranium confers resistance to PFBV

All biotechnology projects should include:

- Creation of the GMO and evaluation of its effectiveness
- Evaluation of the potential risks associated with the GMO

But these activities must be carried out together, not in opposition.

Developers are well advised to use the same tools as risk assessors to put their project into a risk assessment perspective.

France is one of the most anti-GMO countries in Europe

Paris Métro, 2011

We can -and must- do better communication!

Risk analysis to assist decision-making

In the broadest sense:

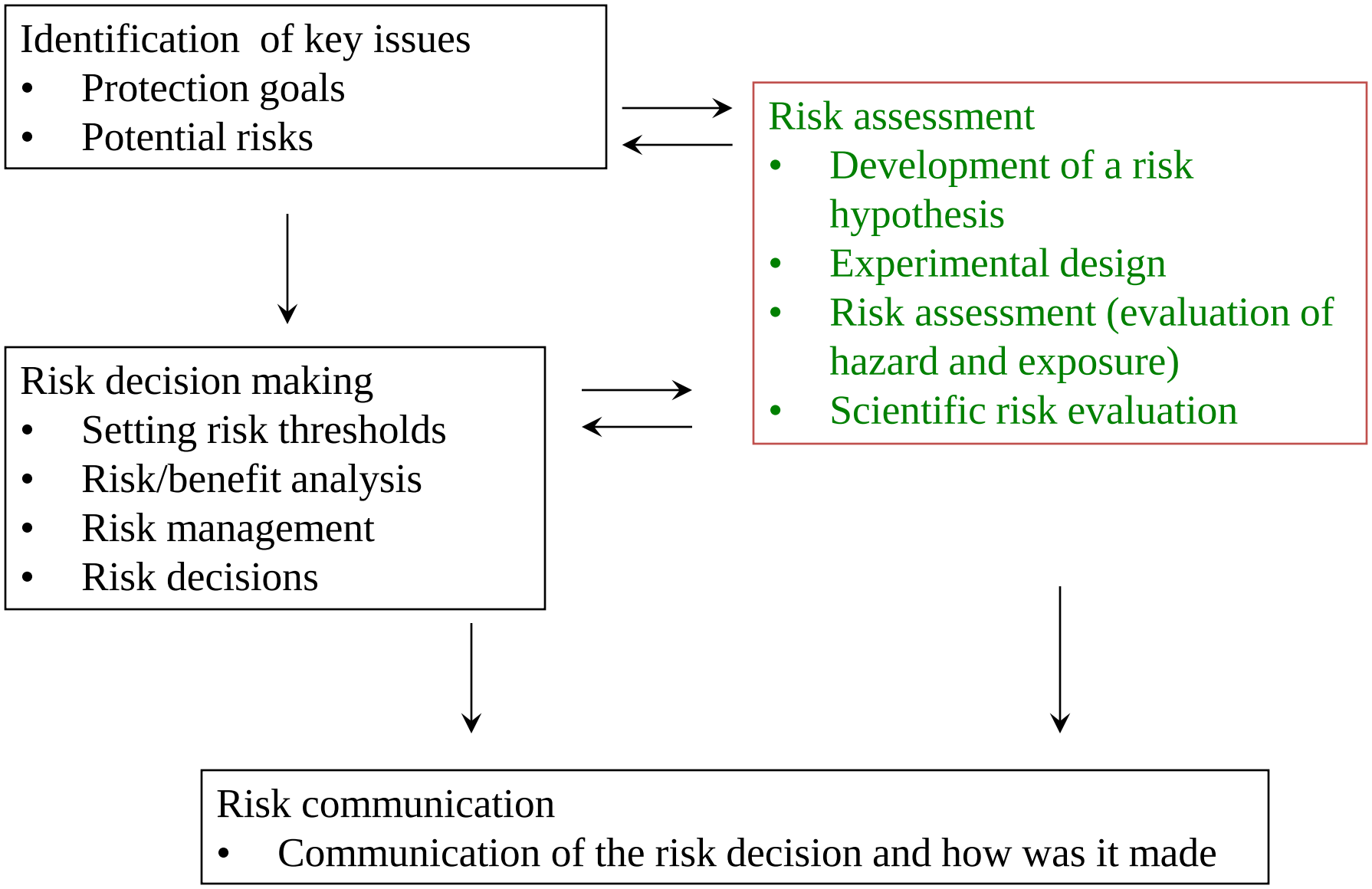
Risk analysis = risk assessment + risk management + risk communication

