GMO Test Methods: Validation, Application and Training Options.

Dr Anne Bridges, November 2005

Consultant, AACC International

Acknowledgements

- **APEC / RDEAB**
- **ILSI International**
- **AACC International**
  (formerly American Association of Cereal Chemists)

Slides

- **Randy Giroux, Cargill**
- **Kim Magin Sutter, Monsanto**
- **Jim Stave, Strategic Diagnostics**
- **Clive James, ISAAA**
- **AEIC**

The 9th APEC/RDEAB Workshop
on Agricultural Biotechnology

Outline

- **Increase in Biotech hectares and distribution, associated regulatory challenges**
- **Supply chain testing**
- **Current status**
- **What are we testing?**
- **Validation – from sampling to reporting**
- **Challenges to trade**
- **ILSI International activities**
- **AACC International activities**

from ISAAA Briefs 32, 2004

Global Status of Biotech Crops in 2004

17 countries have adopted biotech crops

In 2004, global area of biotech crops was 81 million hectares, representing an increase of 20% over 2003, equivalent to 13.3 million hectares.

Source: Clive James, 2004 ISAAA Briefs 32

BIOTECH MEGA-COUNTRIES

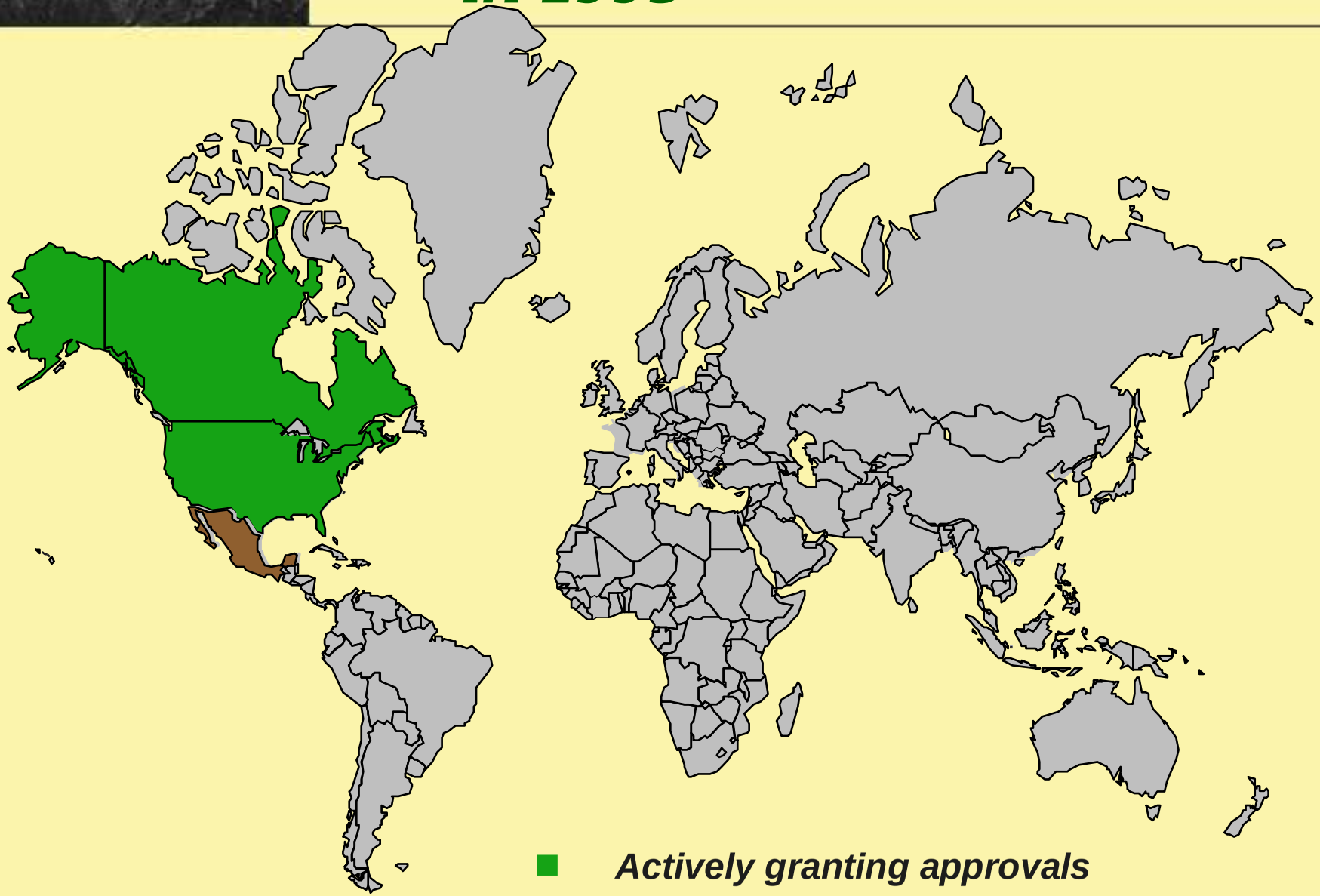
50,000 hectares or more

USA:	47.6 million
Argentina:	16.2 million
Canada:	5.4 million
Brazil:	5.0 million
China:	3.7 million
Paraguay:	1.2 million
India:	0.5 million
South Africa:	0.5 million
Uruguay:	0.3 million
Australia:	0.2 million
Romania:	0.1 million
Mexico:	0.1 million
Spain:	0.1 million
Philippines:	0.1 million

