# GMO Myths and Truths

An evidence-based examination of the claims made for the safety and efficacy of genetically modified crops and foods

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2nd edition

earthopensource

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## Disclaimer

The views and opinions expressed in this report are those of the individual authors and do not represent the official policy, position, or views of any organizations or institutions that the authors may be affiliated with.

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# Contents

# Introduction

We began work on GMO Myths and Truths in 2010, prompted by frequent claims that the case against genetically modifying our food supply had no science behind it. As we had followed the scientific debate and evidence on genetically modified (GM) crops and foods since the early 1990s, we knew that this was untrue.

Another driving factor was the inflated claims that were being made for GM crops. The public was being told that they would make agriculture more sustainable, provide higher yields to feed the world's growing population, reduce pesticide use, help meet the challenges of climate change, provide more nutritious foods, and make farming easier and more profitable.

We knew that these claims were at best questionable and at worst false. GM had not provided a single crop that had sustainably delivered these benefits. On the contrary, a considerable and growing body of scientific evidence pointed not only to potential hazards but also to actual harm from GMOs (genetically modified organisms) to animal and human health and the environment. But this evidence was not reaching the public, campaigners, policy-makers, or even the majority of scientists.

We decided to produce a document explaining the evidence in simple language. Initially we planned a short 10-page document. But it grew – and grew. We finally published the first edition of GMO Myths and Truths as a free download on the Earth Open Source website in June 2012, with more than 120 pages and over 600 references, 280 of them to peer-reviewed papers.

Unexpectedly for such a dry, technical publication, GMO Myths and Truths appeared to hit a nerve. Its publication coincided with a big push for GMO labelling in the United States and campaigners in many states made good use of it. Requests for press interviews flooded in from North America. Well-wishers mailed thousands of copies to the US for those campaigning for GMO food labelling to use and send to their Congressmen and women. Within weeks, GMO Myths and Truths had been translated into Mandarin and published on a Chinese blog. Spanish speakers translated parts for dissemination in South America. In India, where citizens and farmers were smarting from a series of scandals and disasters involving GM Bt cotton, a publishing company asked for our permission to print a few thousand copies under their imprint. They sold them as cheaply as they could manage, given that their target readership was poor villagers and farmers. We were invited to speak in countries all over the world by citizen, government, and industry organizations.

## The critics

Not everyone appreciated GMO Myths and Truths. GMO lobbyists launched attacks against it in online forums. These people are online 24/7, defending GMOs. They criticize GMO Myths and Truths every time someone cites it in an article, blog, or online post. While we may be able to manage a couple of comments in response before we have to do our work or otherwise live our lives, the GMO lobbyists seem to have nothing else to do than defend

GMOs and attack GMO critics again and again, for hours or days on end.

Apart from their supernormal power of never having to sleep, the GMO lobbyists can be distinguished from ordinary people in that:

- There are few of them and their names or aliases pop up again and again under any article on GM published in a significant enough outlet. What normal person is interested in reading and commenting on so many articles on GM, and even in commenting on the comments, unless they are paid to do so?
- There is no learning curve. If normal people make a mistake and it is pointed out, they tend to engage with the challenging evidence or retire from the fray. The lobbyists don't do either. Instead they change the subject or launch personal attacks. And further down (or up) the comments thread, they make the same discredited point over and over again, as if repeating the claim will somehow make it true – or at least, cause many readers to think it must be true.
- They all use the same industry talking points at the same time, sometimes for weeks or months, until the narrative of choice changes. Then they all change message as a unified chorus. At one time the line is "Golden rice will make the lame walk and the blind see"; at another it's "GMO isn't just Monsanto – let's have more 'public good' GMOs, paid for out of public funds!" Seemingly there is no space for original thought in the pro-GMO lobby.
- They are often unpleasant, angry, and hostile.

The lack of accuracy of these lobbyists is legendary. For instance, one gleefully wrote that "no one" was reading our "silly report". It was hard to take this seriously, considering the online statistics – there were 120,000 complete downloads just weeks after publication, with hundreds of thousands more reading it online.

## Questions and comments

Over the two years since GMO Myths and Truths was published, we have received a large number of comments and questions – most positive, a few negative. The most educational were the negative comments, as they challenged us to refine our approach. This has contributed significantly to the strength of this second edition, which contains a considerable amount of material that addresses critics' comments.

The following are an assortment of comments from both sides of the debate, with our replies. All the comments and questions are genuine, but we have edited out the profanities and misspellings.

### Question: Has GMO Myths and Truths had any effect on the pro-GMO lobby?

Answer: It's hard to measure, but we have certainly noticed a shift in their arguments. They've given up claiming there isn't any science at all to support opposition to GMOs. Clearly, all anyone needs to do to counter that argument is to open up GMO Myths and Truths.

Now GMO proponents have taken to arguing that all the science casting doubt on GMO safety is “discredited” or (in the words of EU chief scientist Anne Glover) “contested”.[1] Our reply is: Do they seriously think the science on the GMO industry side is uncontested? If so, they need to read our report. They will find that those disagreeing with GMO proponents’ claims of safety include hundreds of eminent scientists, many of whom have published their data and arguments in peer-reviewed papers.

### Comment: Your report is not peer-reviewed and published in a scientific journal.

Answer: Our aim was not to write a technical paper for other scientists. If it were, we would have gone down the peer-reviewed publication route. Instead we wanted to translate science into language that anyone can understand. GMO Myths and Truths does not contain any new scientific research (we have just compiled what is already in the scientific literature) – and it is far too long for publication in a scientific journal.

Having said that, GMO Myths and Truths has been read and used by many scientists. But our bottom line is that everything should be understandable by the public at large.

### Comment: GMO Myths and Truths uses many sources that are not peer-reviewed, including media articles.

Answer: GMO Myths and Truths contains hundreds of references to peer-reviewed studies. In some areas, peer-reviewed status is vitally important. For example, the vast majority of the findings we cite on toxic effects or environmental harm from GMOs are from peer-reviewed papers. Exceptions are made in special cases, such as the unpublished industry studies on the Flavr Savr tomato and the 2012 study on NK603 GM maize by Professor Gilles-Eric Séralini’s team, which passed peer review and remained in publication for over a year before being retracted by a journal editor for unscientific reasons.

In such cases, we make it clear why we are citing these papers.

However, for some types of information, we use other sources, such as media articles, well-evidenced NGO reports, documents from government regulatory and international agencies, and court rulings. This is because many political, economic, and legal developments involving GMOs do not make their way into peer-reviewed publications in scientific journals. For such topics, a report or a media article is often the best source available.

We also cite reports written by scientists Dr Charles Benbrook and Dr Doug Gurian-Sherman which did not appear in peer-reviewed scientific journals. Nevertheless we consider them reliable because they are based on data on pesticide use and crop yield collected by US and other government agencies, from peer-reviewed studies, and from controlled university trials. And the major sources cited by Benbrook and Gurian-Sherman are publicly available, so anyone can check them out for themselves.

In short, while peer-reviewed publication is the cornerstone of scientific communication, we can’t allow that fact to make us stupid. That you love your children, that your dog is called Joe, or that gravity is still operating in the area you live and work in, are all pieces of information that will most likely never appear in a peer-reviewed publication. But that doesn’t make them any less true.

Finally, we always cite our sources. We also encourage readers to follow them up and make up their own minds about the reliability of the information provided and our interpretation of it. This is in contrast with many publications by GMO proponents, including some in peer-reviewed scientific journals, which rely for their ability to convince on the likelihood that readers will not ask for the sources – or, where sources are given, that readers will not examine them to check that they are being cited accurately. If readers did examine them, they would often find that the sources do not support the GMO proponents' claims.

### Question: How do I know which sources are peer-reviewed?

Answer: There is no easy formula that enables readers to sort the peer-reviewed from the non-peer-reviewed data. Usually, a paper that is published in a scientific journal, that contains original, empirical data derived from actual testing, and that is referenced in the following style will be peer-reviewed:

> Smith G, Jones L. Occurrence of estrogenic endocrine disruptors in groundwater in the US Midwest. Am J Chem Toxicol. 2005;64:229-40.

But not every article published in a peer-reviewed scientific journal is itself peer-reviewed. Reviews, editorials, opinion pieces, and comment articles may or may not be peer-reviewed.

Conversely, some reports produced by reputable NGOs are peer-reviewed prior to publication. Some government agencies and regulatory authorities, stung by accusations that their opinions on GMOs and pesticides are not peer-reviewed, argue that they have a system of internal peer review.

Many industry studies, such as the safety studies on pesticides and GMOs submitted in support of regulatory authorization, are not peer-reviewed or published and therefore lack any external scrutiny outside the regulatory bodies that consider the application for authorization. The industry studies on pesticides are kept secret under commercial confidentiality rules. Thus there is no way for concerned citizens or independent scientists to verify that the regulators who reviewed the data on the pesticide made the right decision in approving it for commercial use.

Peer review itself is not a guarantee of reliability, nor is it failsafe. Many papers of dubious quality make their way into peer-reviewed journals; and some arguably better papers struggle to find acceptance in such journals. Nevertheless, many believe that in spite of its limitations, peer-reviewed publication is the best quality control system that scientists have come up with so far.

### Question: Parts of GMO Myths and Truths are very technical. Not exactly bedtime reading, is it?

Answer: Correct. It is a reference work. While some interesting stories of deception and spin are included, there is also a lot of technical material. Unfortunately the most technical chapter is the first one, where we explain the genetic engineering process. It is the foundation for everything else. But we've arranged the report in such a way that you don't have to read from beginning to end but can dip into the parts that are most useful at any one time. And for those who don't have time or patience to read the detail, we've provided a summary of each myth in the "Myth at a glance" sections.

If it's understandable, even if it's not engaging bedtime reading, we'll have achieved our aim. As a motivation to persist through the technical parts, it may help to bear in mind that GMO firms are radically changing our food supply and we owe it to ourselves and our families to try to understand what they are doing and why.

### Comment: Your report is biased and one-sided. It doesn't address the numerous studies finding GMOs are safe and beneficial.

Answer: In fact we do address many reviews and individual studies that conclude GMOs are safe and beneficial – and explain the possible reasons why they may have reached those conclusions. Sometimes it's a matter of "don't look, don't find": the study design was so weak that it was unable to find harm from GMOs even where it existed. At other times, harm was found but was ignored or rationalized away, either by the authors of the individual study or by the authors of the review citing the study.

The world of GMO studies is not what it seems at first glance. For example, a list of several hundred studies that were claimed to show GMO safety turned out to show nothing of the sort on closer examination (see Myth 2.3). It is padded with articles irrelevant to GMO safety and contains many papers that provide evidence for harm. We aim to equip members of the public with the tools to make their own judgments on such lists of studies.

### Comment: I found a mistake in the first edition of GMO Myths and Truths.

Answer: Thank you for pointing that out. We have corrected it. While we have done our best to avoid mistakes in this second edition, we are only human. Please let us know of any you find, as we take accuracy very seriously.

The broader issue about accuracy is that we should apply equal standards to both sides of the debate. No one is right all the time, but it is galling to see that critics of GMOs are held to an impossible standard of perfection while GMO proponents regularly get away with barefaced lies as standard practice. Frequently, GMO critics buy into this double standard, torturing themselves over a misplaced reference while GMO proponents construct entire articles on the basis of fabrications.

The important thing is that people on both sides of the debate should correct their mistakes where they are pointed out.

### Comment: The GMO debate isn't just about science.

Answer: We agree. Science doesn't happen in a vacuum, which is why we've tried to give some of the political and economic context. But governments claim to make decisions about GMOs on the basis of science, so we have placed science at the centre of our report.

You may find that once you present policy-makers with the scientific evidence in GMO Myths and Truths, they are not in the least interested in it. In our experience, such people are more likely to belong to the rabidly pro-GMO camp. There you have your proof that their stance on GMOs has nothing to do with science. And then you can move the debate on by arguing on the basis of politics or (more likely) ideology. If none of this works and they are determined to foist GMOs onto an unwilling populace, you may need to give up trying to reason with them and start a probe into bribery and corruption!

## The update

The science on GMOs moves quickly, with new studies coming out virtually every week. Almost as soon as the first edition of GMO Myths and Truths was published, it was out of date. We quickly realized we had to write an updated version. As time passes, the evidence demonstrating environmental, health, and social harm from GMO crops and foods increases. It is therefore not surprising that the movement to label, restrict, or ban them also gets stronger.

We have included some of the most important new papers in this second edition. We've clarified the text, provided more information and explanation where asked, and addressed some of the criticisms that were offered. We hope you find it useful.

## References


1. EurActiv.com. Chief EU scientist backs damning report urging GMO "rethink." 2013. Available at: http://www.euractiv.com/science-policymaking/chief-eu-scientist-backs-damning-news-530693.

# Summary

Genetically modified (GM) crops and foods are promoted on the basis of a range of far-reaching claims from the industry and its supporters. They say that GM crops:

- Are an extension of natural breeding and do not pose different risks from naturally bred crops
- Are safe to eat and can be more nutritious than naturally bred crops
- Are strictly regulated for safety
- Increase yields
- Reduce pesticide use
- Benefit farmers and make their lives easier
- Bring economic benefits
- Benefit the environment
- Can help solve problems caused by climate change
- Reduce energy use
- Will help feed the world.

However, a large and growing body of scientific and other authoritative evidence shows that these claims are not true. On the contrary, evidence presented in this report indicates that GM crops:

- Are laboratory-made, using technology that is totally different from natural breeding methods, and pose different risks from non-GM crops
- Can be toxic, allergenic or less nutritious than their natural counterparts
- Are not adequately regulated to ensure safety
- Do not increase yield potential
- Do not reduce pesticide use but increase it
- Create serious problems for farmers, including herbicide-tolerant "superweeds", compromised soil quality, and increased disease susceptibility in crops
- Have mixed economic effects and disrupt markets
- Harm soil quality, disrupt ecosystems, and reduce biodiversity
- Do not offer effective solutions to climate change
- Are as energy-hungry as any other chemically-farmed crops
- Cannot solve the problem of world hunger but distract from its real causes – poverty, lack of access to food and, increasingly, lack of access to land to grow it on.

Based on the evidence presented in this report, there is no need to take risks with GM crops when effective, readily available, and sustainable solutions to the problems that GM

technology is claimed to address already exist. Conventional plant breeding, in some cases helped by safe modern technologies like gene mapping and marker assisted selection, continues to outperform GM in producing high-yield, drought-tolerant, and pest- and disease-resistant crops that can meet our present and future food needs.

The quality and efficacy of our food production system depends only partly on crop genetics. The other part of the equation is farming methods. What is needed are not just high-yielding, climate-ready, and disease-resistant crops, but productive, climate-ready, and disease-resistant *agriculture*.

# 1. The genetic engineering technique

The World Health Organization defines genetically modified organisms (GMOs) as "organisms in which the genetic material (DNA) has been altered in a way that does not occur naturally".[1] European legislation is more specific, defining GMOs as organisms in which "the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination".[2]

Typically genetic engineering involves manipulating an organism's genetic material (genome) in the laboratory by the insertion of one or more new pieces of DNA or by the modification of one or more of the base unit letters of the genetic code. This re-programmes the cells of the genetically modified organism to make a new protein or to modify the structure and function of an existing protein. Genetic modification (GM) confers new properties or "traits" that are not naturally present in the organism.

Among the manipulations included within GM are:

- ➜ Transferring of genes from related and/or totally unrelated organisms
- ➜ Modifying information in a gene ("gene editing")
- ➜ Moving, deleting, or multiplying genes within a living organism
- ➜ Splicing together pieces of existing genes, or constructing new ones.

When incorporated into the DNA of an organism, genetically modified genes modify the functional characteristics – the traits – of an organism. The most common traits in the GM crops currently on the market are the expression of proteins designed to kill insects that try to eat the crop or to make the crop tolerant to an herbicide. However, in theory, the new proteins expressed in GM crops could have a wide range of functions.

## What is DNA?

DNA stands for deoxyribonucleic acid. DNA molecules are found in the nucleus of every cell. Within the DNA molecule are segments called genes, which can number in the tens of thousands. Genes contain the instructions that guide the development and functioning of all known living organisms and viruses.

The main role of DNA is the storage of biological information. Information stored within genes is expressed as physical characteristics or traits, such as height, dark skin, red hair, or blue eyes.

There are four subunits of the DNA molecule, called "bases". These are the "letters" of the genetic alphabet. Information is stored in DNA in the sequence of these letters, just as information is stored on this page in the sequence of the letters of our 26-letter alphabet.

Each gene is a specific sequence of genetic letters and can be likened to a blueprint, recipe, or code for a specific protein or set of proteins. The genome of an organism is the collection of all the genes needed to construct, either directly or indirectly, all components of the organism's cells.

Most genes encode information for proteins, which can function in any of four different ways:

- As the structural building blocks of an organism's body, forming physical structures such as cell walls and organs
- As enzymes – proteins that catalyze the biochemical reactions needed to maintain life
- As intracellular signalling and regulatory molecules, controlling the function of genes, metabolic pathways, cells and organs
- As regulatory molecules or peptide hormones that govern many physiological processes from outside the cells.

The latest estimates indicate that humans have around 21,000 different genes that code for proteins, roughly the same number as a fruit fly. Crop plants, on the other hand, such as rice, wheat, maize and soybeans, contain 30,000–50,000 genes. Clearly, the information content rather than the quantity of genes is most important in determining the characteristics of an organism.

Regions of DNA that contain protein-encoding genes constitute only a small proportion of the DNA present in any human, animal or plant (approximately 3–5%). Until recently the non-coding DNA was thought to be largely non-functional and was referred to by some scientists as "junk DNA". But it has now been discovered that "junk DNA" is far from non-functional and contains thousands of elements that are vital for the control of gene function.

It also used to be thought that one gene coded for one protein. However, since the number of protein functions in humans and other mammals is estimated at more than 200,000, it is clear that there must be ways of obtaining more than one protein from a given gene. It is now known that most genes (at least 60%) encode for more than one protein.

Furthermore, more and more proteins are being found to be localized to multiple sites within cells and organs and to perform more than one function. Many cellular functions are now known to be performed by groups of proteins clustered together. So a large diversity of cellular and organ functions can be obtained from a limited number of genes.

Finally, it is worth noting that many genes do not encode proteins. Rather, they produce ribonucleic acid (RNA) copies of themselves of various sizes. These RNA molecules perform structural, regulatory, and catalytic roles, and are involved in vital cellular processes, including the manufacture of proteins and controlling the function of other genes. For example, RNA molecules can control how much of a certain protein is made from a given gene.

In summary, it is now obvious that gene organisation within DNA is not random and that control of gene function consists of a finely balanced, highly complex network of interactions, which scientists do not fully understand. It is also evident that, because the genes of an organism are an interconnected network, a single disturbance in gene organisation or function can affect multiple gene systems, with serious downstream consequences in terms of the cellular function and health of the organism.

It is also important to keep in mind that because of the complexity of gene systems, the effects of even a single disturbance are not predictable. This is illustrated by the fact that altering a single letter of the genetic code of a single gene can be a significant step leading to cancer, a disease that involves alterations in the function of multiple genes, proteins and cellular systems.

Except in a few circumstances, every cell of an organism (human, animal, plant) contains the whole genome of that organism: that is, the total collection of genetic information specifying, either directly or indirectly, all aspects of the structure and function of the organism.

When cells multiply and reproduce themselves, the total genome is duplicated ("DNA replication") before the cell divides. The complete genome is passed on to both "daughter" cells. The manufacture of all types of proteins from the information contained in genes is a multistep series of reactions:

1. The corresponding genes are copied into messenger ribonucleic acid (mRNA), a process known as transcription.
2. After transcription, the mRNA is transported out of the cell's nucleus to its outer compartment, known as the cytoplasm.
3. Once in the cytoplasm, the genetic information within mRNA is decoded or "translated" to build the desired proteins.

This process is summarized in what is known as the central dogma of molecular biology: DNA makes RNA makes protein.

## Genetic engineering theory and practice

Just as magnetic tape can be used to store electronic information such as music or video, DNA stores genetic information. And just as a sound engineer cuts and splices magnetic tape to make a complete recording of a song, genetic engineers use the techniques of genetic modification or genetic engineering to cut and splice DNA. They use these techniques to isolate, modify and move DNA and the genetic information it carries between both related and unrelated organisms.

The central concept of genetic engineering is that by cutting and splicing the DNA of an organism, new functions, characteristics, or traits can be introduced into that organism. The assumption is that the resulting organism will be identical to the non-genetically modified original, except that it will have the new trait that is conferred by the new gene introduced by the genetic engineer.

This is a simple and elegant concept. But the actual practice of genetic engineering is not so simple and elegant. The genetic engineering process is not precise or predictable. Genes do not function as isolated units but interact with each other and their environment in complex ways that are not well understood or predictable. The genetic engineering process can disrupt the host organism's genome or genetic functioning in unexpected ways, resulting in unpredictable and unintended changes in the function and structure of the genetically modified organism. This in turn can result in the presence of unexpected toxins or allergens or altered nutritional value and the engineered organism can have unexpected and harmful effects on the environment.

## References


1. World Health Organization (WHO). 20 questions on genetically modified foods. 2002. Available at: http://www.who.int/foodsafety/publications/biotech/20questions/en/index.html.
2. European Parliament and Council. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Off J Eur Communities. 2001:1–38.

## 1.1 Myth: Genetic engineering is just an extension of natural breeding

## Truth: Genetic engineering is different from natural breeding and poses special risks

### Myth at a glance

GMO proponents claim that genetic engineering is just an extension of natural plant breeding. But genetic engineering is technically and conceptually different from natural breeding and entails different risks. The difference is recognized in national and international laws.

GMO proponents claim that genetic engineering is just an extension of natural plant breeding. They say that genetically modified (GM) crops are no different from naturally bred crops, apart from the deliberately inserted foreign GM gene (transgene) and the protein it is intended to make.

But GM is technically and conceptually different from natural breeding and poses different risks. This fact is recognized in national and international laws and agreements on genetically modified organisms (GMOs). For example, European law defines a GMO as an organism in which "the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" and requires the risks of each GMO to be assessed.[1]

The Cartagena Protocol on Biosafety,[2] an international agreement signed by 166 governments worldwide that seeks to protect biological diversity from the risks posed by GM technology, and the United Nations food safety body, Codex Alimentarius, agree that GM differs from conventional breeding and that safety assessments should be required before GM organisms are used in food or released into the environment.[3,4]

In 1999 the UK's Advertising Standards Authority ruled that Monsanto's advertisements about GM foods and crops were misleading in claiming that genetic modification was an extension of traditional breeding methods.[5]

Today, few public comment forums on GM crops and foods are complete without claims from GMO promoters to the effect that "We've been genetically modifying crops for millennia". This conveys essentially the same message as Monsanto's advertisements and seems to have the same intent: to reassure the public that nothing radical or new is being done to their food. This message is scientifically inaccurate and misleading.

Indeed, industry tries to play both sides in its presentation of GMOs. It tells patent offices worldwide that the GM process is totally different from natural breeding and so the generation of a GM crop constitutes a non-obvious "inventive step", thus making the GM crop patentable. On the other hand, it tells the public that the GM process is little different from natural breeding and that therefore GM foods are as safe as non-GM foods.

Both arguments cannot be correct. And technically speaking, the GM transformation process is radically different from natural breeding.

Natural breeding can only take place between closely related forms of life (cats with cats, not cats with dogs; wheat with wheat, not wheat with tomatoes or fish). In this way, the genes that carry information for all parts of the organism are passed down the generations in an orderly way.

GM, in contrast, is an artificial laboratory-based technique that is specifically designed to enable the transfer of genes between unrelated or distantly related organisms. It even enables the introduction of synthetic DNA into the genome of living organisms.

In an attempt to reassure the public and regulators about GMO safety, GMO developer companies are now focusing on transferring genes from a related organism or the same organism (so-called "cisgenesis"). For example, a gene from one potato may be inserted into another variety of potato. However, even in cisgenesis, a new GM gene unit may contain genetic elements from other organisms, including bacteria or viruses. Cisgenesis also involves the same laboratory methods that are used in genetic engineering and thus carries the potential for unexpected knock-on effects (see Myth 1.4).

## The steps of genetic modification

The steps by which GM crops are created make it clear that genetic engineering is not an extension of natural breeding. It is not natural, as the particular combinations of genes put together in the GM gene cassette and the manner in which it is inserted into the host organism would never occur in nature.

### 1. Isolation of the gene of interest

Genetic engineering confers a new trait on an organism by introducing the gene for a trait into the genome of that organism. The first step in that process is to identify the gene for the trait of interest and to isolate it. Using existing knowledge about the genome of a given organism, the gene of interest encoding the desired trait is identified and "cloned". That means the gene is physically isolated and propagated in a GM bacterium as part of a DNA molecule known as a plasmid. The vast majority of currently commercialized GMOs are engineered to tolerate being sprayed with one or more herbicides or to produce one or more insecticides.

