

# IMPLICAZIONI SANITARIE DEGLI OGM

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# Safety first

NATURE|Vol 447|24 May 2007

**Intervention: Confronting the Real Risks  
of Genetic Engineering and Life on a  
Biotech Planet**

by Denise Caruso

Hybrid Vigor Institute: 2006. 272 pp.  
\$17.95

**Allison Snow**

In *Intervention*, Denise Caruso challenges scientists to do a better job of evaluating the safety of genetically modified organisms (GMOs) and communicating unbiased findings to the public. Caruso, who founded the non-profit Hybrid Vigor Institute, examines with a healthy dose of scepticism the recent history of the regulatory policies affecting biotechnology in the United States. How, for example, can the Department of Agriculture



# THE SAFETY “ QUESTION ”

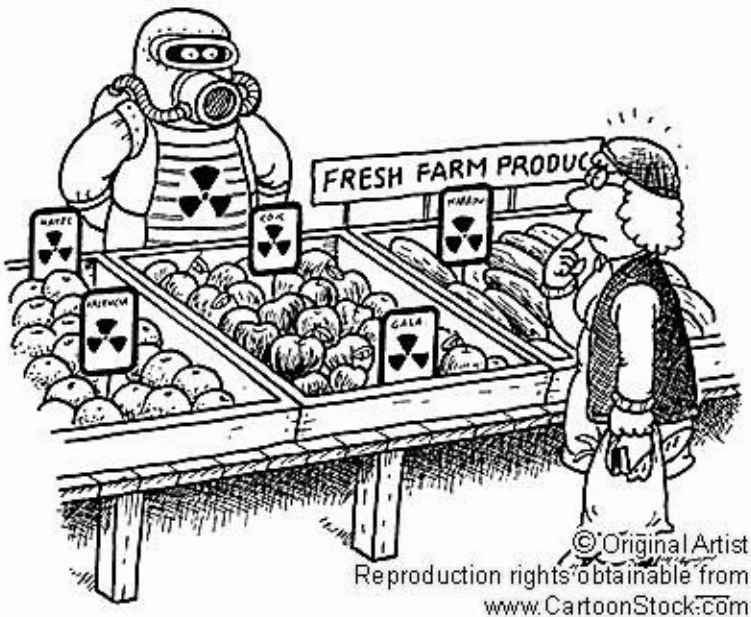




**“ IF GM FOOD IS SAFE,  
WHERE’S THE  
EVIDENCE ? “**

**J. Domingo, *Science*, 288:1748-1749, June 9, 2000**

# RECORDED HEALTH EFFECTS OF GMO



- Spreading of antibiotic resistance
- Recorded deaths from GM
- Allergic reactions
- Food intolerance
- Lowered nutritional supply
- Hepatorenal dysfunction
- Toxin's production
- Cancer and degenerative disease
- unexpected effects
- Viral and Bacterial illness
- Superviruses
- Resurgence of infectious diseases



# ANTIBIOTIC RESISTANCE

- Antimicrobial resistance is one of our most serious health threats. Infections from resistant bacteria are now too common, and some pathogens have even become resistant to multiple types or classes of antibiotics (antimicrobials used to treat bacterial infections).
- The loss of effective antibiotics will undermine our ability to fight infectious diseases and manage the infectious complications common in vulnerable patients undergoing chemotherapy for cancer, dialysis for renal failure, and surgery, especially organ transplantation, for which the ability to treat secondary infections is crucial.
- When first-line and then second-line antibiotic treatment options are limited by resistance or are unavailable, healthcare providers are forced to use antibiotics that may be more toxic to the patient and frequently more expensive and less effective.
- Even when alternative treatments exist, research has shown that patients with resistant infections are often much more likely to die, and survivors have significantly longer hospital stays, delayed recuperation, and long-term disability.
- Efforts to prevent such threats build on the foundation of proven public health strategies: immunization, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment and education

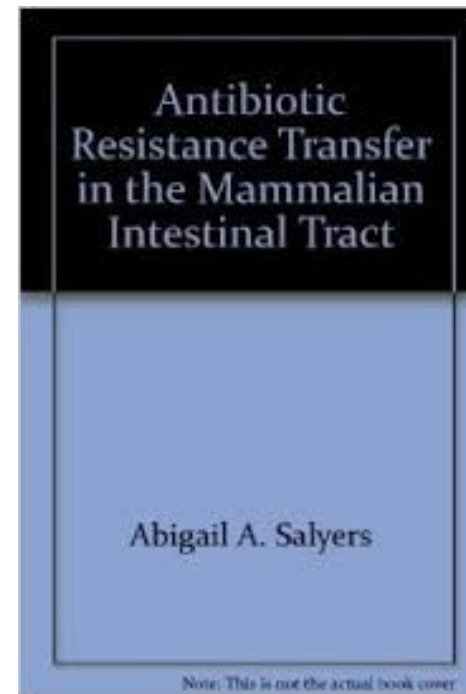


# AMPICILLIN-RESISTANT GENES

NATURE|Vol 435|2 June 2005

## Ampicillin threat leads to wider transgene concern

SIR — We are concerned by the suggestion, in your Editorial “Don’t rely on Uncle Sam” (*Nature* 434, 807; 2005), that the US Food and Drug Administration does not consider the presence of the ampicillin-resistance gene in Syngenta’s unapproved variety of genetically modified *Bt10* maize to represent



In addition, it is worth noting that the ampicillin-resistance gene in *Bt10* maize and other genetically modified crops is a remnant of the bacterial plasmid inserted into these varieties, and would therefore function very efficiently if taken up by bacteria as a result of horizontal gene transfer.

