

EU Regulatory Framework and Status of Genetically Modified Crops

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EAAP workshop 8, Antalya, September 16th, 2006



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Program



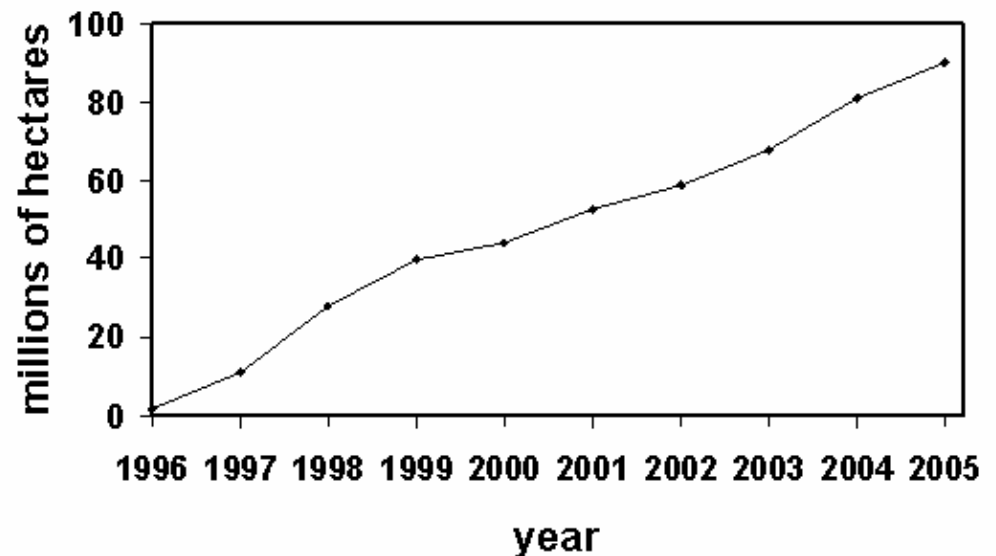
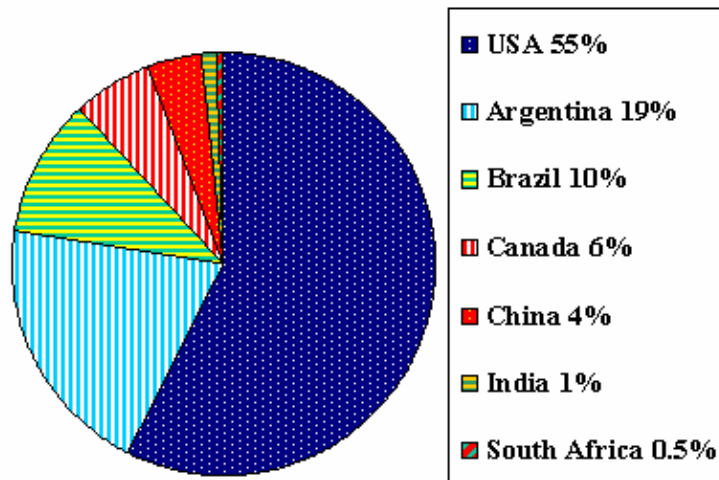
- Introduction, GM crops
- GM crops in the EU
- Safety assessment of GMOs
- Research on GM food safety
- Conclusions



Introduction

The worldwide area of genetically modified crops has rapidly increased

Total area,
1996-2005



Nations,
2005



Introduction

Examples of herbicide-resistant genetically modified crops are soybean and canola

Soybean



before after
herbicide-application

Canola



Introduction

Insect-resistant maize and cotton are grown commercially on a large scale

Maize



Cotton



Introduction

“Golden rice” with additional β -carotene is an example of a future biotech crop



GM crops in the EU



GM crops in the EU

Regulations on GMOs in the EU

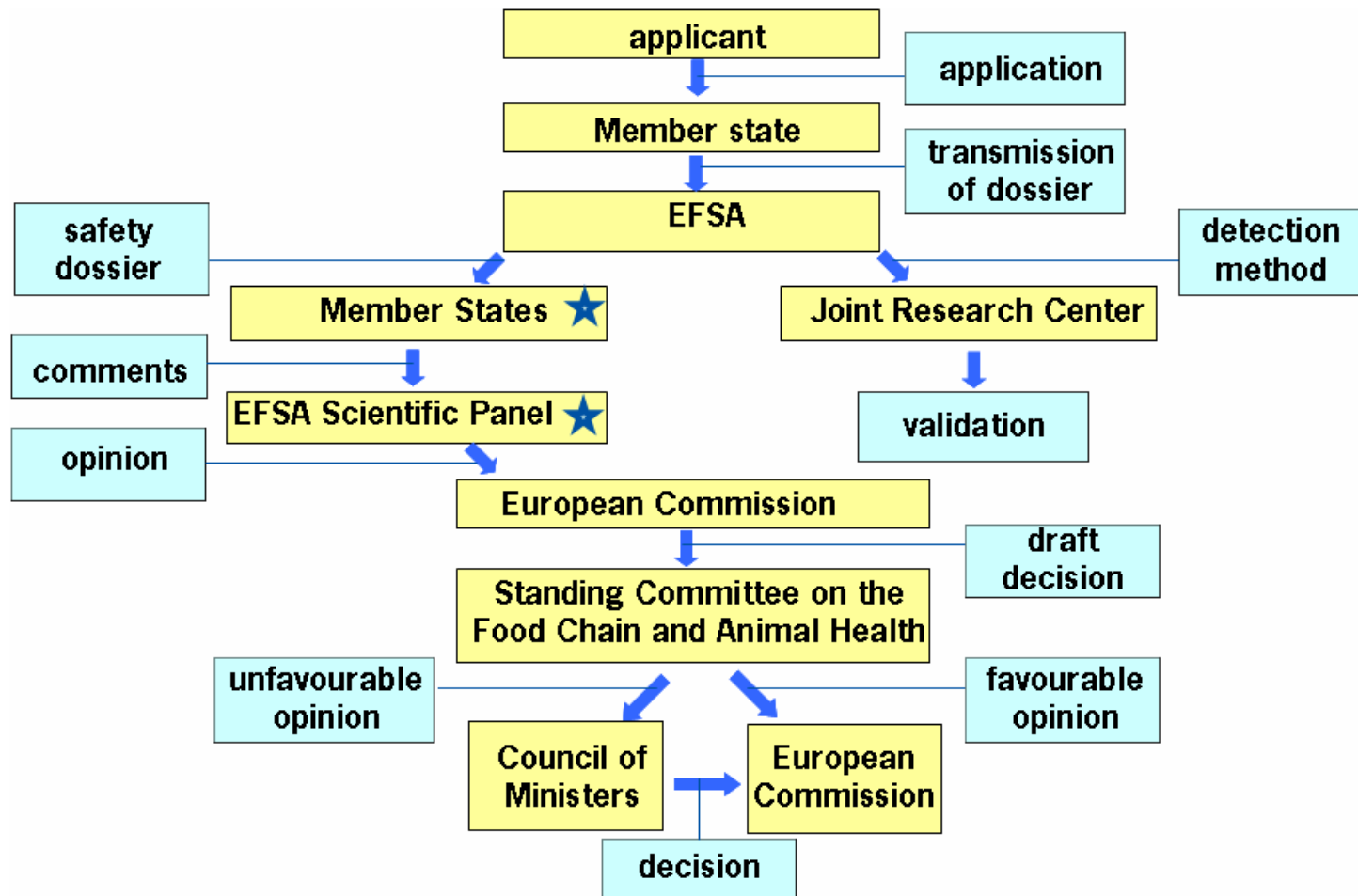


- Environmental release (cultivation, import)
 - Directive 2001/18
- Food and Animal Feed
 - Regulation 1829/2003
- Labelling and Traceability of Food and Feed
 - Regulation 1830/2003
- Seeds and propagating material
 - Thresholds for adventitious presence of GM seeds in seedlots for conventional seeds (in preparation)
- Also co-existence, trans-boundary, contained use



