Relevance of modelling for assessing spatial and temporal effects of GMOs – Upscaling.

Frédérique Angevin[1], Nathalie Colbach[2], Antoine Messéan[1], Claire Lavigne[3]

1: INRA, UAR 1240, Eco-innov, F-78850 Thiverval Grignon - France
2: INRA, UMR1210, Biologie et Gestion des Adventices, F-21000 Dijon, France
3: INRA, UR1115, Plantes et Systèmes de culture Horticoles, F-84000 Avignon, France.

Gene flow is a common phenomenon for crop species and its implications for Genetically Modified Plants have raised new concerns. Undesirable effects related to gene flow may result in ecological or agronomic considerations (persistence of feral plants, creation of new weeds; impacts on biodiversity) as well as in commercial considerations (adventitious presence of GMOs in conventional crop production affecting its competitiveness in the marketplace). Consequently, the coexistence between different types of crops has become a major issue and has to be addressed *per se* whatever are the actual ecological, agronomic and safety impacts.
On-farm gene flow occurs both in time and in space, through pollen flow as well as through seed dispersal. Several factors are involved: crop biology, landscape fragmentation, environmental conditions, crop management and post-harvesting practices. For helping in the elaboration of co-existence rules, for assessing their feasibility and their consequences as well as for setting up monitoring and control schemes, one should be able to forecast the fate of GM plants at the landscape level in the wide range of agro-ecosystems. Specific field experiments are necessary for understanding the basic phenomena involved but are difficult to extrapolate for such a perspective even if several studies have been carried out in order to broaden the scope of the evaluation: the inter-institute platforms in France or the Farm Scale Evaluation programme in the UK.
For addressing such a challenge, modelling is a key element. Models reproduce the functioning of agro-systems and take into account the relevant factors and processes as well as their interactions. They thus allow simulating the behaviour of various agro-systems in non-observed situations and on a long term basis.

Testing non-target organisms – the ecological approach

Gabor L Lövei
University of Aarhus, Faculty of Agricultural Sciences, Department of Integrated Pest Management, Flakkebjerg Research Centre, DK-4200 Slagelse, Denmark

This contribution calls for reconsidering several concepts in GMO risk assessment. The term “non-target” is ecologically misleading, because it artificially dissects an ecological system into component parts (“target” vs. “non-target”) - not always possible nor wise. The main reason for doing pre-release testing is because we have to consider the impact of new technologies on ecosystem services that are strained by combined human activities. We should test ecosystem service providers, not “non-target organisms”.
All organisms cannot and should not be tested. Only some species are important in any ecosystem as ecosystem service providers - many are not. The challenge is how to identify these species. There is no universally useful test organism. The Cartagena Protocol, by calling for case-by-case testing, recognises this. I shall present the selection matrix developed by an international team to solve the tst species selection riddle and show that selection criteria applied so far follow no specific logic: it has been *ad hoc*, opportunistic selection.
The agreed laboratory procedure is to create a “worst case scenario”. Laboratory tests done so far are mostly not “worst case”. Tests so far have been mostly too short, a single-effect tests, under simplistic conditions. Easy and feasible methodological improvements can be suggested. The tiered system terminology is unwise because it creates an analogy to pesticide testing that cannot be followed. Gm plants are not inert chemicals and therefore the same systems cannot be used when testing for risk assessment. Due to important agent-environment interactions, a “no effect” laboratory test is no mandate to stop testing. Higher level testing (semi-field and field scale) has to follow, at least until we know more about these interactions.
The statistical evaluation methods should take example from the risk assessment in other disciplines, such as pharmaceutical testing, and use the equivalence testing as evaluation method, not the usual statistical methods of testing a null hypothesis as routinely used in biological research. Finally, when summarising available evidence, the personalised opinion summaries now common should be replaced by evidence-based methods, also known as “systematic review”.

Managing the Footprint of Agriculture: Towards a Comparative Assessment of Risks and Benefits for Novel Agricultural Systems

Chris Pollock
University of Wales, Aberystwyth and Chair, UK Advisory Committee on Releases to the Environment (ACRE)

Against a background of greater awareness of the significant ecological footprint of modern agriculture, the current legislation on release of GM organisms into the environment obliges us to consider the wider implications of cultivation/release. The farm-scale evaluations of herbicide-tolerant crops (FSEs) determined the impact of novel weed control strategies on within- and around-field biodiversity against a null hypothesis that HT crop management would have no effect. In all cases, the null hypothesis was disproven, but the differences between crops were larger than the within-crop differences between conventional and HT managements. I shall briefly summarise these data and consider the implications for regulation.

An ACRE sub-committee considered the wider implications of the FSEs and concluded that there were significant issues that we felt should be addressed relating to the current regulatory framework. We are concerned that regulation is partial (in that only novel GM crops are subject to this scrutiny despite the much larger impact of changes in conventional management and the development of new conventional varieties) and that no account is taken of the balance between benefit and disbenefit. We have proposed, for discussion purposes, a framework by which such considerations could be addressed and I will describe some examples of the outputs from this process.

ACRE considers that the time is right to begin a debate about the future regulation of novel agricultural processes. As agriculture is increasingly expected to be multifunctional, we support the development of a robust, cost-effective evidence-based framework for consideration of the balance between impact and delivery and see little scientific justification for restricting this to one particular technology.

Non-target arthropod risk assessment of insect-resistant GM crops

Jörg Romeis*, Detlef Bartsch, Franz Bigler, Marco P. Candolfi, Marco M.C. Gielkens, Susan E. Hartley, Richard L. Hellmich, Joseph E. Huesing, Paul C. Jepson, Raymond Layton, Hector Quemada, Alan Raybould, Robyn I. Rose, Joachim Schiemann, Mark K. Sears, Anthony M. Shelton, Jeremy Sweet, Zigfridas Vaituzis, Jeffrey D. Wolt

** Agroscope Reckenholz-Tänikon Research Station ART, Reckenholzstr. 191, 8046 Zurich, Switzerland (joerg.romeis@art.admin.ch)*

An international initiative has been established within the "Western Palaearctic Regional Section" (WPRS) of the "International Organization for Biological Control" (IOBC) with the aim of establishing generic and scientifically rigorous environmental risk assessment (ERA) guidelines for insect-resistant, genetically modified (IRGM) crops, focusing on terrestrial non-target arthropods (NTA's). The activity involves scientists from public research institutes, regulatory agencies, the agricultural biotechnology industry and a commercial testing laboratory.

The proposed consensus approach consists of an adaptation of the tiered approach to risk assessment that is accepted internationally within regulatory toxicology and environmental sciences, and versions of which are already in use in established and effective regulatory systems for GM crops. The approach has a strong focus on the formulation and testing of clearly stated risk hypotheses, making maximum use of available data and using formal decision guidelines to progress between testing stages (or tiers). During the problem formulation stage, the relevant differences between the GM plant and its non-GM counterparts are identified in order to focus the ERA on the areas of greatest concern or uncertainty. Testable scientific hypotheses are developed that are subsequently addressed in the analytical phase of the risk assessment. If a lack of significant differences is established, the ERA can emphasize the effects of the insecticidal protein. A typical risk hypothesis may be that the insecticidal protein does not cause any harm to NTA's at the concentration expressed in the field. The assessment of this hypothesis frequently leads to toxicity tests on selected arthropod species. For practical reasons surrogate species will be selected that are appropriate for a specific IRGM crop and are available and amenable for testing.

Hazard assessment tests are usually conducted using elevated protein doses in the laboratory, following standardized testing protocols. This assures a high level of confidence in the conclusions drawn from the data and applicability for further ERAs. Prior to testing, the objectives of the individual studies need to be defined, and specific measurement endpoints described that address the risk hypotheses (and are related to earlier defined assessment endpoints). Testing protein concentrations that are several times higher than those present in the field increases the likelihood that a hazard will be detected should one be present. Higher tier tests that are, for example, conducted in the field are more realistic but highly complex. They have a high intrinsic uncertainty for showing hazards but more certainty for showing whether hazards pose a risk. Higher tier studies should thus only be conducted when they can further reduce uncertainty in the risk assessment, and only when justified by detection of potentially adverse effects in the lower tiers of testing. Thus, effective tiered processes prevent costly and unnecessary testing.

We are confident that the tiered evaluation of potential hazards with representative indicator/surrogate species provides a rigorous and effective basis for estimating risk that minimizes the likelihood of false negatives. It requires testing of clearly stated relevant hypotheses and thereby minimizes collection of data that are irrelevant to the risk assessment. It is thus seen as the most rigorous approach, from both scientific and regulatory standpoints, for determining the potential of IRGM plants to adversely affect NTA's.

Please consult the following reference for more details and the affiliations of all authors: Romeis *et al*. (2006) Moving through the tiered and methodological framework for non-target arthropod risk assessment of transgenic insecticidal crops. Proceedings of the 9th International Symposium on the Biosafety of Genetically Modified Crops, pp. 62-67. (http://www.isbr.info/symposia/)

Predicting the long-term effects of GM crops

Peter H. van Tienderen
Institute for Biodiversity and Ecosystem Dynamics (IBED)
Universiteit van Amsterdam, Kruislaan 318, 1098 SM Amsterdam.

An increasing number of thorough studies report the difficulties in predicting long-term effects for environmental risk assessment (ERA), but also show progress in designing a structured approach to ERA. In addition, the ESFA guidelines state: "*GMO applicants are obliged to provide adequate data to allow the assessment of the potential long-term adverse effects* ...". It is then up to the applicant and risk assessors for making any prediction.

When looking at long-term effects, some processes are accumulations of small effects in time. They often work at timescales of decades if not longer before any detectable change takes place: e.g. the population dynamics of competing species, selection on rare (trans-)genes, random drift and other stochastic processes, the dynamics of metapopulations. This could mean that fundamental knowledge, experiments and (model) extrapolations rather than observations of actual changes is needed: proper species-specific screening methods and experiments comparing GM and non-GM plants, and models integrating the data. In other processes something emerges that was not previously anticipated. For instance, the first step in the introgression of crop genes into wild relatives depends on gene flow and the presence of wild relatives, the second on the viability and fertility of the F1 hybrid. But in later steps things become more and more complex: the outcome possibly depends on the effects of linkage drag, decline of heterosis, effects of epistasis and different genetic backgrounds, occurrence of transgressive phenotypes, and perhaps even compensatory mutations or epigenetic changes affecting the expression of a gene. This may lead to new phenotypes and hence changes in the distribution and abundance of species.

The case-by-case, step-by-step approach in ERA has clear advantages, but in effect has also undesirable side-effects: there has been limited attention to systematically develop both generic and system-specific knowledge, and it is not well-developed who is responsible for doing this. This makes it unclear what applicant should deliver as '*adequate data*', resulting potentially in wasted efforts and slow regulatory processes.

