# GMOs in animal agriculture: time to consider both costs and benefits in regulatory evaluations


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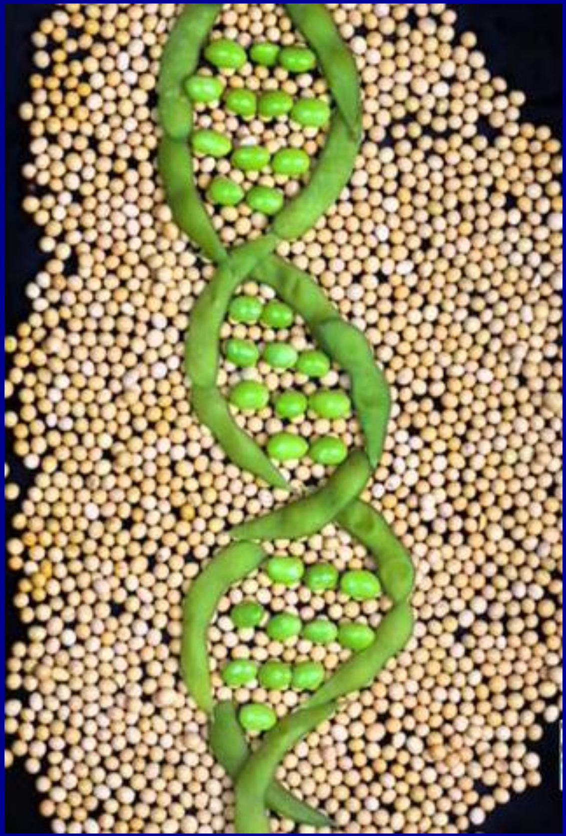
UCDAVIS ANIMAL SCIENCE

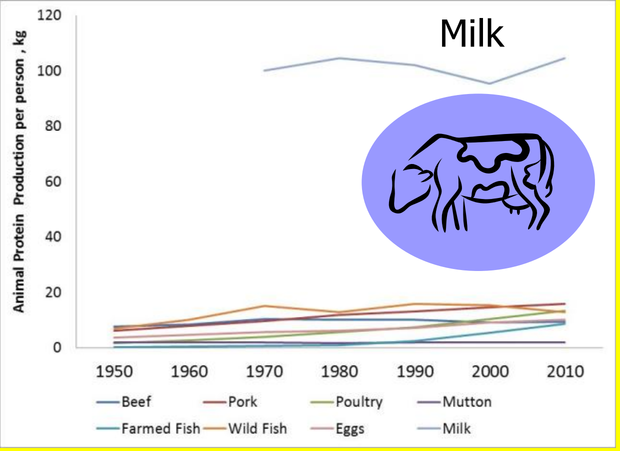


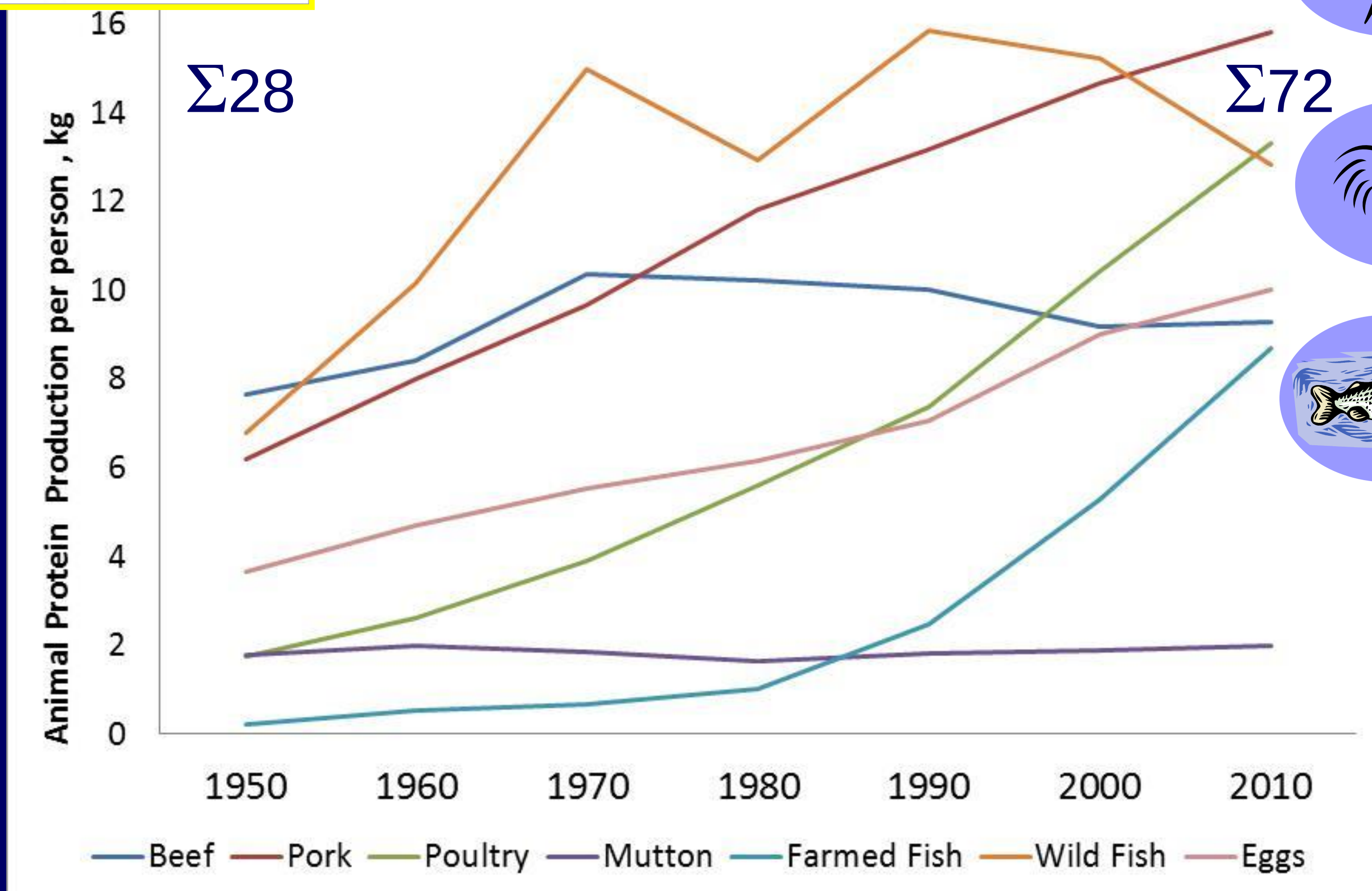
http://animalscience.ucdavis.edu/animalbiotech

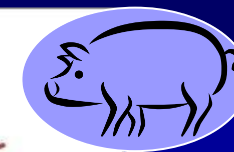
# Overview

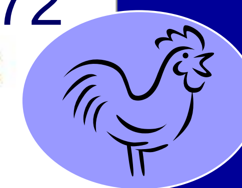
- Global demand for animal protein
- Global production of genetically engineered (GE, biotech, GM, GMO, transgenic) crops
- Global livestock populations as consumers
- Review of animal GE feeding studies
- Importance of correct experimental design
- Regulatory evaluations should consider both reasonable and unique risks and benefits of GE, and consequences of regulatory inaction

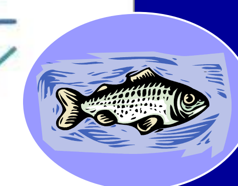
# World Animal Protein Production Per Person, kg (excl. milk) 1950-2010







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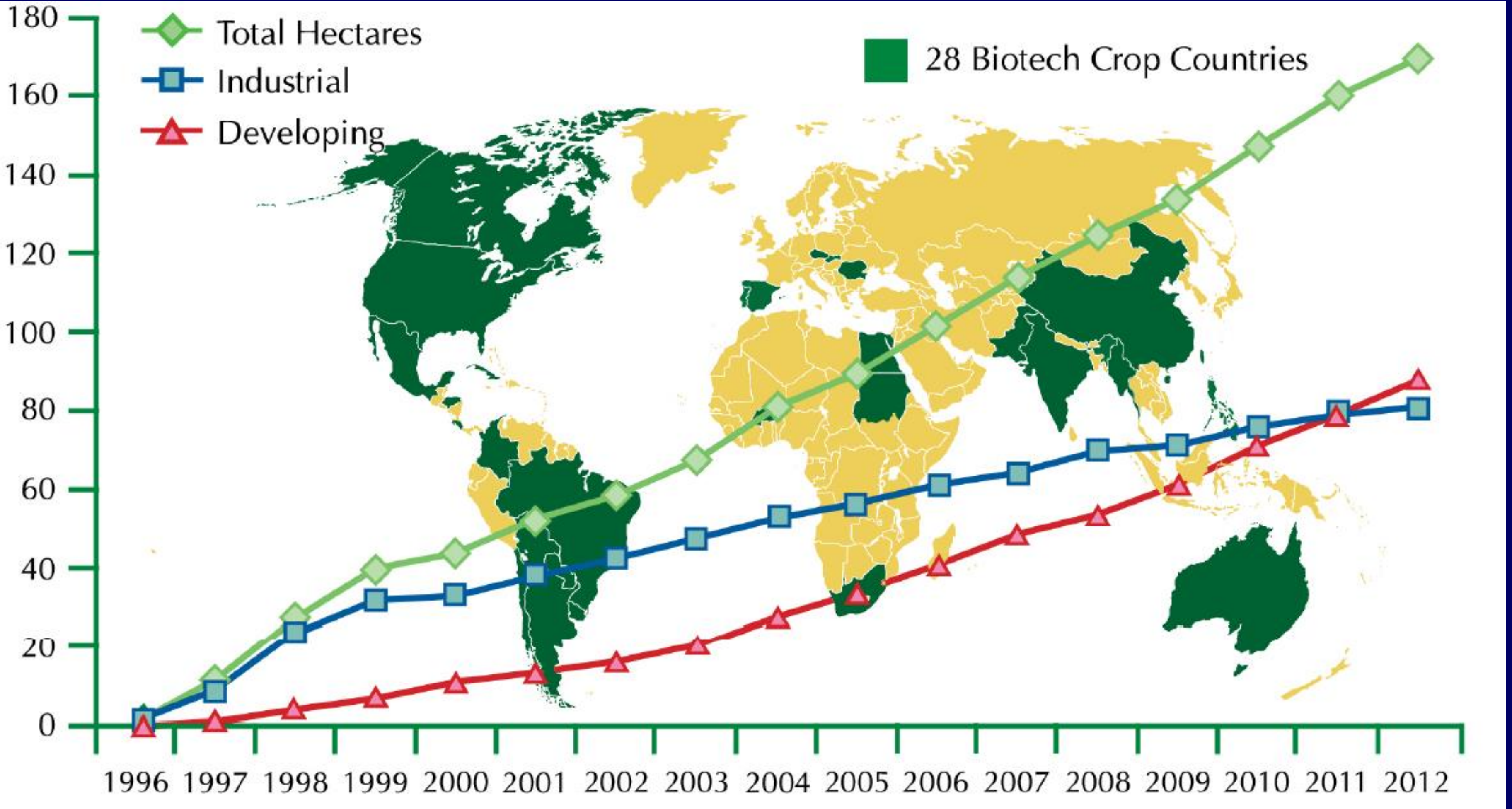
Data compiled by Earth Policy Institute *www.earth-policy.org*