GM crops in the EU

EU approval procedure for GM food and feed



GM crops in the EU

GM crops approved for environmental release

<i>Crop</i>	<i>Trait</i>	<i>Applications</i>
Soya	Herbicide resistant	Import
Radicchio	Herbicide resistant	Breeding
Maize	Herbicide resistant Insect resistant	Cultivation, import
Canola	Herbicide resistant Hybrid system	Breeding, cultivation, import



GM crops in the EU

GM crop products approved as novel foods

Crop

Trait

Canola oil

Herbicide resistant
Insect resistant



Cotton seed oil

Herbicide resistant
Hybrid system



Maize

Herbicide resistant
Insect resistant



Soya

Herbicide resistant



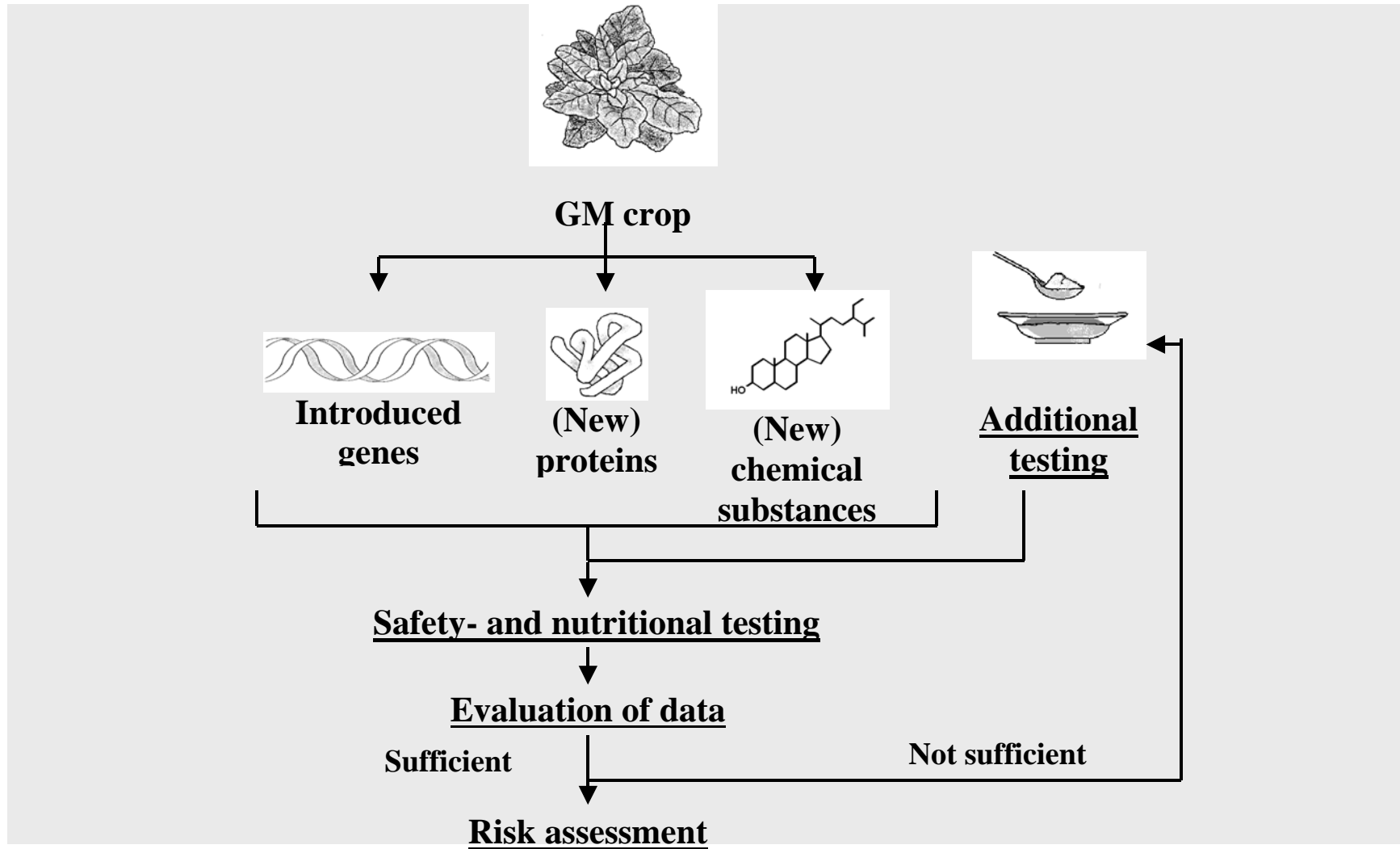
GM crops in the EU

Labelling and traceability of GM foods

- All GM foods and food ingredients
 - Also without detectable transgenic material
- Documentary system for traceability
- Thresholds for adventitious presence:
 - 0.5% (evaluated)
 - 0.9% (approved)
- Organic products GMO-free
- "GMO-free" label in some member states



Safety assessment



Safety assessment

The safety assessment of GM products follows an international consensus approach

Comparative safety assessment

Substantial equivalence

Starting point

Comparison of phenotype, composition

Comparator with history of safe use



FAO/WHO, OECD, ILSI



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Safety assessment

A number of specific safety issues are commonly addressed (I)

Toxicity

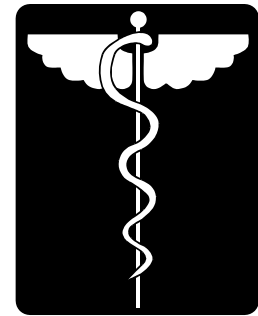
Bioinformatics, degradability, animals

Allergenicity

Bioinformatics, degradability, animals, clinical

Gene transfer

Antibiotic resistance, clinical relevance, likelihood of transfer



Safety assessment

A number of specific safety issues are commonly addressed (II)

Unintended effects

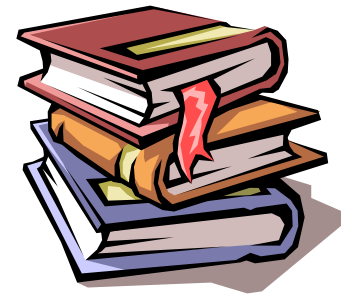
Composition, profiling (future)