### 2. Cutting and splicing – generation of the GM gene cassette for introduction into the plant

Before being used to produce a GM plant, the gene of interest must be joined up with appropriate genetic control elements that will allow it to be switched on within its new plant host, so that it will efficiently produce the protein that it encodes. Other elements are also spliced into or around the gene for various purposes. Most prominent among the genetic control elements that are spliced to the gene of interest are "promoter" and "termination" sequences.

The promoter marks the beginning of the gene. It attracts and binds multi-protein complexes, called the gene expression machinery. This machinery reads the DNA sequence of the gene and synthesizes a complementary messenger RNA (mRNA) copy of the gene sequence. The termination element, as the name implies, marks the end of the gene and causes the synthesis process to stop.

Promoter and termination elements must be sourced from organisms that will allow them to work in the GM plant. These can be from either plants or, more frequently, plant viruses such as the cauliflower mosaic virus (CaMV). Promoters from plant viruses are usually preferred because they are more potent than plant gene promoters, allowing the GM gene to be expressed at higher levels and hence allowing higher production of the GM protein.

If the gene of interest is not from a plant (for example, if it is from a bacterium or animal), it is typically modified in other ways as well, to make it more compatible with the gene expression machinery of the recipient plant cells.

Genetic engineers use a variety of enzymes to cut DNA into specific sequences and to splice the various pieces of DNA into the plasmid that carries the cloned gene or gene of interest. The result of many cutting and splicing steps is the complete genetically engineered construct, called the gene cassette.

For example, the gene of interest in first-generation GM Roundup® Ready soy, maize, cotton and canola encodes an enzyme (CP4 EPSPS), which confers tolerance to Roundup herbicide. The CP4 EPSPS gene was isolated from a naturally occurring soil bacterium. In order to ensure that the CP4 EPSPS gene is switched on appropriately in plants, it is linked to the CaMV 35S promoter, which is derived from the cauliflower mosaic virus. The CP4 EPSPS gene is also linked at its leading end to a gene fragment called a signal sequence, obtained from the petunia, a flowering plant. This is to ensure that the CP4 EPSPS enzyme localizes to the right place within the plant cells. Finally, a sequence that functions to terminate mRNA synthesis is spliced to the end of the CP4 EPSPS gene. This termination sequence is taken from a second bacterial species, Agrobacterium tumefaciens (A. tumefaciens).

Therefore the first-generation Roundup Ready GM tolerance GM gene cassette combines gene sequences from four diverse organisms: two species of soil bacteria, a flowering plant, and a plant virus. These all end up in the genetically engineered agricultural crop. This graphically illustrates the extreme combinations of genetic material that can be brought about by the GM process. This is something that would never occur naturally.

In addition to the gene(s) that confer traits relevant to the final crop, another gene unit is often included in the gene cassette along with the gene of interest. This additional gene unit functions as a selectable marker, meaning that it expresses a function that can be selected for. Typically this is survival in the presence of an antibiotic or herbicide. The GM gene itself can be used as a surrogate marker gene if it encodes resistance to a herbicide. When the marker gene (along with the other gene(s) in the cassette) is successfully engineered into the genome of the recipient plant cells, those cells are protected from the antibiotic or herbicide. The genetic engineer can then separate the cells that have integrated the GM gene cassette from the majority of other cells in the culture by exposing the culture to the antibiotic or herbicide. Only the cells that have been successfully engineered and are therefore resistant to the antibiotic or herbicide survive exposure.

### 3. GM gene cassette insertion into cultured plant cells

To introduce the GM gene cassette into the genome of the recipient plant, millions of cells from that species are subjected to the GM gene insertion (transformation) process. This is done by growing cells from the recipient plant or pieces of tissue from the plant in culture in dishes, tubes, or flasks, a system known as "tissue culture", and then using methods described below to insert the gene cassette into the recipient plant cells. This results in one or more of the GM gene cassettes being inserted into the DNA of some of the plant cells present in the tissue culture. The inserted DNA is intended to re-programme the cells' genetic blueprint, conferring completely new properties on the cell.

The process of inserting the GM gene cassette is carried out in one of two ways. The first way is with a "gene gun", which randomly shoots microscopic gold or tungsten nanoparticles coated in GM DNA into the plant cells in a process called particle bombardment or biolistics. In a few instances, the nanoparticles end up in the nucleus of the plant cells and in an even smaller number of cases, the DNA on the particles gets incorporated into the DNA of the plant cell. This is a completely random process that genetic engineers have no ability to control. They do not fully know what processes are involved in the DNA insertion process and have no control over when it occurs or where in the DNA of the plant cell it will occur.

The second mechanism of gene insertion is by infection of the cultured cells with the soil bacterium A. tumefaciens. In its natural form, A. tumefaciens infects plants at wound sites, causing grown gall disease, a type of tumour. The infection process involves the actual insertion of DNA from A. tumefaciens into the DNA of the infected plant. The genetic engineer uses the natural ability of A. tumefaciens to insert DNA into the genome of infected plants to insert the GM gene cassette into the DNA of plant cells in culture. This is done by first linking the GM gene cassette to a piece of A. tumefaciens DNA called the Ti plasmid. This modified DNA is then introduced back into A. tumefaciens. Then the plant cells in culture are infected with the A. tumefaciens that contains the GM gene cassette-Ti plasmid DNA complex.  A small fraction of the plant cells exposed to the A. tumefaciens are successfully infected and incorporate the GM gene cassette into their own DNA. As with biolistics, the A. tumefaciens insertion process is random and the genetic engineer has no way of controlling where in the plant cell genome the GM gene cassette will be inserted. It is hit or miss.

At this point in the process, the genetic engineer has a tissue culture consisting of millions of plant cells. Some will have picked up the GM gene cassette, whilst the vast majority will not have done so. The genetic engineer now needs to select out the cells that have not picked up the GM genes and discard them from the process.

### 4. Selection of the modified plant cells

Depending on the type of marker genes that are part of the GM gene cassette (herbicide-tolerant or antibiotic-resistant), the plant tissue culture that has undergone the GM transformation process is treated with either a herbicide or an antibiotic, to kill all cells except those that have successfully incorporated the GM gene cassette into their own DNA and switched it on. Only the cells that have incorporated the marker gene into their genome and are expressing it will be resistant to the chemical and survive exposure.

Only a small percentage of GM gene cassette insertion events result in expression of the GM genes in the plant cells.

### 5. Hormone treatment

The few plant cells that have successfully incorporated the GM gene cassette and survived the chemical treatment are then further treated with plant hormones. The hormones stimulate the genetically modified plant cells to proliferate and differentiate into small GM plants that can be transferred to soil and grown to maturity.

### 6. Verification of the GM transformation

Once the GM plants are growing, the genetic engineer examines them and discards any that are deformed or do not seem to be growing well. The remaining plants are tested so as to identify one or more that express the GM genes at the desired high levels and locations within the plant. Out of many hundreds or thousands of GM plants produced, only a few may fit this requirement. These are selected as candidates for commercialization.

Each of these GM plants carries the same GM gene cassette, but it will be inserted at a different location in the genome of the plant. The GM gene will express at different levels in different GM plants and even in different parts of the same GM plant.

At this stage the GM plants have not been assessed for health and environmental safety or nutritional value. This part of the process is described in later chapters.

## The GM transformation process is highly inefficient

The GM transformation process is a complex multistep process in which each step needs to work as intended in order to produce the desired result. The GM gene cassette must be successfully inserted and the gene of interest switched on so that it produces the protein it encodes, while at the same time, all other properties of the plant, including fertility, must be preserved.

This is a very inefficient process. The process of GM gene insertion into the plant cell DNA occurs only rarely. Most inserted GM genes fail to function, either due to integration into regions of the plant genome that are not permissive for gene activation or to natural plant defence mechanisms that silence or switch off of the "invading" foreign gene.

GM gene cassettes currently used by genetic engineers do not possess any elements that are able to overcome these limitations of the transformation process. Therefore obtaining GM plants that are good candidates for taking forward for potential commercialization is a long, arduous, labour-intensive, and expensive process[6,7] (see Myth 6.4).

## How unnatural is genetic engineering and does it matter?

Some aspects of plant genetic engineering are unique to the GM process and do not occur in other types of plant breeding. They include the artificial construction of the GM gene cassette, which contains new synthetic genes and combinations of gene control elements that have never existed before in nature.

Also, genetic engineering enables genes to be transferred not only between different species but also between different kingdoms – for example, from animals or humans into plants. Therefore genetic engineering evades natural barriers between species and kingdoms that have evolved over millennia. Moreover, genetic engineering can introduce purely synthetic genes, thus, for better or worse, expanding the range of possible genes to the frontiers of the human imagination.

The fact that the GM transformation process is unnatural and artificial does not automatically make it undesirable or dangerous. It is the consequences of the procedure, combined with the current lack of systematic assessment of potential risks, that give cause for concern, as detailed in subsequent sections.

## Contained and uncontained use of GM technology

GM technology is used in both contained and uncontained systems. "Contained use" means that the use of GM technology does not result in the deliberate release into the environment of a living GMO that is capable of reproducing and spreading.

In Europe, all laboratory and industrial uses of GM technology are regulated by the Contained Use Directive.[10] Containment can be physical, in the form of barriers preventing escape, chemical, or biological (by genetically crippling the GMO so that it cannot reproduce).

Contained medical uses of GM technology include diagnosis of disease and manufacture of pharmaceuticals and GM viruses used to deliver somatic (non-germline and thus non-inheritable) gene therapy. Contained uses of GM technology in plant breeding are confined to the laboratory and include identification of genes of interest and study of their functions and protein products under normal and disease conditions.

We oppose non-contained uses of GM technology but support contained use, as long as containment is effective. There is always risk of escape during contained use, either due to physical or biological "leakiness". However, for most current and envisioned applications, the benefits outweigh the risks when strong and well-designed containment strategies are employed.

## Horizontal gene transfer – should we worry?

The movement of genetic material between unrelated species through a mechanism other than sexual reproduction is called horizontal gene transfer, or HGT. Genetic engineering can be seen as intentional horizontal gene transfer. Reproduction, in contrast, is known as vertical gene transfer, because the genes are passed down through the generations from parent to offspring.

GM proponents argue that horizontal gene transfer occurs spontaneously in nature and that therefore genetic engineering is only speeding up a natural process, or making it more precise.

It is true that horizontal gene transfer occurs in lower organisms relatively frequently – for example, between different species of bacteria.[8] HGT has evolutionary benefits from the perspective of microorganisms.

However, in higher organisms HGT occurs only under special circumstances. An example is infection with viruses, resulting in the development of endogenous retroviruses (ERVs). These are viruses that write themselves into the host's own DNA. When they do this to a germline cell – a cell involved in reproduction (a sperm or egg cell) the genes for that virus are passed down to the offspring and become a permanent part of the genome of the descendants.

Human endogenous retroviruses (HERVs), the inherited remnants of past retroviral infections in our ancestors, are estimated to make up as much as 8% of the human genome.[9]

The fact that HGT has taken place does not mean that infection with such retroviruses is safe or desirable. Nor does this in any way justify commercializing GMOs without testing their impacts on health and the environment. All we know is that some people survived these retroviral infections, which changed their DNA, and that we are descended from the survivors. Virtually all of these HERVs are not expressed: that is, cellular mechanisms have silenced any effect that they might have on cellular or organismic functioning. However, the silenced HERV sequences have been passed down the generations and any side-effects due to the presence of those sequences remain unknown. It may well be that the only people who survived HERV insertion were those whose cells had the capacity to silence HERV gene expression.

The existence of HERV sequences in the human genome is evidence that horizontal gene transfer events do occur on an evolutionary timescale. But the fact that they occur does not provide evidence that HGT is "normal", harmless, or beneficial, particularly in the short timescale relevant to direct genome changes via genetic engineering.

Another example of HGT happening in nature is infection with A. tumefaciens, a bacterium with a natural ability to carry and transfer part of its DNA to the cells of the plants that it infects, thereby causing crown gall disease, a type of plant tumour. For this reason, A. tumefaciens is a valued tool of genetic engineers.

It is important to note that the above examples of "natural" HGT into higher organisms are

## Muddying the waters with imprecise terms

GMO proponents often use the terminology relating to genetic modification incorrectly, blurring the line between genetic modification and conventional breeding.

For example, they claim that conventional plant breeders have been "genetically modifying" crops for centuries by selective breeding and that GM crops are no different. But this is incorrect. The term "genetic modification" is recognised in common usage and in national and international laws as referring to the use of laboratory techniques, mainly recombinant DNA technology, to transfer genetic material between organisms or modify the genome in ways that would not take place naturally, bringing about alterations in the genetic makeup and properties of the organism.

The term "genetic modification" is sometimes wrongly used to describe marker-assisted selection (MAS). MAS is a relatively uncontroversial branch of biotechnology that can speed up conventional breeding by identifying natural genes that confer important traits. MAS does not involve the risks and uncertainties of genetic modification. It is supported by organic and sustainable agriculture groups worldwide, with objections mostly focusing on patenting issues.

Similarly, "genetic modification" is sometimes wrongly used to describe tissue culture, a method that is used to select desirable traits or to reproduce whole plants from plant cells in the laboratory. In fact, while genetic modification of plants as carried out today is dependent on the use of tissue culture, tissue culture is not dependent on GM. Tissue culture can be used for many other purposes, including some safe and useful ones.

Using the term "biotechnology" to mean genetic modification is inaccurate. Biotechnology is an umbrella term that includes a variety of processes through which humanity harnesses biological functions for useful purposes. For instance, fermentation in wine-making and breadmaking, composting, the production of silage, marker-assisted selection (MAS), tissue culture, and even agriculture itself, are all biotechnologies. GM is one among many biotechnologies.

GM proponents' misleading use of language may be due to unfamiliarity with the field, or may represent deliberate attempts to blur the line between controversial and uncontroversial technologies in order to win public acceptance of GM.

pathogenic processes. They illustrate the fact that in nature, the HGT process often causes disease in the infected organism. The result of the HGT process is the introduction into the host organism of a retrovirus that can play a role in cancer development (in the case of HERVs) or tumour-causing DNA sequences (in the case of A. tumefaciens infection of a plant). This is evidence that such processes cannot be assumed to be benign and may be harmful. So these examples are not an argument in favour of genetic engineering of our food supply, but rather an argument counselling against its use.

It is also important to note that unlike the GM transformation process, HGT by A. tumefaciens does not modify the germ cells of the plant and so does not affect future generations of the infected plant.

In nature, the question of whether any given example of horizontal gene transfer is beneficial or harmful is answered over long periods of co-evolution and natural selection. It cannot be answered based on the limited knowledge of the genetic engineer or under the limited timescales in which GMO introduction takes place. Neither can it be answered by the inadequate "safety assessment" regimes that are currently used in GMO regulatory processes around the world.

## GM attempts to override host plant gene regulatory mechanism

The random insertion of the GM gene cassette at the vast majority of locations within the plant cell DNA results in little or no expression of the transgene. This "silencing" of the GM gene cassette, including any associated antibiotic selectable marker gene present, is in part due to the plant's natural response to invasion by foreign DNA, as occurs, for example, in the case of infection by viruses. This silencing occurs despite that fact that in most cases plant genetic engineers use the powerful 35S cauliflower mosaic virus (CaMV) promoter or similar powerful promoters in an effort to overcome GM gene inactivation.

Consequently the selection procedure of plants via the GM transformation process actively selects for purely fortuitous events in which the GM gene cassette, plus any associated antibiotic marker gene, has inserted into those rare sites within the plant's DNA that allow it to function. These rare sites are by definition regions within the plant cell DNA where active host genes and their control elements are located. In other words, the GM plants contain GM gene cassette insertions into regions of the DNA where their own genes are active (gene regions represent only a tiny fraction of the total genome). This fact maximizes the chances that the plants' host gene function will be disturbed – with unexpected downstream consequences to their biochemistry and performance.

In addition, the use of potent plant promoters such as the CaMV to switch on GM genes has other potential downsides. The CaMV promoter functions in all the different types of cells within the plant. Such ubiquitous expression is necessary in cases such as when the GM crop is engineered to tolerate being sprayed with a herbicide, to ensure that the plant survives.

But in other situations, ubiquitous GM gene expression is not so desirable. For example, GM maize engineered with the insecticidal Bt toxin gene obtained from bacteria aims to target either the corn borer or rootworm pest. Therefore the GM Bt toxin gene only needs to be expressed in stems, corn cobs, and roots, in order to ensure protection from these pests. However, the use of the CaMV promoter to drive expression of the Bt toxin transgene unit (as is the case in all current GM crops) results in the presence of this insecticide in all plant structures, not just the stems, cobs, and roots. This in turn increases the possibility of toxic effects on non-target insect populations that may feed on the pollen of these Bt GM crops, such as bees and butterflies. Thus valuable pest predator or pollinator insect populations may be harmed when feeding on Bt GM crops.

In conclusion, the use of ubiquitous promoters such as the CaMV in an effort to override the host plant's gene regulation systems and force expression of the GM gene at high levels may have undesirable effects on plant biochemistry, crop performance and the surrounding environment.

In contrast, in natural breeding and even in mutation breeding (mutagenesis), which exposes plants to radiation or chemicals to induce genetic mutations (inheritable changes), the plants' own gene regulation systems remain active.

In other words, scientists use genetic engineering to bypass the plants' natural gene regulation systems and to re-programme their genetic functioning. Natural breeding, on the other hand, uses the inherent genetic potential in plants and does not deliberately disrupt their gene regulation system.

## Conclusion

Genetic engineering is different from natural/conventional plant breeding and poses special risks, as is recognized in national and international biosafety laws. The genetic engineering and associated tissue culture processes are highly mutagenic, leading to unpredictable changes in the DNA and proteins of the resulting GM crop that can in turn lead to unexpected toxic, allergenic and nutritional effects.

## References


1. European Parliament and Council. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Off J Eur Communities. 2001:1–38.
2. Secretariat of the Convention on Biological Diversity. Cartagena Protocol on Biosafety to the Convention on Biological Diversity. Montreal; 2000. Available at: http://bch.cbd.int/protocol/text/.
3. Codex Alimentarius. Foods derived from modern biotechnology (2nd ed.). Rome, Italy: World Health Organization/ Food and Agriculture Organization of the United Nations; 2009. Available at: ftp://ftp.fao.org/codex/Publications/Booklets/Biotech/Biotech_2009e.pdf.
4. Codex Alimentarius. Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants: CAC/GL 45-2003; 2003.
5. GeneWatch UK. ASA rules that Monsanto adverts were misleading: GeneWatch UK complaints upheld [press release]. http://www.genewatch.org/article.shtml?als[cid]=492860&als[itemid]=507856. Published August 10, 1999.
6. Phillips McDougall. The cost and time involved in the discovery, development and authorisation of a new plant biotechnology derived trait: A consultancy study for Crop Life International. Pathhead, Midlothian; 2011.
7. Goodman MM. New sources of germplasm: Lines, transgenes, and breeders. In: Martinez JM, ed. Memoria Congresso Nacional de Fitogenetica. Univ Autonimo Agr Antonio Narro, Saltillo, Coah, Mexico; 2002:28–41. Available at: http://www.cropsci.ncsu.edu/maize/publications/NewSources.pdfDoolittle WF. Lateral genomics. *Trends Cell Biol.* 1999;9(12):M5-8.
8. Hughes JF, Coffin JM. Evidence for genomic rearrangements mediated by human endogenous retroviruses during primate evolution. *Nat Genet.* 2001;29:487-9. doi:10.1038/ng775.
9. European Parliament and Council. Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms. 2009. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32009L0041:EN:NOT.

# 1.2 Myth: Genetic engineering is precise and the results are predictable

# Truth: Genetic engineering is crude and imprecise, and the results are unpredictable

## Myth at a glance

GMO proponents claim that GM is a precise technique that allows genes coding for the desired trait to be inserted into the host plant with no unexpected effects. But the genetic engineering and associated tissue culture processes are imprecise and highly mutagenic. They lead to unpredictable changes in the DNA, proteins, and biochemical composition of the resulting GM crop, which can result in unexpected toxic or allergenic effects and nutritional disturbances, as well as unpredictable effects on the environment.

GMO proponents claim that GM is a precise technique that allows genes coding for the desired trait to be inserted into the host plant with no unexpected effects.

The first steps of making a GM plant – isolating the desired gene and cutting and splicing it to form the GM gene cassette in the laboratory – is indeed precise. But the subsequent steps are not. In particular, the process of inserting a GM gene cassette into the DNA of a plant cell is crude, uncontrolled, and imprecise. It causes mutations – inheritable changes – in the plant's DNA blueprint.[1] These mutations can alter the functioning of the natural genes of the plant in unpredictable and potentially harmful ways.[2,3] Other procedures associated with producing GM crops, including tissue culture, also cause mutations.[1]

In addition to the unintended effects of mutations, there is another way in which the GM process generates unintended effects. Proponents of GM crops paint a simplistic picture of GM technology that is based on a naïve and outdated understanding of how genes are organised within DNA and how they work. They imply that they can insert a single gene with laser-like precision and insertion of that gene will have a single, predictable effect on the organism and its environment.

But manipulating one or two genes does not just produce one or two desired traits. Instead, just a single change at the level of the DNA can give rise to multiple changes within the organism.[2,4] Such changes are known as pleiotropic effects. They occur because genes do not act as isolated units but interact with one another and are regulated by a highly complex, multi-layered network of genetic and epigenetic processes (epigenetic effects are inheritable changes in gene expression or cells caused by mechanisms other than changes in the underlying DNA sequence). Components of the GM gene, and the functions and structures that the GM genes confer on the organism, interact with other functional units of the organism.

Because of these diverse interactions, and because even the simplest organism is extremely complex, it is impossible to predict the impacts of even a single GM gene on the organism. The complexity of living systems makes it even more challenging to predict the impact of any given GMO on its environment.

In short, unintended, uncontrolled mutations and complex interactions at multiple levels within the organism occur during the GM process, giving rise to unpredictable changes in function as a result of the insertion of even a single new gene.

A seemingly simple genetic modification can give rise to unexpected and potentially harmful changes in the resulting GMO and the foods produced from it. The unintended changes could include alterations in the nutritional content of the food, toxic and allergenic effects, poor crop performance, and the emergence and spread of characteristics that harm the environment.

It is unlikely that potentially harmful changes would be picked up by the inadequate tests carried out in support of GMO authorizations. Even when changes are detected, they are often dismissed as irrelevant without further investigation.

These unexpected changes are especially dangerous because the release of GMOs into the environment is irreversible. Even the worst chemical pollution diminishes over time as the pollutant is degraded by physical and biological mechanisms. But GMOs are living organisms. Once released into the ecosystem, they do not degrade and cannot be recalled, but propagate and multiply in the environment, passing on their GM genes to future generations. Each new generation creates more opportunities for the GMO to interact with other organisms and the environments, generating even more unintended and unpredictable side-effects.

## The GM process is highly mutagenic

The process of creating a GM plant is highly mutagenic. This means it damages the DNA, creating changes in the genome. Mutations can be beneficial or harmful. Very infrequently, a specific mutation can benefit the functioning of the organism. Such changes are the basis of evolution through natural selection. Much more frequently, mutations can harm the organism, for example, by giving rise to birth defects and cancer.

The GM process involves three kinds of mutagenic effects, as follows.[1,2]

### 1. Insertional mutagenesis

Genetic modification or the genetic engineering of an organism always involves the insertion of a foreign GM gene cassette into the genome (DNA) of the recipient organism. The insertion process is uncontrolled, in that the site of insertion of the foreign gene is random. The insertion of the GM gene cassette interrupts the normal sequence of the letters of the genetic code within the DNA of the plant, causing what is called insertional mutagenesis. This can occur in a number of different ways:

- The GM gene can be inserted into the middle of one of the plant's natural genes. Typically this blocks the expression of – "knocks out" – the natural gene, destroying its function. Less frequently the insertion event will alter the natural plant gene's structure and the structure and function of the protein for which it encodes.
- The GM gene can be inserted into a region of the plant's DNA that controls the expression of one or more genes of the host plant, unnaturally reducing or increasing the level of expression of those genes.
- Even if the GM gene is not directly inserted into a gene of the host plant or its control elements, its mere presence within a region of the plant's DNA where host genes are located and active can alter the normal pattern of gene function – that is, the level at which a given gene is switched on. Thus it can alter the balance of the genes' resulting protein products. The inserted gene can compete with gene expression control elements within the DNA of the host plant for the binding of regulatory proteins. The result will be marked disturbances in the level and pattern of expression of the host plant's natural genes.

Since the insertion of the GM gene is an imprecise and uncontrolled process, there is no way of predicting or controlling which of the plant's genes will be influenced and how.

## 2. Genome-wide mutations

In most cases, the insertion process is not clean. In addition to the intended insertion, fragments of DNA from the GM gene cassette can be inserted at multiple random locations in the genome of the host plant. Each of these unintended insertions is a mutational event that can disrupt or destroy the function of other genes in the same ways as the full GM gene, described under "Insertional mutagenesis", above.

It is estimated that there is a 53–66% probability that any insertional event will disrupt a gene.[1] Therefore, if the genetic modification process results in one primary insertion and two or three unintended insertions, it is likely that at least two of the plant's genes will be disrupted.