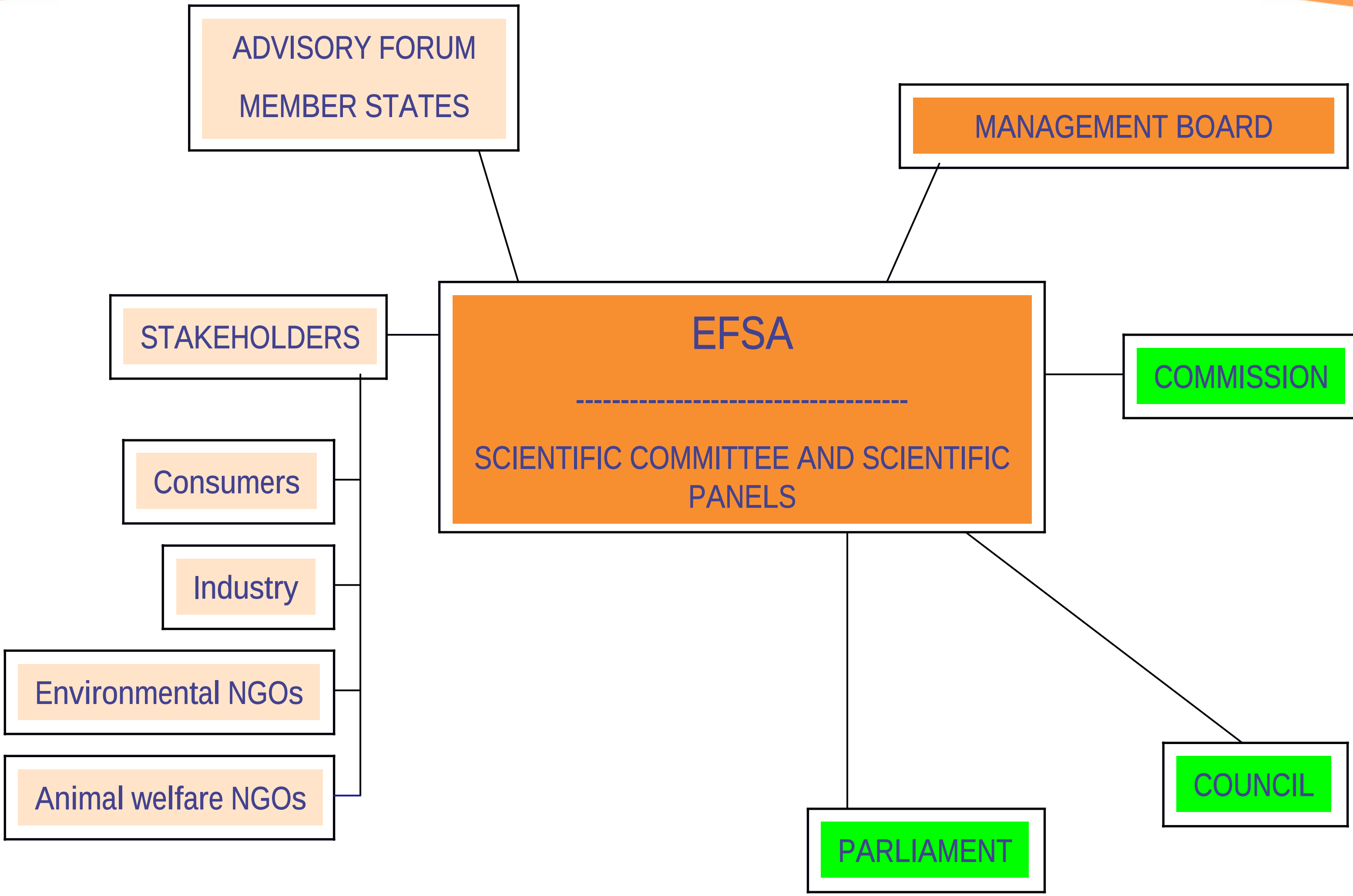
A complement to the case-by-case dogma to reduce the present regulatory congestion is needed, focusing on delivering both generic and system-specific baseline information on the ecology of crops, feral populations and wild relatives, as well as the specifics of the crop/wild hybridization process. The goal would be to identify vulnerable crop systems given the species that occur in and around the agricultural setting, and identify crop-wild combinations where hybridization is likely to proceed; To distinguish cases whose dynamics are driven by external forcing, *i.e.*, the (local) effects would disappear again if the cultivation of the GM crop is discontinued, and cases that progress to a global scale and are potentially irreversible; To identify uncertain and relatively safe crop/trait combinations. With this added the case-by-case approach could function with much greater efficiency, allowing for better prediction of long-term effects. However, GM crop monitoring will be the only way to feed back to the ERA whether predictions were good or bad.

The European Food Safety Authority: working together

HERMAN B.W.M. KOËTER
Deputy Executive Director and Director of Science

Separate risk assessment from risk management

- EFSA is fully independent of the Commission in its scientific work;
- Close cooperation with the Commission and Member States;
- EFSA shares the area of risk communication with the Commission and Member States.


ADVISORY FORUM
MEMBER STATES
MANAGEMENT BOARD
STAKEHOLDERS
EFSA

SCIENTIFIC COMMITTEE AND SCIENTIFIC PANELS
COMMISSION
Consumers
Industry
Environmental NGOs
Animal welfare NGOs
COUNCIL
PARLIAMENT

Scientific activities (work themes):

- Providing scientific opinions, guidance and advice in response to questions;
- Assessing the risk of regulated substances and development of proposals for risk-related factors;
- Monitoring of specific animal health risk factors and diseases;
- Development, promotion and application of new and harmonized scientific approaches and methodologies for hazard and risk assessment of food and feed.

Scientific activities (work themes):

- Providing scientific opinions, guidance and advice in response to questions;
- Assessing the risk of regulated substances and development of proposals for risk-related factors;
- Monitoring of specific animal health risk factors and diseases;
- Development, promotion and application of new and harmonized scientific approaches and methodologies for hazard and risk assessment of food and feed.

Investing in food science: focus areas

- Harmonization of detection methodology for chemical and microbiological contaminants in food/feed;
- Improving the risk assessment process (e.g., environment, transparency, animal health and welfare, specific substances);
- Methodologies to detect and recognise emerging risks;
- Exposure assessment modelling (chemical and microbiological).

Investing in food science (2)

- Organization of open scientific EFSA meetings, to discuss in-depth topical and sensitive issues related to EFSA's mission : EFSA Science Colloquia;
- Adequate follow-up on EFSA Scientific Colloquia (e.g. development of Guidance Documents);
- Active participation in and monitoring of scientific projects, conferences and other scientific meetings in Member States.

Science Colloquia

1. Setting threshold levels for Dioxins and PCBs (2004);
2. Qualified Presumption of Safety of micro-organisms (2004);
3. Collection of European Food Consumption Data (2005);
4. Principles of risk assessment of animal health and welfare (2005);
5. Consumption based dietary guidelines (2006);
6. Risk/benefit analysis (2006);
7. Cumulative risk assessment of pesticides (2006)

Scientific Colloquium Series of the European Food Safety Authority N° 5 March 2006

EFSA SCIENTIFIC COLLOQUIUM 8

Environmental Risk Assessment of Genetically Modiefied Plants: Challenges and Approaches

20-21 June 2007 - Tabiano, PR, Italy

Any EFSA Colloquium is:

- an interactive event rather than a passive listening to lectures;
- a platform for scientists to have in-depth discussions on scientific approaches and methods available and tools and data needed for conducting risk assessments;
- an event to explore opportunities and limitations for defining a common understanding of the current state-of-the-art in scientific progress and limitations;
- an opportunity to define further research needs.

An EFSA Colloquium is not:

- An attempt to agree on the details of a preferred strategy or approach, if any;
- An attempt to finalise a blue print for the work ahead of us;
- A “who is right and who is wrong” discussion.

Issues

- The debate on the risk assessment of GMOs is highly politically motivated;
- Too often the safety evaluation of GMOs is compared to that of ‘small’ molecules such as pesticides;
- The case-by-case approach for food and feed safety assessment as mentioned in the GMO Guidance Document is likely to be also the basis for further consideration of the environmental assessment.

Objectives

- Discuss environmental risk assessment approaches and methodologies in light of current scientific progress;
- Address specific issues, including:
  - Long-term effects
  - Environmental fitness
  - Defining non-target species and assess effects
  - Effects on life cycles of production systems
  - Risks versus benefits

A free and open debate should be the basis for further guidance

Thank you
for sharing your views with EFSA

Thank you
for being frank, open and constructive

Managing the Footprint of Agriculture: Towards a Comparative Assessment of Risks and Benefits for Novel Agricultural Systems

Chris Pollock

Chairman, Advisory Committee on Releases to the Environment

SYNOPSIS

- ACRE
- The reasons for the trials
- The broad findings of the trials
- Their implications
- The work of the ACRE Wider Impacts Sub-Group
- Conclusions

The Advisory Committee on Releases to the Environment (ACRE)

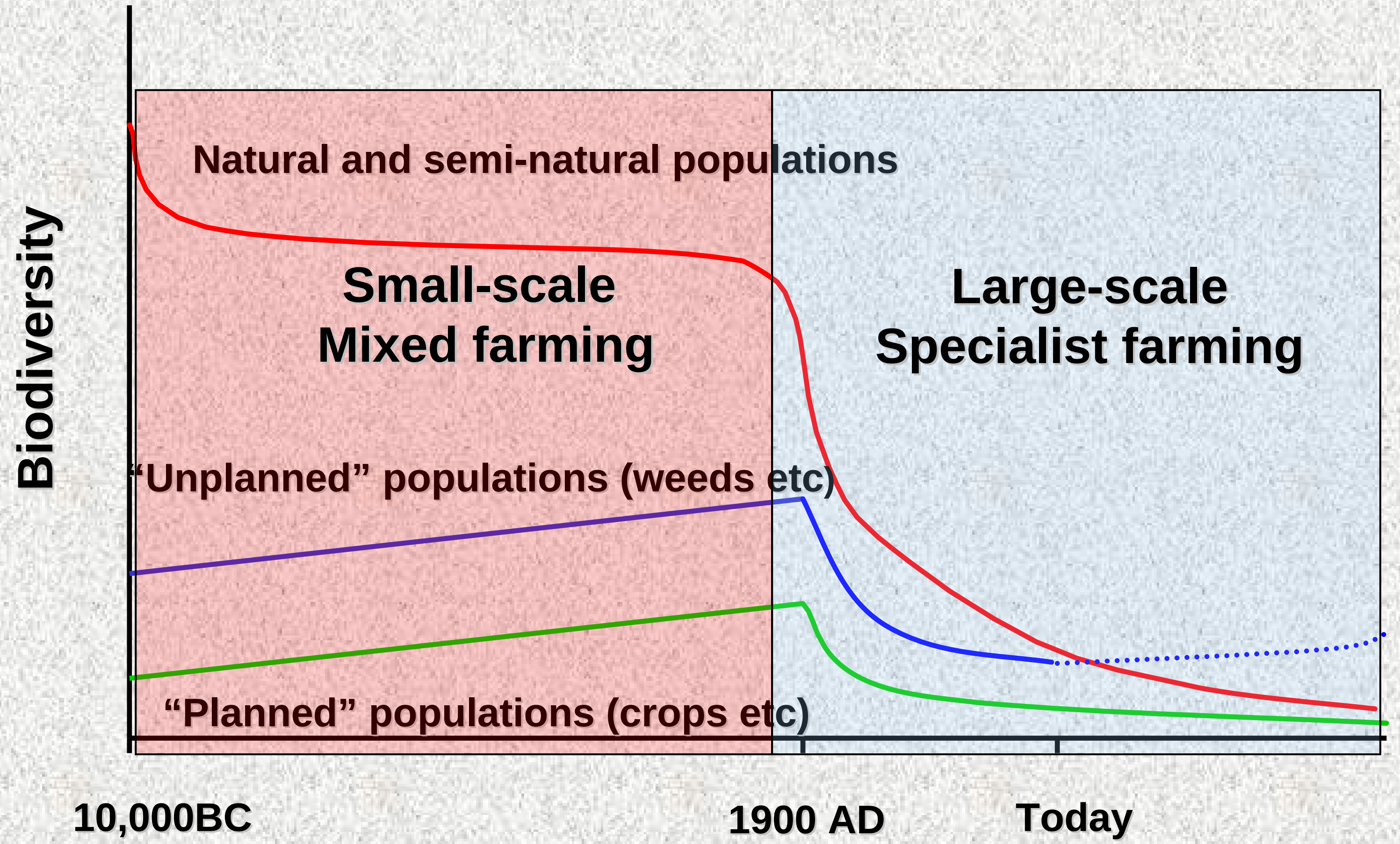
- ACRE is an independent scientific advisory committee established in 1993
- The Committee provides statutory advice to the UK government regarding environmental risks associated with genetically modified organisms.
- ACRE works within the legislative framework that implements EU Directive 2001/18/EC.

