Food Safety Assessment of GM Crops

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Seminar on GM Coffee, International Coffee Organization, ICO, London, May 17, 2005

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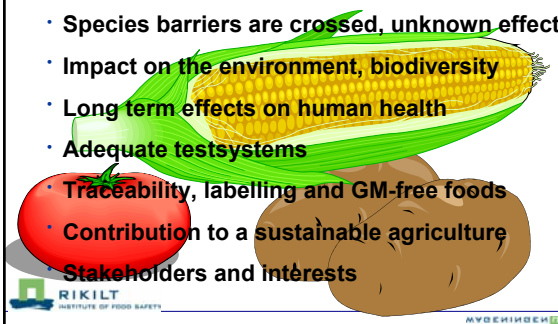
Debate on Genetically Modified Food Crops

- Species barriers are crossed, unknown effects
- Impact on the environment, biodiversity
- Long term effects on human health
- Adequate testsystems
- Traceability, labelling and GM-free foods
- Contribution to a sustainable agriculture
- Stakeholders and interests



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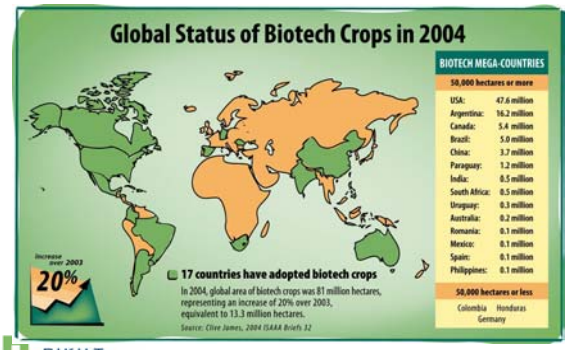

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First Generation of Modified Food Plants with Agronomical Traits

- Improved disease resistance (viruses, fungi)
- Improved pest resistance (lepidoptera, beetles)
- Tolerance for herbicide (glyphosate, glufosinate)
- Slow ripening

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Future Transgenic Crops

Golden rice	provitamin A
Iron-fortified rice	transgenic for ferritin
Tomato	β-carotene / lycopene enriched
Lupin	higher methionine levels
Maize	detoxification of mycotoxins
Insect resistant maize	transgenic for avidin
Cassava	detoxification of cyanogens
Fructan-beet	non caloric sweetener
Alfalfa	transgenic phytase, P-availability
Canola	vitamin E enriched
Coffee-beans	caffeine-free

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Future Transgenic Crops

Crop	*trait*	*transgene*
Rice	+ provit.A	phytoene synthase (daffodil)
		phytoene desaturase (Erwinia)
		lycopene cyclase (daffodil)
Rice	iron↑	ferritin (Phaseolus)
		metallothionein (rice)
		phytase (mutant, Aspergillus)
Cassava	cyanogen↓	hydroxynitril lyase

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Future Transgenic Crops

Crop	*trait*	*transgene*
Tomato	provit.A↑& lycopene↑	lycopene cyclase (Arabidopsis)
Tomato	provit.A↑	phytoene desaturase (Erwinia)
Tomato	flavonoids↑	chalcone isomerase (Petunia)
Lupin	methionine↑	seed albumin (sunflower)
Maize	fumonisin↓	de-esterase+de-aminase (μbial)
Maize	insect res.	avidin (chicken)

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Future Transgenic Crops

Crop	*trait*	*transgene*
Beet	+fructans	1-sucrose:sucrose fructosyl transferase
Alfalfa	+phytase	phytase (Aspergillus)
Canola	vit.E↑	γ-tocopherol methyl transferase (Arabidopsis)
Coffee	caffein↓	antisense xanthosine-N-7-methyl transferase (coffee)

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Nutritional and Safety Assessments of Foods and Feeds Nutritionally Improved through Biotechnology

Prepared by a Task Force of the ILSI International Food Biotechnology Committee

IFT's Comprehensive Reviews in Food Science and Food Safety, Volume 3, 2004

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New Healthy Diets and Major Uncertainties

- Which compounds/fruits/vegetables
- Bioavailability of compounds
- Interaction between components
- Matrix effects on availability of nutrients
- Current (non)-nutrient levels and variability
- Losses of compounds through food processing
- Scientific evidence of risk/benefits ???

