Food Safety

an essential public health priority

建立基因改造食品科學性風險評估體系

國家科學委員會
第161次會議
92.7.9

高文彥博士
高級研究員
行政院衛生署食品衛生處

Food safety initiative
World Health Organization

基因改造食品安全嗎?

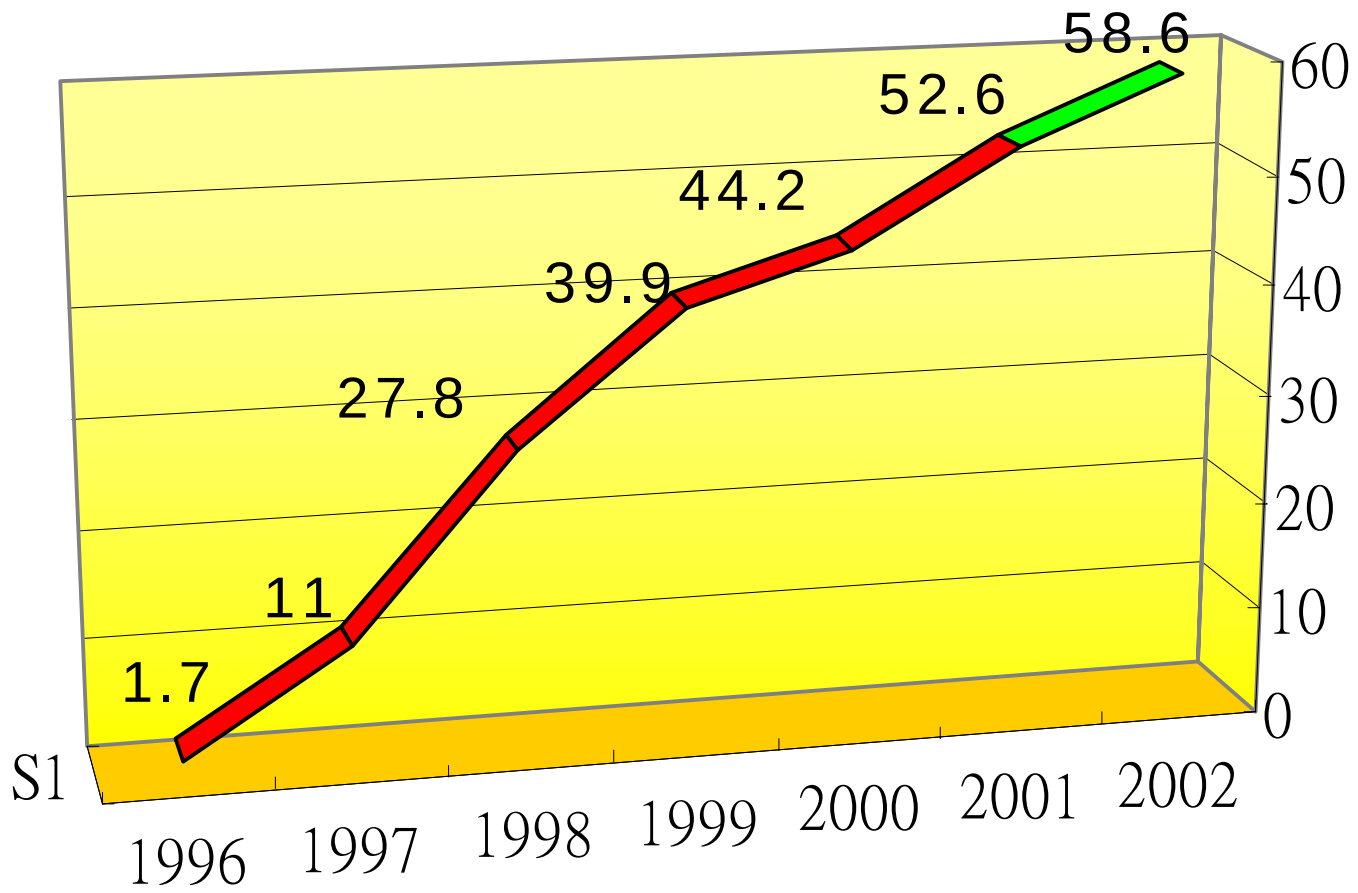
世界衛生組織(WHO):

GM foods currently available on the international market have passed risk assessments and are not likely to present risks for human health.

現今國際市場上的基因改造食品均已通過安全風險評估，不大可能會對人體健康導致危害。

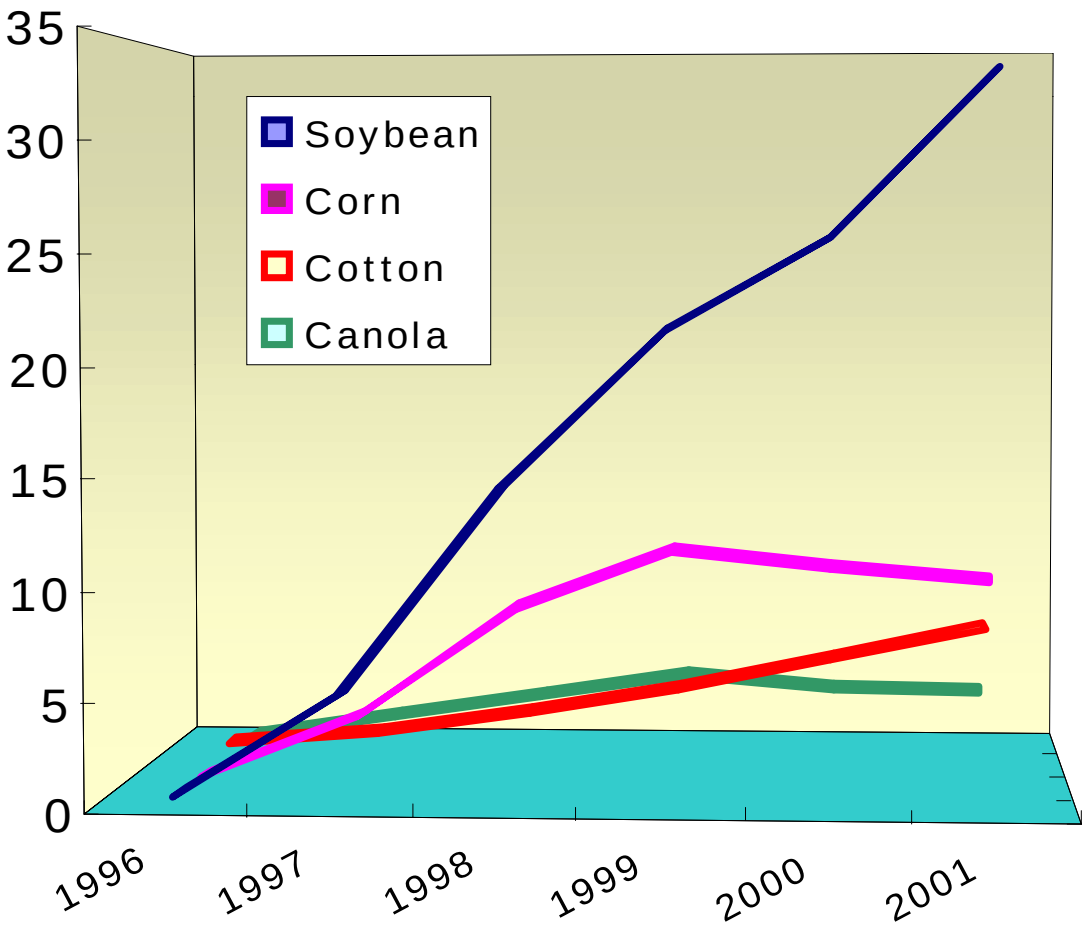
- 2002年10月15日“基因改造食品常見問答20題” http://www.who.int/fsf/

全球生產面積快速增加...