# The livestock revolution

- **Demand for livestock products is expected to continue growing strongly through the middle of this century**
- Unlike the supply-led Green Revolution, the “Livestock Revolution” is driven by demand resulting from population growth, rising affluence in developing countries and urbanization
- **For more than a decade, the strongest increases in animal protein production have been in the developing world**
- From the early 1970s to the mid-1990s, the volume of meat consumed in developing countries grew almost three times as much as it did in the developed countries
- **Since 1995 developing countries produce more meat and dairy products than are produced in developed countries**

Delgado, C. L. 2003. Rising consumption of meat and milk in developing countries has created a new food revolution. Journal of Nutrition 133:3907S-3910S

# Global Area of Genetically Engineered (GE) crops
# Million hectares (1996-2013)

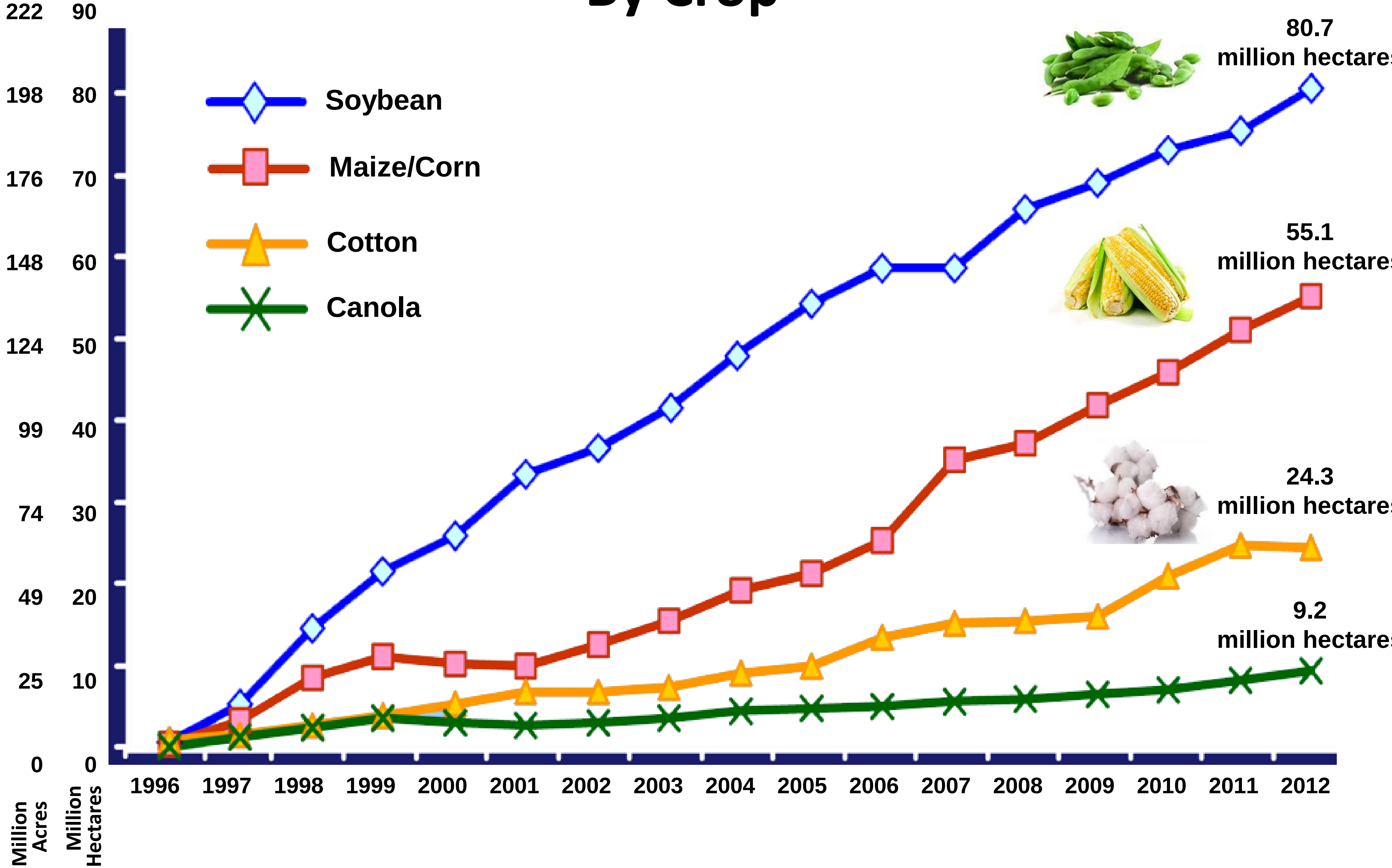



*A record 17.3 million farmers, in 28 countries, planted 170.3 million hectares (420 million acres) in 2012, a sustained increase of 6% or 10.3 million hectares (25 million acres) over 2011.*



**Source: Clive James, 2012 ISAAA Brief 44-2012 http://www.isaaa.org**

# Global Area of Genetically Engineered (GE) Crops 1996 – 2012 By Crop

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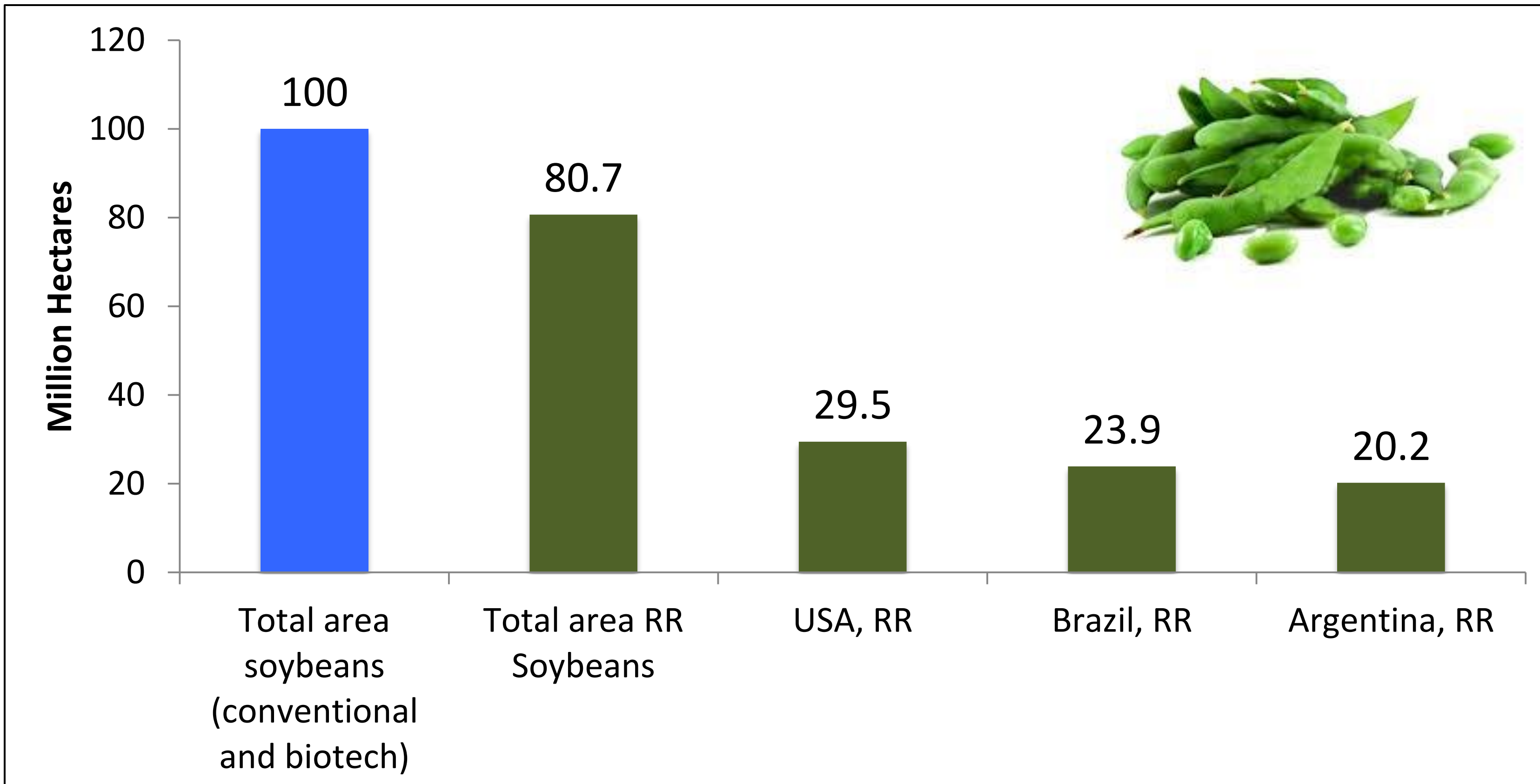
Source: Clive James, 2012 ISAAA Brief 44-2012 http://www.isaaa.org

# Soybeans, 2012

- In 2012, GE soybeans accounted for 47% of all GE crop area
- 81% of all soybeans grown were GE
- 11 countries grew “RoundUp-Ready” (RR) GE Soybeans