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International Food Safety Strategies for Foods Derived from Modern Biotechnology

- International Food Biotechnology Council (1990)
- OECD Group of National Experts on Safety in Biotechnology, 1993, 1994, 1996
- OECD Task Force on the Safety of Novel Foods and Feed, 1998-present
- FAO/WHO Expert Consultations, 1991, 1996, 2000, 2001, 2003
- CODEX Task Force on Foods Derived from Biotechnology, 1999-2004
- EU, 1996-present
- ILSI, Task Forces,1996 - present

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Food and Agriculture Organization of the United Nations

World Health Organization

Safety aspects of genetically modified foods of plant origin

Report of a Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology

World Health Organization, Headquarters
Geneva, Switzerland
29 May - 2 June 2000

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Codex Principles for Risk Analysis and Guidelines for Safety Assessment of Foods Derived from Modern Biotechnology 2003

- Principles for the Risk Analysis of Foods Derived from Modern Biotechnology (CAC/GL 44 -2003)
- Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (CAC/GL 45 -2003)
- Guideline for the Conduct of Food Safety Assessment of Foods Produced Using Recombinant-DNA Microorganisms (CAC/GL 46 -2003)

Http://www.codexalimentarius.net

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Safety Evaluation of Foods

- Foods are *complex* mixtures of nutrients, vitamins, minerals and other health-beneficial substances.
- Foods contain also anti-nutrients, and natural toxins
- Safety evaluation of whole foods as performed with single chemicals or food additives is not possible.

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Concept of Substantial Equivalence OECD, 1993

- Traditional foods are considered to be safe, through their history of use (empirical evidence)
- Traditional foods serve as comparator for GM foods
- Concept of *Substantial Equivalence (SE) or Comparative Safety Assessment (CSA)*

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Substantial Equivalence or Comparative Safety Assessment

- Is not a safety assessment in itself
- It identifies but does not characterise the hazard
- Is the starting point of the assessment, rather than the endpoint
- Structures the safety assessment of a GM food relative to its conventional counterpart

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Substantial Equivalence or Comparative Safety Assessment

***A Systematic Comparison of*:**

- Agronomic properties
- Morphological characteristics
- Compositional parameters

of the GM organism and its closest traditional counterpart

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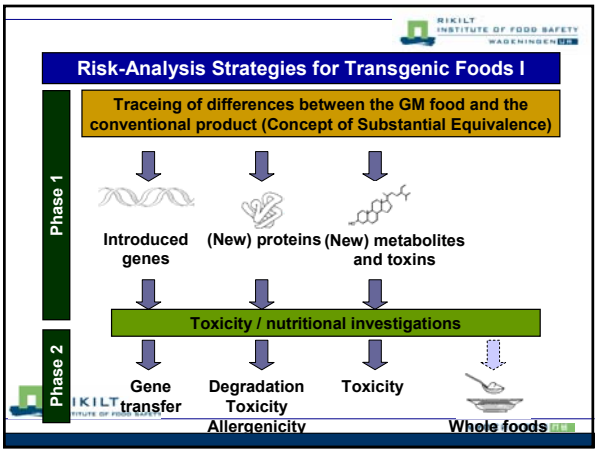

Risk-Analysis Strategies for Transgenic Foods II

Phase 3

Intake studies

- **Role of the product in the diet**
- **Intake of the product by the consumer**

Phase 4

Risk assessment of transgenic foods

Long-Term Effects

- Very little known about long-term effects of any foods
- Wide genetic variability, dietary changes over time
- Pre-market safety assessment should provide already assurance that the GM food is as safe as its conventional counterpart
- Epidemiological studies are unlikely to identify adverse effects
- Randomised Controlled Trials could be used to investigate long-term effects,but are difficult to conduct

Long-Term Effects

- A 90-days study is the minimum requirement to test the safety of repeated consumption of a food
- Additional studies may be considered on a case-by-case basis (proliferative changes observed in a 90-days study)
- Highest dose levels should not cause nutritional imbalance and lowest levels should be comparable to anticipated human intake

OECD Task Force on the Safety of Novel Foods and Feed

OECD Consensus documents:

- Crop components to be compared: key food and feed nutrients, antinutrients, and toxicants
- *Completed*: soybean and low-erucic acid rapeseed, potato, sugar beet, maize, rice
- *In progress*: wheat, sunflower, and cotton

www.oecd.org/document/9/0.2340.en 2649 34391 1812041 1 1 1 37437.00.html.