（百萬公頃）

GM作物 - 四大生產作物



36.5 大豆

12.4 玉米

6.8 棉花

3.0 油菜

（百萬公頃）

耐農藥/抗蟲能力（第一代）

Bt抗蟲
玉米

傳統
玉米

Source: Monsanto

(Input Traits)

改變營養組成（第二代）

黃金米可以防治維生素A缺乏症
成為健康食品

(Output Traits)

生產醫藥與工業用（第三代）

(Output Traits)

［複製人! 和我有什麼關係］陳文君著 泛亞 2001

基因改造動物

由台灣動物科技研究所研究成功的複製豬「酷比三號」，八日在第三屆台灣國際生物科技大展記者會中亮相。

「酷比三號」是全球第一例雙基因轉殖複製豬。

(中央社記者鄭傑文攝91.8.8)

簡介

GM作物產品的開發過程

發現與單離有用基因

基因工程

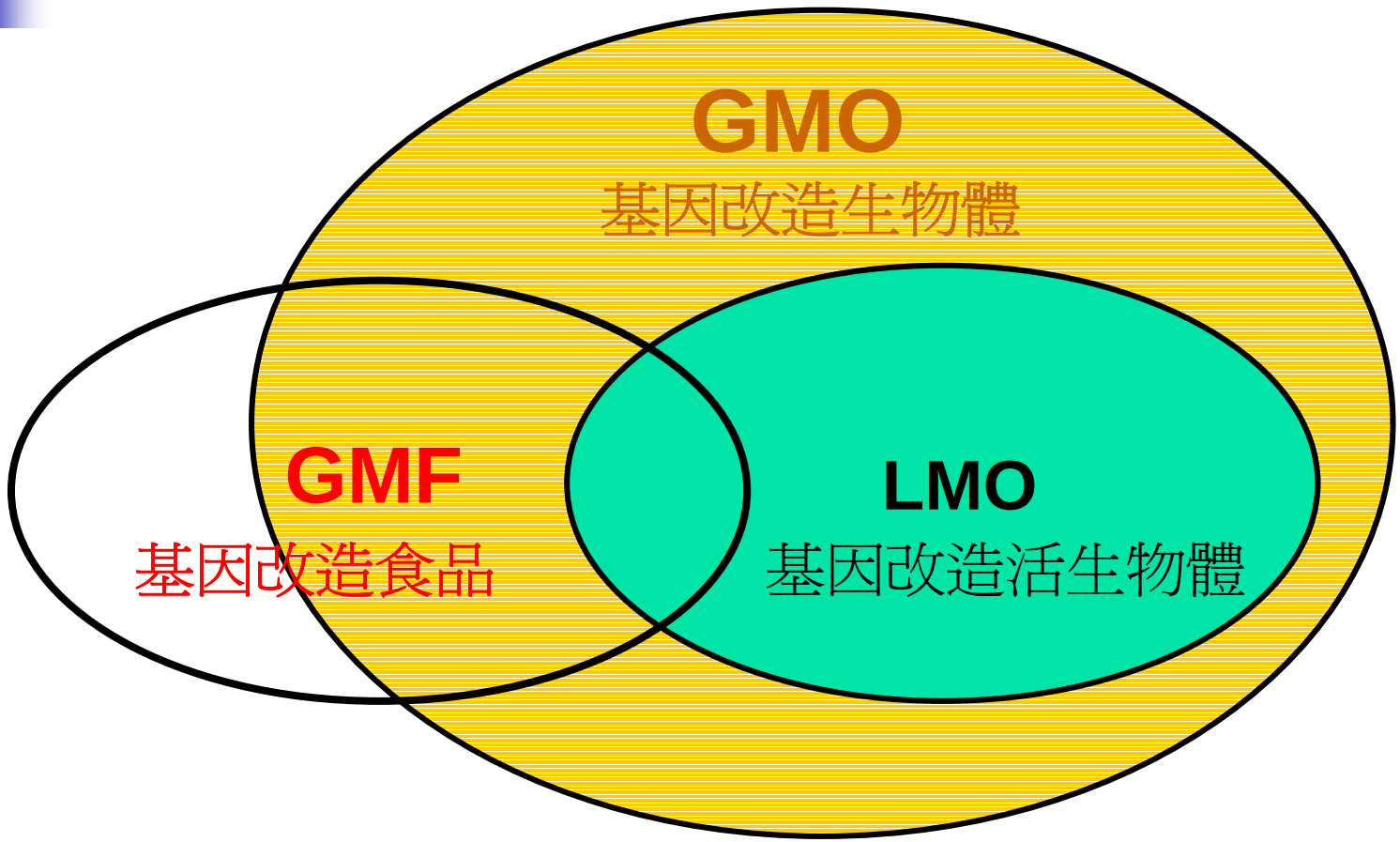
田間試驗

食品安全評估

商業化

Development of a GM plant variety can take 6 to 12 years at a cost ranging from $50 million to $300 million, Bio-ERA said. Even then, "companies must face risks of market acceptance.“ - 2/20/2003 Reuters

GMOs v. GMF



基因改造產品之管理

上、中、下游的管理架構

1. 國科會（實驗室）：基因重組實驗守則
2. 農委會（農作物）：基因轉殖...
3. 衛生署（食物）： 基因改造...

行政院科技顧問組 → 行政院生物技術產業指導小組

風險評估：聯合國食品標準委員會(Codex)規範

聯合國糧農組織

世界衛生組織

聯合國食品標準委員會基因改造食品臨時特別工作小組

Codex *Ad Hoc* Intergovernmental Task Force on Foods Derived From Biotechnology

第三次會議,日本,橫濱, 2002年3月4-8日

1. **Draft *Principles* for the Risk Analysis of Foods Derived from Modern Biotechnology** (風險分析原則)
2. **Draft *Guideline* for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants** (植物性基改食品風險評估準則)
3. **Draft Annex on the Assessment of Possible Allergenicity** (致過敏性評估方法)
4. **Papers on Traceability** (文件追蹤指針 – 未達成決議)
5. **Consideration of Analytical Methods** (檢驗方法 – 未達成決議)

風險評估：聯合國食品標準委員會(Codex)規範

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Codex *Ad Hoc* Intergovernmental Task Force on Foods Derived From Biotechnology

