

# Achievements and setbacks in genetic engineering 1973-2013

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Molecular genetics 1960-1970



Genetic engineering 1970-80



Revolutions in biology



Revolutions in medicine, agriculture, forensic science

.....



Powerful

Proven **benefits** for science and society

Proven as **safe** and probably safer than  
conventional food, feed, crops.

One of the safest new technology ever invented

No damage to people, animals or the environment  
40 years

Huge potential to increase productivity worldwide



1970s

**Diabetes** epidemic

Looming shortage of **pig** insulin



Isolate human insulin gene - instruction



Transfer to a single bacterial cell



Multiply that cell - factory



**Purify human insulin**

**1982: on the market**



**1973: First molecular cloning. Cohen and Boyer**

**1982: First major product. Human insulin**

40 years since the technology was invented

Today we have extensive knowledge of the science and  
experience of using the technology

40 years of safe science



**An example from the food industry: cheese production**



**1960s**

Cheese production increasing  
rapidly

Milk clotted with calf rennet

From 4<sup>th</sup> stomach of neonatal calf

Looming shortage of calf rennet  
(Chymosin)





Isolate calf chymosin gene



Transfer to a single bacterial cell



Multiply that cell



**Purify calf chymosin (rennet)**

GM chymosin on the market as FPC in 1990

Fermentation-Produced Chymosin (Rennet)

**90% US and UK cheese made with  
GM FPC**

One way of making vegetarian cheese !



Molecular genetics 1960-1970



Genetic engineering 1970-80



**Revolutions in biology**



Revolutions in medicine, agriculture, forensic  
science





California Institute of Technology  
1966-70



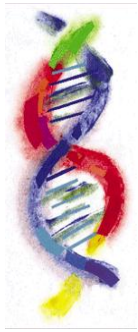
## The isolation of a gene

David McConnell

Research proposal to the National Science Council of Ireland

1970





Nobel prizewinners  
related to Genetics and Molecular Biology  
2000-

**Medicine**

- 2012 - [Gurdon, Yamanaka](#)
- 2010 - [Edwards](#)
- 2009 - [Blackburn, Greider, Szostak](#)
- 2008 - [zur Hausen, Barre-Sinoussi, Montagnier](#)
- 2007 - [Capecchi, Evans, Smithies](#)
- 2006 - [Fire, Mello](#)
- 2004 - [Axel, Buck](#)
- 2002 - [Brenner, Horvitz, Sulston](#)
- 2001 - [Hartwell, Hunt, Nurse](#)

**Chemistry**

- 2009 - [Ramakrishnan, Steitz, Yonath](#)
- 2008 - [Shimomura, Chalfie, Tsien](#)
- 2006 - [Kornberg](#)
- 2004 - [Ciechanover, Hershko, Rose](#)



## Some remarkable scientific discoveries

Many genes are *split* – introns and exons

Some genes are mobile within a genome

Some genes are rearranged

Some genes transfer naturally between *widely different* species

Some diseases are caused by proteinaceous particles – eg BSE

RNA interference

Circular RNAs

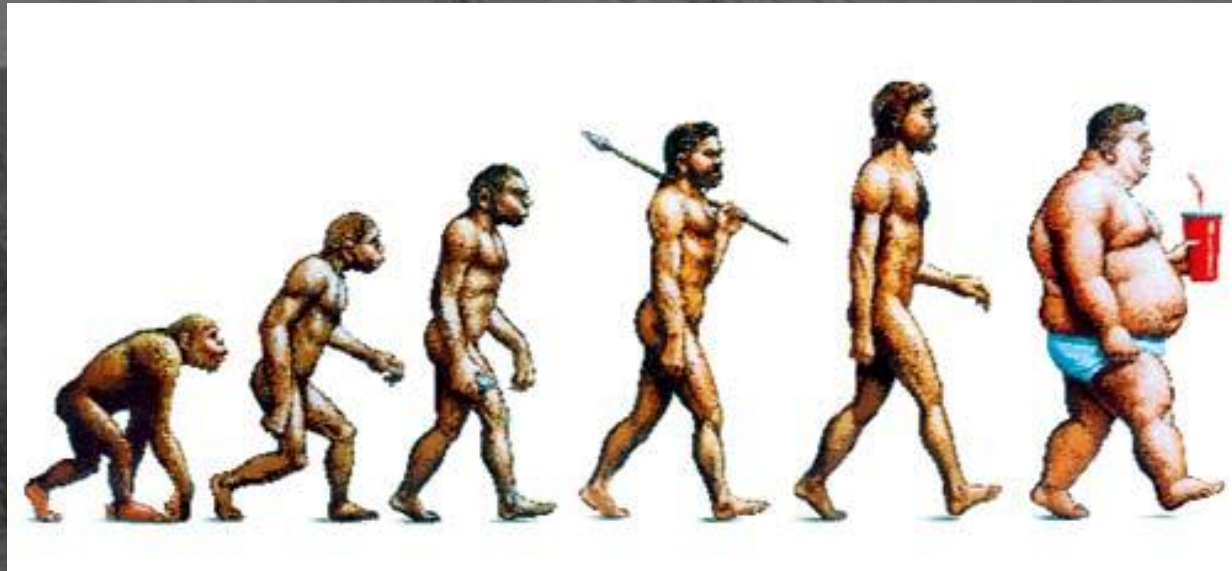
All *Homo sapiens* share a common ancestor - 200,000 years ago

*Homo sapiens* and chimps – 7 million years ago





**Ape to man: 7 million years**



**Has evolution ended?**





98% chimp and proud of it

## **Achievements in medicine**

Well known and well accepted worldwide

Impact on Irish medical practice

Impact on Irish pharmaceutical industry



## **Impact on Irish medical practice**

Treatment of diabetes

Triple therapy for AIDS

Vaccination against Human Papilloma Virus

Rheumatoid arthritis (ENBREL)

