Using problem formulation to construct fit-for-purpose environmental risk assessments of regulated stressors

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Environmental risk assessments (ERAs)

- Performed to evaluate the likelihood of adverse effects in the environment occurring as a result of exposure to biological, physical or chemical stressors.

- ERAs must be “fit-for-purpose”
  
  • Focus on the key aspects that the assessments must consider
  
  • Provides relevant information for decision-makers

FACILITATE DECISION MAKING
Using problem formulation to construct fit-for-purpose risk assessments

**Fit-for-purpose**

“using the right tool to adequately answer the risk managers questions”

**VALIDITY**
- The assessment measures exactly what we set out to measure

**RELIABILITY**
- Consistent
- As accurate as possible
- As realistic as possible

**TRANSPARENCY**
- Clearly explains the logic of what has been done, how and why it has been done
In the EU, ERAs for different stressors are covered by different regulations, e.g.:

- **Pesticides (EC) No 1107/2009**
  - Well codified risk assessments, tiered approaches with specific data requirements and trigger values that guide the assessment

- **Genetically modified crops: Directive 2001/18/EC**
  - Case-by-case risk assessments with a set of data requirements expected for all types of products.

Emerging technologies such as: gene drive modified mosquitoes, RNA interference-based genetically modified plants and pesticides, etc raise questions on whether existing ERA tools can be readily applied.

How to ensure that the ERAs are fit-for-purpose?
Problem formulation

- Implicitly used by risk assessors.
- Early described more explicitly in the frame of the EPA pesticide risk assessment (USEPA, 1992\(^1\)).
- Identified as a useful tool for organizing and harmonizing ERAs for GM crops.
- Now used explicitly in ERAs for GMOs submitted to EFSA (e.g. EFSA, 2010\(^2\)) and other countries (e.g. India)
- Could be useful for new technologies under development

PF helps ensuring that the assessment will be fit-for-purpose (validity, reliability, transparency)

Using problem formulation to construct fit-for-purpose risk assessments

Problem formulation in the environmental risk assessment for genetically modified plants

Jeffrey D. Wolt · Paul Keese · Alan Raybould · Julie W. Fitzpatrick · Moisés Burachik · Alan Gray · Stephen S. Olin · Joachim Schiemann · Mark Sears · Felicia Wu

Putting problem formulation at the forefront of GMO risk analysis

When applying risk assessment and the broader process of risk analysis to decisions regarding the dissemination of genetically modified organisms (GMOs), there are a number of issues that are not easy to resolve in practice. Further, in almost all situations regarding the environmental impact of GMOs, the approach is underpinned by limited information about the species involved and their reactions to environmental factors. Thus, there is a need to develop a framework for addressing the complex issues associated with GMOs.

Problem Formulation in Environmental Risk Assessment for Genetically Modified Crops: A Practitioner’s Approach

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Abstract
Problem Formulation, a tried and tested aspect of Environmental Risk Assessment (ERA), is increasingly being applied to assess the potential risks associated with the cultivation of genetically modified (GM) crops. The first step in the ERA, problem formulation is a way of focussing on those aspects of the environment which most need protection or are most at risk of harm, framing relevant scenarios in which they may be harmed and devising a plan

Safety Assessment of Food and Feed Derived from GM Crops: Using Problem Formulation to Ensure “Fit for Purpose” Risk Assessments

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Abstract
All genetically modified (GM) crops intended for use in food and feed must be assessed for their safety to humans and animals. The data and methodology used to conduct these assessments has been developed over many years. International organisations like the Food and Agriculture Organization (FAO) of the United Nations, the World Health Organization (WHO) and the Organisation for Economic Cooperation and Development (OECD) have been facilitating the harmonisation of food and feed risk assessment methodologies. The Codex Alimentarius Commission, established by FAO and WHO in 1963, has developed harmonised international food standards, guidelines and codes of practice and promoted coordination of all food standards work undertaken by international governmental and non-governmental organisations.
What is Problem Formulation?

Allows the organization of the risk assessment in a transparent and logical way

- Considers the relevant Protection goals
- Relevant available information is compiled to address key questions
- Facilitates an initial risk characterization to establish:
  - If the risk characterization can be completed with available information
  - If more information is necessary
- If more information is needed, problem formulation allows:
  - The development of a clear analysis plan, or
  - The identification of the information needed to facilitate decision making
Using problem formulation to construct fit-for-purpose risk assessments

PROBLEM FORMULATION

PROTECTION GOALS

GATHERING RELEVANT INFORMATION

INITIAL RISK CHARACTERIZATION

CONCLUSION OR

IDENTIFY MISSING INFORMATION
PROTECTION GOALS:

- Different regulatory frameworks may have different protection goals.

  A good understanding of the protection goals set in the regulatory framework within which we are operating is essential.

- Usually the protection goals set by policy are very broad and not always clear. They need to be translated to more operative protection goals that can then be translated to testable hypothesis.