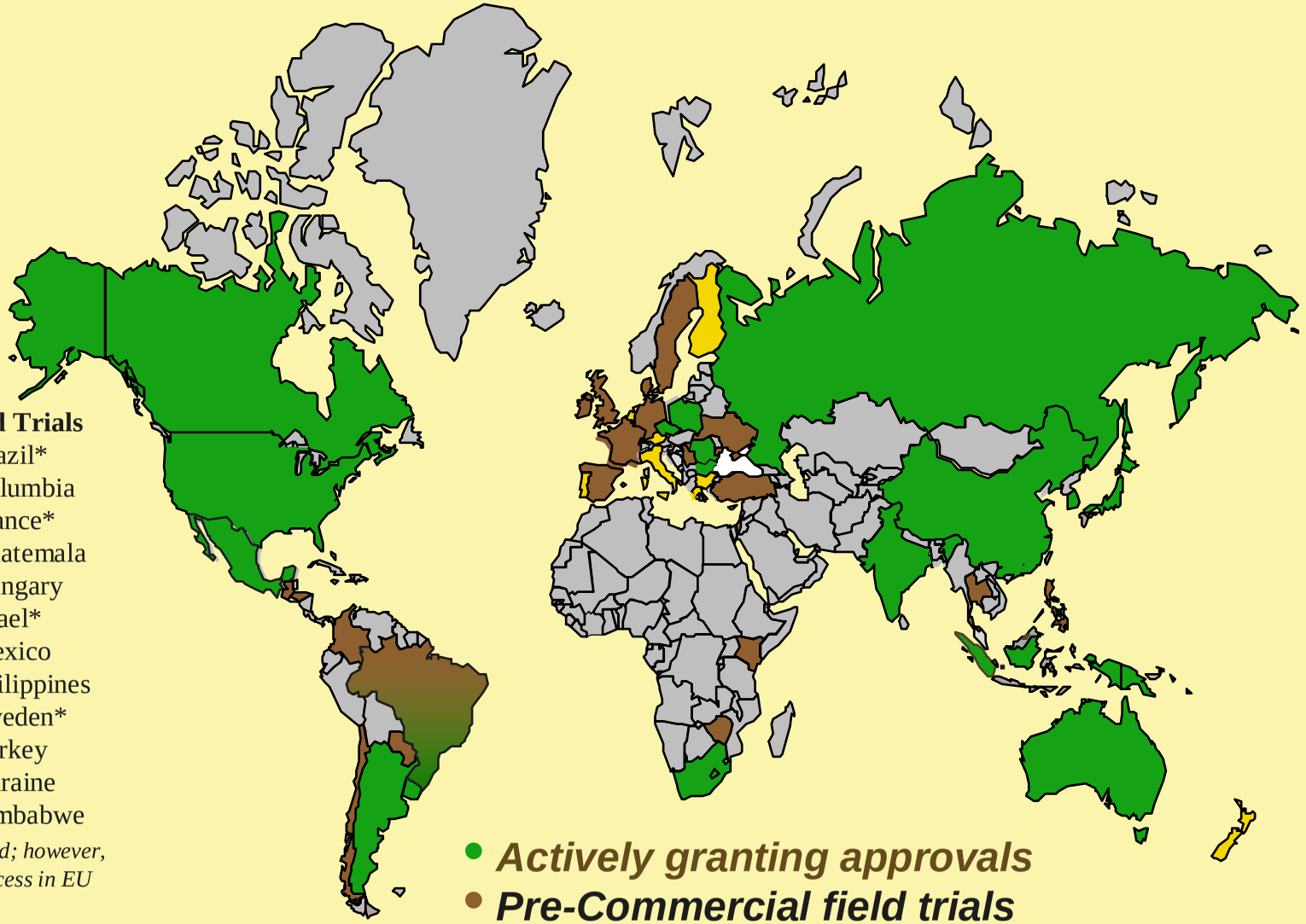
50,000 hectares or less

Colombia Honduras
Germany

Global Regulatory Situation in 1995



Global Regulatory Situation in 2002



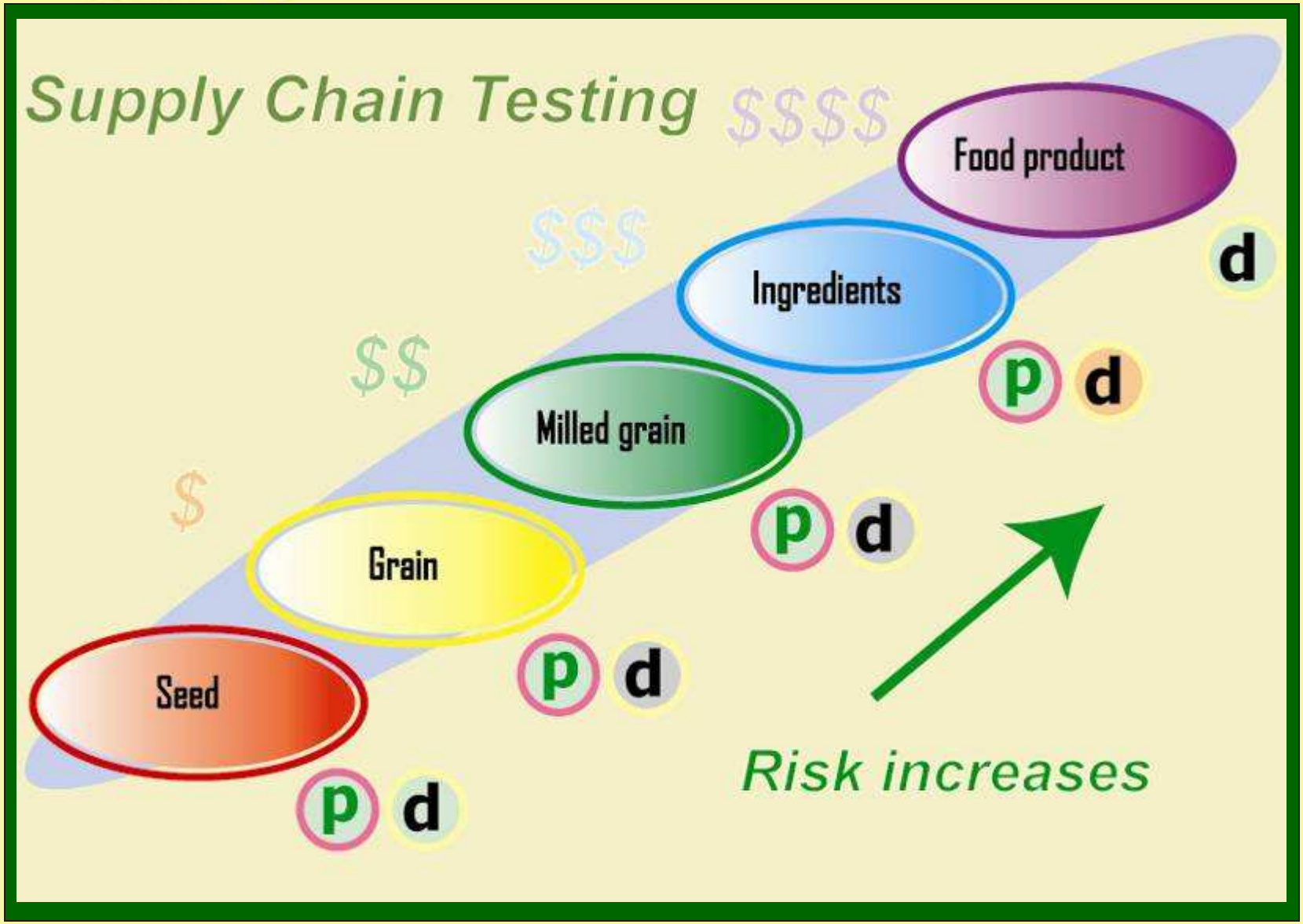
Conducting Field Trials

Belgium*	Brazil*
Chile	Columbia
Denmark*	France*
Germany*	Guatemala
Honduras	Hungary
Ireland	Israel*
Kenya	Mexico
Paraguay	Philippines
Spain*	Sweden*
Thailand	Turkey
UK*	Ukraine
Yugoslavia	Zimbabwe