Risk assessment (RA) – identifies sources of potential harm, assesses the likelihood that harm will occur, and the consequences if harm does occur

Risk management (RM) – evaluates which risks identified in the RA require management and selects and implements the plans and actions required to ensure those risks are controlled

Risk communication - involves an interactive dialogue between stakeholders and risk assessors and risk managers to actively inform the RA and RM processes

Risk assessment in the risk analysis context



After Johnson et al. 2007, Trends Pl.Sci. 12, 1-5

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Problem: if risk communication includes from the stakeholders, how should risk assessors and decision makers take into account non-scientific concerns??

What is risk assessment???

Risk is a function of exposure and harm:

Risk = *f*(Exposure x Harm)

The evaluation must take into account both the harm (nature and scope of potential damage, undesirable effects) and the exposure (probability, likelihood).

The objectives of biosafety research: evaluate the harm and/or the exposure to harm.

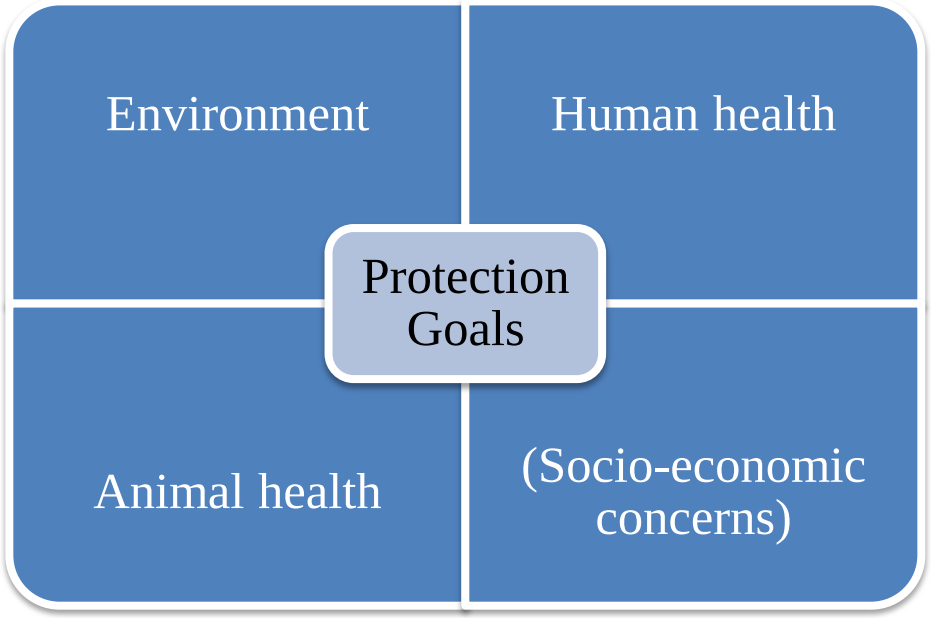
Approach:

- Science-based (hypothesis-driven)
- Case by case and step by step

Protection goals are the starting point for risk assessment

- Defined by country regulations as part of environmental policy
- Often formulated in legal terms using normative concepts such as "sustainability, integrity, acceptability,…"

- Can be widely interpreted
- Often impossible to prove or falsify
- Too vague to be scientifically assessed



why do some find it hard to decide?