Using problem formulation to construct fit-for-purpose risk assessments.

HIGH LEVEL PROTECTION GOAL

OPERATIONAL PROTECTION GOAL

TESTABLE HYPOTHESIS
Using problem formulation to construct fit-for-purpose risk assessments

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Using problem formulation to construct fit-for-purpose risk assessments

Evaluating environmental risks of genetically modified crops: ecological harm criteria for regulatory decision-making

Development of a framework based on an ecosystem services approach for deriving specific protection goals for environmental risk assessment of pesticides


EMBO reports

Optimising environmental risk assessments

Yann Devos, Jörg Romme, Robert Luttik, Angelo Maggioni, Joe N Perry, Reinhold Schoonjans, Franz Streissl, Jose V Tarazona & Theo CM Brock

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Optimising environmental risk assessments

Accounting for ecosystem services helps to translate broad policy protection goals into specific operational ones for environmental risk assessments

Yann Devos, Jörg Romme, Robert Luttik, Angelo Maggioni, Joe N Perry, Reinhold Schoonjans, Franz Streissl, Jose V Tarazona & Theo CM Brock

Regular products such as genetically modified organisms (GMOs), plant protection products (PPPs) or feed additives for livestock are subject to environmental risk assessment before they can be approved for use in agriculture. This assessment aims to evaluate any possible risk that the deployment of such products may pose to the environment. Robust environmental risk assessments require an explicit formulation of potential problems that are possible to identify and evaluate exposure assessment and potential adverse effects from potential optimisation. The actual risk is then characterised by testing specific hypotheses about the likelihood and severity of these

To support regulatory decision-making, these protection goals can vary between jurisdictions, but their overall aim is to minimise harm to the environment, including biodiversity and ecosystems, caused by human activities.

However, policy protection goals, such as protecting biodiversity, are often too general and vague to be useful for scientific risk assessment, and need to be translated into specific, operational ones. Because protecting everything every time is not always realistic, operational protection goals, also termed specific protection goals, have to delineate the environmental components that need to be protected, what and how

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Protection goals in environmental risk assessment: a practical approach

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Protection goals in environmental risk assessment: a practical approach

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Abstract Policy protection goals are set up in most countries to minimise harm to the environment, humans and animals caused by human activities. Decisions on whether to approve new agricultural products, like pesticides or genetically modified (GM) crops, take into account these policy protection goals. To support decision-making, applications for approval of commercial uses of GM crops usually comprise an environmental risk assessment (ERA). These risk assessments are analytical tools, based on science, that follow a conceptual model that includes a problem formulation step where policy protection goals are considered. However, in most countries, risk assessors face major problems in that policy protection goals set hypotheses that can be used in ERAs. Examples are provided to show how this approach can be applied to two areas of environmental concern relevant to the ERAs of GM crops.

Keywords Environmental risk assessment - Genetically modified crops - Protection goals - Assessment endpoints - Policy - Regulation

Introduction Environmental risk assessments (ERAs) are an essential part of regulatory decision-making for genetically modified crops (GMCs) and pest control products. ERAs provide a framework for assessing the potential risks of introducing new agricultural products, such as pesticides or genetically modified (GM) crops, to the environment, human health, and animal health. The purpose of this study is to develop a framework for integrating policy protection goals into environmental risk assessment (ERA) for genetically modified crops (GMCs). To achieve this, we will explore the relationship between policy protection goals and environmental risk assessment (ERA) and propose a conceptual model for incorporating policy protection goals into the ERA process. We will then illustrate the application of this model through case studies of policy protection goals for GMCs and pest control products. The results of this study will provide guidance for regulatory agencies and stakeholders on how to effectively incorporate policy protection goals into the ERA process and improve the decision-making process for introducing new agricultural products.
Using problem formulation to construct fit-for-purpose risk assessments

**Broad**

- **Policy Protection Goals**: What the country policy is
- **Operational Protection Goals**: Aspects of the country policy that will be included in the risk assessment
- **Assessment Endpoints**: What will be assessed based on the characteristics of the product and the potential harm it can cause
- **Measurement Endpoints**: What will be measured to assess risk for the chosen assessment endpoints. Based on testable hypothesis.

**Specific**
Using problem formulation to construct fit-for-purpose risk assessments

PROBLEM FORMULATION

PROTECTION GOALS

GATHERING RELEVANT INFORMATION

INITIAL RISK CHARACTERIZATION

CONCLUSION

OR

IDENTIFY MISSING INFORMATION
GATHERING RELEVANT INFORMATION:

Collection of information relevant to the hypotheses formulated that may help prove or disprove the hypotheses

There are different sources of these sort of information

- From studies conducted within the regulatory package
  - e.g. Ecotox studies
- Relevant peer reviewed publications
  - e.g. information related to the compounds or class of compounds
- Previous risk assessments
  - e.g. risk assessment conducted in other countries
Using problem formulation to construct fit-for-purpose risk assessments

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IDENTIFY MISSING INFORMATION
INITIAL RISK CHARACTERIZATION

Risk = \( f \) (Hazard, Exposure)

If there is no exposure or the hazard is very low (no toxicity found), the risk can be considered low.