DNA based diagnostic procedures



## **Impact on Irish pharmaceutical industry**



Wyeth Biopharma  
Pfizer  
Dublin  
\$2 billion  
2000 staff



Biotechnology  
revolution

Enbrel

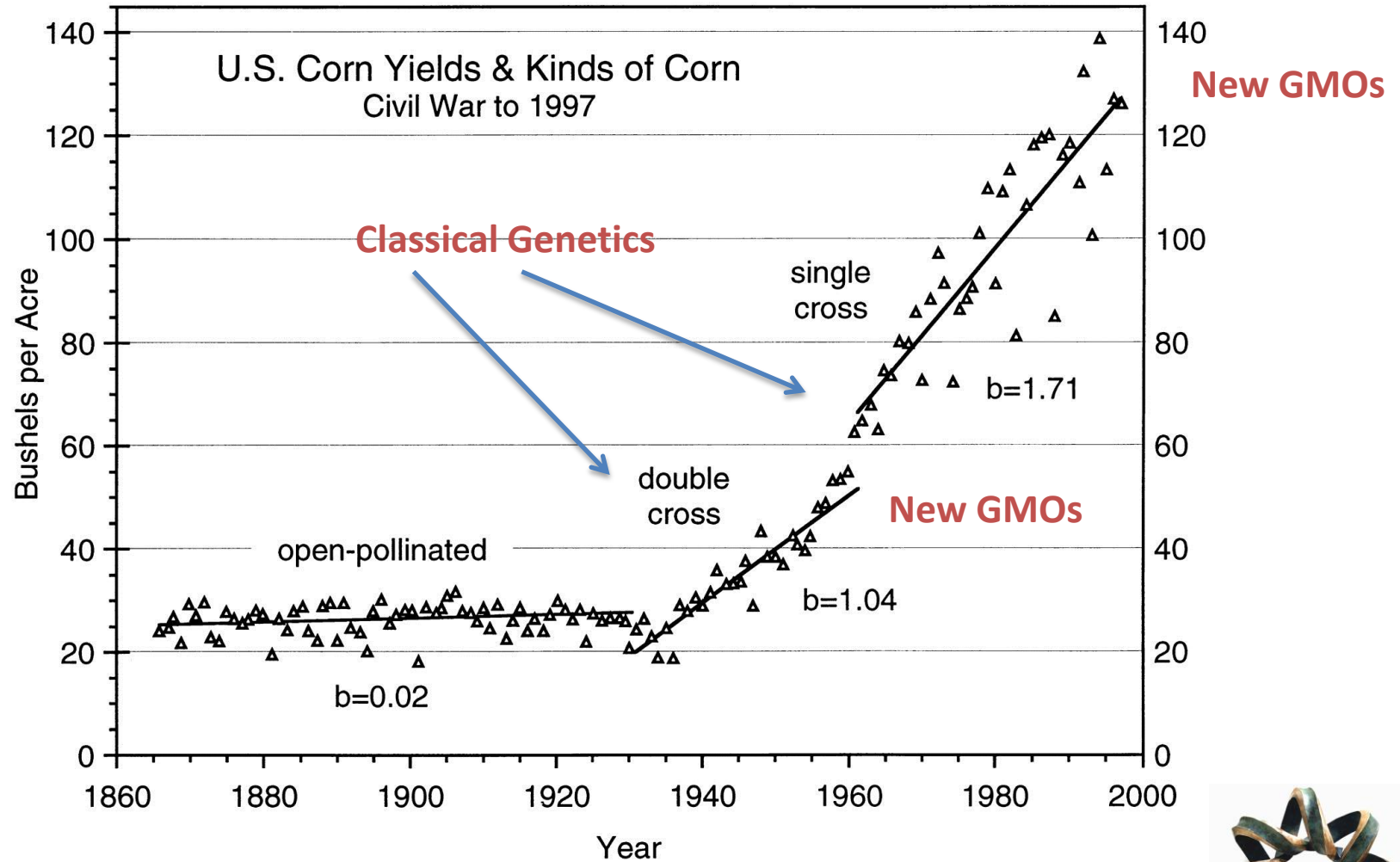
Some remarkable achievements in agriculture