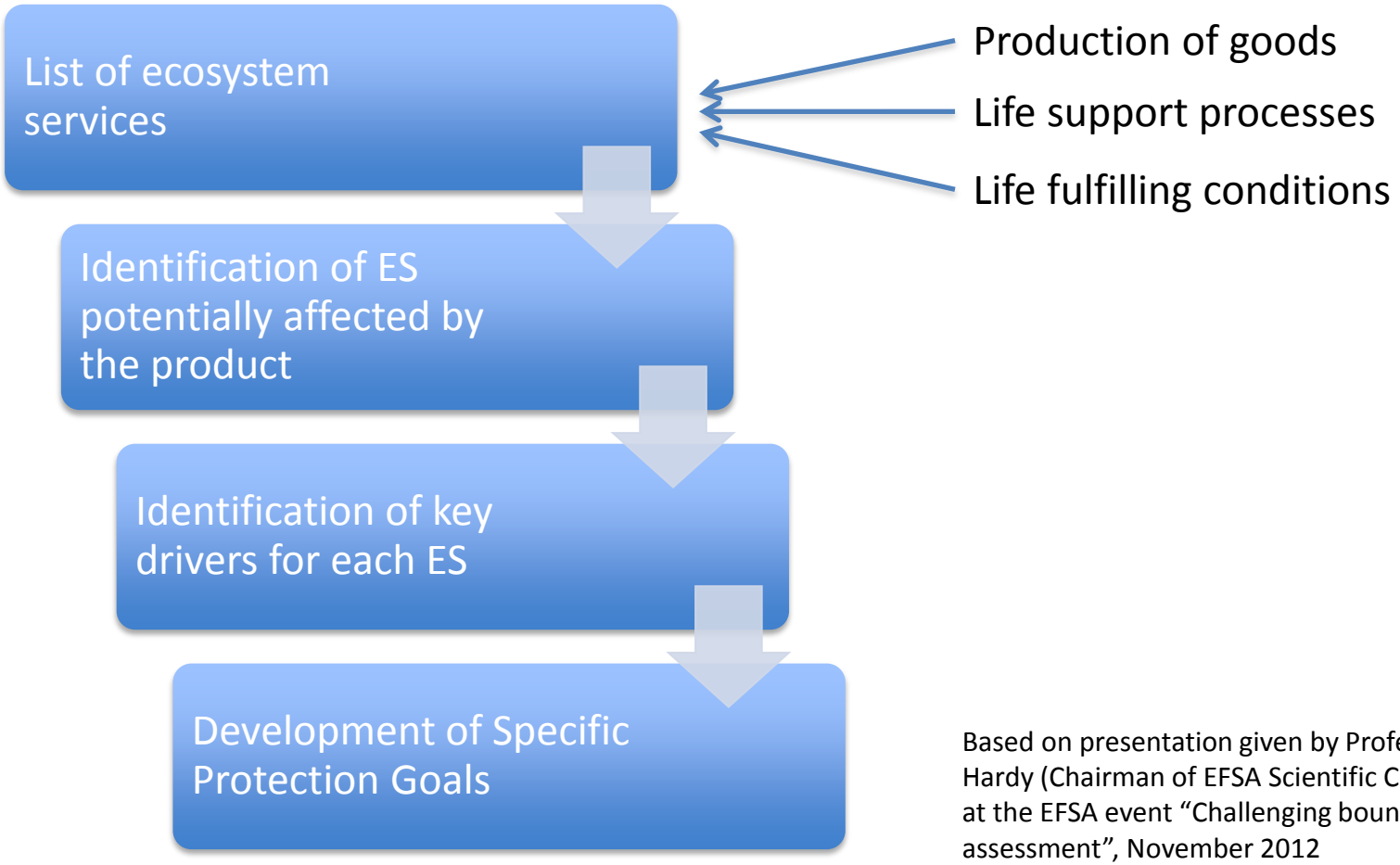
This risk assessment-policy gap stems partly from normative and imprecise policy language, but is rooted more fundamentally in society's uncertain expectations for the environment. (Evans et al., 2006: Environment International, 32, 1066-1071)

Strategies to address the difficulties in risk assessment:

- Analyse in terms of ecosystem services
- Establish a checklist of concerns and pertinent data
- Use problem formulation to focus concerns

Environmental Risk Assessment

- Attempting translation – Ecosystem service



Based on presentation given by Professor Tony Hardy (Chairman of EFSA Scientific Committee) at the EFSA event "Challenging boundaries in risk assessment", November 2012

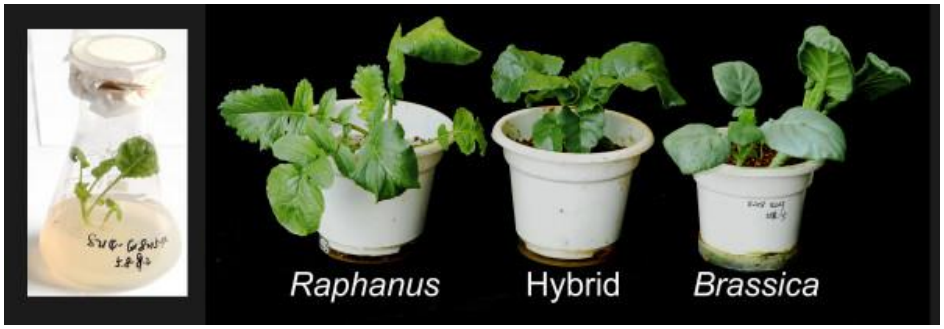
Environmental Risk Assessment

- In the absence of clearly defined protection goals, risk assessors have identified specific areas of concern

1) Persistence/invasiveness
2) Plant-to-micro-organism gene transfer
3) Interaction with target organisms
4) Interaction with non-target organisms
5) Impact of the specific cultivation, management and harvesting techniques
6) Effects on biogeochemical processes
7) Effects on human and animal health.