第四次會議,日本,橫濱, 2003年3月11-14日

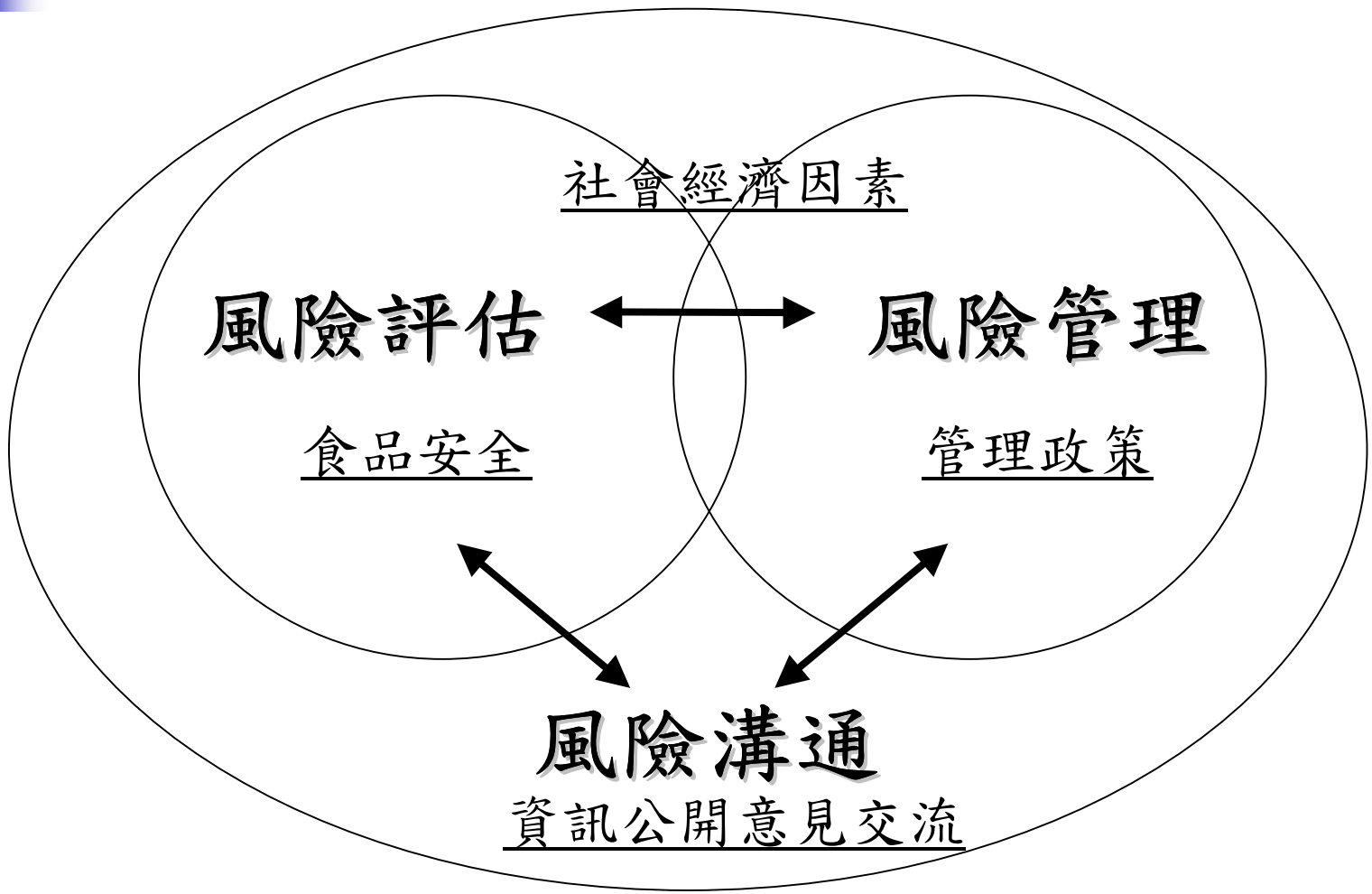
1. **Draft *Guideline* for the Conduct of Food Safety Assessment of Foods Produced using Recombinant-DNA Microorganisms** (微生物製造基改食品風險評估準則)
2. **Draft Annex on the Assessment of Possible Allergenicity (Proteins)** (微生物蛋白致過敏性評估方法)
3. **Open discussion on Traceability**
4. **Potential future work**

安全評估

Principles for the Risk Analysis

- Risk Assessment
- Risk Management
- Risk Communication
- Consistency
- Capacity Building and Information Exchange
- Review Processes

基因改造食品風險分析



以科學為基礎之安全評估

nature

21 March 2002 Volume 416 Issue no 6878

In search of sound science

Quality standards for US federal research could be useful — but only if industry acts

'Sound science' is one of those phrases repeated so often by politicians in recent years that it has come close to losing all meaning. In endless debates over this or that piece of environmental or health regulation, each side invokes 'sound science' to mean anything that supports its end of the argument.

Now US government agencies are being asked to bring more precision to the term. They will soon be required by law to ensure that the scientific information they disseminate meets standards for "quality, objectivity, utility, and integrity" (see page 249).

The move seems to have started as a manoeuvre by industry-backed groups — which helped to draft the law — to make it harder to enact federal regulations. But it could nevertheless prompt a useful discussion of what constitutes 'quality' research, and what the role of science should be in shaping policy.

In public discussion of guidelines for implementing the new law, scientists have argued, p
peer review assures qua
page 258), and Presider
a wary eye on federal r
'reproducibility'. By th
supporting 'influential
enough for others to ac

In a world where ev
science', that standard
new law simply to gum
or keeps sending scient
before accepting their
that happens, scientists
another kind of transpa
required to come clean

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安全評估三原則

1. 實質等同 (Substantial Equivalence)
2. 個案分析(Case-by-case)
3. 逐步完善(Stepwise)

安全評估三原則 –

Substantial Equivalence (OECD, 1993)

- Existing traditional foods considered safe
- Traditional foods can serve as a basis for the safety assessment of GM foods
- comparison of similarities and differences which should be further assessed regarding their impact on the safety and nutritional status of the GM foods
- investigate differences for safety, include:
  - composition: macronutrients, micro nutrients, anti-nutrients, toxins.

安全評估三原則 – Case-by-case

2001-2002年衛生署審理之申請案件

#	種類	品　名	轉殖品系	申 請 者	核准日期	備　註
1	大豆	耐嘉磷塞基因改造黃豆	40-3-2 (RRS)	孟山都遠東股份有限公司	91.07.22	有效日期至96.07.22
2	玉米	抗蟲基因改造玉米	MON810	孟山都遠東股份有限公司	91.10.15	有效日期至96.10.15
3	玉米	耐嘉磷塞基因改造玉米	GA21	孟山都遠東股份有限公司	核給臨時許可	91.06.03通過食品安全書面審查；唯檢驗方法尚待確立
4	玉米	耐嘉磷塞基因改造玉米	NK603	孟山都遠東股份有限公司	92.04.11	有效日期至97.04.11
5	玉米	抗蟲/耐固殺草基因改造玉米	Bt11	台灣先正達股份有限公司	核給臨時許可	92.03.31通過食品安全書面審查
6	玉米	抗蟲基因改造玉米	Event176	台灣先正達股份有限公司	核給臨時許可	92.03.31通過食品安全書面審查
7	玉米	耐固殺草基因改造玉米	T25	拜耳作物科學(前台灣安萬特股份有限公司)	91.08.16	有效日期至96.08.16

安全評估三原則 - Stepwise

Codex *Guideline* for the Conduct of Food Safety Assessment

聯合國糧農組織

世界衛生組織

- Unintended Effects
- Framework (a stepwise process)

1. **Description of the recombinant-DNA plant**
2. **Description of the donor organism(s)**
3. **Description of the genetic modification**
4. **Characterization of the genetic modification(s)**
5. **Safety assessment**
6. **Other considerations**

GM作物 – 四大議題

I. 食品安全	**Food Safety**
II. 環境生態	Environmental Safety
III. 社會倫理	ELSI(ethical, legal, social issues)
IV. 國際貿易	Trade

Based on Sound Science...