Nutritional value

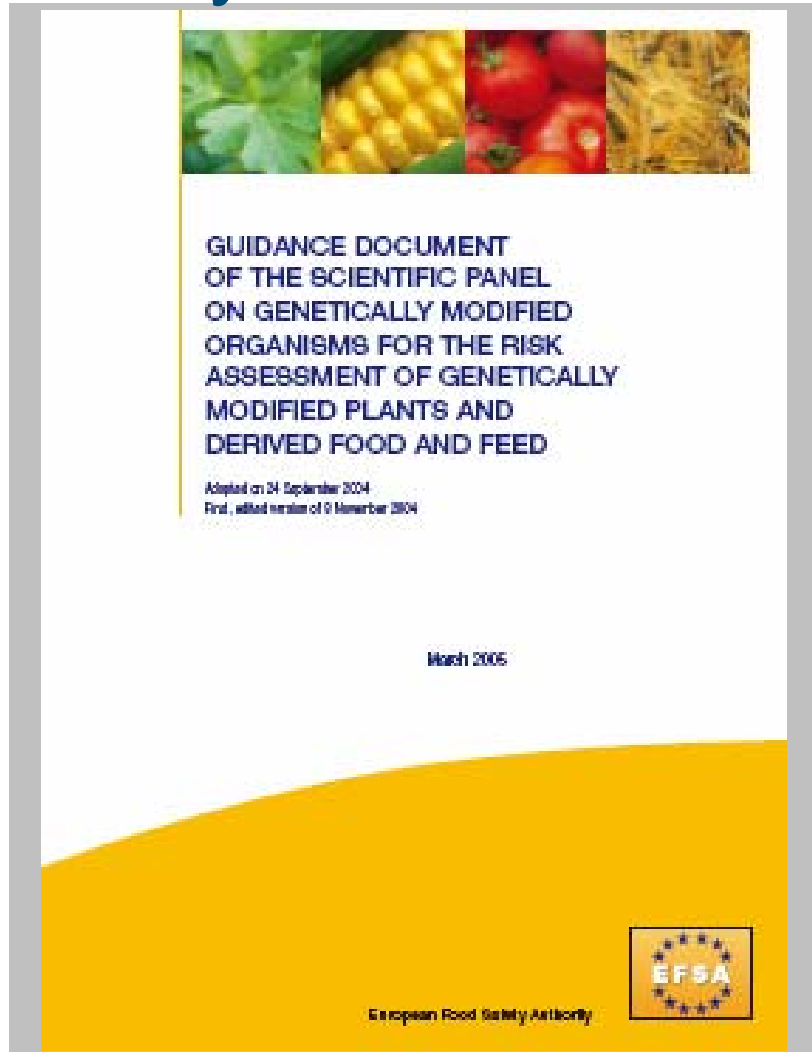
Composition, target animals

Pesticide residues

Residue data, metabolism



Safety assessment



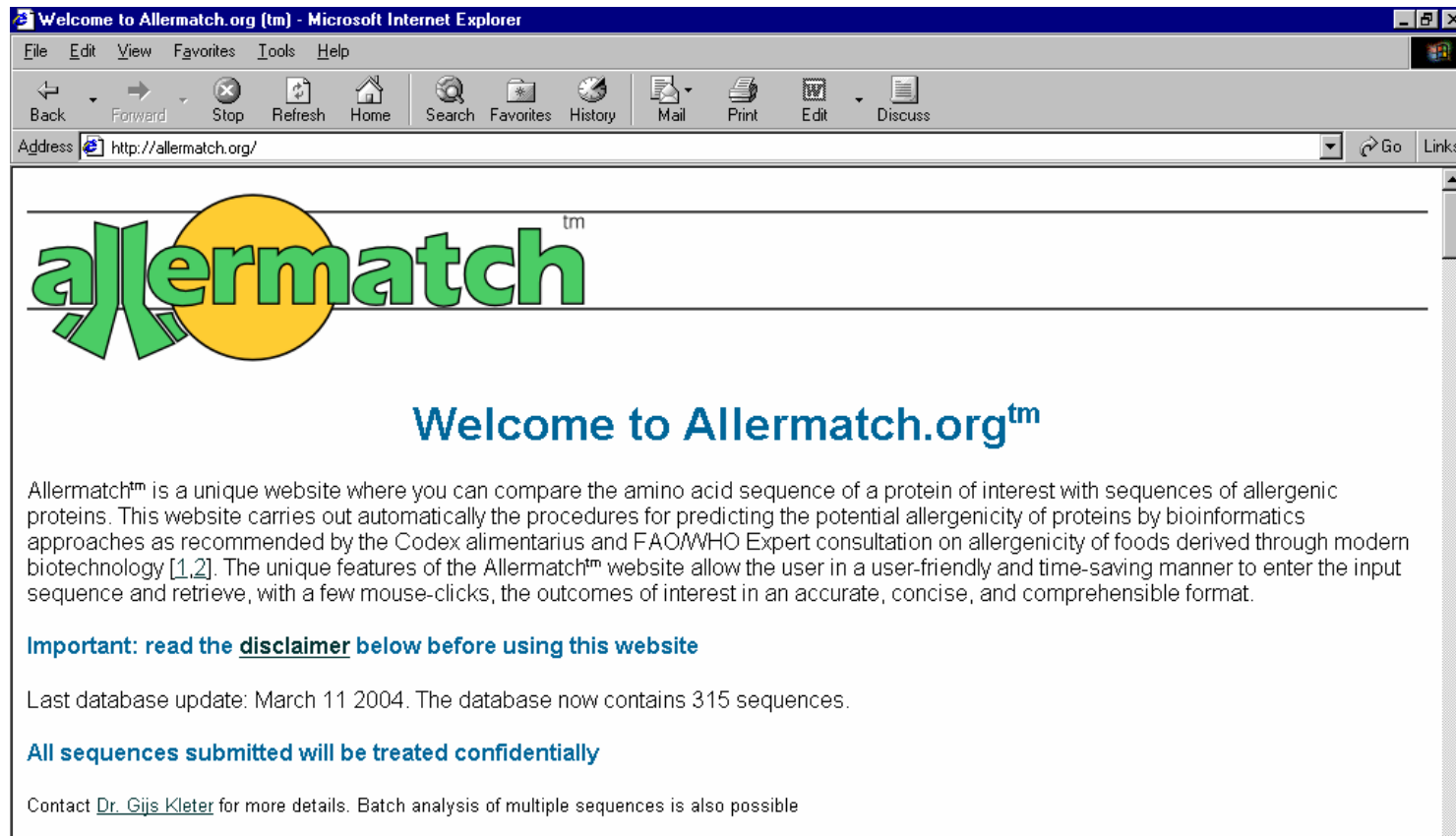
http://www.efsa.eu.int/science/gmo/gmo_guidance/660_en.html



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Safety assessment

Allermatch[™] (www.allermatch.org) for bioinformatic prediction of similarity of proteins with allergens



Safety assessment

Example: model sequence Zea m 14, start search

The screenshot shows a web browser window titled "Allermatch: Allermatch - Microsoft Internet Explorer". The address bar shows the URL "http://www.allermatch.org/allermatch.py/form". The page content includes a navigation menu on the left with links: Home, Search, Database, Publication, Introduction, Example, About us, Feedback, Disclaimer, Copyright, Thanks, and References. The main heading is "Allermatch allergen finder: Input Form". Below this, a paragraph states: "This webpage has three analysis modi to identify a relationship between your input sequence and an allergen from the database". A bulleted list describes the three analysis methods: 80 amino acids sliding window, Full Alignment (Fasta), and Wordmatch. A text input field labeled "Copy Paste your Amino Acid sequence here:" contains the sequence: "aiscgqvasaiaapcisyargqgsgpsagccsgvrslinnaarttdrraacnclknaaagvsglnagnaasipskcgvsipytiiststdcervn". Below the input field, the "Algorithm:" section has three radio buttons: "Do an 80 amino acids sliding window alignment" (selected), "Look for a small exact wordmatch", and "Do a full fasta alignment". To the right of the first radio button is a text input field with the value "35" and the label "Cutoff Percentage (only applicable to the 80 amino acids sliding window)". To the right of the second radio button is a text input field with the value "6" and the label "Wordlength (only applicable to the exact wordmatch search)". Below the radio buttons is a "Select a database:" section with a dropdown menu showing "SwissProt and WHO-IUIS". At the bottom left of the form is a "Go" button.

Allermatch allergen finder: Input Form

This webpage has three analysis modi to identify a relationship between your input sequence and an allergen from the database

- 80 amino acids sliding window. The input sequence is chopped up in 80 amino acids windows. For each 80 amino acids window, the program counts which allergen it hits (with an specific identity).
- Full Alignment. Use Fasta to perform a full alignment.
- Wordmatch: Look for an exact hit of 6 amino acids in a sequence in the database

Copy Paste your Amino Acid sequence here:

aiscgqvasaiaapcisyargqgsgpsagccsgvrslinnaarttdrraacnclknaaagvsglnagnaasipskcgvsipytiiststdcervn

Algorithm:

☒ Do an 80 amino acids sliding window alignment Cutoff Percentage (only applicable to the 80 amino acids sliding window)

☐ Look for a small exact wordmatch Wordlength (only applicable to the exact wordmatch search)

☐ Do a full fasta alignment

Select a database:



Safety assessment

Example: output list, 16 hits besides Zea m 14

Allermatch: Allermatch - Microsoft Internet Explorer

Bestand Bewerken Beeld Favorieten Extra Help

Vorige Zoeken Favorieten

Adres <http://allermatch.org/allermatch.py/search> Ga naar Links

Google Search Check AutoLink AutoFill Options

6 Amino Acid Wordmatch

Database : SwissProt and WHO-IUIS

No	Db	Allergen Id	No of exact wordmatches	% of exact wordmatches	External db	Species Name	Detailed Information
*1	*2	*3	*4	*5	*6	*7	*8
1	AL	al_Zea_m_14	88	100.00	P19656 ^S	Zea mays	Go
2	AL	al_Pru_d_3	10	11.36	P82534 ^S	Prunus domestica	Go
3	WI	wi_Cit_s_3.0102	4	4.55	CAH03799 ^N	Citrus sinensis	Go
4	AL	al_Mal_d_3	4	4.55	Q9M5X7 ^S	Malus domestica	Go
5	WI	wi_Fra_a_3.0101	3	3.41	CAC86258 ^N	Fragaria x ananassa	Go
6	SP	sp_Pyr_c_3	3	3.41	Q9M5X6 ^S	Pyrus communis	Go
7	WI	wi_Fra_a_3.0203	2	2.27	AAY83343 ^N	Fragaria x ananassa	Go



