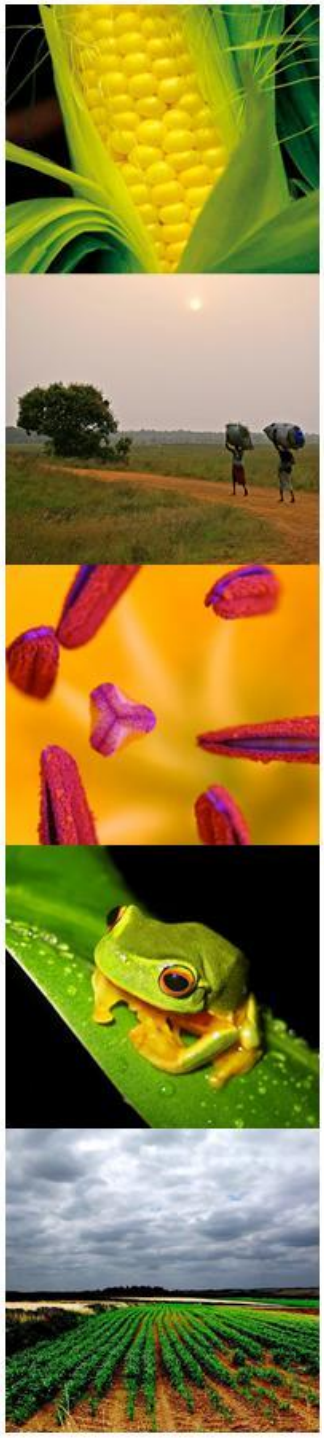

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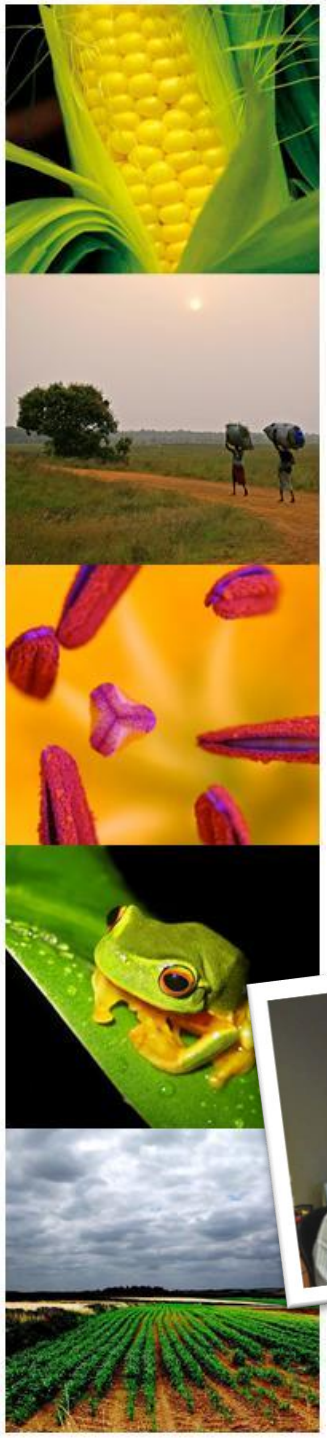
GMO RISK ANALYSIS SHORT COURSE

University of Pretoria, 4 September 2019

science & innovation
Department:
Science and Innovation
REPUBLIC OF SOUTH AFRICA

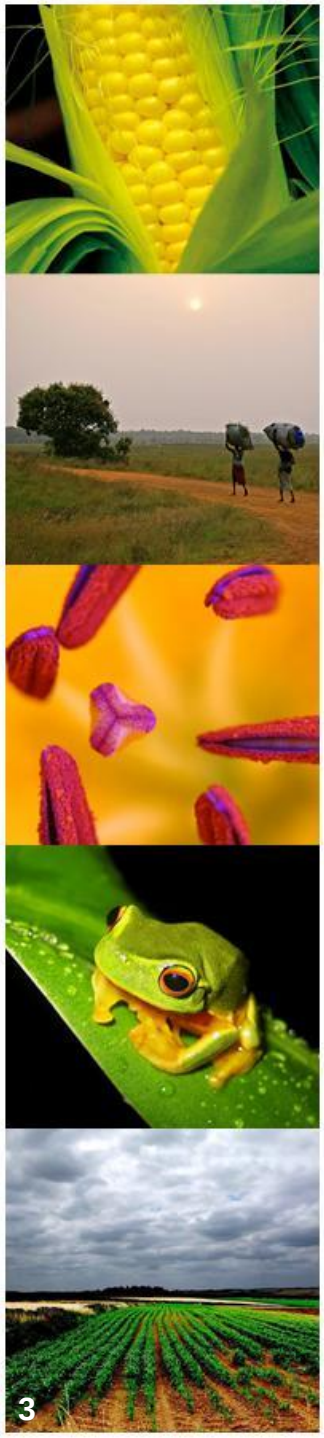
technology innovation AGENCY



Important Risk Analysis Concepts

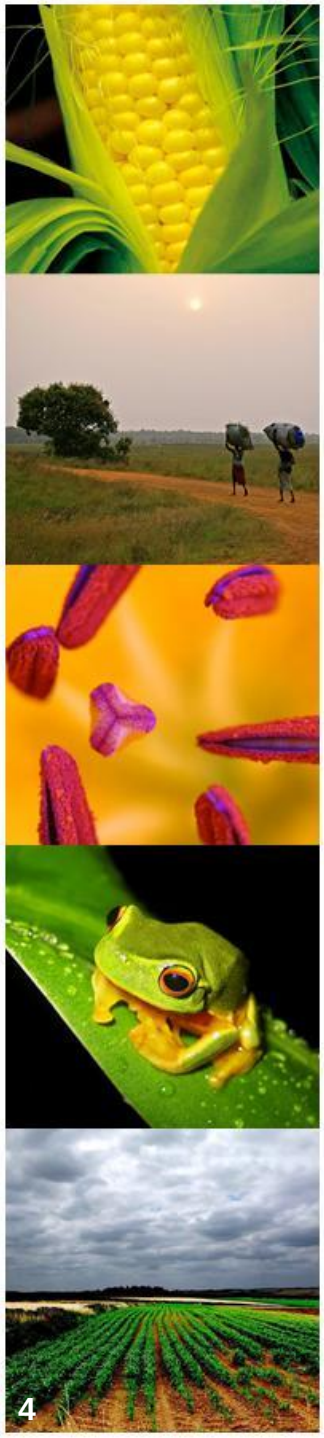
James Rhodes, MSc

Biosafety South Africa, james@biosafety.org.za



OVERVIEW

- Harms
- Hypothesis testing
- Tiered assessments
- Risk management
- Risk thresholds
- Sources of reliable information
- Uncertainty



RISK ANALYSIS OF GMOs: SETTING THE CONTEXT

- The risk assessment cannot proceed until it is clear as to what it is that needs to be protected.