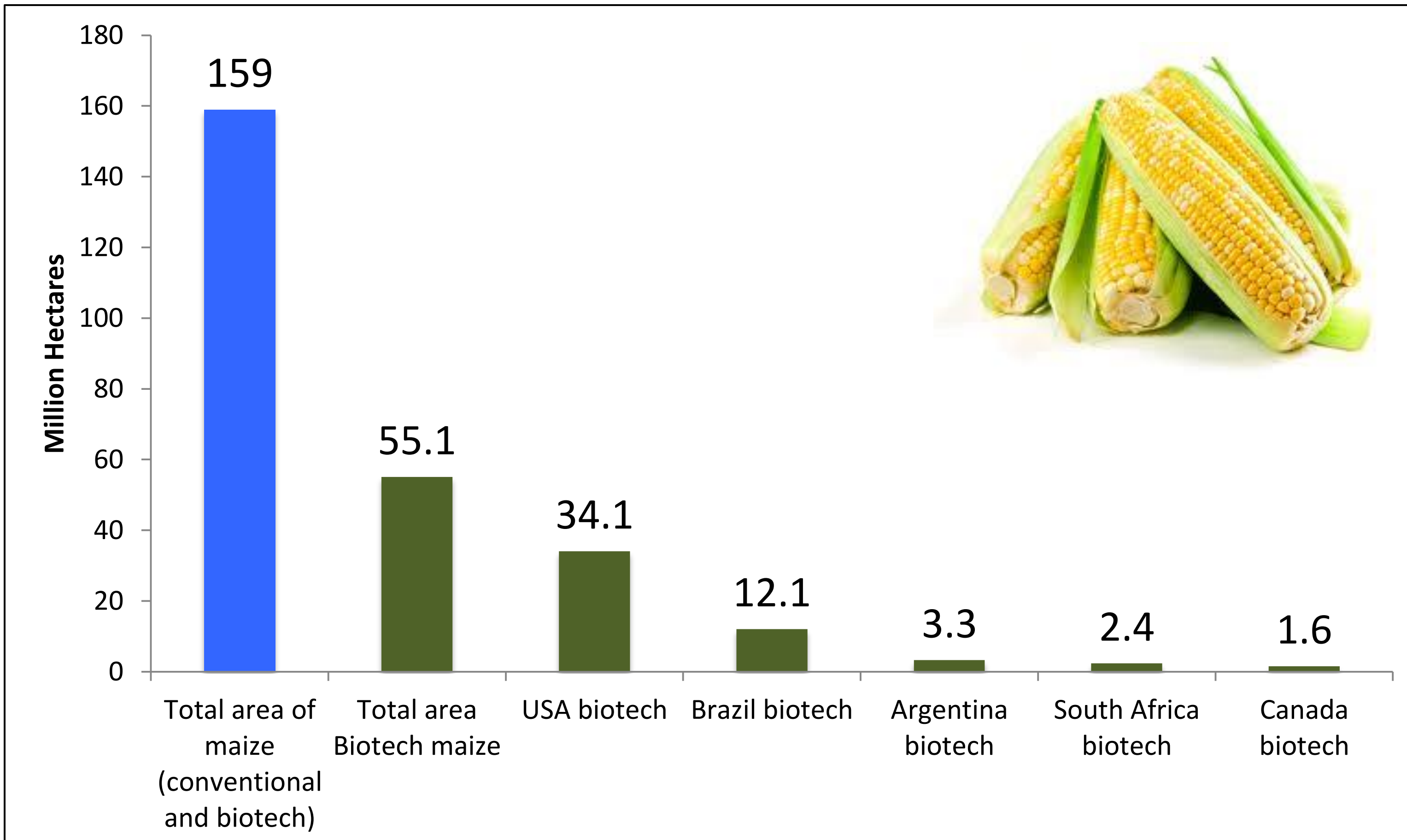





Source: Clive James, 2012 ISAAA Brief 44-2012 http://www.isaaa.org

# Maize (Corn), 2012

- 35% of all maize area was GE
- 17 countries grew GE maize
- Brazil grew by 3 million hectares from 2011 to 2012
- 5 EU countries  grew 130,000 hectares of Bt GE maize

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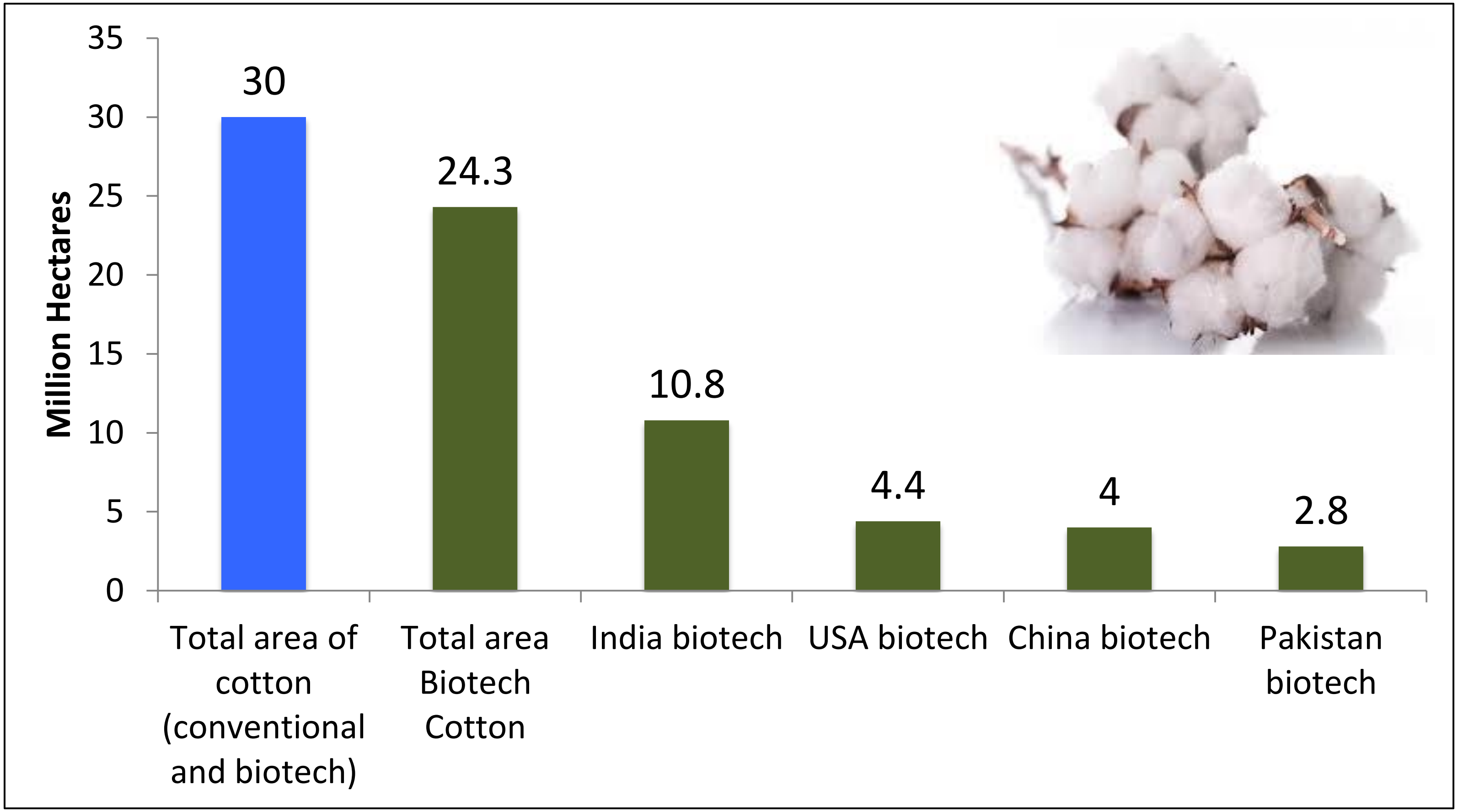
Source:  Clive James, 2012 ISAAA Brief 44-2012  http://www.isaaa.org

# Cotton, 2012

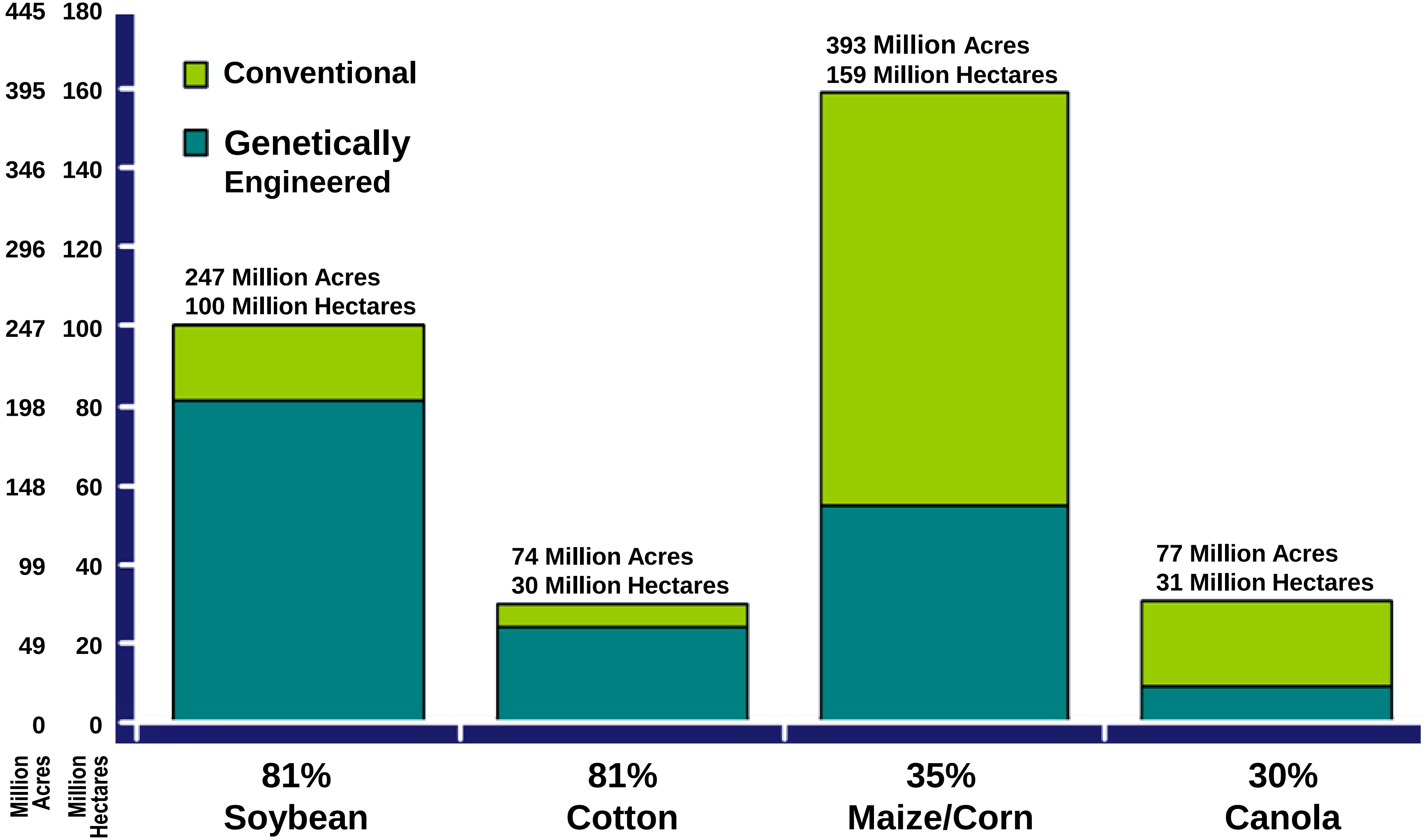
- 81% of all cotton area was GE
- Global area of GE cotton 24.3 million hectares
- 15 countries grew GE cotton