Safety assessment

Example: detailed information for allergen Pru d 3

Allermatch: Allermatch - Microsoft Internet Explorer

Bestand Bewerken Beeld Favorieten Extra Help

Vorige Zoeken Favorieten

Adres <http://allermatch.org/allermatch.py/search> Ga naar Links

Google Search ABC Check AutoLink AutoFill Options

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[Copyright](#)
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[References](#)

Allergen Id	al_Pru_d_3
Allermatch™ Database	SwissProt and WHO-IUIS
Allergen Name	Pru d 3
Source database	SwissProt
Accession Id	P82534
External link	http://www.expasy.org/cgi-bin/niceprot.pl?P82534
Species Name	Prunus domestica
English Name	garden plum
Remark	no remarks
Size mature protein	91 aa
Sequence	itcgqvssnlapcinyvkgggavppaccngirvnlnlarttadrraacnclqslgsipg vnpnnaaalpgkcgvnvpykisastncatvk

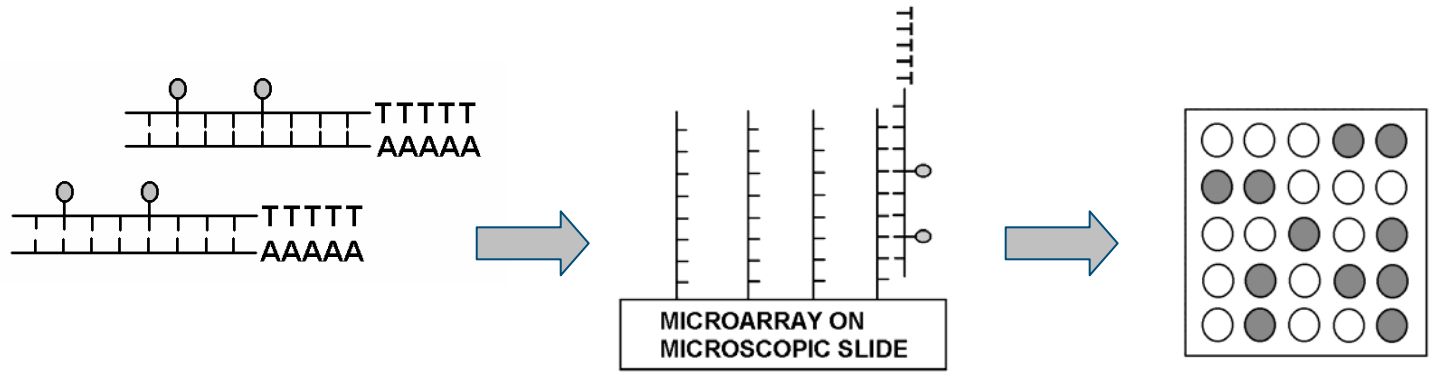
Input Sequence

The # denotes which parts of the input sequence have an exact 6 aa match against this specific database sequence

```
0 : aiscgqvsaaiapcisyargggggsagccsgvrslinnaarttadrraacnclknaaagv
0 : #####
60 : sglagnaasipskcgvsipyttiststdcervn
60 :
```

Research on GM food safety

mRNA profiling with microarrays



**Synthesize cDNA
from mRNA**

**Hybridize to
microarray**

**Hybridization
pattern**



Tomato gene expression during the subsequent stages



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Tomato illustration: E. Kok, MSc

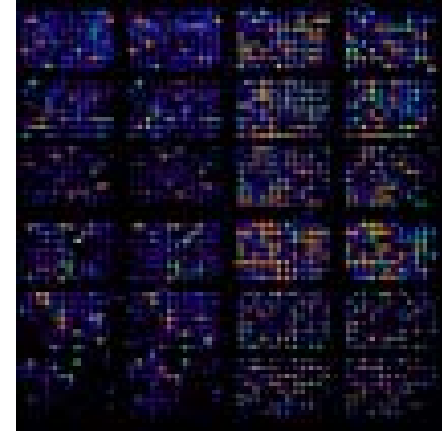
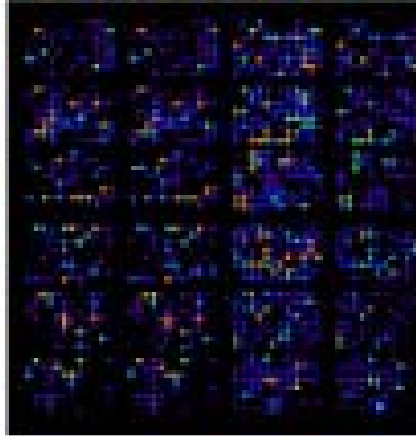
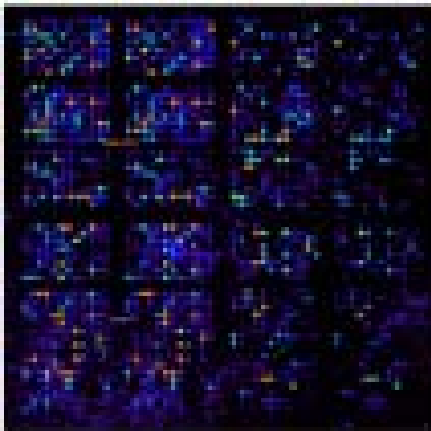
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Microarray analysis of tomato development

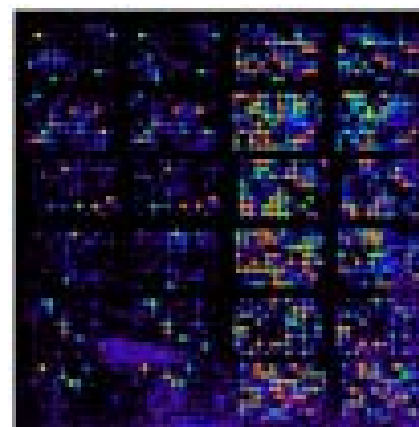
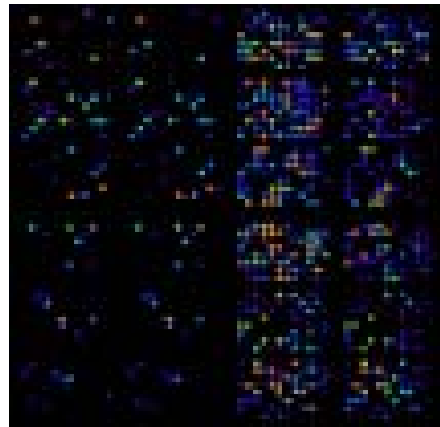
Green