- Management / protection goals can be inferred from policy

  - Assessment endpoints must be defined from these protection goals. These must be an unambiguous expression of the environmental endpoint that must be evaluated

    E.g. of assessment endpoints
    - Population sizes of a species of importance
    - Concentration of certain chemicals in waterways

RISK ANALYSIS OF GMOs: SETTING THE CONTEXT

- The identification of assessment endpoints is a key component in risk analysis
  - Harm would be detected if there is an adverse change to an assessment endpoint
  - The greater this adverse change the greater the harm
  - Harm can incorporate other elements such as the ability to reverse such harm
  - Benefits?
- Risk assessment then tests these assessment endpoints
  - E.g. will cultivation have an adverse effect on the population size of a chosen species of importance

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RISK ANALYSIS OF GMOs: SETTING THE CONTEXT

- must link measurement endpoints with assessment endpoints
- Measurement endpoints are measurable responses related to the assessment endpoint e.g.
    - species richness
    - diversity indices
    - intensity of disease symptoms
    - yield/production

RISK ANALYSIS OF GMOs: SETTING THE CONTEXT

- Nature and type of consequences

GENERIC CRITERIA FOR CONSEQUENCES

e.g.- negative effects on valued organisms (including protected species)

CONSEQUENCE CRITERIA (ASSESSMENT ENDPOINS)

e.g.- reduced population size of a valued lepidopteron

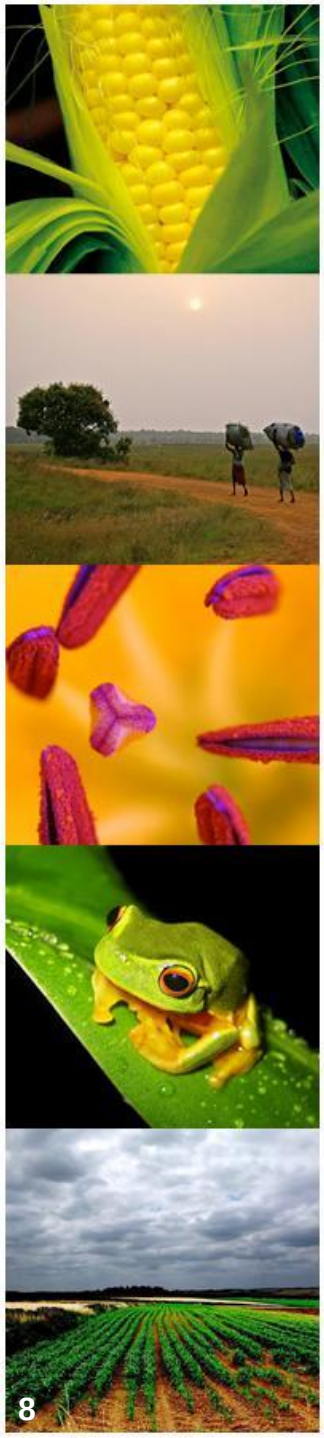
-production of a chemical toxic to protected mammals

MEASURABLE PROPERTIES FOR SPECIFIC CONSEQUENCE CRITERIA (MEASUREMENT ENDPOINTS)

e.g. -population morbidity

-presence and abundance

-biochemical, physiological, physical or development abnormalities

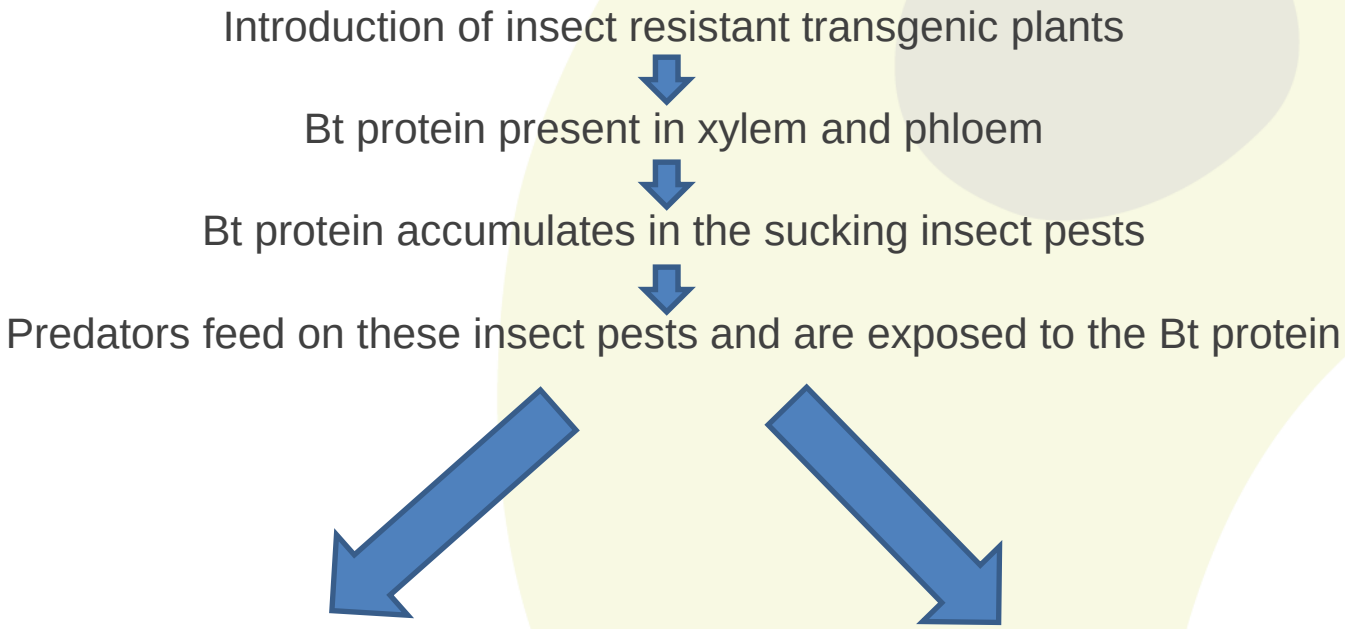


RISK ANALYSIS OF GMOs: RISK ASSESSMENT
PROBLEM FORMULATION/ HYPOTHESIS TESTING

- Problem formulation can be employed to simplify the risk analysis process
  - still allows a rigorous scientific evaluation
  - makes risk analysis more accessible to different stakeholders
- This can be done by hypothesizing a testable chain of events that can lead to harm.
- Use measurement endpoints previously identified to come up with a hypothesis to harm.
- If it is a linear chain falsifying the hypothesis only requires falsifying one link
- If the chain is branched master links can be identified which if falsified would also falsify the risk hypothesis

RISK ANALYSIS OF GMOs: RISK ASSESSMENT
HYPOTHESIS TESTING

Conceptual model



Risk Hypothesis

Exposure to Bt by sucking insect pests leads to the decrease of predator and parasitoid abundances or to sub lethal effects leading to the disruption of synchrony between prey and predators.