(http://www.defra.gov.uk/environment/acre/index.htm)

Concerns have been raised by conservation bodies that many novel agricultural systems have increased adverse effects on wildlife

In general, increased intensification and “agro-efficiency” reduces energy capture by the non-farmed components on farms (e.g. weeds in fields and field boundaries)

Changes in biodiversity attributable to the development of agriculture



Redrawn from Edwards & Hilbeck, 2001

HT CROPS

- Intended to provide more effective weed control
- Concern that this could impact on wildlife (with some indirect supporting evidence)
- Proper exercise of precautionary principle to measure these effects before license

ACRE RECOMMENDED FIELD-SCALE TRIALS OF HT CROPS

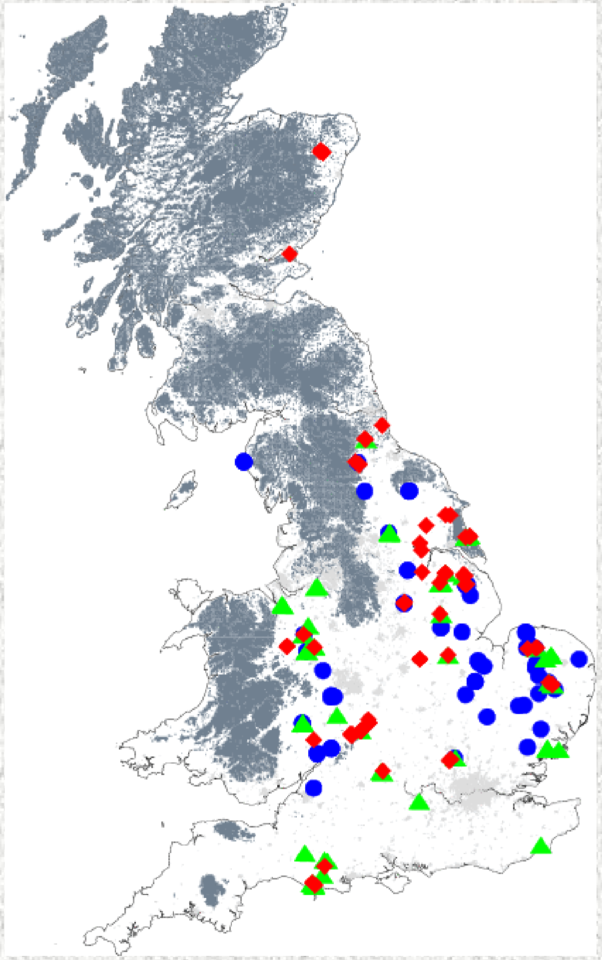
The null hypothesis was that there would be no differences between HT and conventional crops in terms of impact on biodiversity

Centre for Ecology & Hydrology
NATURAL ENVIRONMENT RESEARCH COUNCIL

SITE SELECTION

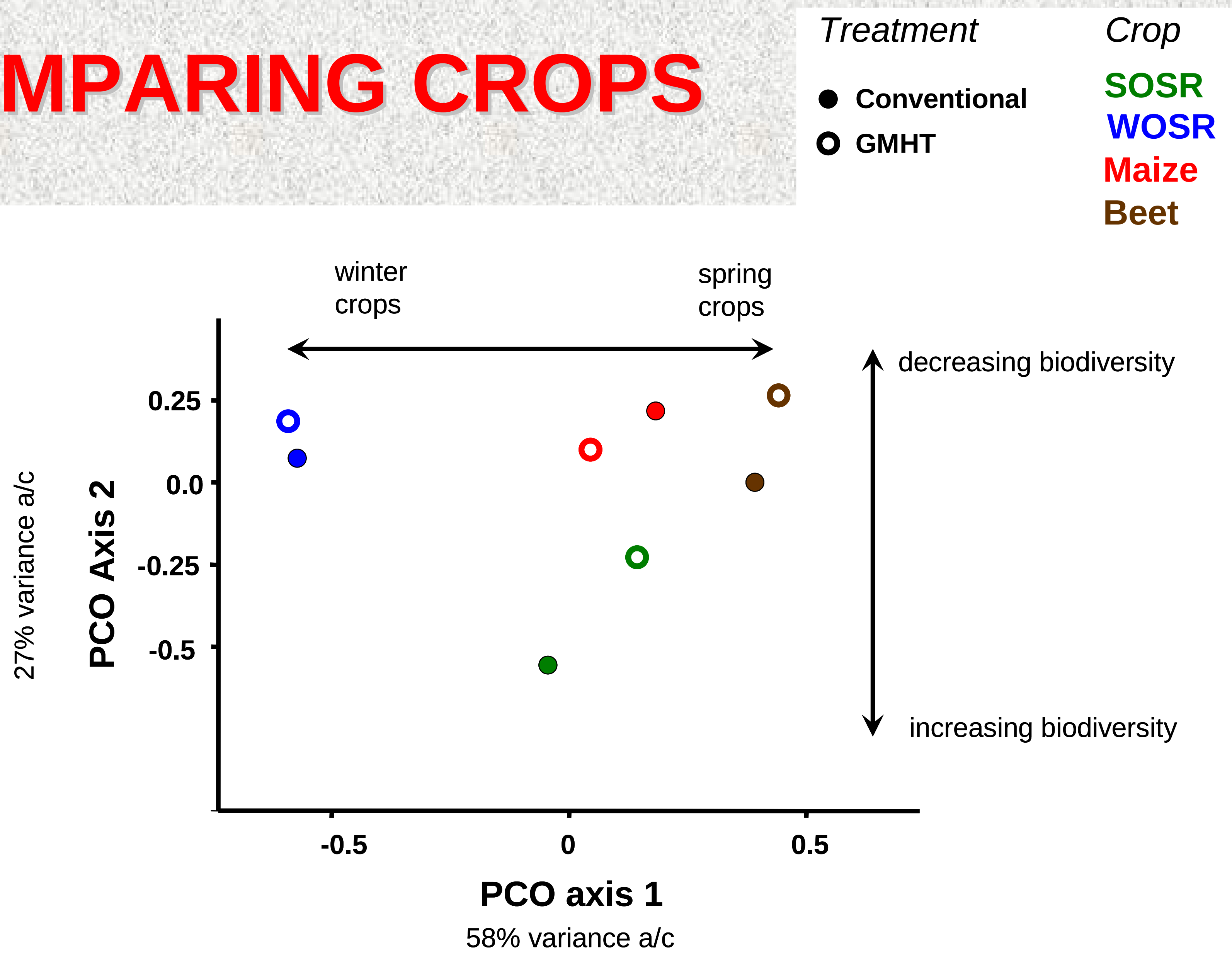
ROTHAMSTED RESEARCH

- 66 beet sites
- 68 maize sites
  - 9 following sites
- 67 spring oilseed rape sites
- Split fields
- Crop management as per normal practice



Scottish Crop Research Institute

COMPARING CROPS



DIFFERENCES BETWEEN CROPS AND TREATMENTS

- **Greater between crops than GM and Conv for same crops**
- **Biodiversity of Winter OSR is the most distinctive**

GM CROPS AND DICOTS

- GM beet, spring OSR, winter OSR, produced fewer dicot seeds and biomass
- GM maize produced more dicot seeds and biomass
- All crops likely to impact populations of granivorous birds

IN SUMMARY .....

- Differences greatest for in-field weeds
- Differences are driven by herbicide regimes
- Differences between crops greater than between GM and conventional

ACRE ADVICE TO MINISTERS

- Permit cultivation of GMHT maize under the FSE conditions within the current consent to 2006
- Renewal would need to show that the advantages to wildlife were maintained under new conventional herbicide regime (no atrazine)
- Any cultivation of rape and beet would require evidence of effective mitigation

RESPONSE

- Ministers accepted ACRE's advice
- Applications for cultivation withdrawn
- Ministers asked ACRE to consider the wider implications of the FSE results

OUTCOME

In May this year, ACRE published

Managing the Footprint of Agriculture:

Towards a Comparative Assessment of Risks and Benefits for Novel Agricultural Systems

EVIDENCE IN SUPPORT OF CHANGE

- Canadians assess novelty rather than concentrating on technology
- Norwegians include benefits of GMOs
- Experts briefed ACRE on developing methodolgies that could be used
- UK and EU Sustainability targets emphasise the need to consider balance of benefits and disbenefits

MAIN CONCLUSIONS (1)

- **Existing regulatory system is partial, inconsistent and only concerned with impact**
- **As agriculture is required to balance delivery of ecosystem services with food production, the balance between impact and benefit is increasingly important**

MAIN CONCLUSIONS (2)

- We propose a matrix-based assessment of impacts and benefits to encourage evidence-based and objective-led regulation of novel agricultural technologies
- Eight criteria are used to develop an overall view of impacts and benefits

CSA PRINCIPLES

- Take account of benefits as well as risks
- Be evidence-based
- Recognise the need to assess impact on a limited scale before widespread use
- Be based on comparison with current crops and practices
- Protect opportunities for innovation by taking into account the impacts of current practice
- Be straightforward to apply
- Be sensitive to the competitiveness of UK agriculture

The matrix

	Benefits	Magnitude of effect/difference	Negative Impacts	Magnitude of effect/difference	Potential for Mitigation
Management System and inputs required					
Persistence/invasiveness					
Environmental goods and services -Biodiversity					
Environmental goods and services -Water					
Environmental goods and services -Soils					
Environmental goods and services -Energy Balance					
Latency/cumulative effects					
Reversibility of effects					
Social Factors					
Economic Factors					
Overall assessment of sustainability					

WORKED EXAMPLES TO ILLUSTRATE HOW THE CSA MIGHT BE USED

1. Japanese knotweed
2. Winter wheat
3. Biocontrol of the European corn borer with *Trichogramma*
4. The energy crop Miscanthus
5. Bt cotton
6. Herbicide tolerant amenity grasses developed through GM or conventional means
7. American Mink

EXAMPLE 5

Benefits and negative impacts of Bt cotton for bollworm control compared to conventionally managed non-GM cotton

CSA Bt cotton compared to non-GM cotton (page 1)

	Benefits	Magnitude of difference	Negative Impacts	Magnitude of difference	**Potential for Mitigation**
Management System and inputs required	**Bt cotton is easier to manage for farmers as few or no insecticide sprays are required and farm workers are less likely to be exposed to toxic insecticides. Bt cotton gives farmers the opportunity to develop integrated pest management systems to keep other pests below economically damaging levels. Fewer insecticide applications required than in non-GM cotton.**	**High**	**Bt cotton provides a continuous high level of plant resistance, which exerts a higher selection pressure than sprayed insecticides (resistance management regimes were therefore implemented in several countries for Bt cotton at the time of commercialization, see below). Bt cotton seeds are more expensive. Use of water and fertiliser the same in both conventional and Bt cotton. Some insecticide applications to Bt cotton can still be required in areas where pests other than bollworms cause economic damage.**	**Low**	
Persistence/ invasiveness			**Cotton does have the potential to hybridise with feral *Gossypium hirsutum* populations and some wild *Gossypium* relatives in limited geographic locations. Upland cotton is a poor coloniser.**	**Low**	**None required**
Environmental goods and services ***– Biodiversity***	**More non-target arthropods survive in Bt cotton. No chronic long-term effects of Bt cotton were observed.**	**High**	**Bt cotton likely to reduce food supply for some specialist natural enemies that feed on the target pest more than insecticides do.**	**Low**	**Maintain below economic threshold levels of pests**
Effects on environmental goods and services -Water	**The growing of Bt cotton results in less synthetic insecticide entering water courses.**	**High**			**None**

CSA Bt cotton compared to non-GM cotton (page 2)

	Benefits	Magnitude of difference	Negative Impacts	Magnitude of difference	**Potential for Mitigation**
Effects on environmental goods and services -Soils	**The growing of Bt cotton results in less synthetic insecticide entering soils.**	**High**	**Bt toxin enters soil with decaying plant material but no negative effect on soil organisms known. See latency and cumulative effects**	**Low**	**None required**
Effects on environmental goods and services -Energy Balance					
Latency/ cumulative effects			**Incorporation of plant residues after harvest introduces Bt toxins into soil. Cry toxins can adsorb and bind to clays and humic substances in soil and have been detected in some soils three years after incorporation of plant biomass. Evolution of C into CO_2 during decomposition has been reported to be reduced during decomposition of Bt cotton compared to non-Bt cotton. No significant effects on soil organisms of Cry toxins released into soil have been found.**	**Low**	**None required**
Reversibility of effects			**Reversible as long as cropping not permitted in regions where introgression into populations of wild species and feral populations is possible.**	**Low**	

CSA Bt cotton compared to non-GM cotton (page 3)

	Benefits	Magnitude of difference	Negative Impacts	Magnitude of difference	**Potential for Mitigation**
Social Factors	**Bt cotton is easier to manage for farmers as few or no insecticide sprays are required and farm workers are less likely to be exposed to toxic insecticides.**	**High**		**None**	**None Required**
Economic Factors	**Yield gains and an increase in yield security have been reported for Bt cotton, particularly from developing countries.**	**High**	**The performance of GM crops depends heavily on the suitability of the local varieties into which genes are inserted. GM Bt seeds are more expensive for farmers than conventional seeds. These factors combined mean that the benefits of this crop may be dependent on region. Yield and profit reductions relative to non-Bt hybrids have been reported in some areas.**	**Low**	**None**

EXAMPLE 5: CONCLUSIONS

Compared to cotton sprayed with insecticides, Bt cotton has major benefits in terms of the environment, yield security and human health. The environmental disbenefits appear marginal in comparison.

EXAMPLE 6: GM VS NON-GM HT RYEGRASS

- Benefit in terms of effectiveness and cheapness of management
- Disbenefits in terms of:
  - Increased spraying over non-HT
  - Negative effects on non-target biodiversity
  - High risk of escape of trait into wild populations (alternative control strategies more damaging)

GM VS NON-GM HT RYEGRASS

- Conclusions that the approach offered advantages over non-HT but also had potential disadvantages that would have to be mitigated.
- Phenotype would be similar for GMHT and non-GMHT, so similar balance of benefit and disbenefit.