Breaker

Turning



Light red



Red



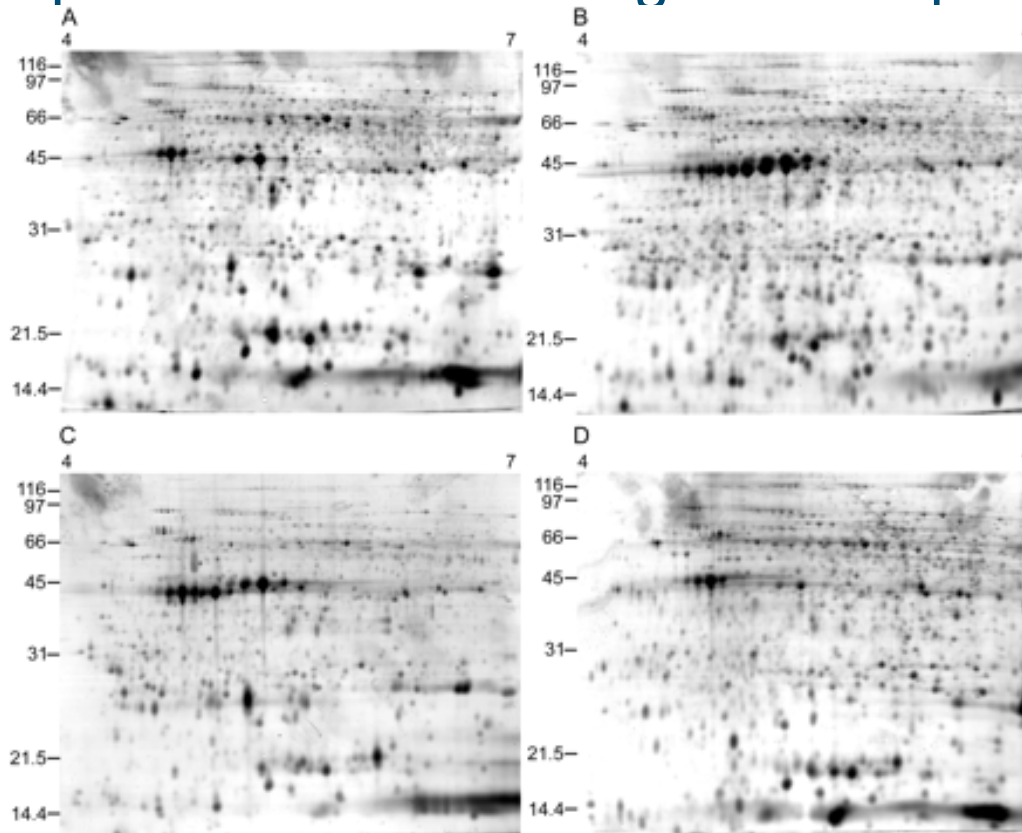
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Illustration: E. Kok, MSc

Research on GM food safety

Potato proteomics with 2-D gel electrophoresis

Cv. Désirée



Cv. Maris
Piper

Landrace

S. phureja

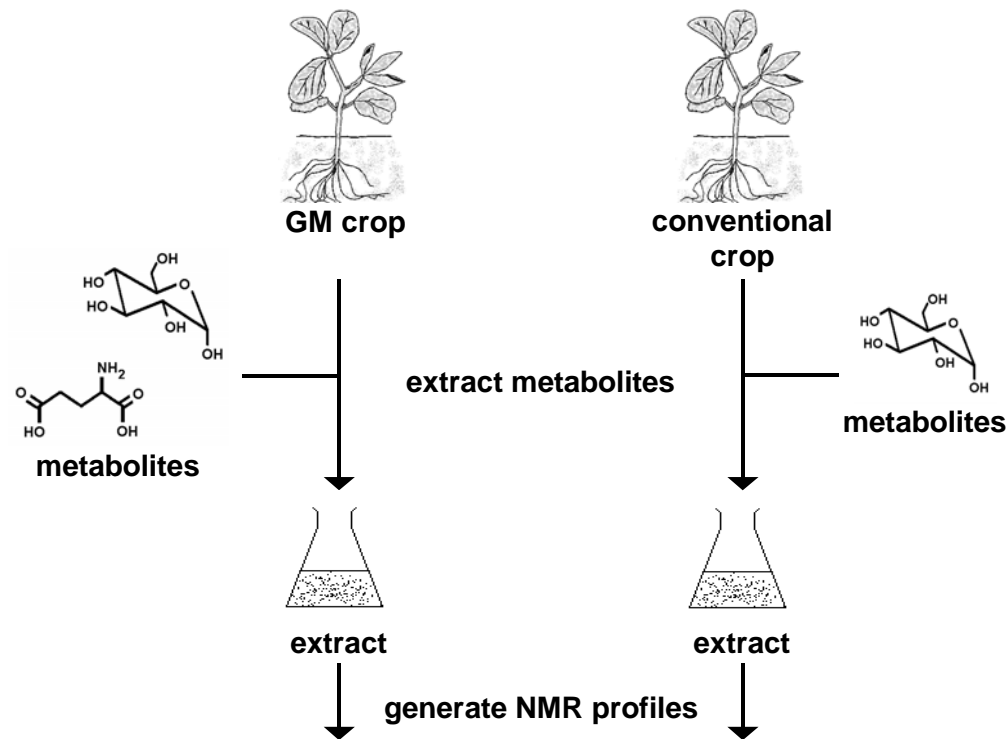
Lehesranta et al. (2005) Plant Physiology 138:1690-1699



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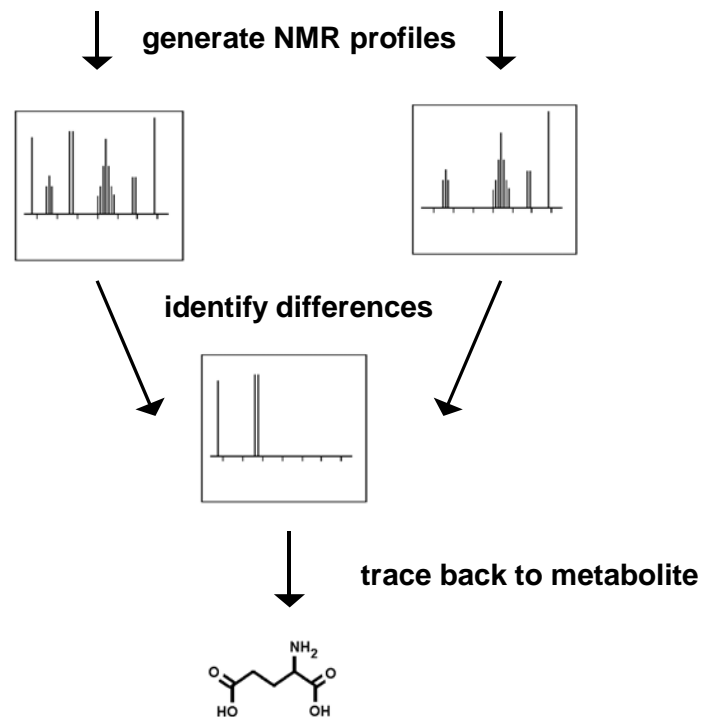
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Profiling using liquid-chromatography coupled to nuclear magnetic resonance (LC-NMR)