EFSA Panel on Genetically Modified Organisms (GMO); Guidance on the environmental risk assessment of genetically modified plants. EFSA Journal 2010;8(11):1879.

Concern
Persistence/invasiveness



- "Weediness", "Escape"
- Includes consideration of sexually compatible species (vertical gene transfer)
- Enhanced fitness:
  - more persistent, exacerbating weed problems
  - may reduce the diversity/abundance of valued flora and fauna.
- Reduced fitness:
  - may decrease the fitness of hybrid offspring.

Concern

Horizontal gene transfer

- Extremely unlikely in plants & animals

Concern

Target organisms

- Likelihood that the TO will develop resistance

- Environmental and agronomic:
  - compromise other pest control products
  - destabilise pest control strategies
  - lead to increased pesticide use.

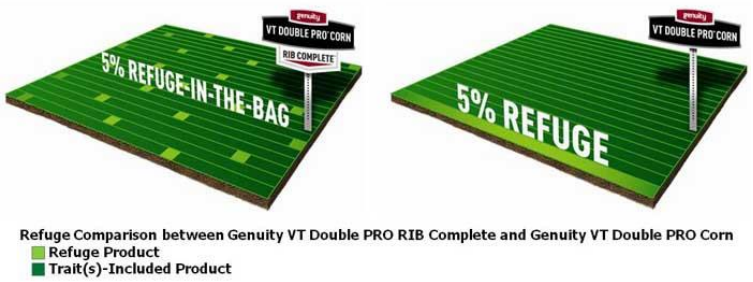
- Strategies to
  - delay or prevent the occurrence of resistance
  - prevent undesired changes in the interaction between the TO and GMO

Concern

Non target organisms

- Species directly and/or indirectly exposed to the GMO plant, and which are not targets of the newly expressed metabolite(s).
- Effect on biodiversity and its functioning at several levels
- Receiving environment
- Directly and/or indirect (e.g. through food web interactions, scale of adoption) potentially harmful effects to species guilds involved in ecosystem functions

Concern
Impact of techniques

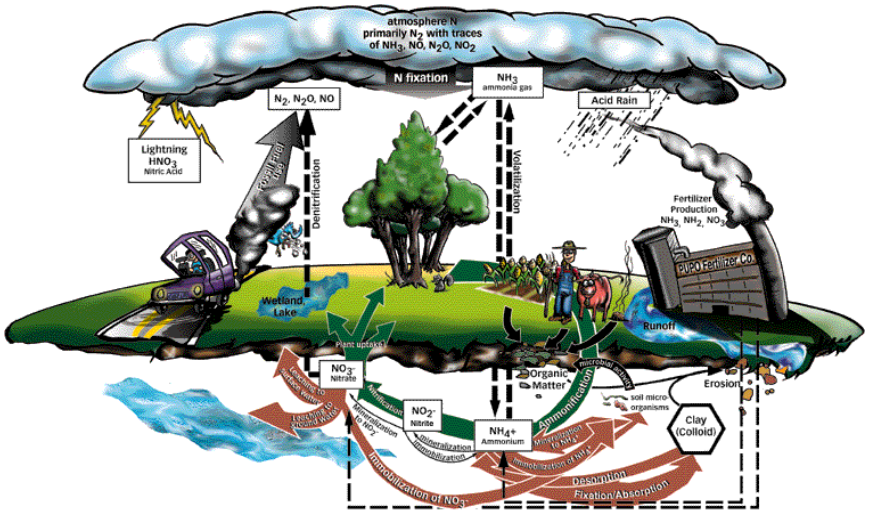


Refuge Comparison between Genuity VT Double PRO RIB Complete and Genuity VT Double PRO Corn
Refuge Product
Trait(s)-Included Product

- Can the specific GM management and production systems -if needed- lead to greater, similar or lower adverse environmental effects than the current systems they are likely to replace?