基因改造食品安全性評估方法

- 毒素
- 過敏原
- 營養組成
- 基因轉移 (HGT, or Gene flow)
- 抗生素標識基因

基因改造食品之安全性評估

基因改造馬鈴薯事件

- 1998年 英國
- 普茲泰(Arpad Pusztai*)
- 老鼠組織病變免疫降低
- 不為科學界接受

* Ewen SW, Pusztai A. Lancet. 1999 Oct 16;354(9187):1353-4

基因改造食品之安全性評估

星連(StarLink)玉米事件

- 2000年 美國、日本(台灣)
- 飼料級玉米
- 含Cry9C (Bt的一種)
- 疑似致過敏
  (CDC證實沒有臨床過敏案例)
- 全面禁止

星連玉米(StarLink)

食品安全評估 –

有致過敏疑慮：

1. **模擬消化試驗**

   SGF stability, pH2

   > 4hr

2. **熱穩定試驗**

   90°C > 19 min

"There is no evidence to indicate that Cry9C is or is not a potential food allergen." - US EPA, 2000.

SGF: Simulated Gastric Fluid(人造胃液)

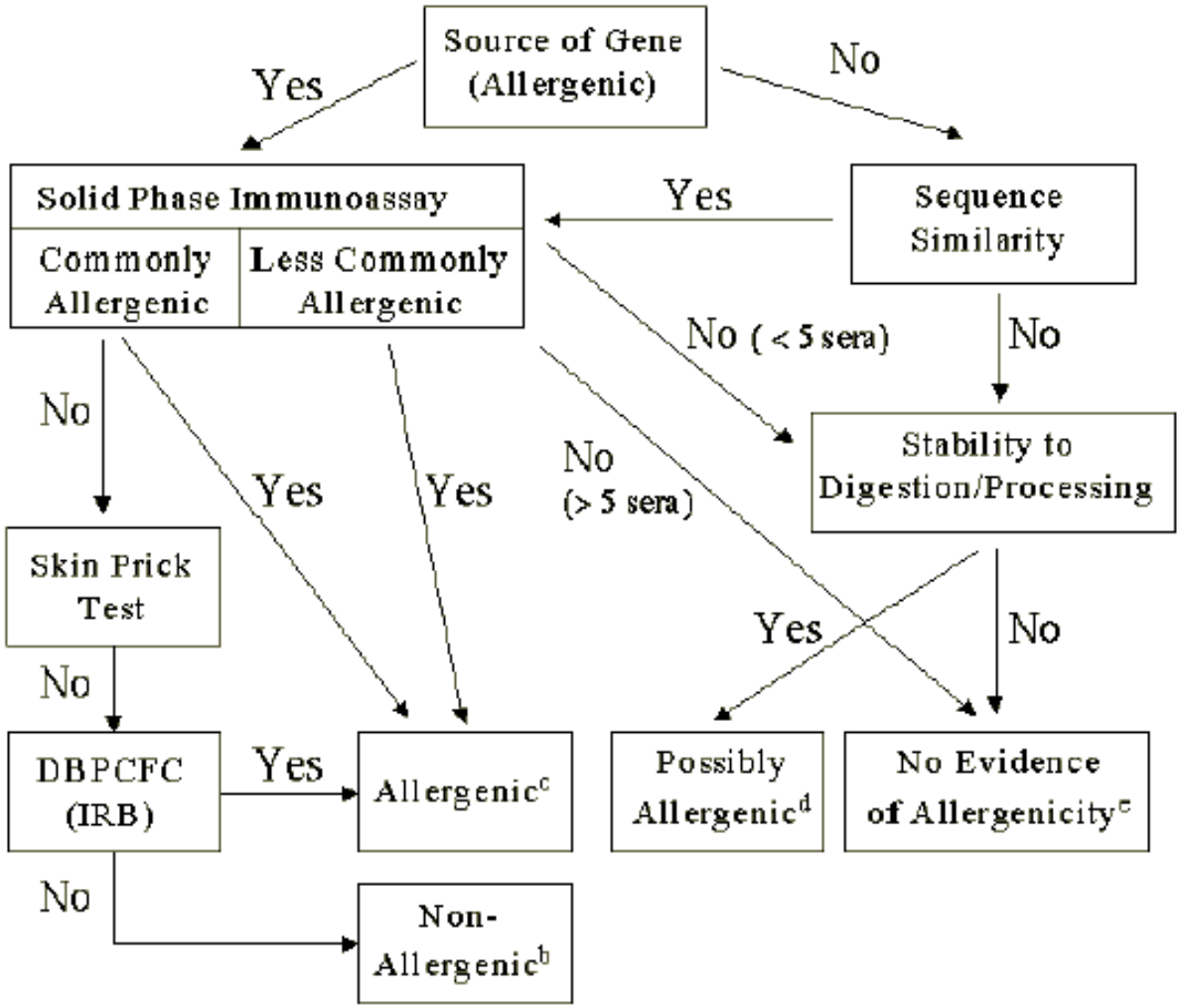
過敏性評估:消化穩定性試驗之存疑

Pepsin/test	Stability of protein in SGF (min)		
Protein ratio(w/w)	10:1	1:1	1:10
Food allergens			
b-lactoglobulin B	120	120	120
ovalbumin	5	60	120
papain	0	0	0
Nonallergenic proteins			
Zein	60	60	120
Pea lectin	5	120	120
Cytochrome c	0	0.5	0.5
Sucrose synthetase	0	0	0

Source: Fu, *et al*. 2002.