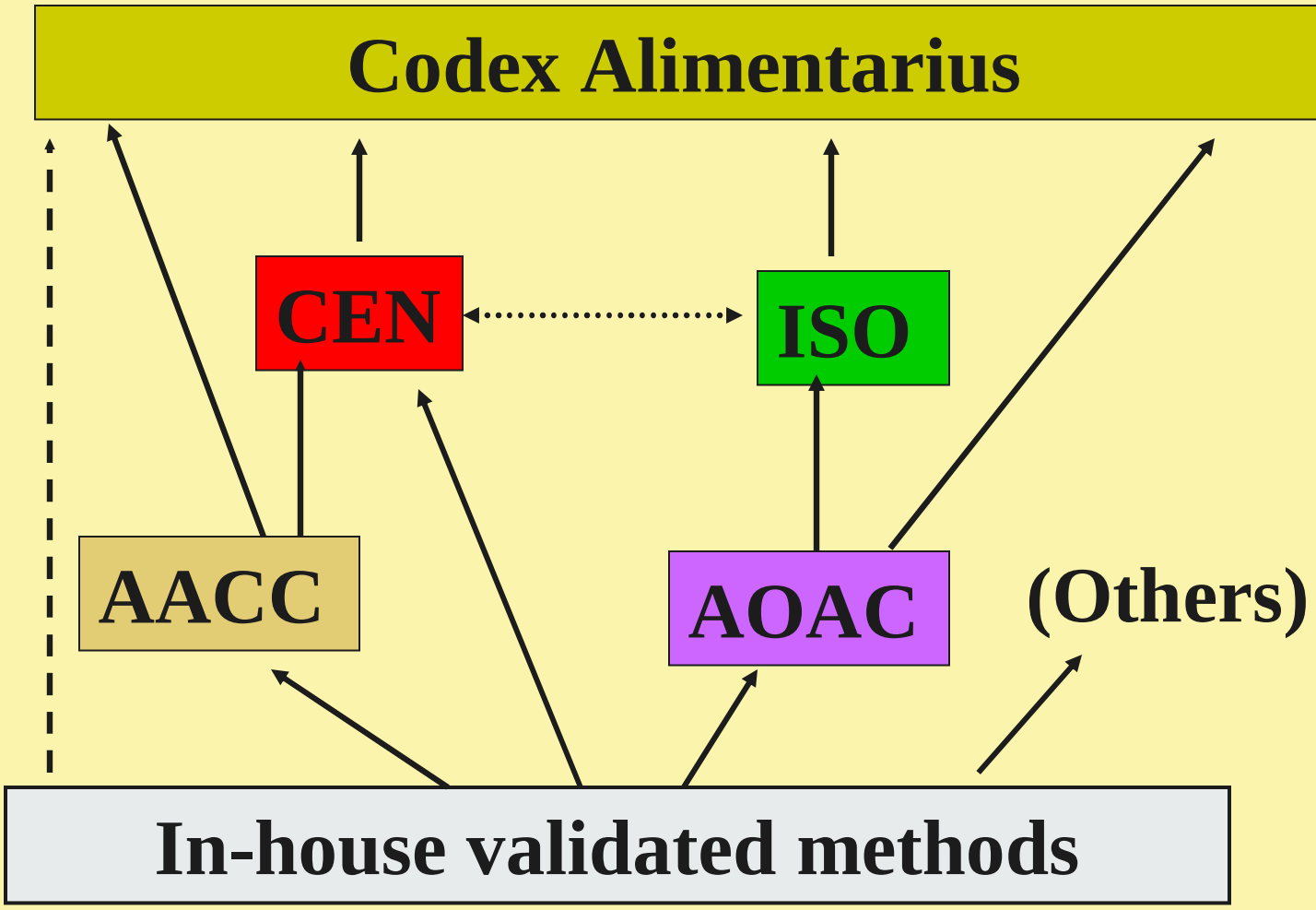
** Field trial approved; however, overall approval process in EU and Brazil is delayed*

- ***Actively granting approvals***
- ***Pre-Commercial field trials***
- ***Commercialisation delayed***

Testing along the Chain



Coordination of Standardisation Initiatives



The Issue

Need for standardised methods to test for Agbiotech products is multi-faceted:

- **Research and development**
- **Seed quality**
- **Adventitious presence in conventional seed**
- **Compliance with country specific thresholds for grain and food**
- **Testing for unapproved events**
- **Identity preservation and support of consumer choice labeling**

Detection Methods in Agbiotech Industry: State of the Art

- **No single method will detect all biotechnology-derived products**
- **Methods are product specific**
- **Lack of reference materials**

Detection Methods in Agbiotech Industry: State of the Art

Each method has natural applications and limitations

- **Some traits may not express a detectable protein in grain**
- **PCR is susceptible to contamination**
- **Antibodies may cross react**
- **Analysis time and cost are important considerations**

What is method validation?

"The process of establishing the performance characteristics and limitations of a method and the identification of influences which may change these characteristics and to what extent."

EURACHEM Guide

What is the goal of validating methods?