Source: Clive James, 2012 ISAAA Brief 44-2012 http://www.isaaa.org

# Global Adoption Rates (%) for Principal GE Crops, (Million Acres, Million Hectares) 2012

**53% of the global area (conventional and GE) of these crops are GE (50% in 2011)**

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Source: Clive James, 2012 ISAAA Brief 44-2012 http://www.isaaa.org

# Global livestock populations are the major consumers of GE crops

70-90% of harvested GE biomass is fed to food producing animals

Flachowsky G, Schafft H, Meyer U: 2012 **Animal feeding studies for nutritional and safety assessments of feeds from genetically modified plants: a review.** *(Journal of Consumer Protection and Food Safety)* **:**179–194.

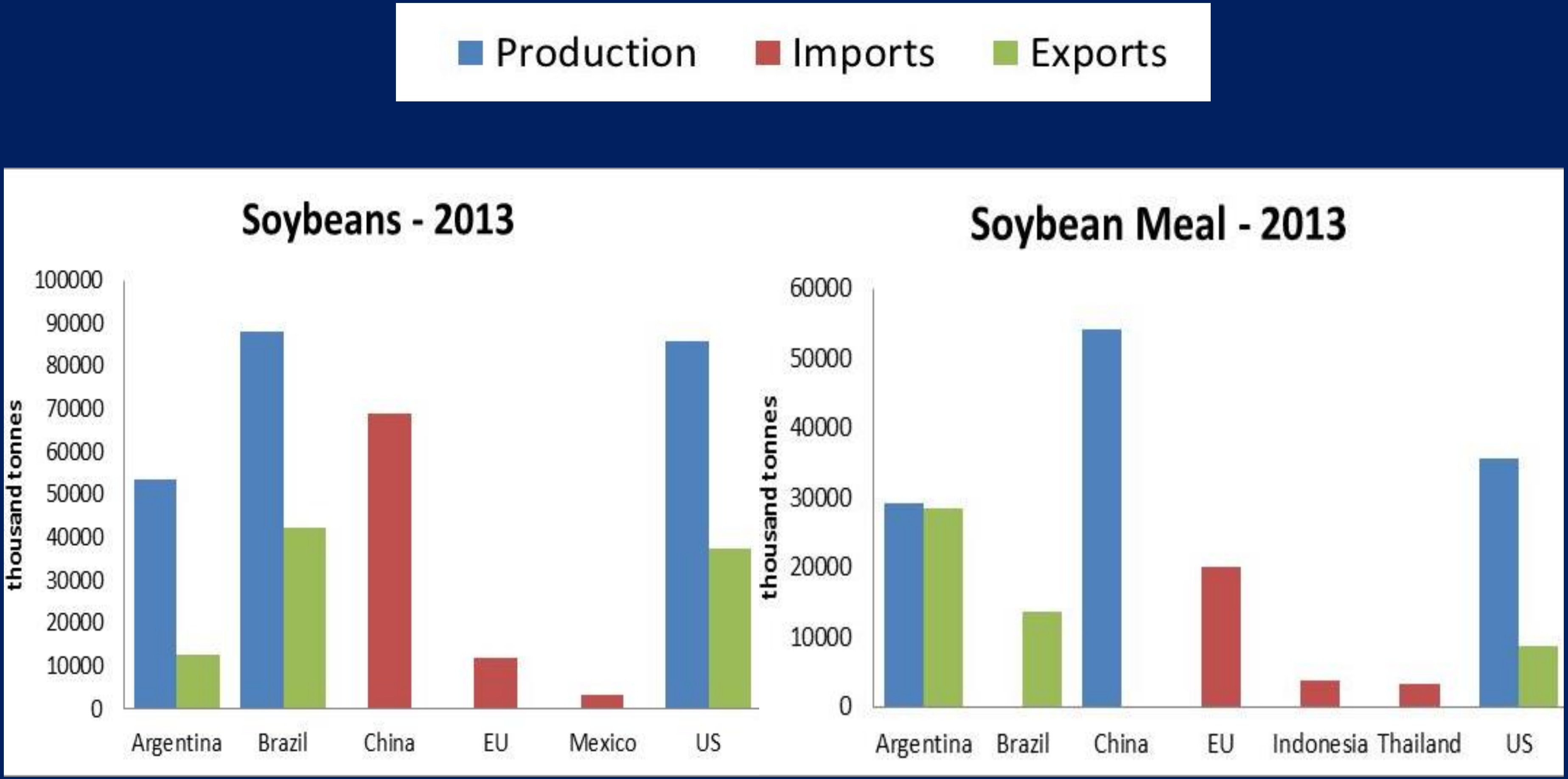
# Share of global crop trade accounted for by GE crops 2011/12

## (million tonnes)

| | Soybeans | Maize (Corn) | Cotton | Canola |
|---|---|---|---|---|
| Global production | 238 | 883.5 | 27.0 | 61.6 |
| Global trade (exports) | 90.4 | 103.4 | 10.0 | 13.0 |
| Share of global trade from GE producers | 88.6 (98%) | 70.0 (67.7%) | 7.15 (71.5%) | 9.9 (76%) |
| Share of global trade that may be GE | 96.7% | 67.7% | 71.5% | 76% |

Brookes G, Barfoot P: 2013 **GM crops: global socio-economic and environmental impacts 1996–2011.** PG Economics Ltd: UK;. www.pgeconomicscouk/pdf/2013globalimpactstudyfinalreportpdf.

# Three top producers, importers and exporters of soybeans and soybean meal (thousand tonnes)




**Oilseeds world market and trade. September 2013** http://www.fas.usda.gov/oilseeds/Current

# Global livestock populations are the major consumers of GE crops

- For climatic and agronomic reasons, the European Union (EU) is unable to produce most of the oilseed meal and other protein-rich feedstuffs required to feed its livestock
- 80% of all livestock feed in the European Union (EU) is imported
- 98% of EU soybean meal is imported from Brazil, the USA, and Argentina; ~ 80% of this imported soybean meal animal feed is GE
- If the EU were not able to import soybean protein from outside the EU it would only be able to replace 10-20% of imports by high protein substitutes, resulting in a substantial reduction in animal protein production, exports and consumption, and a very significant increase in animal protein imports and cost in the EU*

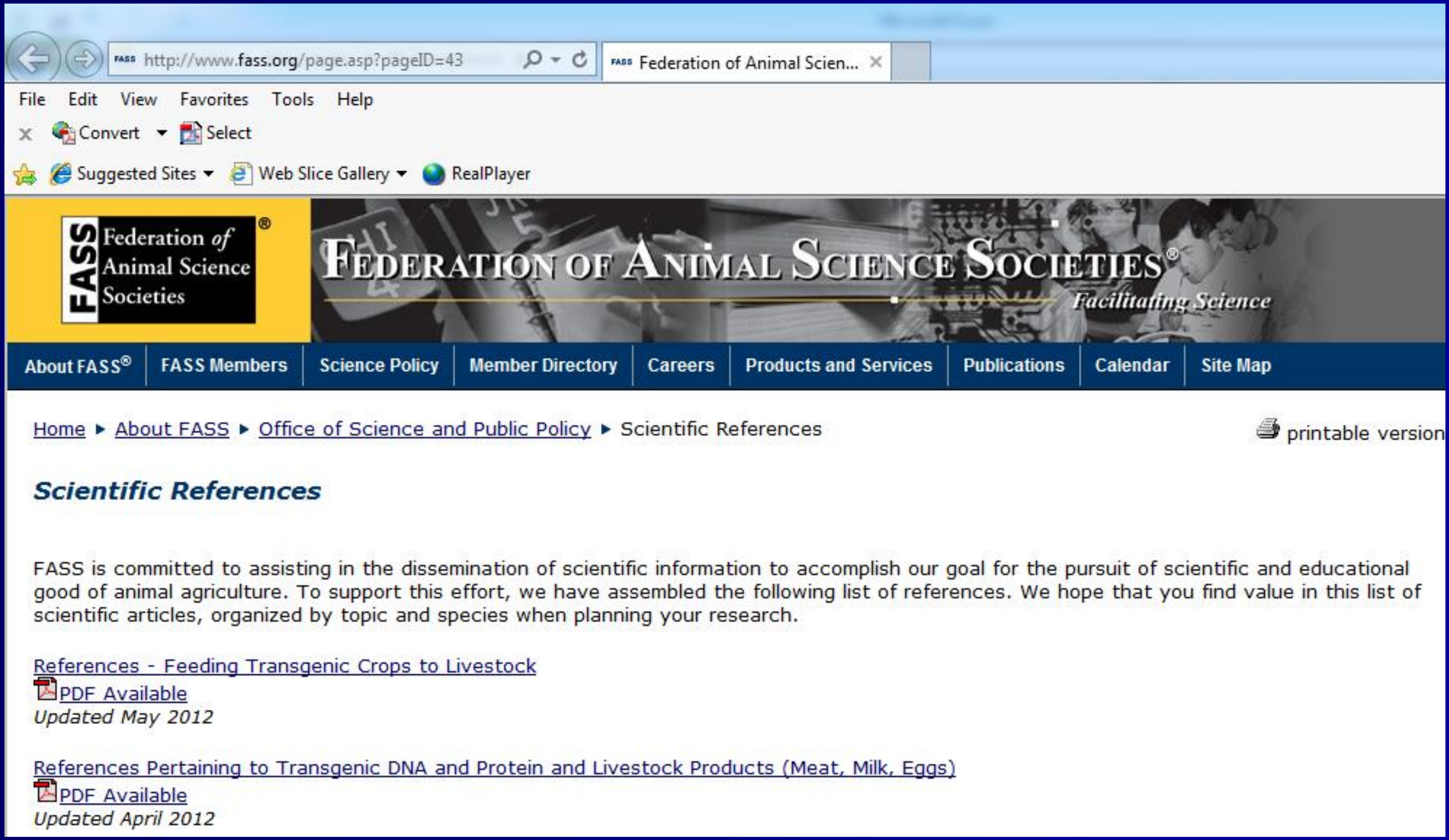
* Directorate-General for Agriculture and Rural Development. 2007. **Economic impact of unapproved GMOs on EU feed imports and livestock production**. http://ec.europa.eu/agriculture/envir/gmo/economic_impactGMOs_en.pdf