Risk Conclusion: The risk is low

If the exposure levels are not known or the level of hazard is not known.

Need more information to make a risk conclusion.
Using problem formulation to construct fit-for-purpose risk assessments

Example:

No protein expressed in pollen, low risk to pollinators
QUALITATIVE RISK MEASURES

When the risk cannot be quantified, qualitative measures can be used.

<table>
<thead>
<tr>
<th>HAZARD</th>
<th>RISK ESTIMATE</th>
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<tr>
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PROBLEM FORMULATION

PROTECTION GOALS

GATHERING RELEVANT INFORMATION

INITIAL RISK CHARACTERIZATION

CONCLUSION OR IDENTIFY MISSING INFORMATION
Identifying missing information

If the initial risk characterization can not be completed more data may be needed

- Characterization of hazard
- Characterization of exposure

The data must be relevant to the assessment endpoints and risk hypotheses formulated

The purpose always is to collect data that facilitates decision making

(“need to know” versus “nice to know”)

Implementation: Pathways to Harm

Proposed activity

Specify events that must occur for the particular use to lead to the defined harm

Event A → Hypothesis 1
Event B → Hypothesis 2
Event C → Hypothesis 3

Defined harm

Choice of hypothesis depends on definition of harm & decision-making criteria

Slide based on material provided by Dr. A. Raybould
Proposed activity

- Specify events that must occur for the particular use to lead to the defined harm

Defined harm

RISK CHARACTERIZATION

- Hypotheses are false, not tested or only weakly tested: High risk/high uncertainty
- At least one hypothesis is corroborated after rigorous testing: pathway blocked: Negligible risk
- Several hypotheses are corroborated after less rigorous testing: Low risk (weight of evidence)

Slide based on material provided by Dr. A. Raybould
Pathways to Harm
Example: assessing the potential population decline of a valued species of butterfly due to the cultivation of Bt maize

- **Cultivation of Bt maize**
- The Bt protein is expressed in pollen
- Bt pollen reaches butterfly food plant
- Butterfly eats Bt pollen
- The Bt protein is toxic to the butterfly
- **Population decline**

- **No Bt protein in pollen**
- **No pollen on food plant**
- **Pollen not eaten**
- **Pollen not toxic**
- **Toxicity has no effect on population**

*Slide based on material provided by Dr. A. Raybould*
Pathways to Harm
Example: assessing the potential population decline of a valued species of butterfly due to the cultivation of Bt maize

Cultivation of Bt maize
- The Bt protein is expressed in pollen
  - Bt pollen reaches butterfly food plant
    - Butterfly eats Bt pollen
      - The Bt protein is toxic to the butterfly
        - Toxicity has no effect on population
          - Population decline

The expression study shows that the Bt protein is not expressed in pollen
- No Bt protein in pollen
  - No pollen on food plant
    - No exposure
      - Low risk
Cultivation of Bt maize

The Bt protein is expressed in pollen

Bt pollen reaches butterfly food plant

Butterfly eats Bt pollen

The Bt protein is toxic to the butterfly

Population decline

No Bt protein in pollen

No pollen on food plant

Pollen not eaten

Pollen not toxic

Toxicity has no effect on population

Once the path is blocked a risk conclusion can be made

Testing all the hypothesis is not always useful/necessary

Example: assessing the potential population decline of a valued species of butterfly due to the cultivation of Bt maize
Pathways to Harm
Example: assessing the potential population decline of a valued species of butterfly due to the cultivation of Bt maize

- Cultivation of Bt maize
  - The Bt protein is expressed in pollen
    - No Bt protein in pollen

- Bt pollen reaches butterfly food plant
  - No pollen on food plant

- Butterfly eats Bt pollen
  - Pollen not eaten

- The Bt protein is toxic to the butterfly
  - Pollen not toxic

- Toxicity has no effect on population

Population decline

Gather further information on toxicity of the protein

No information that allows ruling out potential hazard
Protection goals: clear definition of what is being assessed and what is regarded as harmful

Gathering relevant data: data relevant to the assessment endpoints and risk hypotheses

Initial risk characterization: a pathway to harm can be used

Conclusion: can be reached when pathways are clearly blocked

Identifying missing information: when a pathway cannot be blocked with existing information, a clear plan for collection of key data can be drawn
Summary

- ERAs are conducted to **facilitate decision making**, they must be **fit-for-purpose**.
- Problem formulation provides a useful method for ERAs that can be applied to any kind of stressor.

Problem formulation can be implemented using pathways to harm:

- Taking into account relevant protection goals to define the specific harms
- Formulating hypotheses to test the events that constitute the pathway
- Making risk conclusions with existing information, or
- Identifying information that must be gathered to continue the assessment
Thank you for your attention!