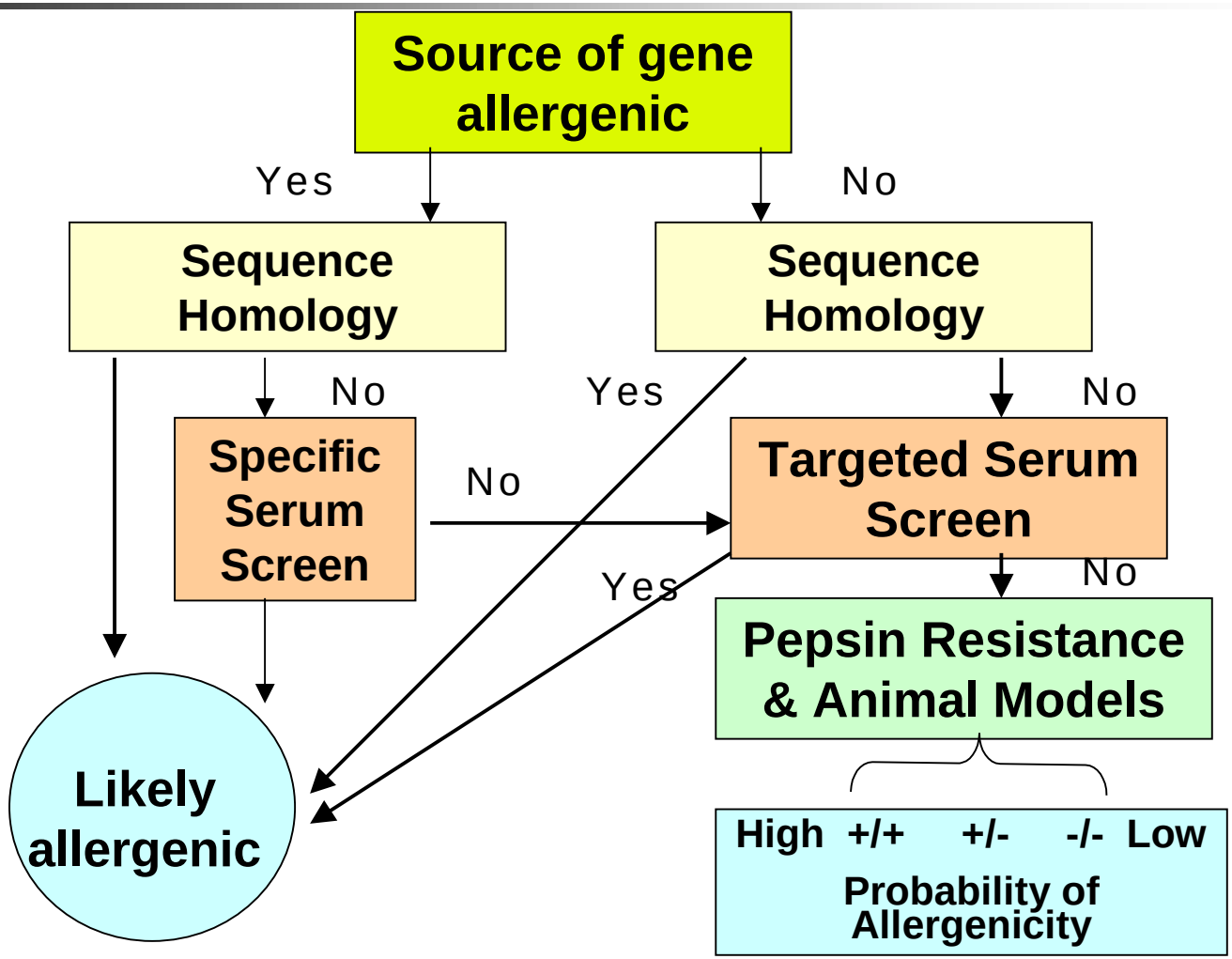
過敏性評估:

FAO/WHO 2000 Decision Tree



過敏性評估:

FAO/WHO 2001 Decision Tree



Case Study

「神秘DNA事件」

(August 2001)
Molecular Characterization of the genetic modification

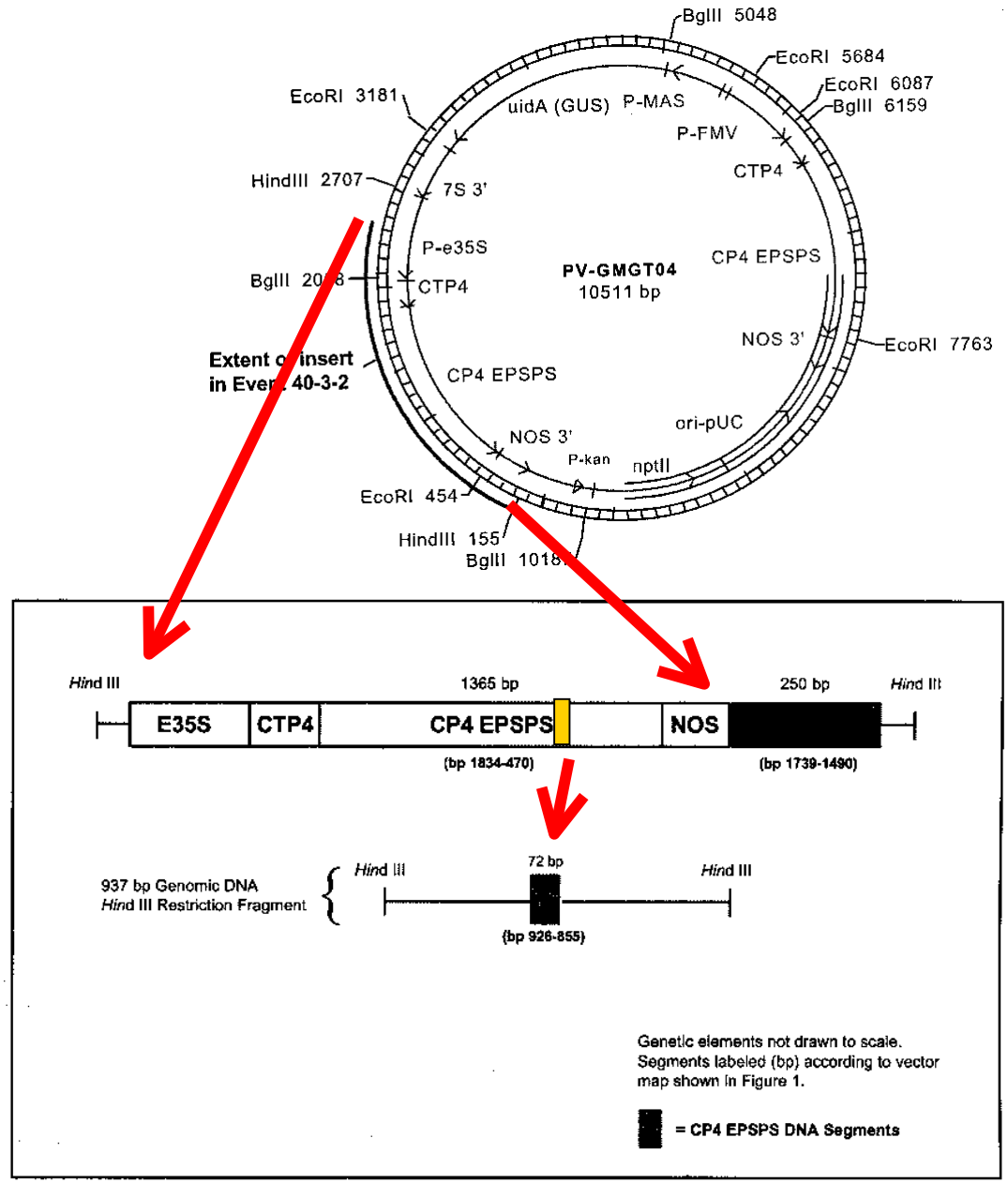


Figure 2 **Updated molecular characterization of RR soybean event 40-3-2.**

Windels P. *et al.* (2001)

Horizontal Gene Transfer (HGT)?