The Achilles Heel of GM

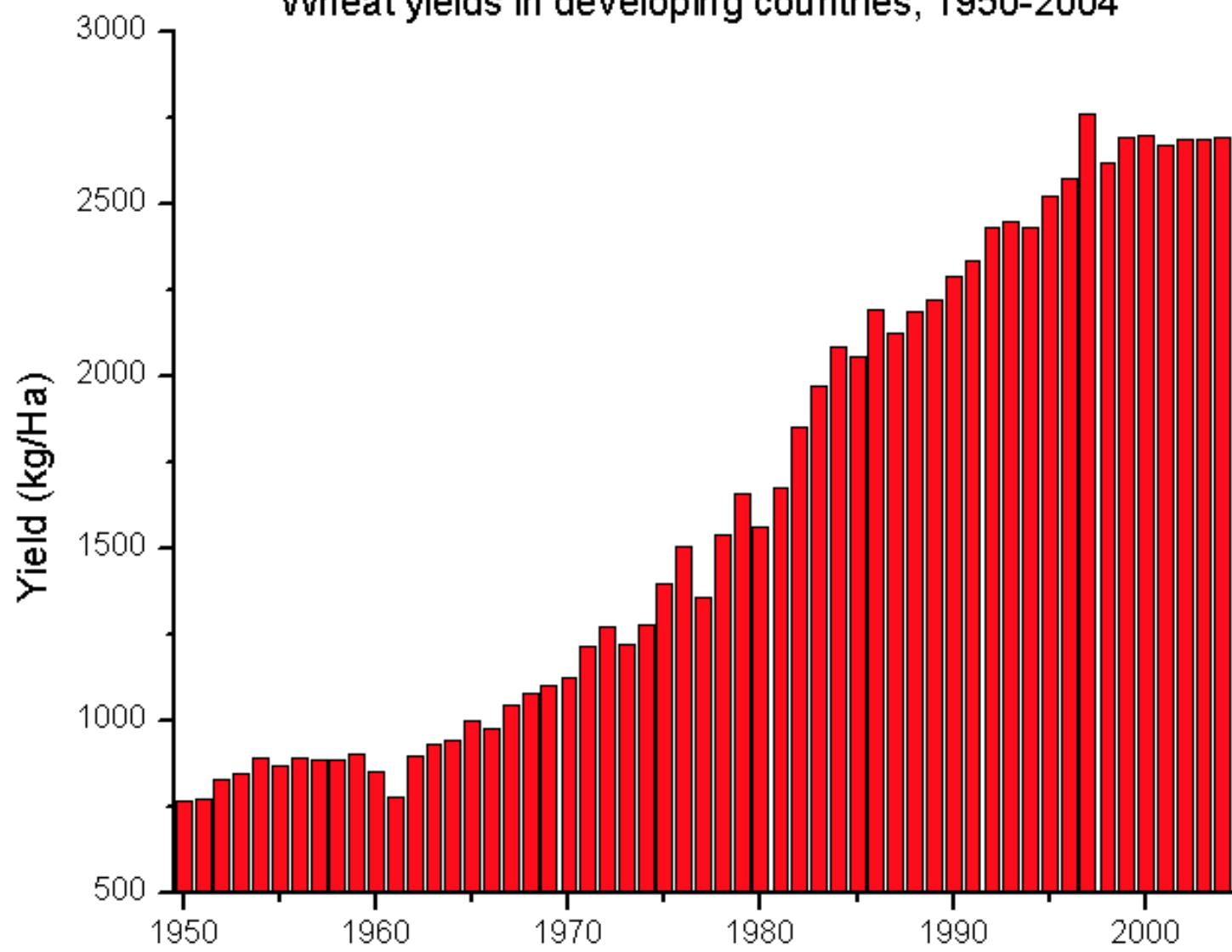




## Classical genetics in agriculture

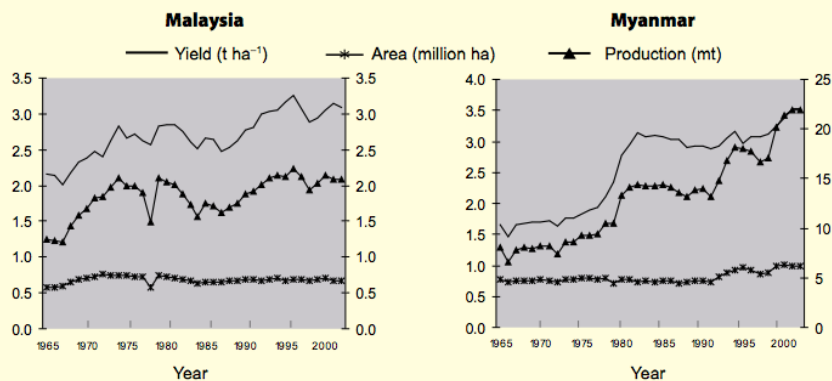
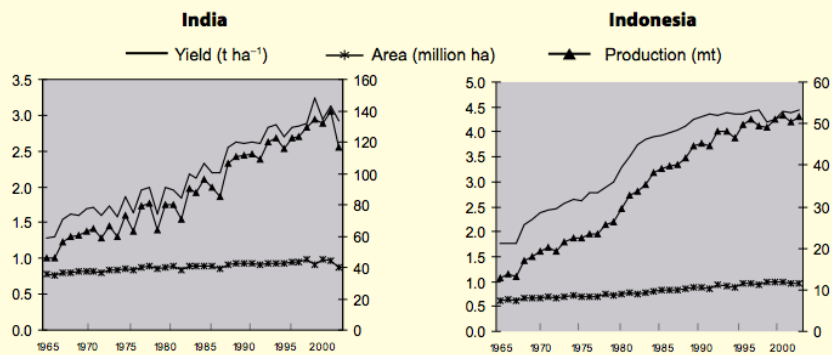
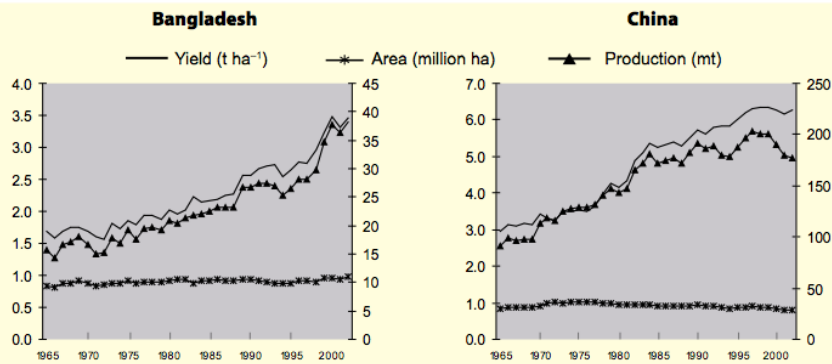


Wheat yields in developing countries, 1950-2004



Source: FAO





1965 – 2000

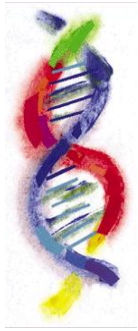
Area under cultivation – flat

Yield - 2-4 x increase

Production - 2-4 x increase



Fig. 1. Rice production (mt), area (million ha), and yield ( $t\ ha^{-1}$ ) from 1965 to 2002 in major rice-growing countries. Numbers to the left refer to yield and numbers to the right refer to both area and production.



# Green Revolution

**Norman Borlaug**

Rice

International Rice Research  
Institute (IRRI), Manila

Wheat and maize

Centro Internacional de  
Mejoramiento de Maíz y Trigo  
(CIMMYT), Mexico City

**Nobel prizewinner in Peace**  
**1970**



Key development in GM technology

**Molecular cloning in plants**

**Schell, van Montagu, Chilton**

**1983**



Isolate a gene – one molecule



Transfer to a single cell



Culture that cell to produce a plant



**Multiply the plant (GMO)**



## **Classical genetics**

Dealing with more than 100,000 genes

Chemical mutagenesis

Radiation mutagenesis

Uncontrollable randomness

## **Molecular genetics**

Dealing with one or a few genes

Genes from any species

No mutagenesis of the plant

Highly specific genetic modification

Highly controlled

## Classical genetics

Dealing with more than 100,000 genes

Chemical mutagenesis

Radiation mutagenesis

Uncontrollable randomness



**Cooking - messy**

## Molecular genetics

Dealing with one or a few genes

Genes from any species

No mutagenesis of the plant

Highly specific genetic modification

Highly controlled



**Engineering - precise**



Unpredictable genome  
modifications<sup>1</sup> in traditional  
and GMO breeding.

Traditional farming



Thousands of years



Classical Genetics 1930-



Molecular Genetics 1983-



Genetically modified genome



Genetically engineered genome



# BT Toxin

Produced by *Bacillus thuringiensis* - a bacterium

Kills insects

BT toxins are **proteins**

Many different kinds

Each kills a specific group of insects





# GMO plants which produce the BT Toxin

Have one extra gene for BT

The toxin is produced in the leaves

The insect larvae eat the leaves

The larvae are killed

Nothing killed but organisms that eat the leaves

BT is safe for higher animals – birds, mammals etc

**A GREEN TECHNOLOGY**



## Tobacco



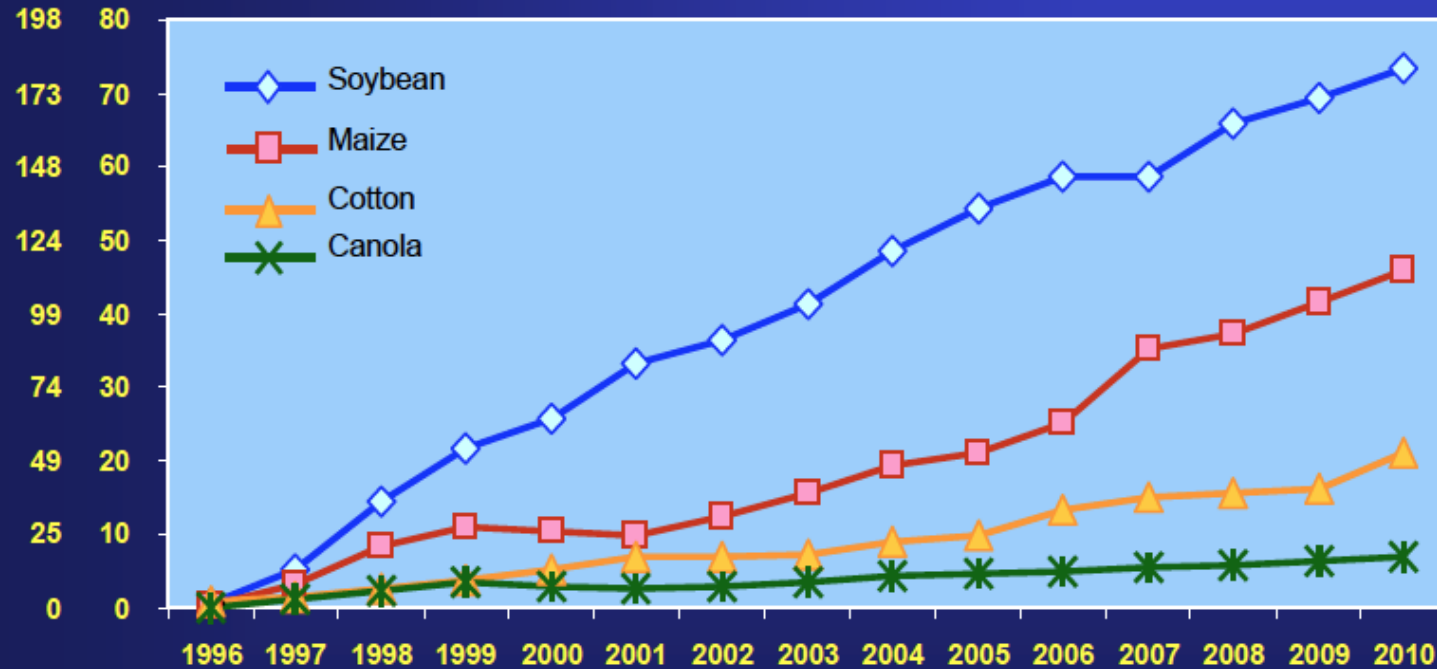
Tony Kavanagh. Smurfit Institute of Genetics