Evidence from research indicates that the genetic modification process can also trigger other kinds of mutations – rearrangements and deletions of the plant's DNA, especially at the site of insertion of the GM gene cassette[1] – which are likely to compromise the functioning of genes important to the plant.

## 3. Mutations caused by tissue culture

Three steps of the genetic modification process take place while the host plant cells are being grown in a process called cell culture or tissue culture. These steps include:

1. The initial insertion of the GM gene cassette into the host plant cells
2. The selection of plant cells into which the GM gene cassette has been successfully inserted

3. The development of GM plant cells into GM plantlets with roots and leaves with the help of plant hormones.

The process of tissue culture is itself highly mutagenic, causing hundreds or even thousands of mutations throughout the host cell DNA.[1,2] Since tissue culture is obligatory to all three steps described above and these steps are central to the genetic engineering process, there is abundant opportunity for tissue culture to induce mutations in the plant cells.

In the case of plants that are vegetatively propagated (that is, not through seeds but through tubers or cuttings), such as potatoes, all the different types of mutations in a given GM plant resulting from the GM transformation process will be present in the final commercialized crop.

In the case of soy, maize, cotton, and oilseed rape (canola), the initial GM plant can be back-crossed (bred) with the non-GM parent variety to achieve closer genetic similarity. This back-crossing enables many, but not all, of the mutations incurred during the GM transformation process to be "bred out".

However, given the fact that hundreds of genes may initially be mutated during insertion of the GM gene cassette and during tissue culture, there is a significant risk that a gene or genes crucial to some important property, such as disease- or pest-resistance, could be damaged. In another example, a gene that plays a role in controlling biochemical reactions in the plant could be damaged, making the plant allergenic or toxic, or altering its nutritional value.

The genetic engineer will not be able to detect and eliminate many such harmful mutations because their effects will not be obvious under the conditions of the development process. But these mutations would still be present in the commercialized crop and could cause problems. For instance, the non-GM parent crop may contain a gene that confers resistance to an insect pest. In the laboratory and greenhouse where the GM crop is developed, that insect will not be present and so the genetic engineers would have no way of knowing that the insect resistance gene present in the GM plants had been damaged. Only after the crop has been commercialized would it be discovered that the plants were no longer able to resist the insect pest.

## How GM selects for host gene mutational effects

The GM gene cassette that is inserted into the host plant's DNA (step 1 in "3. Mutations caused by tissue culture", above) normally carries a selectable marker gene. Most commonly the marker gene confers antibiotic resistance on cells that have successfully incorporated the GM gene cassette into their DNA and expressed the genes in that cassette. As discussed in Myth 1.1, the antibiotic resistance marker gene enables the genetic engineer to identify which plant cells have successfully incorporated the GM gene cassette into their genome. Alternatively, a GM gene conferring tolerance to a herbicide can be used for selection of transformed plants.

It is important to note that either the antibiotic or herbicide-based selection process relies on the expression of these marker genes. This expression is required in order to make the plant resistant to the antibiotic or tolerant to treatment with the herbicide. If this gene does not express its protein, it will not confer resistance to the antibiotic or herbicide, and the cell will die upon exposure to it.

Not all regions of the plant cell DNA are *permissive* for the gene expression process to take place. In fact, the vast majority of any cell's DNA is *non-permissive*. Any gene present in such a region of the plant's genome will be silent – that is, it will not be expressed. Because the process of inserting the GM gene cassette (containing the GM gene(s) of interest and any associated antibiotic resistance marker genes) is essentially random, most insertions will occur in non-permissive regions of the plant cell DNA and will not result in expression of either the marker gene or the GM gene. Such cells will not survive exposure to the antibiotic or herbicide. Only when the GM gene cassette, including the antibiotic resistance marker gene, happens to have been inserted into a functionally permissive region of the plant cell DNA will the cell express the marker gene and survive exposure to the antibiotic or herbicide.

Permissive regions are areas of DNA where genes or control elements important to the functioning of the recipient plant cells are present and active. Thus, selection for antibiotic or herbicide resistance selects for cells into which the gene cassette has been inserted into a permissive region of DNA. Since these are also the regions that carry genes and control elements important to the function of the recipient plant cell, insertions in these regions carry a greatly increased likelihood of damaging the expression of genes important to the cellular function and even survival of the recipient plant cell.

In short, the selection for GM gene insertions in the GM transformation procedure maximizes the likelihood that incorporation of the GM gene will damage one or more genes that are active and important to the functioning of the host plant.

We conclude from this analysis of the mechanisms by which genetic modification can cause mutations that genetic modification is not the elegant and precisely controlled scientific process that proponents claim, but depends on a large measure of luck to achieve the desired outcome without significant damage. We also conclude that it is unwise to commercialize GM crop varieties without thorough assessment of potential harmful effects to health and the environment.

## Is GM technology becoming more precise?

Technologies have been developed that are intended to target GM gene insertion to a predetermined site within the plant's DNA in an effort to obtain a more predictable outcome and avoid the complications that can arise from random insertional mutagenesis.[5,6,7,8,9,10]

Some of these technologies use nucleases or "genome scissors" which allow the cutting of DNA and the insertion of new DNA in any position in the chromosomes. The most popular of these new genome scissors are TALENs (transcription activator-like effector nucleases), ZFNs (zinc finger nucleases), and most recently CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats).

These genome scissors are a combination of a unit to recognize specific regions of the

DNA and an enzyme to cut both strands of the DNA at a sequence determined by the genetic engineer. When the cell senses that this double-strand DNA break has occurred, it stimulates the cell's machinery to repair it.

There are two possible outcomes. First, simply allowing the repair to proceed where the cut ends of the DNA are joined back together again (a process known as "non-homologous end-joining") introduces a mutation at the site of cutting by the genome scissors. This is because non-homologous end-joining repair is not perfect, and in the majority of cases, base units of DNA are lost from the ends of the DNA during the joining process.

Second, at the same time that the genome scissor gene is introduced into the plant cell, the genetic engineer can also introduce a separate DNA molecule that has the same regions in it as the region that he is trying to modify in the host genome, but which also contains a gene coding for the desired additional trait. The artificial gene that has been introduced can align with the corresponding region of the host cell's DNA. In some instances the cell uses this second introduced DNA molecule as a guide to repair the double-stand DNA break in a process known as "homologous recombination". The final result is the repair of the double-strand DNA break, but with the incorporation of the artificial gene at this pre-determined site.

By using these methods, genes can be knocked-out (silenced) or mutated, or new DNA including whole gene units can be inserted.

Proponents claim that these technologies offer "targeted genome editing".[11] However, these GM transformation methods are not failsafe. Two studies found that ZFNs caused unintended genomic modifications in off-target sites in human cell lines.[12,13] The simple word for "modifications in off-target sites" is "mutations". That is, these techniques can cause unintended mutations in other locations in the genome, causing a range of potentially harmful side-effects. In another investigation using human cells, CRISPR was found to cause unintended mutations in many regions of the genome.[14]

Biotechnologists still know only a fraction of what there is to be known about the genome of any species and about the genetic, biochemical, and cellular functioning of our crop species. That means that even if they select an insertion site that they think will be safe, insertion of a gene at that site could cause a range of unintended effects, such as disturbances in gene expression or in the function of the protein(s) encoded by that gene.

Even if there is no disturbance at the level of the gene, there may be disturbance at the level of the protein for which the gene encodes. For example, a plant may have an enzyme that is normally inhibited by a herbicide, meaning that the plant will die if that herbicide is applied. If the plant is genetically modified to alter the enzyme so that it is not inhibited by the herbicide (genetic engineered for herbicide tolerance), there may be knock-on effects. Enzymes are not totally specific. If the activity of the enzyme is changed, the plant's biochemistry could be altered in the process, causing unknown chemical reactions with unknown consequences.

Moreover, because tissue culture must still be carried out for these new targeted insertion methods, the mutagenic effects of the tissue culture process remain a major source of unintended damaging side-effects.

Effects could include:

- Unexpected toxins or allergens, or an alteration in nutritional value
- Reduced ability of the GM crop to resist disease, pests, drought, or other stresses
- Reduced productivity or vigour
- Unexpected environmental effects, such as increased weediness.

According to a German newspaper, plants produced using these technologies are already being grown in greenhouses. The independent research institute Testbiotech says it is not known whether any of the plants have been released into the environment, adding, "There is, however, a clear lack of regulation to ensure that these plants, which are genetically modified organisms, undergo risk assessment."[15]

## Rapid Trait Development System: GM or not?

The biotechnology companies BASF and Cibus have developed oilseed rape and canola with a technique called RTDS (Rapid Trait Development System).[16] According to Cibus, RTDS is a method of altering a targeted gene by utilizing the cell's own gene repair system to specifically modify the gene sequence in situ, and does not involve inserting foreign genes or gene expression control sequences. The Gene Repair Oligonucleotide (GRON) that effects this change is a chemically synthesized oligonucleotide,[17] a short, single-stranded DNA and/or RNA molecule.

Cibus markets its RTDS crops as non-transgenic and as produced "without the insertion of foreign DNA into plants". The company adds that crops developed using this method are "quicker to market with less regulatory expense".[16] Cibus says that the RTDS method is "all natural", has "none of the health and environmental risks associated with transgenic breeding", and "yields predictable outcomes in plants".[18]

However, GM is a process, and the definition of genetic modification does not depend on the origin of the inserted genetic material. Crops created with RTDS can and should be described as GMOs, since RTDS alters the genome in a manner that would not occur naturally through breeding or genetic recombination. The fact that no foreign DNA is inserted into the recipient plant's genome is immaterial.

In addition, RTDS still involves tissue culture, which introduces genome-wide mutations. Some or all of these mutations (the latter in vegetatively propagated plants, e.g. potatoes) will be present in the final marketed product. Also, there will inevitably be off-target effects from the RTDS process. The intent of the RTDS process is specific targeting, but this technique is new and the research has not been done to assess the frequency and extent of off-target effects. The old saying, "Absence of evidence of harm is not evidence of the absence of harm," is pertinent here.

To assess the fidelity and efficacy of the RTDS process and the extent to which unintended alterations take place at other locations in the genome during RTDS, many different studies will be needed. For instance, one important class of studies that must be carried out is whole genome sequencing of RTDS GMOs. Structural and functional analysis of the proteins present in RTDS GMOs (proteomics), as well as analysis of metabolites present (metabolomics) would also be required. In parallel, the functional performance of these RTDS GMOs should be assessed. The agronomic performance, the impact on the environment, and the quality and safety of the food derived from these RTDS-derived GMOs all need to be investigated, including via long-term toxicological feeding studies.

Even changing a single gene, whether it encodes an enzyme, a structural protein, a peptide hormone, or a regulatory protein, can cause unintended functional or structural disturbances at the level of the cell and the organism as a whole.

RTDS is a genetic modification process, albeit more targeted than other recombinant DNA techniques. Any crops or other organisms produced in this way must be treated in exactly the same way as crops altered using old-fashioned recombinant DNA techniques, namely thorough evaluation of functionality, utility, and safety.

"New" does not necessarily mean "better" or "safer". RTDS and the other methods described above are new and they were designed to be more specific. This is a laudable intention, but empirical evidence needs to be gathered on the safety and efficacy of these new techniques.

It is interesting to note that the biotech company Cibus, in its publicity materials for the RTDS method, acknowledges the imprecision of standard genetic modification using recombinant DNA techniques.[18]

## Conclusion

Genetic engineering and the associated tissue culture processes are imprecise and highly mutagenic. They lead to unpredictable changes in the DNA, proteins, and biochemical composition of the resulting GMOs, which can result in unexpected toxic or allergenic effects and nutritional disturbances, as well as unpredictable effects on the environment.

## References


1. Latham JR, Wilson AK, Steinbrecher RA. The mutational consequences of plant transformation. *J Biomed Biotechnol.* 2006;2006:1–7. doi:10.1155/JBB/2006/25376.
2. Wilson AK, Latham JR, Steinbrecher RA. Transformation-induced mutations in transgenic plants: Analysis and biosafety implications. *Biotechnol Genet Eng Rev.* 2006;23:209–238.
3. Schubert D. A different perspective on GM food. *Nat Biotechnol.* 2002;20:969. doi:10.1038/nbt1002-969.
4. Pusztai A, Bardocz S, Ewen SWB. Genetically modified foods: Potential human health effects. In: D'Mello JPF, ed. *Food Safety: Contaminants and Toxins.* Wallingford, Oxon: CABI Publishing; 2003:347–372. Available at: http://www.leopold.iastate.edu/news/pastevents/pusztai/0851996078Ch16.pdf.
5. Kumar S, Fladung M. Controlling transgene integration in plants. *Trends Plant Sci.* 2001;6:155–9.
6. Ow DW. Recombinase-directed plant transformation for the post-genomic era. *Plant Mol Biol.* 2002;48:183-200.
7. Li Z, Moon BP, Xing A, et al. Stacking multiple transgenes at a selected genomic site via repeated recombinase-mediated DNA cassette exchanges. *Plant Physiol*. 2010;154:622-31. doi:10.1104/pp.110.160093.
8. Shukla VK, Doyon Y, Miller JC, et al. Precise genome modification in the crop species Zea mays using zinc-finger nucleases. *Nature*. 2009;459(7245):437-41. doi:10.1038/nature07992.
9. Townsend JA, Wright DA, Winfrey RJ, et al. High-frequency modification of plant genes using engineered zinc-finger nucleases. *Nature*. 2009;459(7245):442-5. doi:10.1038/nature07845.
10. Shen H. CRISPR technology leaps from lab to industry. Nature. 2013. doi:10.1038/nature.2013.14299.
11. Wood AJ, Lo T-W, Zeitler B, et al. Targeted genome editing across species using ZFNs and TALENs. Science. 2011;333(6040):307. doi:10.1126/science.1207773.
12. Pattanayak V, Ramirez CL, Joung JK, Liu DR. Revealing off-target cleavage specificities of zinc-finger nucleases by in vitro selection. *Nat Methods.* 2011;8(9):765-770. doi:10.1038/nmeth.1670.

13. Gabriel R, Lombardo A, Arens A, et al. An unbiased genome-wide analysis of zinc-finger nuclease specificity. *Nat Biotechnol*. 2011;29(9):816-823. doi:10.1038/nbt.1948.
14. Fu Y, Foden JA, Khayter C, et al. High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells. *Nat Biotechnol*. 2013;31(9):822-826. doi:10.1038/nbt.2623.
15. Then C. *Free trade for "high-risk biotech"? Future of genetically engineered organisms, new synthetic genome technologies and the planned free trade agreement TTIP – a critical assessment*. Munich, Germany: Testbiotech; 2013. Available at: http://www.testbiotech.org/sites/default/files/Testbiotech_Future_Biotech.pdf.
16. Cibus. BASF and Cibus achieve development milestone in CLEARFIELD® production system [press release]. Undated. Available at: http://www.cibus.com/press/press012709.php.
17. Cibus. What is RTDS™? The Rapid Trait Development System in brief. 2013. Available at: http://www.cibus.com/rtds.php.
18. Cibus. The evolution of plant breeding: RTDS™ versus other technologies. Undated. Available at: http://www.cibus.com/pdfs/RtdsSketch4_LoRes.pdf.

# 1.3 Myth: Genetic engineering of crops is no more risky than mutation breeding, which is widely accepted and not regulated

## Truth: Genetic engineering and mutation breeding are both risky and should be strictly regulated

### Myth at a glance

GM proponents often compare GM with radiation- or chemical-induced mutation breeding (mutagenesis) and claim that these methods are even more mutagenic than GM and at least as disruptive to gene expression. They argue that crops developed by mutation breeding are widely viewed as safe and have not caused health problems; and that therefore GM crops should not be subjected to stricter regulation than mutation-bred crops.

Some GM proponents imply that mutagenesis is equivalent to conventional breeding.

However, while mutagenesis is used in conventional breeding, mutation breeding is not the same as conventional breeding. Mutation breeding is unpredictable and risky, and crops produced in this way should be as strictly regulated as GM crops.

GM proponents often compare GM with mutation breeding (mutagenesis), which they say has been used for decades in conventional plant breeding and is not controversial. They argue that mutation breeding is used by conventional plant breeders and that mutation-bred plants have a history of safe use and do not cause ill health.[1] GM proponents also say that genetic modification is more precise than mutation breeding, and imply that therefore, GM plants should not be regulated any more strictly than those produced by mutation breeding.[2]

However, these arguments are flawed, for the reasons explained below.

### What is mutation breeding?

The physical form of an organism's genetic blueprint is the sequence of the four "bases", or "letters" (A, G, C, T) of the genetic alphabet. The sequence in which these four "letters" are linked together to form the DNA molecule determines the information contained in that molecule, just as the sequence in which the 26 letters of our alphabet are placed on this page determines its information content.

You can change the meaning of a sentence by changing the sequence of letters in the sentence, and you can change the "meaning" of a gene or its associated genetic control elements by changing the sequence of letters within the genetic code of that gene or control element. Mutations are physical alterations in the sequence of the four letters of the genetic alphabet within the DNA.

Mutation breeding is the process of exposing plant seeds to mutagens – physical or chemical agents that damage the DNA, causing mutations. In practice, these agents are either ionizing radiation (X-rays or gamma rays) or compounds that physically or chemically react with DNA.

The types of mutations that can be created range from a change in a single genetic letter (for example, "A" can be replaced with "C", or "G" with "T"), to the deletion of one or many letters, to rearrangements of small or large stretches of the DNA sequence.

This process of change in the DNA is known as mutagenesis. Mutagenesis can completely destroy the function of a gene – "knockout" its function – or it can cause the gene to direct the cell to produce one or more proteins with altered function. In addition, mutagenesis can alter the functioning of the genetic control elements associated with a gene or genes and thus alter the amount, timing, or location of the protein products produced from them. The resulting plant is called a mutant.

It is a fortuitous and infrequent event when a mutation improves the functioning of an organism. More often, mutations are damaging or silent (no observable effect). Damage can range from death of the plant, to minor reductions in productivity or vigour, to changes in the function or structure of the organism, and even to the quality or safety of the food derived from the crop plant.

Once plants carrying radiation-induced mutations have been created, they are crossed with other crop varieties using conventional breeding (the same process is used with GM crop varieties). However, mutation breeding is not in itself conventional breeding.

## Where did radiation-induced mutation breeding come from?

Mutation breeding using radiation started in the 1920s. It became more widely used in the 1950s, after the US atomic bombing of Japan at the end of World War II in 1945. In the wake of the devastation, there was a desire to find uses for the "peaceful atom" that were helpful to humanity. Atomic Gardens were set up in the US and Europe, and even in Japan, with the aim of creating high-yielding and disease-resistant crops. They were laid out in a circle with a radiation source in the middle that exposed plants and their seeds to radiation. This caused mutations in the plants, which radiation enthusiasts hoped would be beneficial. Public relations campaigns euphemistically described the plants as "atom energized".

However, the results of these projects were poorly documented and do not qualify as scientific research. It is unclear whether any useful plant varieties emerged from Atomic Garden projects.[3]

Today, radiation-induced mutation breeding is carried out in laboratories. This branch of plant breeding retains strong links with the nuclear industry. The only database of crop varieties generated using radiation- and chemically-induced mutation breeding is maintained by the UN Food and Agriculture Organization in partnership with the International Atomic Energy Agency.[4] Many studies and reports that promote radiation-induced mutation breeding are sponsored by organizations that also promote nuclear energy.[5,6]

## Is mutation breeding widely used?

Mutation breeding is not a widely used or central part of crop breeding. It is a minor footnote to the advances that conventional breeding has brought to agriculture, although a handful of crop varieties have apparently benefited from it. The database maintained by the UN Food and Agriculture Organisation and the International Atomic Energy Agency keeps track of plant varieties that have been generated using mutation breeding and cross-breeding with a mutant plant.[4] The database contains only around 3,000 such plant varieties, and this number includes not only food crop plants but also ornamental plants.[7] It also includes not only the primary mutant varieties generated through mutagenesis, but also any varieties that have been created by crossing the primary mutant varieties with other varieties by conventional breeding. Thus the actual number of primary mutant varieties is a fraction of the 3,000 varieties listed in the database.

Conventional breeding, in contrast, has produced millions of crop varieties. The Svalbard seed vault in the Arctic contains over 770,000 seed varieties.[8] In 2009 its seed stocks were estimated to represent one-third of our most important food crops.[9] So quantitatively speaking, mutation breeding has proved to be of only marginal importance in crop development.

## Why isn't mutation breeding more widely used?

The process of mutagenesis is risky, unpredictable, and does not efficiently generate beneficial mutations. Studies on fruit flies suggest that about 70% of mutations will have damaging effects on the functioning of the organism, and the remainder will be either neutral or weakly beneficial.[10]

Because of the primarily harmful effects of mutagenesis, living organisms have DNA repair mechanisms to correct mutations and minimize their impacts. The primarily harmful effect of mutations is reflected in the policies of regulatory agencies around the world, which are designed to minimize or eliminate exposure to radiation and other manmade mutagens.

In plants as well as fruit flies, mutagenesis is a destructive process. One textbook on plant breeding states, "Invariably, the mutagen kills some cells outright while surviving plants display a wide range of deformities."[11] Experts conclude that most such induced mutations are harmful and lead to unhealthy and/or infertile plants.[11,12]

A report by the UK government's GM Science Review Panel concluded that mutation breeding "involves the production of unpredictable and undirected genetic changes and many thousands, even millions, of undesirable plants are discarded in order to identify plants with suitable qualities for further breeding."[13]

Occasionally, mutagenesis may give rise to a previously unknown feature that may be beneficial and can be exploited. Commercially useful traits that have emerged from mutation breeding include the semi-dwarf trait in rice, the high oleic acid trait in sunflower, the semi-dwarf trait in barley, and the low-linolenic acid trait in canola (oilseed rape).[7,14,15] It is interesting to note that all of these traits are the result of destruction of the function of one or more natural genes, not the remodelling or fine-tuning of genes or the proteins they encode. This reflects the brute-force nature of the mutation breeding technique.

The process of screening out undesirable mutants and identifying desirable ones for further breeding has been likened to "finding a needle in a haystack".[11] The problem is that only certain types of mutations, such as those affecting shape or colour, are obvious to the eye. These plants can easily be discarded or kept for further breeding as desired. But other more subtle changes may not be obvious, yet nonetheless can have important impacts on the health or performance of the plant. Such changes can only be identified by expensive and painstaking testing.[11]

In retrospect, it is fortunate that mutation breeding has not been widely used because that has reduced the likelihood that this risky technology could have generated crop varieties that are toxic, allergenic, reduced in nutritional value, vulnerable to pests or environmental stressors, or harmful to the environment.

## Why worry about mutations caused in genetic engineering?

GMO proponents make four basic arguments to counter concerns about the mutagenic aspects of genetic engineering.

### 1. "Mutations happen all the time in nature"

GMO proponents say that mutations happen all the time in nature as a result of various natural exposures, for example, to ultraviolet light, so mutations caused by genetic engineering of plants are not a problem.

In fact, mutations in nature are a low-frequency event.[7] And comparing natural mutations with those that occur during genetic modification is like comparing apples with oranges. Every plant species has encountered environmental mutagens, including certain types and levels of ionizing radiation and chemicals, throughout its natural history and has evolved mechanisms for preventing, repairing, and minimizing the impacts of any mutations caused. But plants have not evolved mechanisms to repair or compensate for the insertional mutations that occur during genetic modification. Also, the high frequency of mutations caused by tissue culture during the process of developing a GM plant is likely to overwhelm the plant's repair mechanisms.

Homologous recombination events that move large stretches of DNA around a plant's genome do occur in nature. But the mechanisms of homologous recombination are very precise, and rarely cause mutations. Also, the DNA sequences that undergo rearrangement during homologous recombination are already part of the plant's own genome, not DNA that is foreign to the species.

In addition, if mutations were to occur that compromised the quality of the food produced by the plant, for instance, by producing unexpected toxins, the long co-evolution process between humans and their food crops would have enabled such harmful mutants to be eliminated from the breeding process.

## 2. "Conventional breeding is less precise and more disruptive to gene expression than GM"

Some GMO proponents cite a study by Batista and colleagues[16] to argue that chemical- or radiation-induced mutagenesis, used in "conventional" breeding, is less precise and more disruptive to gene expression than GM. They term radiation-induced mutagenesis "conventional radiation treatment" and argue on the basis of papers discussing mutation-bred crops that "conventional plant breeding causes mutations" – appearing to imply that mutation breeding is synonymous with conventional breeding. They add that plants developed in this way are widely accepted and have not caused ill health in consumers.[1]

However, such arguments misrepresent the study of Batista and colleagues and the nature of conventional breeding and mutation breeding. Batista and colleagues did not compare conventional breeding with GM, but radiation-induced mutation breeding with GM.[16]

Mutation breeding is not the same as conventional breeding. While radiation- and chemical-induced mutation breeding has been used in tandem with conventional breeding, it is not in itself conventional breeding. Mutation breeding only escaped regulation because of the widespread ignorance about the potential effects of mutations in food crops at the time that the method began to be used in crop breeding.