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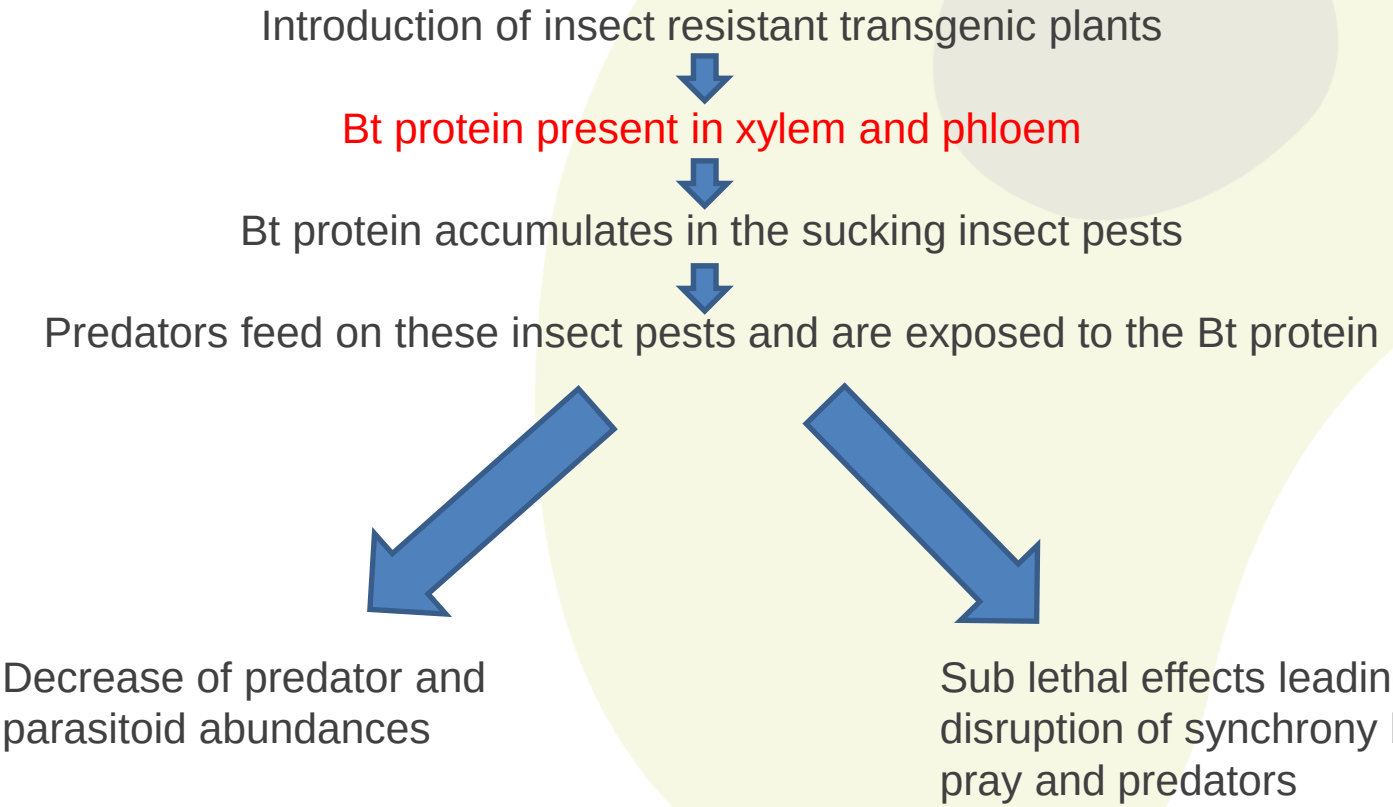
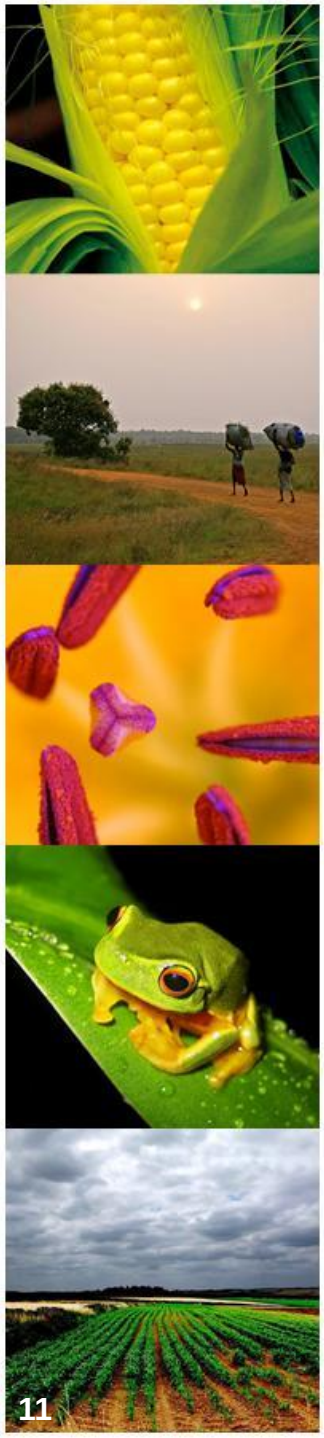
Conceptual model





RISK ANALYSIS OF GMOs: RISK ASSESSMENT
TIERED ASSESSMENT

- Tiered assessment can be used
  - Logical, science-based approach to assessing hazard to non-target organisms
- Early tiers are simple, worst-case exposure scenarios using surrogate species
  - laboratory assays
  - higher control
  - lower realism
- Tests only proceed to higher tiers if lower tier studies show adverse effects and if exposure is probable
- Higher tiers are more realistic, but also more complicated
  - The tiered approach system is cost effective, minimizes environmental risk

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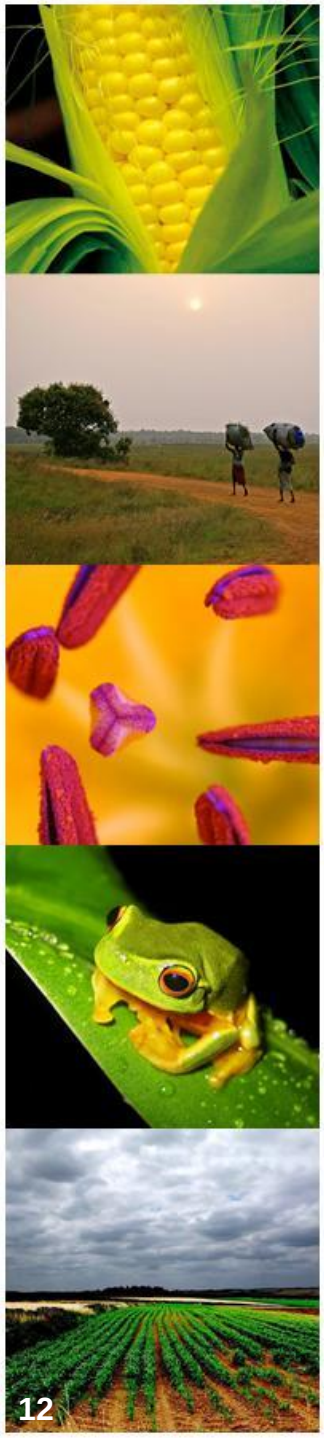
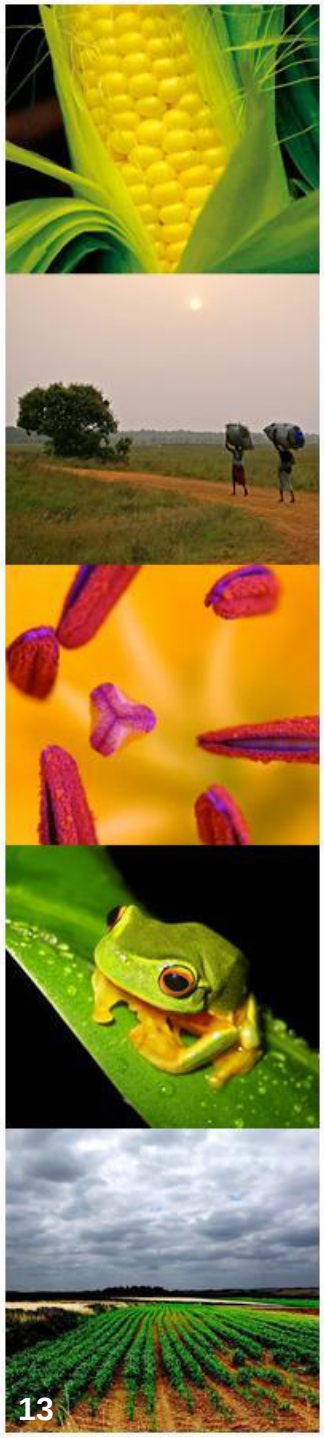


RISK ANALYSIS OF GMOs: RISK DECISION MAKING RISK MANAGEMENT

- Uncertainty is generally highest during early stage development of a GM crop.
  - the risks may not be fully characterised and are managed by reducing the likelihood of risks occurring
  - manage unacceptable consequences e.g. to manage volunteers that may contain a vaccine that may mix with following crops.
  - field trials enable regulators the opportunity to gain familiarity with the crop
  - enables the generation of relevant biosafety data to reduce uncertainties/ characterise risks
    - e.g. efficacy; higher tier field studies
  - this can result in changes in license conditions and feed into evaluations of the same or similar GMOs



RISK ANALYSIS OF GMOs: RISK DECISION MAKING
RISK MANAGEMENT

- Contained use
  - Different physical containment levels (CL1-4/ BL 1-4/ BL1-4-P)
  - Can be applied to all contained use applications (laboratories, screenhouses, greenhouses, pilot plants)
  - Containment levels provide administrative controls, work practices and procedures, equipment and facility features required to achieve a designated level of containment
  - The aim is to prevent propagules from inside the containment area to enter the outside environment