CONCLUSIONS

- FSEs demonstrated proper application of the precautionary principle
- They confirmed the impact on biodiversity of conventional systems as well as GMHT
- Logical application of the precautionary principle is to assess all new agricultural practices for impacts on the natural environment
- Risks should be set against benefits
- The debate on regulatory change now has to go out into Europe

Guidance of the GMO Panel for the risk assessment of GM plants and derived food and feed

Dr Suzy Renckens

Head GMO Unit

Scientific co-ordinator GMO Panel

Mandate of the GMO Panel (1)

- **to deliver opinions on scientific questions relating to genetically modified organisms such as micro-organisms, plants and animals.**
  - **questions related to genetically modified food and feed including the derived products** (applications under Regulation 1829/2003)
  - **questions related to the deliberate release into the environment of GMOs** (applications under Directive 2001/18/EC or Regulation 1829/2003)
  - **general questions** (eg safeguard clauses)

Mandate of the GMO Panel (2)

- **To provide risk assessment guidance to applicants on preparation and presentation of applications**
  - GM plants and derived food and feed
  - GM microorganisms for food and feed use

'Living' documents, updated whenever needed

- **To provide scientific advice**

- **To initiate 'self-tasks'** (own initiatives)

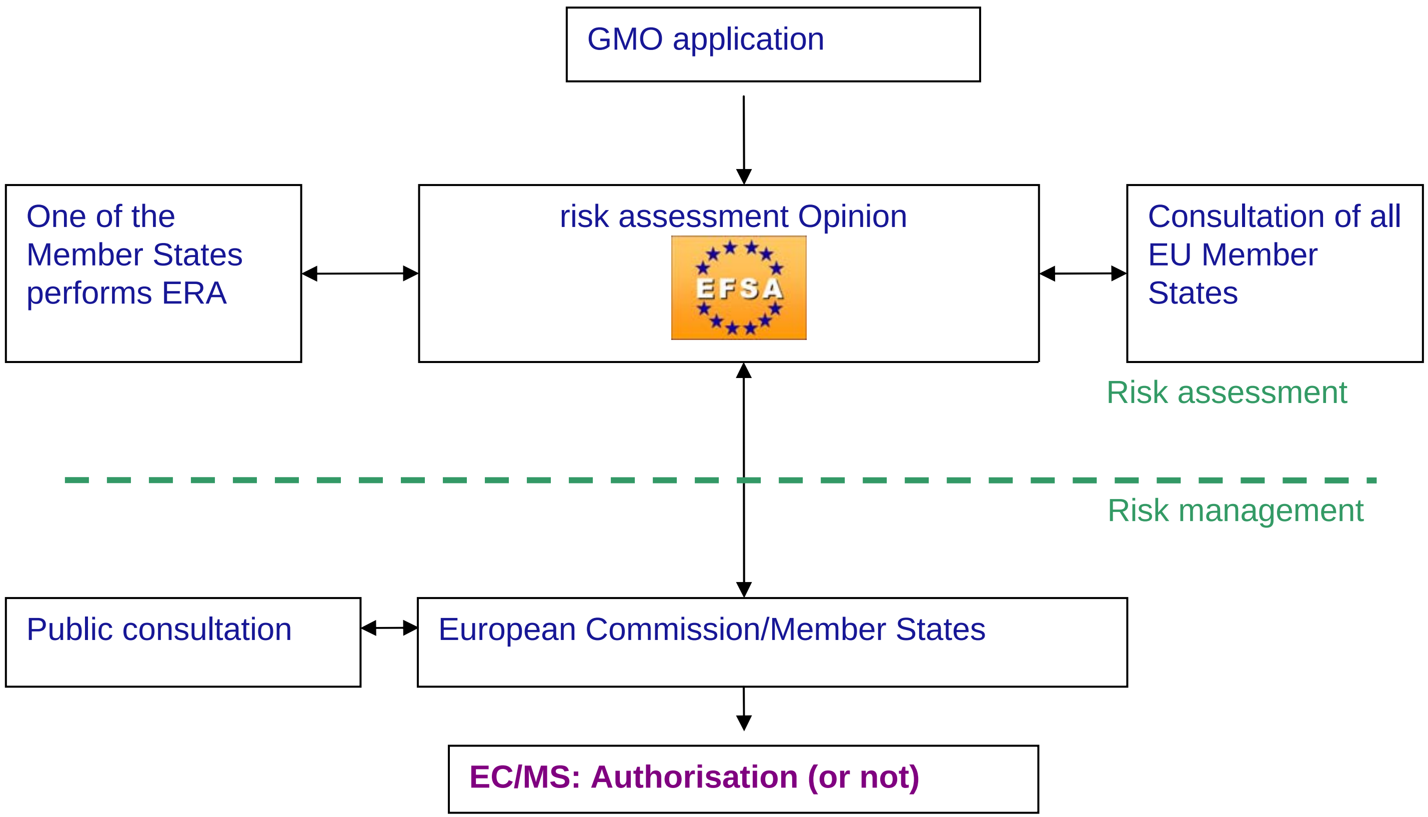
Directive 2001/18/EC on the deliberate release into the environment of GM organisms

- ***Case by case*** **environmental risk assessment prior to any release**
- **Introduction of GMOs in the environment follows a ‘ step by step’ procedure**
- **Establish common methodology to carry out the environmental risk assessment**
- **Assessment of potential cumulative long-term effects**
- **Mandatory post-market environmental monitoring**
- **Initial assessment by rapporteur Member State**
- **Consultation of EFSA in case of diverging opinions MS**

Regulation (EC) 1829/2003 on GM Food and Feed

- **Scope:**
  - GMOs for food and feed use
  - Food/feed consisting or containing GMOs
  - Food/feed produced from GMOs
- Risk assessment under responsibility of EFSA (Consultation Member States)
- Post-market monitoring of GM food or feed where appropriate
- Methods for sampling, identification and detection of GM food and feed to be provided by the applicant
- Detection methods validated by the Community Reference Laboratory

Regulation (EC) 1829/2003 - GM food & feed



EFSA GM Plant Guidance

- Guidance for the risk assessment of GM plants and derived food and feed in accordance with EU legislation
  - Written consultation + stakeholder consultation meeting
- Guidance on Post Market Environmental Monitoring
  - 3 consultation workshops on Post Market Environmental Monitoring
- Guidance for the renewal of existing products
  - Written consultation

Objective

- **To provide a general concept of risk assessment of GMOs**
  - Requirements for food/feed safety assessment
  - Requirements for environmental risk assessment
  - Outline an Environmental Monitoring Plan

- **Guidance document is not a protocol for carrying out specific analytical, toxicological and nutritional testing or feed trials**

Key elements in the assessment of GMOs

European Food Safety Authority

- **Characterization of donor and host organism**
- **Molecular characterization of the genetic modification event**
- **Analysis of agronomical and compositional properties**
- **Specific toxicity / allergenicity / nutritional testing**
- **Post-market monitoring**
- **Environmental risk assessment**
- **Post-market environmental monitoring**

Safety Assessment Strategy for GM Crops: Two-step Procedure

1. **Identification of differences between the GM and non-GM crop: intended and unintended changes**

2. **Assessment of the environmental and/or food/feed safety and nutritional impact of identified differences**

   – ***Concept of Familiarity***
   – ***Comparative Safety Assessment***

Comparative safety assessment approach

- **Underlying assumption:**
  - **Traditionally cultivated crops have gained a history of generally accepted use (environment/ consumer/ animals)**
  - **These crops can therefore serve as a *baseline* for the environmental and food/feed safety assessment of GM crops**

Comprehensive approach

- **Case-by-case assessment**
- **The available evidence determines the extent of specific testing (tiered approach, feeding trials yes/no)**
- **All the available information should be taken into account**

Environmental Risk Assessment

- Mechanism of interaction between the GM plant and target organisms (if applicable).
- Potential changes in the interactions of the GM plant with the biotic environment resulting from the genetic modification
- Persistence and invasiveness
- Selective advantage or disadvantage
- Potential for gene transfer
- Interactions between the GM plant and target organisms
- Interactions of the GM plant with non-target organisms

Environmental Risk Assessment (2)

European Food Safety Authority

- Effects on biogeochemical processes.
- Impacts of the specific cultivation, management and harvesting techniques
- Potential interactions with the abiotic environment
- Mechanism of interaction between the GM plant and target organisms (if applicable)
- Environmental Monitoring Plan

‘Self task’ activities to address scientific concern

European Food Safety Authority

- Biosafety of antibiotic resistance marker genes
- Post-market environmental monitoring of GM crops (general surveillance)
- The use of animal feeding trials for the safety evaluation of whole GM foods/feed
- Improve the approaches for allergenicity assessment of GMOs
- Statistical considerations for the safety evaluation of GMOs

Cooperation with MS (Art 36)

- **Nominated institutions within Member States**

- **In area of GMO risk assessment:**
  - **Study on safety of Cry proteins**
  - **Herbicide tolerant plants**
  - **Guidance on GM animals**

GMO Consultations

European Food Safety Authority

- Broad public and Member State consultation before adoption of opinions relating to risk assessment approaches and guidance documents
  - Stakeholders (applicants, NGOs, ...)
  - Risk assessors from MS
  - Academia (highly welcomed)

Grazie

Looking forward to a fruitful colloquium

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Economic Affairs DEA
Agroscope Reckenholz-Tänikon Research Station ART

Non-target arthropod risk assessment of insect-resistant GM crops

Jörg Romeis *et al.*

EFSA Scientific Colloquium 8
Environmental Risk Assessment of Genetically Modified Plants – Challenges & Approaches
20-21 June 2007, Tabiano, Italy

An activity organized by the IOBC/WPRS working group
GMOs in Integrated Plant Production

IOBC
International **O**rganisation for **B**iological and Integrated **C**ontrol of Noxious Animals and Plants

IOBC
OILB

http://www.iobc-wprs.org/

Participating scientists

Detlef Bartsch, Franz Bigler, Marco P. Candolfi, Marco M.C. Gielkens, Susan E. Hartley, Richard L. Hellmich, Joseph E. Huesing, Paul C. Jepson, Raymond Layton, Hector Quemada, Alan Raybould, Jörg Romeis, Robyn I. Rose, Joachim Schiemann, Mark K. Sears, Anthony M. Shelton, Jeremy Sweet, Zigfridas Vaituzis, Jeffrey D. Wolt

IOBC
OILB

Objective

To develop a **scientifically-sound**, **generic**, and **pragmatic** approach to assessing the risks of **insecticidal transgenic crops** to non-target organisms, with emphasis on **terrestrial arthropods**, that **meets the needs of environmental decision makers**

Background

Application of the **‚tiered approach‘**

- accepted internationally within regulatory toxicology and environmental sciences
- versions of which are already in use in established and effective regulatory systems for GM crops

US EPA /USDA-Aphis White Paper

http://www.epa.gov/pesticides/biopesticides/pips/non-target-arthropods.pdf

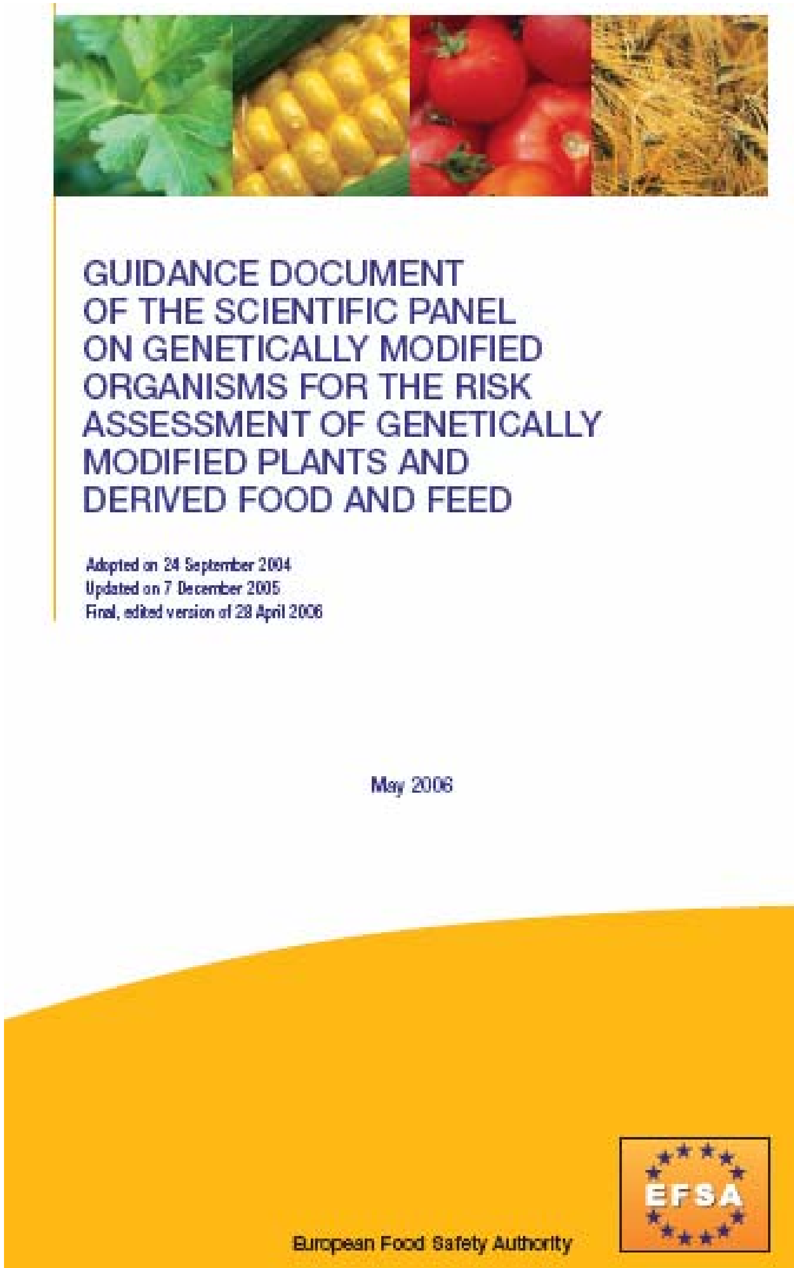
Garcia-Alonso et al. (2006)