Batista and colleagues' research actually provides strong evidence to support the argument that GM is highly disruptive to gene expression. The study found that in rice varieties developed through radiation-induced mutation breeding, gene expression was disrupted even more than in varieties generated through genetic modification. They concluded that for the rice varieties examined, mutation breeding was more disruptive to gene expression than genetic engineering.[16]

Batista and colleagues did not compare GM with conventional breeding, but compared two highly disruptive methods – genetic engineering and mutation breeding – and concluded that genetic engineering was, in the cases considered in their study, the less disruptive of the two methods.

One GM proponent nonetheless concludes, based on the Batista paper, that "the potential for harm in both cases is trivial".[2] But this was not the conclusion that Batista and colleagues drew from their findings. They concluded that all crop varieties produced by either mutation breeding or genetic engineering should be subjected to safety assessment.[16]

We agree with the conclusions of Batista and colleagues. While their study does not examine enough GM crop varieties and mutation-bred crop varieties to enable generalized conclusions about the relative risks of mutation breeding and genetic engineering, it does provide evidence that both methods significantly disrupt gene regulation. It also suggests that crops generated through these two methods should be assessed for safety with similar levels of rigour. The fact that the risks of mutation breeding have been overlooked by regulators does not justify overlooking the risks of GM crops as well.

Significantly, an expert committee of the US National Research Council concluded that genetic engineering was more likely to cause unintended changes than all other crop development methods *except* mutation breeding.[17]

Regulations around the world should be revised to treat mutation-bred crops with the same sceptical scrutiny with which GM crops should be treated.

### 3. "More mutations occur as a result of natural breeding than of genetic engineering"

GM proponents say that in conventional breeding, traits from one variety of a crop are introduced into another variety by means of a genetic cross. They point out that the result is offspring that receive one set of chromosomes from one parent and another set from the other. They further point out that for some genes, the maternal and paternal versions will be identical, but for many other genes, the maternal and paternal versions will be different. Thus there is the potential that the genetic makeup of the offspring will deviate from that of either parent by as much as 50%. That is, tens of thousands of the genes carried by the offspring could be different from the genes carried by one of the parents.

They suggest that the result is a patchwork that contains tens of thousands of deviations from the DNA sequence and genetic information present in the chromosomes of either parent. They imply that these deviations can be regarded as tens of thousands of mutations, and conclude that because we don't require crop varieties resulting from such genetic crosses to undergo biosafety testing before they are commercialised, we should not require GMOs, which they claim contain only a few mutations, to be tested.

But this is a spurious argument. The versions of a gene – called alleles – contributed by both the mother and father are typically not different due to recent mutagenic events. These alleles are established versions of the gene that have survived the process of natural selection over the ages because they confer distinct, useful characteristics onto the individual that carries them.

Thus the genome and phenotype of the offspring resulting from a genetic cross of two varieties is not the result of random mutations, but of the precise combination of genetic material contributed by both parents. This is a natural mechanism operating on the level of the DNA to generate diversity within a species, yet at the same time preserve the integrity of the genome with letter-by-letter exactness.

Genetic engineering, on the other hand, is an artificial laboratory procedure that forces foreign DNA at random into the DNA of the cells of a plant. Once the engineered gene is introduced into the nucleus of the cells, it breaks randomly into the DNA of the plant and inserts into that site. This process results in at least one insertional mutation. However, other steps in the genetic engineering process generate hundreds, possibly even thousands, of mutations throughout the plant's DNA.[18]

For these reasons, conventional breeding is far more precise and carries fewer mutation-related risks than genetic engineering.

## 4. "We will select out harmful mutations"

GM proponents say that even if harmful mutations occur, that is not a problem. They say that during the process of developing a GM crop, the GM plants undergo many levels of screening and selection and the genetic engineers will catch any plants that have harmful mutations and eliminate them during this process.[1]

The process of gene insertion during genetic modification selects for insertion of engineered GM gene cassettes into regions of the host (recipient) plant cell genome where many genes are being actively expressed. Insertion of GM sequences into such regions has a high inherent potential to disrupt the function of active genes native to the plant's genome.

In some cases, the disruption will be fatal – the engineered cell will die and will not grow into a GM plant. In other cases, the plant will compensate for any disturbance in the function of genes, or the insertion will occur at a location that seems to cause minimal disruption of the plant cell's functioning. This is what is desired. But just because a plant grows vigorously and has a healthy green colour does not mean that it is safe to eat and safe for the environment. It could have a mutation that causes it to produce substances that harm consumers or to damage the ecosystem.

Genetic engineers do not carry out detailed screening that would catch all plants producing potentially harmful substances. They introduce the GM gene(s) into hundreds or thousands of plant cells and grow them out into individual GM plants. If the gene insertion process has damaged the function of one or more plant cell genes that are essential for survival, the cell will not survive this process. So plants carrying such "lethal" mutations will be eliminated. But the genetic engineer is often left with several thousand individual GM plants, each of them different, because:

- The engineered genes have been inserted in different locations within the DNA of each plant
- Other mutations or disturbances in host gene function have occurred at other locations in the plants through the mechanisms described above.

How do genetic engineers sort through the GM plants to identify the one or two they are going to commercialise? They do a test that allows them to find the few plants, among many thousands, that express the desired trait at the desired level. Of those, they pick some that look healthy, strong, and capable of being bred on and propagated.

That is all they do. Such screening cannot detect plants that have undergone mutations that cause them to produce substances that are harmful to consumers or lack important nutrients.

It is unrealistic to claim that genetic engineers can detect all hazards based on obvious differences in the crop's appearance, vigour, or yield. Some mutations will give rise to changes that the breeder will see in the greenhouse or field, but others will give rise to changes that are not visible because they occur at a subtle biochemical level or manifest only under certain circumstances. So only a small proportion of potentially harmful mutations will be eliminated by the breeder's superficial inspection. Their scrutiny cannot ensure that the plant is safe to eat.

Some agronomic and environmental risks will be missed, as well. For instance, during the GM transformation process, a mutation may destroy a gene that makes the plant resistant to a certain pathogen or a specific environmental stress like extreme heat or drought. But that mutation will be revealed only if the plant is intentionally exposed to that pathogen or stress in a systematic way. GM crop developers are not capable of screening for resistance to every potential pathogen or environmental stress. So mutations can sit like silent time bombs within the GM plant, ready to "explode" at any time when there is an outbreak of the relevant pathogen or an exposure to the relevant environmental stress.

An example of this kind of limitation was an early – but widely planted – variety of Roundup Ready soy. It turned out that this variety was much more sensitive than non-GM soy varieties to heat stress and more prone to infection.[19]

## Conclusion

Like genetic engineering, radiation-induced mutagenesis is risky and mutagenic. It is not widely used in plant breeding because of its high failure rate. Comparing genetic engineering with radiation-induced mutagenesis and concluding that it is safe is like comparing a game of Russian Roulette played with one type of gun with a game of Russian Roulette played with another type of gun. Neither is safe.

A more useful comparison would be between genetic engineering and conventional breeding that does not involve radiation- or chemical-induced mutagenesis. This is the method that has safely produced the vast majority of our crop plants over millennia and that is most widely used today. It is also far more successful. All the increases in crop yield achieved around the world in the last several decades are due to conventional breeding, not genetic engineering.

## References


1. Academics Review. The use of tissue culture in plant breeding is not new. 2014. Available at: http://bit.ly/I7fPc9.
2. Genetic Literacy Project. GMOs vs. mutagenesis vs. conventional breeding: Which wins? 2013. Available at: http://www.geneticliteracyproject.org/2013/12/03/gmos-vs-mutagenesis-vs-conventional-breeding-which-wins/#.U1JJHscwLn0.
3. Anon. Atomic gardens: Interview with Paige Johnson. *Pruned*. http://pruned.blogspot.com/2011/04/atomic-gardens.html. Published April 20, 2011.
4. Food and Agriculture Organization (FAO) and International Atomic Energy Agency (IAEA). Mutant variety database (MVGS). 2010. Available at: http://mvgs.iaea.org/.
5. Kodym A, Afza R. Physical and chemical mutagenesis. *Methods Mol Biol*. 2003;236:189-204. doi:10.1385/1-59259-413-1:189.
6. Novak FJ, Brunner H. Plant breeding: Induced mutation technology for crop improvement. *IAEA Bull*. 1992;4:25–33.
7. Jain SM. Mutagenesis in crop improvement under the climate change. *Romanian Biotechnol Lett*. 2010;15:88–106.
8. Ministry of Agriculture and Food (Norway). Svalbard Global Seed Vault secures future seed. 2013. Available at: http://bit.ly/GF2cqY.
9. BBC News. More seeds for "doomsday vault." http://news.bbc.co.uk/1/hi/sci/tech/7912543.stm. Published February 26, 2009.
10. Sawyer SA, Parsch J, Zhang Z, Hartl DL. Prevalence of positive selection among nearly neutral amino acid

replacements in Drosophila. *Proc Natl Acad Sci USA*. 17;104:6504-10. doi:10.1073/pnas.0701572104.
11. Acquaah G. *Principles of Plant Genetics and Breeding*. Oxford, UK: Wiley-Blackwell; 2007. Available at: http://bit.ly/17GGkBG.
12. Van Harten AM. *Mutation Breeding: Theory and Practical Applications*. London: Cambridge University Press; 1998.
13. GM Science Review Panel. *First report: An open review of the science relevant to GM crops and food based on interests and concerns of the public*. 2003.
14. Ahloowalia BS, Maluszynski M, Nichterlein K. Global impact of mutation-derived varieties. *Euphytica*. 2004;135:187–204.
15. Maluszynski M, Szarejko I. Induced mutations in the Green and Gene Revolutions. In: Tuberosa R, Phillips RL, Gale M, eds. Bologna, Italy: Avenue Media; 2003.
16. Batista R, Saibo N, Lourenco T, Oliveira MM. Microarray analyses reveal that plant mutagenesis may induce more transcriptomic changes than transgene insertion. *Proc Natl Acad Sci USA*. 4;105:3640-5. doi:10.1073/pnas.0707881105.
17. National Research Council. *Safety of genetically engineered foods: Approaches to assessing unintended health effects*. Washington, DC: The National Academies Press; 2004. Available at: http://www.nap.edu/catalog.php?record_id=10977.
18. Latham JR, Wilson AK, Steinbrecher RA. The mutational consequences of plant transformation. *J Biomed Biotechnol*. 2006;2006:1–7. doi:10.1155/JBB/2006/25376.
19. Coghlan A. Monsanto's Roundup-Ready soy beans cracking up. *New Sci*. 1999. Available at: http://www.biosafety-info.net/article.php?aid=250.

# 1.4 Myth: Cisgenesis is a safe form of GM because no foreign genes are involved

## Truth: Cisgenesis shares many of the risks associated with transgenic genetic engineering

### Myth at a glance

Cisgenesis (sometimes called intragenesis) is a type of genetic engineering involving artificially transferring genes between organisms from the same species or between closely related organisms that could otherwise be conventionally bred.

Cisgenesis is presented as safer and more publicly acceptable than transgenic genetic engineering, in which GM gene cassettes containing genes from unrelated organisms are introduced into the host organism's genome.

However, in cisgenesis, the GM gene cassette will still contain DNA elements from other unrelated organisms like bacteria and viruses.

Cisgenesis is as mutagenic as transgenesis, and cisgenes can have the same disruptive effects as transgenes on the genome, gene expression, and a range of processes operating at the level of cells, tissues and the whole organism.

Thus cisgenic GMOs pose most of the same risks to health and the environment as transgenic GMOs. Experiments confirm that cisgenesis can result in important unanticipated changes to a plant.

Cisgenesis, sometimes called intragenesis, is a type of genetic engineering involving artificially transferring genes between organisms from the same species or between closely related organisms that could otherwise be conventionally bred. For example, a cisgenic GM potato engineered to resist blight was developed using a gene taken from a wild potato.[1]

Proponents claim that cisgenesis is safer than transgenesis, as purportedly it involves transfer of genetic material only between members of the same species and no foreign genes are introduced.[2,3] Some scientists are calling for complete deregulation of cisgenic plants on the grounds that they carry no additional risks than naturally bred plants.[4,5,6]

Proponents also hope that cisgenics will overcome public resistance to GM. An article on the pro-GM website Biofortified, "Cisgenics – transgenics without the transgene", bluntly states the public relations value of cisgenics: "The central theme is to placate the misinformed public opinion by using clever technologies to circumvent traditional unfounded criticisms of biotechnology."[7]

However, cisgenesis still carries many of the risks associated with transgenic genetic engineering, for the following reasons.

### 1. No truly cisgenic GMOs exist

The word "cisgenic" (meaning "same descent") implies that only genes within the genome of the same or closely related species are being manipulated. But no GMO has ever been or is likely to be created using only DNA from its own species. Some of the genetic information in the supposedly cisgenic organism does indeed come from close to home (the same species), which might suggest that there would be less likelihood of unpredictable outcomes.

However, although it is possible to isolate a gene from maize, for instance, and then put it back into maize, this will not be a purely cisgenic process. In order to put the gene back into maize, it is necessary to link it to other sequences, at least from bacteria, and possibly also from viruses, other organisms (potentially from different species), and even synthetic DNA.[8,9]

Therefore "cisgenic" gene transfer inevitably uses sequences foreign to the recipient organism. So "cisgenic" actually means "partly transgenic". Unpredictability and risk from cross-species genetic information is not avoided.

For example, the cisgenic plants engineered by Rommens and colleagues (2004), who claim to have made "the first genetically engineered plants that contain only native DNA", were produced using genetic modification mediated by the soil bacterium Agrobacterium tumefaciens – an organism from a different species.[10]

### 2. Cisgenic GMOs use the same mutagenic transformation techniques as transgenic GMOs

Cisgenic plants are created using the same highly mutagenic transformation techniques[11] used to create other transgenic plants.[12] The process of inserting any fragment of DNA, whether cisgenic or transgenic, into an organism via the GM transformation process carries risks (see Myths 1.1, 1.2). Insertion takes place in an uncontrolled manner and results in at least one insertional mutation event within the DNA of the recipient organism. The insertional event will interrupt some sequence within the DNA of the organism and may interfere with any natural function that the interrupted DNA carries. For instance, if the insertion occurs in the middle of a gene, the gene's function will likely be destroyed. As a result, the organism will lose the protein function that the gene encodes, with potential negative consequences for cellular and organ processes.

Although the main gene of the GM gene cassette may be cisgenic, the cassette will in all cases be inserted randomly into the genome of the recipient organism, that is, at a site other than its "natural" location. The location at which the cassette is inserted will influence the structure of the genome, which can influence the expression of genes in the whole region of the genome unpredictably. Furthermore, the regulatory sequences contained in the GM gene cassette can have unpredictable effects on the expression of genes located nearby.

In addition, cisgenesis, like transgenic genetic engineering, invariably involves the tissue culture process, which has wide-scale mutagenic effects on the plant host DNA.

## Experimental evidence that cisgenesis can be as unpredictable as transgenesis

In arguing for less stringent regulatory oversight of cisgenic plants, Schouten and colleagues (2006) argue that unlike transgenic plant breeding, "cisgenesis does not add an extra trait" and that there is an "equivalence of products resulting from cisgenesis and traditional breeding including mutational breeding".[5]

But such claims have been thrown into question by a series of experiments using the model plant Arabidopsis thaliana.[13,14,15,16] These experiments assessed whether introduction of a cisgene introduced unanticipated trait changes. They also looked for differences between breeding methods by comparing plants where either genetic engineering or "conventional" breeding using chemical mutagenesis was used to introduce the identical trait into the identical genetic background. The trait deliberately introduced was herbicide resistance.

The results showed that trait introduction via a cisgene can result in plants that differ in unanticipated and dramatic ways from their conventionally bred counterparts. The differences observed would have important agronomic and ecological implications for commercial varieties.[9]

Differences included:

- Levels of outcrossing were higher in all GM lines carrying the cisgene as compared to the conventionally bred plants[15]
- When grown under field conditions, both the GM and conventional herbicide-resistant plants showed decreased total seed numbers as compared to the herbicide-sensitive wild-type parents. However, when nutrients were added to field-grown plants, only the GM plants still showed a fitness decrease.[13,14]

These results do not support the claims made by Schouten and colleagues.[5] They show instead that a cisgene can introduce important unanticipated changes into a plant.

## Conclusion

Cisgenesis is transgenesis by another name. Cisgenic GMOs pose most of the same risks as transgenic GMOs. The gene cassette developed to transfer a cisgene will also include DNA sequences from at least one other species, and therefore the gene cassette as a whole will be transgenic. In addition, cisgenesis involves tissue culture, a highly mutagenic process. The only difference between cisgenic and transgenic crops is the choice of organism from which the main gene of interest is taken. Experiments confirm that cisgenesis can result in important unanticipated changes to a plant.

# References


1. Jones JDG, Witek K, Verweij W, et al. Elevating crop disease resistance with cloned genes. Philos Trans R Soc B Biol Sci. 2014;369(1639):20130087. doi:10.1098/rstb.2013.0087.
2. Rommens CM. Intragenic crop improvement: Combining the benefits of traditional breeding and genetic engineering. J Agric Food Chem. 2007;55:4281-8. doi:10.1021/jf0706631.
3. Rommens CM, Haring MA, Swords K, Davies HV, Belknap WR. The intragenic approach as a new extension to traditional plant breeding. Trends Plant Sci. 2007;12:397-403. doi:10.1016/j.tplants.2007.08.001.
4. Schouten HJ, Krens FA, Jacobsen E. Cisgenic plants are similar to traditionally bred plants. EMBO Rep. 2006;7(8):750-753. doi:10.1038/sj.embor.7400769.
5. Schouten HJ, Krens FA, Jacobsen E. Do cisgenic plants warrant less stringent oversight? Nat Biotechnol. 2006;24(7):753-753. doi:10.1038/nbt0706-753.
6. Viswanath V, Strauss SH. Modifying plant growth the cisgenic way. ISB News. 2010.
7. Folta K. Cisgenics – transgenics without the transgene. Biofortified. 2010. Available at: http://www.biofortified.org/2010/09/cisgenics-transgenics-without-the-transgene/.
8. Rommens CM. All-native DNA transformation: a new approach to plant genetic engineering. Trends Plant Sci. 2004;9(9):457-464. doi:10.1016/j.tplants.2004.07.001.
9. Wilson A, Latham J. Cisgenic plants: Just Schouten from the hip? Indep Sci News. 2007. Available at: http://www.independentsciencenews.org/health/cisgenic-plants/.
10. Rommens CM, Humara JM, Ye J, et al. Crop improvement through modification of the plant's own genome. Plant Physiol. 2004;135(1):421-431. doi:10.1104/pp.104.040949.
11. Schubert D, Williams D. "Cisgenic" as a product designation. Nat Biotechnol. 2006;24(11):1327-1329. doi:10.1038/nbt1106-1327.
12. Wilson AK, Latham JR, Steinbrecher RA. Transformation-induced mutations in transgenic plants: Analysis and biosafety implications. Biotechnol Genet Eng Rev. 2006;23:209–238.
13. Bergelson J, Purrington CB, Palm CJ, Lopez-Gutierrez JC. Costs of resistance: A test using transgenic Arabidopsis thaliana. Proc Biol Sci. 1996;263:1659-63. doi:10.1098/rspb.1996.0242.
14. Purrington CB, Bergelson J. Fitness consequences of genetically engineered herbicide and antibiotic resistance in Arabidopsis thaliana. Genetics. 1997;145(3):807-814.
15. Bergelson J, Purrington CB, Wichmann G. Promiscuity in transgenic plants. Nature. 1998;395:25. doi:10.1038/25626.
16. Bergelson J, Purrington C. Factors affecting the spread of resistant Arabidopsis thaliana populations. In: Letourneau D, Elpern Burrows B, eds. Genetically Engineered Organisms. CRC Press; 2001:17-31. Available at: http://www.crcnetbase.com/doi/abs/10.1201/9781420042030.ch2.

# 2. Science and regulation

*"Monsanto should not have to vouchsafe the safety of biotech food. Our interest is in selling as much of it as possible. Assuring its safety is the FDA's job."*
– Philip Angell, Monsanto's director of corporate communications (the FDA is the US government's Food and Drug Administration, responsible for food safety)[1]

*"Ultimately, it is the food producer who is responsible for assuring safety."*
– US Food and Drug Administration (FDA)[2]

*"It is not foreseen that EFSA carry out such [safety] studies as the onus is on the [GM industry] applicant to demonstrate the safety of the GM product in question."*
– European Food Safety Authority (EFSA)[3]

## References


1. Pollan M. Playing God in the garden. New York Times Magazine. http://www.nytimes.com/1998/10/25/magazine/playing-god-in-the-garden.html. Published October 25, 1998.
2. US Food and Drug Administration (FDA). Statement of policy: Foods derived from new plant varieties. FDA Fed Regist. 1992;57(104):22984.
3. European Food Safety Authority (EFSA). Frequently asked questions on EFSA GMO risk assessment. 2006. Available at: http://www.cibpt.org/docs/faq-efsa-gmo-risk-assessment.pdf.

## 2.1 Myth: GM foods are strictly tested and regulated for safety

## Truth: GM foods are safety tested by the developer companies and regulation varies from non-existent to weak

### Myth at a glance

Claims that GM foods are extensively tested and strictly regulated are false. At best, they are tested for safety by the companies that want to commercialize them. The tests are weak and inadequate to show safety.

GM foods were first allowed into the human food supply in the US, based on the claim that they are Generally Recognized as Safe (GRAS) – despite the fact that none has ever fulfilled the strict legal criteria that define GRAS status.

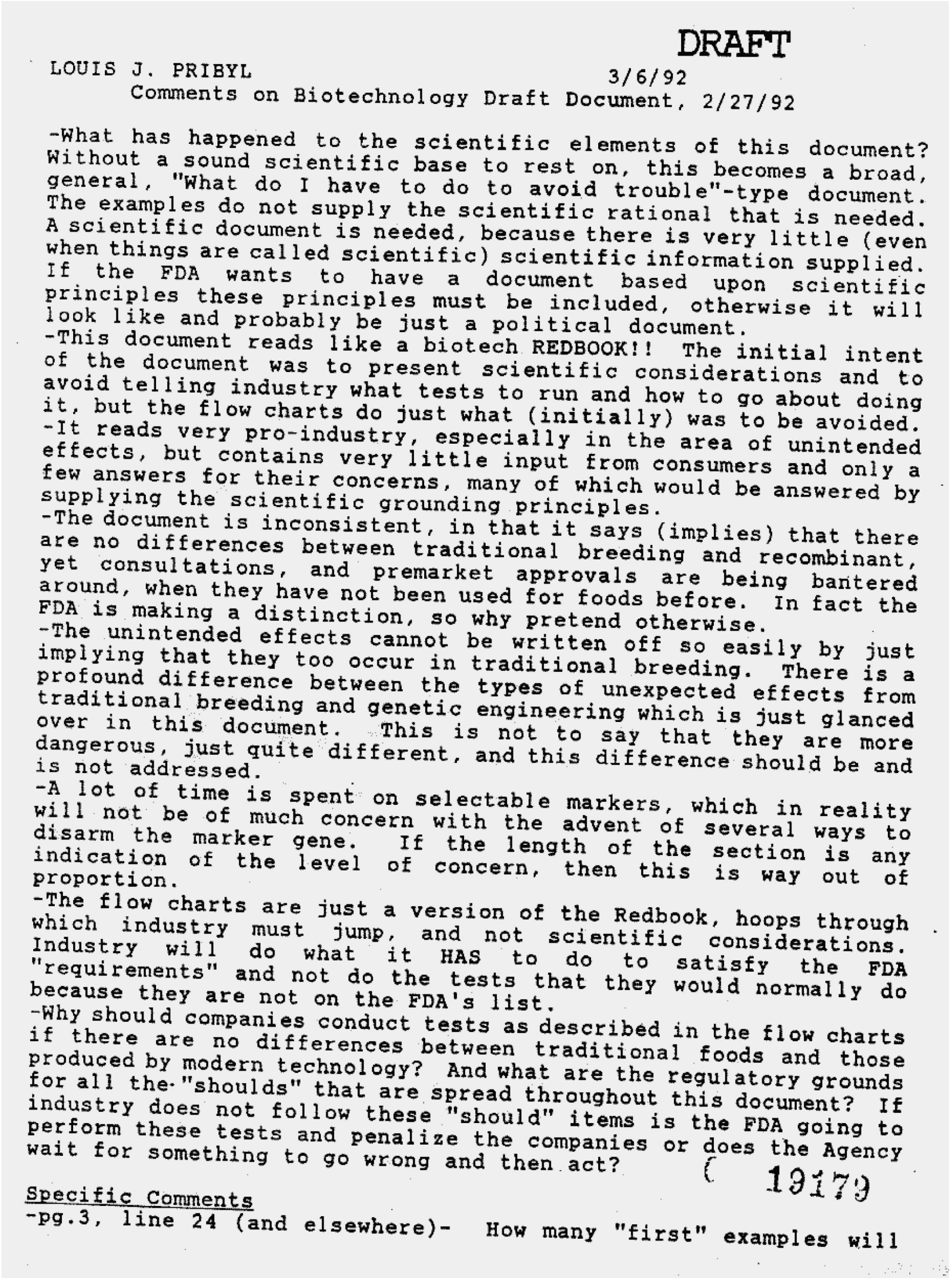
In many countries, GM foods are approved by regulators as "substantially equivalent" to non-GM crops, but when this assumption is tested scientifically, GM crops are often found to have unexpected and unintended differences.