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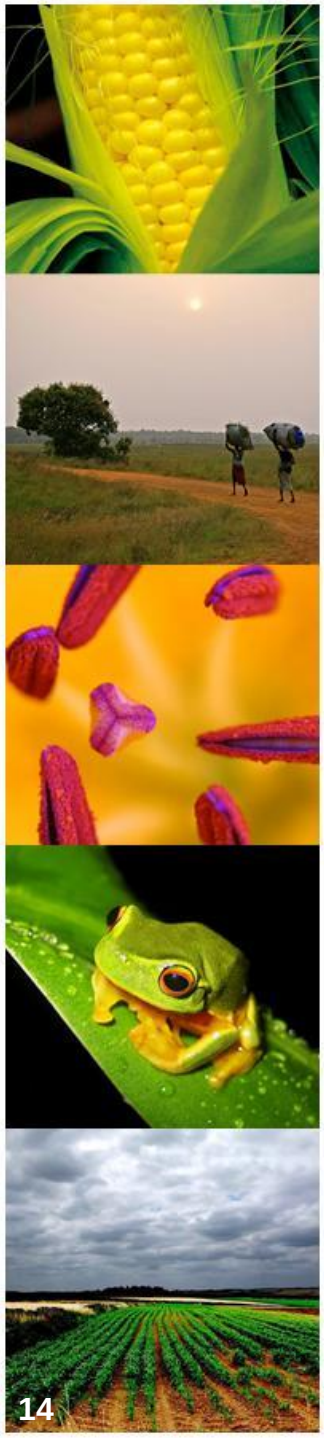
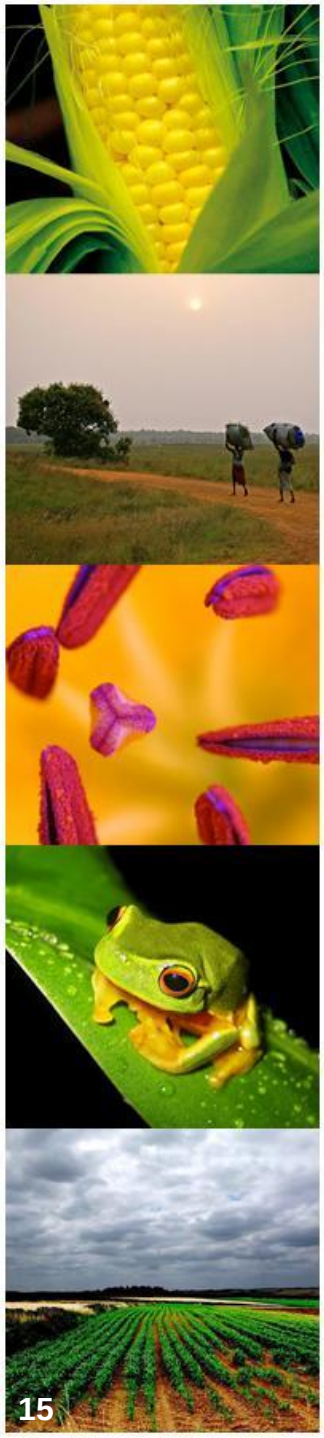


RISK ANALYSIS OF GMOs: RISK DECISION MAKING RISK MANAGEMENT

- Field Trials
  - Controls to restrict gene flow (isolation distances, guard rows)
  - controls to restrict access (fences)
  - limited size, duration and locations
  - not used for human of animal feed



RISK ANALYSIS OF GMOs: RISK DECISION MAKING
RISK MANAGEMENT

GUARD ROWS

ISOLATION DISTANCES

RISK ANALYSIS OF GMOs: RISK DECISION MAKING
RISK MANAGEMENT

CONTROL OF VOLUNTEERS

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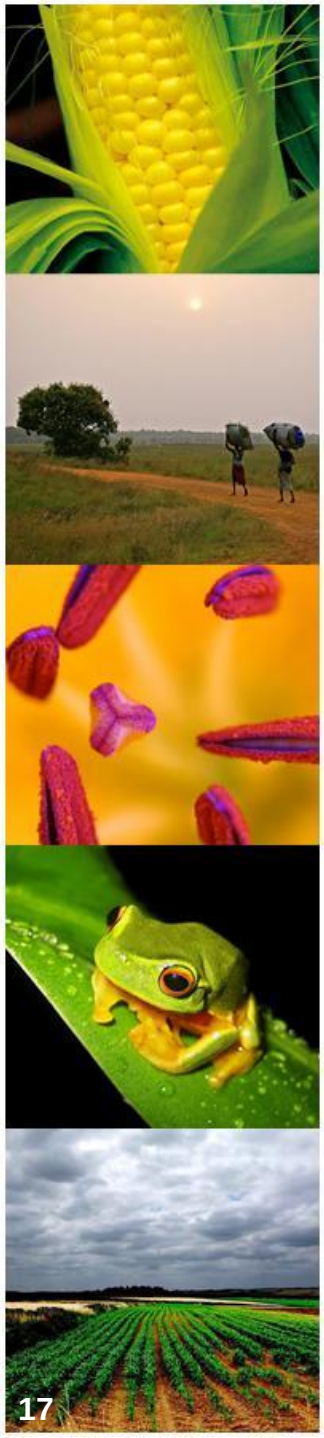

RISK ANALYSIS OF GMOs: RISK DECISION MAKING
RISK MANAGEMENT

- The focus on commercial/ unconfined release is on thorough risk assessment with few or no risk mitigation strategies

- Risk management may be used to
  - decrease the complexity of an ERA e.g. in the US GM cotton cultivation is banned in areas where feral cotton grows.
  - Risk management may be used to reduce data requirements

- A risk management plan should be monitored for efficacy and to ensure compliance with permit conditions

- Technology suppliers must educate users of the technology e.g.
  - planting of refuges for *Bt* crops.
  - rotation of herbicides for *HT* crops

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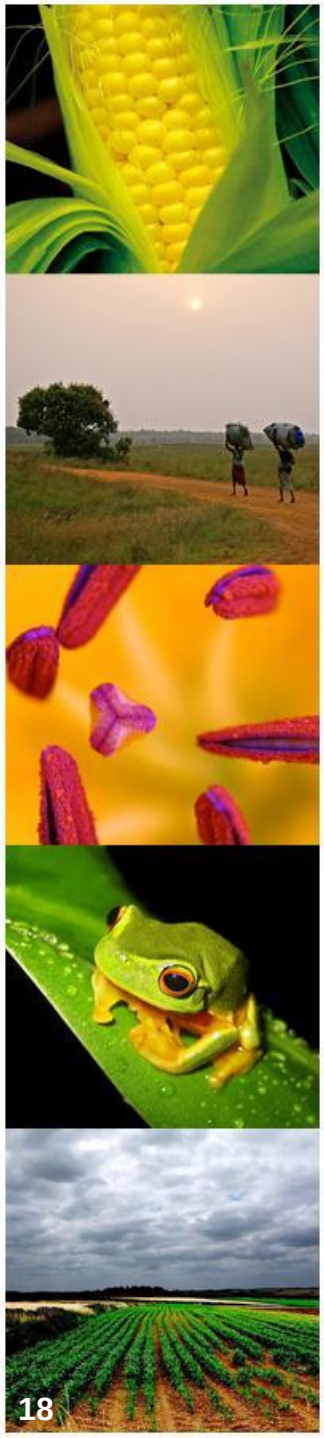

RISK ANALYSIS OF GMOs: RISK DECISION MAKING
ACCEPTABLE THRESHOLDS OF RISK

- No such thing as zero risk
  - therefore we accept some level of uncertainty or risk
  - the question is "are the risks acceptable?"