Monsanto vs. Percy Schmeiser

(產品: 加拿大芥花油)

- 2001.4.2.
- 種植基因改造油菜花 (GM Canola)

智財權爭議:

孟山都生物科技種子訴訟糾紛
加拿大農夫敗訴！

* http://www.fct-cf.gc.ca ; http://www.percyschmeiser.com

基因改造實驗動物流入食品市場

Research Piglets Sold as Food Hard to Find, FDA Accused of Lax Biotech Regulation

02/07/2003

- **WHO:** 美國伊利諾大學 **(University of Illinois – Urbana/Champaign)**
- **WHEN: 4/2001 – 1/2003**
- **WHAT: 386**頭 基因改造實驗乳豬 販售給肉品商

The ProdiGene Incident

WHO - ProdiGene Inc. (College Station, TX)

WHAT - edible vaccine grown in corn

WHEN - 11/13/2002 USDA investigation

WHY - Contamination of 155 Acre soybeans

RESULTS:

1. **$250,000 罰鍰 + $3,000,000 USDA補償款 + $1,000,000 保證金**
2. **美國加強聯邦法規: 68FR11337**

基因改造食品與WTO

Tuesday, 13 May, 2003

US launches GM trade war

The United States - and twelve other agricultural exporting nations - want the EU to repeal its five-year moratorium on GM foods, or face trade sanctions under World Trade Organisation (WTO) rules.

基因改造食品與WTO

世界貿易組織 (WTO)

GMO 相關協定

1. 食品衛生檢驗與動植物檢疫措施協定
   Sanitary and Phytosanitary Measures (SPS)
2. 技術性貿易障礙協定
   Technical Barrier to Trade (TBT)

基因改造食品與WTO

基因改造食品成爲主要議題

因爲許多國家：

1. 禁止基因改造食品
2. 實施標示制度

有關GMOs之文件數

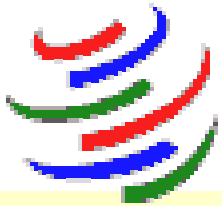
年度	TBT	SPS
1995	1	4
1996	2	1
1997	11	0
1998	11	5
1999	20	2
2000	14	20
2001	25	37
2002	43	74
2003(1-6)	19	43
合計	**146**	**186**

基因改造食品、WTO與CBD

CBD 聯合國生物多樣性公約組織

© 2002 - Secretariat of the Convention on Biological Diversity
United Nations Environment Programme

WORLD TRADE ORGANIZATION



Cartegena Protocol on Biosafety(生物安全議定書)

Article 1. Objective

The objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of **living modified organisms (LMOs)** resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on **transboundary movements**.

World Trade Organization (WTO)

…is the only international organization dealing with the global rules of trade between nations. Its main function is to ensure that trade flows as smoothly, predictably and freely as possible.