Examples of regulatory failure are common and include unscientific procedures, sloppy practices, and the failure to recognize and address important types of risk. Regulatory lapses are often linked to conflicts of interest among regulators.

Industry and some government sources claim that GM foods are strictly regulated.[1,2] But GM food regulatory systems worldwide vary from voluntary industry self-regulation (in the US) to weak (in Europe). None are adequate to protect consumers' health. All rely on safety testing done by the company that wishes to commercialize the genetically modified organism (GMO) in question.

As criticism has mounted of the deficiencies in GM food regulatory systems, the message from pro-GM lobbyists has shifted, from "GM foods are strictly regulated" to "GM foods are no more risky than non-GM foods, so why regulate them at all?" They point out that each time a plant breeder develops a new variety of apple or beetroot through conventional breeding, we do not demand that it be tested toxicologically, and there is no reason to think that GM foods will be any more toxic.

But this argument is spurious. Humans have co-evolved with their food crops over millennia and have learned by long – and doubtless sometimes bitter – experience which plants are



DRAFT

LOUIS J. PRIBYL 3/6/92

Comments on Biotechnology Draft Document, 2/27/92

-What has happened to the scientific elements of this document? Without a sound scientific base to rest on, this becomes a broad, general, "What do I have to do to avoid trouble"-type document. The examples do not supply the scientific rational that is needed. A scientific document is needed, because there is very little (even when things are called scientific) scientific information supplied. If the FDA wants to have a document based upon scientific principles these principles must be included, otherwise it will look like and probably be just a political document.
-This document reads like a biotech REDBOOK!! The initial intent of the document was to present scientific considerations and to avoid telling industry what tests to run and how to go about doing it, but the flow charts do just what (initially) was to be avoided.
-It reads very pro-industry, especially in the area of unintended effects, but contains very little input from consumers and only a few answers for their concerns, many of which would be answered by supplying the scientific grounding principles.
-The document is inconsistent, in that it says (implies) that there are no differences between traditional breeding and recombinant, yet consultations, and premarket approvals are being bantered around, when they have not been used for foods before. In fact the FDA is making a distinction, so why pretend otherwise.
-The unintended effects cannot be written off so easily by just implying that they too occur in traditional breeding. There is a profound difference between the types of unexpected effects from traditional breeding and genetic engineering which is just glanced over in this document. This is not to say that they are more dangerous, just quite different, and this difference should be and is not addressed.
-A lot of time is spent on selectable markers, which in reality will not be of much concern with the advent of several ways to disarm the marker gene. If the length of the section is any indication of the level of concern, then this is way out of proportion.
-The flow charts are just a version of the Redbook, hoops through which industry must jump, and not scientific considerations. Industry will do what it HAS to do to satisfy the FDA "requirements" and not do the tests that they would normally do because they are not on the FDA's list.
-Why should companies conduct tests as described in the flow charts if there are no differences between traditional foods and those produced by modern technology? And what are the regulatory grounds for all the "shoulds" that are spread throughout this document? If industry does not follow these "should" items is the FDA going to perform these tests and penalize the companies or does the Agency wait for something to go wrong and then act? ( 19179

Specific Comments

-pg.3, line 24 (and elsewhere)- How many "first" examples will

Comments on the FDA's policy to release GMOs into the food supply by FDA microbiologist Dr Louis Pribyl. Dr Pribyl castigates the FDA for the lack of a scientific basis to its GMO policy. This document is one of many that were released as a result of a lawsuit brought against the FDA by the Alliance for Bio-Integrity (http://www.biointegrity.org/).

toxic and which are safe to eat. There would have been casualties along the way, but the survivors would have learned from any mistakes and would only have developed their food crops from plants that were proven safe over many years of use.

With GM foods, we do not have the luxury of long periods of experimentation by our ancestors. And unlike our ancestors, we show no sign of learning from the mistakes of genetic engineering, since signs of toxicity in animal feeding experiments with GM foods are routinely dismissed (see Chapter 3).

## How GMOs first entered world markets

GM foods were first commercialized in the US in the early 1990s. The US Food and Drug Administration (FDA) allowed the first GM foods onto world markets in spite of its own scientists' warnings that genetic engineering is different from conventional breeding and poses special risks, including the production of new toxins or allergens that are difficult to detect.[5,6,7,8,9,10]

For example, FDA microbiologist Dr Louis Pribyl stated: "There is a profound difference between the types of unexpected effects from traditional breeding and genetic engineering". He added that several aspects of genetic engineering "may be more hazardous".[10]

Dr E. J. Matthews of the FDA's Toxicology Group warned that "Genetically modified plants could … contain unexpected high concentrations of plant toxicants".[7]

Gerald Guest, director of FDA's Center for Veterinary Medicine (CVM), called for GM products to be demonstrated safe prior to marketing, on the grounds that "animal feeds derived from genetically modified plants present unique animal and food safety concerns."[6]

FDA official Linda Kahl protested that the agency was "trying to fit a square peg into a round hole" by "trying to force an ultimate conclusion that there is no difference between foods modified by genetic engineering and foods modified by traditional breeding practices." Kahl stated: "The processes of genetic engineering and traditional breeding are different, and according to the technical experts in the agency, they lead to different risks."[5]

Several FDA scientists called for more rigorous scientific data to be presented by the companies before GMOs were released onto the market, and specifically for safety and toxicological testing.[6,7,10]

However, FDA administrators, who expressly admitted that the agency had been following a government agenda to "foster" the growth of the biotech industry,[11] disregarded their scientists' concerns, refused to regulate GM foods, and permitted them to enter the market without any testing or labelling.

The creation of this policy was overseen by the FDA's deputy commissioner of policy,

> *"One thing that surprised us is that US regulators rely almost exclusively on information provided by the biotech crop developer, and those data are not published in journals or subjected to peer review… The picture that emerges from our study of US regulation of GM foods is a rubber-stamp 'approval process' designed to increase public confidence in, but not ensure the safety of, genetically engineered foods."*
> – David Schubert, professor and head, Cellular Neurobiology Laboratory, Salk Institute, commenting on the findings of a review of GMO regulation that he co-authored[3,4]

**Biotechnology Consultation Agency Response Letter BNF No. 000001**

Return to inventory: Completed Consultations on Foods from Genetically Engineered Plant Varieties

See also Biotechnology: Genetically Engineered Plants for Food and Feed and about Submissions on Bioengineered New Plant Varieties

**See FDA's memo on BNF No. 000001 for further details**

January 27, 1995

Ms. Diane Re
Regulatory Affairs
The Agricultural Group of Monsanto
700 Chesterfield Parkway North
Chesterfield, MO 63198

Dear Ms. Re:

This is in regard to your genetically modified glyphosate-tolerant soybean about which you initiated consultations with the agency in June 1993. The new soybean variety has been rendered tolerant to glyphosate by expression of a 5-enolpyruvylshikimate-3-phosphate synthase from the bacterium *Agrobacterium sp.* strain CP4.

As part of bringing your consultation with FDA regarding this product to closure, you submitted a summary of your safety and nutritional assessment of the new soybean variety on September 2, 1994. On September 19, 1994, you also made a detailed oral presentation of the data that support your submission. It is our understanding that these communications were intended by Monsanto to inform FDA of the steps taken to ensure that this product complies with the Federal Food, Drug, and Cosmetic Act. Further, it is our understanding that, based on the safety and nutritional assessment you have conducted, you have concluded that the new soybean variety is not materially different in composition, safety, or any other relevant parameter from soybean varieties currently on the market and that it does not raise issues that would require premarket review or approval. All materials relevant to this consultation have been placed in a file that has been designated BNF 0001 and that will be maintained in the Office of Premarket Approval.

Based on the description of the data and information presented during the consultations, the new soybean variety does not appear to be significantly altered within the meaning of 21 CFR 170.30(f)(2). We have no additional questions concerning the product at this time. However, as you are aware, it is Monsanto's continued responsibility to ensure that foods the firm markets are safe, wholesome, and in compliance with all applicable legal and regulatory requirements.

Sincerely yours,

Alan M. Rulis, Ph.D.
Acting Director
Office of Premarket Approval
Center for Food Safety
and Applied Nutrition

Letter from the US FDA's Center for Food Safety and Applied Nutrition to Monsanto regarding its GM glyphosate-tolerant soybean. The letter confirms that the FDA is not liable if any safety concerns are identified with the soybean.

Michael Taylor, who was appointed to the post in 1991. Prior to joining the FDA, Taylor had been in private practice at King & Spalding, a law firm that represented the GM crop developer company Monsanto. In 1998 he became Monsanto's vice president for public policy.[12,13] By 2010 he was back at the FDA as its deputy commissioner for foods.[14]

Taylor's career is often cited as an example of a type of conflict of interest known as the "revolving door". The term describes the movement of personnel between roles as regulators and the industries affected by the regulation.

## The US regulatory process for GMOs

Contrary to popular belief, the US FDA does not have a mandatory GM food safety assessment process and has never approved as safe any GM food that is currently on the market. It does not carry out or commission safety tests on GM foods. Instead, the FDA operates a *voluntary* pre-market review programme, in which it looks at whatever data the manufacturer chooses to provide.

Although all GM foods commercialized to date have gone through this lenient process, there is no legal requirement for them to do so. Companies are allowed to put any GMO on the market that they wish without even notifying the FDA. And even though they might theoretically be held liable for any resulting harm to consumers, it would be extremely difficult to prove such harm in court.

The outcome of the FDA's voluntary assessment is not a conclusion, underwritten by the

FDA, that the GMO is safe. Instead it consists of the FDA sending the company a letter stating that:

- The company has provided the FDA with a summary of research that it has conducted assessing the GM crop's safety
- Based on the results of the research done by the company, the company has concluded that the GMO is safe
- The FDA has no further questions
- The company is responsible for placing only safe foods in the market
- If a product is found to be unsafe, the company may be held liable.[15]

This process does not guarantee – or even attempt to scientifically investigate – the safety of GM foods. Therefore although it may protect the image of GM foods, it does not protect the public.

## The US government is not impartial regarding GM crops and foods

The US government cannot be relied upon to regulate GMOs. It is not an impartial authority, given its aim to "foster" the growth of the biotechnology industry.[11] And not only is the US Department of Agriculture (USDA) influenced by that same policy, it even has financial interests in GM technology, owning 1.2% of all public-sector US agricultural biotechnology patents granted between 1982 and 2001.[16]

Through its embassies and agencies, the US government promotes GM crops globally and sometimes even pressures other governments to accept them. This was made clear by diplomatic cables disclosed by Wikileaks, which revealed that:

- The US embassy in Paris recommended that the US government launch a retaliation strategy against the EU that "causes some pain" as punishment for Europe's reluctance to adopt GM crops.[17]
- The US embassy in Spain suggested that the US government and Spain draw up a joint strategy to help boost the development of GM crops in Europe.[18]
- The US State Department is trying to steer African countries towards acceptance of GM crops.[19,20]

This strategy of exerting diplomatic pressure on national governments to adopt GM crops is undemocratic as it interferes with their ability to represent the wishes of their citizens. It is also inappropriate to use US taxpayers' money to promote patented products owned by individual private companies to further the companies' economic goals. A 2003 paper found that nearly three-quarters (74%) of agricultural biotechnology patents were privately owned.[16]

## FDA presumes that GMOs are "generally recognized as safe"

The US FDA claims that GM foods can be marketed without prior testing or oversight because they are "generally recognized as safe" or GRAS.[21]

However, GM foods do not meet the GRAS criteria, which are strict. According to US statutory law and FDA regulations, a food that does not have a history of safe use prior to 1958 cannot qualify as GRAS unless it satisfies two requirements:

- There must be an overwhelming expert consensus that it is safe; and
- This consensus must be based on scientific evidence generated through "scientific procedures", which "shall ordinarily be based upon published studies".[22]

Because GM foods have never met either requirement, they cannot legally be classified as GRAS. At the time the FDA made its presumption that all GM foods are GRAS, there was not even expert consensus about their safety within the FDA (as attested by the statements of the agency's scientists detailed above). The FDA's biotechnology coordinator admitted there was no such consensus outside the agency either.[23]

Moreover, no such scientific consensus has emerged since then. For instance, in 2001 an expert panel of the Royal Society of Canada issued an extensive report declaring that it is "scientifically unjustifiable" to presume that GM foods are safe.[24] Over the following years, many hundreds of experts have signed various formal statements declaring that the safety of GM foods has not been established and is subject to reasonable doubt. In 2013 nearly 300 scientists and experts signed a statement rejecting claims of a scientific consensus on GMO safety, either for human or animal consumption or for the environment.[25]

Even if there had been such a consensus, GM foods would still have failed to meet the GRAS standard because there has never been adequate technical evidence to establish that even one GM food is safe, especially because the law requires that the data must demonstrate a "reasonable certainty" the food will not be harmful.[22]

## The sham of substantial equivalence

Worldwide, regulators approve GM foods as safe based on the concept of "substantial equivalence". Substantial equivalence assumes that if a GMO contains similar amounts of a few basic components such as protein, fat, and carbohydrate as its non-GM counterpart, then the GMO is substantially equivalent to the non-GMO and no rigorous safety testing is required.

The concept of substantial equivalence as applied to GMOs was first put forward by the industry and the Organization for Economic Cooperation and Development (OECD), a body dedicated not to protecting public health but to facilitating international trade.[28,29]

Until recently there has been no legal or scientific definition of substantial equivalence. For example, it has not been established how different a GM crop is allowed to be in its constituents from the non-GM parent line, or how different it can be from other varieties of the crop, before it is deemed non-substantially equivalent and regulatory action is triggered.[30] Such regulatory action could comprise a ban or a requirement for in-depth, long-term toxicological testing.

In 2013, after years of criticism over the lack of scientific definition of substantial equivalence, the EU instituted a regulation defining limits on the extent to which a GMO

*"The concept of substantial equivalence has never been properly defined; the degree of difference between a natural food and its GM alternative before its 'substance' ceases to be acceptably 'equivalent' is not defined anywhere, nor has an exact definition been agreed by legislators. It is exactly this vagueness that makes the concept useful to industry but unacceptable to the consumer... Substantial equivalence is a pseudo-scientific concept because it is a commercial and political judgment 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."*
– Erik Millstone, professor in science and technology policy, University of Sussex, UK, and colleagues[26]

*"Substantial equivalence is a scam. People say that a potato has vaguely the same amount of protein and starch and stuff as all other potatoes, and therefore that it is substantially equivalent, but that is not a test of anything biological."*
– Professor C. Vyvyan Howard, medically qualified toxicopathologist, then at the University of Liverpool, in testimony to the Scottish Parliament Health and Community Care Committee[27]

*"In one interpretation, to say that the new [GM] food is 'substantially equivalent' is to say that 'on its face' it is equivalent (i.e. it looks like a duck and it quacks like a duck, therefore we assume that it must be a duck – or at least we will treat it as a duck). Because 'on its face' the new food appears equivalent, there is no need to subject it to a full risk assessment to confirm our assumption. This interpretation of 'substantial equivalence' is directly analogous to the reasoning used in approval of varieties derived through conventional breeding. In both cases, 'substantial equivalence' does not function as a scientific basis for the application of a safety standard, but rather as a decision procedure for facilitating the passage of new products, GM and non-GM, through the regulatory process."*
– The Royal Society of Canada[24]

can differ from the non-GM comparator and still qualify as equivalent.[31]

Claims of substantial equivalence for GM foods have been widely criticized and revealed as scientifically inaccurate by independent researchers[32,33,34,35] and by the Royal Society of Canada.[24] A useful analogy to help us understand what is meant by substantial equivalence is that of a BSE-infected cow and a healthy cow. They are substantially equivalent to one another, in that their chemical composition is the same. The only difference is in the shape of a protein (prion) that constitutes a minute proportion of the total mass of the cow. This difference that would not be picked up by current substantial equivalence assessments. Yet few would claim that eating a BSE-infected cow is as safe as eating a healthy cow.

When claims of substantial equivalence are tested, they are often found to be untrue. Using molecular analytical methods, GM crops have been shown to have a different composition to their non-GM counterparts. This is true even when the two crops are grown under the same conditions, at the same time and in the same location – meaning that the changes are not due to different environmental factors but to the genetic modification.

Examples include:

- GM soy had 12–14% lower amounts of isoflavones, compounds that play a role in sex hormone metabolism, than non-GM soy.[36]
- GM soy had 27% higher levels of a major allergen, trypsin-inhibitor, than the non-GM parent variety, despite the Monsanto authors' claim that the GM soybean was "equivalent" to the non-GM soybean. In order to reach the conclusion of "equivalence", the Monsanto authors compared plants grown at different locations and different times, increasing the range of variability with irrelevant data. Good scientific practice in a test of substantial equivalence requires the GM plant to be compared with the non-GM isogenic (with the same genetic background) variety, grown at the same time in the same conditions.[37]
- Canola (oilseed rape) engineered to contain vitamin A in its oil had much reduced vitamin E and an altered oil-fat composition, compared with non-GM canola.[38]
- Experimental GM rice varieties had unintended major nutritional disturbances compared with non-GM counterparts, although they were grown side-by-side in the same conditions. The structure and texture of the GM rice grain was affected and its nutritional content and value were dramatically altered. The authors said that their findings provided "alarming information with regard to the nutritional value of transgenic rice" and showed that the GM rice was not substantially equivalent to non-GM.[39]
- Experimental GM insecticidal rice was found to contain higher levels of certain components than non-GM rice. Differences were caused by both genetic manipulation and environmental factors. However, differences in sucrose, mannitol, and glutamic acid were shown to have resulted specifically from the genetic manipulation.[40]
- Commercialized MON810 GM maize had a markedly different profile in the types of proteins it contained compared with the non-GM counterpart when grown under the same conditions.[35] These unexpected compositional differences also showed that the MON810 maize was not substantially equivalent to the non-GM isogenic comparator, even though worldwide regulatory approvals of this maize had assumed that it was.[41]
- Bt maize of the variety MON810 Ajeeb YG showed significant differences from its isogenic non-GM counterpart, with some values being outside the range recorded in the scientific literature. Some fatty acids and amino acids present in the non-GM maize were absent in the Bt maize. The researchers concluded that the genetic modification process had caused alterations in the maize that could result in toxicity to humans and animals.[42]

Altered nutritional value is of concern for two reasons: first, because it could directly affect the health of the human or animal consuming it by providing an excess or shortage of certain nutrients; and second, because it is an indicator that the genetic engineering process could have altered biochemical processes in the plant. This could signify that other unexpected changes have also occurred that might impact human or animal health, such as altered toxicity or allergenicity.

Indeed, the Bt maize MON810 Ajeeb YG and its non-GM counterpart, which were found to be compositionally different,[42] were tested in a rat feeding study and the GM variety was found to cause organ toxicity.[43,44]

## Different environmental conditions produce wide variations in protein expression

A comparison of GM maize MON810 and the isogenic non-GM parent variety grown in two different locations revealed a total of 32 different proteins that were expressed at significantly different levels in fresh leaf tissue from GM maize compared to non-GM. These proteins belonged to three main functional categories: (1) carbohydrate and energy metabolism, (2) genetic information processing, and (3) stress response.[45]

The differences were influenced by environmental conditions, since different proteins were expressed differentially in the two locations studied. The evidence also suggested that gene expression in non-GM maize was more stable, less influenced by environmental factors, than in GM maize.[45]

This study did not measure specific parameters related to food safety or environmental impact, but identified 32 differences in the expression of specific proteins in GM and non-GM maize plants.[45] However, it would be informative to extend this study by carrying out additional research to assess whether health impacts of MON810 maize reported by other researchers[44,46,47,48] might be linked to one or more of the protein (proteomic) changes observed in this study.

## Herbicide residues in GM herbicide-tolerant crops mean they are not substantially equivalent to non-GM crops

Over 80% of GM crops worldwide are engineered to tolerate glyphosate herbicides. These GM crops are approved by regulators on the grounds that they are substantially equivalent to the non-GM parent crops. This assumption was tested in a comparative analysis of GM glyphosate-tolerant soy, non-GM soy cultivated under a conventional "chemical" regime, and non-GM soy grown organically. All crops tested were grown in Iowa, USA.[49]

The GM soy was found to contain high residues of glyphosate and its breakdown product AMPA. Conventional and organic soybeans contained neither of these chemicals.[49]

Organic soybeans showed the healthiest nutritional profile, with more sugars, such as glucose, fructose, sucrose and maltose, and significantly more protein and zinc and less fibre than conventional and GM soy. Organic soybeans also contained less total saturated fat and omega-6 fatty acids than conventional and GM soy.[49]

Using 35 different nutritional variables to characterise each soy sample, the researchers were able to discriminate GM, conventional and organic soybeans without exception.[49]

The study showed that GM glyphosate-tolerant soy is not substantially equivalent to non-GM soy, not only because of the herbicide residues in the GM soy, but because of the different nutritional profile.[49]

## Europe's comparative safety assessment: Substantial equivalence by another name

Europe has controversially adopted the concept of substantial equivalence in its GM food assessments – but under another name. The European Food Safety Authority (EFSA) does not use the discredited term "substantial equivalence" but has allowed industry to replace it with another term with the same meaning: "comparative assessment" or "comparative safety assessment".

The story of how the comparative safety assessment made its way into Europe's GMO regulatory system is, like the formation of the US FDA's biotech policy, a tale of revolving doors and conflicts of interest with industry.

The change of name from "substantial equivalence" to "comparative safety assessment" was suggested in a 2003 paper on risk assessment of GM plants.[50] The paper was co-authored by Harry Kuiper, then chair of EFSA's GMO Panel, with Esther Kok. In 2010 Kok joined EFSA as an expert on GMO risk assessment.[51] In their 2003 paper, Kuiper and Kok freely admitted that the concept of substantial equivalence remained unchanged and that the name change was in part meant to deflect the "controversy" that had grown up around the term.[50]

At the same time that Kuiper and Kok published their 2003 paper, they were part of a task force of the GMO industry-funded International Life Sciences Institute (ILSI), that was working on re-designing GMO risk assessment.[29] In 2004 Kuiper and Kok co-authored an ILSI paper on the risk assessment of GM foods, which defines comparative safety assessment. The other co-authors include representatives from GM crop companies that sponsor ILSI, including Monsanto, Bayer, Dow, and Syngenta.[52]

EFSA has followed ILSI's suggestion of treating the comparative safety assessment as the basis for GM safety assessments. EFSA has promoted the concept in its guidance documents on assessment of environmental risks of GM plants[53] and of risks posed by food and feed derived from GM animals,[54] as well as in a peer-reviewed paper on the safety assessment of GM plants, food and feed.[55]

In 2013 the EU Commission incorporated the industry- and EFSA-generated concept of the comparative safety assessment into its new regulation on GM food and feed.[31]

A major problem with the comparative safety assessment is that, as the name suggests, the authorities are beginning to treat it as a safety assessment in itself, rather than as just the first in a series of mandatory steps in the assessment process. In other words, EFSA and the EU Commission are moving towards a scenario in which if the GMO passes this weak test – and many have, in spite of having significant differences from the non-GM comparators – then they may not be subjected to further rigorous testing.

## What is the comparative assessment?

This comparative assessment consists of a comparison of the newly developed GM variety with its closest non-GM relative, normally the parent variety. The non-GM relative has the same genetic background as the GMO, but without the genetic modification, so it is called the isogenic (genetically the same) variety.

A comparison is made of the composition of the GMO compared with the non-GM isogenic variety, with regard to the levels of certain basic components such as carbohydrate, protein, and fat. If they fall roughly within the same range, the GMO is deemed substantially equivalent to the non-GM isogenic variety. The effects of feeding the GMO and its non-GM isogenic variety to animals are also compared in a short animal feeding study.

## The right and wrong way to do a comparative assessment

The proper scientific method of carrying out a comparative assessment is to grow the GM crop and its non-GM isogenic comparator side-by-side under the same conditions. This method ensures that any differences found in the GM crop, or in animals that eat it in a feeding trial, are understood to arise from the genetic modification and not from environmental factors such as different growing conditions. It also fulfills the intent of the EU Directive, which is to enable differences "arising from the genetic modification" to be identified and assessed.[56]

If differences are found between the GM crop and the correct comparator, this is a sign that the genetic engineering process has caused disruption of the structure and/or function of the native genes of the host plant. Further investigations should then be carried out to look for other unintended changes. These would include in-depth toxicological testing and "stress testing", in which the crop is subjected to challenges in the laboratory that it might encounter in the field, such as exposure to crop diseases and simulated adverse weather conditions.

In contrast, comparisons with unrelated or distantly related varieties grown at different times and in different locations introduce and increase external variables and serve to mask rather than highlight the effects of the genetic engineering process. Such practices undermine the aim of the GMO comparative assessment, which is to identify any unintended disruption to gene structure and function – and consequent biochemical composition – brought about by the genetic engineering process.