# Global Area of Biotech Crops, 1996 to 2010: By Crop (Million Hectares, Million Acres)



M Acres



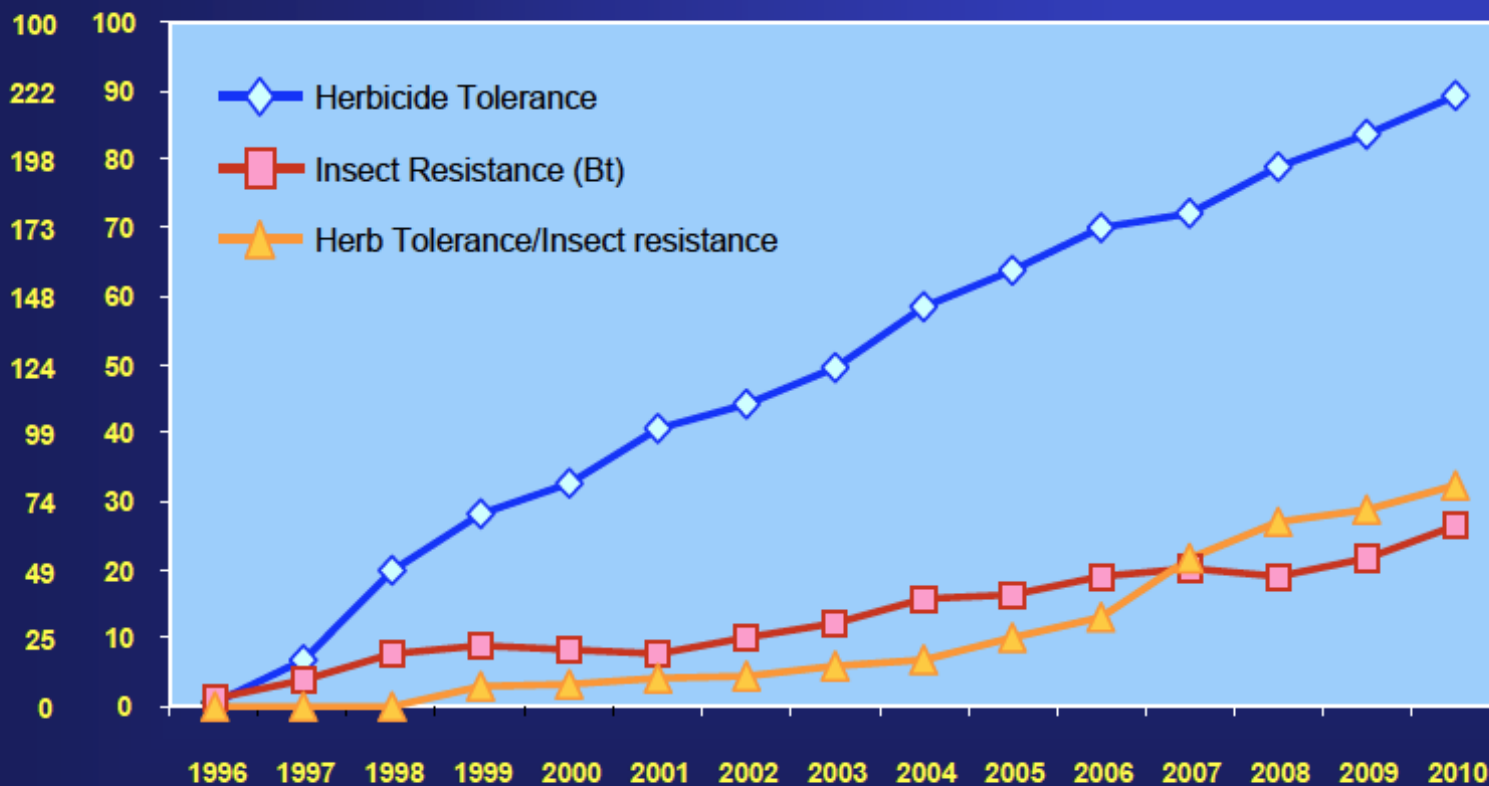
Source: Clive James, 2010



# Global Area of Biotech Crops, 1996 to 2010: By Trait (Million Hectares, Million Acres)



M Acres



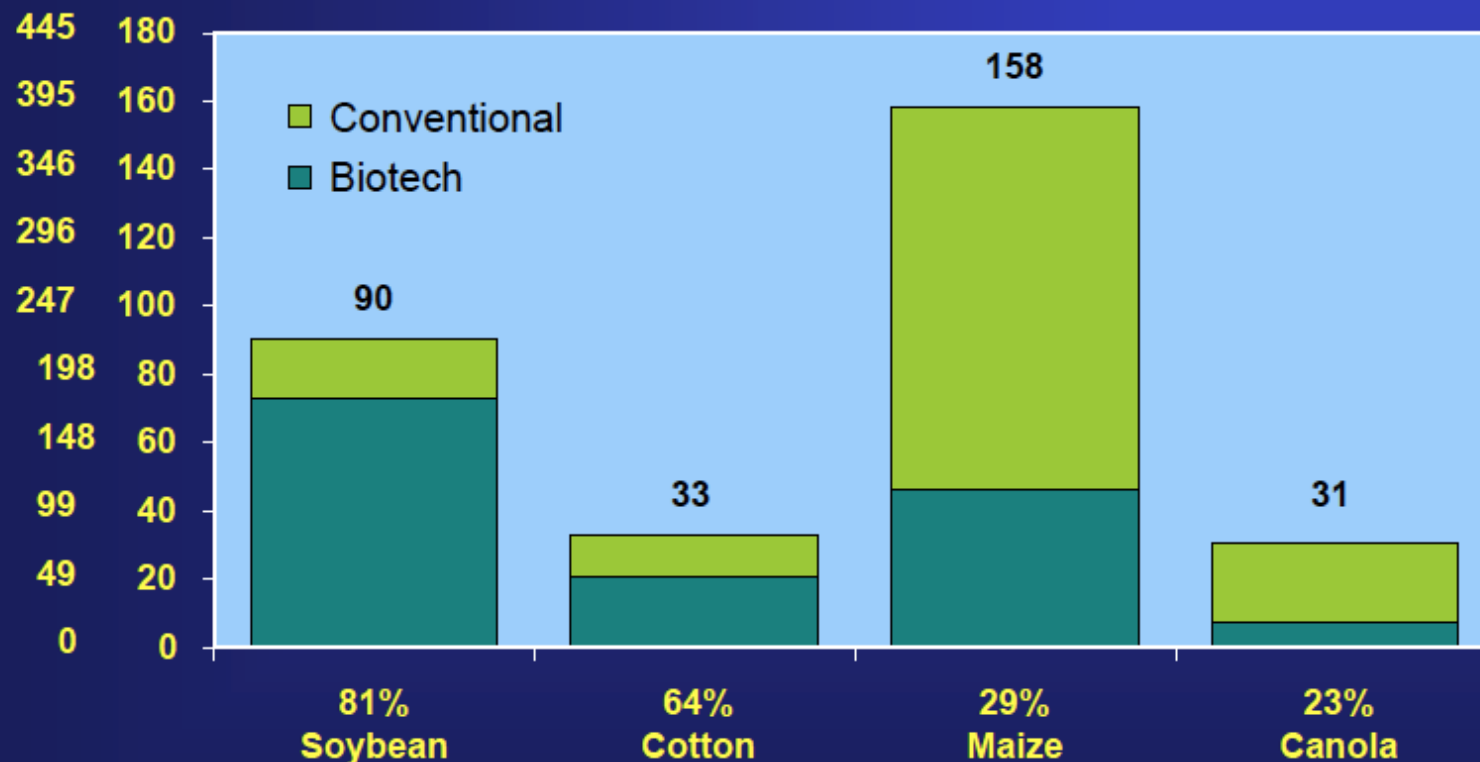
Source: Clive James, 2010



# Global Adoption Rates (%) for Principal Biotech Crops (Million Hectares, Million Acres), 2010



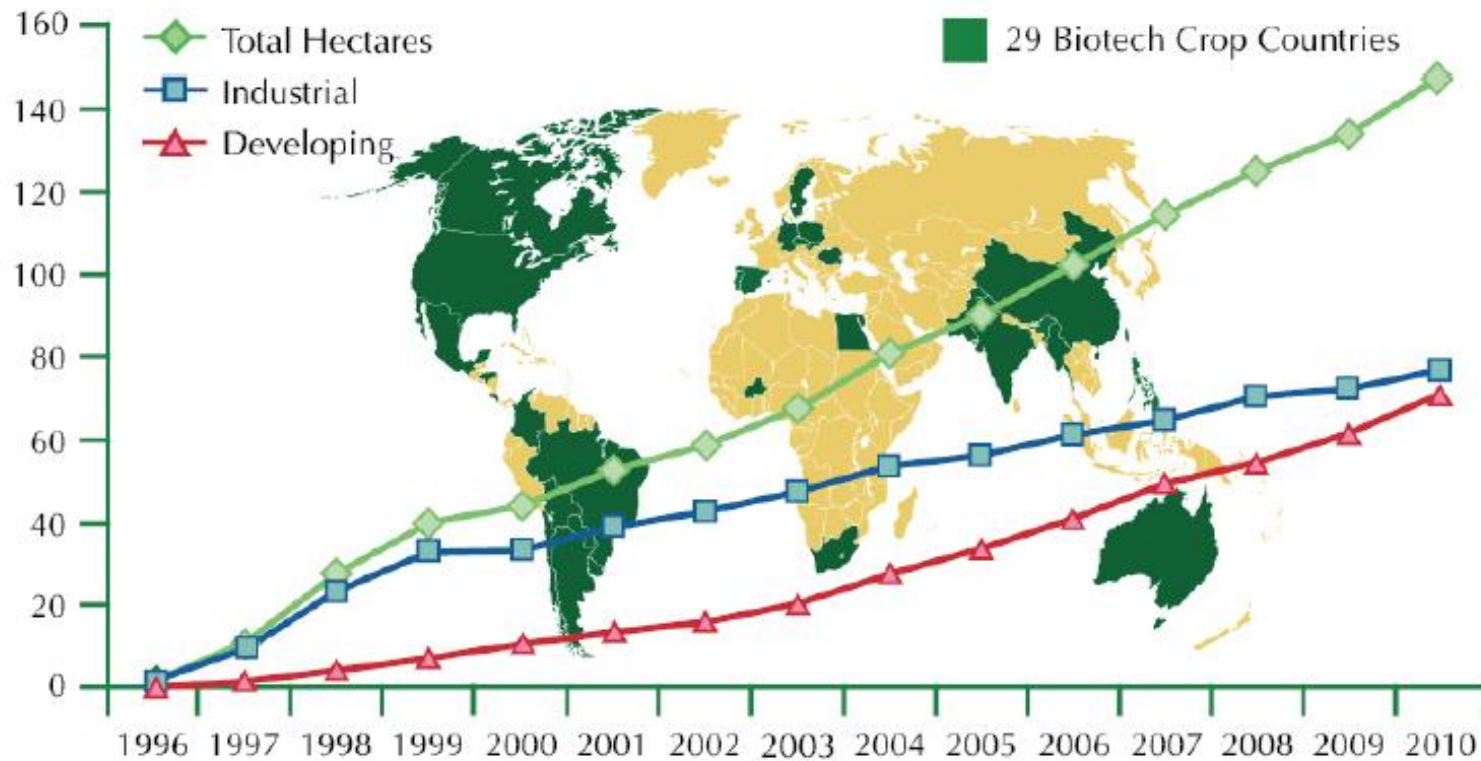
M Acres



Source: Clive James, 2010



## GLOBAL AREA OF BIOTECH CROPS Million Hectares (1996-2010)



*A record 15.4 million farmers, in 29 countries, planted 148 million hectares (365 million acres) in 2010, a sustained increase of 10% or 14 million hectares (35 million acres) over 2009.*

Source: Clive James, 2010.



	% acreage USA	
	1997	2013
Herbicide-tolerant soybean	17	93
Herbicide-tolerant cotton	10	82
Herbicide-tolerant corn	4	85
Bt corn	8	76
Bt cotton	15	75



**Economic gains at the US farm level of ~\$78 B 1996 to 2010**

**40% due to reduced production costs (less ploughing, fewer pesticide sprays and less labor)**

**60% due to substantial yield gains of 276 million tons.**

**Reduction of 443 million kg a.i. of pesticides.**

**91 million hectares of land saved (Brookes and Barfoot, 2012,).**

**HT- increase in no- till: reduction in erosion, soils much healthier, organic matter, less soil compaction, better H<sub>2</sub>O usage.**





## **GMO success – 4 crops**

Cotton, maize, soybean, canola.