Methods are:

- **Sensitive, specific (LOD, LOQ)**
- **“Fit for purpose”**
- **Applicable**
- **Practical**

Test results are:

- **Accurate/precise**
- **Comparable, method to method**
- **Predictable, same results lab to lab**

International Guidelines Exist

ISO 5725 – International Standard for Validating a Method

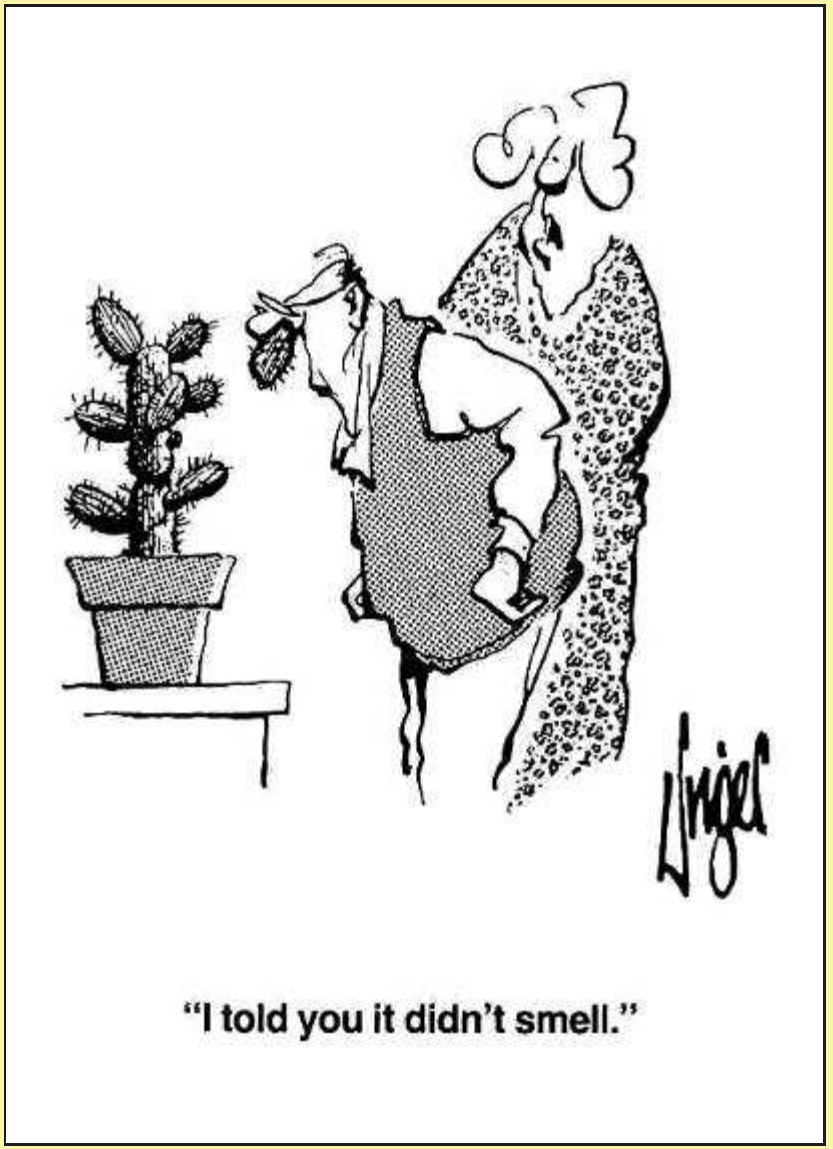
General principles and definitions

- Basic method for the determination of repeatability and reproducibility of a standard measurement method
- Intermediate measures of the precision of a standard measurement method.
- Basic methods for the determination of the trueness of a standard measurement method
- Alternative methods for the determination of the precision of a standard measurement method
- Use in practice of accuracy values
- Guidelines for the evaluation of conformity with specified requirements

Guidelines for AOAC, IUPAC, AACC International

Validation of Methods

- **Within a Laboratory**
- **Between Laboratories**
  "Approved Methods"
  AACC, AOAC, ISO,
  IUPAC etc
- **Proficiency testing**
  GIPSA



Methods scheduled for, or completed validation (April 2005)

- **Corn: MON810, Bt11, NK603, GA21, Mon863, T25, 1507, NK603 x MON 81, MON 863 x MON 810, Bt176, GA21 x MON810, NK603 x MON863, MON810 x MON 863 x NK603, 1507 x NK603, 59122, MIR604**
- **Rice: LLRICE62**
- **Canola: Ms8, Rf, Rf, Rf2, Ms1, Topas 19/2, T45, GT73, Ms1xRf1, Ms1xRf2, Ms8xRf3**
- **Cotton: MON 1445, MON 531, MON 531 x MON 1445, MON 15985 x MON 1445, MON 15985, LL25**
- **Sugar beet: RUR H7**
- **Potato: EH92-527-1**
- **Soy: 40-3-2**

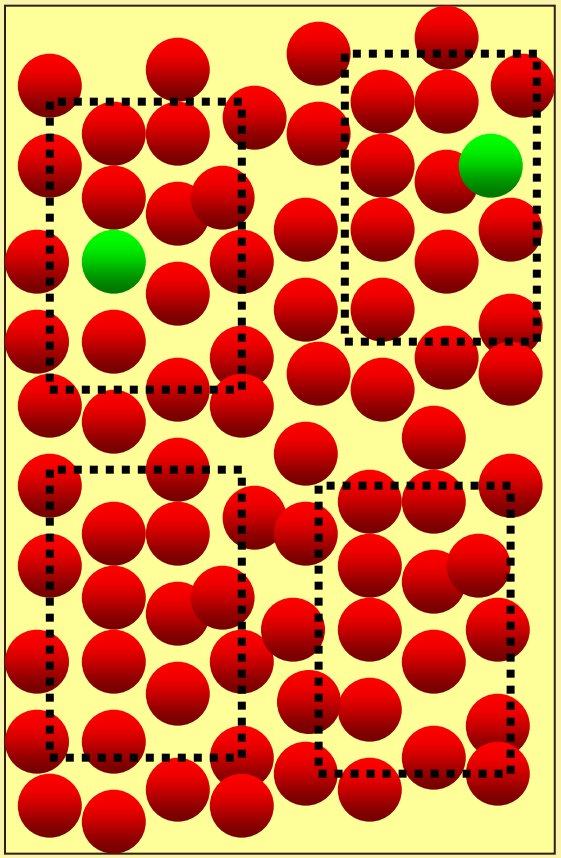
http://gmo-crl.jrc.it/statusofdoss.htm,
in red: validation finished

