

# Annex 7



# Issues Raised by Member States on Risk Assessment Approaches for GMOs

Harry A. Kuiper  
Special meeting of the EFSA Advisory Forum on GMO risk assessment in Europe  
13 November 2007, Brussels

1. Standardization/harmonization of test procedures and methods for safety evaluation
2. Definition of test parameters and biological endpoints
3. Statistical analysis of results of field trials and feeding experiments
4. Biological significance of identified differences
5. Allergenicity testing
6. Use of omic-technologies for safety assessment (unintended effects)

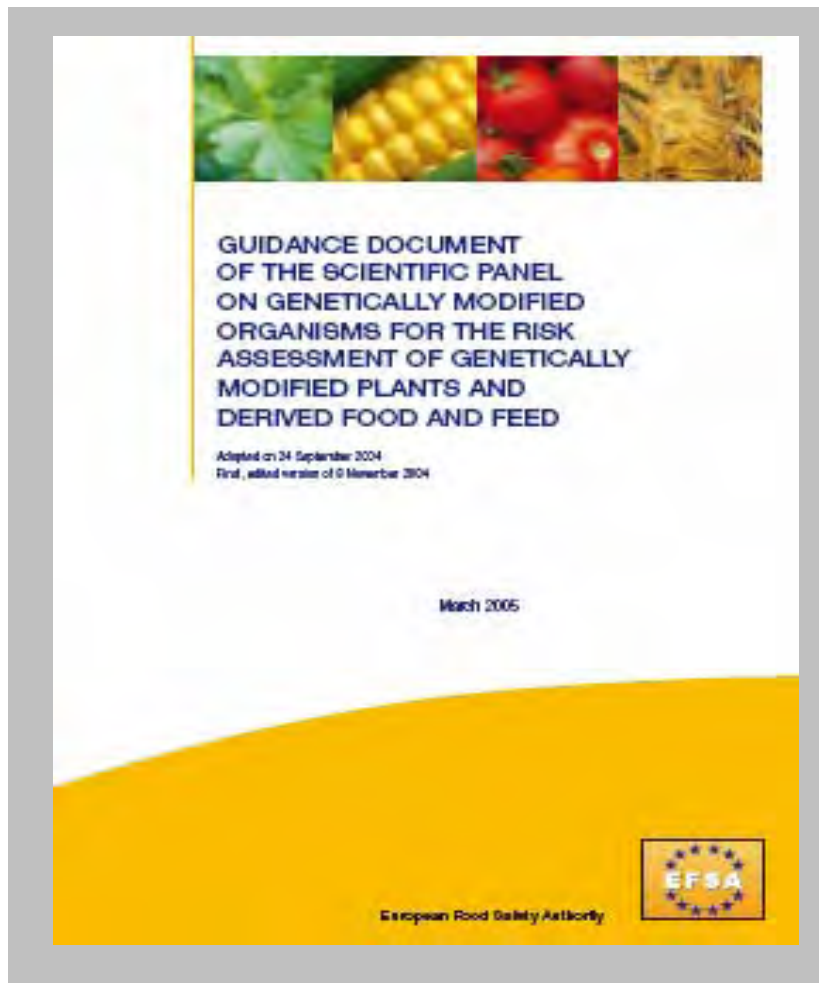
7. Assessment of long-term effects (combined intake)
8. Risk assessment of GM animals, trees, non-food/feed purposes
9. Gene stacking
10. Simplification of procedures in case no unexpected outcomes have been identified

- **Guidance for the risk assessment of GM plants and derived food and feed**
- **Guidance on Post Market Environmental Monitoring**
- **Guidance for the risk assessment of GM microorganisms for food and feed use**
- **Guidance for the renewal of existing products**
- **Guidance for stacked events**

# Self Tasking Activities

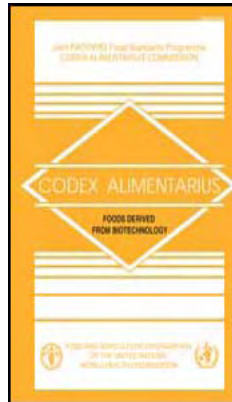
- Use of antibiotic marker genes in GM plants (April 2004)
- Guidance for post-market environmental monitoring ( December 2005)
- Safety and nutritional assessment of GM plant derived food/feed – the role of animal feeding trials (November 2007 )
- Guidance for the risk assessment of GM plants used for non-food/feed purposes (ongoing)
- Working group on new approaches for the allergenicity assessment (ongoing)
- Working Group on statistical approaches in comparative assessment of GMOs (ongoing)