Concern

Biogeochemical processes



- Movement, transformation and storage of energy, water, carbon, nitrogen and other elements in ecosystems

Concern

Human & animal health

- Persons working with the GMO, coming into contact with it or exposed to products such as pollen or dust from processed material

Environmental Risk Assessment

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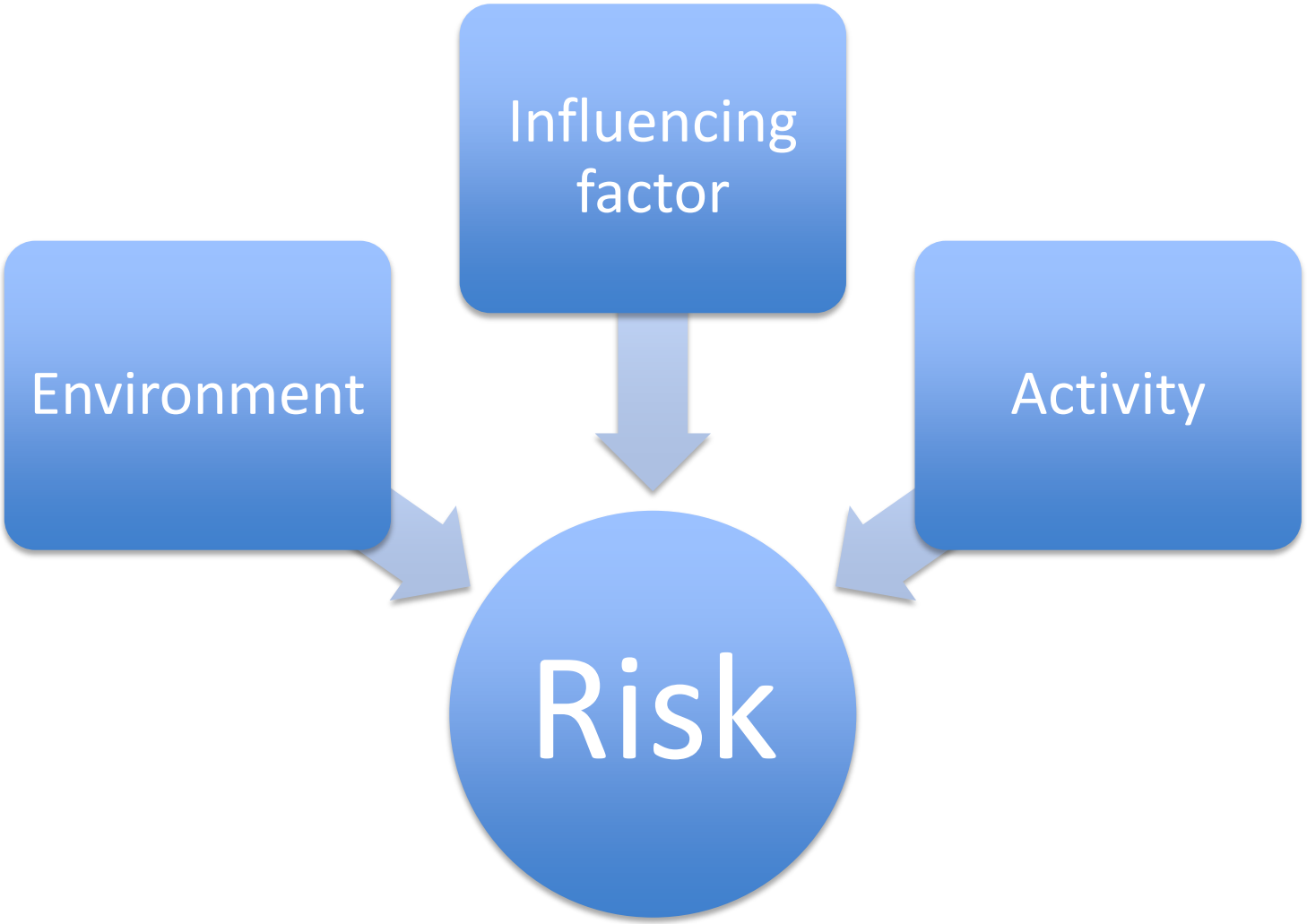
Scope