Once the *Bt10* maize incident has been dealt with, we feel there should be a review of the general question of horizontal gene transfer from GMOs. There is no reason to



# A SIGNIFICANT RISK

*Journal of Antimicrobial Chemotherapy*

DOI: 10.1093/jac/dkh419

Advance Access publication 24 September 2004

**Comment on: An assessment of the risks associated with the use of antibiotic resistance genes in genetically modified plants: report of the Working Party of the British Society for Antimicrobial Chemotherapy**

K. L. Goodyear\* on behalf of the Defra Antimicrobial Resistance Coordination (DARC) Group

*DARC Group Secretariat, Policy Division, Veterinary Medicines Directorate, Woodham Lane, New Haw, Addlestone KT15 3LS, Surrey, UK*

- In the veterinary field in the UK (and in many other countries), a significant number of species of veterinary bacteria remain fully susceptible to b-lactam compounds, such as ampicillin, despite continued therapeutic use of these compounds for decades. Considered against this background of extremely low or no detected resistance in certain bacterial species of veterinary origin, **any occasional transfer of resistance genes to these organisms would be a very significant event** and we do not feel that the potential hazard to animal health should be characterized as slight in such circumstances.
- As a consequence, if it became necessary to use much more potent antimicrobials in the animal health field, then **there could be significant consequences for the consumer through the food chain**, because increased use of such potent antimicrobials would be likely to provide greater selective pressure for the emergence of resistance to such compounds in bacteria in animals.



# GM GENES FOUND IN HUMAN GUT

Netherwood T., et al.

Assessing the survival of transgenic plant DNA in the human gastrointestinal tract

*Nat. Biotechnol.* 2004, 22: 204-209.

- These findings indicate that DNA released from bacteria or food sources (GMO) within the mouth has the potential to transform naturally competent bacteria
- "To my knowledge this study demonstrated clearly that you can get GM plant DNA in the gut bacteria. Everyone used to deny that this was impossible. Results suggests that you can get antibiotic marker genes spreading around the stomach which would compromise antibiotic resistance. This can happen even at very low levels after just one meal."
- M. Antonio (senior lecturer in molecular genetics at King's College Medical School, London) *The Guardian* July 17, 2004

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FEMS Microbiology Letters 191 (2000) 71–77

Letters

www.fems-microbiology.org

Survival of free DNA encoding antibiotic resistance from transgenic maize and the transformation activity of DNA in ovine saliva, ovine rumen fluid and silage effluent

Paula S. Duggan<sup>a</sup>, Philip A. Chambers<sup>a</sup>, John Heritage<sup>a,\*</sup>, J. Michael Forbes<sup>b</sup>

<sup>a</sup> Division of Microbiology, School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, UK

<sup>b</sup> Centre for Animal Sciences, Leeds Institute for Plant Biotechnology and Agriculture (LIPA), University of Leeds, Leeds LS2 9JT, UK

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Jan. 1999, p. 6–10  
0099-2240/99/\$04.00+0

Vol. 65,

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Fate of Free DNA and Transformation of the Oral Bacterium  
*Streptococcus gordonii* DL1 by Plasmid DNA  
in Human Saliva

DERRY K. MERCER,<sup>1\*</sup> KAREN P. SCOTT,<sup>1</sup> WENDY A. BRUCE-JOHNSON,<sup>1</sup>  
L. ANNE GLOVER,<sup>2</sup> AND HARRY J. FLINT<sup>1</sup>

Rowett Research Institute, Bucksburn,<sup>1</sup> and Department of Molecular and Cell Biology,  
University of Aberdeen, IMS, Foresterhill,<sup>2</sup> Aberdeen, Great Britain

Gene Transfer in the Gastrointestinal Tract

TRUDY NETHERWOOD,<sup>1,2\*</sup> R. BOWDEN,<sup>1,2</sup> P. HARRISON,<sup>1,2</sup> A. G. O'DONNELL,<sup>2</sup>  
D. S. PARKER,<sup>1</sup> AND H. J. GILBERT<sup>1</sup>

Department of Biological and Nutritional Sciences<sup>1</sup> and Department of Agriculture and Environmental Science,<sup>2</sup>  
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Received 26 April 1999/Accepted 9 August 1999

The maximum in vivo transfer rate of plasmid pAMβ1 in the gut was 0.03 transconjugant per recipient cell, and this rate could be simulated in vitro only by forced filter mating. Transfer was not detected in liquid culture matings. Our findings demonstrate that in vitro methods, such as forced filter mating and liquid mating, underestimate the in vivo rates of gene transfer.