## **Two traits**

Herbicide tolerance and insect resistance.

## **A few countries dominate**

Adopted by US, Canada and developing countries – Brazil, Argentina, China, South Africa, India

**All developed by private sector in the U.S.**



## **World Health Organization (2005)**

**“GMOs offer potential of increased ag  
productivity, improved nutritional  
values that can contribute directly to  
enhancing human health and  
development”**

**[http://www.who.int/foodsafety/biotech/  
who\\_study/en/index.html](http://www.who.int/foodsafety/biotech/who_study/en/index.html)**



Papaya in Hawaii

BT cotton

Golden Rice





## Papaya ringspot virus



Non GM papaya

GM papaya



## Papaya production in Hawaii, 1992-2001

	Year	Total	Puna
PRSV appears	1992	55,800	53,010
	1994	56,200	55,525
	1996	37,800	34,195
GM seed used	1998	35,600	26,750
	2000	53,000	40,290





## BT cotton: Bollweevil resistance



GM

nonGM

BT cotton: Bollweevil resistance

93% of Indian cotton (Nature 2012)



## The Golden Rice project: Non-profit, humanitarian



Igor Potrykus (Zurich) and Peter Beyer (Freiburg)



## Carotene (Provitamin A) deficiency

WHO

Vitamin A deficiency

670,000 children die each year from Vitamin A deficiency

Vitamin A deficiency is the number one cause of preventable blindness among children in developing countries

As many as 350,000 children go blind each year



## Golden Rice

Rice kernels are carotene deficient

Made GM rice which produces carotene (1999 - 2002)

Gifted to Golden Rice Project.