		RISK ESTIMATE			
LIKELIHOOD ASSESSMENT	**Highly likely**	Low	Moderate	High	High
	Likely	Low	Low	Moderate	High
	Unlikely	Negligible	Low	Moderate	Moderate
	Highly unlikely	Negligible	Negligible	Low	Moderate
		Marginal	**Minor**	**Intermediate**	**Major**
		CONSEQUENCE ASSESSMENT			

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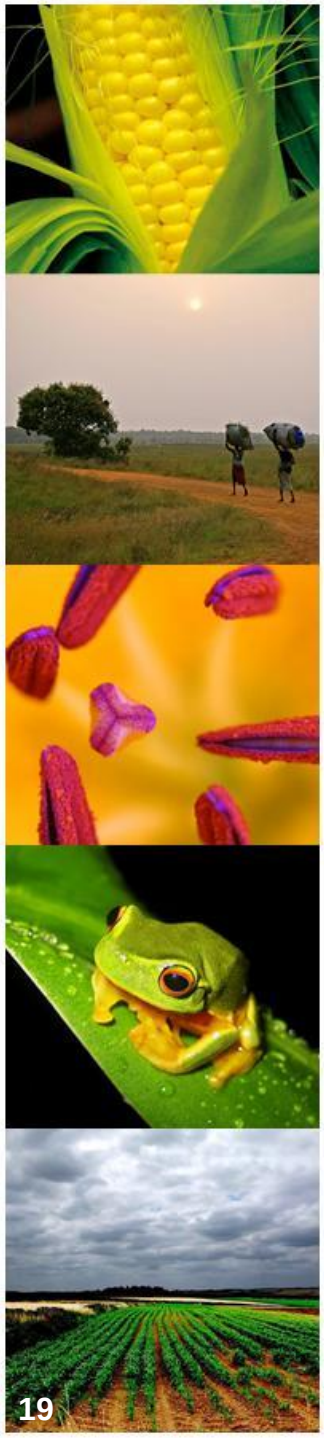
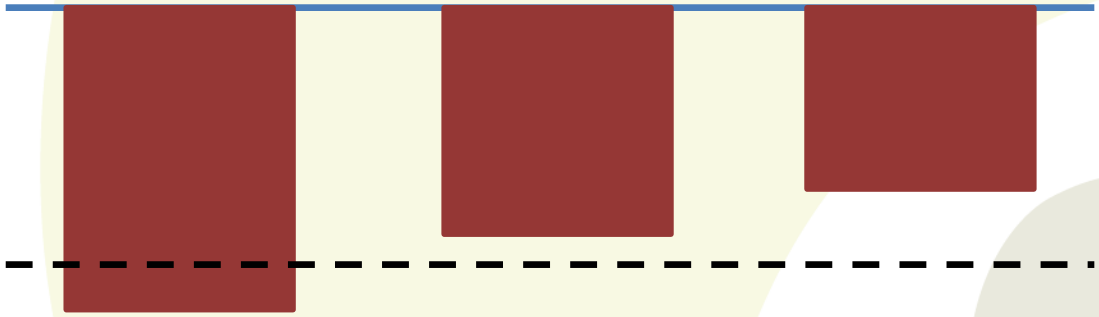
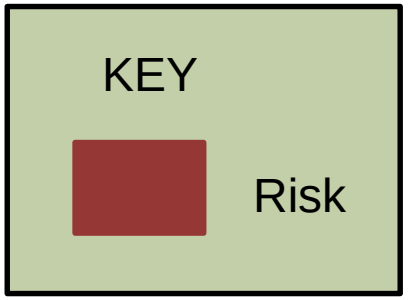


RISK ANALYSIS OF GMOs: RISK DECISION MAKING
ACCEPTABLE THRESHOLDS OF RISK



Acceptable threshold of risk



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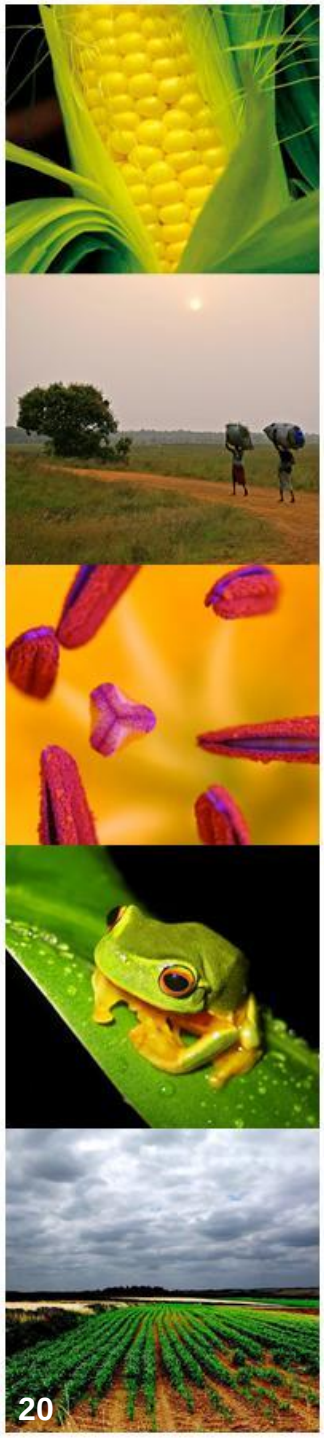
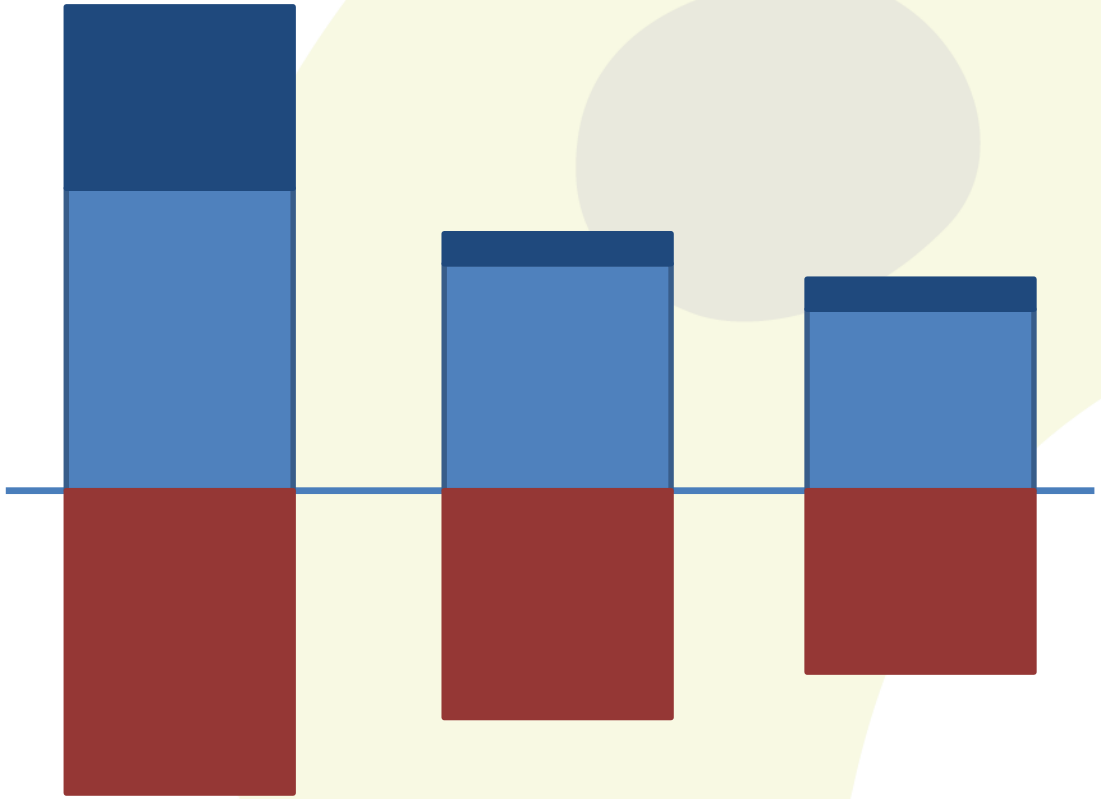