# ALLERGY

## NIEHS News

### Allergies à la Carte Is There a Problem with Genetically Modified Foods?

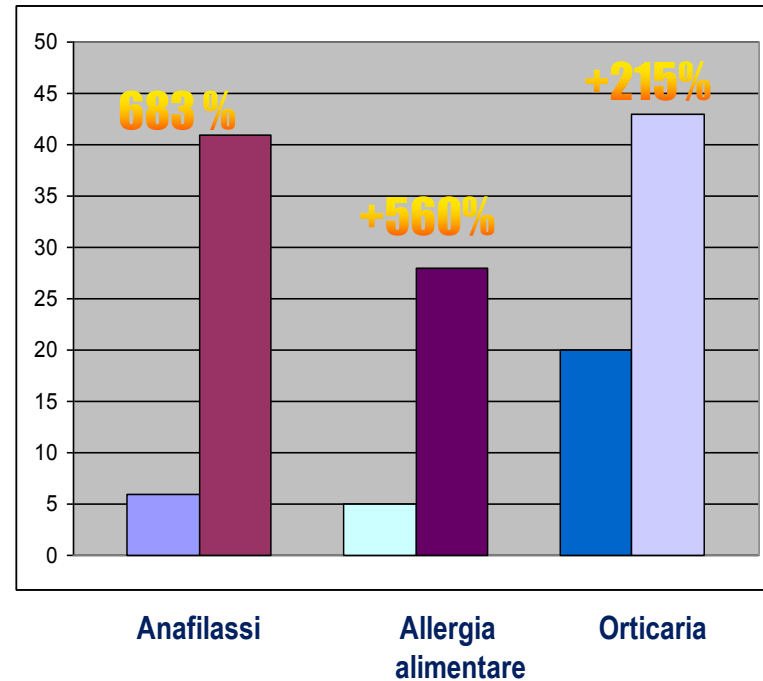
What's in a name? Ask genetically modified (GM) foods. They go by many names, ranging from the sinister ("Frankenfoods") to the adoring ("super crops"), depending on who's doing the naming. Although there are clear benefits to the use of this technology—for example, genetic modification could reduce the amount of allergenic substances in foods

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*British Medical Journal*, 2001

1990-2001



# ALLERGIC REACTIONS

- In 1996 Brazil-nut genes were spliced into soybeans by Pioneer Hi-Bred company. About 28% of individuals were allergic to this new food. The product was removed from the market before any fatalities occurred.
- **“ The next case could be less than ideal and the public less fortunate ”**
- M. Nestle, Nutrition Department NYU
- New England J Medecine, Editorial

- “Current methods for assessment have not been validated as robust indicators of safety; alternative strategies including animal models and immunoassays need to be developed”.

## Genetically Modified Foods | Mini-Monograph

### Introduction: What Are the Issues in Addressing the Allergenic Potential of Genetically Modified Foods?

Dean D. Metcalfe

Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA

There is growing concern among the general public and the scientific community regarding the potential toxicity of genetically modified organisms (GMOs). The use of biotechnology to enhance pest resistance or nutritional value has raised a number of fundamental questions including the consequences of insertion of reporter genes, the spread of resistance genes to surrounding plants, and the use of suicide genes to prohibit reuse of seed from engineered plants. Of particular interest is the ability of proteins from GMOs to elicit potentially harmful immunologic responses, including allergic hypersensitivity. The lack of information of the potential toxicity of these products suggests a need to identify the critical issues and research needs regarding these materials and to develop testing strategies to examine the allergenicity of these compounds. *Key words:* biotechnology, decision tree, food allergy, genetically modified crops, IgE, immunology, sensitization. *Environ Health Perspect* 111:1110–1113 (2003). doi:10.1289/ehp.5810 available via <http://dx.doi.org/> [Online 19 December 2002]

target tissues. If such a reaction is severe may result in profound hypotension or be life threatening. This latter reaction is called anaphylaxis.

However, not all reactions to foods on an immunologic basis are IgE mediated. There are non-IgE-mediated delayed reactions particularly in infants and children, to substances as milk protein. These reactions lead to vomiting, diarrhea, and failure to thrive. Such reactions are sometimes termed “food-induced enterocolitic syndrome” (Lake 1997). The food component induces such reactions and the mechanism



# THE STARLING AFFAIR

## nature biotechnology

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### GMO contamination of seeds

*To the editor:*

Since November, the transgenic maize variety Starlink has turned up in nearly one-tenth of 110,000 grain tests performed by US federal inspectors, according to the US Department of Agriculture. It is becoming increasingly obvious that the prevalence of Aventis's StarLink, which has yet to be approved for human consumption, is far greater than the small area of crop land on which it originally was grown.

On June 11, 2001, the Centers for Disease Control and Prevention (CDC) published an investigation into human health effects associated with the transgenic corn. The investigation found that 28 subjects had experienced apparent allergic reactions after ingestion of the transgenic corn.

The authors suggest that processing of the chips could have uncovered an antigenic epitope that might not have been present in the raw corn. This is based on evidence that cooking, heating, or baking can change protein conformation.

The patient investigated by Sutton et al<sup>1</sup> had complained of 3 allergic reactions after consumption of processed foods containing the transgenic corn at different time periods.

A factor that needs to be considered here is the influence of the food matrix. It is relevant to point out that the patient in question had originally consumed processed corn products while he experienced the reactions. The effect of other ingredients or food additives present in the processed corn products on the properties of the Cry9C protein needs to be examined because Martin-Orue et al<sup>2</sup> had earlier raised the possible influence of food matrices, which are the components of the human diet, on the extent of transgenic DNA degradation and also the ability to form complexes with proteins, including digestive enzymes.