Environmental Biosafety Research 5, 57-65

Background

EFSA GMO Panel suggests application of

- Tiered approach to risk assessment
- Comparative approach
  - concept of ‚familiarity‘
  - concept of ‚substantial equivalence‘


GUIDANCE DOCUMENT OF THE SCIENTIFIC PANEL ON GENETICALLY MODIFIED ORGANISMS FOR THE RISK ASSESSMENT OF GENETICALLY MODIFIED PLANTS AND DERIVED FOOD AND FEED

Adopted on 24 September 2004
Updated on 7 December 2005
Final, edited version of 28 April 2006

May 2006

European Food Safety Authority

EFSA

Involvement of scientists from diverse institutions

- Public research institutes
- Agricultural biotechnology industry
- Regulatory agencies
- Commercial testing laboratory

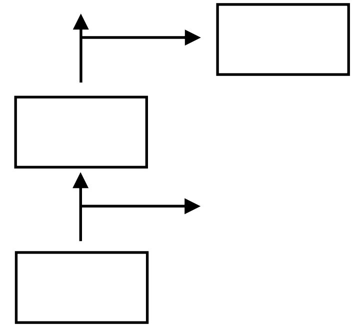
The group has experience in the application of the tiered risk assessment from a research and regulatory perspective

Subgroups - Topics

Problem formulation

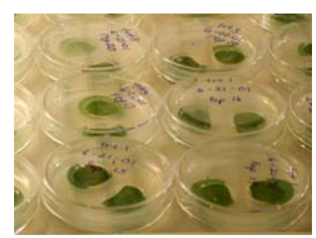
?

Framework



Species selection

Study design



Conceptual risk assessment framework

Predictable pathway for requesting, acquiring, organizing and evaluating data

- **Evaluation of need**
- **Problem formulation** (construct hypotheses)
- **Hypothesis testing** (existing and new data)
- **Overall risk assessment**
- **Risk management and communication**

Problem Formulation

I. Defines **scope of the risk assessment**

- Identifies **assessment endpoints** reflecting **management goals** (protection goals, policy)
- Generates relevant **risk hypotheses** concerning the likelihood of unacceptable harmful events (changes to assessment endpoints)
- Identifies **data requirements** (data to provide powerful tests of the risk hypotheses)

Problem Formulation

II. Considers **precursor information**

identify meaningful differences between the GM plant and its non-transformed comparators besides the introduced trait

Crop/plant characterization

Agronomic/ morphological characterization

- Dormancy
- Growth
- Reproduction
- Seed dispersal
- Volunteer potential
- Insect-, disease-plant interactions
- …

Compositional analysis

- Macro- and micronutrients
- Toxicants
- Anti-nutrients
- …

Problem Formulation

II. Considers **precursor information**

identify meaningful differences between the GM plant and its non-transformed comparators besides the introduced trait

- ► if **No**, the remaining ERA is focused on the expressed trait as stressor (insecticidal protein)
- ► if **Yes,** then the novel or different characters of the plant become additional stressors that also need to be evaluated

Stressor characterization

- Expression profile (time, tissue, level, etc.)
- Agronomic practice (location, timing, area, etc.)

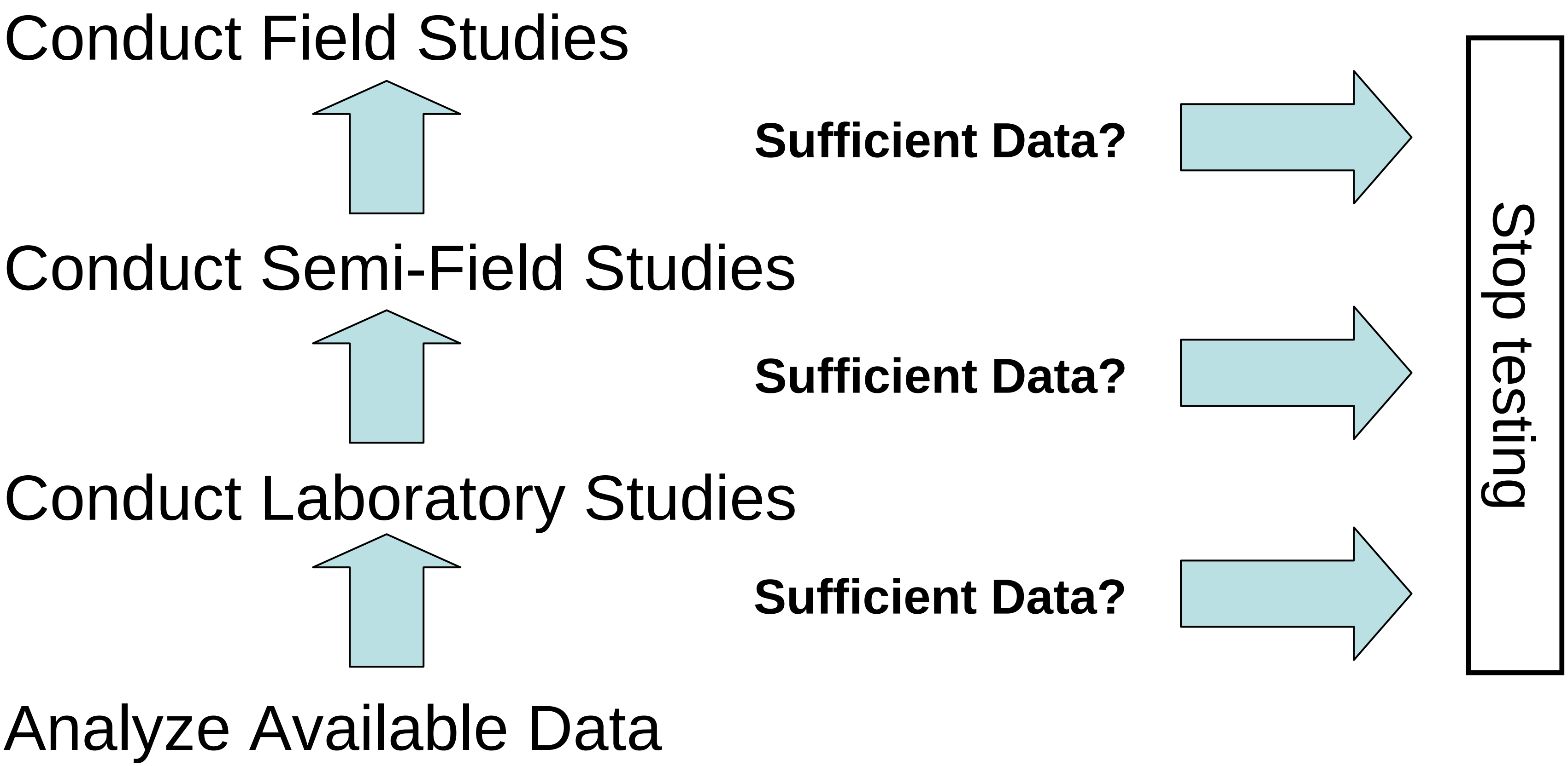
➡ **Identifies NTOs likely to be exposed**

- Mode of action
- Spectrum of activity against pests (or NTOs)

➡ **Identifies NTOs likely to be sensitive**

➢ **Guides risk assessment and testing requirements**

Properties of the framework (how to test)



Move through the framework to acquire sufficient data to make a regulatory decision

How to move within the framework

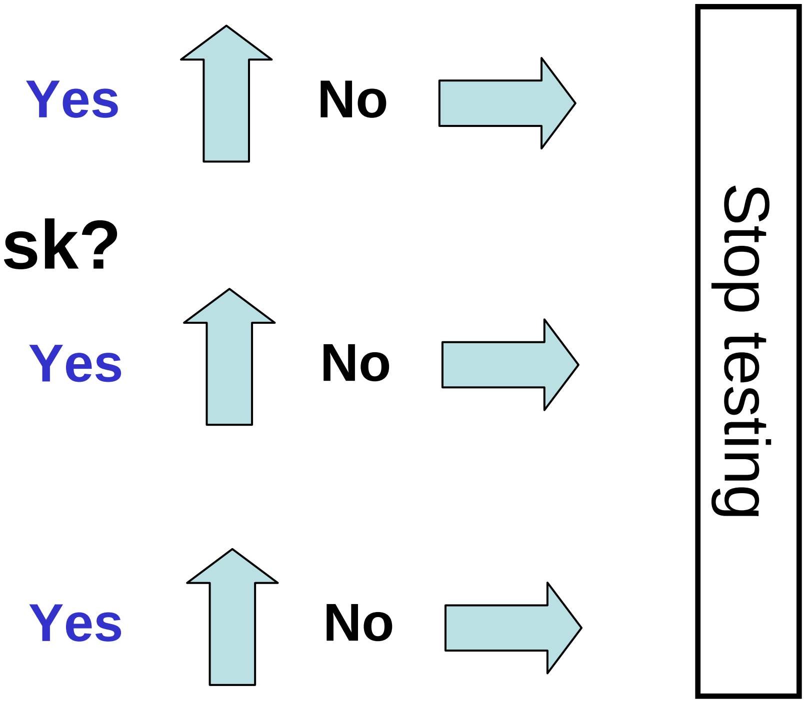
Is there <u>really</u> a risk?

Does the hazard pose a risk?

Is there a hazard?

Is there conceivable risk?

(Potential hazard <u>and</u> exposure)



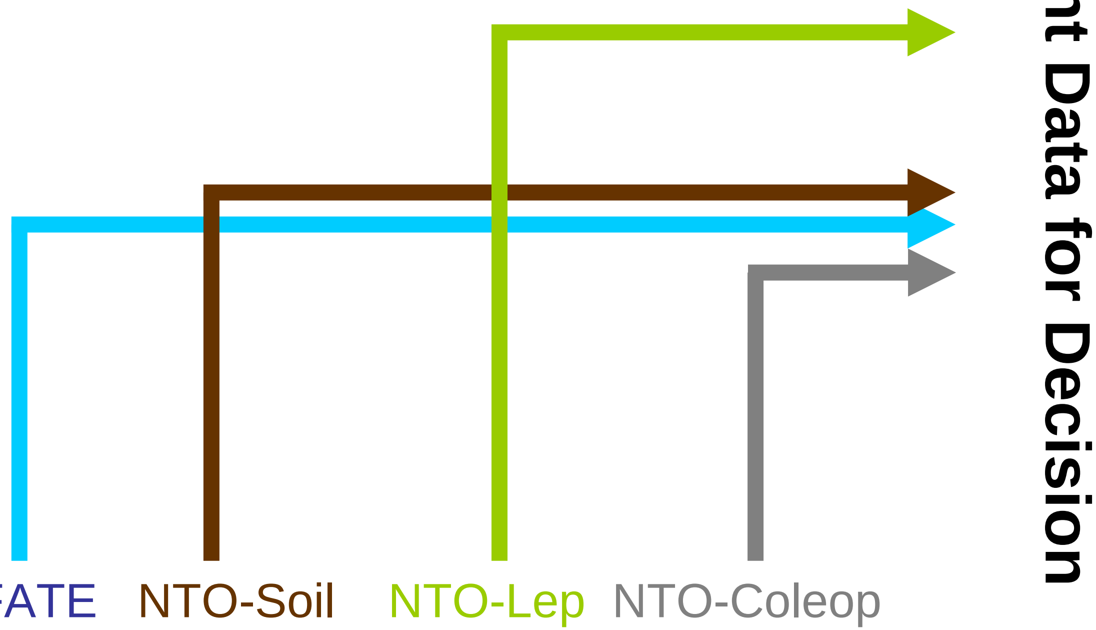
Example framework

Field Studies

Semi-Field Studies

Laboratory Studies

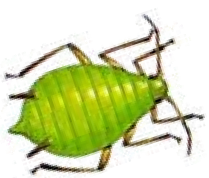
Previous Data

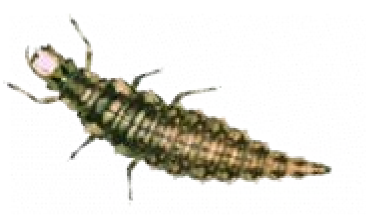


Not all hypotheses require the same testing

Species selection

Select **appropriate** species to serve as **surrogates** for ecologically and economically important non-target organisms **that can be tested** to provide **relevant data** at **proportionate costs** in the laboratory.