Plants

•Diversity – Survival, propagation, life cycle,






Scope

Influencing factors

Animals

•Diversity – Environment, level of control





Scope

Influencing factors

Scope

Environment

- Different compartments
- Level of management

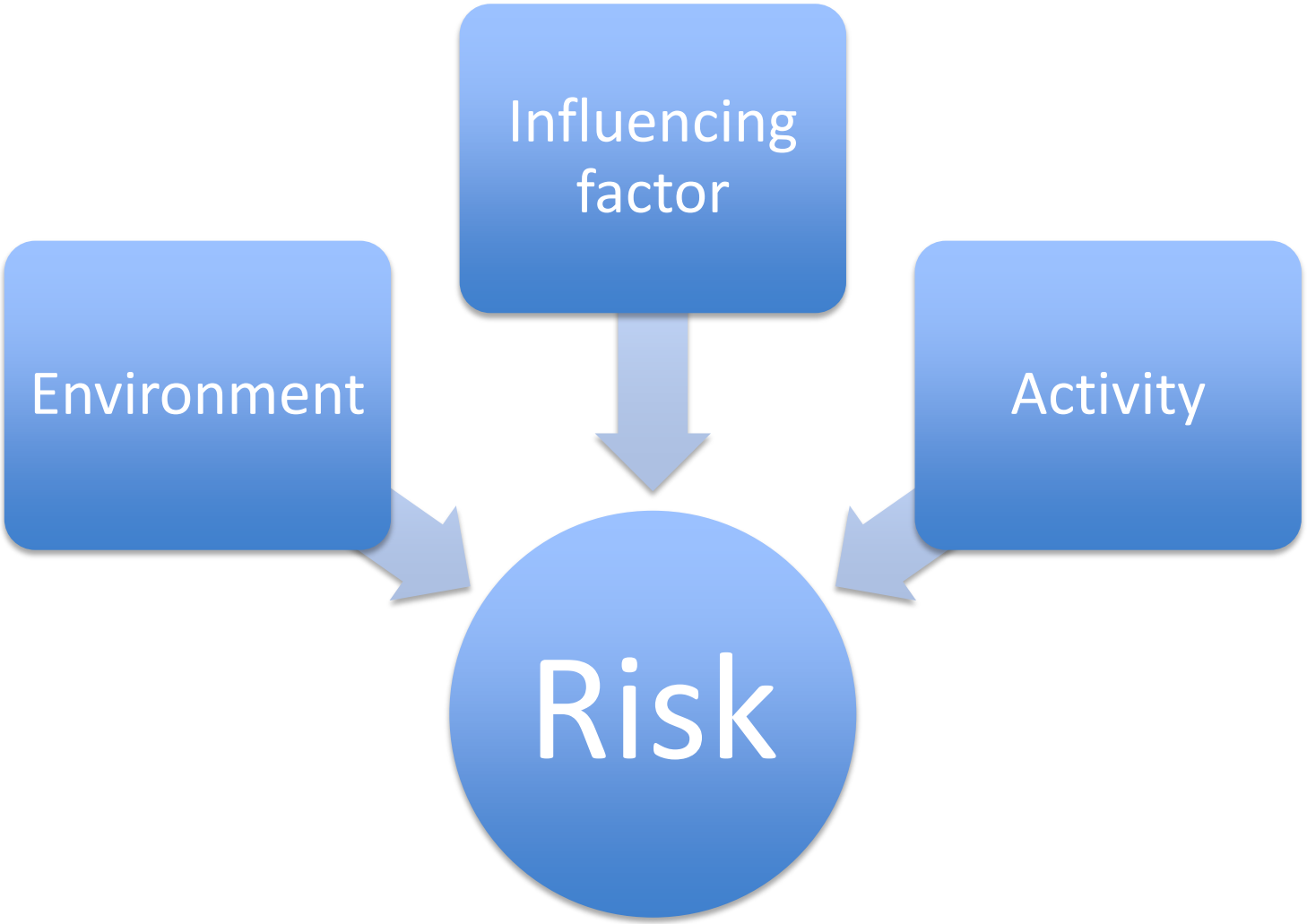
Scope
Environment

- Level of detail

Scope

Activity

Scope



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Several factors have contributed to the perception of a need for better tools for GMO risk assessment

With the increasing size of the dossiers, it becomes desirable to simplify.