# ULTRASTRUCTURAL CHANGES

*J. Anat.* (2002) **201**, pp409–415

## BRIEF COMMUNICATION

### Ultrastructural analysis of pancreatic acinar cells from mice fed on genetically modified soybean

Manuela Malatesta,<sup>1</sup> Chiara Caporaloni,<sup>1,2</sup> Luigia Rossi<sup>3</sup>, Serafina Battistelli,<sup>1</sup> Marco B. L. Rocchi,<sup>4</sup> Francesco Tonucci<sup>2</sup> and Giancarlo Gazzanelli<sup>1</sup>

<sup>1</sup>Istituto di Istologia e Analisi di Laboratorio, <sup>2</sup>Istituto di Chimica Biologica 'G. Fornaini', and <sup>4</sup>Istituto di Biomatematica, University of Urbino, Urbino, Italy

<sup>3</sup>Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, Perugia, Italy

CELL STRUCTURE AND FUNCTION 27: 173–180 (2002)  
© 2002 by Japan Society for Cell Biology

### Ultrastructural Morphometrical and Immunocytochemical Analyses of Hepatocyte Nuclei from Mice Fed on Genetically Modified Soybean

Manuela Malatesta<sup>1\*</sup>, Chiara Caporaloni<sup>1,2</sup>, Stefano Gavaudan<sup>2</sup>, Marco B.L. Rocchi<sup>3</sup>, Sonja Serafini<sup>1</sup>, Cinzia Tiberi<sup>1</sup>, and Giancarlo Gazzanelli<sup>1</sup>

<sup>1</sup>Istituto di Istologia e Analisi di Laboratorio, via Zeppi s.n., University of Urbino, 61029 Urbino (PU), Italy.

<sup>2</sup>Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, via Salvemini 1, 06126 Perugia, Italy.

<sup>3</sup>Istituto di Biomatematica, Località Crocicchia, University of Urbino, 61029 Urbino (PU), Italy, and <sup>4</sup>Istituto di Chimica Biologica 'G. Fornaini', via Saffi 2, University of Urbino, 61029 Urbino (PU), Italy

- Rats fed with the GMO for prolonged periods (up to 8 months) showed minor pancreatic alterations (with reduction of pancreatic enzyme efficiency, RNA activity and post-transcriptional RNA processing) and significant changes in liver cell nuclear ultrastructure (morphological modifications of nuclear pores, nucleoles and the nuclear membrane), indicative of increased metabolism and the capacity of a diet based on GMOs to specifically interfere with liver cell nuclear activity. Similar results were also found in rat testicles. The alterations were reversible, but still demonstrate how brief exposure to GM food can cause major ultrastructural modifications in cells of the adult organism



# GONADAL EFFECTS

## Ultrastructural analysis of testes from mice fed on genetically modified soybean

L. Vecchio,<sup>1\*</sup> B. Cisterna,<sup>1</sup> M. Malatesta,<sup>2</sup> T.E. Martin,<sup>3</sup> M. Biggiogera<sup>1</sup>

<sup>1</sup>Laboratorio di Biologia Cellulare e Neurobiologia, Dipartimento di Biologia Animale, University of Pavia and Istituto di Genetica Molecolare del CNR, Pavia, Italy; <sup>2</sup>Istituto di Istologia ed Analisi di Laboratorio, University of Urbino "Carlo Bo", Urbino, Italy; <sup>3</sup>Department of Molecular Genetics and Cell Biology, University of Chicago, IL, USA

\*Present address: Centre of Electron Microscopy, University of Lausanne, Switzerland

- We have focussed our attention on Sertoli cells, spermatogonia and spermatocytes by means of immunoelectron microscopy. Our results point out that the immunolabelling for Sm antigen, hnRNPs, SC35 and RNA Polymerase II is decreased in 2 and 5 month-old GM-fed mice, and is restored to normal at 8 months. In GM-fed mice of all ages considered, the number of perichromatin granules is higher and the nuclear pore density lower. Moreover, we found enlargements in the smooth endoplasmic reticulum in GM-fed mice Sertoli cells.
- These findings suggest that, during the 2-8 months interval, a transient transcriptional decrease occurs in mice fed on the GM-diet.



# DEATHS AND GENETICALLY MODIFIED FOODS



- In 1989 dozens of Americans died and several thousands were afflicted and impaired by a genetically altered version of the food supplement L-Tryptophan obtained by means of GM-modifying bacteria.
- A settlement of 2 billion dollars was paid by Showa Denko, Japan's third largest chemical company.

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★ Performing your original search, *Tryptophan produced by Showa Denko and epidemic eosinophilia-myalgia syndrome*, in PubMed will retrieve [2 records](#).

*J Rheumatol Suppl.* 1996 Oct;46(81-8):discussion 89-91.

**Tryptophan produced by Showa Denko and epidemic eosinophilia-myalgia syndrome.**

[Kilbourne EM, Philen RM, Kamb ML, Falk H.](#)

**Author information**

**Abstract**

Evidence from an array of scientific studies strongly supports the conclusion that ingestion of products containing L-tryptophan (LT) produced by Showa Denko KK caused the 1989 epidemic of eosinophilia-myalgia syndrome (EMS) in the United States. In case-control studies of EMS, LT exposure was essentially universal among cases but rare among controls. Of 6 manufacturers of LT, only LT manufactured by Showa Denko KK was clearly associated with illness. The data meet other Hill criteria for inferring a causal relationship. Consistent findings were found in multiple independently conducted studies. There was a dose-response effect, with risk of illness increasing as a function of the amount of tryptophan consumed. The extremely small p values observed in the multiple independently conducted studies effectively rule out the possibility that the tryptophan-EMS association was the result of chance. Moreover, no potential confounding factor or bias explains the association. The incidence of EMS in the United States diminished abruptly once LT containing products were recalled.