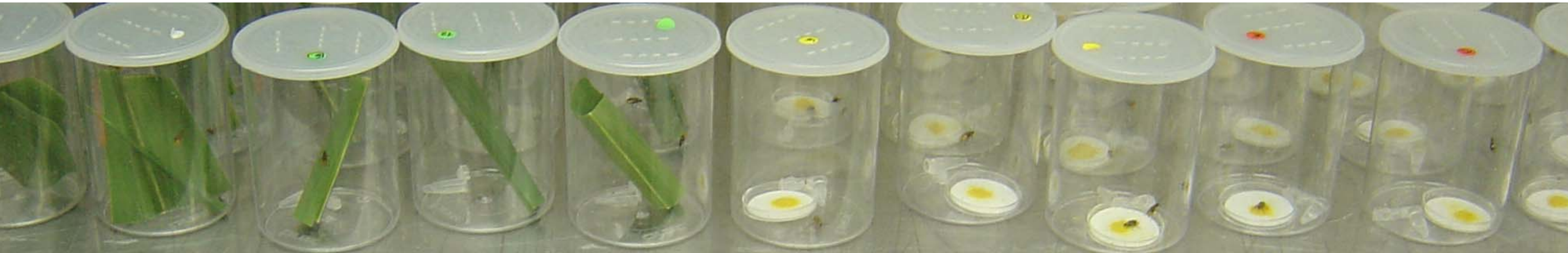
Species selection - criteria

- Representation of different **ecological functions**
- Representation of the receiving **environment**
- Information about the **stressor** (specificity, exposure profile)
- **Amenability** for testing
- **Availability** of test methods
- **Taxonomic recognition**
- **Anthropocentric values**

Adoption of the surrogate species concept

Study design – general requirements

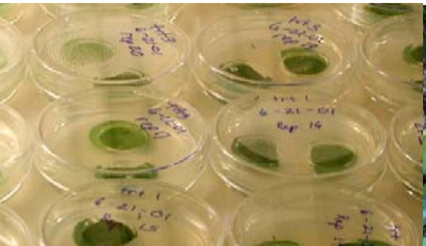
- Purpose and **objectives** of the study clearly defined (directed by problem formulation)
- Study must provide data that are **interpretable** and can be related to an assessment endpoint
- Study results should assist decision-making by **reducing uncertainty** in the risk assessment



Higher tier testing

Conduct only when they

- **Reduce uncertainty** in the risk assessment
- **Are justified** by detection of unacceptable risks at lower tiers of testing
- When early tier studies are not possible
- Can be performed under conditions and rigour necessary to produce interpretable results




Study design – considerations

(i) Specific measurement endpoints

- Depend on purpose of study
- Should be related to assessment endpoints

(ii) Life-stage to be tested

Selection criteria

- Level of likely exposure (e.g., adult *vs.* larva)
- Sensitivity to the insecticidal compound
- Amenability to testing („validated“ test system)

Study design – considerations

(iii) Availability of test protocols

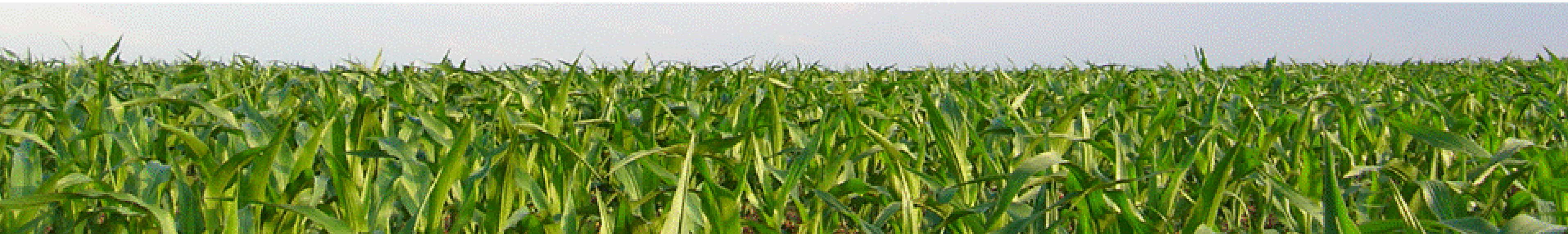
- modified to account for
  - oral exposure pathways
  - mode of action of insecticidal proteins

(iv) Test validation (quality control standards)

- Assures repeatability, interpretability and quality of the study
- GLP standards recommended / mandatory
- Need for complete study/ data reconstruction

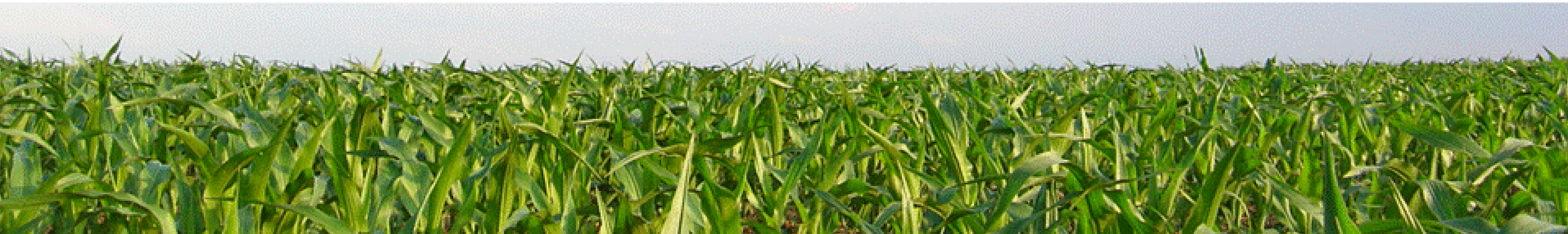
Conclusions (I)

- Tiered evaluation of potential hazards with representative surrogate species provides a **rigorous and effective** basis for characterizing risk
- It thus minimizes the likelihood of false negatives which could result in the release of hazardous insect-resistant GM plants



Conclusions (II)

- The tiered approach ensures testing of clearly stated relevant hypotheses
- It thereby minimizes collection of data that are irrelevant to the risk assessment
- Decisions about acceptable risk can be made in a reasonable period of time



For details see

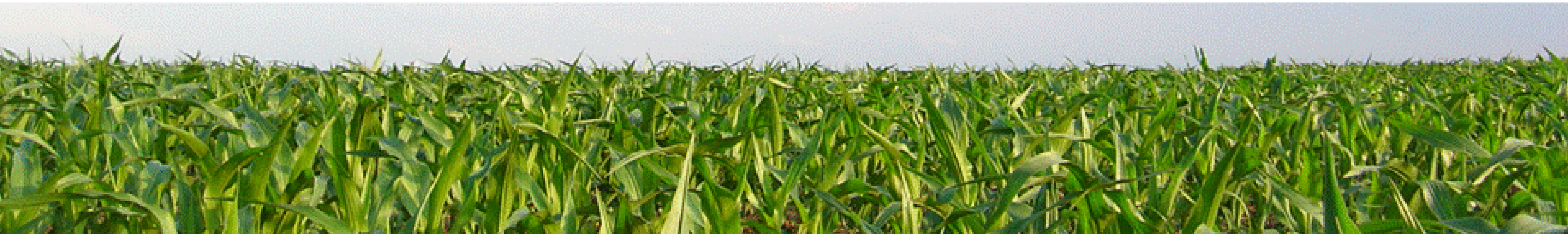
Romeis J, Bartsch D, Bigler F, Candolfi MP, Gielkens MMC, Hartley SE, Hellmich RL, Huesing JE, Jepson PC, Layton R, Quemada H, Raybould A, Rose RI, Schiemann J, Sears MK, Shelton AM, Sweet J, Vaituzis Z, Wolt JD (2006)

Moving through the tiered and methodological framework for non-target arthropod risk assessment of transgenic insecticidal crops.

Proceedings of the 9th International Symposium on the Biosafety of Genetically Modified Organisms, 24-29 September 2006, Jeju Island, South Korea, pp. 62-67.

http://www.isbr.info/symposia/

Contact: joerg.romeis@art.admin.ch



European Food Safety Authority

Colloquium 8

Environmental Risk Assessment of Genetically Modified Plants: Future Challenges

20 -21 June 2007, Tabiano, Italy

Jeremy Sweet : Vice Chairman EFSA GMO Panel

BACKGROUND

- ENVIRONMENTAL RISK ASSESSMENT is an evolving science
- ERA is only as good as current knowledge and experience
- ERA Methods based on experience of applying scientific methods
- **>>Always scope for improvement**

Objectives

- Review Environmental Risk Assessment :
  Approaches and Methods
- How do we examine the effects on different Biota at both species and population levels ?
- Do we focus too much on effects on organisms and not enough on impacts on receiving environments ?
- How do we anticipate effects of long term, large scale cultivation of multiple GM crops in changing agricultural environments (due to economic, political other considerations) ?

OBJECTIVES

- Open scientific meeting
- Brain storming
- Your ideas
- Think outside the box (no bars or constraints)
- Individual comments not reported
- No media, press etc…

Focus of Colloqium : 1

- Testing Effects on Non-Target organisms: Approaches and Methods:
- Talks:
  - Joerg Romeis
  - Gabor Lovei
- Working Group :
  - Chairman: Jozef Kiss
  - Rapporteur: Guy Poppy

Focus of Colloqium: 2

- Upscaling : Objectives, Approaches, Methods ….
- Talk: Frederique Angevin
- Working Group :
  - Chairman: Joe Perry
  - Rapporteur: Salvatore Arpaia

Focus of Colloqium: 3

- **Long Term Effects : Objectives, Approaches, Methods……**
- **Talk: Peter van Tienderen**
- **Working Group :**
  - Chairman: Detlef Bartsch
  - Rapporteur: Simon Butler

Focus of Colloqium: 4

- **Broadening the Scope of ERA:** Biodiversity effects, Life cycle analysis, Risk benefit analysis ……….
- **Talk : Chris Pollock**
- **Working Group:**
  - Chairman: Joachim Schiemann
  - Rapporteur: Rosie Hails

Environmental RISK Assessment Colloquium

~ Plenary Presentations

~ Working Groups

~ Rapporteur Reports : Messages to EFSA on scope for developing ERA methods or approaches.

>> Establish EFSA Self tasking/Working group activities …. ?

~ EFSA publication of Proceedings of Colloqium

~ Review Paper in Scientific Journal ?

Predicting the long term effects of GM crops

Peter van Tienderen

How to put risks in the right perspective..

Why?

GMO applicants are obliged to provide adequate data to allow the assessment of the potential long-term adverse effects on both the human/animal health and environmental aspects of a GMO as part of their application, as described in the EFSA Guidance Document.

Types of (slow) processes in plant populations

1. Accumulation of (known) small effects (or chances) in time

2. New events that may occur (much) later

1. Accumulation of (known) small effects in time

- *Population dynamics (e.g. Lotka-Volterra)*
- *Selection*
- *Drift*
- *Metapopulation dynamics*

Back Search Favorites

Address http://fisher.forestry.uga.edu/popdyn/index.html

Population Dynamics in Java

Site Index

- Introduction
- Density Independence
- Density Dependence
- Age-Structured Population Growth
- Binomial Sampling
- Likelihood Function
- Statistical Power
- Lotka-Volterra Competition
- Lotka-Volterra Predation
- Maximum Sustained Yield
- Harvest Compensation
- Diploid Selection
- Genetic Drift

Welcome to *Population Dynamics in Java*. This site contains applets programmed in Java from Sun Microsystems. Viewing these applets requires the appropriate Java Runtime Environment (JRE). If you are using Netscape or Mozilla, no additional software is required; it contains the most current Java plug-in. Otherwise, please download the JRE appropriate to your system.