RISK ANALYSIS OF GMOs: RISK DECISION MAKING

ACCEPTABLE THRESHOLDS OF RISK



KEY

Risk

\+ Benefit

Net benefit (benefit - risk)

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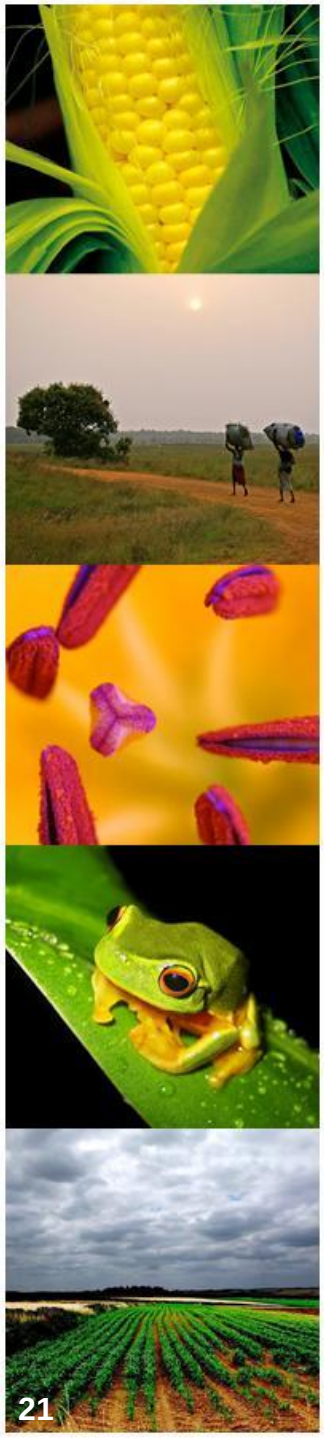
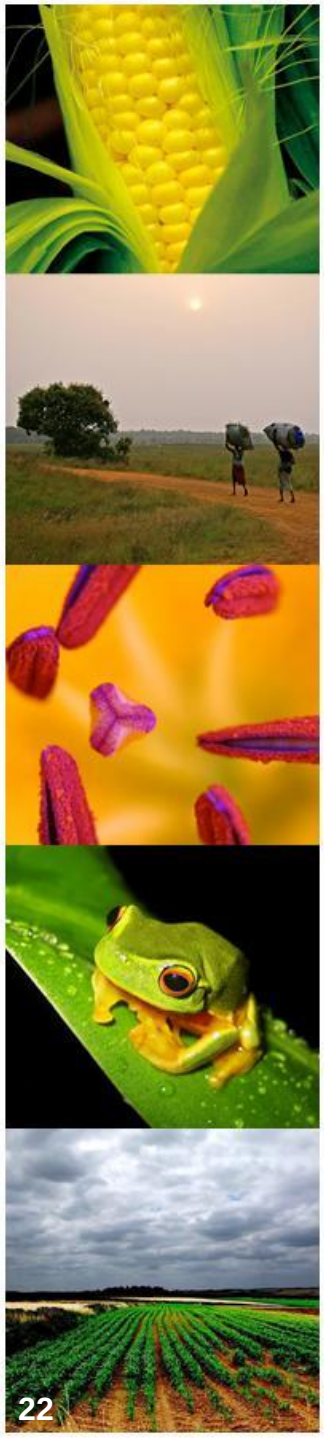


RISK ANALYSIS OF GMOs: RISK DECISION MAKING
ACCEPTABLE THRESHOLDS OF RISK

- Are the risks acceptable taking into account proposed risk management options?
- Insufficient information- ask for more information
- Approve with minimal risk management (including monitoring) conditions
- Approve with practical risk management conditions
- Refuse the application if one or more of the identified risks pose unacceptable risks



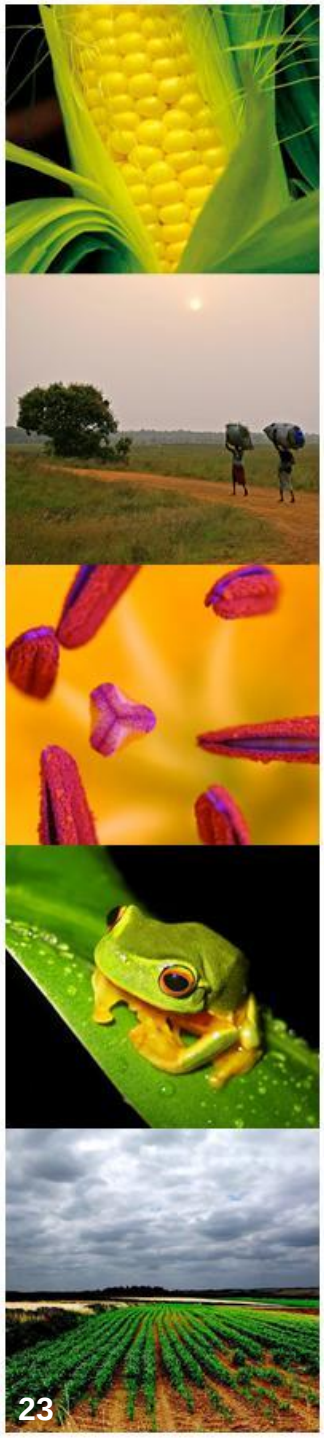
RISK ANALYSIS OF GMOs: RISK DECISION MAKING MONITORING

- Monitoring can be defined as the systematic measurement of variables and processes over time, guided by specific, well defined reasons for collecting the data, for example, to ensure certain standards or conditions are being met or to examine potential changes.

- Environmental monitoring includes:

  - Case specific monitoring is well defined, hypothesis driven and is generally aimed at confirming that the assumptions used in the risk analysis are correct

  - General surveillance on the other hand is aimed at identifying effects which were not anticipated in the risk analysis and is therefore based on consent as opposed to strict hypotheses



RISK ANALYSIS OF GMOs: RISK DECISION MAKING MONITORING

- Possible harms, assessment endpoints, risk acceptance criteria, threshold values, risk management practices, etc. should be integrated into a possible monitoring plan for the particular GMO.

- Monitoring should take into consideration already implemented risk management activities