This, however, is the method favoured by the GMO industry, both in the compositional analyses it performs on its products[37,57] and in the animal feeding trials it carries out on its GMOs for regulatory authorizations. In these animal feeding trials, it compares the GMO diet not only with the non-GM isogenic comparator diet, but also with a range of "reference" diets containing varieties grown in different locations.[58,59] The effect is to hide the effects of the genetic modification on the plant amid the "noise" created by the external variables.

## GMOs would not pass an objective comparative safety assessment

Scientists and even the Royal Society of Canada have heavily criticized the use of substantial equivalence and the comparative safety assessment as the basis of safety assessments of GM crops.[4, 24,26,60]

Yet if the comparative safety assessment were applied objectively and systematically with proper controls, most GMOs would not pass even this weak test of safety. This is because as explained above ("The sham of substantial equivalence"), many studies on GM crops show that they are not substantially equivalent to the non-GM counterparts from which they are derived. There are often significant differences in the levels of certain nutrients and types of proteins, which could impact allergenicity, toxicity, or nutritional value.

The GMO industry and its supporters have sidestepped this problem by widening the range of comparison. Adopting a method used by Monsanto in analyses of its GM soy,[37,57] they no longer restrict the comparator to the GM plant and the genetically similar (isogenic) non-GM line, grown side-by-side under the same conditions and at the same time. Instead they use as comparators a range of non-isogenic varieties grown at different times and in different locations.

In some cases the spurious comparators are modern varieties that have been recently grown and analyzed, but in other cases they are historical varieties on which data has been gathered in the literature. Some of this "historical" data even dates back to before World War II.[60] It may have been analyzed by different researchers using methods that vary in sensitivity, accuracy and reliability. Anyone familiar with the fundamental principles of the experimental sciences will recognize that comparisons to such data are not meaningful.

Despite the loose approach taken in these comparative assessments, they often reveal significant differences in composition between the GMO and the diverse comparator dataset used by the company applying for approval of the GMO. This reveals that the properties of the GMO are outside the range of the non-GMO comparator data, including even the historical data. But even in these extreme cases, according to scientists who have served in regulatory bodies, the differences are dismissed as not being "biologically relevant".[60]

## The ILSI database

The industry-funded International Life Sciences Institute (ILSI) has created a database of crop varieties,[61] including historical or unusual varieties that have untypically high or low levels of certain components. It appears that the primary purpose of this database is to provide "comparative data" that allow industry to argue that the constituents of their GMOs are within the normal range of variation, regardless of how deviant they are from the norm and from the appropriate comparator, which is the relevant non-GM isogenic line grown in the same conditions. EFSA experts use this industry database as the basis of the compositional comparison in GMO risk assessments.[29]

If, on the basis of this "comparative safety assessment", EFSA experts judge the GM crop to be equivalent to the comparator non-GM crops, it is assumed to be as safe.[29,62] Further rigorous tests that could reveal unexpected differences, such as long-term animal feeding trials and environmental stress tests, are not required.[29] Instead, a limited check is carried out.

## EFSA disregards advice of its own head of GMO risk assessment

Joe Perry, the chair of EFSA's GMO Panel, has admitted that the ILSI database cannot be relied upon for risk assessment purposes. Perry said: "At the present time we can't trust the ILSI database. There is not sufficient environmental information from where these trials were done and that's why we insist that the commercial reference variety should be planted simultaneously with the GM and the non-GM. Otherwise I think we are in an unsafe situation and I would worry that the limits would be too wide."[63]

Although Perry's statement implies that comparison with the isogenic line is EFSA policy, this does not seem to be the case, since EFSA used the ILSI database as the basis of the risk assessment of SmartStax, a stacked trait GM maize to which eight genetically modified genes had been added.[64] Moreover, EFSA did not confine its comparison of the GM maize with a commercial reference variety "planted simultaneously", as Perry said EFSA requires. Instead, EFSA compared one of the parent GM maize varieties used to develop the stacked trait crop and its non-GM isogenic parent variety grown in "various field trials" in "different field trial locations", on two different continents, and at different times.[64] This is antithetical to good scientific practice, which tests one variable at a time.

In spite of all the "noise" introduced by these irrelevant data, statistically significant differences in composition were still found between the parent GM maize and the non-GM comparator. But EFSA dismissed these differences on the basis that the values fell within the "natural variation" found in unspecified "literature" and in the ILSI database. EFSA was able to conclude that the GM stacked maize was "equivalent" to existing "commercial maize varieties",[64] with the result that it was not considered necessary to perform further detailed risk assessment on this stacked trait crop.

## EFSA weakens the comparative assessment by widening the range of comparators

An EU Directive of 2001 was strict in stipulating that the comparator against which the GMO should be assessed for safety should be the non-GM genetically similar (isogenic) parent – "the non-modified organism from which it is derived".[56] The non-GM isogenic parent would have the same genetic background as the GM crop, but without the GM transformation. This would enable differences "arising from the genetic modification" to be identified and assessed, without the confounding factor of different environmental conditions in which the crops are grown.

In line with this Directive, the EU Regulation of 2003 on GM food and feed stipulated that the comparator against which the GMO should be assessed for safety should be the non-GM "conventional counterpart".[65]

Until 2011 EFSA followed the principle of using the correct comparator in its Guidance documents and Opinions. But in a Guidance document published in late 2011,[66] EFSA legitimized unscientific industry practice by widening the range of acceptable comparators beyond the non-GM isogenic comparator. In doing so, EFSA arguably departed from EU legislative requirements.[65,56]

EFSA even proposed to allow the use of other GM crops, rather than the usual non-GM isogenic line, as comparators for stacked trait crops containing multiple GM traits. And remarkably, EFSA stipulated that in some cases, plants from different species could be accepted as comparators.[66]

EFSA's approach is in line with industry's practices. But whether it complies with EU regulation is questionable.

The result of this lax regulatory process is that almost any GMO could pass through the regulatory process unchallenged. This forces consumers and farmers into the role of experimental guinea pigs. Any unexpected effects of a GMO that has entered the market via this channel will only be revealed post-commercialization, in the form of ill effects on humans or animals that eat the GMO, or poor crop performance in farmers' fields.

## Industry-backed lobbying to weaken the criteria for comparative assessment

There has been intense lobbying pressure on regulators to allow a wider range of comparison for GMOs beyond the non-GM isogenic variety. As part of this drive, some scientists have published papers in scientific journals explaining away significant alterations in a GM plant compared with the non-GM isogenic comparator by widening the range of comparison and recommending this practice to regulators. They compare the GM plant not only with the non-GM parent plant from which it is derived, but with a wide range of different varieties of the plant. Two examples of such papers follow.

### 1. Catchpole and colleagues (2005)

This study evaluated levels of certain metabolites (breakdown products) in GM potatoes and compared these levels not only with levels in the non-GM parent lines but also with levels in other non-GM potato varieties. The authors found significant differences in the levels of one metabolite, rhamnose, in a GM potato variety, as compared with the levels in the non-GM isogenic parent line grown in the same conditions. But they believed that this was not important because the GM variety had rhamnose levels that were "typical of potato cultivars".[67]

The authors were explicit about the lobbying purpose of their study: "The cultivar-based compositional heterogeneity [differences] we describe emphasizes the importance of comparison with a range of equivalent cultivars and not solely the parental line."[67] They were recommending widening the range of comparison used in the comparative assessment of GM crops to a range of different varieties. This effectively hides the significant difference between a GM crop and its non-GM isogenic control.

The authors also emphasized the conclusion that regulators were supposed to reach: that the GM potatoes were "substantially equivalent to traditional cultivars".[67]

### 2. Ricroch and colleagues (2011)

This review of safety assessment methods for GM crops[68] took the same approach as

Catchpole and colleagues (above). Ricroch and colleagues disagreed with the principle of EU Directive 2001/18, which states that the non-GM isogenic line should be used as the comparator for the risk assessment.[56] They argued that the natural range of variation of certain components in different non-GM lines was greater than the variation between the GM and the isogenic non-GM parent line.

Also, the authors argued that compared with any differences brought about by the genetic engineering of a crop compared with the isogenic non-GM parent line, different "environmental conditions usually have a larger impact".[68]

This is entirely our point – environmental conditions create large differences in plants. But the aim of the comparative assessment in EU regulatory practice is to exclude differences caused by environmental conditions, so that any differences caused by the GM process ("arising from the genetic modification", as EU Directive 2001/18 states) can be identified.[56] The differences caused by different environmental conditions are confounders, or confusing elements, in this process. With that in mind, the proper comparator for the GMO is the non-GM isogenic variety, grown side-by-side under the same conditions.

The lobbying point made by Ricroch and colleagues is the same as that of Catchpole and colleagues: "These observations indicate that the current regulatory burden on GE crops should be lowered... the time may have come to simplify the risk assessment of modern biotechnology products, and therefore reduce cost." Like Catchpole and colleagues, Ricroch and colleagues affirmed the "validity" of the concept of substantial equivalence – the basis for the non-regulation of GM crops by the US government.[68]

Both sets of authors did not want the GMO to be compared with the non-GM isogenic counterpart, arguably because of the significant differences that are generally found. Instead they wanted to compare it with a range of other non-GM plants – masking the differences in the GM plant compared with the non-GM isogenic variety – amid the "noise" created by irrelevant data on a wide range of varieties grown in a range of conditions.

In summary, these authors are in conflict with the spirit and letter of EU legislation as well as scientific rigour. What they are recommending is the equivalent in chemicals risk assessment of:

1. Carrying out a toxicological experiment that finds that a certain chemical causes a certain type of cancer in 40% of the test group of animals as compared with control cancer rates of 0-5%, then...
2. Dismissing the significance of the finding on the grounds that in a certain town where carcinogenic chemicals are manufactured, 40% of the population has this type of cancer, and...
3. Concluding that the cancer incidence in this experiment is within the natural range of variation and that therefore the chemical is safe.

Such a conclusion would rightly be derided. But it is no different in principle from invoking the "natural range of variation" to conclude that GM crops are safe.

## Comparative assessment does not directly assess safety

Comparative assessment or assessment of substantial equivalence measures the composition of the GMO and of some comparators and on that basis comes to a conclusion on whether the GMO is significantly different from the comparators. This compositional analysis says nothing directly about the safety of a GMO for human or animal consumption or about its potential impacts on the environment.

Even if the comparative assessment were correctly carried out using the isogenic non-GMO variety as comparator, it still would not be able to establish the safety or otherwise of a GM crop. It can only find what the researcher is looking for. It cannot find unexpected toxins or allergens or changes in nutrients that may have been caused by the GM process. The only way to look for such unexpected changes is long-term toxicological and nutritional testing in animals. Such testing screens broadly for harmful impacts of consuming the GMO. When such tests are carried out on GM foods, as discussed in Chapter 3, they often expose problems with the GM food tested against the non-GM food.

The comparative assessment also cannot predict the responses of a GM crop to environmental stresses. Such responses can only be known by testing the GMO under different environmental stress conditions. Similarly, it is not possible to predict environmental impacts of the GMO from a comparative assessment, and these too must be tested.

Such tests should be carried out in controlled, enclosed conditions in order to prevent the introduction of the GMO into the wider environment until evidence is obtained that it is stable and safe.

## Masking effects of a GM diet

In parallel with the trend of widening the range of comparators used in the comparative assessment of GMOs, industry and regulators have adopted an equally unscientific approach to assessing the health effects of a GMO in animal feeding trials. When, as is often the case, a feeding trial reveals statistically significant differences between the animals fed a GM diet, as compared with those fed a non-GM diet, these changes are often dismissed as being "not biologically meaningful" or as being within the range of normal biological variation (see Chapter 3 for a discussion of this practice and how it places public health at risk).

These practices run counter to good scientific method and seem to be part of a strategy for masking the effects of the GMO by introducing into the data analysis additional data from other experiments, often carried out under different and non-comparable conditions. This greatly widens the apparent "natural range of variation" to the point where the results for the GMO fall within this artificially widened range. This generates a convenient answer – that the GMO is no different from non-GM comparators – but in no way assures safety for the consumer or the environment.

## GMO assessment turns its back on science


The medical biologist and immunologist Dr Frédéric Jacquemart, president of the independent scientific research group Inf'OGM and a member of France's High Council for Biotechnology, analyzed EFSA's risk assessment of Monsanto's insecticidal GM maize MON810 as an example of the unscientific nature of GMO evaluations. Unscientific practices used by Monsanto in its dossier and accepted by EFSA (and other regulators around the world) include:

- Assuming that the Bt toxin protein expressed by the GM maize is the same as, and as safe as, the natural Bt protein, when in fact the protein in GM maize is a hybrid and truncated protein with different biological and toxicological properties.
- Introducing irrelevant comparison data, from experiments carried out on a range of crops grown in a wide range of conditions, into studies on a GM crop. This has the effect of masking differences between the GM crop and the corresponding non-GM crop that were caused by the GM process and allows a false conclusion of equivalence to be drawn between the two.
- Accepting claims of equivalence between the GMO and the non-GM comparator even though equivalence has not been proven. The tests performed by industry have historically not been capable of proving equivalence. A European regulation passed in 2013 addresses this problem by setting criteria for equivalence and non-equivalence,[31] but this has not been applied to MON810.
- Allowing industry to select which data it presents in order to reach the desired conclusion, without requiring industry to disclose all of the studies it has carried out or the criteria it used in selecting the data submitted.
- Failing to require a power analysis in animal toxicological feeding studies. The power analysis ensures that the experiment uses the appropriate number of animals to enable the researchers to detect the effect that is being looked for. If a study finds no effect from the GM diet, without a power analysis that demonstrates that a sufficient number of animals was used, one cannot determine whether the negative result was because there truly was no effect or whether the study used too few animals to detect the effect.

The report notes that stating that nothing of concern was seen in a study is only valid "if one looks", and points out that the evaluations done as part of the regulatory process create the appearance of having looked, but are "designed not to find anything". The report concludes that while evaluations of GMOs are "passed off as rigorous studies, directly based on data", in fact they are "a parody of science, aimed at political decision-makers and the public".[85]

## Proof of equivalence not required in Europe until 2013

Before 2013, the degree of similarity that a GMO needed to have to its non-GMO counterpart in order to pass the comparative assessment was never defined. Previous to that time, all GMOs were approved without any objective criteria for similarity or dissimilarity being in place. A regulation passed in 2013 changed this situation and demands proof of equivalence within defined limits.[31] However, the GMOs commercialized previous to this date have not been subject to this requirement and the regulation will not be retrospectively applied to them.

## Regulatory process is based on industry studies

Many governments, including those of the EU, Japan, Australia, and New Zealand, have an agency that reviews GM crops before commercialization. Some agencies make a judgment regarding the safety of those crops for consumption and the environment. Others, for example, the US FDA, make no such judgment. In Europe, the relevant agency is the European Food Safety Authority (EFSA) and the final decision to approve or reject the GMO is made by a vote by representatives of the governments of the member states. In Australia and New Zealand, the agency is FSANZ.

Worldwide, safety assessments of GMOs by government regulatory agencies are not scientifically rigorous. Nowhere in the world do the relevant agencies carry out or commission their own safety tests prior to GMO commercialization. Instead, they make decisions regarding the safety of the GMO based on studies commissioned and controlled by the very same companies that stand to profit from the crop's approval.

The problem with this system is that industry studies have an inbuilt bias. Published reviews that evaluate studies assessing the safety and hazards of risky products or technologies have shown that industry-sponsored studies, or studies where authors are affiliated with industry, are much more likely to reach a favourable conclusion about the safety of the product than studies carried out by scientists independent of industry.

The most notorious example is industry studies on tobacco, which succeeded in delaying regulation for decades by sowing confusion about the health effects of smoking and passive smoking.[69,70] A similar bias has been found in industry studies on other products, including pharmaceuticals,[71,72] medical products,[73] and mobile phone technology.[74]

The GMO field is no exception. A review of scientific studies on the health risks of GM crops and foods showed that either financial or professional conflict of interest (author affiliation to industry) was strongly associated with study outcomes that cast GM products in a favourable light.[75]

## Grey literature and lack of transparency

Lack of transparency of industry data is a major problem with the GMO regulatory process. The animal feeding and other safety studies that companies submit to regulatory agencies are often unpublished at the time the GMO is approved. This means that they are not available for scrutiny by the public or independent scientists. Unpublished studies fall into the category of so-called "grey literature" and are of unknown reliability.

Such grey literature stands in stark contrast with the standard quality control method traditionally used by the scientific community: peer-reviewed publication. The peer-reviewed publication process is far from perfect and is subject to biases of various kinds. Yet it is still the best method that scientists have come up with to ensure reliability. Its strength lies in a multi-step quality control process:

- The editor of the journal reads the study. If he judges it as potentially acceptable for publication in the journal, he sends it to qualified scientists ("peers") to evaluate. They give feedback, including any suggested revisions, which are passed on to the authors of the study.
- Based on the outcome of the peer review process, the editor publishes the study, rejects it, or offers to publish it with revisions by the authors.
- Once the study is published, it can be scrutinized and repeated (replicated) or extended by other scientists. Replication is the cornerstone of scientific reliability, because if other scientists were to do the same experiment but come up with different findings, this could challenge the findings of the original study.

In the US, significant portions of the industry data on GMOs submitted to regulators are classified as confidential business information and are shielded from public scrutiny.[76]

The lack of access to industry studies has resulted in the public being deceived over the safety of GMOs. For example, in Europe, industry's raw data on Monsanto's GM Bt maize variety MON863 (approved for food and feed use in the EU in 2005) were only forced into the open through court action by Greenpeace. Scientists at the independent research organization CRIIGEN in France analyzed the raw data and found that Monsanto's own feeding trial on rats revealed signs of liver and kidney toxicity that had been kept hidden from the public.[77,78]

Since this case and perhaps as a result of it, transparency has improved in Europe and the public can obtain industry toxicology studies on GMOs from EFSA on request, along with other safety data submitted by the developer company. Only a small amount of information, such as the genetic sequence of the GMO, can be kept commercially confidential.[79]

However, the problem of the lack of transparency of industry data in Europe is far from solved. In 2013 EFSA published the full Monsanto dossier of data on the GM maize NK603 as part of its transparency initiative[80] after the safety of the maize was cast into doubt by a study carried out by the team of Professor Gilles-Eric Séralini at the University of Caen, France.[81] Monsanto responded by threatening legal action against EFSA for publishing its data.[82] (The French study was subsequently retracted by Food and Chemical Toxicology, the journal that published it, in highly questionable circumstances: see Chapter 3.)

Moreover, industry safety data on pesticides is still kept secret under commercial confidentiality agreements between industry and regulators.[83] This is relevant to GMO safety because most GM crops are engineered to tolerate being sprayed with herbicide (herbicides are technically pesticides): that is, they can absorb the herbicide and survive.

Therefore GM crops are likely to contain higher levels of specific pesticides.[49] Yet the public cannot see the studies that form the basis of pesticide approvals. In Europe, all that is accessible to the public is the report on the industry studies drawn up by the authorities of the "rapporteur" member state, responsible for liaising between industry and the EU authorities for the application for authorization of that particular pesticide.[83]

This secrecy was challenged in a 2012 court case brought by Pesticide Action Network Europe and Greenpeace Netherlands to force disclosure of the industry studies on glyphosate. Astonishingly, however, the German court prioritized commercial interests over public health and ruled that the studies must remain secret.[84]

## Industry and the US government design the GMO regulatory process worldwide

Agricultural biotechnology corporations have lobbied long and hard on every continent to ensure that the weak safety assessment models developed in the US are the norm globally. Working through the US government or groups that appear to be independent of the GMO industry, they have provided biosafety workshops and training courses to smaller countries that are attempting to grapple with regulatory issues surrounding GMOs. The result has been models for safety assessment that favour easy approval of GMOs without rigorous assessment of health or environmental risks.

For example, a report by the African Centre for Biosafety (ACB) described how the Syngenta Foundation, a nonprofit organization set up by the agricultural biotechnology corporation Syngenta, worked on "a three-year project for capacity building in biosafety in sub-Saharan Africa". The Syngenta Foundation's partner in this enterprise was the Forum for Agricultural Research in Africa (FARA), a group headed by people with ties to Monsanto and the US government.

The ACB identified the Syngenta Foundation/FARA project as part of an "Africa-wide harmonization of biosafety policies and procedures" that would "create an enabling environment for the proliferation of GMOs on the continent, with few biosafety checks and balances".[86]

In India, the US Department of Agriculture led a "capacity building project on biosafety" to train state officials in the "efficient management of field trials of GM crops"[87] – the first step towards full-scale commercialization. And in 2010, a scandal erupted when a report from India's supposedly independent national science academies recommending release of GM Bt brinjal (eggplant/aubergine) for cultivation was found to contain 60 lines of text copy-pasted almost word for word from a biotechnology advocacy newsletter – which itself contained lines extracted from a GMO industry-supported publication.[88]

## Regulatory failures around the world

There is a constant stream of revelations about the lack of competence, objectivity, and transparency of GMO regulatory bodies around the world. Individuals who sit on GMO regulatory bodies are frequently found to have conflicts of interest in the form of professional or financial affiliation with the GMO industry or ownership of patents on GMO technology.

A few examples of this compromised regulatory system follow.

### India: "public sector" GM Bt cotton infected with Monsanto's gene

A taxpayer-funded project of the Indian Council of Agricultural Research (ICAR) to commercialize a "public sector" variety of GM Bt cotton came to an ignominious end when the crop was found to carry a Monsanto-patented GM gene. The crop also failed in the field and was withdrawn.[89]

An inquiry revealed that the developers of the Bt cotton variety had submitted three different maps of the inserted GM gene unit sequence to different authorities. The maps showed that even the developers of the GMO did not understand its genetic makeup.[90]

It was also reported that the scientist responsible for conducting the molecular analysis of the GM Bt cotton variety, Ishwarappa S. Katageri from the University of Agricultural Sciences in Dharwad, did not do so because he did not have the technical skills to carry out such studies and was not even aware of any methodology to differentiate various events.[90]

Such tests are mandatory for regulatory assessments in India. Yet the regulators, the Genetic Engineering Appraisal Committee (GEAC) and the Review Committee on Genetic Manipulation (RCGM), seemingly did not notice these lapses. Indeed, Katageri had sat on the RCGM as a regulator for years.[90]

### India: Regulatory breakdown left GM Bt cotton farmers vulnerable

In 2012, faced with conflicting reports of the performance and prospects of GM crops in India, an expert committee of the Indian Parliament was tasked with looking into the matter. The committee was especially concerned to investigate reports of an escalation in farmer suicides since the introduction of GM Bt cotton. Critics of GM crops in India have linked the suicides to failure of the Bt cotton crop and farmer indebtedness resulting from high seed costs.

After gathering evidence from all stakeholders, the committee visited villages in the cotton growing belt of Vidarbha in the state of Maharashtra to interview Bt cotton farmers. In spite of strenuous efforts by the Maharashtra state government to divert them elsewhere,[91] the committee visited a Monsanto showcase village. According to a previously published article in The Times of India authored by a journalist on a Monsanto-sponsored field trip, thanks to Bt cotton, "not a single person" in this village had committed suicide.[92]

But the visiting committee members talked to farmers in the Monsanto model village and heard a very different account, according to an article in The Hindu by the award-winning journalist P. Sainath. The farmers said there had been 14 suicides in the village, most of them since Bt cotton was introduced. Many of the remaining farmers had given up farming altogether or switched to soybeans.[91]

In their final report, the committee noted that while seed companies had benefited from selling Bt cotton, "The poor and hapless farmers have received more of the costs than the benefits". They concluded that there are better options than GM crops for increasing food production and demanded a ban even on GM crop field trials.[93]

It is reasonable to ask why, if this assessment is true, so many farmers in India adopted Bt cotton. The committee's report addressed this question and partly blamed the "craze" for cultivating Bt cotton because of its "perceived advantages", leading to a situation where traditional non-GM seeds had been "almost wiped out".[93]

The "craze" interpretation is backed up by a peer-reviewed study by the anthropologist Glenn Davis Stone, who is not an opponent of GM Bt cotton. Stone concluded that seed "fads" were responsible for the widespread adoption of Bt cotton, helped along by "agricultural deskilling" and aggressive marketing campaigns by seed companies.[94]

According to the Indian Parliament expert committee, the other part of the answer lies in the failure of the government regulatory bodies, which should protect the interests of the public and farmers. The committee noted "with concern the grossly inadequate and antiquated regulatory mechanism for assessment and approval" of GM crops; the "serious conflict of interest of various stakeholders involved in the regulatory mechanism"; and "the total lack of post commercialization, monitoring and surveillance".[95]

### Worldwide: Lack of regulation of a new type of GMO based on gene-silencing technology

In 2013 a peer-reviewed study was published by Professor Jack Heinemann and colleagues suggesting that government GMO regulators are failing to consider important risks of a new type of GM plants and related technologies.[96]

While most existing GM plants are designed to make new proteins, these new-type GM plants and products are designed to make a form of genetic information called double-stranded RNA (dsRNA). The dsRNA molecules are short (21-23 base unit) gene function regulatory molecules which are designed to alter the way genes are expressed – by silencing or activating them. This process of gene expression alteration is broadly called RNA interference (RNAi) and is at the basis of post-transcriptional gene silencing (PTGS) in plants.