It is necessary to improve the quality of communication with the stakeholders, and to engage them better in the process.

With new, more complex traits, such as resistance to drought or to salinity, an evaluation based simply on the equivalence between a GMO and non-GMOs may be less effective.

Request to USDA for reregulation of squash resistant to two viruses (1992)

Less than 50 pages

Asgrow Seed Company
subsidiary of The Upjohn Company

Agricultural Division

H.D. Quemada, Ph.D.
Associate Director
Vegetable Biotechnology
9612-50-1
Telephone No. (616)
Faxsimile No. (616) 384-2726

July 13, 1992

Biotechnology, Coordination, and Technical Assistance
Biotechnology, Biologics, and Environmental Protection
U.S. Department of Agriculture, APHIS
6505 Belcrest Road, Room 850
Hyattsville, MD 20782

PETITION FOR DETERMINATION OF REGULATORY STATUS

Gentlemen:

Enclosed is a copy of a petition for determination on the regulatory status of *Cucurbita pepo* L. cultivar YC77E ZW-20 which has been modified to be resistant to watermelon mosaic virus-2 (WMV-2) and zucchini yellow mosaic virus (ZYMV), which is currently deemed a "regulated article". Based on the data and information contained in the enclosed petition, we believe that there is no longer "reason to believe" that the modified squash plant should be deemed to be a regulated article. The modified squash plant does not present a plant pest risk and is not otherwise deleterious to the environment. The enclosed petition does not contain confidential business information.

The undersigned certifies that, to the best of our knowledge and belief, this petition includes all data, information, and views relevant to the matter, whether favorable or unfavorable to the position of the undersigned, which is the subject of the petition.

Recent applications for unrestricted release…!

Several factors have contributed to the perception of a need for better tools for GMO risk assessment

With new, more complex traits, such as resistance to drought or to salinity, an evaluation based simply on the equivalence between a GMO and non-GMOs may be less effective.

Examples:

Bt toxin gene: no interaction with host biology; no changes expected

Modify metabolic pathway: several changes expected, not surprising if there are others

Modify expression of a transcription regulator: may have highly complex effects on expression of many genes (may be needed for desirable effect)

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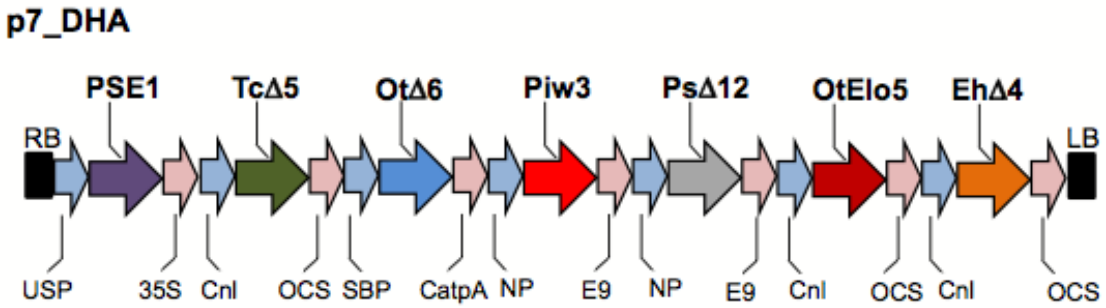

Seven transgenes from 14 organisms

Ruiz-Lopez et al. 2014. Plant J. 77, 198-208

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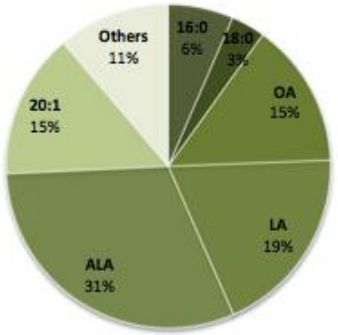
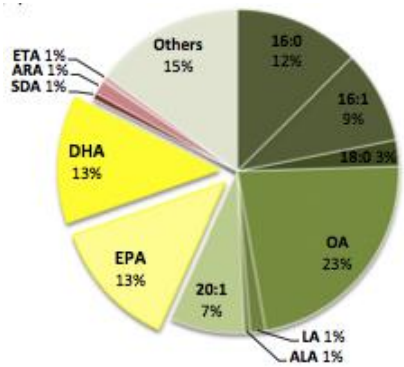
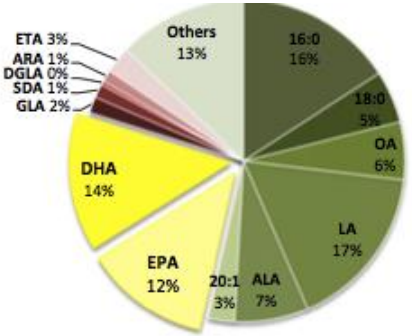
Wild-type seeds