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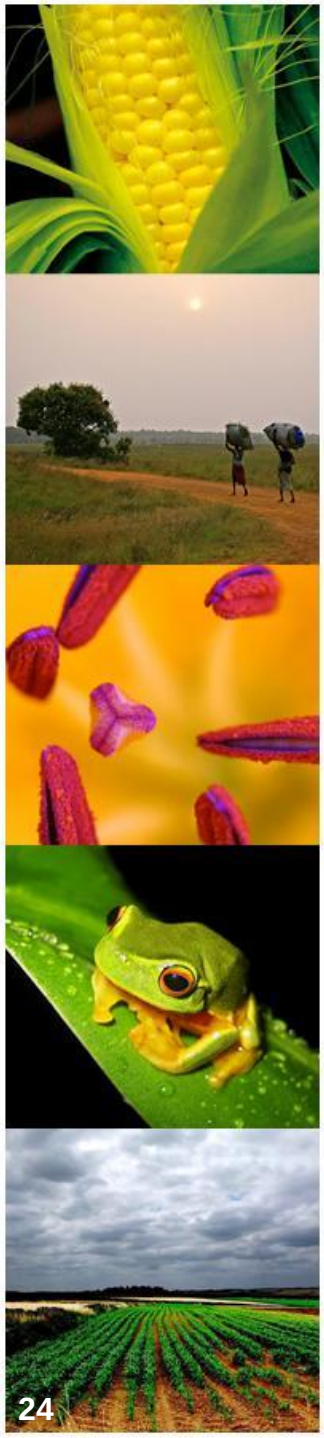
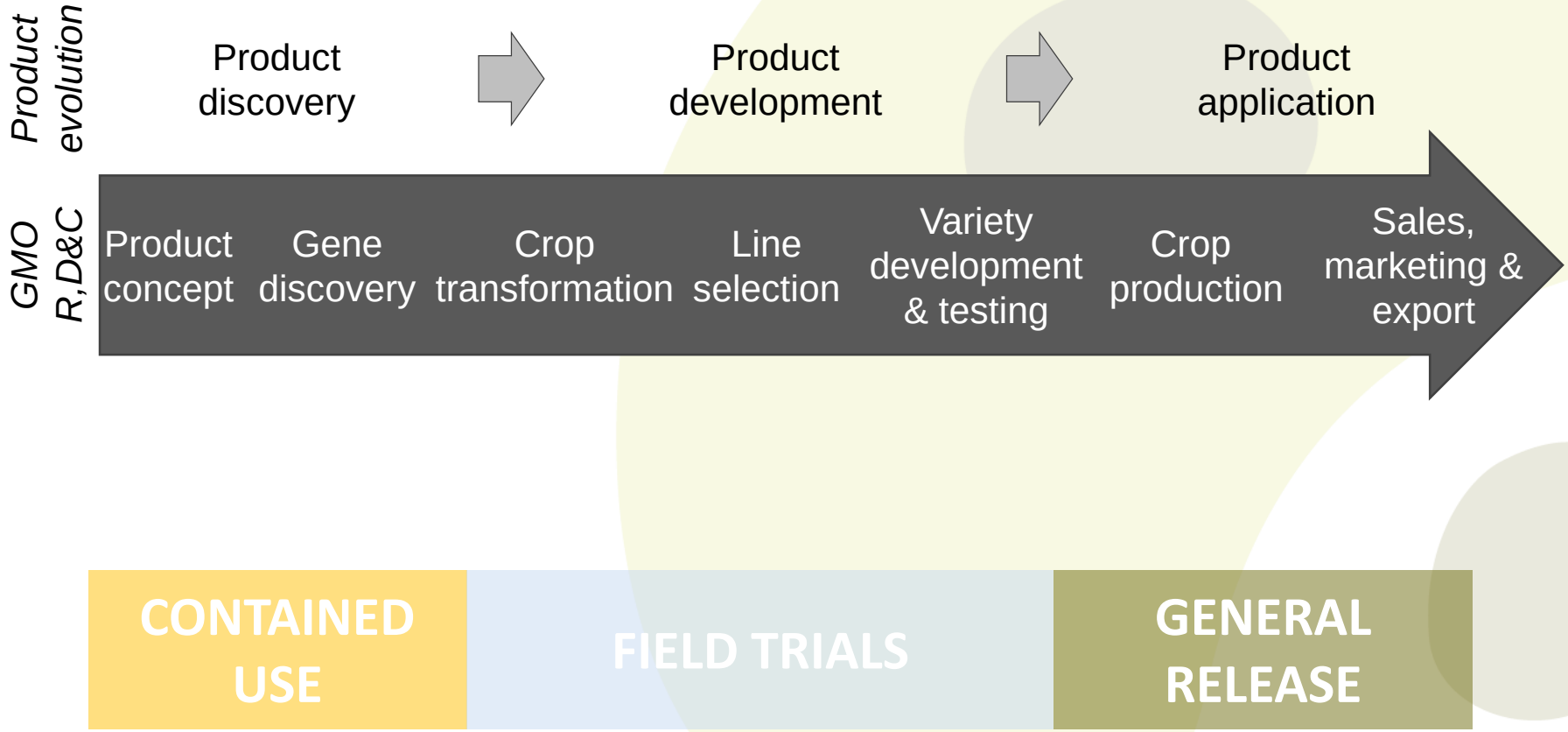


RISK ANALYSIS OF GMOs
RISK COMMUNICATION

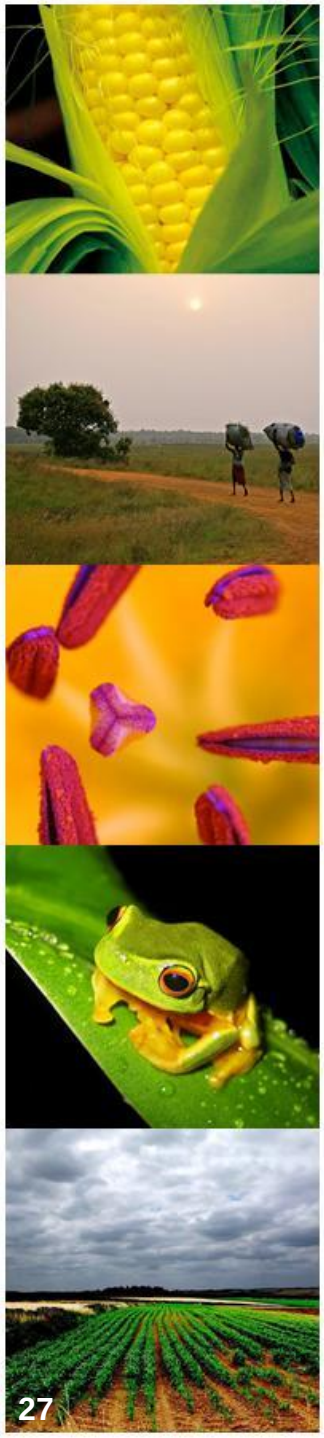
- Establishes a dialogue between decision makers and stakeholders to provide open, transparent and consultative risk based regulation of GMOs

- It is an important component of risk analysis

    - should include an explanation of the risk assessment findings and reasoning for any imposed risk management conditions



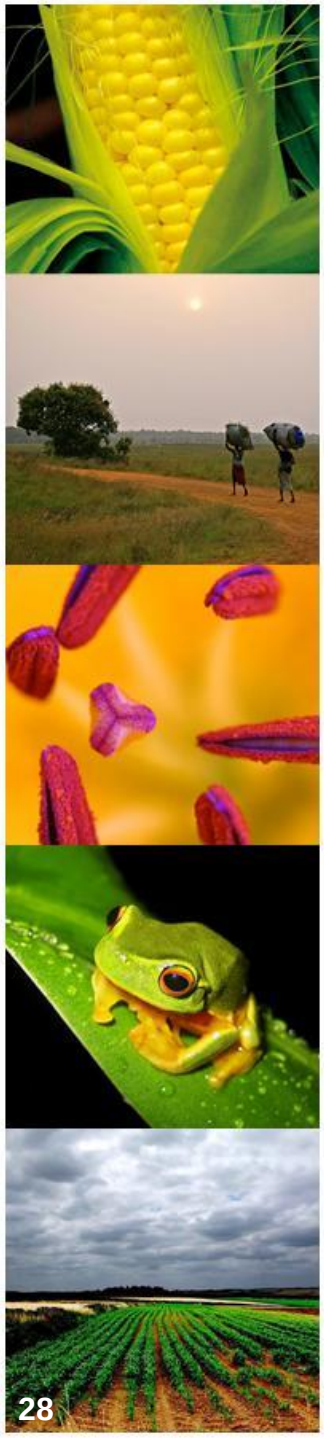
THE BIOTECH PRODUCT DEVELOPMENT PIPELINE



RISK ANALYSIS OF GMOs
SOURCES OF RELIABLE INFORMATION

	Reliability	Appropriateness
Increasing value	Validated studies conducted according to international protocols meeting defined standards.	Experimental data on the GMO and/or parent organism in the Australian environment.
	Peer reviewed literature—strongly supported reports, models, theories.	Experimental data on the GMO and/or parent organism overseas.
	Peer reviewed literature—single report, model, theory.	Experimental data on modified traits in other organisms.
	Opinion of an expert familiar with the GMO, parent organism, modified traits, ecology.	Experimental data on related surrogate systems.
	General biological principles.	
	Other technical reports, specialist literature, government reports, etc.	
	Experience of no reports of a problem.	
	Unsubstantiated statements.	