11 September 2003 enter into force!

LMOs v. GMOs v. GMF

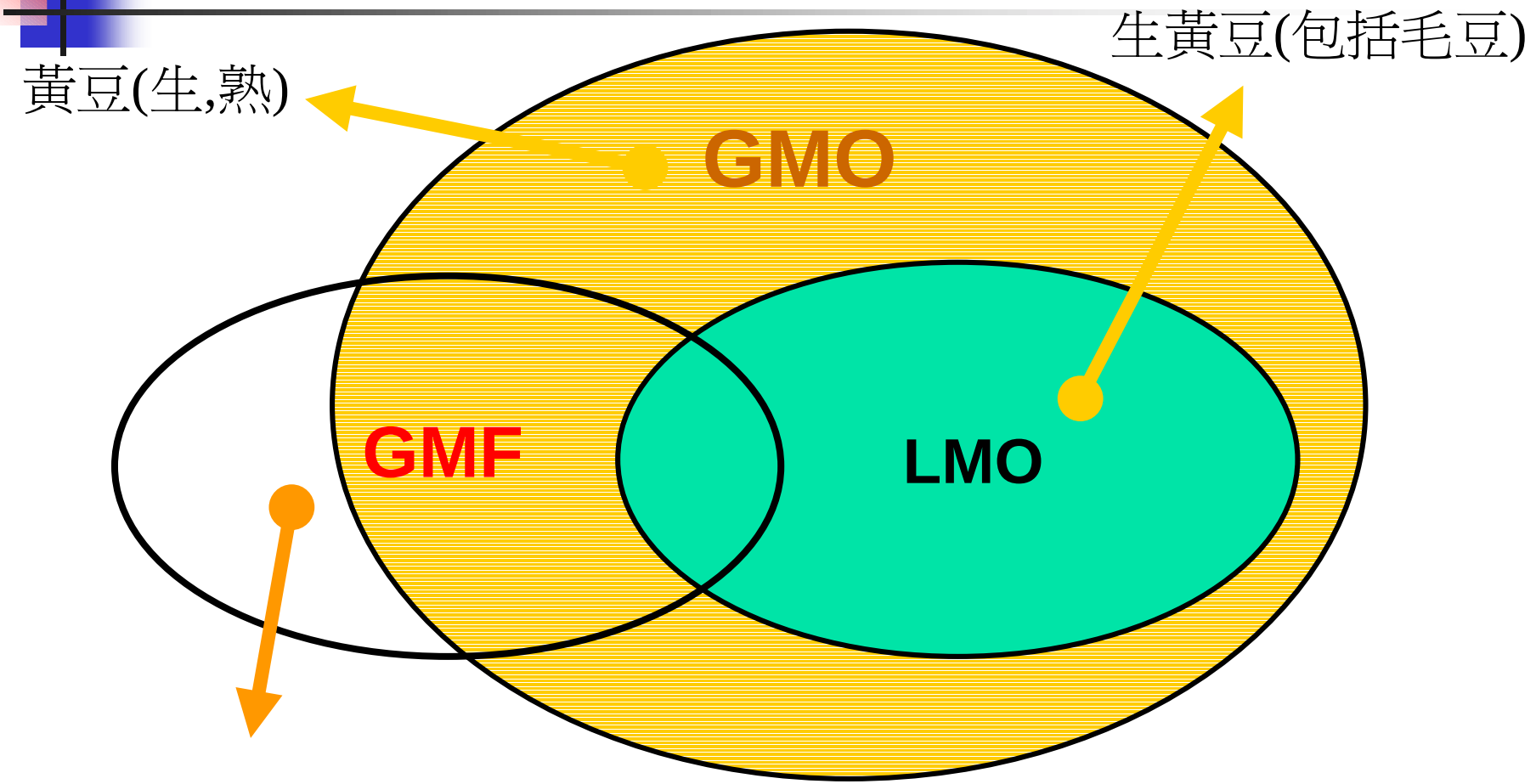


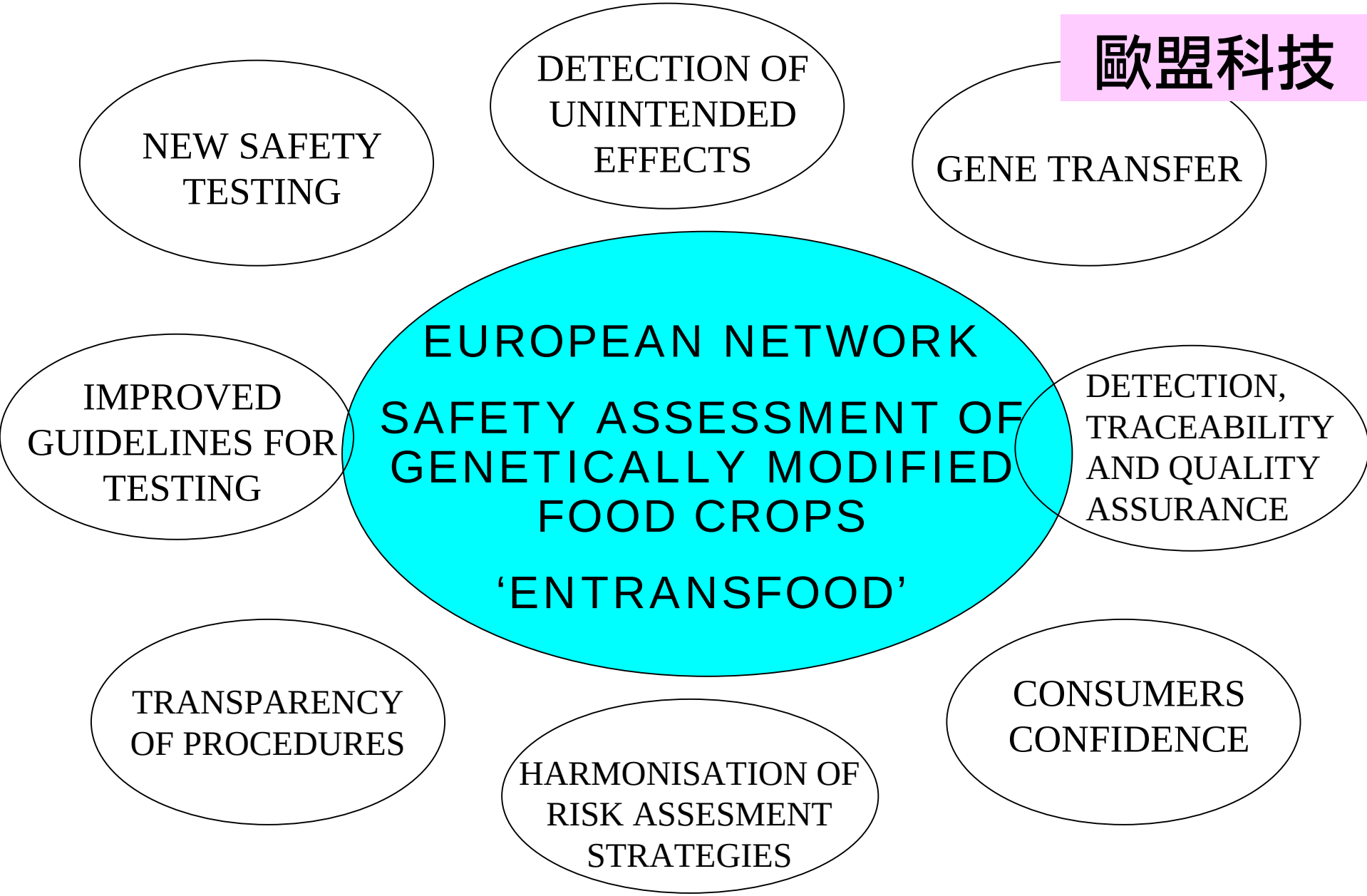
Table: History of EC-Supported GMO Safety Projects

歐盟科技

Programme	Number of Projects
Fifth Framework Programme (1998-2000 only)	
Cell Factory Key Action	5
Food, Nutrition and Health Key Action	5
Fourth Framework Programme (1994-1998)	
Biotechnology (II)	18
Agriculture and Fisheries (FAIR)	2
Standards, Measurement and Testing	1
International Cooperation	5
Third Framework Programme (1990-1994)	
Biotechnology (I)	9
Agriculture and Agro-Industry (AIR)	2
Second Framework Programme (1987-1991)	
Biotechnology (BRIDGE)	14
Food-linked Agro-Industrial Research (FLAIR)	1
First Framework Programme (1984-1987)	
Biotechnology Action Programme (BAP)	19
TOTAL Number of Projects	**81**