# There have been hundreds of animal feeding studies using GE crops

| Animal species/ category | Number of experiments | Nutritional assessment |
|---|---|---|
| Ruminants | | No unintended effects in composition (except lower mycotoxin concentration in Bt-plants) |
| Dairy cattle | 23 | |
| Beef cattle | 14 | |
| Others | 10 | |
| Pigs | 21 | |
| Poultry | | No significant differences in digestibility and poultry health as well as no biological relevant unintended effects on performances of animals and composition of food of poultry origin |
| Broilers | 48 | |
| Laying hens | 12 | |
| Other poultry | 1 | |
| Others (fish, rabbits etc.) | 8 | |

Flachowsky G, Schafft H, Meyer U: 2012 **Animal feeding studies for nutritional and safety assessments of feeds from genetically modified plants: a review.** *(Journal of Consumer Protection and Food Safety)* **:**179–194.

# Federation of Animal Science Societies' (FASS) maintains a list of animal feeding studies with GE (transgenic) crops




http://www.fass.org/page.asp?pageID=43

Food and Chemical Toxicology 50 (2012) 1134–1148

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Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Review

# Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review

Chelsea Snell [a], Aude Bernheim [b], Jean-Baptiste Bergé [c], Marcel Kuntz [d], Gérard Pascal [e], Alain Paris [f], Agnès E. Ricroch [b,*]

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[b] *AgroParisTech, 16, rue Claude Bernard, 75231, Paris, Cedex 05, France*
[c] *Anthala, 239, chemin de Saint Claude, 06600 Antibes, France*
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A R T I C L E I N F O

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Multigenerational studies
Systematic review

A B S T R A C T

The aim of this systematic review was to collect data concerning the effects of diets containing GM maize, potato, soybean, rice, or triticale on animal health. We examined 12 long-term studies (of more than 90 days, up to 2 years in duration) and 12 multigenerational studies (from 2 to 5 generations). We referenced the 90-day studies on GM feed for which long-term or multigenerational study data were available. Many parameters have been examined using biochemical analyses, histological examination of specific organs, hematology and the detection of transgenic DNA. The statistical findings and methods have been considered from each study. Results from all the 24 studies do not suggest any health hazards and, in general, there were no statistically significant differences within parameters observed. However, some small differences were observed, though these fell within the normal variation range of the considered parameter and thus had no biological or toxicological significance. If required, a 90-day feeding study performed in rodents, according to the OECD Test Guideline, is generally considered sufficient in order to evaluate the health effects of GM feed. The studies reviewed present evidence to show that GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed.

# Meta-analysis of long-term and multigenerational animal feeding trials

- Published long-term feeding studies using a GE-based diet ranged from 110-728 days
- The longest multigenerational study involved 10 generations.
- The authors concluded that none of the long-term or multigenerational studies they evaluated revealed any new effect that had not been found in the 90-d rodent toxicology study

"*The studies reviewed present evidence to show that GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed*."

Snell C, Bernheim A, Berge JB, Kuntz M, Pascal G, Paris A, Ricroch AE. 2012. **Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: a literature review.** *Food Chem Toxicol* **50:**1134–1148.

## Review of data from 60 high-throughput '-omics' comparisons between GE and non-GE crop lines and 17 recent long-term animal feeding studies, and 16 multigenerational studies on animals

- The '-omics' comparisons revealed that the genetic modification has less impact on plant gene expression and composition than that of conventional plant breeding. Moreover, environmental factors (such as field location, sampling time, or agricultural practices) have a greater impact than transgenesis.

*"None of these -omics profiling studies has raised new safety concerns about GE varieties; neither did the long-term and multigenerational studies on animals"*

Ricroch AE: **Assessment of GE food safety using '-omics' techniques and long-term animal feeding studies.** *N Biotechnol* 2012, **30**: 349-354.

# Billions of animals have eaten GE feed for the last 15 years

In 2011 in the United States alone

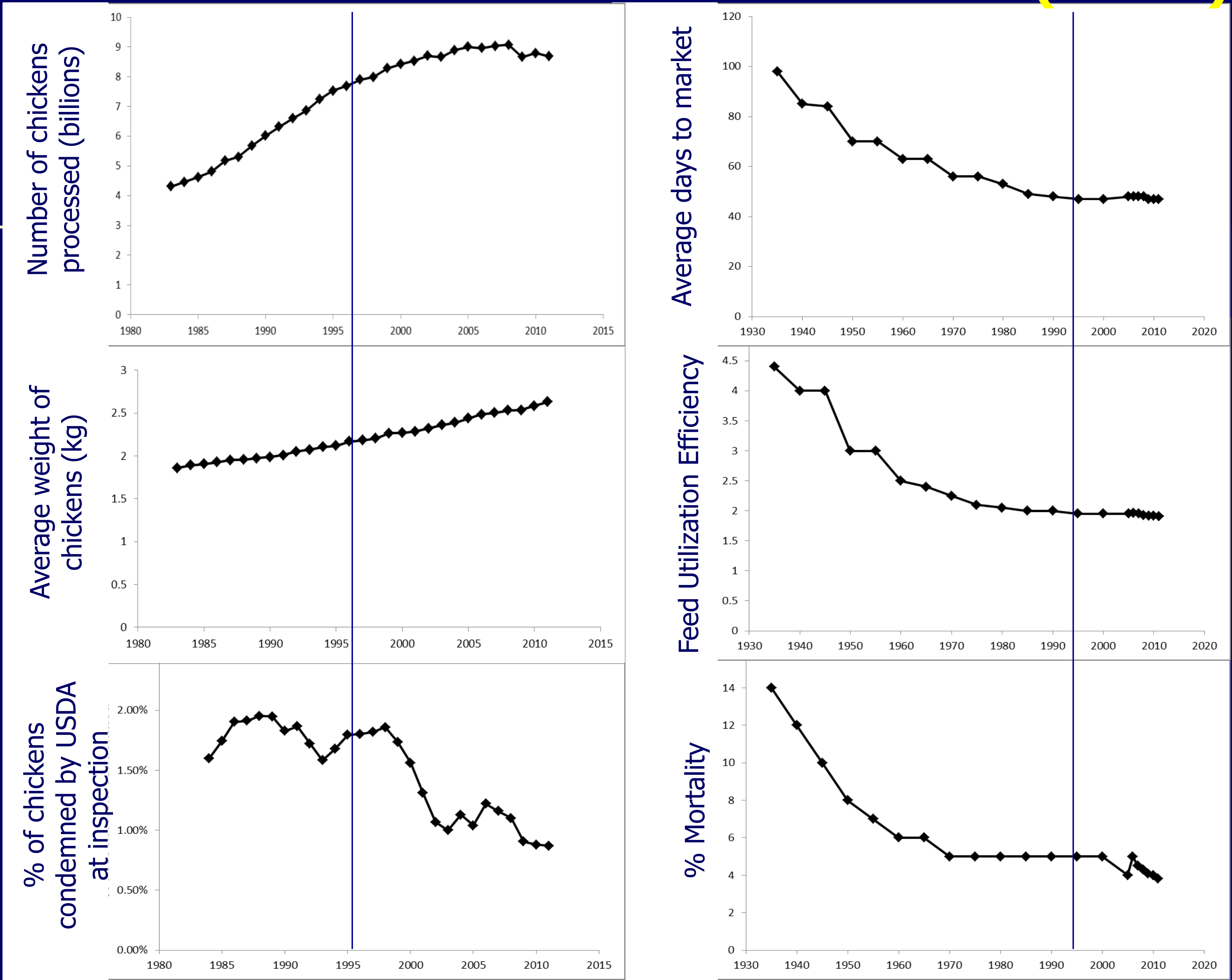
9 billion broiler chickens
weighing over 22.5 billion kg live weight

consumed

30 million tonnes of corn (~ 88% GE)
13.6 million tonnes of soy (~ 94% GE)

Van Eenennaam, A. L. 2013. **GMOs in animal agriculture: time to consider both costs and benefits in regulatory evaluations.** Journal of Animal Science and Biotechnology. 4:37.

# United States commercial broiler data (USDA)



# In some published animal feeding studies, differences have been observed in test parameters measured in animals fed GE feed

Many of these differences could not be interpreted or associated with the GE test material, due to deficiencies in the experimental design including:

- lack of information on the source and production of the GM test material
- lack of appropriate controls
- lack of information on the composition of the administered diet
- the use of diets that are potentially unbalanced nutritionally
- lack of dose response
- insufficient or no information on natural variations in test parameters

This information is needed to place differences potentially observed between the GE test material and its control into the appropriate biological context.