# EFSA Guidance document for GM Plants and derived Food and Feed



[http://www.efsa.eu.int/science/gmo/gmo\\_guidance/660\\_en.html](http://www.efsa.eu.int/science/gmo/gmo_guidance/660_en.html)

- 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)



## Underlying assumption:

- Traditionally cultivated crops have gained a history of safe use for the environment/consumer/animals
- These crops can therefore serve as a *baseline* for the safety assessment of GM crops

**Concept of Familiarity**

**Concept of Substantial Equivalence**

**Comparative Safety Assessment**

- Molecular Characterization of the Modification Process and rec.DNA Organism
- Agronomical and Phenotypical Characterization
- Food/Feed Safety Assessment
- Environmental Risk Assessment
- Comprehensive Risk Assessment
  - *All available evidence should be considered*
  - *Iterative process*

# What is the Appropriate Comparator and Natural Background

- Extent of Equivalence
- Natural variations
- Many factors influence the composition of GMOs
- Statistical significant differences *by chance*
- Biological relevance of stat. significant differences
  
- *Working Group on statistical approaches in comparative assessment of GMOs (ongoing)*

## National Academy of Sciences, 2004

- Selecting from homogeneous population
- Selection from heterogeneous population
- Crossing of existing approved varieties
- rDNA technology (Agrob.) using genes from closely related species
- Conventional pollen based crossing closely related species
- Conventional crossing distant species and/or embryo rescue
- Somatic hybridisation
- Somaclonal variation
- rDNA biolistic transfer genes from closely related species
- rDNA (Agrob.) transfer genes from distally related species
- rDNA biolistics gene transfer from distally related species
- Mutation breeding, chemical mutagenesis, ionising radiation

lower

higher

# Analysis of (Un)Intended Effects

- Plant
- Tissue
- DNA
- mRNA
- Proteins
- Metabolites

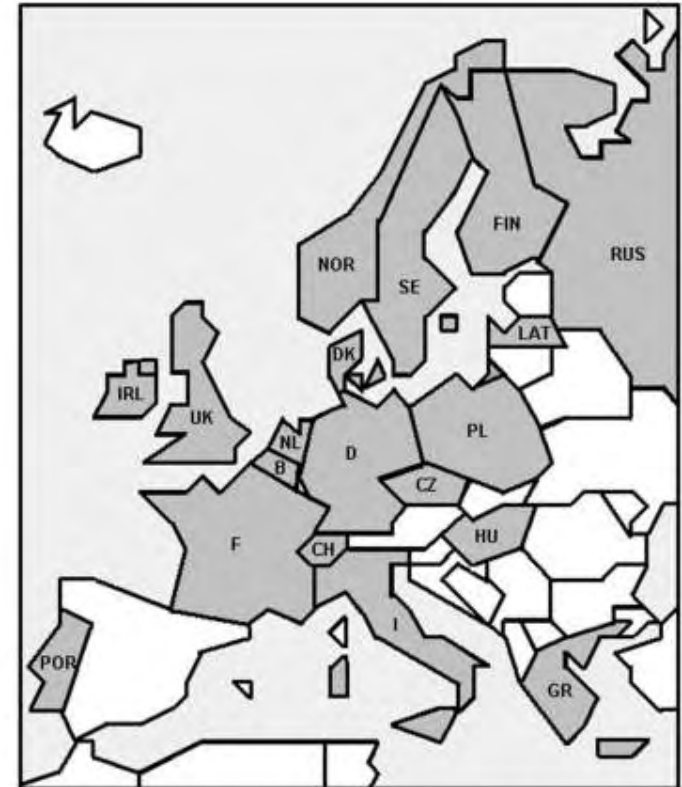


- Phenotypic alterations
- Phenotypic alterations
- DNA analysis
- Genomics
- Proteomics
- Metabolomics