Methods submitted to ISO and/or Codex

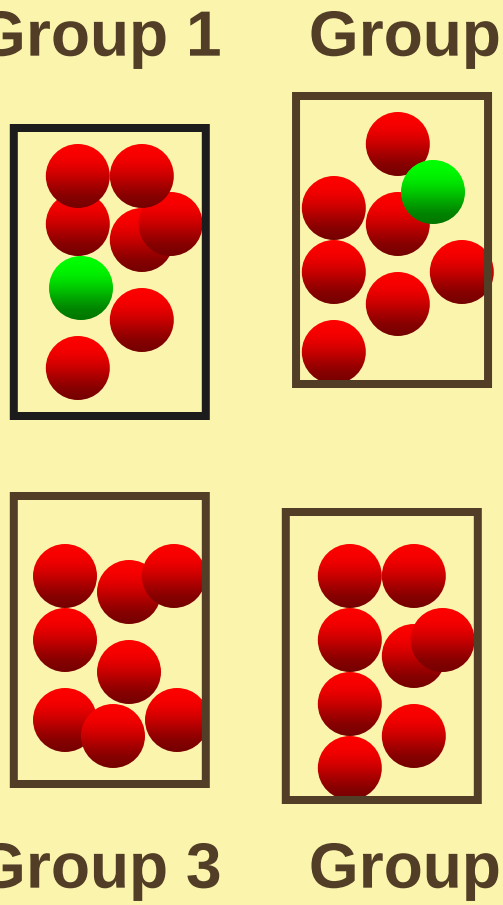
CODEX and ISO	Number of methods:				
	Total	Taxon	Screening	Events /construct	Protein
JRC/EU	6	1	3	1	1
Germany	19	6	1	12	0
Japan	22	2	0	20	0
Switzerland	3	1	1	1	0
USA	3	0	0	0	3
China	expected				

Historical data – more expected in the near future

Probability of Detecting 0.1% with 700 Bean Sample Size



3000 beans of <0.1%



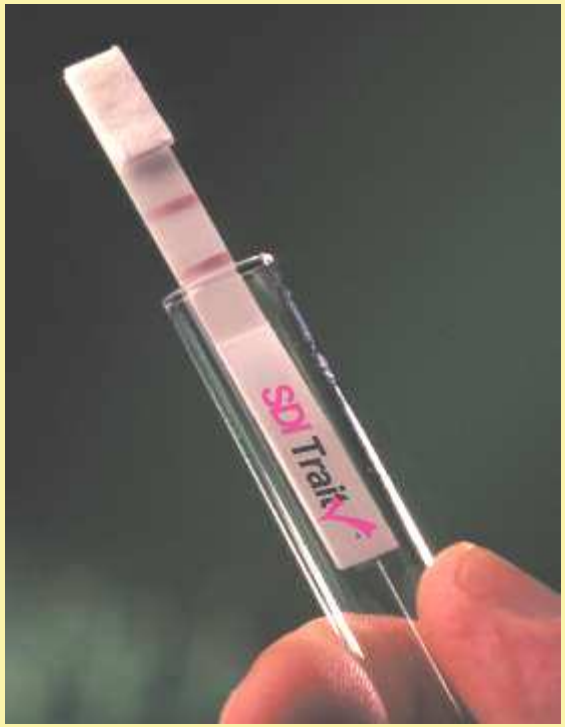
50%

4 samples of 700 beans

Tools for Measurement

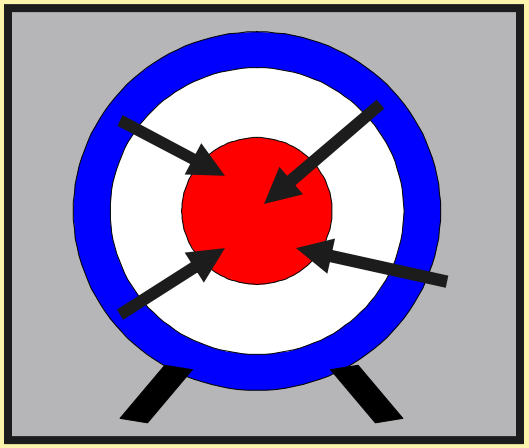
- **Methods of detection….**

  Protein, DNA
- **Harmonised methods, important to engage in international trade**

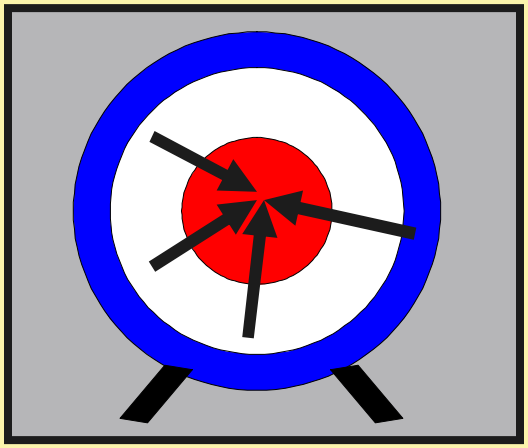


What are we testing?

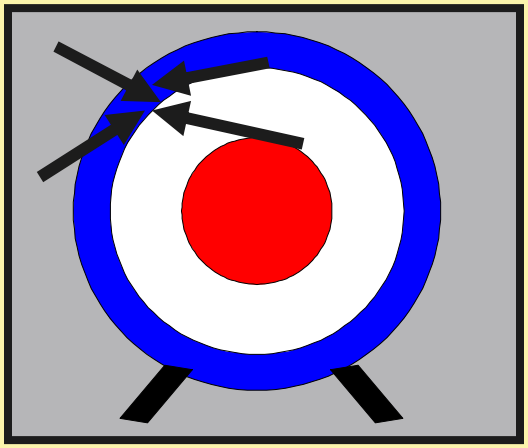
Accuracy and Precision



Accuracy



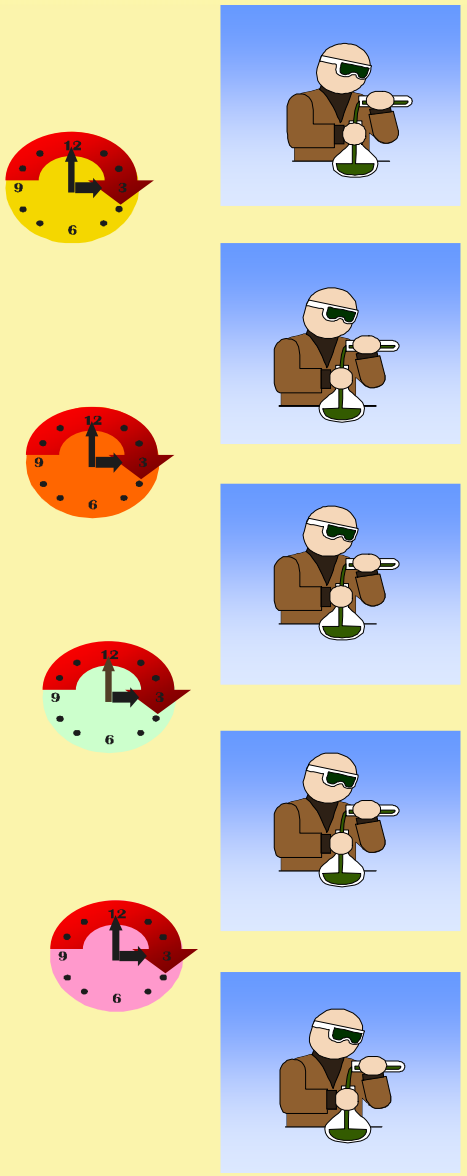
Accuracy and Precision



Precision

Repeatability of a method (r)