Kuiper, H.A., Kok, E.J., Davies, H.V. (2013) **New EU legislation for risk assessment of GM food: no scientific justification for mandatory animal feeding trials**. Plant Biotechnol. J., doi: 10.1111/pbi.12091

Food and Chemical Toxicology xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

# Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize

Gilles-Eric Séralini [a,*], Emilie Clair [a], Robin Mesnage [a], Steeve Gress [a], Nicolas Defarge [a], Manuela Malatesta [b], Didier Hennequin [c], Joël Spiroux de Vendômois [a]

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A R T I C L E   I N F O

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Roundup
NK603
Rat
Glyphosate-based herbicides
Endocrine disrupting effects

A B S T R A C T

The health effects of a Roundup-tolerant genetically modified maize (from 11% in the diet), cultivated with or without Roundup, and Roundup alone (from 0.1 ppb in water), were studied 2 years in rats. In females, all treated groups died 2–3 times more than controls, and more rapidly. This difference was visible in 3 male groups fed GMOs. All results were hormone and sex dependent, and the pathological profiles were comparable. Females developed large mammary tumors almost always more often than and before controls, the pituitary was the second most disabled organ; the sex hormonal balance was modified by GMO and Roundup treatments. In treated males, liver congestions and necrosis were 2.5–5.5 times higher. This pathology was confirmed by optic and transmission electron microscopy. Marked and severe kidney nephropathies were also generally 1.3–2.3 greater. Males presented 4 times more large palpable tumors than controls which occurred up to 600 days earlier. Biochemistry data confirmed very significant kidney chronic deficiencies; for all treatments and both sexes, 76% of the altered parameters were kidney related. These results can be explained by the non linear endocrine-disrupting effects of Roundup, but also by the overexpression of the transgene in the GMO and its metabolic consequences.



**“This report describes the first life-long rodent (rat) feeding study investigating possible toxic effects rising from an Roundup-tolerant GM maize”**

# A recent example of poor experimental design is the long-term toxicity study of a herbicide-tolerant GM maize NK603
**(Seralini *et. al.* 2012 *Food Chem Toxicol* 50:4221–4231)**

The key limitations of the study include:

- use of a rat strain with a well-known spontaneous occurrence of mammary tumors in female rats,
- small number of animals used in the various test groups,
- lack of reference controls or data on natural variations of test parameters,
- lack of data on the agronomic, compositional and phenotypic characteristics of the test and control materials,
- use of unconventional statistical methods and
- lack of power analysis prior to the start of the study.

The deficiencies noted in this study render any claims of the authors regarding long-term adverse effects of GM maize NK603 highly disputable and scientifically unfounded.

Kuiper, H.A., Kok, E.J., Davies, H.V. (2013) **New EU legislation for risk assessment of GM food: no scientific justification for mandatory animal feeding trials.** Plant Biotechnol. J., doi: 10.1111/pbi.12091

# Highly-publicized yet poorly-designed animal feeding studies have real world consequences

"Within hours, the news had been blogged and tweeted more than 1.5 million times. Lurid photos of tumor-ridden rats appeared on websites and in newspapers around the world, while larger-than-life images of the rats were broadcast across the USA on the popular television show Dr. Oz.

Activists destroyed a GM soybean consignment at the port of Lorient, France, in order to denounce the presence in the food chain of a product they considered to be toxic. The Russian Federation and Kazakhstan banned imports of the maize variety used in the study, Peru imposed a 10-year moratorium on GM crops and Kenya banned all imports of GM food."

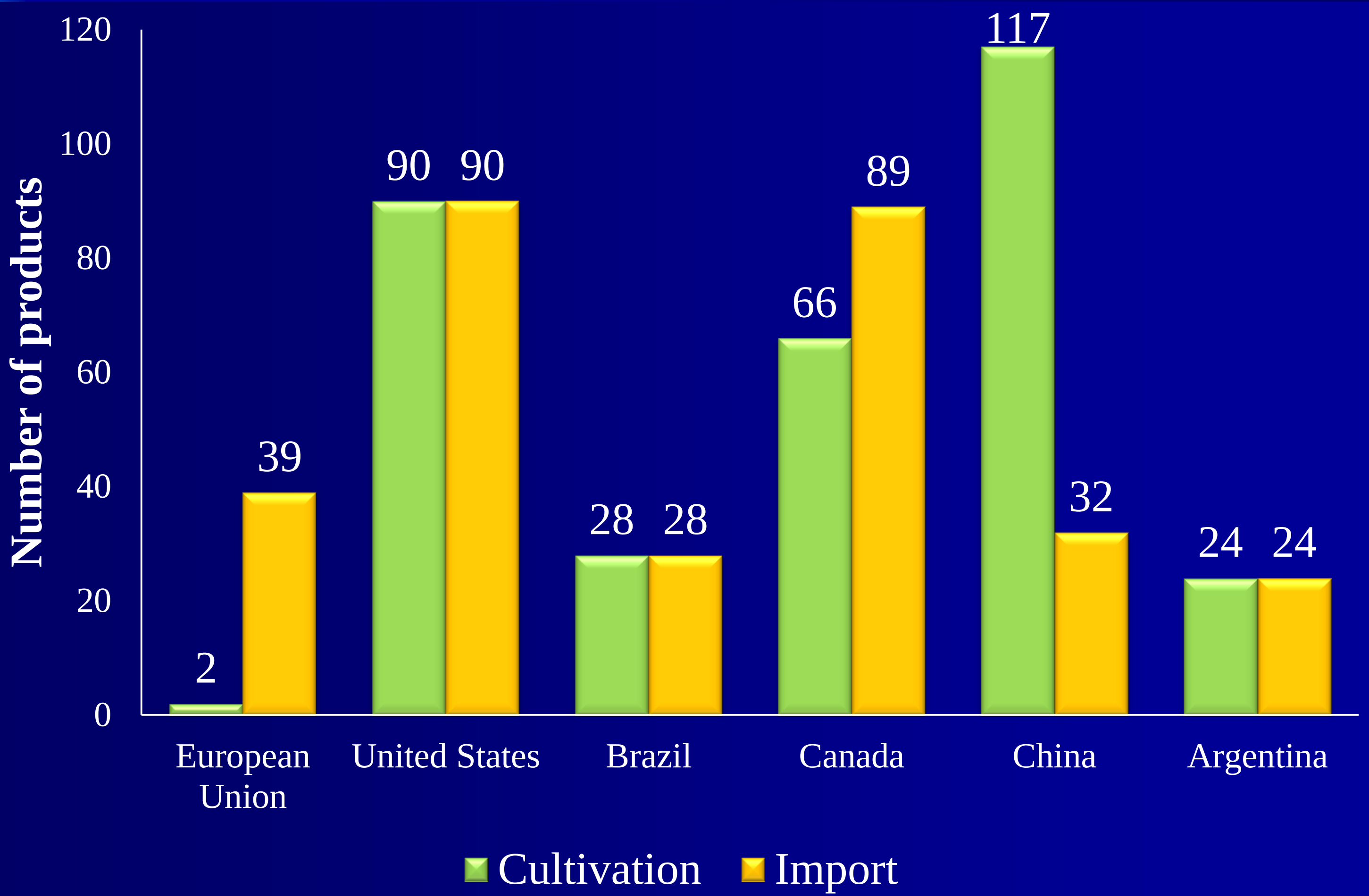
Arjó G, Portero M, Piñol C, Viñas J, Matias-Guiu X, Capell T, Bartholomaeus A, Parrott W, Christou P. 2013. **Plurality of opinion, scientific discourse and pseudoscience: an in depth analysis of the Séralini et al. study claiming that Roundup™ Ready corn or the herbicide Roundup™ cause cancer in rats.** Transgenic Res. 22:255-67.

# Regulatory implications

On June 2013, the European Commission published a Regulation (EU) No 503/2013 requiring an obligatory 90-day whole food/feed rodent feeding study for regulatory approval of each GE crop event. Depending on the outcome of this study, a 2-year long-term GE feeding study in rats may also be requested, on a case-by-case basis.

This Regulation passed despite the fact that the European Food Safety Authority (EFSA) questioned the need to provide such studies for the risk evaluation of each GE crop application as follows: ***"When 'molecular, compositional phenotypic, agronomic and other analyses have demonstrated equivalence of the GM food/feed, animal feeding trials do not add to the safety assessment"***

# Number of genetically engineered (GE) products approved for cultivation and import in different countries




Van Eenennaam, A. L. 2013. **GMOs in animal agriculture: time to consider both costs and benefits in regulatory evaluations.** Journal of Animal Science and Biotechnology. 4:37 .