ILSI Crop Composition Database: Establishing Natural Variability in Crop Composition

Contact
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Washington, DC 20005
Phone: (202) 659-0074
Fax: (202) 659-3859
E-mail: lkurtyka@ilsi.org

www.cropcomposition.org

Importance of High Quality Crop Composition Data

- Composition studies are a key factor in the substantial equivalence evaluation process
- Assesses important nutritional and anti-nutritional endpoints
- Provides for an assessment of “unexpected” or “pleiotropic” effects
- Composition analyses form the baseline for studies of nutritionally enhanced crops

Scope of Maize, Soybean and Cottonseed Data

- Years: 1995, 1997 - 2002
- Geographic Regions
  - U.S. and Canada (IL, IN, IA, NE, CO, OH, MO, KS, NC, WI, HI, PA, AR, MN, other)
  - South America (Brazil, Argentina)
  - Europe (France, Germany, Hungary, Italy, Spain)
- Number of Analytes: 114
- Number of Datasets: 1,820
- Number of Datapoints: 70,658

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Food and Agriculture Organization of the United Nations

World Health Organization

Evaluation of Allergenicity of Genetically Modified Foods

Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology

22 - 25 January 2001, Rome, Italy

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Most Common Food Allergens

- More than 170 foods cause food allergies
- Most common foods "The Big Eight":
  - cow's milk
  - eggs
  - fish
  - crustaceans
  - peanuts
  - soybeans
  - tree nuts
  - wheat

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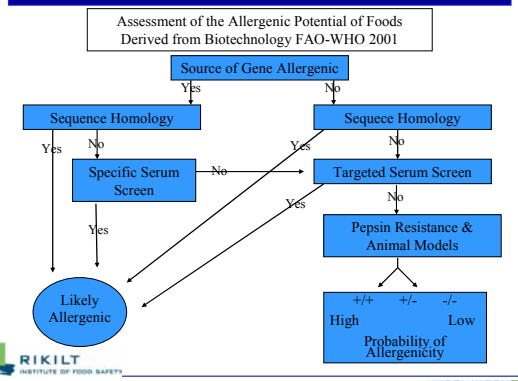
FAO/WHO 2001 Decision Tree



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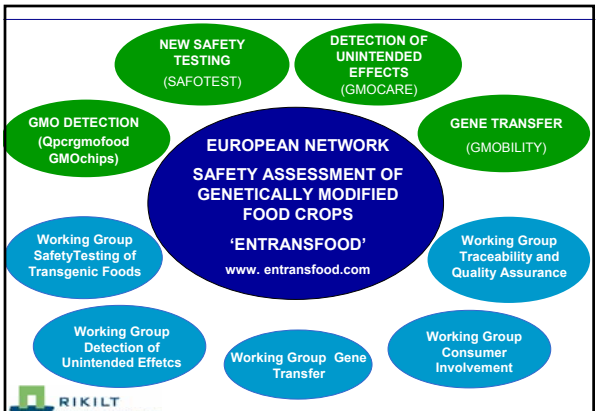

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Thematic Network ENTRANSFOOD

ENTRANSFOOD CONSORTIUM

- Consortium of Experts from Food industries, Plant breeding companies, Universities, Public/Private Research Institutes, Regulatory Agencies, and Consumers organisations
- 45 participants in RTD projects
- 62 participants in Working Groups
- Scientific disciplines: molecular biology, toxicology, biochemistry, plant breeding, analytical chemistry, and social science
- Total costs: € 12.302.449
- EU contribution: € 8.390.776

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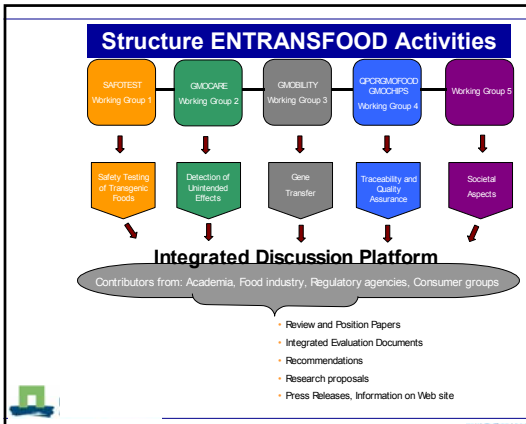
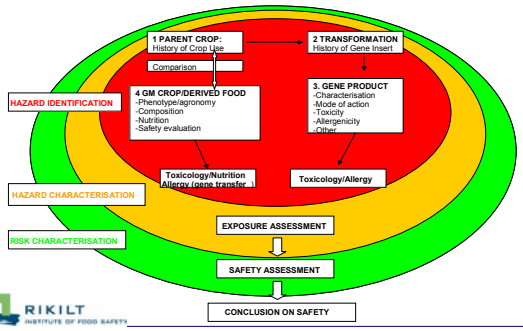
Structure ENTRANSFOOD Activities