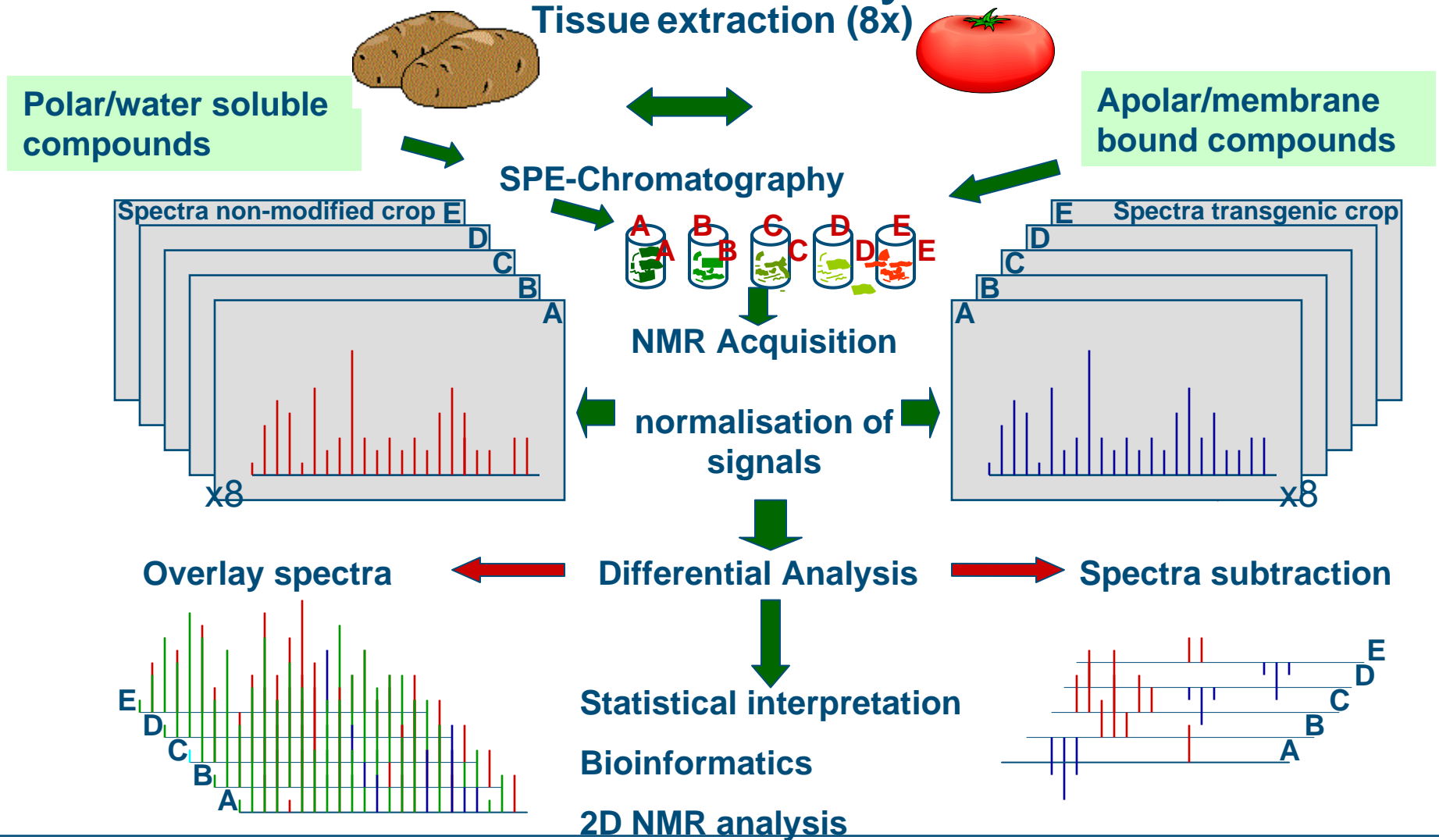


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Profiling using LC-NMR (continued)

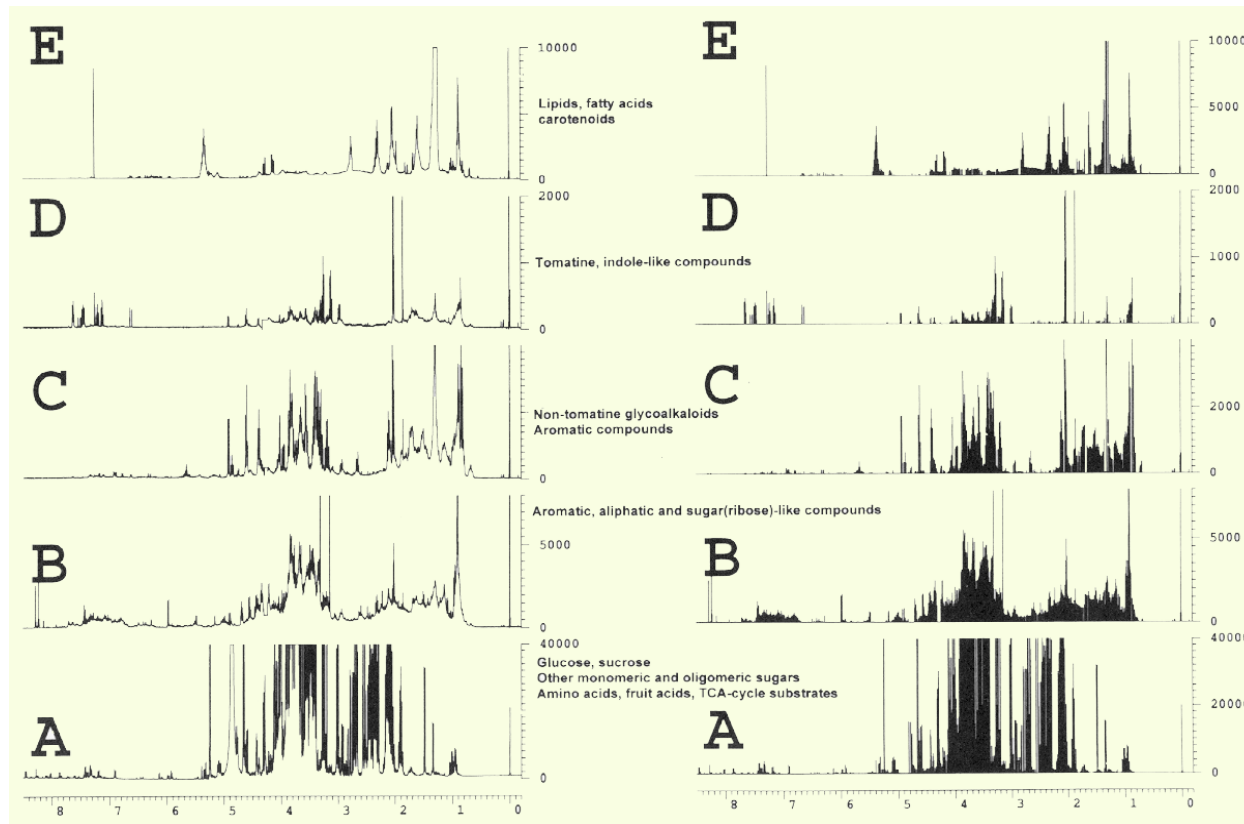


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Chemical fingerprinting with NMR