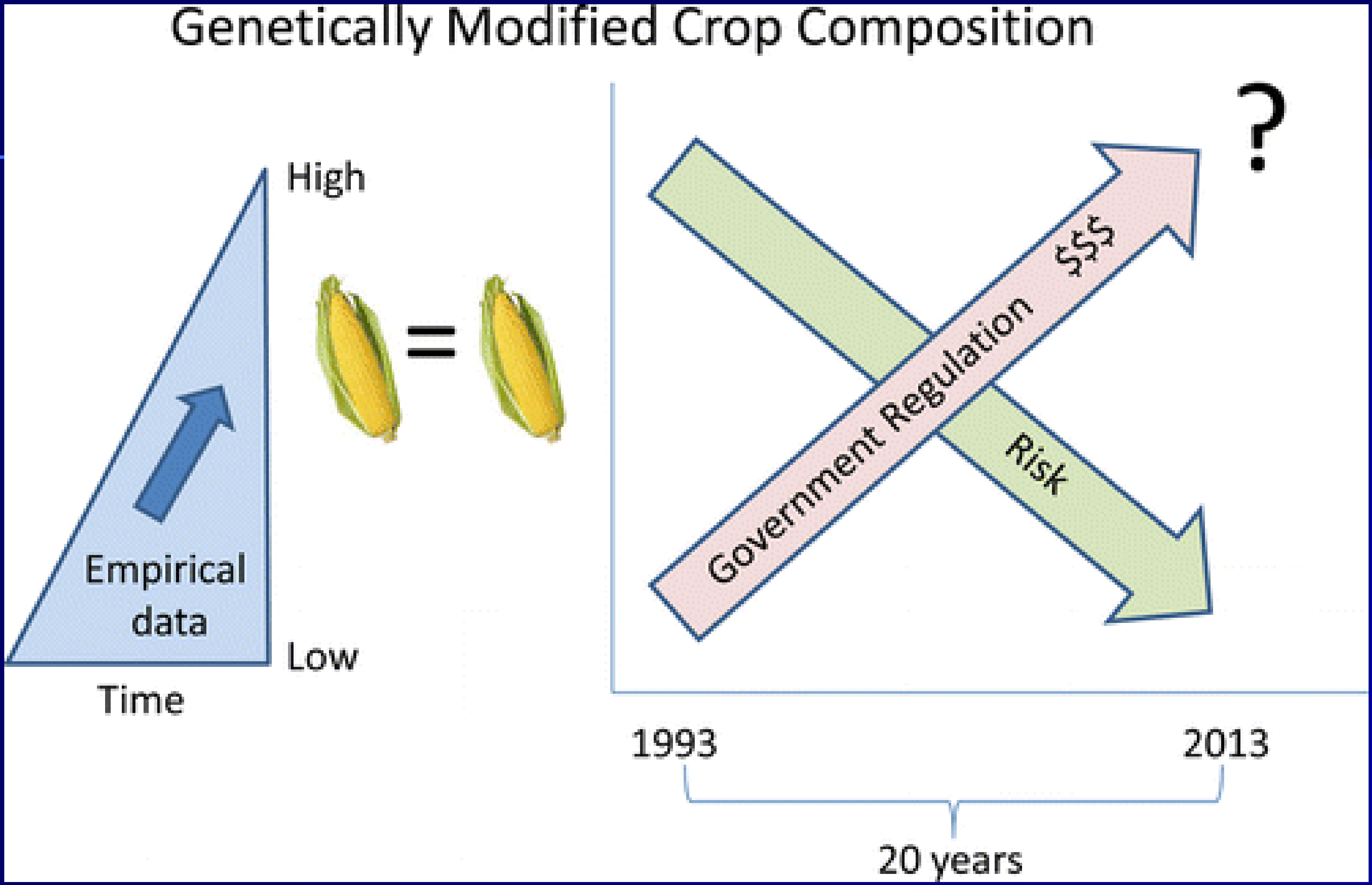
# Importance of correct experimental design and standard protocols in animal feeding studies

Repeated experimental design flaws in animal feeding studies evaluating GE feed are exacerbating the continued controversy associated with the safety of GE food and feed

The Animal Science community has an obligation to conduct and ensure that published animal feeding studies are carried out according to standard protocols to ensure data can be appropriately analyzed and unambiguously interpreted in the absence of confounding factors.

Van Eenennaam, A. L. 2013. **GMOs in animal agriculture: time to consider both costs and benefits in regulatory evaluations**. Journal of Animal Science and Biotechnology. 4:37 .

# Cost of regulations vs. benefit




Herman RA, Price WD: **Unintended compositional changes in genetically modified (gm) crops: 20 years of research.** *J Agric Food Chem* 2013

# Compositional equivalence studies uniquely required for GE crops can no longer be justified on the basis of scientific uncertainty

"Can the millions of dollars spent each year on compositional studies with GE crops can still be generally justified in 2013 or, alternatively, should such studies be hypothesis-driven on the basis of reasonable and unique risks posed by the novelty of certain traits (e.g., intentionally modified biochemical pathways)?"

Herman RA, Price WD: **Unintended compositional changes in genetically modified (gm) crops: 20 years of research.** *J Agric Food Chem* 2013

# When are the benefits that have been (or could be) derived from adoption of GE crops considered?

- During the period 1996–2011 it has been estimated that the cumulative economic benefits from cost savings and added income derived from planting GE crops was USD $49.6 billion in developing countries and USD $48.6 billion in industrial countries

- GE technology has added 110 million tonnes of soybeans and 195 million tonnes of maize to global production of these crops since the introduction of GE crops in the mid-1990s.

Brookes G, Barfoot P: **The global income and production effects of genetically modified (GM) crops 1996–2011.** *GM Crops and Food: Biotechnology in Agriculture and the Food Chain* 2013, **4:**74–83.

# GE insect-resistant (*B.t.*) crops: summary of active ingredient usage and associated percent decrease in amount of active ingredient used 1996–2011

**Table 5.** GM IR maize: summary of active ingredient usage and associated EIQ changes 1996–2011

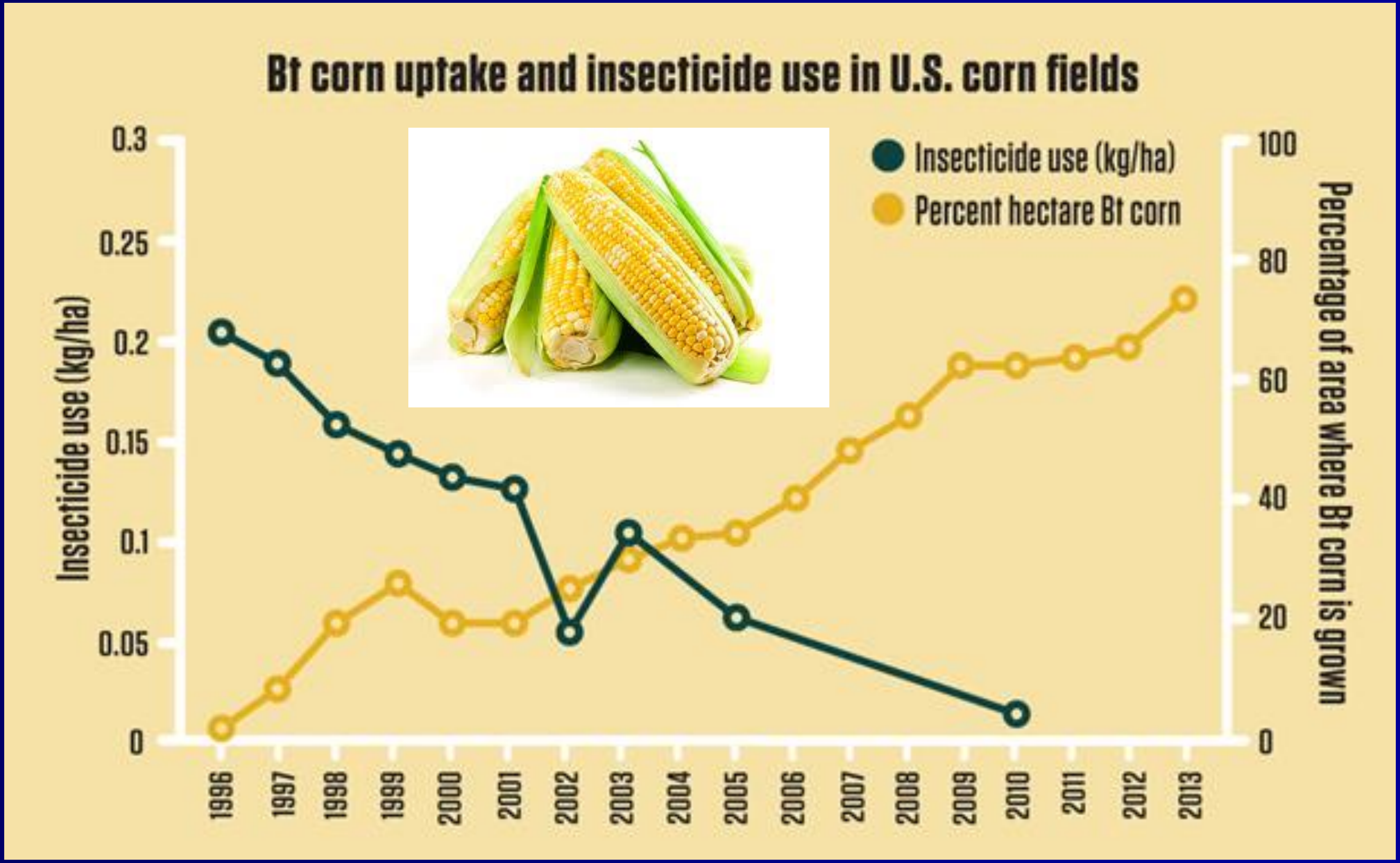
| Country | Change in active ingredient use (million kg) | Percent change in amount of active ingredient used |
|---|---|---|
| USA | –40.7 | –41.9 |
| Canada | –0.5 | –93.8 |
| Spain | –0.4 | –34.3 |
| South Africa | –1.1 | –56.2 |
| Brazil | –7.2 | –75.6 |
| Colombia | –0.1 | –33.0 |
| **Aggregate impact: all countries** | **–50.0** | **–45.2** |


**Table 6.** GM IR cotton: summary of active ingredient usage and associated EIQ changes 1996–2011

| Country | Change in active ingredient use (million kg) | Percent change in amount of active ingredient used |
|---|---|---|
| USA | –11.0 | –16.7 |
| China | –108.7 | –30.3 |
| Australia | –16.8 | –32.4 |
| India | –49.8 | –19.1 |
| Mexico | –1.1 | –9.5 |
| Argentina | –0.8 | –16.2 |
| Brazil | –0.5 | –8.9 |
| **Aggregate impact: all countries** | **–188.7** | **–24.8** |

Brookes G, Barfoot P: **Key environmental impacts of global genetically modified (GM) crop use 1996–2011.** *GM Crops Food* 2013, **4:**109–119.