A number of GMOs have been made using dsRNA gene-silencing technology. Australia's public research institute CSIRO has developed GM wheat and barley varieties where genes have been silenced in order to change the type of starch made by the plant in its grain. Another example is biopesticide plants, which produce a dsRNA molecule designed to silence a gene in insects that eat the plant. The insect eats the plant, and the dsRNA in the plant survives digestion in the insect and travels into the insect's tissues to silence a gene. The insect dies as a result.[96]

Gene silencing may be inherited across generations through epigenetic mechanisms in plants and some kinds of animals that are exposed to gene-silencing dsRNA.[96]

Furthermore, there is massive ongoing investment to develop products that directly transfer dsRNA into the living cells of plants, animals and microbes via their food or by being

### Unexpected effects from gene-silencing technology

A study in honeybees revealed unexpected ecological risks of dsRNA molecules. The study found that the expression of nearly 1,400 of the bees' genes was altered in response to a certain type of dsRNA administered in their food – representing around 10% of known honeybee genes. The findings were a surprise, since this particular dsRNA had been used as a control in honeybee experiments because its gene sequence does not exist in honeybees and thus it was not expected to trigger RNAi responses in the bees.[106]

Another demonstration, this time in humans, was published by Hanning and colleagues. They attempted to predict which genes would be silenced in human cells based on full knowledge of the sequence of the dsRNAs they were using –and failed. They concluded that information-based modeling tools (known as bioinformatics) are insufficient to predict the effects of dsRNAs without specific biological testing.[107]

absorbed through their "skin". This allows dsRNA molecules to be sprayed onto fields of crops to kill insects or weeds, or to be delivered as oral medicine to bees.[97]

Heinemann and colleagues reviewed their experience with three government safety regulators (for either food or the environment) in three different countries over the past ten years. They found that the safety of dsRNA molecules was usually not considered at all. If it was considered, the regulator simply assumed that any dsRNA molecules were safe, rather than requiring evidence that they were safe.[96]

The authors found that government regulators:

- Dismissed the need for any assessment of the sequence of the base unit nucleotides in the dsRNAs produced by GM plants
- Seemed to assume that dsRNAs produced by these plants are much the same as the more fragile single-stranded RNAs (for example, mRNA), and therefore would not survive cooking and digestion
- Claimed that these new dsRNA molecules are safe because humans and non-target animals would not be exposed to them.[96]

On the basis of these assumptions, the regulators did not assess whether the gene regulatory dsRNAs could cause adverse effects by, for example, silencing or activating genes in people or animals that come into contact with the plant when it is grown commercially. Contact could include eating the crop or processed products derived from it, inhaling dust from the crop when harvesting it, or inhaling flour from the crop when baking with it. And regulators made that decision regardless of whether the dsRNA was generated intentionally or unintentionally by the crop. All three regulators decided that there were no risks to be considered, based on assumptions, rather than scientific evidence.[96]

The problem is that all these assumptions are incorrect, as shown by many scientific studies reviewed by Heinemann and colleagues.[96]

For example, a study by Zhang and colleagues showed that short dsRNA gene regulatory molecules produced in non-GM plants can be taken up into the bodies of people who eat the plant. The dsRNA from the plant was found circulating in blood, indicating that it survives cooking and digestion. Research has also shown that:

- At least one dsRNA produced in plants (called MIR168a) can change the expression of genes in mice when the dsRNA is taken up through eating
- One type of dsRNA (MIR168a) can change the expression of a gene in human cells growing in tissue culture.[98]

Another study found a wide range of RNA molecules from many different organisms, including bacteria and fungi as well as other species, in human plasma (a component of blood). The authors concluded that these RNA molecules may be able to influence cellular activities and may thus affect human health.[99]

According to Heinemann and colleagues, these studies show that there is a real risk that novel short dsRNA gene regulatory molecules produced by the new GM crops could survive digestion in people and change how those people's genes are expressed. Therefore regulators should not ignore the specific risks posed by novel dsRNAs in GM foods.[96]

As a result of their analysis, Heinemann and colleagues developed and provided a safety testing procedure for all GM plants that may produce new dsRNA molecules, as well as for products where the active ingredient is dsRNA.[96]

Since the publication of the paper by Heinemann and colleagues, two more have appeared on the topic of dsRNA uptake through food. The first, by Witwer and colleagues,[100] studied dsRNA uptake into primates. The concentration of dietary dsRNA was just at the detection limit, creating uncertainty about how common these molecules are. Therefore the authors encouraged more studies. That should be concerning to regulators, who for years have assumed that dsRNAs could not survive digestion. The new work further justified calls for testing of foods created using RNAi-based technology to confirm the safety of novel dsRNA molecules.

Witwer and colleagues reported poor reproducibility of detection, which they said suggested low levels of dsRNAs.[100] Indeed, it is to be expected that dietary dsRNAs will be present at low levels. However, the paper did not address relevant risk assessment issues, such as:

- Which concentration of dsRNA in blood (or other tissues) matters?
- Which exposure routes (diet, inhalation, contact) matter most?

Witwer and colleagues used different animals and food sources than other investigators, their study had only two animals, and only a very small number (five) of potential dsRNAs were targeted. So while the authors concluded that effects were unlikely, they also carefully acknowledged that their study was too small and the strength of their positive detections too strong to exclude uptake of dsRNA into mammals through food.[100]

The second paper was written by employees of Monsanto and another company that produces dsRNA-containing products (Dickinson and colleagues, 2013).[101] Dickinson and colleagues extended Monsanto's previous study,[102] but failed to find dsRNA of plant origin in mice fed the plants in question.[101] An editorial in the journal Nature Biotechnology claimed that Monsanto's new study facilitated "the process of self-correction" in the literature,[103] effectively implying that Zhang and colleagues' study[98] was wrong.

However, the methodology of the second Monsanto study was severely criticized by some of the original authors of Zhang and colleagues' study.[104] Moreover, on the basis of the evidence in the study by Zhang and colleagues (2012)[98] and the second Monsanto study by Dickinson and colleagues (2013),[101] it is not possible to say either that Zhang and colleagues or the Monsanto authors are wrong. Different groups of researchers working on different groups of animals, using different methodologies and looking for different dsRNA molecules, may reach different conclusions. Both may be correct, or either or both may be wrong.

More importantly, there have been many more successful detections of short dsRNA gene regulatory molecules of plant origin in mammals than there have been failures to detect them, as recorded in a study by Monsanto[102] and in the patent literature.[105]

## Viral Gene VI

A paper published in 2012 by scientists at the European Food Safety Authority (EFSA) revealed that the most common genetic regulatory sequence in commercialized GMOs also encodes a significant fragment of a viral gene.[108] Yet this viral gene, called Gene VI, has been missed in regulatory assessments worldwide, including by EFSA. Regulators failed to identify the gene, to investigate whether it is expressed, and to assess any risks it may pose to human and animal health.

The EFSA researchers discovered that of the 86 different GMOs commercialized to date in the United States, 54 contain portions of Gene VI. They include any with the widely used gene regulatory sequence called the CaMV 35S promoter (from the cauliflower mosaic virus, CaMV).[108]

Among the affected GMOs are some of the most widely grown, including Roundup Ready soybeans, NK603 maize, and MON810 maize.

The EFSA researchers did a computer search of Gene VI DNA sequences to see if there were any similarities to known toxins and found "no significant hits". In fact they did find a similarity between parts of Gene VI and a known allergen, suggesting that it is a "potential allergen". But the authors went on to conclude that Gene VI was probably not an allergen, based on database searches against known allergens.[108]

However, the databases that the EFSA authors used include the Allergy Research and Resource Program database (FARRP) at allergenonline.org.[109] The objectivity of this database is questionable on the grounds that its staff and facilities at the University of Nebraska are funded by the six major biotech companies: Monsanto, Syngenta, Dow, Dupont Pioneer, Bayer, and BASF.[110]

More importantly, databases of allergens only contain information on known allergens. They are not useful for identifying unknown allergens, which would be missed in a computer search such as that which the EFSA authors carried out. And as there are no meaningful animal models for assessing the allergenicity of foods or isolated proteins, hitherto unknown allergens could only be revealed by extensive testing on humans.

Also, Gene VI could express differently, depending on the genetic context in the host plant into which it is inserted. Thus no conclusions of safety can be drawn from the computer exercise.

The EFSA researchers did, however, conclude that the presence of segments of Gene VI "might result in unintended phenotypic changes"[108] – changes in the plant's observable characteristics or traits. Such changes could include the creation of proteins that are toxic or allergenic to humans. The segments of Gene VI could also trigger changes in the plants themselves that could compromise their performance in the field.

The protein produced by Gene VI is known to be toxic to plants.[111] Gene VI is also known to interfere with the basic mechanism of protein synthesis,[112] which is common to humans, animals, and plants, and to disrupt RNA silencing – a biological mechanism shared by humans, animals, and plants. Thus it is reasonable to ask whether the protein produced by Gene VI could be toxic to humans. This question can only be answered by further experiments.

Jonathan Latham, a crop geneticist and plant virologist, and Allison Wilson, a molecular biologist and geneticist, commented that viral genes expressed in plants raise both agronomic and human health concerns because many viral genes function to disable their host in order to facilitate pathogen invasion. They concluded, "The data clearly indicate a potential for significant harm," and recommended that all GM crops containing Gene VI should be recalled. These include numerous commercial GMOs containing a promoter from the figwort mosaic virus (FMV), which were not considered by the EFSA researchers.[113]

After Latham and Wilson's article drew the EFSA researchers' paper to public attention, EFSA published a statement defending its risk assessment of GMOs. But EFSA's response was misleading. It stated, "The viral gene (Gene VI) belongs to a plant virus (cauliflower mosaic virus) that cannot infect animals or humans".[114]

This seems to miss the point of the concerns raised. As Latham and Wilson pointed out in response, Gene VI as found in GM crops is not the same as the natural cauliflower mosaic virus found in vegetables: "Depending on the specifics of its genome integration into commercial GMOs, Gene VI DNA may produce either a simple viral protein fragment or a chimeric (part-viral) protein. In either case the result will not be equivalent in structure, cellular location, or quantity, to any protein produced by the virus."[115] Therefore the safety of Gene VI as found in GMOs cannot be deduced from the qualities or known behaviour of the natural cauliflower mosaic virus.

Safety questions about Gene VI could be answered by analyzing GM crops with CaMV-driven cassettes to see if they express Gene VI and produce a protein product containing it. If Gene VI is expressed, then more in-depth studies should be carried out to investigate the consequences to the plant and the animals and humans that eat it.

## GM salmon

The biotechnology aquaculture company AquaBounty has developed a GM salmon called the AquAdvantage®. The GM salmon is intended to grow faster and reach the market more quickly than natural salmon.

Dr Michael Hansen, senior scientist with the Consumers Union, examined[116] the US Food and Drug Administration's (FDA) assessment of the company's data on the AquAdvantage salmon.[117]

Hansen found that the company data, though "woefully incomplete", raised concerns that the GM salmon could be more allergenic than non-GM salmon. The study used groups of fish that were far too small to enable reliable conclusions to be drawn – only six GM fish were used. Despite the small sample sizes, tests with blood serum from humans who were allergic to salmon still showed a highly statistically significant increase (52%) in allergenic potency of one type of GM salmon ("diploid"), compared with non-GM controls. This means that the process of genetic engineering led to an increase in allergenic potency, at least in this test.[116]

A smaller increase (20%) in allergenic potency was found in the second type ("triploid") of GM salmon. These are the salmon that will be commercialized and eaten by consumers. The FDA stated that the increase was not statistically significant. However, lack of statistical significance could have been due to the very small sample sizes. Hansen believed the FDA should have demanded that the test be repeated with larger sample sizes.[116]

Instead the FDA stated that there were not enough data to enable it to draw a conclusion on the allergenicity of the diploid GM salmon and that the triploid salmon posed "no additional risk" compared with non-GM salmon.

Hansen found the FDA's assessment of the allergenicity data "inadequate" and concluded that there was cause for concern that the salmon "may pose an increased risk of severe, even life-threatening allergic reactions to sensitive individuals".[116]

Hansen highlighted other questionable practices by the FDA, such as reportedly manipulating data on levels of IGF-1, a growth hormone that is linked with cancer, which was found at an average of 40% higher levels in the GM fish compared with controls. The data manipulation, as reported by Hansen, enabled the FDA to conclude that there was no significant difference between the IGF-1 levels for the GM and non-GM salmon.[116]

The FDA even reached a conclusion about growth hormone levels in the salmon flesh, despite having no data at all on growth hormone levels, due to the use of insensitive test methodology. In addition, the FDA allowed the company to select fish for inclusion in studies without specifying that they were chosen randomly.[116]

The FDA also allowed the company to cull out deformed fish prior to selecting fish to include in the studies, on the grounds that it is standard practice in the industry.[117] This may be true, but it is not acceptable scientific practice in a study that is supposed to be designed to examine the effects of genetic modification in salmon. Even the FDA admitted that the culling "may have skewed the population" of fish studied,[117] but it failed to draw the only scientifically valid conclusion, which is to reject the results as insufficient and require additional more rigorous research.

Hansen concluded that the FDA's assessment of the company data was an example of "sloppy science".[116]

## Conclusion

The regulatory regime for GM crops and foods is weakest in the US, the origin of most such crops, but is inadequate in most regions of the world, including Europe. The US assumes that GM foods are "generally recognized as safe" (GRAS), even though they do not meet the legal definition of GRAS. Worldwide, regulators assume that GM crops are safe if certain basic constituents of the GM crop are "substantially equivalent" to those of their non-GM counterparts – a term that has not been legally or scientifically defined. The European regime applies the same concept but terms it "comparative safety assessment".

Often, however, when an in-depth scientific comparison of a GM crop and its non-GM counterpart is undertaken, the assumption of substantial equivalence is shown to be false, as unexpected differences are found.

Today, no regulatory regime anywhere in the world requires long-term or rigorous safety testing of GM crops and foods. Regulatory assessments are based on data provided by the company that is applying to commercialize the crop – the same company that will profit from a positive assessment of its safety.

The regulatory procedure for GM crops is not independent or objective. The GM crop industry, notably through the industry-funded group, the International Life Sciences Institute (ILSI), has heavily influenced the way in which its products are assessed for safety. ILSI has successfully promoted concepts such as the comparative safety assessment, which maximize the chances of a GMO avoiding rigorous safety testing and greatly reduce industry's costs for GMO authorizations.

Examples of regulatory failure are common and include unscientific procedures, sloppy practices, and the failure to recognize and address important types of risk. Regulatory lapses are often linked to conflicts of interest among regulators.

## References


1. European Commission. GMOs in a nutshell. 2009. Available at: http://ec.europa.eu/food/food/biotechnology/qanda/a1_en.print.htm.
2. Monsanto. Commonly asked questions about the food safety of GMOs. 2013. Available at: http://www.monsanto.com/newsviews/Pages/food-safety.aspx.
3. Tokar B. Deficiencies in federal regulatory oversight of genetically engineered crops. Institute for Social Ecology Biotechnology Project; 2006. Available at: http://environmentalcommons.org/RegulatoryDeficiencies.html.
4. Freese W, Schubert D. Safety testing and regulation of genetically engineered foods. Biotechnol Genet Eng Rev. 2004:299-324.
5. Kahl L. Memorandum to Dr James Maryanski, FDA biotechnology coordinator, about the Federal Register document, "Statement of policy: Foods from genetically modified plants." US Food & Drug Administration; 1992. Available at: http://www.biointegrity.org/FDAdocs/01/01.pdf.
6. Guest GB. Memorandum to Dr James Maryanski, biotechnology coordinator: Regulation of transgenic plants – FDA Draft Federal Register Notice on Food Biotechnology. US Department of Health & Human Services; 1992. Available at: http://www.biointegrity.org/FDAdocs/08/08.pdf.
7. Matthews EJ. Memorandum to toxicology section of the Biotechnology Working Group: "Safety of whole food plants transformed by technology methods." US Food & Drug Administration; 1991. Available at: http://www.biointegrity.org/FDAdocs/02/02.pdf.

8. Shibko SL. Memorandum to James H. Maryanski, biotechnology coordinator, CFSAN: Revision of toxicology section of the "Statement of policy: Foods derived from genetically modified plants." US Food & Drug Administration; 1992. Available at: http://www.biointegrity.org/FDAdocs/03/03.pdf.
9. Pribyl LJ. Comments on the March 18, 1992 version of the Biotechnology Document. US Food & Drug Administration; 1992. Available at: http://www.biointegrity.org/FDAdocs/12/ljpp.pdf.
10. Pribyl LJ. Comments on Biotechnology Draft Document, 2/27/92. US Food & Drug Administration; 1992. Available at: http://www.biointegrity.org/FDAdocs/04/04.pdf.
11. Sudduth MA. Genetically engineered foods – fears and facts: An interview with FDA's Jim Maryanski. FDA Consum. 1993:11–14.
12. Bittman M. Why aren't GMO foods labeled? New York Times. http://opinionator.blogs.nytimes.com/2011/02/15/why-arent-g-m-o-foods-labeled/. Published February 15, 2011.
13. Nestle M. Food Politics: How the Food Industry Influences Nutrition and Health. Revised 15 October 2007. University of California Press; 2002.
14. US Food and Drug Administration (FDA). Meet Michael R. Taylor, JD, deputy commissioner for foods. 2013. Available at: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofFoods/ucm196721.htm.
15. US Food and Drug Administration (FDA). Biotechnology consultation agency response letter BNF No. 000001. 1995. Available at: http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/Submissions/ucm161129.htm.
16. Graff GD, Cullen SE, Bradford KJ, Zilberman D, Bennett AB. The public-private structure of intellectual property ownership in agricultural biotechnology. Nat Biotechnol. 2003;21:989-95. doi:10.1038/nbt0903-989.
17. Vidal J. WikiLeaks: US targets EU over GM crops. The Guardian. http://www.guardian.co.uk/world/2011/jan/03/wikileaks-us-eu-gm-crops. Published January 3, 2011.
18. Euractiv.com. US lobbied EU to back GM crops: WikiLeaks. http://www.euractiv.com/global-europe/us-lobbied-eu-back-gm-crops-wikileaks-news-500960. Published January 4, 2011.
19. EINNEWS. Wikileaks document pushes genetically modified food for African countries. http://www.einnews.com/pr-news/248883-wikileaks-document-pushes-genetically-modified-food-for-african-countries. Published December 1, 2010.
20. Laskawy T. Wikileaks: State Dept wants intel on African acceptance of GMOs. Grist. http://www.grist.org/article/2010-11-29-wikileaks-state-dept-wants-intel-on-african-acceptance-of-gmos. Published November 30, 2010.
21. US Food and Drug Administration (FDA). Statement of policy: Foods derived from new plant varieties. FDA Fed Regist. 1992;57(104):22984.
22. US Food and Drug Administration (FDA). CFR - Code of Federal Regulations Title 21, Volume 3 (Revised 1 April 2013): 21CFR170.30. 2013. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=170.30.
23. Maryanski J. Letter from Dr James Maryanski, Biotechnology Coordinator, to Dr Bill Murray, Chairman of the Food Directorate, Canada. Subject: the safety assessment of foods and food ingredients developed through new biotechnology. 1991. Available at: http://www.biointegrity.org/FDAdocs/06/view1.html.
24. Royal Society of Canada. Elements of precaution: Recommendations for the regulation of food biotechnology in Canada. An expert panel report on the future of food biotechnology. 2001. Available at: http://www.rsc.ca//files/publications/expert_panels/foodbiotechnology/GMreportEN.pdf.
25. European Network of Scientists for Social and Environmental Responsibility (ENSSER). Statement: No scientific consensus on GMO safety. 2013. Available at: http://www.ensser.org/increasing-public-information/no-scientific-consensus-on-gmo-safety/.
26. Millstone E, Brunner E, Mayer S. Beyond "substantial equivalence." Nature. 1999;401:525–6. doi:10.1038/44006.
27. Howard CV. GM crops inquiry: Testimony of Prof C. Vyvyan Howard to the Scottish Parliament Health and Community Care Committee, meeting no. 31, 27 November 2002. 2002. Available at: http://archive.scottish.parliament.uk/business/committees/historic/health/or-02/he02-3102.htm.
28. Organisation for Economic Cooperation and Development (OECD). Safety evaluation of foods derived by modern biotechnology: Concepts and principles. OECD Publishing; 1993. Available at: http://dbtbiosafety.nic.in/guideline/OACD/Concepts_and_Principles_1993.pdf.
29. Then C, Bauer-Panskus A. European Food Safety Authority: A playing field for the biotech industry. Testbiotech; 2010. Available at: http://www.testbiotech.de/en/node/431.
30. Levidow L, Murphy J, Carr S. Recasting "substantial equivalence": Transatlantic governance of GM food. Sci Technol Hum Values. 2007;32:26–64.
31. European Parliament and Council. Commission implementing regulation (EU) no. 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Off J Eur Union. 2013. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF.
32. Pusztai A, Bardocz S, Ewen SWB. Genetically modified foods: Potential human health effects. In: D'Mello JPF, ed. Food Safety: Contaminants and Toxins. Wallingford, Oxon: CABI Publishing; 2003:347–372. Available at: http://www.leopold.iastate.edu/news/pastevents/pusztai/0851996078Ch16.pdf.
33. Nodari RO, Guerra MP. Implications of transgenics for environmental and agricultural sustainability. Hist Cienc Saude Manguinhos. 2000;7(2):481-91.
34. Zdunczyk Z. In vivo experiments on the safety evaluation of GM components of feeds and foods. J Anim Feed Sci. 2001;10:195-210.
35. Zolla L, Rinalducci S, Antonioli P, Righetti PG. Proteomics as a complementary tool for identifying unintended side

effects occurring in transgenic maize seeds as a result of genetic modifications. J Proteome Res. 2008;7:1850-61. doi:10.1021/pr0705082.
36. Lappé M, Bailey B, Childress C, Setchell KDR. Alterations in clinically important phytoestrogens in genetically modified herbicide-tolerant soybean. J Med Food. 1999;1:241–245.
37. Padgette SR, Taylor NB, Nida DL, et al. The composition of glyphosate-tolerant soybean seeds is equivalent to that of conventional soybeans. J Nutr. 1996;126:702-16.
38. Shewmaker C, Sheehy JA, Daley M, Colburn S, Ke DY. Seed-specific overexpression of phytoene synthase: Increase in carotenoids and other metabolic effects. Plant J. 1999;20:401–412X.
39. Jiao Z, Si XX, Li GK, Zhang ZM, Xu XP. Unintended compositional changes in transgenic rice seeds (Oryza sativa L.) studied by spectral and chromatographic analysis coupled with chemometrics methods. J Agric Food Chem. 2010;58:1746-54. doi:10.1021/jf902676y.
40. Zhou J, Ma C, Xu H, et al. Metabolic profiling of transgenic rice with cryIAc and sck genes: an evaluation of unintended effects at metabolic level by using GC-FID and GC-MS. J Chromatogr B Anal Technol Biomed Life Sci. 2009;877:725-32. doi:10.1016/j.jchromb.2009.01.040.
41. European Food Safety Authority (EFSA) GMO Panel. Opinion of the scientific panel on genetically modified organisms on a request from the Commission related to the notification (reference C/DE/02/9) for the placing on the market of insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. EFSA J. 2004;2004:1-25.
42. Abdo EM, Barbary OM, Shaltout OE. Chemical analysis of Bt corn “Mon-810: Ajeeb-YG®” and its counterpart non-Bt corn “Ajeeb.” IOSR J Appl Chem. 2013;4(1):55–60.
43. Gab-Alla AA, El-Shamei ZS, Shatta AA, Moussa EA, Rayan AM. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(9):1117–1123.
44. El-Shamei ZS, Gab-Alla AA, Shatta AA, Moussa EA, Rayan AM. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(10):684–696.
45. Agapito-Tenfen SZ, Guerra MP, Wikmark O-G, Nodari RO. Comparative proteomic analysis of genetically modified maize grown under different agroecosystems conditions in Brazil. Proteome Sci. 2013;11(1):46. doi:10.1186/1477-5956-11-46.
46. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
47. Gu J, Krogdahl A, Sissener NH, et al. Effects of oral Bt-maize (MON810) exposure on growth and health parameters in normal and sensitised Atlantic salmon, Salmo salar L. Br J Nutr. 2013;109:1408-23. doi:10.1017/S000711451200325X.
48. Finamore A, Roselli M, Britti S, et al. Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. J Agric Food Chem. 2008;56:11533–39. doi:10.1021/jf802059w.
49. Bøhn T, Cuhra M, Traavik T, Sanden M, Fagan J, Primicerio R. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. Food Chem. 2013. doi:10.1016/j.foodchem.2013.12.054.
50. Kok EJ, Kuiper HA. Comparative safety assessment for biotech crops. Trends Biotechnol. 2003;21:439–444.
51. European Food Safety Authority (EFSA). Annual declaration of interests – Esther Kok. 2010.
52. International Life Sciences Institute (ILSI). Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology, prepared by a task force of the ILSI International Food Biotechnology Committee. Compr Rev Food Sci Food Saf. 2004;3:38–104.
53. European Food Safety Authority (EFSA) GMO Panel. Guidance on the environmental risk assessment of genetically modified plants. EFSA J. 2010;8:1879–1990. doi:10.2903/j.efsa.2010.1879.
54. European Food Safety Authority (EFSA). Guidance on the risk assessment of food and feed from genetically modified animals and on animal health and welfare aspects. EFSA J. 2012;10:2501. [43 pp.].
55. European Food Safety Authority (EFSA) GMO Panel Working Group on Animal Feeding Trials. Safety and nutritional assessment of GM plants and derived food and feed: The role of animal feeding trials. Food Chem Toxicol. 2008;46:S2-70. doi:10.1016/j.fct.2008.02.008.
56. European Parliament and Council. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Off J Eur Communities. 2001:1–38.
57. Taylor NB, Fuchs RL, MacDonald J, Shariff AR, Padgette SR. Compositional analysis of glyphosate-tolerant soybeans treated with glyphosate. J Agric Food Chem. 1999;47:4469-73.
58. Hammond B, Dudek R, Lemen J, Nemeth M. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food Chem Toxicol. 2004;42:1003-14. doi:10.1016/j.fct.2004.02.013.
59. Hammond B, Lemen J, Dudek R, et al. Results of a 90-day safety assurance study with rats fed grain from corn rootworm-protected corn. Food Chem Toxicol. 2006;44:147-60. doi:10.1016/j.fct.2005.06.008.
60. Hilbeck A, Meier M, Römbke J, Jänsch S, Teichmann H, Tappeser B. Environmental risk assessment of genetically modified plants - concepts and controversies. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-13.
61. International Life Sciences Institute (ILSI). ILSI crop composition database: Version 4. 2011. Available at: http://www.cropcomposition.org/query/index.html.
62. European Food Safety Authority (EFSA). Guidance on the submission of applications for authorisation of genetically modified food and feed and genetically modified plants for food or feed uses under Regulation (EC) No 1829/2003. EFSA J. 2011;9:1–27. doi:10.2903/j.efsa.2011.2311.
63. Perry J. Comment by Joe Perry, chair of EFSA's GMO Panel, at EFSA's consultative workshop on its draft guidance for the selection of Genetically Modified (GM) plant comparators, Brussels, 31 March 2011. 2011. Available at: http://