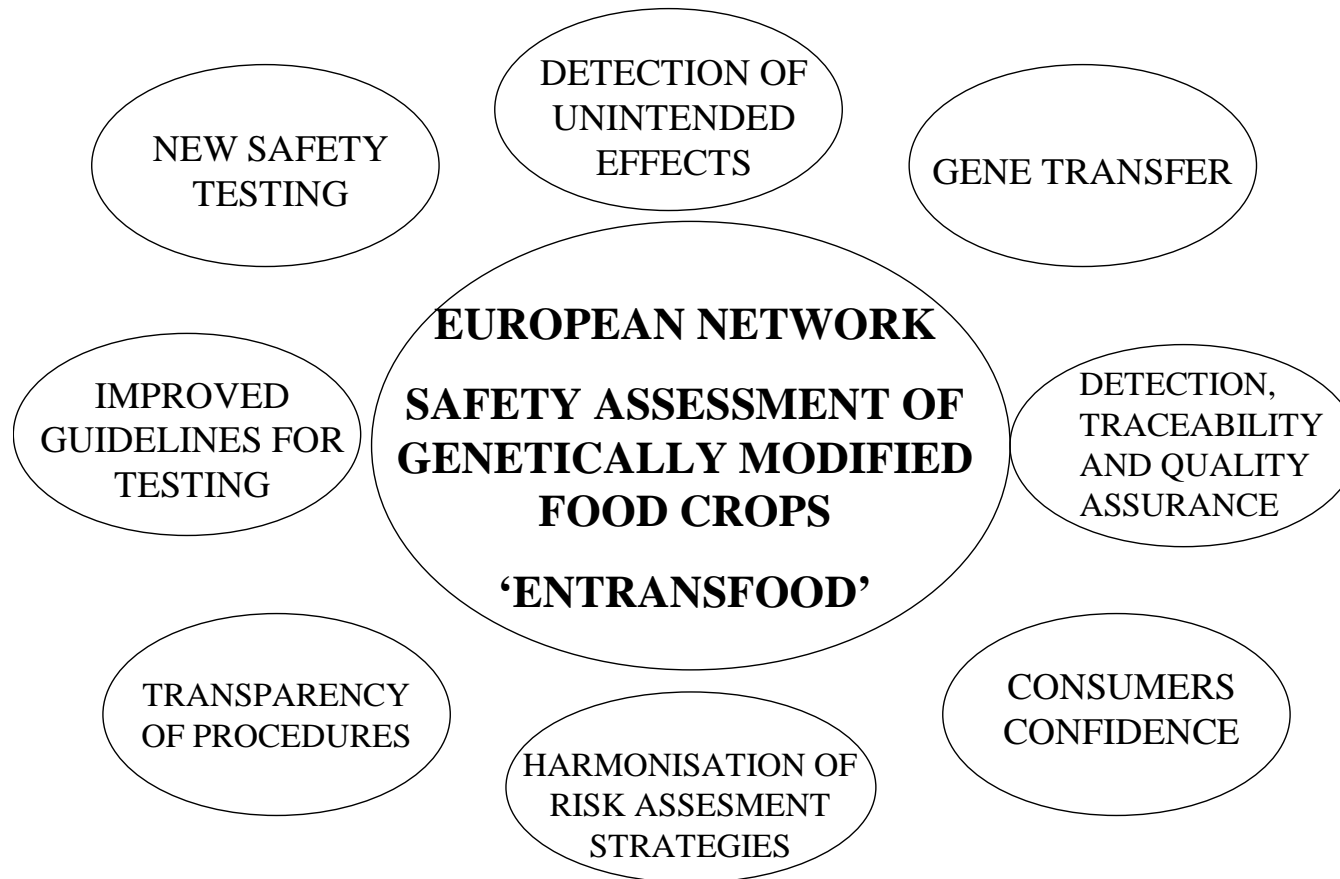


Antisense-exogalactanase RNA tomato (URL);
Noteborn et al. J. Biotechnology 77 (2000): 103-114



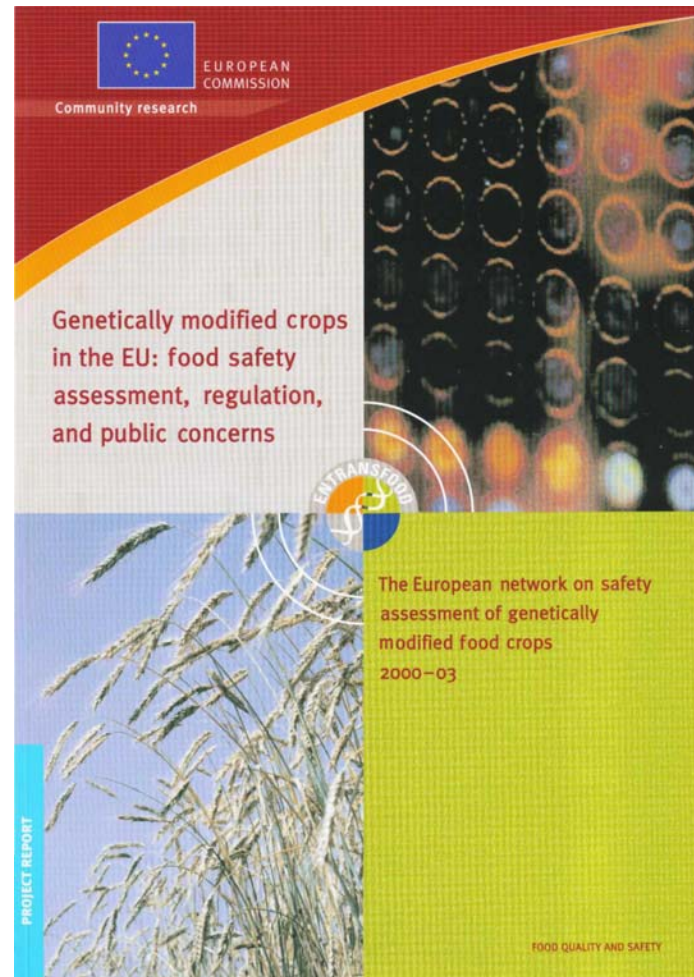
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ENTRANSFOOD (www.entransfood.com)



Research on GM food safety

ENTRANSFOOD Overarching report



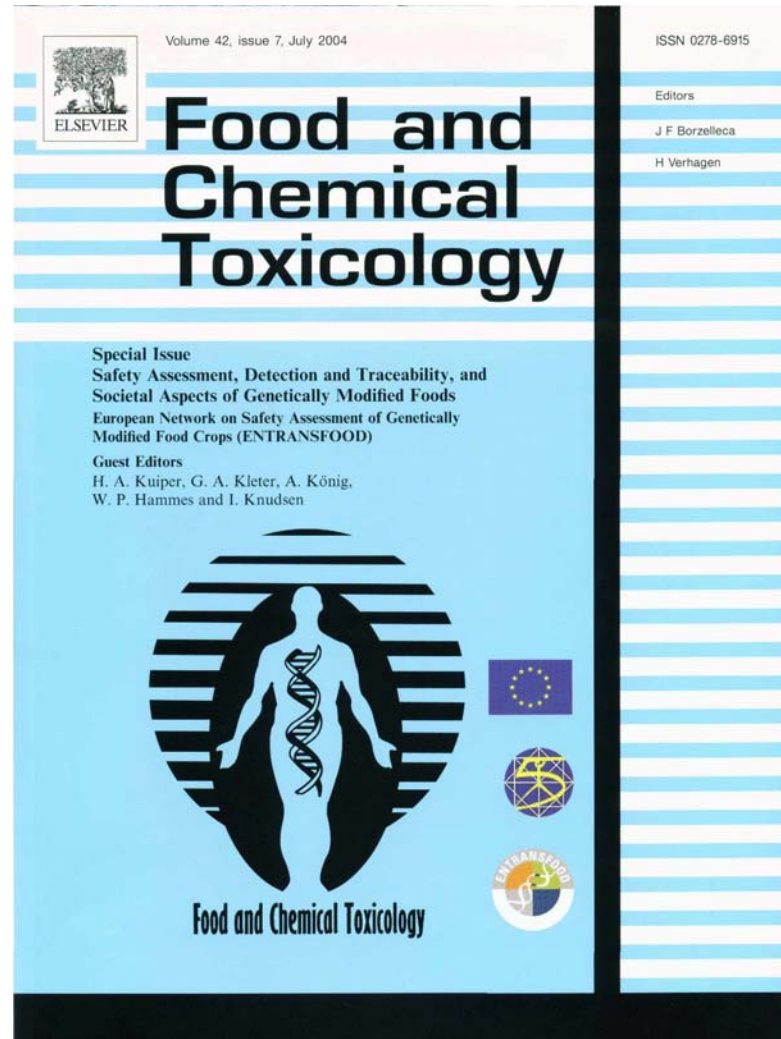
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ENTRANSFOOD

Special issue Food and
Chemical Toxicology

Send reprint requests to:
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Research on GM food safety

SAFE FOODS (www.safefoods.nl)

- "This Integrated Project addresses the issue of how consumer confidence in consumer protection and risk analysis can be restored and strengthened."
- Four-year project
- Kick-off meeting in May 2004