Involved rights to more than 50 patents

(ETH Zurich, U Freiburg, Syngenta, Bayer, Monsanto, Orynova, Zeneca)

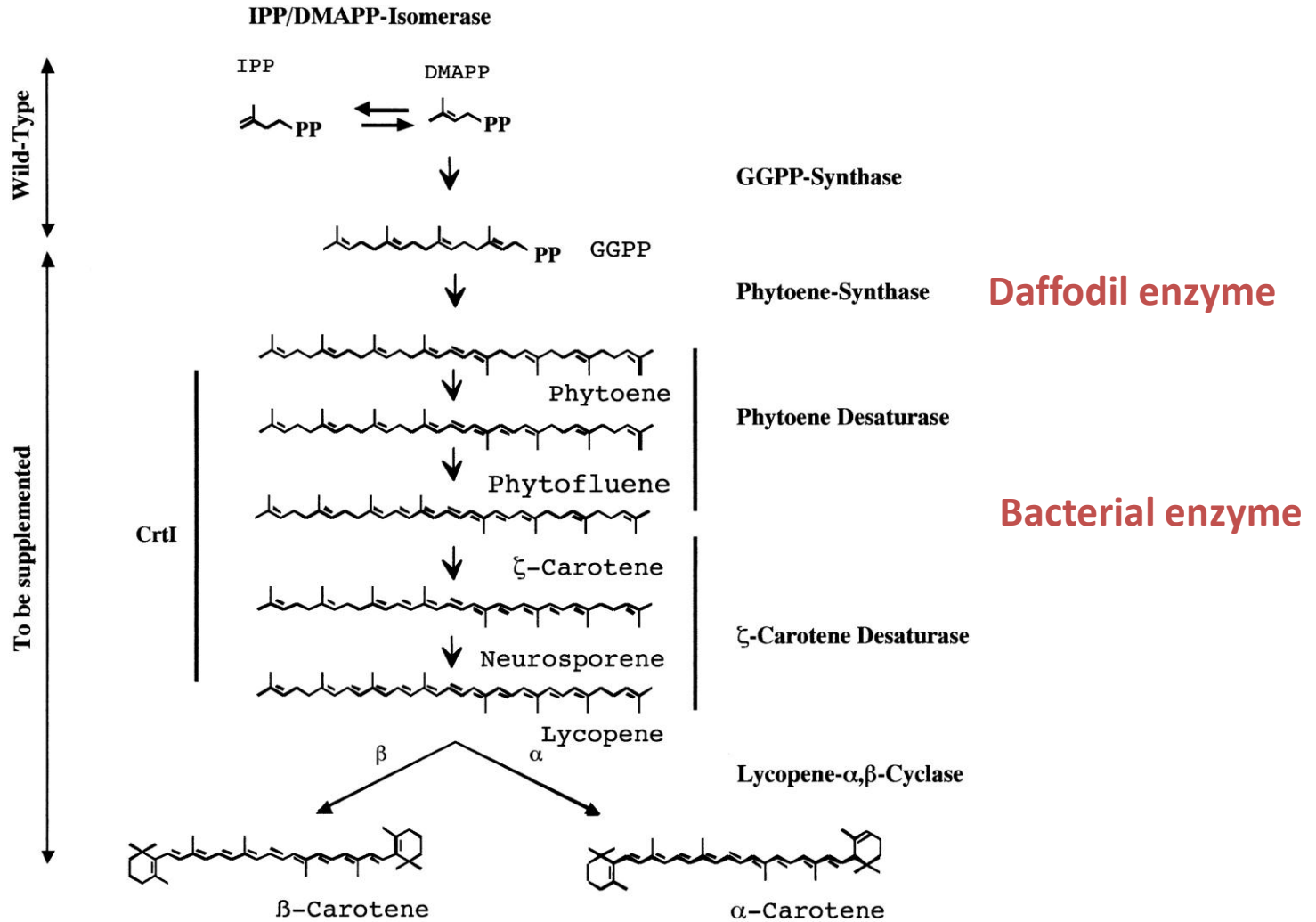
Project located at IRRI, Manila

Led by Dr Gerard Barry

<http://www.goldenrice.org/>



## Provitamin A biosynthetic pathway.



Beyer P et al. J. Nutr. 2002;132:506S-510S

Funded by

Rockefeller Foundation (I.P. and P.B.)  
European Community Biotech Program (P.B., FAIR CT96, 1996–1999),  
Swiss Federal Office for Education and Science (I.P.)  
Swiss Federal Institute of Technology (I.P.).

Gates Foundation

**One of the scientifically most complex GM projects**



## Golden Rice

First field trials Louisiana 2004

American varieties

Further engineering to increase levels of pro-vitamin A

Backcrossing into Asian and other varieties

Now under field trials in Philippines and Bangladesh

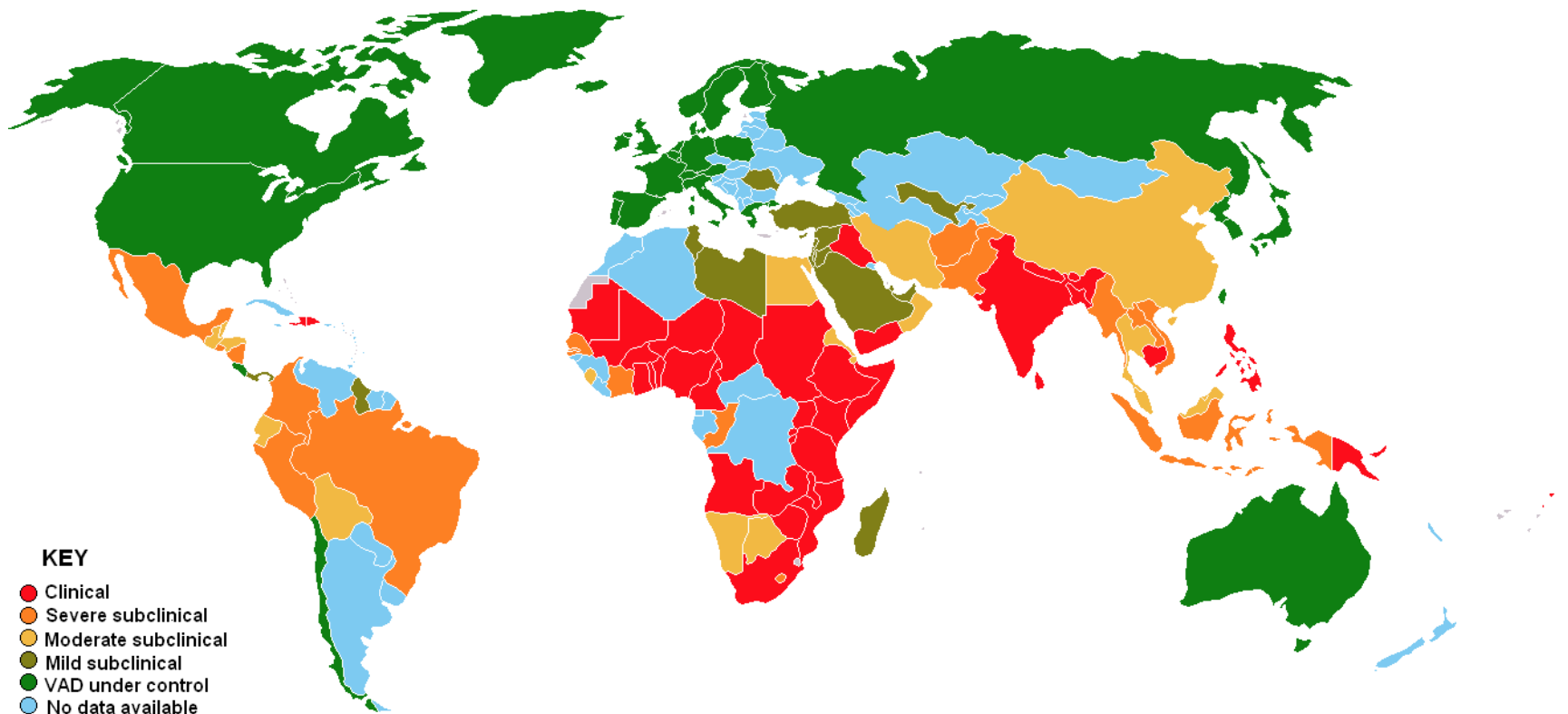
Nutritional and safety trials

For release in 2015









Vitamin A deficiency: Asia, Africa, Latin America: WHO data





Almost all GM food and crop projects have been vehemently opposed by NGOs, especially in Europe, notably Greenpeace