Fish oil



GM seeds



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New Phytologist

New Phytologist (2013) 1
www.newphytologist.com

Research

A novel 5-enolpyruvoylshikimate-3-phosphate (EPSP) synthase transgene for glyphosate resistance stimulates growth and fecundity in weedy rice (*Oryza sativa*) without herbicide

Wei Wang[1], Hui Xia[1], Xiao Yang[1], Ting Xu[1], Hong Jiang Si[1], Xing Xing Cai[1], Feng Wang[2], Jun Su[2], Allison A. Snow[3] and Bao-Rong Lu[1]

A new strategy developed at ICGEB for GMO risk assessment based on problem formulation that will be both:

- Scientifically rigorous
- More accessible to non-specialists
  (follow natural thought processes, avoid jargon…)

(developed through ICGEB courses like this one)

- Well adapted to serve as the basis for communication

GM Crops and Food: Biotechnology in Agriculture and the Food Chain 4:1, 10-15; January/February/March 2013; © 2013 Landes Bioscience

Putting problem formulation at the forefront of GMO risk analysis

Mark Tepfer,[1,2] Monica Racovita[3] and Wendy Craig[3,*]
[1]INRA, UMR1318; Institut Jean-Pierre Bourgin; INRA-Versailles; Versailles, France; [2]INRA, UR407; Station de Pathologie Végétale; INRA-Avignon; Montfavet, France; [3]Biosafety Unit; International Centre for Genetic Engineering and Biotechnology (ICGEB); Trieste, Italy

A brief history of problem formulation

A concept that has developed over several years:

US EPA (1998) Guidelines for ecological risk assessment.

Johnson KL, Raybould AF, Hudson MD, Poppy GM (2007) How does scientific risk assessment of GM crops fit within the wider risk analysis? Trends Plant Sci 12, 1-5.

Hokanson KE, Ellstrand NC, Ouedraogo JT, Olweny PA, Schall BA, Raybould AF (2010) Biofortified sorghum in Africa: using problem formulation to inform risk assessment. Nature Biotech. 28, 900-903.

Wolt JD, Keese P, Raybould A, Fitzpatrick JW, Burachik M, Gray A, Olin SS, Schiemann J, Sears M, Wu F (2010) Problem formulation in the environmental risk assessment for genetically modified plants. Transgenic Res. 19, 425–436.

Tepfer M, Racovita M, Craig W (2013) Putting problem formulation at the forefront of GMO risk analysis. GM Crops & Food 4, 10-15.

Risk assessment based on problem formulation

Instead of accumulation all possible information concerning, for instance plant-gene-environment interactions, to show that nothing is changed by the GMO, start out by examining the potential negative effects that are of concern.

These potential negative effects are then reformulated as risk hypotheses.

Then, through detailed scrutiny of the causal chain that could link the GMO and a negative effect (harm), you can determine of scientific knowledge make it possible to invalidate the causal chain (refutation of the risk hypothesis).

How to proceed, using the problem formulation strategy

1. **Identify protection goals**

2. **Based on these goals, create a catalogue of risk hypotheses**

3. **Prioritization: rank hypotheses according to importance**

4. **For the hypotheses to be examined, create a "pathway to harm"**

5. **Test the risk hypothesis**
- Identify key steps in the pathway, and fit available data to it.
- Determine whether the data allow to break one or more links in the pathway.
- If necessary, gather new data.

6. **If there are still concerns, consider mitigation measures**

7. **Draw conclusions regarding the potential risk**

why do some find it hard to decide?

This risk assessment-policy gap stems partly from normative and imprecise policy language, but is rooted more fundamentally in society's uncertain expectations for the environment.

Until this uncertainty is resolved, the democratic and regulatory effectiveness of risk regulation will be undermined by ad hoc policy decisions abdicated to risk assessors.

(Evans et al., 2006: Environment International, 32, 1066-1071)


Questions?