- **Variability within a lab**
- **Testing the precision under intra-lab conditions**
- **same method**



Reproducibility of a method (R)

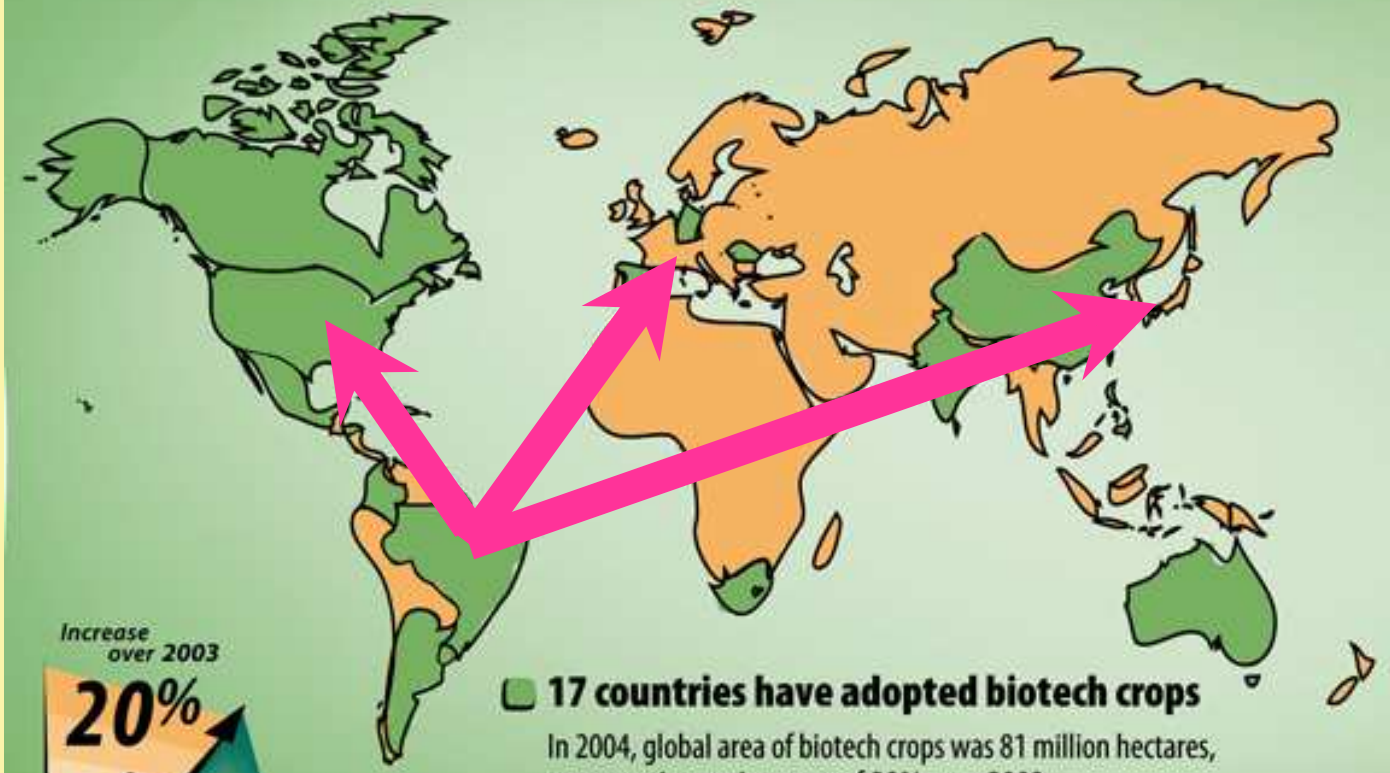
- **Testing the precision under reproducible conditions**
- **same method**

  different laboratories
- **preferably on international level rather than on national level**

CODEX puts emphasis on “fully-validated” methods through collaborative trials

Implications for Trade

Global Status of Biotech Crops in 2004



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Source: Clive James, 2004 ISAAA Briefs 32

Consistent Result for a Product Through the Supply Chain

- **IP chain test results must be consistent with regulatory compliance test results**
- **Methods applied by third-party labs must be consistent to reduce risks of failure**
- **Test methods must be applicable to changes in the material composition as it moves through the chain**

What is the status of detection method performance initiatives?

- **Several initiatives underway to study the performance of GM test methods**
- **Number of organisations working towards standardisation and harmonisation at both national and international levels**

Recognition that all methods are NOT created equal

- **Test providers need to recognise that kits have limitations and need to validate each part and then the sum of the parts**
- **Validating each step individually may not be appropriate for DNA-based test methods**
- **Need international standardisation of the reference materials to be used with test methods**
- **Are grain reference materials appropriate for finished foods?**

Regulations – limits of methods

- **Recognize the variability that exists in a final test result for finished foods and act appropriately**
- **If there are enforcement limits and policies, they need to reflect test variability and imprecision**

ILSI - International Life Sciences Institute

Founded in 1978, the International Life Sciences Institute (ILSI) is a nonprofit, worldwide foundation that seeks to improve the well-being of the general public through the pursuit of balanced science.

Goal is to promote the understanding of science relating to nutrition, food safety, toxicology, risk assessment, and the environment

- by bringing together scientists from academia, government, and industry.

ILSI receives financial support from industry, government, and foundations.