We hope find this site useful. Please send comments and questions to Dr. Chris Fonnesbeck.

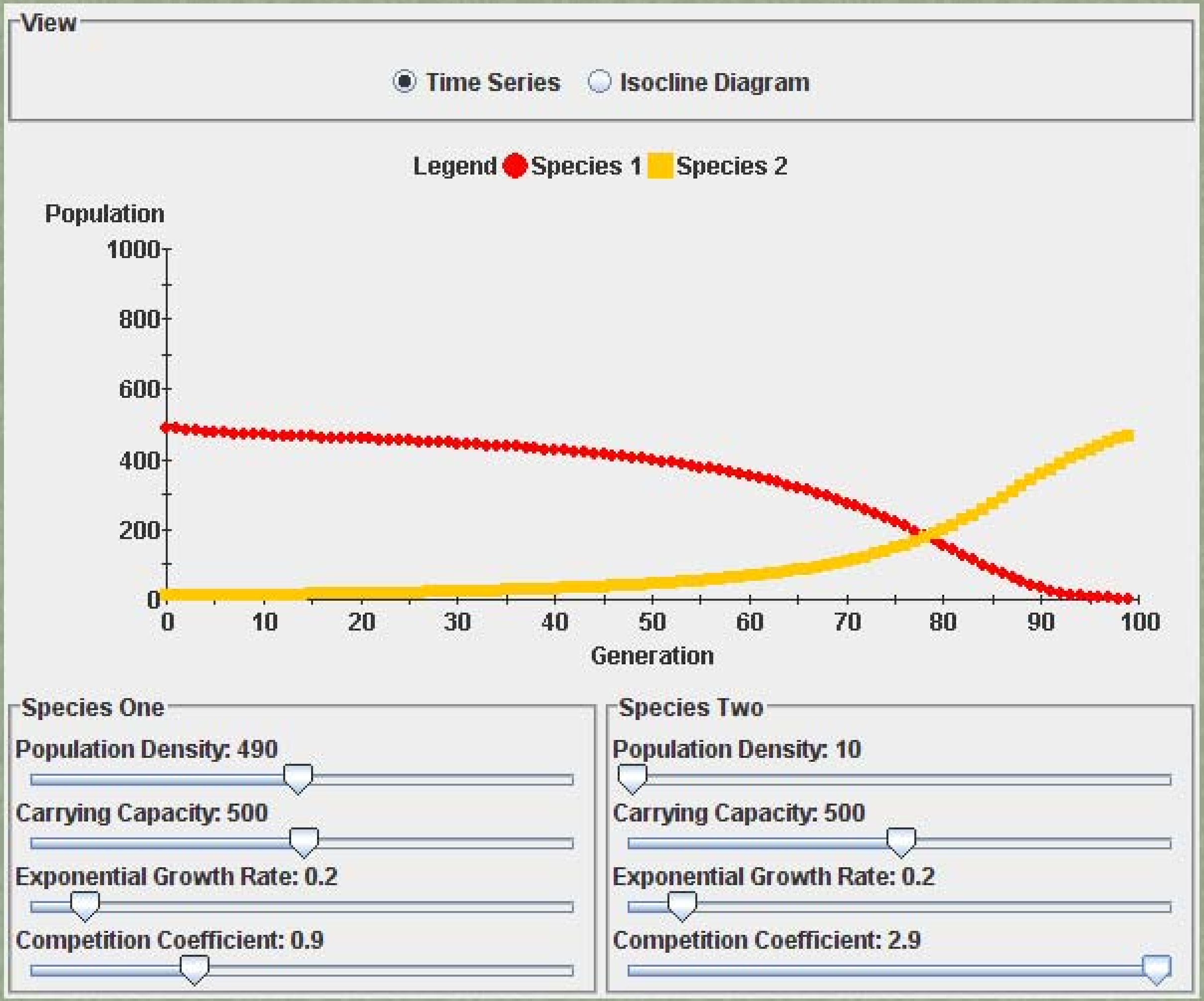
JAVA

by specie 2.

$$dN_1/dt = r_1 * N_1 ((K_1 - N_1 - (a * N_2)) / K_1)$$

We can then do the same for species 2

$$dN_2/dt = r_2 * N_2 (K_2 - N_2 - (b * N_1)) / K_2)$$



Diploid Selection - Microsoft Internet Explorer

File Edit View Favorites Tools Help

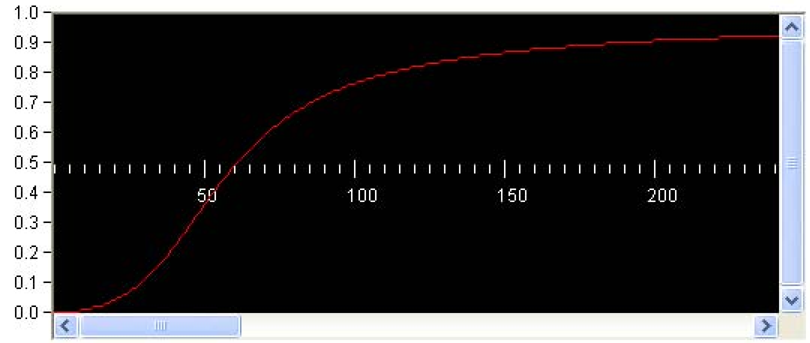
Back Search Favorites

Address http://fisher.forestry.uga.edu/popdyn/DiploidSelection.html Go Links

Site Index

- Introduction
- Density Independence
- Density Dependence
- Age-Structured Population Growth
- Binomial Sampling
- Likelihood Function
- Statistical Power
- Lotka-Volterra Competition
- Lotka-Volterra Predation
- Maximum Sustained Yield
- Harvest Compensation
- Diploid Selection
- Genetic Drift

Diploid Selection



W(AA) 1.1 — 0 0.250 5.0

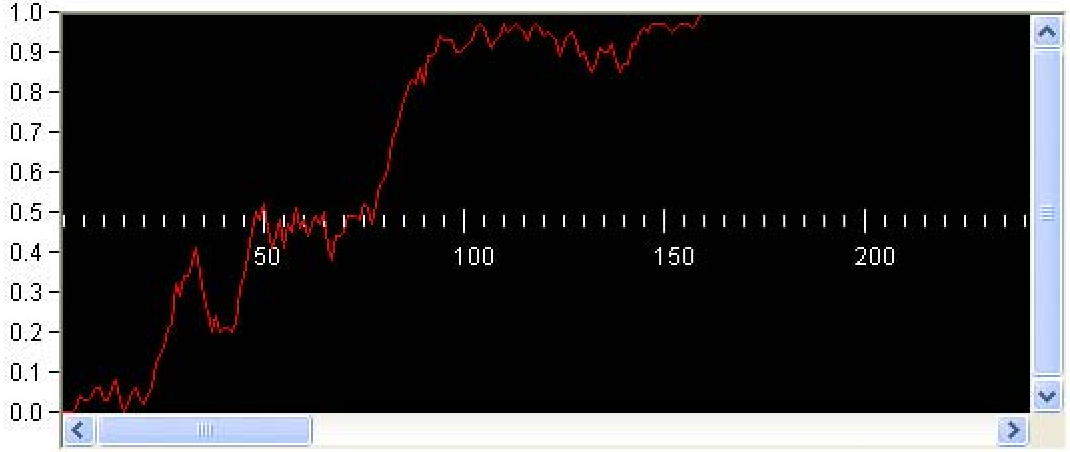
W(Aa) 1.1 — 0 0.250 5.0

W(aa) 1.00 — 0 0.250 5.0

Initial p(A): 0.01 — 0 0.50 1.0

Frequency stabilizes at 0.9880269

Genetic Drift

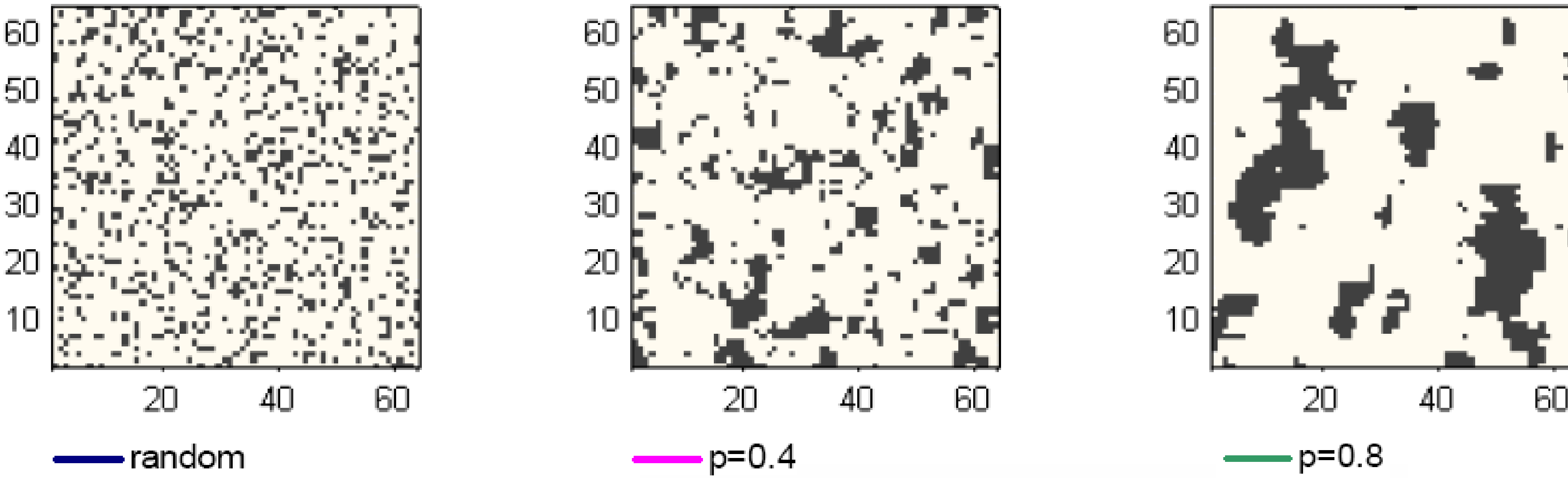


2N 500 (0 — 50 — 100)

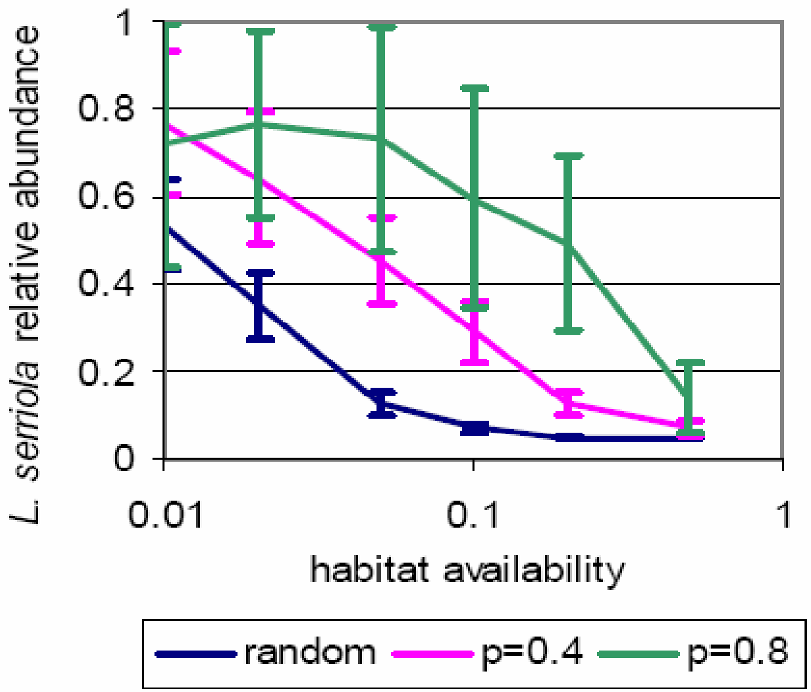
p(A) 0.01 (0 — 0.50 — 1.0)

Run model

Fixation occurs at generation 158



Percent 'wild' remaining after 100 generations



J. Kummer, MSc project

1. Accumulation of (known) small effects in time

- *Population dynamics (e.g. Lotka-Volterra)*
- *Selection*
- *Drift*
- *Metapopulation dynamics*

Sometimes easier to look for differences and extrapolate (model) than to wait for changes to occur

Requires knowledge, models, and experimental protocols for screening

2. New events that may occur (much) later

Changes during the hybridisation process

- *Linkage drag, heterosis, genetic background, transgressive phenotypes, epistatic effects*
- *Compensatory mutations*
- *Breaking of containment / silencing*
- *Results due to stacking*
- *….*