Source: http://europa.eu.int/comm/research/quality-of-life/gmo/index.html

歐盟科技



Source: http://www.entransfood.com/

Participating Projects

- **SAFOTEST**

  Innovative safety testing of GMOs

- **GMOCARE**

  Detection of unintended effects

- **GMOBILITY**

  Gene transfer

- **QPCRGMOFOOD**

  GMO detection and traceability

SAFOTEST Participants

- **Danisch Food and Veterinary Administration (DK)**

  Animal testing

- **Technical University of Munich (GER)**

  Compositional analysis

- **Scottish Crop Research Institute & University of Newcastle (UK)**

  Gene constructs

- **RIKILT (NL)**

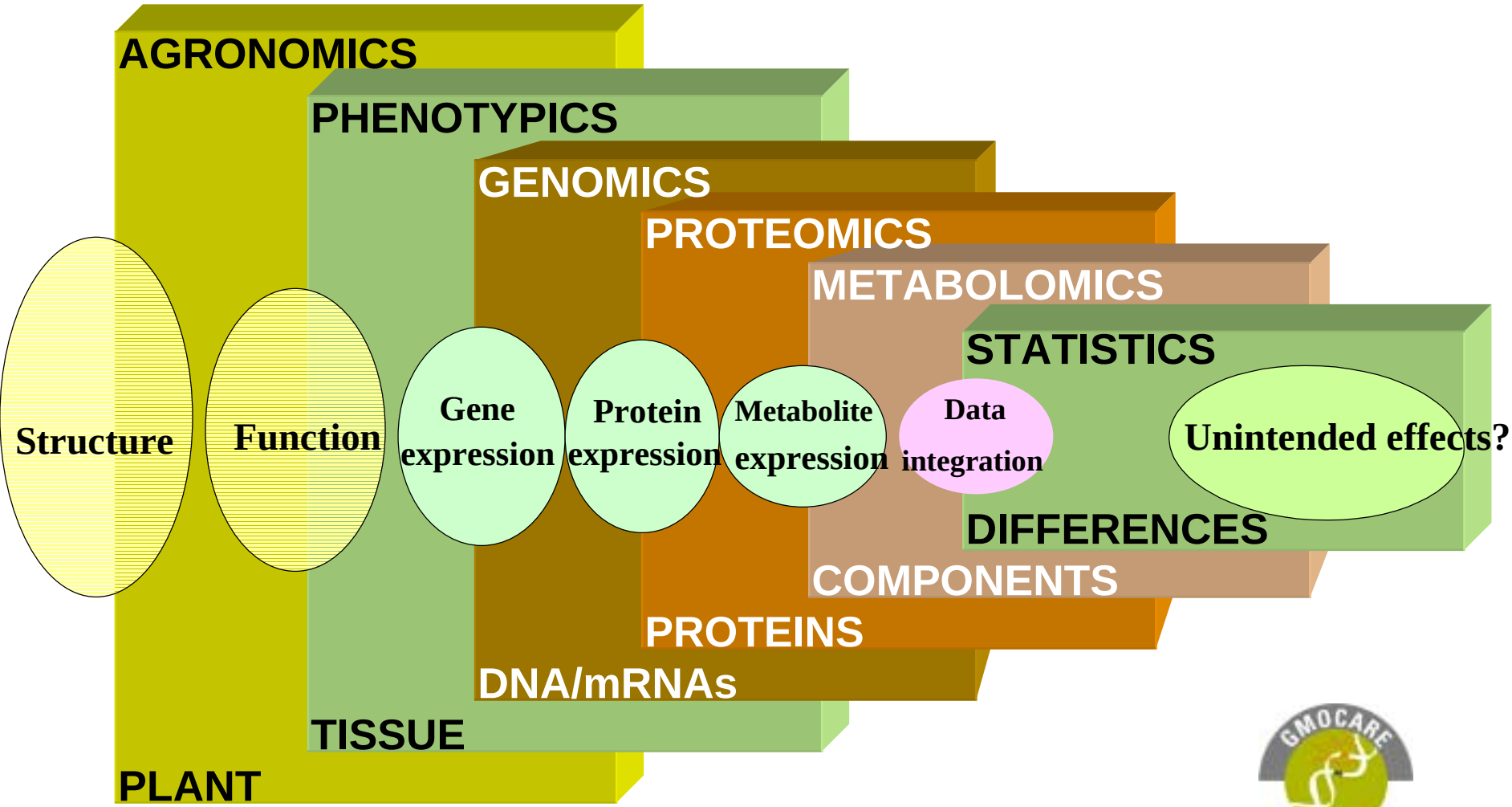
  In vitro, in situ, microarrays

GMOCARE

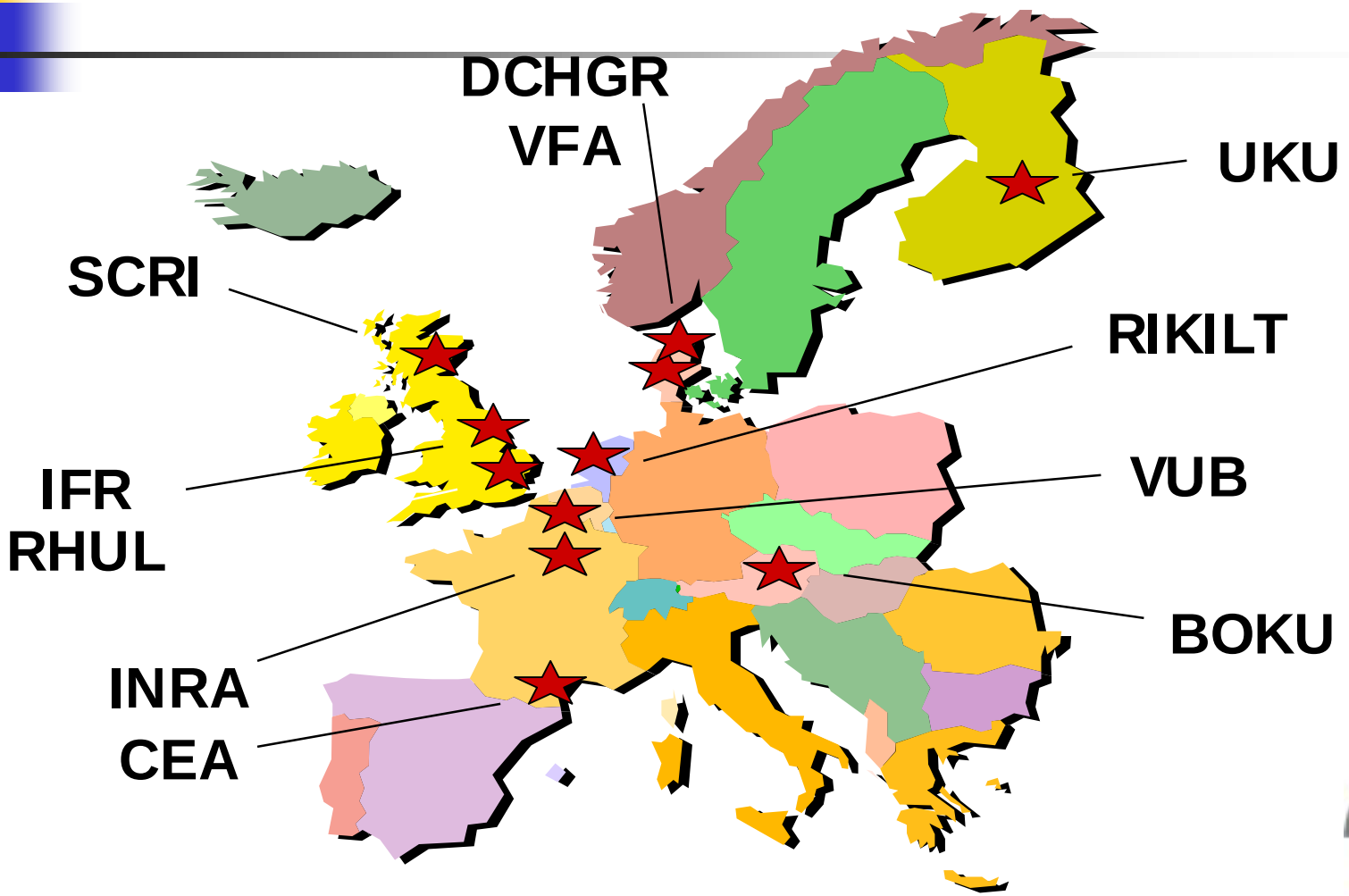
- Analysis of unintended effects
- Chemometry & “omics” , allergenicity
- Experimental GM Crops:
  - potato (5): starch, sugar, lysine, polyamine, glycoprotein
  - tomato (5): carotenoids, phytosterols
  - tobacco (3): lysine, threonine
  - Arabidopsis (6): flavonoids

歐盟科技

Platform of “omics”



GMOCARE Consortium



EUROPEAN NETWORK OF GMO LABORATORIES

JOINT RESEARCH CENTRE

ENGL Inauguration Ceremony and Stakeholders' Meeting

Brussels,
4 December 2002

The representatives of 44 laboratories, designated by EU Competent Authorities sign the Agreement. (http://engl.jrc.it/)

台灣基因改造產品何去何從?

NSTP/AB 農業生物技術國家型科技計畫
National Science and Technology Program for Agricultural Biotechnology

1. 花卉與觀賞植物 – 菊花、文心蘭
2. 植物保護 - 微生物抗拮基因、抗蟲、抗病基因選殖(西瓜、甜瓜)
3. 水產養殖 – 草蝦、魚類
4. 畜產動物用疫苗 – 抗熱、抗病、人類第九凝血因子基因轉殖豬
5. 植物有用基因之利用 – 香蕉、苦瓜、西瓜、甜瓜、毛豆、蕃茄(1)、青花菜(1)、木瓜(1)、水稻(3)、馬鈴薯(1) (進入田間試驗 - 7件)
6. 環境保護 - 瘤胃微生物禽畜廢棄物減量生物技術
7. 保健/藥用植物 – 台灣紅豆杉

台灣基因改造產品何去何從?

螢光魚技術獨步全球為水族市場新寵 商機無窮

中央社(2003-4-27)

螢光魚... 基因改造物種操控 何時失控？

【 2003-06-17/聯合報/A15版/民意論壇 】

基因改造產品(GMO)之管理

行政院科技顧問組
Science and Technology Advisor Group (STAG)
Executive Yuan, R. O. C.

食品資訊網 food.doh.gov.tw

未來工作

一、建議行政院科技顧問組設立常設委員會後，積極進行基因改造產品相關法制之跨部會協調工作，以建立我國風險評估之法規環境。

基因改造產品(GMO)之管理

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未來工作

二、建議國科會、農委會、衛生署及相關部會，積極增加編列科技預算，以加強基因改造產品之生態環境及食品安全科技研究，配合建立符合國際規範之基因改造產品風險評估體系。

國家科學委員會第161次委員會議

建立基因改造食品科學性風險評估體系

92.07.09

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