ILSI International Food Biotechnology Committee (IFBiC)

www.ilsi.org

IFBiC

- Formed in 1998 to address gaps in the science regarding safety of foods and feeds derived from biotech crops
- Comprised of 13 food, feed, and biotech companies

Core Projects

- Outreach activities with a focus on training and education

Task Forces

- Focus on addressing current / future science gaps
- Supported by at least five committee members

IFBiC Core Projects

- Supported by all IFBiC Committee Members
- Harmonization and Capacity Building on food / feed safety assessment in Asia, Latin America, and Africa
- Workshops on Sampling and Detection Methods
- Workshops on Applications of Plant Biotechnology to Nutritional Needs in Developing Countries
- Global Resource Guide

IFBiC Core Projects
Harmonization / Capacity Building

Workshops in Southeast Asia

- Four workshops at the request of the Association of Southeast Asian Nations (ASEAN) 2001-2004 (Singapore, Malaysia, Thailand, and Indonesia)
- Government-to-government training sessions for regulatory decision makers
- Collaborative effort: IFBiC, ILSI SE Asia, ASEAN, Agri-food Veterinary Authority (AVA), Health Canada, and the Food Standards Australia New Zealand (FSANZ)

Workshop in Central America

- June 2004 - Mexico City with Health Canada and U.S. FDA for Mexican Ministry of Health and other regulators

IFBiC Core Projects
Workshops: Latin American / Caribbean Region

- 3-year program of workshops for 25 countries, proposed by OAS, includes USDA-APHIS, ILSI, AgBios, ISAAA, ABSP, ISNAR, CFIA, etc.
  - Capacity-building and training programs in risk assessment of biotechnology-derived foods
  - To disseminate scientific information to government, industry, and academia
  - To promote networking and the development of communication mechanisms
- 1st Workshop - September 2004, Panama City Collaboration with Health Canada and local regulatory experts
- 2nd Workshop - April 18-22, 2005, in Caracas, Venezuela, on analytical methods

IFBiC Core Projects
Program for Biosafety Systems (PBS)

- To address biosafety within a sustainable development strategy, anchored by agriculture-led economic growth, trade, environmental, and food safety issues
- Coordinated by Intl. Food Policy Research Institute (IFPRI)
- Consortium
  - IFPRI, ILSI, Donald Danforth Plant Sciences Center, Michigan State University, New Agri-Tech Strategies, national and sub-regional partner organizations, and CGIAR centers
- IFBiC helps organize 4 workshops on food / feed safety in Asia and Africa in 2005
- Collaboration with Health Canada, Food Safety Australia New Zealand (FSANZ), U.S. Food and Drug Organization (FDA), academic and local regulatory experts

IFBiC Core Projects
Sampling and Detection Methods

Workshops contain theoretical and hands-on training modules

- Collaborative effort among IFBiC, ILSI branches, the EU Joint Research Centre (JRC), the American Association of Cereal Chemists (AACC), and local governments
- Requested by ILSI branches / local governments
- Brazil and Argentina (September 2002)
- India -- two workshops (October 2003)
- Hungary, with FAO and WHO; prior to the Codex Committee on Methods of Analysis and Sampling (CCMAS) (March 2004)
- China (December 2005)

Participated in International Workshop on Detection Methods for Genetically Modified Organisms, Yokohama, Japan (November 2004)

Harmonization of Detection Methods for Products Derived from Modern Biotechnology within NAFTA Countries

Approach

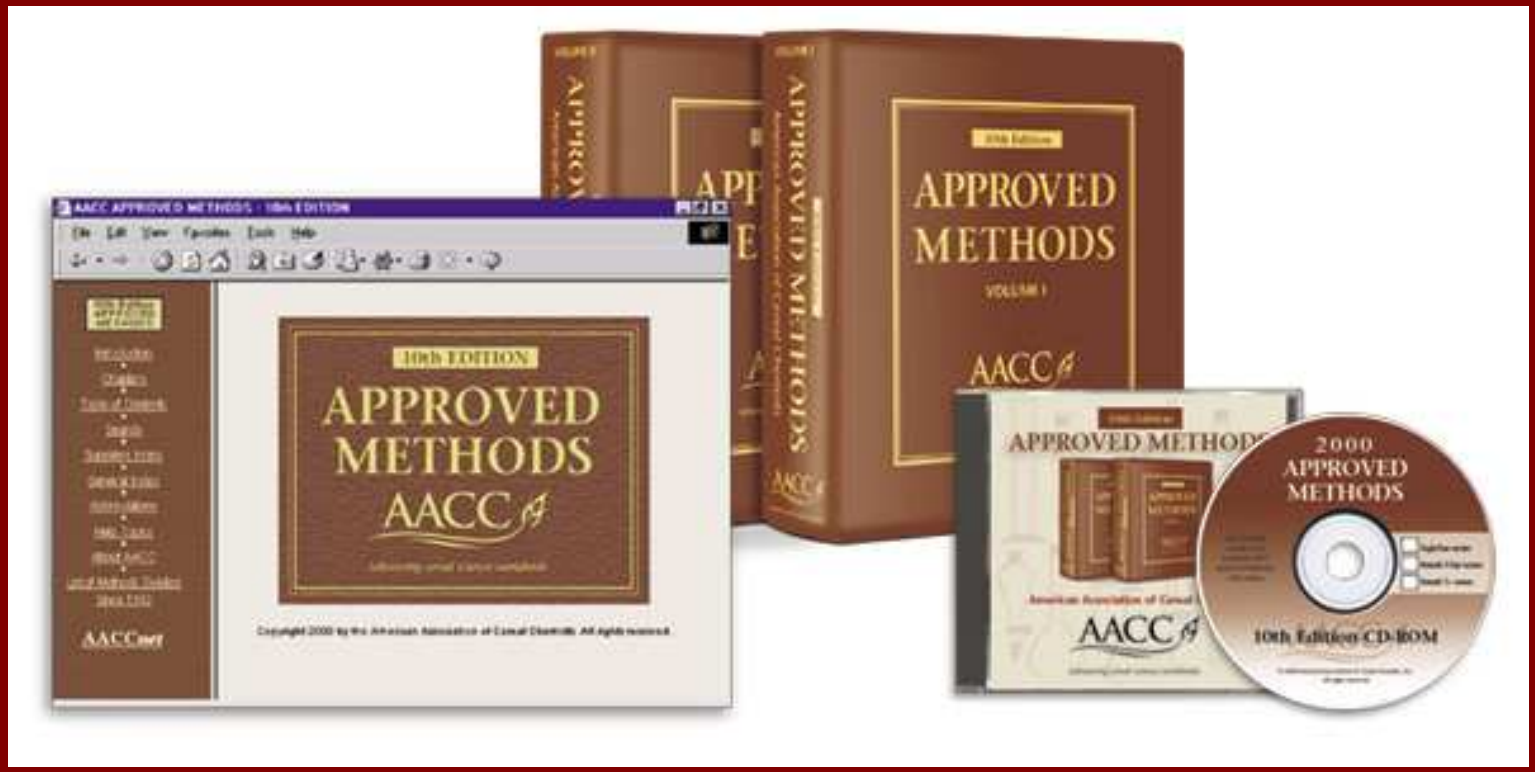
- Prepare a document that summarizes
  - the “state of affairs” for GM-method approaches and validation and the current efforts and initiatives
  - current and pending country policies on detection methods
- Communicate with regulatory agencies
  - The contents of the document and raise awareness of the global activities underway on GM method harmonization and validation
  - Clarify individual regulatory agency approaches and strategies on detection methods
  - Encourage information sharing across agencies
- Conduct a workshop with NAFTA regulators to develop consensus, where possible