**Comment on**

Bias or biology: evaluating the epidemiologic studies of L-tryptophan and the eosinophilia-myalgia syndrome. [*J Rheumatol Suppl.* 1996]  
Epidemiologic studies of the association of L-tryptophan with the eosinophilia-myalgia syndrome: a critique. [*J Rheumatol Suppl.* 1996]

PMID: 8895184 [PubMed - Indexed for MEDLINE]

**Publication Types, MeSH Terms, Substances**

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Bias or biology: evaluating the epidemiologic studies of L-tryptophan [*J Rheumatol Suppl.* 1996]  
Contaminants in L-tryptophan associated with eosinophilia [*Arch Environ Contam Toxicol.* 1993]  
[Review](#) Epidemiology of potential association between L-tryptophan and [*J Clin Epidemiol.* 1995]  
[Review](#) Review of L-tryptophan and eosinophilia-myalgia syndrome. [*J Am Diet Assoc.* 1992]

[See reviews...](#)  
[See all...](#)

**Cited by 2 PubMed Central articles**

L-tryptophan metabolism in pregnant mice fed a high L-tryptophan diet [*Int J Tryptophan Res.* 2013]  
[Review](#) cDNA microarray screening in food safety. [*Toxicology.* 2006]





# METHODOLOGICAL INADEQUACIES



- **LABORATORY EXPERIMENTS** have been very limited. There are no long-term toxicological, oncological, neurological or reproductive studies on GM foods.
- **SAFETY DATA PRESENTATION IS NOT MANDATORY.** Unsatisfactory handling by regulatory agencies.
- **NO SAFETY ASSESSMENT METHODS** are fully reliable. Inadequacy of the Substantial Equivalence Principle.
- **GENETIC CONTROL of CELL FUNCTION is VERY POOR UNDERSTOOD**
- **HUMAN EXPERIENCE with GM** has been **VERY LIMITED** no post-market surveillance studies were realized until now !



# INSURMOUNTABLE BARRIERS

- “The fact is, it is virtually impossible to even conceive of a testing procedure to assess the health effects of genetically engineered foods when introduced into the food chain, nor is there any valid nutritional or public interest reason for their introduction”.
- **Richard LACEY, Professor of Food Safety, Leeds University**

Unfortunately, scientists are not yet able reliably to predict the biochemical or toxicological effects of a GM food from a knowledge of its chemical composition. For example, recent work on the genetics of commercial grape varieties shows that, despite detailed knowledge, going back for centuries, of the chemistry and flavour of grapes and wines, the relationship between the genetics of grapes and their flavour is not understood<sup>3</sup>. Similarly, the relationship between genetics, chemical composition and toxicological risk remains unknown. Relying on the concept of substantial equivalence is therefore merely wishful thinking; it is tantamount to pretending to have adequate grounds on which to judge whether or not products are safe.



THE CONCEPT OF “SUBSTANTIAL EQUIVALENCE” HAS NEVER BEEN PROPERLY DEFINED. IT IS EXACTLY THIS VAGUENESS THAT MAKES THE CONCEPT USEFUL TO INDUSTRY BUT UNACCEPTABLE FOR THE CONSUMER

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Toxicology 181–182 (2002) 427–431

[www.elsevier.com/locate/toxicol](http://www.elsevier.com/locate/toxicol)

Substantial equivalence—an appropriate paradigm for the safety assessment of genetically modified foods?

Harry A. Kuiper\*, Gijs A. Kleter, Hub P.J.M. Noteborn, Esther J. Kok

*RIKILT, Wageningen University and Research Center, P.O. Box 230, 6700 AE Wageningen, The Netherlands*

### An anti-scientific test

Substantial equivalence is a pseudo-scientific concept because it is a commercial and political judgement masquerading as if it were scientific. It is, moreover, inherently anti-scientific because it was created primarily to provide an excuse for not requiring biochemical or toxicological tests. It there-

## Beyond ‘substantial equivalence’

Showing that a genetically modified food is chemically similar to its natural counterpart is not adequate evidence that it is safe for human consumption.

**Erik Millstone, Eric Brunner and Sue Mayer**

two main drawbacks. First, companies did not want to have to conduct toxicological experiments, which would delay access to the

intended to reassure consumers, but it is not clear that it has served, or can serve, that purpose. Although toxicological and bio-



# COULD WE REALLY RELY ON FDA ?

Nature Biotech. 2002

## A different perspective on GM food

David Schubert

**In the United States, the Food and Drug Administration has no mandatory safety approval regulation for GM foods and no specific testing requirements.**

the FDA has no mandatory safety approval regulation for GM foods and no specific testing requirements<sup>2</sup>. There are no all-inclusive mandatory food-safety testing requirements in the United States. The cited testing protocols are only suggestions for producers. There is, however, an effort by a consumer advocacy group, the Center for Science in the Public Interest<sup>3</sup>, to require GM food products to obtain FDA safety approval. With respect to testing technology, Parrot and colleagues claim that “the protein produced in the new host is subjected to extensive biochemical characterization to confirm that the protein produced is the one and only one intended.” However, there is no technique that can assay all cellular proteins. The best to date is 2,528 out of the rice genome of 50,000 genes (a mere 5%)<sup>4</sup>!