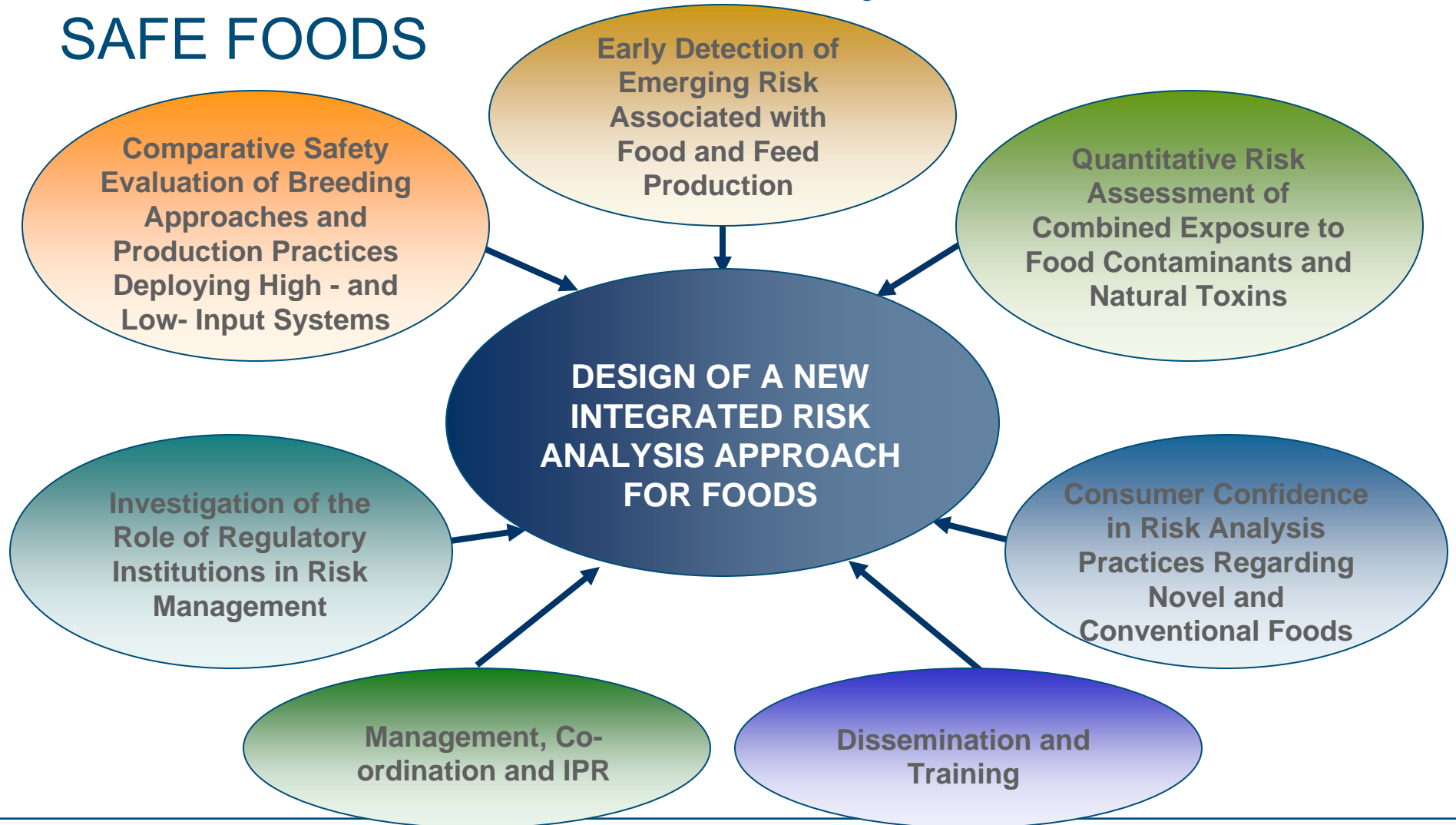


Illustration:

S. Bauer/ARS/K7242-20

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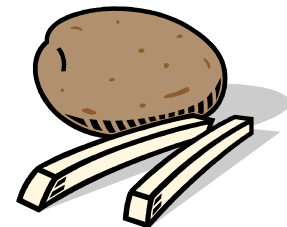
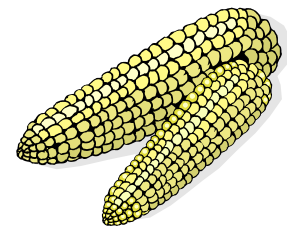
SAFE FOODS



Research on GM food safety

SAFE FOODS Work Package 1

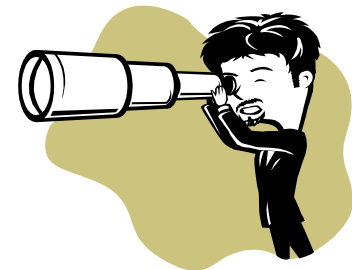
- Comparative evaluation of crops derived through different breeding practices and cultivated according to different agricultural practices
- Potato and maize
- Europe, Africa, and Asia
- Advanced profiling techniques
- Database on natural variation



Research on GM food safety

SAFE FOODS Work Package 2

- Emerging risks in the food and feed chain, high- or low-input agriculture
- Microbiological risks, mycotoxins and other chemical risks
- Framework for early risk identification
- Experts database
- Reviews and recommendations
- Training



Research on GM food safety

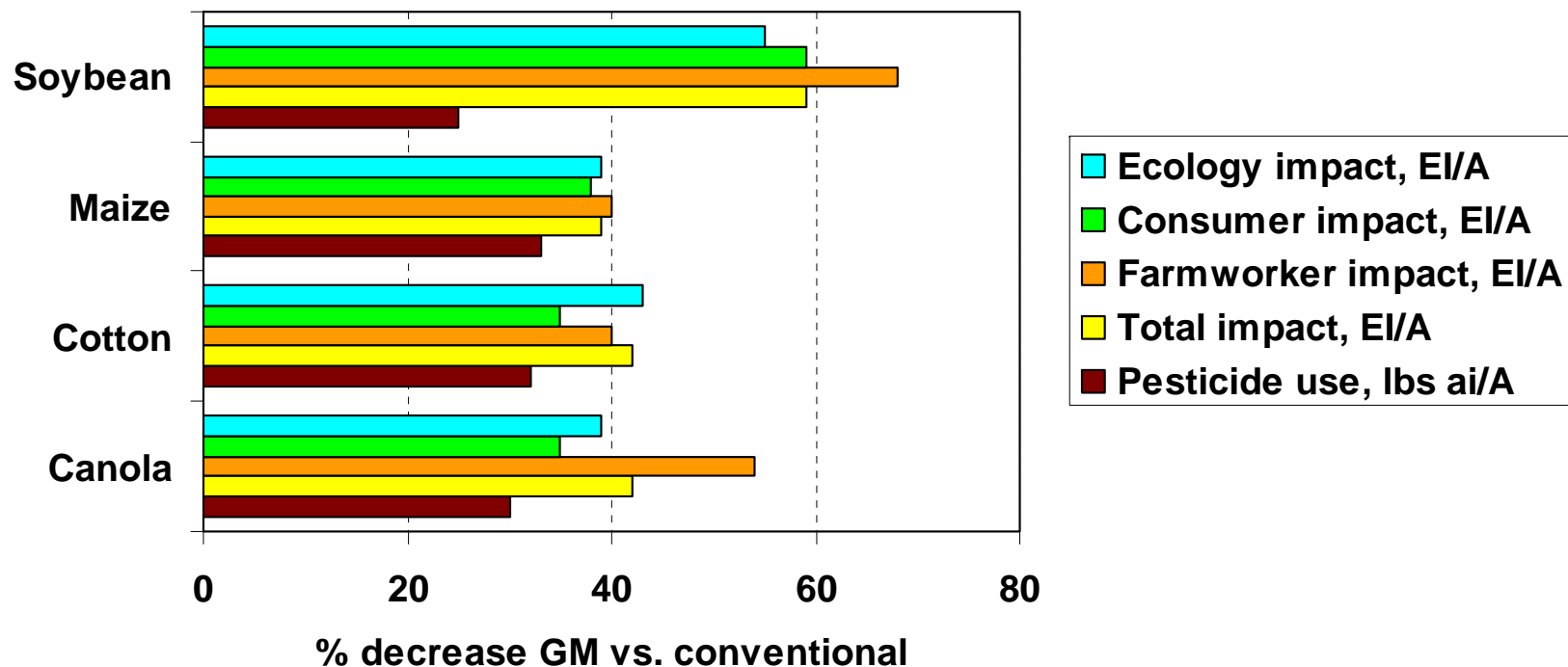
IUPAC Project on impact of pesticides used on GM crops

- Collect data on pesticide use
 - Various surveys, *e.g.* USDA, NCFAP
 - In general, decreased pesticide usage
- Predict environmental impact
 - Indicators such as EIQ
 - Apparent overall decrease in impact
- Consider risks and benefits



Research on GM food safety

IUPAC project: EIQ-methodology applied to HR crops in the US, 2004 (NCFAP data), % change



Conclusions

The new properties of GM crops that are currently on the market are mainly intended for agriculture

The safety assessment of GM foods and feed is based on harmonized international consensus

Research is done on advanced methods for the safety assessment of future crops (GM and conventional)



Acknowledgement

The contributions with materials on profiling of GM crops by the following persons are gratefully acknowledged:

Mrs. E.J. Kok, MSc (tomato microarray)

Dr. H.P.J.M. Noteborn (metabolomics)



Thank you for your attention

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