from OGTR, Risk Analysis Framework 2013



RISK ANALYSIS OF GMOs
UNCERTAINTY

- Uncertainty is intrinsic to risk analysis, e.g.
  - source of risk
  - type and degree of harm
  - the chance of harm occurring
  - the level of risk
  - efficacy of containment
- Risk analysis is part of a process to analyse and address uncertainty
  - always some level of residual uncertainty
  - if uncertainty is critical to decision making further analysis can be carried out such as meta analyses or worst case scenarios

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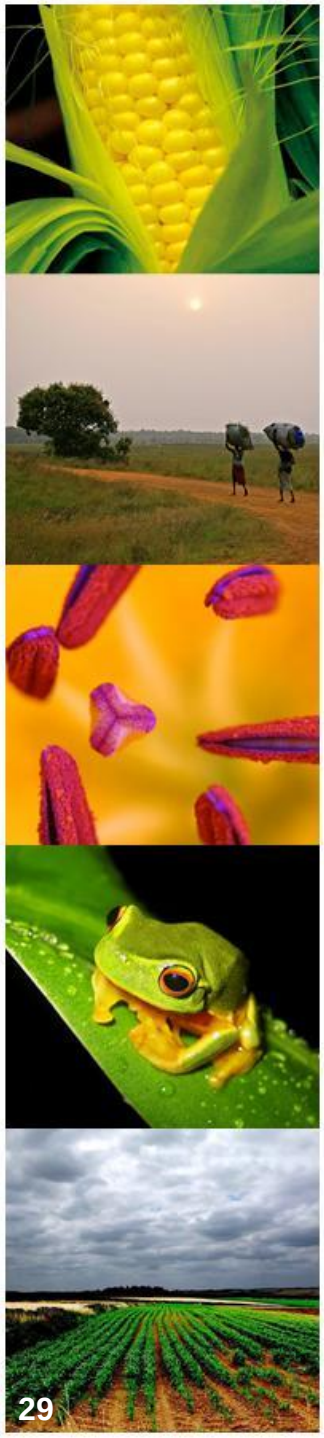
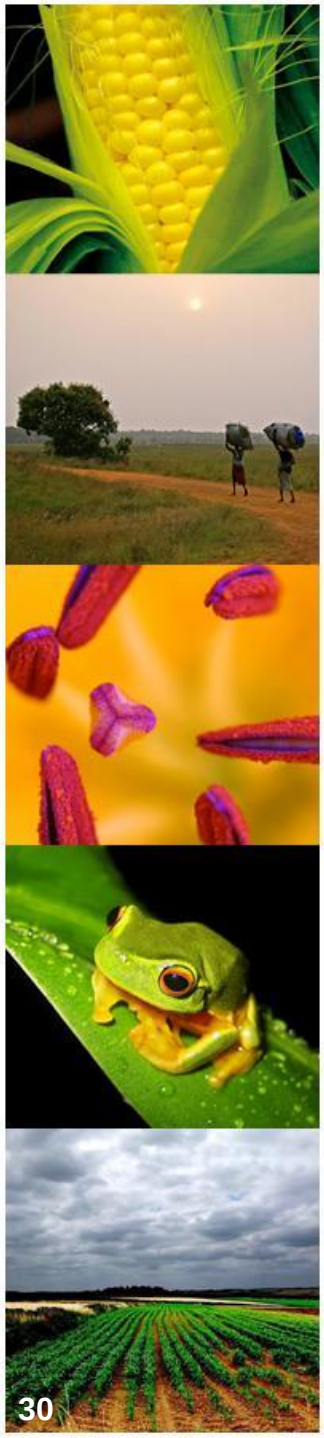


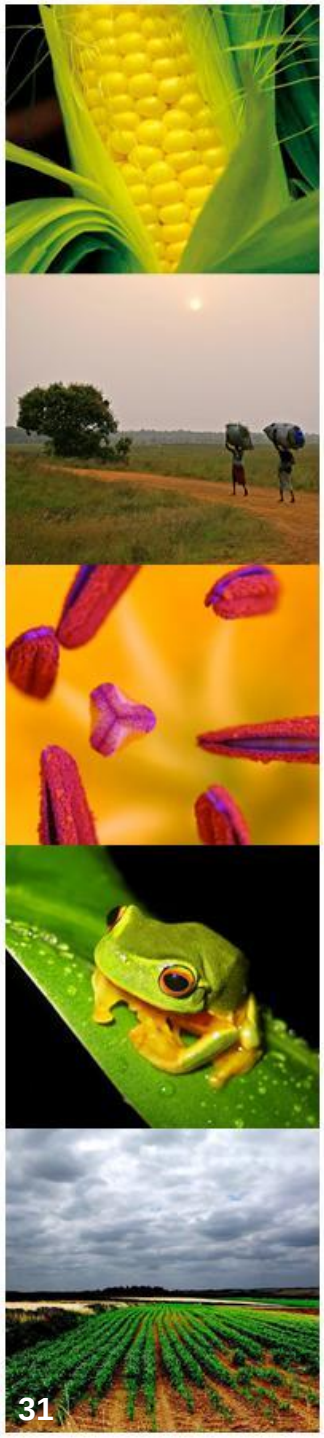
RISK ANALYSIS OF GMOs
UNCERTAINTY

- Approaches to address uncertainty include:
  - establishing parameters for data quality
  - obtaining additional data
  - identifying and correcting errors
  - applying conservative estimates
  - apply upper and lower bound of estimates
  - independent review or expert opinion
  - clear definitions of key words
  - re-evaluation against the context and scope
  - applying additional controls/ containment to manage risk



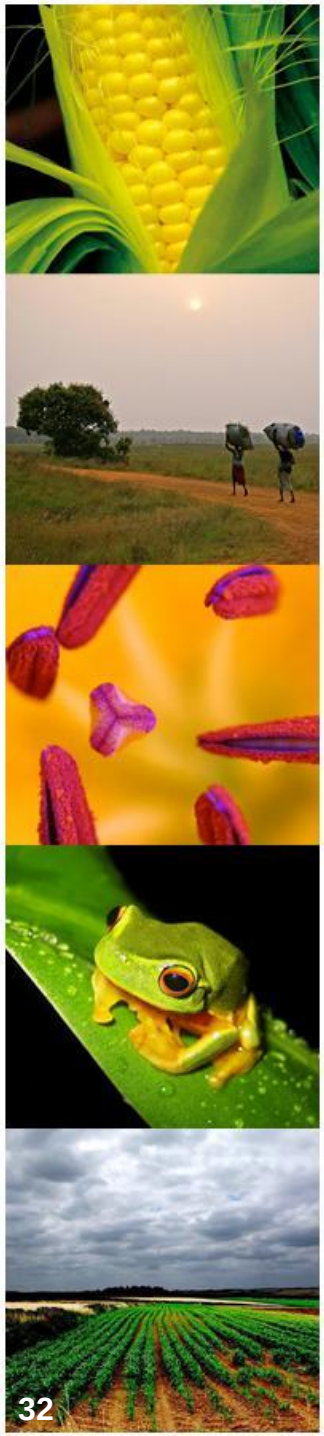
RISK ANALYSIS OF GMOs
UNCERTAINTY

- Explicit consideration of uncertainty
  - increased clarity and credibility
  - highlights areas where more focus is needed
  - more effective communication of risk
- Treatment of uncertainty on a case by case basis



TAKE HOME MESSAGES

- The basis of all regulatory activities associated with GMOs, including risk management options, should be based on a comprehensive risk analysis.
- Approaches such as problem formulation and tiered assessment can simplify the risk analysis process
- Practical risk management may be used to ensure activities occur within an acceptable level of risk (NB for contained and confined activities).
- Ensure that regulatory frameworks are adequate- need to adapt and keep abreast of developments



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THANK YOU

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