I am very pleased that both letters support rigorous testing of GM food and hopefully all involved will back efforts to hasten mandatory rules through the FDA.



# CHILDREN'S HAZARD

A study of GM Vicia Faba an increase in estrogen levels has been found. That finding raises health issues – especially in infant soy formulas. Milk from cows with rBHG contains substantially higher Levels of pus, bacteria and fat. Monsanto's analysis of glyphosate-resistant soya showed the GM-line contained 28% more Kunitz-trypsin inhibitor, a known anti-nutrient and allergen.

Too often the toxicity of GM foods is untested and the potential hazards that they pose to children have not been examined.

**Nobody has evaluated whether intra-uterine and infant exposure to GMFs may have profound permanent and irreversible consequences even in adult life.**

Mmm GMOs. I want to be obese and infertile when I grow up! Thanks Mom!

#justlabelit



someecards  
user card

## Genetically Modified Foods and Children Potential health Risks

Cantani A., Micera M.  
Un. La Sapienza, Roma

Eur Rev Med Pharmacol Sci  
2001, 5: 25-29



!



## UNEXPECTED EFFECTS iii





# A BRIEF SURVEY

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Carbohydrate Research 339 (2004) 2233–2239

RESEARCH

## Synergistic interactions between the genetically modified bacterial polysaccharide P2 and carob or konjac mannan

Michael Ridout, Paul Cairns, Geoffrey Brownsey\* and Victor Morris

*Institute of Food Research, Food Material Science, Norwich Research Park, Colney, Norwich NR4 7UA, UK*

Received 26 April 2004; received in revised form 15 June 2004; accepted 10 July 2004

Available online 14 August 2004

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Journal of Biotechnology 77 (2000) 103–114

[www.elsevier.com/locate/jbiotec](http://www.elsevier.com/locate/jbiotec)

## Chemical fingerprinting for the evaluation of unintended secondary metabolic changes in transgenic food crops

Hub P.J.M. Noteborn\*, Arjen Lommen, Robert C. van der Jagt, Joop M. Weseman

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Food and Chemical Toxicology 42 (2004) 1089–1125

Food and Chemical Toxicology

[www.elsevier.com/locate/foodchemtox](http://www.elsevier.com/locate/foodchemtox)

## Unintended effects and their detection in genetically modified crops<sup>☆</sup>

F. Cellini<sup>a</sup>, A. Chesson<sup>b</sup>, I. Colquhoun<sup>c</sup>, A. Constable<sup>d</sup>, H.V. Davies<sup>e</sup>, K.H. Engel<sup>f,\*</sup>,  
A.M.R. Gatehouse<sup>g</sup>, S. Kärenlampi<sup>h</sup>, E.J. Kok<sup>i</sup>, J.-J. Leguay<sup>j</sup>, S. Lehesranta<sup>h</sup>,  
H.P.J.M. Noteborn<sup>i</sup>, J. Pedersen<sup>k</sup>, M. Smith<sup>l</sup>



# ROUNDUP'S ENZYMATIC-ENDOCRINE EFFECTS

## Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase

*Sophie Richard, Safa Moslemi, Herbert Sipahutar, Nora Benachour, and Gilles-Eric Seralini*

Laboratoire de Biochimie et Biologie Moléculaire, USC-INCRA, Université de Caen, Caen, France

- Roundup is always more toxic than its active ingredient. We tested the effects of glyphosate and Roundup at lower nontoxic concentrations on aromatase, the enzyme responsible for estrogen synthesis. The glyphosate-based herbicide disrupts aromatase activity and mRNA levels and interacts with the active site of the purified enzyme, but the effects of glyphosate are facilitated by the Roundup formulation in microsomes or in cell culture.
- We conclude that endocrine and toxic effects of Roundup, not just glyphosate, can be observed in mammals. We suggest that the presence of Roundup adjuvants enhances glyphosate bioavailability and/or bioaccumulation.



# TOXIC SECONDARY METABOLITES PRODUCTION

*J. Agric. Food Chem.* 2005, 53, 7766–7776

JOURNAL  
AGRICULTURE  
FOOD CHEM

## Toxic Secondary Metabolite Production in Genetically Modified Potatoes in Response to Stress

DEREK MATTHEWS,<sup>\*,†</sup> HUW JONES,<sup>†</sup> PAUL GANS,<sup>†</sup> STEVEN COATES,<sup>‡</sup> AND  
LYDIA M. J. SMITH<sup>†</sup>

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(Cambridge) Ltd., Cambridge CB4 0WA, United Kingdom

PERGAMON

Phytochemistry 62 (2003) 959–969

[www.elsevier.com/locate/phytochem](http://www.elsevier.com/locate/phytochem)