# FP6 EU Project SAFE FOODS

- Integrated Project
- Coordinators:
  - *Dr. H. A. Kuiper*
  - *Dr. H.J.P. Marvin*
- April 2004-March 2008
- Project Participation:
  - *37 partners*
  - *21 countries*
- Budget:
  - *14,628,000 € total*
  - *11,576,000 € EU contribution*

} *RIKILT*



CHINA



SOUTH AFRICA



# Workpackage 1: Comparative Safety Evaluation of Breeding Approaches and High-and Low-Input Production Systems



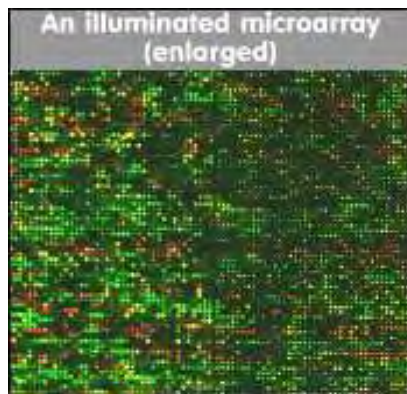
**Does diversification in agricultural production systems lead to diversification in risk?**

# The 'OMICS' approach

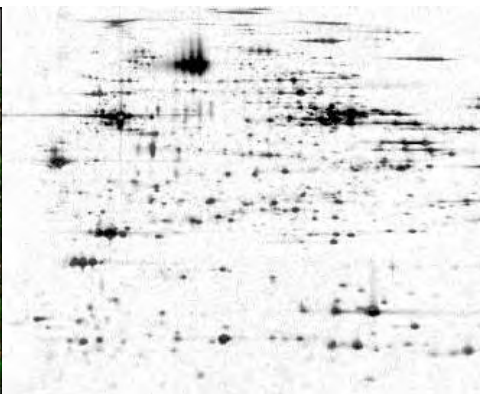
**“Unbiased” approaches**  
**Data rich: reducing uncertainty**  
**Multivariate analysis, PCA**