IFBiC: Going Forward

- Continue providing science-based information on food safety and safety assessment, especially for products derived using new technologies
- Provide training and support capacity building in food safety assessment
- Address science gaps in the safety assessment for agricultural biotechnology products
- Build scientific basis for evaluating second generation biotech products
- Build enhanced synergies between food and biotech companies; food safety experts, nutritionists and biotech experts

www.aaccnet.org

AACC Approved Methods



Summary

- **Testing needs to be effective, consistent, and predictable along the supply chain to satisfy commercial IP and/or traceability requirements**
- **Test method developers need to validate methods using internationally acceptable approaches, to demonstrate they are “fit for purpose” and transferable to practical testing environments**
- **The testing marketplace for Agbiotech products needs standards and standardisation**
- **Testing thresholds need to be appropriate based on the sampling and test precision needs**

www.fao.org

FAOBioDeC
Biotechnologies in Developing Countries

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It is possible to search **records** using a combination of fields to be selected and terms searched within them. Relationships of AND, OR and AND NOT can also be specified between the fields.

Search Clear

Products / technologies: GMOs
Trait / technique: Herbicide resistance
Sub trait / sub technique description:
Species description:
Country/Territory: China
Region: All:
Status: All:

Sort results by: Species
Field Connector: AND
Maximum number of records: 50 100 200

Search Clear

http://usbiotechreg.nbii.gov/

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Search the U.S. Database of Completed Regulatory Agency Reviews

This database contains information on genetically engineered crop plants intended for food or feed that have completed all recommended or required reviews for planting, food, or feed use in the United States. This database will be updated regularly. The overall content and scope of the database may change in the future to ensure that the database continues to meet user needs.

Product Search

Common Name:	Chickory Corn Cotton
Scientific Name:	Oryza sativa Solanum tuberosum Zea mays
Trait Category:	None Pest Resistance Insect Resistance
Applicant:	BASF

www.agbios.com

agbios :: GM Database

:: Information on GM Approved Products

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:: Query Page

- New database query

:: Product Related Info

Documents

1. Cotton biology facts
2. Product summary prepared by Monsanto

Figures

3. Plasmid map of PV-GHBK04

:: Synopsis

- Overview of all products in database

:: Recent Updates

Canada, US: changes since January 1, 2002.

1. 15985- Insect resistance Cotton
2. X81359- Herbicide tolerance Sunflower
3. Vector 21-41- Plant quality Tobacco
4. LLCotton25- Glufosinate Cotton
5. MON863- Insect resistance Maize
6. GT200- Herbicide tolerance Argentine Canola
7. HCN92- Glufosinate Argentine Canola
8. MS1, RF1 =>PGS1- Herbicide tolerance + fertility Argentine Canola
9. MS1, RF2 =>PGS2- Herbicide tolerance + fertility Argentine Canola
10. TC1507- Herbicide tolerance + insect

:: Database Product Description

Show full record | Print this page

MON-ØØ531-6, MON-ØØ757-7 (MON531/757/1076)

Host Organism / Variety	*Gossypium hirsutum* L. (Cotton) Bollgard®
Trait	Resistance to lepidopteran pests including, but not limited to, cotton bollworm, pink bollworm, tobacco budworm.
Trait Introduction Method	*Agrobacterium tumefaciens*-mediated plant transformation.
Proposed Use	Production of cotton for fibre, cottonseed and cottonseed meal for livestock feed, and cottonseed oil for human consumption.
Company Information	Monsanto Company

:: Summary of Regulatory Approvals

Country	Environment	Food and/or Feed	Food	Feed	Marketing
Argentina	1998		1998	1998	
Australia	1996		1996	1996	
Canada			1996	1996	
China	1997		1997	1997	
India	2002				
Japan	1997		1997	1997	
Mexico	1997		1997	1997	
South Africa	1997		1997	1997	
United States	1995	1995			

Click on the country name for country-specific contact and regulatory information.

Notes

http://biotech.jrc.it/

Biotechnology & GMOs Information Website

EUROPEAN COMMISSION
DIRECTORATE GENERAL
Joint Research Centre
ihcp

Deliberate releases and placing on the EU market of Genetically Modified Organisms (GMOs)

The purpose of this web site, managed by the Joint Research Centre of the European Commission on behalf of the Directorate General for the Environment is to publish information and to receive comments from the public regarding notifications about deliberate field trials and placing on the market of genetically modified organisms, as defined in Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001.

- Click here for more information.
- Visit the Biotechnology and GMOs Unit website.
- Links

KEEP YOU INFORMED!
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Deliberate release into the environment of GMOs for any other purposes than placing on the market		Placing on the market of GMOs as or in products
Plants	Organisms other than plants	All products
		
Browse notifications	Browse notifications	Browse and comment
Download the SNIF application form in Word or RTF format	Download the SNIF application form in Word or RTF format	
List of Main Traits	List of Main Traits	

Contact the Webmaster

www.foodstandards.gov.au

FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

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- Bovine Spongiform Encephalopathy (BSE)
- Caffeine
- Folate
- Food additives
- Food irradiation
- Food labelling
- Food Safety Information

FSANZ Home > What's in Food > GM Foods > GM Current Applications and Approvals

Current Applications and Approvals

(Updated March 2004)

All applications for genetically modified food must be assessed on a case-by-case basis by FSANZ. The assessment report for each application is available by clicking on the link below.

Genetically modified foods and their approval status (in chronological order)

.	Product	Application Number	Proponent	Status
SOYBEAN	Glyphosate tolerant soybean	A338	Monsanto Australia	Approved 2000
.	High oleic acid soybeans	A387	Du Pont	Approved 2000
.	Glufosinate ammonium tolerant soy	A481	Bayer Crop Science	Approved 2004
CANOLA	Glyphosate tolerant canola GT73	A363	Monsanto Australia	Approved 2000