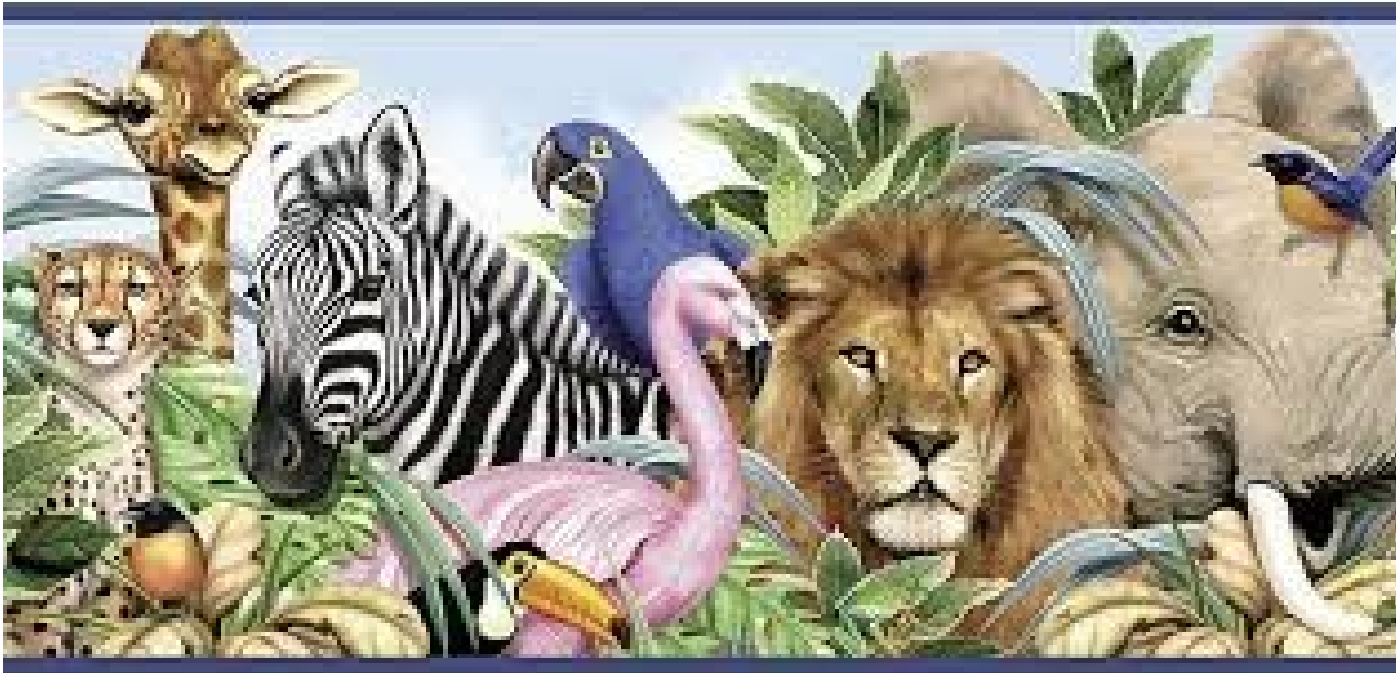
Monitoring changes in anthocyanin and steroid alkaloid glycoside content in lines of transgenic potato plants using liquid chromatography/mass spectrometry

Maciej Stobiecki<sup>a,\*</sup>, Iwona Matysiak-Kata<sup>b</sup>, Rafał Frański<sup>c</sup>, Jacek Skała<sup>d</sup>, Jan Szopa<sup>b</sup>

- In conclusion, the results of this study clearly demonstrate that the introduction of anti-invertase and maize RIP genes into potato can result in significant changes in the levels of glycoalkaloids and sesquiterpenes in tuber tissue. An observation from this study, which may be of some concern, is the high levels of total glycoalkaloids found in GM Ssamples. Mean levels frequently reached twice the accepted threshold of 20 mg/100 g, with some individual samples exceeding 72 mg/100 g; clearly, tubers destined for human consumption containing these levels of glycoalkaloids could represent a significant health concern.
- Transgenic potato plants showed the expected changes in anthocyanins synthesis level. A significant decrease in anthocyanin level was observed when the plant was transformed with a corresponding antisense construct. The transformation of potato plants was also accompanied by significant changes in steroid alkaloid glycosides (SAG) level in transgenic potato tuber.



# ANIMAL STUDIES



# IMMUNE ALTERATIONS

JOURNAL OF  
AGRICULTURAL AND  
FOOD CHEMISTRY

*J. Agric. Food Chem.* XXXX, xxx, 000 A

## Intestinal and Peripheral Immune Response to MON810 Maize Ingestion in Weaning and Old Mice

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- Weaning and old mice were fed a diet containing MON810 or its parental maize for 30 and 90 days. MON810 maize induced alterations in the percentage of T and B cells and of CD4<sup>+</sup>, CD8<sup>+</sup>,  $\gamma\delta$ T, and  $\alpha\beta$ T subpopulations of rats, at the gut and peropheral sites.
- An increase of serum IL-6, IL-13, IL-12p70, and MIP-1 $\beta$  after MON810 feeding was also found.