## Profiling techniques

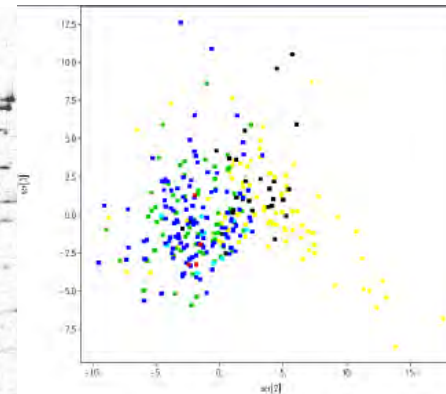
### Transcriptomics



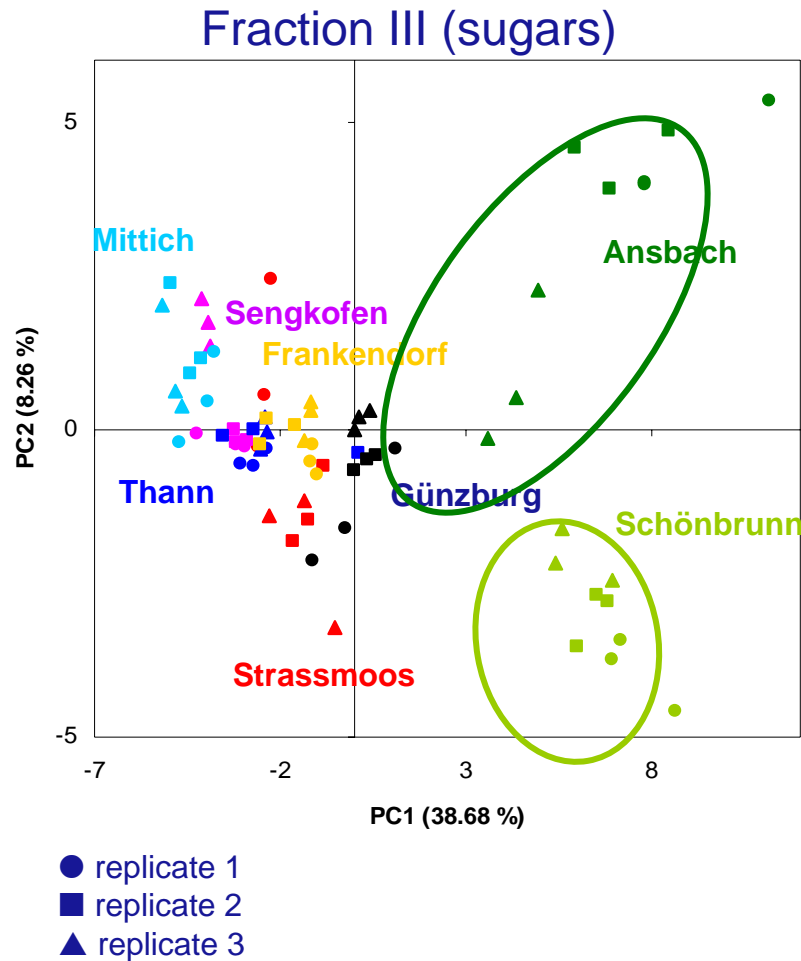
### Proteomics



### Metabolomics



# Influence of location

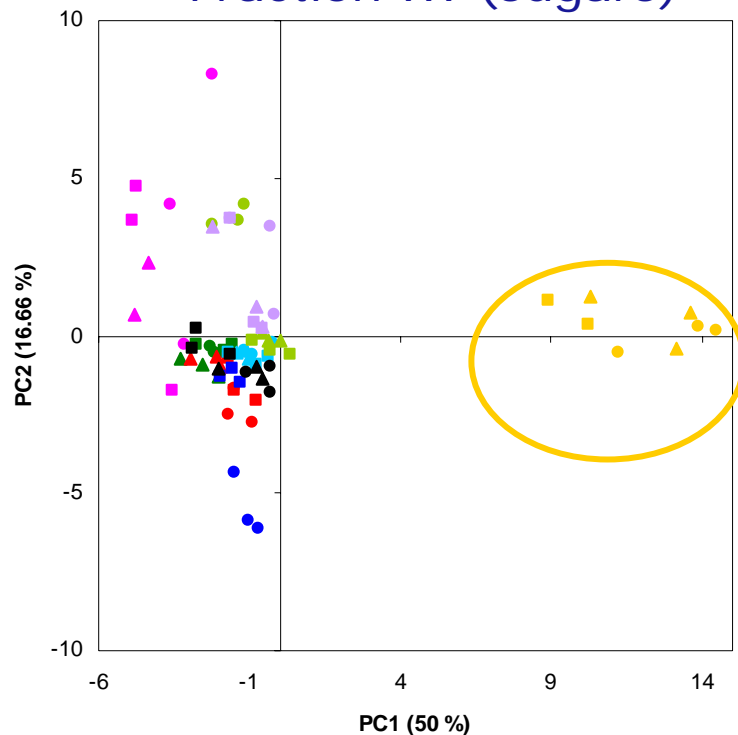


1 Variety Lukas grown at different locations in Bavaria

Agricultural practice  
or location?

# Influence of variety

Fraction III (sugars)



- replicate 1
- replicate 2
- ▲ replicate 3
- Spezi
- Shorty
- Gomera
- Amadeo
- Expert
- Lukas
- Flavi
- Fangio
- Pontos

Different varieties grown at one location (Frankendorf/Bavaria)

- overlap of 8 varieties
- clear separation of one variety (Fangio)

# Profiling Techniques

- Enormous potential for detection of alterations at the genome, proteome and/or metabolite expression level
- In theory: complete set of information on DNA - proteins - metabolites
- In practice:
  - difficulties to determine “natural” baseline for comparison
  - validation and standardization
  - analysis of large data sets with bioinformatic techniques
  - limited availability of data on profiles and natural variations

# Long-Term Adverse Effects of GM Foods and Derived Products

- Fundamental pillar of the EFSA risk assessment approach
- Very little is known about potential long term effects of ***any foods*** on human health
- Sensitivity and predictivity of animal models
- When should the performance of animal feeding trials with whole GM foods/feed be considered?

## **“Safety and Nutritional Assessment of GM Plants and derived food and feed: The role of animal feeding trials”**

**EFSA GMO Panel, November 2007**