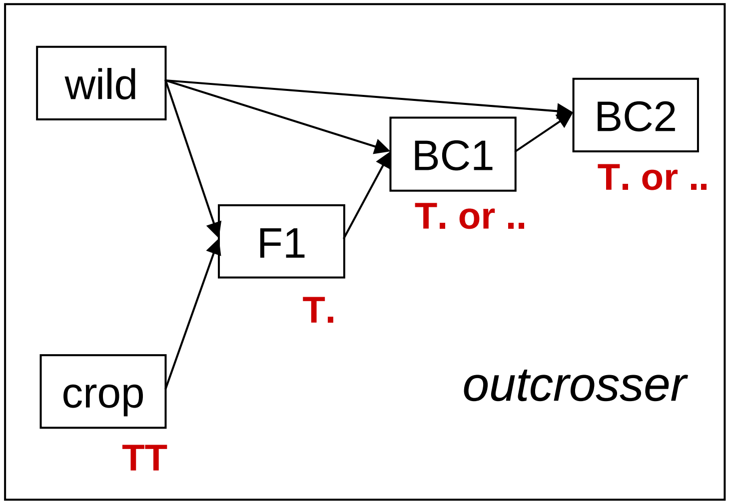
Later changes in ecology

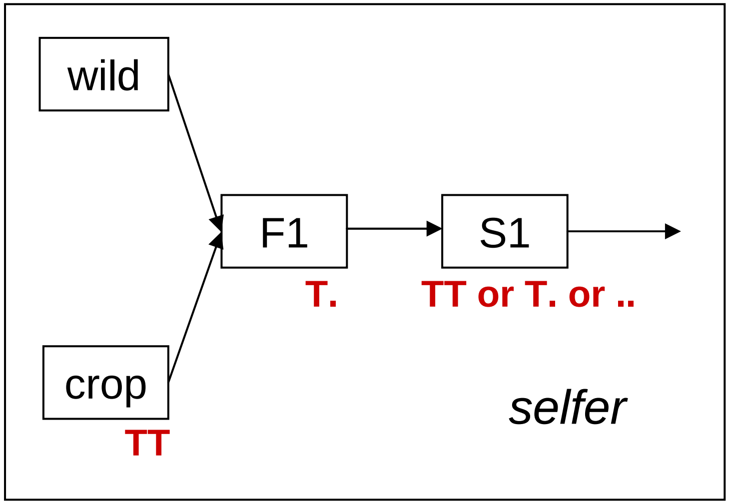
- *Invasiveness, range expansion (e.g. stress related)*
- *In response to external (e.g. climatic) changes*

Introgression of genes into wild relatives

Barriers for transgenes:

- Escape from GM crop
- Escape from first generation hybrid
- Fitness of later generations





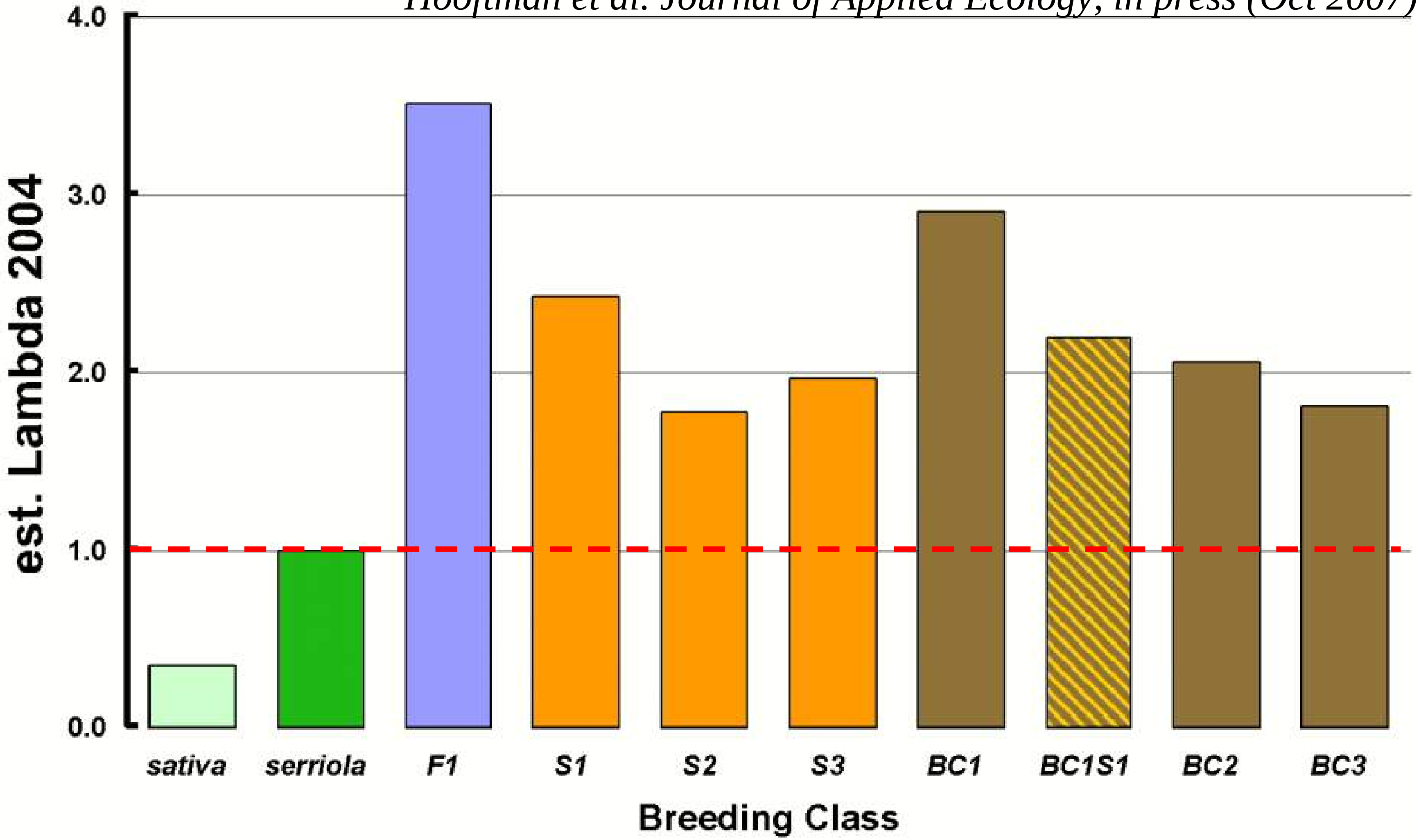
T: transgene

Wild and cultivated lettuce

L. serriola *L. serriola x L. sativa* *Lactuca sativa*

Fitness per breeding class

Hooftman et al. Journal of Applied Ecology, in press (Oct 2007)



2. New events that may occur (much) later

Changes during the hybridization process

Changes in ecology

Are very difficult to predict, require ‘what if’ scenarios
Require species / crop / wild specific information

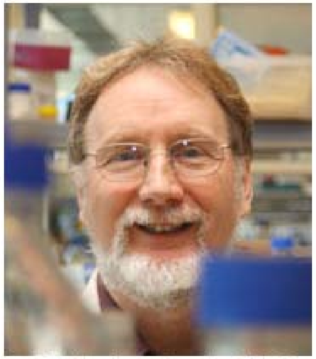
Benefits of the case-by-case, step-by-step approach

- Precautionary principle

- Monitoring

Media Release

GM pea study backs case-by-case risk assessment


Dr TJ Higgins, Deputy Chief of CSIRO Plant Industry

Reference: 05/212

Research by CSIRO to genetically modify peas to resist insect attack and reduce the use of chemical sprays has been discontinued because the GM peas did not satisfy all categories of a stringent risk assessment process.

17 November 2005

The Deputy Chief of CSIRO Plant Industry, Dr TJ Higgins, says the findings – published this week in the Journal of Agricultural and Food Chemistry – demonstrate the effectiveness of case-by-case evaluation of GM plants and the important role science can play in decision-making around the introduction of GM crops.

The GM field peas were developed by CSIRO Plant Industry to protect Australia's $100 million field pea industry from the pea weevil Bruchus pisorum, which can cause yield losses of up to 30 per cent each year if left uncontrolled.

Although this GM breed of field pea proved almost 100 per cent effective against pea weevil attacks, research led by immunologists Dr Simon Hogan and Professor Paul Foster at the John Curtin School of Medical Research (JCSMR), with CSIRO, showed that the GM peas caused an immune response in mice.

Following discussions with the scientists conducting the study, CSIRO decided not to progress development of these GM field peas.

"This work strongly supports the need for case-by-case examination of plants developed using genetic modification and the importance of decision-making based on good science," Dr Higgins says.

"Even though this GM field pea research will not be progressed further, the technology is very valuable and we're considering applying it to other research," he says.

The CSIRO research team used a gene from beans to block the activity of alpha-amylase, an enzyme important for digestion of starch.

Weevil larvae feeding on starch in the developing pea seed are unable to digest the starch and starve.
"We asked why there was a reaction to the GM peas and not beans, which also have the alpha-amylase inhibitor, and which humans have been eating

FAST FACTS

- Genetically Modified (GM) field peas were developed by CSIRO Plant Industry
- Following discussions with the scientists conducting the study, CSIRO decided not to progress development of these GM field peas
- Although this GM breed of field pea proved almost 100 per cent effective against pea weevil attacks, research showed that the GM peas caused an immune response in mice

PRIMARY CONTACTS

Dr TJ Higgins (BAgSc MSc PhD)
Deputy Chief
CSIRO Plant Industry
Phone: 61 2 6246 5037
Fax: 61 2 6246 5062
Email: Tj.Higgins@csiro.au

Prof Paul Foster
Research Center School of Biomedical Sciences Faculty of Health
University of Newcastle
Phone: 61 2 4923 6719
Email: Paul.Foster@newcastle.edu.au

Dr Simon Hogan
University of Cincinnati, USA
Phone: 1 513 636 6620
Email: Simon.Hogan@chmcc.org

RELATED AREAS

- News & Events
- Media Centre
- CSIRO Plant IndustryFarming & Food

Drawbacks of the case-by-case, step-by-step approach

Less attention to develop generic & crop/system specific information

- Who are responsible for this?
- Unclear what applicants should deliver as ‘*adequate data*’
- Wasted energy, slow procedures

Consensus Documents for the Work on Harmonisation of Regulatory Oversight in Biotechnology

send print

"Note: Some of the following documents have an ".ENG" extention. To open files with an ".ENG" extention, save them changing the file extention to ".PDF", then open them using Adobe Acrobat."

These consensus documents comprise technical information for use during the regulatory assessment of products of biotechnology and are intended to be mutually recognised among OECD Member countries. They focus on the biology of organisms (such as plants, trees or micro-organisms) or introduced novel traits.

These documents are updated to take into account new knowledge on the topic. In order to assist in this, it is possible to make comments to the OECD on the Biotechnology Consensus Documents.

At the present time, the following consensus documents have been published:

Consensus Document on the Biology of the Native North American Larches: Subalpine Larch (*Larix Lyalli*), Western Larch (*Larix occidentalis*) and Tamarack (*Larix laricina*)
No. 41, 2007, ENV/JM/MONO(2007)7

Consensus Document on Biology of *Pinus banksiana* (Jack Pine)
No 40, 2006, ENV/JM/MONO(2006)28

Consensus Document on the Biology of Western White Pine (*Pinus Monticola* Dougl.ex D. Don.)
No 38, 2006, ENV/JM/MONO(2006)16

Consensus Document on Information Used in the Assessment of Environmental Applications Involving Acidithiobacillus
No 37, 2006, ENV/JM/MONO(2006)3

Don't miss

- Conference, Workshop
- Documents
- Product Database
- Regulatory Contacts
- Field Trials in Member Countries
- IANB
- Contact Us
- Site Map

OECD Observer

» Article on Unique Identifier, 2004
» Biotechnology: New food for thought, 1999

Newsletter

» OECD Biotechnology Update

Focus on Harmonization of Regulatory Oversight in Biotechnology

Information needed

- Screening protocols
- Ecology of crops, feral populations, and wild relatives
- Specifics of the crop/wild hybridisation process
- Models to assess vulnerabilities
- Potentially dangerous crop-trait combinations
- Back to case-by-case guidelines for E.R.A.

Types of (invasive) processes

- Internally driven
  - *Autonomous, acceleration, positive feedbacks, irreversible*

    Which crops / wild relatives / traits?
    Consequences for E.R.A.?

- External forcing
  - *Influx driven, no/negative feedbacks, reversible*

    Which crops / wild relatives / traits?
    Consequences for E.R.A.?