Stepwise Procedure for Safety Testing



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Unintended Effects in GMO's,

Random integration of transgenes

⇒ **insertional mutagenesis**
⇒ **disruption of endogenous gene functions**
- **gene activation / inactivation**
- **production of new proteins**

⇒ **changes in**
- **phenotype**
- **enzymes**
- **metabolites**
- **toxins?**

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Unintended Effects in Conventional Breeding

Potato glycoalkaloids
- Pest resistance: glycoalkaloids up
- Cases of human poisoning

Celery
- Furanocoumarins
- Insect / Fusarium resistance
- Contact dermatitis in field workers

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ANALYSIS OF (UN)INTENDED EFFECTS

Plant	Phenotypic alterations
Tissue	Phenotypic alterations
DNA	DNA analysis
mRNA	Genomics
Proteins	Proteomics
Metabolites	**Metabolomics**

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Safety Assessment of GM Food

Unintended effects

Specific analysis
⇒ targeted approach

Profiling techniques
⇒ non-targeted approach

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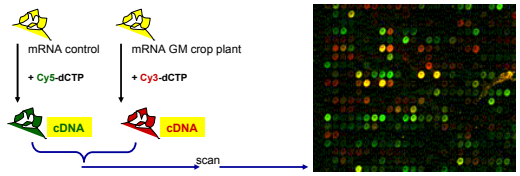
www.entransfood.com

GMOCARE

DNA Micro-Array Technology

Analysis of differential gene expression due to genetic modification



- Take GM crop plant/mutant/control
- Isolate mRNA
- Label RNA in RT-PCR reaction
- Combine equal amounts
- Hybridize to microarray
- Laser scanning of array
- Data analysis
- Identify (un)intended effects
- In vitro/in vivo validation

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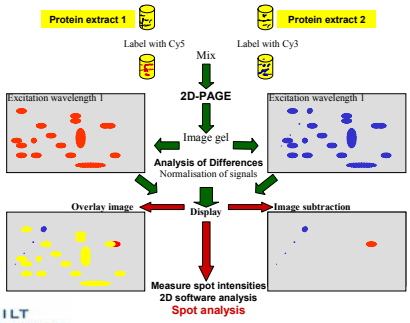
Proteomics



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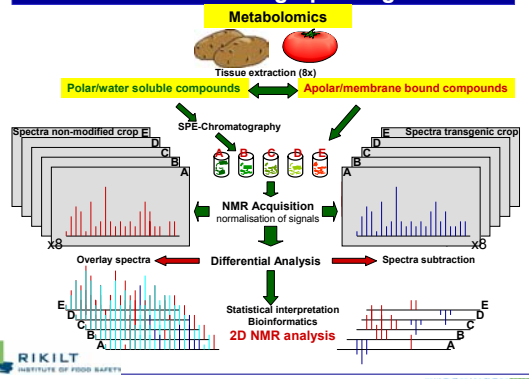
Chemical Fingerprinting



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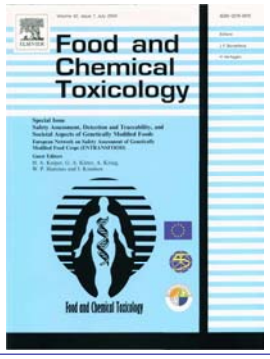
Special Issue Food and Chemical Toxicology



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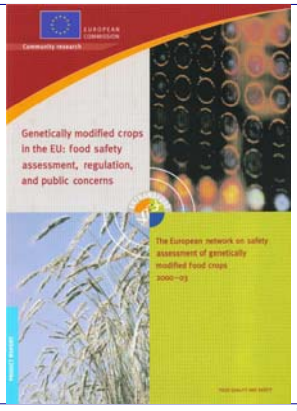

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Conclusions

1. The Comparative Safety Assessment strategy (Substantial Equivalence) is robust and adequate to identify hazards of GM foods, which are subsequently further investigated
2. Unexpected alterations in the composition of GM foods are thoroughly screened for by single compound analysis and profiling methods. The latter methods should be further developed and validated

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Conclusions

3. GM foods with health-benefit properties are still under development and need thorough investigations of safety and health claims
4. Transparency in the risk analysis process and interactive dialogue between all stakeholders about the risks and benefits of the GM technology is necessary in order to restore public trust in GM foods

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