# Overall insecticide use in the United States has declined 0.6% per year




http://www.washingtonpost.com/blogs/wonkblog/files/2013/08/bt-corn.png

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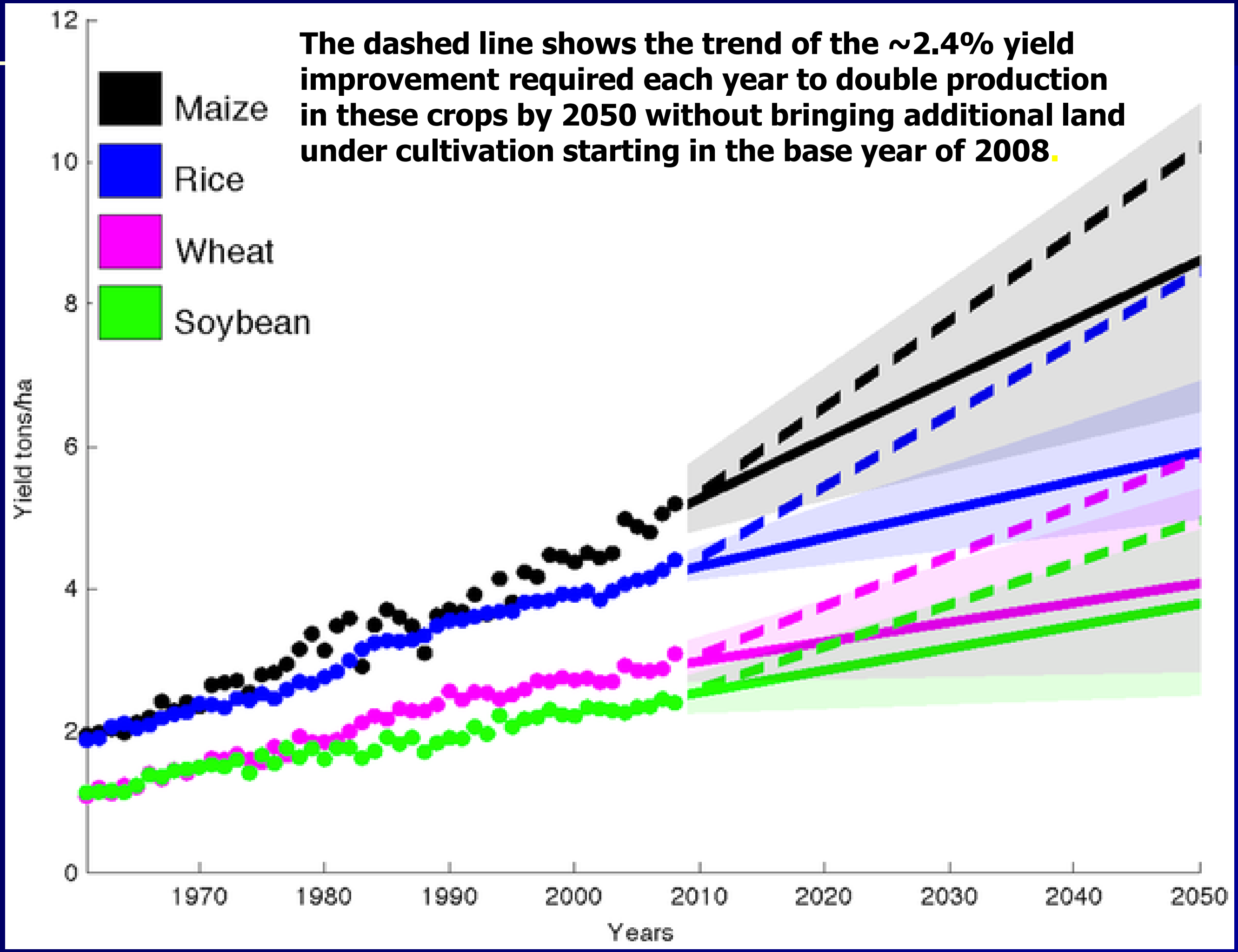
# Observed area-weighted global yield shown using closed circles and projections to 2050 using solid lines for maize, rice, wheat, and soybean.




Ray DK, Mueller ND, West PC, Foley JA (2013) **Yield Trends Are Insufficient to Double Global Crop Production by 2050**. PLoS ONE 8(6): e66428. doi:10.1371/journal.pone.0066428

# The lives saved and/or harms avoided by risk assessment and regulatory evaluations should be balanced against both the costs and deferred potential benefits

There are many current (increased yields, reduced insecticide use, improved feed quality), and potential future benefits of GE including "second generation" crops with enhanced nutritional characteristics and durability.

Improvements in crops especially in developing countries will almost certainly fall to public sector researchers, who are now putting existing GE events on the shelf and discontinuing the development of new projects due to escalating regulatory costs.

Herman RA, Price WD: **Unintended compositional changes in genetically modified (gm) crops: 20 years of research.** *J Agric Food Chem* 2013

# Regulatory costs involved in performing animal feeding studies

In 2007 it was estimated that the range of costs involved with animal performance and safety studies (typically a 90-day whole food/feed rodent feeding study) for approval of a GE crop ranged from USD $300,000–845,000.

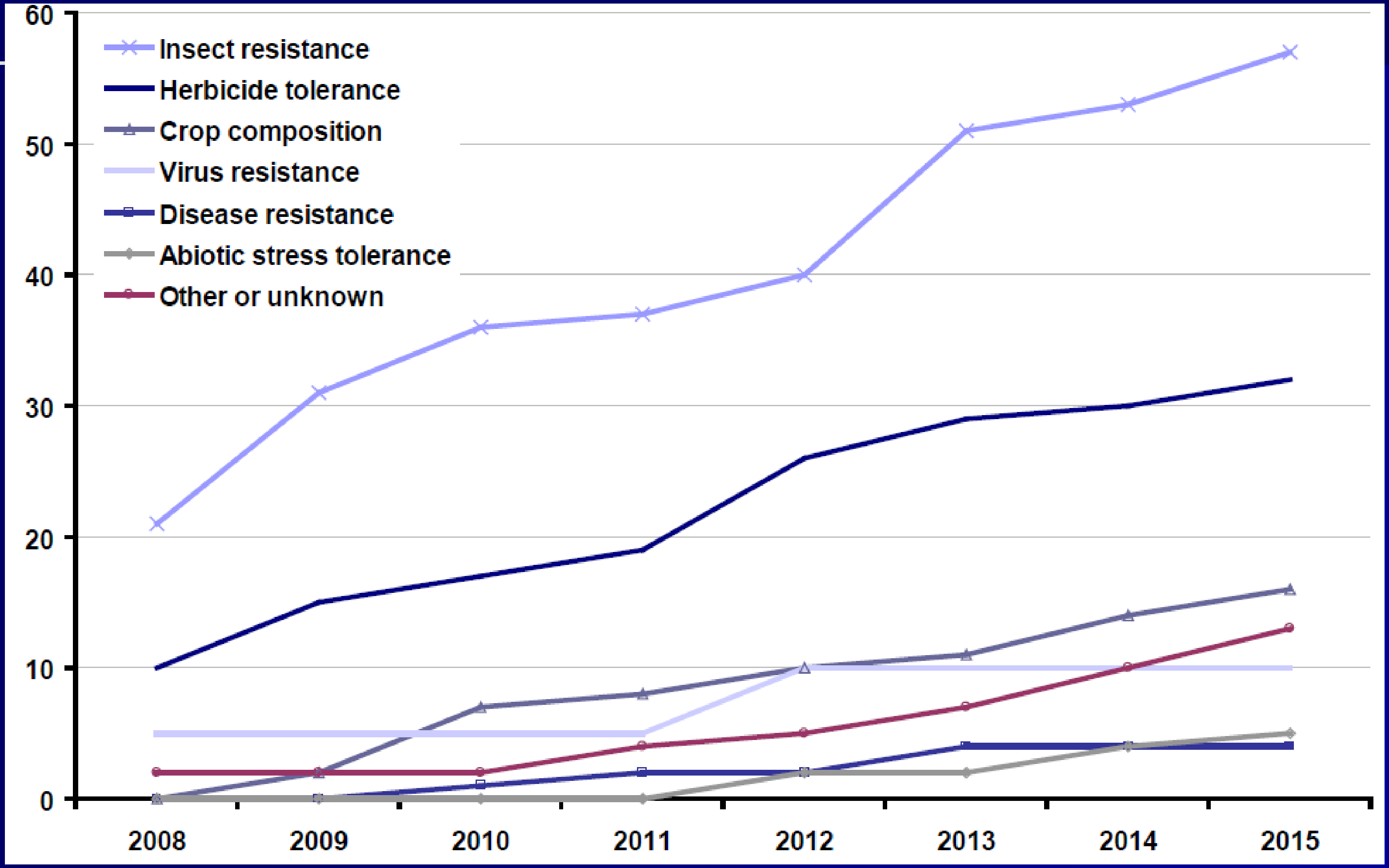
Mandating GE feeding studies on long-lived target species such as cattle would be orders of magnitude more costly

Additionally the cost of rendering the animals would need to be factored into regulatory evaluations as animals would not be able to enter the food supply if fed an "as-yet" unapproved GE crop variety

**Would the value of the information justify the cost?**

Van Eenennaam, A. L. 2013. **GMOs in animal agriculture: time to consider both costs and benefits in regulatory evaluations.** Journal of Animal Science and Biotechnology. 4:37 .

# Projected number of events in GE crops, worldwide, by trait




Stein, A.J., & Rodríguez-Cerezo, E. (2009a, July). **The global pipeline of new GM crops: Implications of asynchronous approval for international trade** (JRC Technical Report EUR 23486 EN). Seville, Spain: European Commission, Joint Research Centre, Institute for Prospective Technological Studies. http://ipts.jrc.ec.europa.eu/publications/pub.cfm?id=2420.

## When GE crops have substantial changes in plant composition (altered output traits), target species feeding studies measuring digestibility or availability of nutrients may be needed for evaluation of animal performance

- Second generation GE crops may not be "substantially equivalent". Whether this represents a safety concern will depend on the novel trait and/or phenotype
- Mandatory animal feeding studies for regulatory purposes should be reserved for GE crops where the novel phenotype results in a reasonable food safety concern that remains unanswered following all other analyses
- Need to consider both the reasonable and unique risks and benefits associated with the use of GE crops, and weigh them against those associated with existing crop varieties, and those of regulatory inaction

# Conclusions

- Regulations triggered by the **process** used to make a product are inconsistent with science-based risk assessment unless there is something inherently risky about the process, as compared to existing methods
- A substantial body of evidence shows that GE crops are no more risky than conventionally bred crops
- Mandating animal feeding studies for regulatory approval based on the process used to make a GE crop, rather than on reasonable unaddressed food safety concerns associated with the novel trait and/or phenotype, cannot be justified based on the weight of scientific evidence

# Thanks for inviting me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