“If you plan to destroy test fields to prevent responsible testing and development of Golden Rice for humanitarian purposes, you will be accused of contributing to a crime against humanity.”

Dr. Ingo Potrykus to Greenpeace,  
February 2001



“Protestors from two anti-GMO groups, KMB and Sikwal-GMO, yesterday vandalized a field of genetically modified (GM) "golden rice" in the Bicol region of the Philippines.”

Science *Insider* 9 August 2013



## Summary

The EU eats **IMPORTED** GM food

– soy, corn etc

The EU uses **IMPORTED** GM animal feed

The EU uses GM enzymes in food processing

– cheese, bread, beer, whiskey, fruit juice .....

The EU uses **IMPORTED** GM cotton

In essence the EU uses but does not grow GM crops





Why?

EU public and political opinion has been negative

Science has been sidelined

The regulatory system has **paralysed** the technology



Weak public science

*44% of Germans think non-GM tomatoes do not contain genes*

Uninformed media

Uninformed politicians

Uninformed civil servants

Weak political leadership

Strong anti-scientific NGO

Naïve scientists



## EU GMO regulatory system

Slow, complex, conservative, highly politicised, unreliable and damaging

EU has approved 67 GM crops (USA 202)

2 carnations and 2 crops *cultivation*

**Maize Mon 810**

**Potato BPS-25271-9**

Other are permits are for imported feed or food

[https://www.isaaa.org/gmapprovaldatabase/approvedeventsin/default.asp?  
CountryID=EU&Country=European%20Union](https://www.isaaa.org/gmapprovaldatabase/approvedeventsin/default.asp?CountryID=EU&Country=European%20Union)





## Timelines for GM products with a positive EFSA safety opinion and awaiting Commission action:

**timelines not compliant with EU law**      **timelines compliant for the moment**

Product	EFSA Opinion	Days waiting for the Commission to schedule vote at committee level <sup>1</sup> : maximum: 3 months	Days waiting for the Commission to schedule vote in Appeal Committee maximum: 2 months <sup>2</sup>	Days after Council/ Appeal vote - waiting for approval
1507 maize (c)	03/03/2005	voted after 1462 days	1131 days and counting	
Bt11 maize (ipc)	19/05/2005	voted after 1385 days	1131 days and counting	
LL Rice62 (ffip)	30/10/2007	1613 days and counting		
NK603 maize (ffipc)	11/06/2009	1007 days and counting		
MON810 maize (ffipc)	30/06/2009	1006 days and counting		
MS8xRF3 rapeseed(ff)	22/09/2009	922 days and counting		
GT73 oilseed rape(ffip)	15/12/2009	838 days and counting		
MON863 maize (ffip)	30/03/2010	733 days and counting		
MON89034x1507xMON88017x 59122 maize (ffip)	27/09/2010	552 days and counting		
MON89034x1507xNK603 maize (ffip)	27/09/2010	552 days and counting		
MON531 cotton (ffip)	16/09/2011	198 days and counting		
MON88017 maize (c)	10/11/2011	143 days and counting		
MON1445 cotton (ffip)	16/12/2011	107 days and counting		
GA21 maize (ffipc)	16/12/2011	107 days and counting		
MON87701xMON89788 soybean (ffip)	15/02/2012	46 days and counting		
MON 531xMON1445 cotton (ff)	28/03/2012	5 days and counting		

ff=food, feed and industrial use    i=import    p=processing    c=cultivation

Product	EFSA Opinion	Commission vote (max 3 months)	Vote on appeal (Max 2 months)
1057 Maize	3.3.05	4 years	> 4 years
Bt11 Maize	19.5.05	3.8 years	> 4 years

**"In terms of the risk management stage, nearly all respondents, whether [member state] Competent Authorities or stakeholders, believed this was not fully operational"**

**- EU Report on the state of the biotech regulatory system**

## Objections

## Answers

Safety

As safe as *modern* farming/food

Protection of traditional farming/food

No different from *modern* farming/food

Protection of the environment

No different from *modern* farming/food

Role of multinational industries in agriculture

No different from *modern* farming



# Professional Scientific and/or Medical bodies with an opinion on safety of GMOs

## Generally Positive

- ✓ The U.S. National Research Council (NRC)
- ✓ U.S. National Academy of Sciences (NAS)
- ✓ The American Medical Association, (AMA)
- ✓ U.S. Department of Agriculture (USDA)
- ✓ U.S. Environmental Protection Agency (EPA)
- ✓ U.S. Food and Drug Administration (FDA)
- ✓ European Food Safety authority (EFSA)
- ✓ American Society for Plant Biology (ASPB)
- ✓ World Health Organization (WHO)
- ✓ Food and Agriculture Organization (FAO)
- ✓ Royal Society (London)
- ✓ Brazil National Academy of Science,
- ✓ Chinese National Academy of Science
- ✓ Indian National Academy of Science
- ✓ Mexican Academy of Science
- ✓ Third World Academy of Sciences

## Generally Negative

From all our experience with traditionally bred 'genetically modified' crop varieties, and from basic biological science we know that there is no sensible argument for specific regulations for 'genetically engineered' crops.

The results from extensive 'biosafety research' with 'genetically engineered' varieties, and experience from all previous deregulations confirm this view.

It does not make sense, therefore, to maintain the present 'extreme precautionary' GMO regulation, even if it would not prevent use of the technology for the solution of severe humanitarian problems.

The scientific community has the duty of stressing this point to the media, politicians and the public. Keeping a low profile is irresponsible.

Igor Potrykus 2005



## Lesson

GM farming should be regulated in the same way as nonGM farming

GM food and feed should be regulated in the same way as nonGM food and feed

The principle of equivalence

GM = nonGM



European Academies Science Advisory Council  
(EASAC)

*Planting the future: opportunities and  
challenges for using crop genetic improvement  
technologies for sustainable agriculture*

June 2003

“The regulatory framework for crop genetic improvement technologies must be reformulated appropriately”

European Academies Science Advisory Council  
(EASAC)

*Planting the future: opportunities and  
challenges for using crop genetic improvement  
technologies for sustainable agriculture*

June 2013

**“There is no validated evidence that GM crops have greater adverse impact on health and the environment than any other crops developed by alternative technologies used in plant breeding. There is compelling evidence that GM crops can contribute to sustainable development goals with benefits to farmers, consumers, the environment and the economy”**



The present EU regulations are unnecessary, expensive and damaging

Undermining EU farming and industry

Undermining GMOs in developing world

Discriminating in favour of US multinationals

Discriminating against public science,  
university science and start-up biotech companies

*(Cannot afford to deal with the regulations)*

Inhibiting innovative plant genetics

Anti-science

Anti-intellectual



Greenpeace opposes Golden Rice and all GM (GE crops)

“Greenpeace opposes the release of GE crops, including 'Golden' rice, into the environment.”