# HEPATO-RENAL TOXICITY

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**Environmental  
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## New Analysis of a Rat Feeding Study with a Genetically Modified Maize Reveals Signs of Hepatorenal Toxicity

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- Health risk assessment of genetically modified organisms (GMOs) cultivated for food or feed is under debate throughout the world, and very little data have been published on mid- or long-term toxicological studies with mammals. One of these studies performed under the responsibility of Monsanto Company with a transgenic corn MON863 has been subjected to questions from regulatory reviewers in Europe, where it was finally approved in 2005.
- **We observed that after the consumption of MON863, rats showed slight but dose-related significant variations in growth for both sexes, resulting in 3.3% decrease in weight for males and 3.7% increase for females.**
- **Chemistry measurements reveal signs of hepatorenal toxicity, marked also by differential sensitivities in males and females.**
- **Triglycerides increased by 24-40% in females (either at week 14, dose 11% or at week 5, dose 33%, respectively); urine phosphorus and sodium excretions diminished in males by 31-35% (week 14, dose 33%) for the most important results significantly linked to the treatment in comparison to seven diets tested.**
- **With the present data it cannot be concluded that GM corn MON863 is a safe product.**





# TUMORS



Food and Chemical Toxicology

journal homepage: [www.elsevier.com/locate/foodchemtox](http://www.elsevier.com/locate/foodchemtox)

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

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# UNEXPECTED THREATS

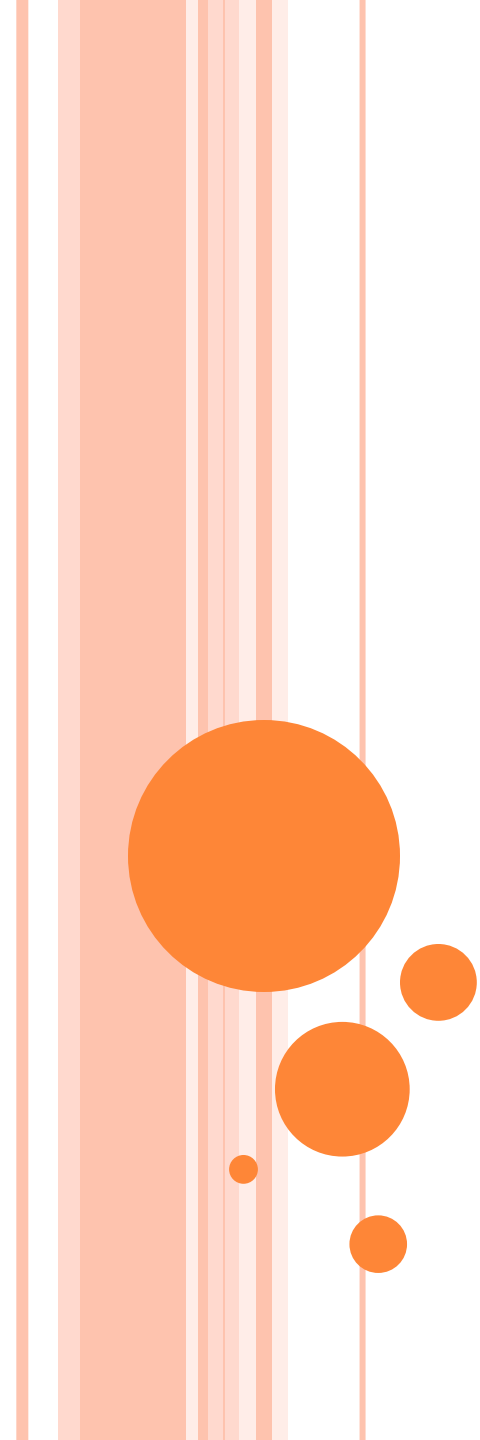
- Terminator technology that renders seed infertile to guarantee seed corporations' yearly sales may eventually be abused for economic warfare. If terminator crops become widespread, it would be easy for a transnational company that controls the technique to stop sales to a specific country or region for political or economic purposes. After some years of planting such seeds, only limited quantities of other seed would be available, thus agriculture could be paralyzed, leading to serious economic crisis and/or famine



- The Sunshine Project. An introduction to biological weapons, their prohibition, and the relationship to biosafety. April 2002.

- The American Society for Microbiology coded a long series of rules to identify and label agents and substances that could be used by terrorists. Among these, GMOs are in category F: GMOs are generally first and second class agents of infection (Category A [UN2814 or UN2900], Category B [UN3373]) or else substances or organisms in class 9 (miscellaneous dangerous goods)
- American Society of Microbiology. *Sentinel Laboratory: Guidelines for suspected agents of bioterrorism*, in: *Biological Safety: Principles and Practice*, 4<sup>th</sup> ed., Fleming D.O. & Hunt D.L. (Eds.), ASm Press, Washington DC, 2006.
- Just a few bushels of “pharmacorn” producing a swine vaccine could, if strategically planted by terrorists, contaminate virtually the entire US corn supply and close international markets to us for years
- Gilmore R. US food safety under siege? *Nat Biotechnol.* 2004, 22: 1503-1505.





# IN RISK ASSESSMENT, ONE HAS TO ADMIT IGNORANCE

**Hoffman-Riem H., Wynne B.**

*Nature*, 2002 Mar 14; 416: 123

# CONCLUSIONS



A vast scientific literature has raised specific questions that governments, companies and scientists *have to answer*. Indignant tirades and partisan speculations are unacceptable. Transgenic supporters' accusations of unscientific arguments should be *returned to the sender*, and the discussion resumed on an equal footing of mutual attention and respect, without prejudice or ideological preconceptions







**Dopo le petunie nella  
soia, i batteri nel mais,  
ecco una nuova  
proposta  
per un nuovo  
organismo  
geneticamente  
modificato:**

**IL SALE NELLA ZUCCA**