The

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has become an insurgent outlier – ideologically extreme:

scornful of compromise;

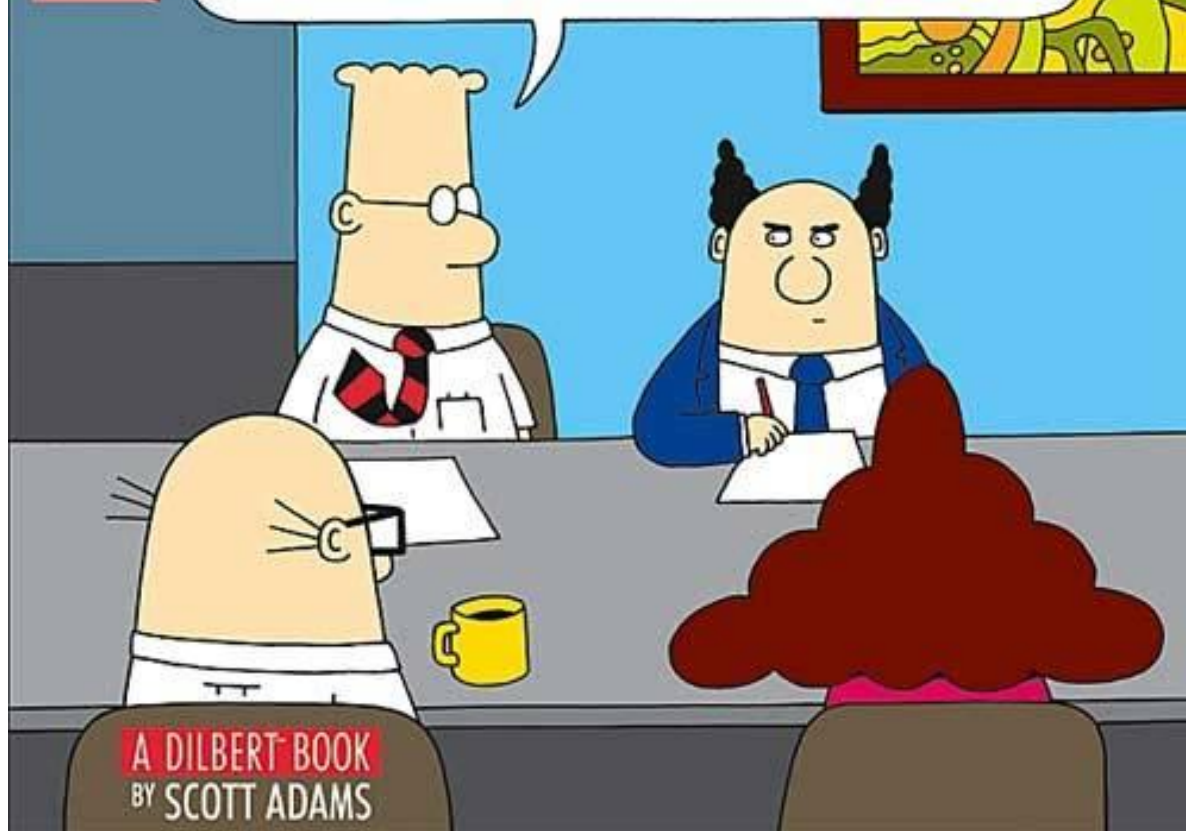
unpersuaded by the conventional understanding of facts,  
evidence and science.





**DILBERT**

**WHEN DID  
IGNORANCE  
BECOME A POINT OF VIEW?**



Wrong activism has done tremendous damage to the humanitarian use of this great technology. Let's hope that with increasing acceptance and the accumulated experience using GM crops around the world, more and more developing countries will find ways to benefit from the many useful traits in the pipeline in the near future and that many children will have access to biofortified rice and other crops.

[http://www.goldenrice.org/Content1-Who/who4\\_IP.php](http://www.goldenrice.org/Content1-Who/who4_IP.php)



Marvellous science

Wonderful technology

Remarkable achievements

Extraordinary potential for boosting agriculture  
and  
ameliorating hunger and disease



GM crops

2012

Alfalfa (*Medicago sativa*)  
Argentine Canola (*Brassica napus*)  
Bean (*Phaseolus vulgaris*)  
Carnation (*Dianthus caryophyllus*)  
Chicory (*Cichorium intybus*)  
Cotton (*Gossypium hirsutum* L.)  
Creeping Bentgrass (*Agrostis stolonifera*)  
Flax (*Linum usitatissimum* L.)  
Maize (*Zea mays* L.)  
Melon (*Cucumis melo*)  
Papaya (*Carica papaya*)  
Petunia (*Petunia hybrida*)  
Plum (*Prunus domestica*)  
Polish canola (*Brassica rapa*)  
Poplar (*Populus* sp.)  
Potato (*Solanum tuberosum* L.)  
Rice (*Oryza sativa* L.)  
Rose (*Rosa hybrida*)  
Soybean (*Glycine max* L.)  
Squash (*Cucurbita pepo*)  
Sugar Beet (*Beta vulgaris*)  
Sugarcane (*Saccharum* sp.)  
Sweet pepper (*Capsicum annuum*)  
Tobacco (*Nicotiana tabacum* L.)  
Tomato (*Lycopersicon esculentum*)  
Wheat (*Triticum aestivum*)





Pest resistance

– insects, fungi, nematodes, viruses ...

Herbicide tolerance

Drought tolerance

GM traits

Nitrogen assimilation

2012

Salt tolerance

Nutritional value

Allergen reduction

Shelf life

Chemical quality (starch)

Bioplastic production

Etc etc etc





Plant making bioplastic

PolyOHbutyrate

## The pipeline

100s of cases developed in the public sector

Including Egypt, Kenya, South Africa,  
Zimbabwe, China, India, Indonesia, Malaysia,  
Pakistan, Philippines, Thailand, Argentina,  
Brazil, Costa Rica, and Mexico.

GMO rice, maize, pearl millet, sorghum,  
wheat, potatoes, cassava, sweet potatoes,  
melons, cucumbers, squash, watermelons,  
tomatoes, bananas, plantain, beans, papaya,  
sunflower, soybean, groundnut, chickpea, oil  
palm, cabbage, cauliflower, cacao, mango .....

Ireland: Blight-tolerant potatoes ????



97 genes approved for use in one or more countries

- 10 virus resistance
- 23 herbicide resistance
- 24 insect resistance



**"We cannot turn back the clock on agriculture and only use methods that were developed to feed a much smaller population. ....**

**Farmers across the world must have access to current high-yielding crop-production methods as well as new biotechnological breakthroughs that can increase the yields, dependability, and nutritional quality of our basic food crops. We need to bring common sense into the debate on agricultural science and technology, and the sooner the better!"**

**- Norman E. Borlaug**

**"Responsible biotechnology is not the enemy; starvation is."**

**- President Jimmy Carter**



?What is Life?

Charles Jencks

National Botanic Gardens

Unveiled by James Watson 2013