www.efsa.europa.eu/en/events/event/gmo110331.htm#playvideo.
64. European Food Safety Authority (EFSA) Panel on Genetically Modified Organisms (GMO). Scientific Opinion on application (EFSA-GMO-CZ-2008-62) for the placing on the market of insect resistant and herbicide tolerant genetically modified maize MON 89034 x 1507 x MON 88017 x 59122 and all sub-combinations of the individual events as present in its segregating progeny, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Dow AgroSciences and Monsanto. EFSA J. 2010;8(9):1–37.
65. European Parliament and Council. Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Off J Eur Union. 2003;268:1–23.
66. European Food Safety Authority (EFSA) Panel on Genetically Modified Organisms (GMO). Guidance document on selection of comparators for the risk assessment of GM plants: Adopted on 14 April 2011. EFSA J. 2011;9:1–20.
67. Catchpole GS, Beckmann M, Enot DP, et al. Hierarchical metabolomics demonstrates substantial compositional similarity between genetically modified and conventional potato crops. Proc Natl Acad Sci USA. 2005;102:14458-62. doi:10.1073/pnas.0503955102.
68. Ricroch AE, Berge JB, Kuntz M. Evaluation of genetically engineered crops using transcriptomic, proteomic, and metabolomic profiling techniques. Plant Physiol. 2011;155:1752-61. doi:10.1104/pp.111.173609.
69. Michaels D. Doubt is Their Product: How Industry's Assault on Science Threatens Your Health. Oxford University Press; 2008.
70. Barnes DE, Bero LA. Why review articles on the health effects of passive smoking reach different conclusions. JAMA. 1998;279:1566-70.
71. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. Br Med J. 2003;326:1167. doi:10.1136/bmj.326.7400.1167.
72. Lexchin J. Those who have the gold make the evidence: How the pharmaceutical industry biases the outcomes of clinical trials of medications. Sci Eng Ethics. 2011. doi:10.1007/s11948-011-9265-3.
73. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. JAMA. 2003;289:454-65.
74. Huss A, Egger M, Hug K, Huweiler-Müntener K, Röösli M. Source of funding and results of studies of health effects of mobile phone use: Systematic review of experimental studies. Environ Health Perspect. 2007;115:1–4.
75. Diels J, Cunha M, Manaia C, Sabugosa-Madeira B, Silva M. Association of financial or professional conflict of interest to research outcomes on health risks or nutritional assessment studies of genetically modified products. Food Policy. 2011;36:197–203.
76. Waltz E. Under wraps – Are the crop industry's strong-arm tactics and close-fisted attitude to sharing seeds holding back independent research and undermining public acceptance of transgenic crops? Nat Biotechnol. 2009;27(10):880–882. doi:10.1038/nbt1009-880.
77. Séralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
78. CRIIGEN. Revelations on the toxicity of GMOs – CRIIGEN reveals serious anomalies observed in rats fed on GMOs. 2005. Available at: http://www.criigen.org/SiteEn/index.php?option=com_content&task=blogcategory&id=20&Itemid=87.
79. Dalli J. GMOs: Towards a better, more informed decision-making process. http://bit.ly/zj8BZu. Published March 17, 2011.
80. European Food Safety Authority (EFSA). EFSA promotes public access to data in transparency initiative [press release]. 2013. Available at: http://www.efsa.europa.eu/en/press/news/130114.htm.
81. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
82. Starling S. Monsanto threatens to sue EFSA over publication of maize GM data. Food Navigator. http://www.foodnavigator.com/Legislation/Monsanto-threatens-to-sue-EFSA-over-publication-of-maize-GM-data. Published March 8, 2013.
83. Antoniou M, Habib MEM, Howard CV, et al. Teratogenic effects of glyphosate-based herbicides: Divergence of regulatory decisions from scientific evidence. J Env Anal Toxicol. 2012;S4:006. doi:10.4172/2161-0525.S4-006.
84. Administrative Court of Braunschweig. Pesticide Action Network Europe and Greenpeace Netherlands vs the Federal Republic of Germany, represented by Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL): 2A1033/12. 2012.
85. Jacquemart F. GMO expertise: Assessment turns its back on science. Inf'OGM; 2012. Available at: http://www.infogm.org/IMG/pdf/brochure_eval_couv_text_eng.pdf.
86. Swanby H. Ongoing concerns about harmonisation of biosafety regulations in Africa. Melville, South Africa: African Centre for Biosafety; 2009. Available at: http://www.biosafety-info.net/file_dir/2484217664b02137ac5049.pdf.
87. Ministry of Environment and Forests (India). Genetic Engineering Approval Committee (GEAC) and Cartagena Protocol on Biosafety (CPB). 2010. Available at: http://web.archive.org/web/20121208120227/http://moef.nic.in/divisions/cs/GEAC.htm.
88. Mudur GS. Experts admit GM brinjal report fault. The Telegraph (India). http://www.telegraphindia.com/1100927/jsp/nation/story_12986605.jsp. Published September 26, 2010.
89. Jishnu L. Untangling India's Bt cotton fraud. Down To Earth. http://www.downtoearth.org.in/content/untangling-india-s-bt-cotton-fraud. Published February 15, 2012.
90. Jishnu L. ICAR's shoddy science. Down to Earth. http://www.downtoearth.org.in/content/icar-s-shoddy-science#troubling. Published January 15, 2013.
91. Sainath P. Reaping gold through cotton and newsprint. The Hindu. http://www.thehindu.com/opinion/columns/

sainath/reaping-gold-through-cotton-and-newsprint/article3401466.ece. Published June 16, 2012.
92. Shrivastav S. Reaping gold through Bt cotton. Times of India. http://articles.timesofindia.indiatimes.com/2011-08-28/special-report/29937803_1_bt-cotton-cry1ac-bollgard-ii. Published August 28, 2011.
93. Ministry of Agriculture Committee on Agriculture 2011-2012 (India): Fifteenth Lok Sabha. Cultivation of genetically modified food crops – Prospects and effects: 37th Report. New Delhi, India; 2012.
94. Stone GD. Agricultural deskilling and the spread of genetically modified cotton in Warangal. Curr Anthropol. 2007;48.
95. Lok Sabha Secretariat Committee on Agriculture (2011–12). Thirty-seventh report of the committee on cultivation of genetically modified food crops – Prospects and effects [press release]. 2012. Available at: http://bit.ly/ZbsG8e.
96. Heinemann J, Agapito-Tenfen SZ, Carman J. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. Environ Int. 2013;55:43–55.
97. Carman J, Heinemann J, Agapito-Tenfen S. A briefing document for non-specialists describing the lack of regulation of a new class of products and GM crops based on dsRNA technology. http://gmwatch.org/latest-listing/52-2013/14698. Published March 21, 2013.
98. Zhang L, Hou D, Chen X, et al. Exogenous plant MIR168a specifically targets mammalian LDLRAP1: Evidence of cross-kingdom regulation by microRNA. Cell Res. 2012;22(1):107-126. doi:10.1038/cr.2011.158.
99. Wang K, Li H, Yuan Y, et al. The complex exogenous RNA spectra in human plasma: An interface with human gut biota? PLoS ONE. 2012;7(12):e51009. doi:10.1371/journal.pone.0051009.
100. Witwer KW, McAlexander MA, Queen SE, Adams RJ. Real-time quantitative PCR and droplet digital PCR for plant miRNAs in mammalian blood provide little evidence for general uptake of dietary miRNAs: Limited evidence for general uptake of dietary plant xenomiRs. RNA Biol. 2013;10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23770773.
101. Dickinson B, Zhang Y, Petrick JS, Heck G, Ivashuta S, Marshall WS. Lack of detectable oral bioavailability of plant microRNAs after feeding in mice. Nat Biotechnol. 2013;31(11):965-967. doi:10.1038/nbt.2737.
102. Zhang Y, Wiggins BE, Lawrence C, Petrick J, Ivashuta S, Heck G. Analysis of plant-derived miRNAs in animal small RNA datasets. BMC Genomics. 2012;13:381. doi:10.1186/1471-2164-13-381.
103. The editors of Nature Biotechnology. Receptive to replication. Nat Biotechnol. 2013;31(11):943-943. doi:10.1038/nbt.2748.
104. Chen X, Zen K, Zhang C-Y. Reply to Lack of detectable oral bioavailability of plant microRNAs after feeding in mice. Nat Biotechnol. 2013;31(11):967-969. doi:10.1038/nbt.2741.
105. Lam E. Edible transgenic plants as oral delivery vehicles for RNA-based therapeutics. 2012. Available at: http://patentscope.wipo.int/search/en/detail.jsf?docId=WO2012135820&recNum=40&docAn=US2012031830&queryString=microRNA&maxRec=4460.
106. Nunes F, Aleixo A, Barchuk A, Bomtorin A, Grozinger C, Simões Z. Non-target effects of Green Fluorescent Protein (GFP)-derived double-stranded RNA (dsRNA-GFP) used in honey bee RNA interference (RNAi) assays. Insects. 2013;4(1):90-103. doi:10.3390/insects4010090.
107. Hanning JE, Saini HK, Murray MJ, et al. Lack of correlation between predicted and actual off-target effects of short-interfering RNAs targeting the human papillomavirus type 16 E7 oncogene. Br J Cancer. 2013;108(2):450-460. doi:10.1038/bjc.2012.564.
108. Podevin N, du Jardin P. Possible consequences of the overlap between the CaMV 35S promoter regions in plant transformation vectors used and the viral gene VI in transgenic plants. GM Crops Food. 2012;3:296–300. doi:10.4161/gmcr.21406.
109. University of Nebraska-Lincoln. About AllergenOnline. 2010. Available at: http://www.allergenonline.org/about.shtml.
110. Shetterly C. The bad seed: The health risks of genetically modified corn. Elle. 2013. Available at: http://www.elle.com/beauty/health-fitness/healthy-eating-avoid-gmo-corn.
111. Takahashi H, Shimamato K, Ehara Y. Cauliflower mosaic virus gene VI causes growth suppression, development of necrotic spots and expression of defence-related genes in transgenic tobacco plants. Mol Gen Genet. 1989;216:188–194.
112. Park HS, Himmelbach A, Browning KS, Hohn T, Ryabova LA. A plant viral "reinitiation" factor interacts with the host translational machinery. Cell. 2001;106:723-33.
113. Latham J, Wilson A. Regulators discover a hidden viral gene in commercial GMO crops. Indep Sci News. 2013. Available at: http://independentsciencenews.org/commentaries/regulators-discover-a-hidden-viral-gene-in-commercial-gmo-crops/.
114. European Food Safety Authority (EFSA). FAQ on inserted fragment of viral gene in GM plants. 2013. Available at: http://www.efsa.europa.eu/en/faqs/faqinsertedfragmentofviralgeneingmplants.htm.
115. Latham J, Wilson A. Is the hidden viral gene safe? GMO regulators fail to convince. Indep Sci News. 2013. Available at: http://independentsciencenews.org/commentaries/gmo-regulators-hidden-viral-gene-vi-regulators-fail/.
116. Hansen M. Comments of Consumers Union on genetically engineered salmon, Food and Drug Administration docket no. FDA-201034-N-001, Veterinary Medicine Advisory Committee Meeting. 2010. Available at: http://www.consumersunion.org/pdf/CU-comments-GE-salmon-0910.pdf.
117. US Food and Drug Administration (FDA) Veterinary Medicine Advisory Committee. Briefing packet: AquAdvantage salmon. 2010. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM224762.pdf.

# 2.2 Myth: Independent studies confirm that GM foods and crops are safe

# Truth: Independent research on GM foods is difficult or impossible to carry out, but many studies that have been carried out find problems

## Myth at a glance

In-depth food safety studies on GM crops and foods carried out by scientists independent of the GMO industry are rare. They are hampered by the difficulty of accessing GM seeds and the non-GM parent varieties from the developer companies.

Those scientists who have managed to carry out such research and have found risks from the genetically modified organism (GMO) tested have suffered persecution. Some have paid with their careers and funding.

Claims that the climate for independent researchers has improved in recent years remain unproven.

It is often claimed that many independent studies on GM crops show they are safe.[1] But it is unclear whether those who make this claim have investigated the potential industry funding and/or industry affiliations of the authors of studies published in scientific journals. In these days of increasing industry funding of public universities and research institutes, it cannot be assumed that academic authors are independent.

A review of scientific studies on the health risks of GM crops and foods that did investigate funding sources found that either financial or professional conflict of interest (author affiliation to industry) was strongly associated with study outcomes that cast GM products in a favourable light. Conclusions of safety were also found to be associated with studies in which source of funding was not declared. Furthermore, there was a strong connection between undeclared funding and author affiliation to industry.[2]

Genuinely independent studies on GM foods and crops are rare, for two reasons: because independent research on GM crop risks is not supported financially; and because industry uses its patent-based control of GM crops to restrict independent research.

Research that has been suppressed includes assessments of health and environmental safety and agronomic performance of GM crops. Permission to study GM crops is withheld or made so difficult to obtain that research is effectively blocked. For example, researchers are often denied access to commercialized GM seed and the non-GM isogenic seed.[3,4]

Even if permission to carry out research is given, GM companies typically retain the right to block publication.[3,4] An editorial in Scientific American reported, "Only studies that the seed companies have approved ever see the light of a peer-reviewed journal. In a number of cases, experiments that had the implicit go-ahead from the seed company were later blocked from publication because the results were not flattering."[5]

## Scientists protest

In 2009, 26 scientists took the unusual step of making a formal complaint to the US Environmental Protection Agency. They wrote, "No truly independent research can be legally conducted on many critical questions involving these crops."[6]

In response to the controversy that followed, a new licensing agreement for researchers on GM crops was reached between US Department of Agriculture (USDA) scientists and Monsanto in 2010. However, this agreement is still restrictive. It only applies to agronomic, not food safety research, and only to USDA scientists.[7] Given that the USDA has a policy of supporting GM crops and the companies that produce them (see 2.1: "The US government is not impartial regarding GM crops and foods"), perhaps Monsanto does not see USDA scientists as a threat.

## Is the problem of access to research materials solved?

In 2013 Nathanael Johnson, a food writer at the online magazine Grist, looked into the question of access to materials for GMO research as part of his series of articles on GM. Johnson concluded that before 2009, some scientists really did have trouble doing their work due to patent restrictions, but that now "the problem is largely fixed", due to research agreements being reached between GMO seed companies and universities.[8]

Johnson's source was the pro-GMO plant scientist Kevin Folta, who told him that obtaining seeds was "no problem" and that researchers could obtain them from "me, any of my colleagues that work in corn here at my university, or any of the thousands of other independent researchers in the USA... Seeds are available through Academic Research Licenses, no questions asked from most companies." Folta added that it was even possible to "have the transgenic plants made for well under $1,000" at various universities in the US.[8]

## Information that Johnson ignored or discounted

For his research for this and other articles on GM, Johnson had also corresponded with the independent scientist Dr Judy Carman, who has researched the effects of feeding GMOs to pigs.[9] Johnson had asked Carman for her opinion on Folta's claims. Carman told Johnson:

"GM crops are under patent protection. This means that you cannot go to a seed merchant to buy GM seeds to test. If you do, you will be presented with a legal contract (a technology user agreement[10]) to sign that states that you will not do any research on the seeds and you will not give them to anyone else to do research on, either. I know, because we tried this approach and I've seen the agreements.[11]

"The way US schools get access to GM crops is by signing legal agreements with GM companies to be able to access the patented materials and patented methods that allow them to be able to do GM crop work. They usually do this using commercial in-confidence agreements that you and I cannot see. So we cannot see the conditions placed upon the researchers and the institutions involved, but there has been some protest from scientists about the conditions placed upon them that has been published in scientific journals.

"Also, clearly, GM companies will only reach these agreements with US schools that they approve of. They would not reach agreement with schools they do not approve of. The schools they approve of tend to be schools that work in partnership with the GM company to make GM crops where both can benefit financially. These legal agreements would certainly not allow the school to pass GM material on to me, particularly where the patent on the GM crop is not owned by them but by a GM crop company. Doing that would violate laws."[11]

Carman had tried approaching GM companies directly to source GM seeds and the non-GM isogenic varieties for her toxicology study on pigs.[9] In a more detailed version of the explanation she had provided to Johnson, she wrote, "We wrote to three GM companies asking if we could obtain GM crops from them. One company didn't reply. One wanted to have all the details of our study before considering the possibility (and then they would probably say no).

"Monsanto gave us a legal document to sign that said that we agreed that we would give them the results of the study before we published. Even if we had agreed, there was no guarantee that they would give us seed, so if we had signed and Monsanto had not given us any seed to test, we would still have been legally bound to give them all our results before we published."

Carman concluded: "No self-respecting independent scientist would sign such documents. And we didn't."[12]

Carman also told Johnson that contrary to Folta's claim, it was not possible make a GM crop, field test it and grow enough of it to feed to animals for a toxicology study for $1,000. She added that this would be illegal: "Taking a patented gene and putting it in a crop myself or asking someone to do it for me would violate quite a few laws."[11]

Johnson, however, discounted many of Carman's points, even though they were based on first-hand experience, choosing instead to believe the claims of Folta that the problem of access to seeds had been "largely fixed".[8]

Carman's account was backed by her co-author on the GMO feeding study in pigs,[9] US farmer Howard Vlieger, who also sent his views to Johnson and the editor of Grist – and was also ignored. In the 1990s Vlieger had run his own tests on GM Bt corn and the non-GM parent variety on his farm, with no restrictions. Now, things were very different. Vlieger says, "A bag of patented [GM] traited seed cannot even be unloaded on a dealer's property unless the dealer has signed a technology agreement with the patent holder of the seed."[13] These technology agreements forbid use of the seeds for research.

As for the universities that Folta claimed were happy to help independent researchers with GMO studies, Vlieger found just the opposite. He had approached researchers, funding in hand, at several universities asking them to carry out studies on GM crops and the glyphosate herbicide that most GM crops are engineered to tolerate. But the researchers were unwilling even to consider delving into such questions. Vlieger said, "The reaction was the same every time. They told us it would be 'very unhealthy' for the career of any researcher to get involved with any research that may shed negative light on a GM crop or glyphosate."[13]

It is clear from these accounts that relationships between GM seed companies and universities are a restrictive rather than a liberating influence on independent research. It is unlikely that any university would risk upsetting the GM seed companies that provide it with an ongoing source of research funding by facilitating critical research on their products.

## Another researcher finds problems accessing materials

Another researcher who had extreme difficulty accessing materials was Professor Gilles-Eric Séralini, a molecular biologist at the University of Caen who decided to carry out a long-term rat feeding study on a GMO.[14]

The first difficulty was financial. Séralini would have liked to test Roundup Ready soy as well as the two principal types of GM maize (herbicide-tolerant and Bt insecticidal), on adult mammals and during development in the uterus. But this would have multiplied by five his already considerable budget.

The second problem was technical. In order to test a Bt insecticidal maize, Séralini would have had to isolate the Bt toxin from the maize, but he lacked the technical facilities to do so.

As a solution to the first and second problems, Séralini decided to study a GM maize,

*"Unfortunately, it is impossible to verify that genetically modified crops perform as advertised. That is because agritech companies have given themselves veto power over the work of independent researchers… Research on genetically modified seeds is still published, of course. But only studies that the seed companies have approved ever see the light of a peer-reviewed journal. In a number of cases, experiments that had the implicit go-ahead from the seed company were later blocked from publication because the results were not flattering… It would be chilling enough if any other type of company were able to prevent independent researchers from testing its wares and reporting what they find… But when scientists are prevented from examining the raw ingredients in our nation's food supply or from testing the plant material that covers a large portion of the country's agricultural land, the restrictions on free inquiry become dangerous."*
– Editorial, Scientific American[5]

NK603, which is engineered to tolerate Roundup herbicide. Accessing Roundup was easy – he just had to buy it from a store.

The third difficulty proved more challenging: accessing the GM maize and the non-GM isogenic parent variety for the rats' diets. Cultivation of NK603 maize is not authorized in Europe for commercial purposes, though it is allowed for research. However, no farmer wanted to take the risk of breaching his technology agreement with Monsanto, which forbids the use of GM seed for research. Séralini approached farmers in Spain, Romania, and the US without success. Eventually a farm school in Canada agreed to grow the crops, but on the strict condition that the school was not named, "out of fear of reprisal from the seed suppliers".[14]

Clearly the climate for independent research on GMOs is far from healthy and open. Johnson's assertion that it has improved in recent years remains unproven and, based on current experience, unfounded.

## Researchers who publish studies that find harm from GM crops are attacked

Sometimes, against the odds, independent researchers succeed in carrying out critical research on GMOs. But their problems are by no means over – in fact, they are just beginning. This is because the GMO seed industry and its allies use a range of public relations strategies to discredit and silence scientists who publish critical research.[15]

In some cases pro-GM scientists have bullied the journal editor to try to persuade him not to publish the study. If the research does make it into publication, they criticize it as "bad science", identifying any flaw or limitation (which all studies have) and claiming that this invalidates all the findings. Needless to say, they do not apply the same standards to studies claiming that the GMO tested is safe. Often, they make personal attacks against the researchers.

Scientific debate is nothing new and is to be welcomed: it is the way that science progresses. A researcher publishes a study; another researcher thinks that certain aspects could be improved upon and refines the design to address any uncertainties; these findings in turn are added to the database of knowledge for future researchers to build on. But the trend of attempting to silence or discredit research that finds problems with GMOs is unprecedented and has grown in parallel with the commercialization of GM crops.

Unlike in traditional scientific debate, the criticism does not consist of conducting and publishing further research that could confirm or refute the study in question. Instead, the critics try to "shout down" the study on the basis of claims that are spurious or not scientifically validated. Sometimes they put forward alternative explanations for any harmful effects found in order to remove the blame from the GM crop. Yet these should be viewed as untested hypotheses, unless and until a new experiment is carried out to test them.

The following are just a few examples of cases in which researchers have been targeted over their critical research on GMOs.

## Gilles-Eric Séralini

In 2007 Professor Gilles-Eric Séralini and his research team published a re-analysis of a Monsanto 90-day rat feeding study that the company had conducted and submitted in support of its application for market approval of GM Bt maize MON863. Approval was granted for MON863 to be used in food and feed in the EU in 2005. Monsanto tried to keep the feeding trial raw data secret, claiming commercial confidentiality, but it was forced into the open by a court ruling in Germany.[16]

The Séralini team's re-analysis of the Monsanto raw data showed that the rats fed GM maize had signs of liver and kidney toxicity and differences in weight gain, compared with controls. Séralini and colleagues concluded that it could not be assumed that the maize was safe. They asked for studies performed on GMOs for regulatory purposes to be extended beyond 90 days so that the consequences of such initial signs of toxicity could be investigated.[16]

After Séralini and his team published this and other papers showing harmful effects from GM crops and the glyphosate herbicide used with GM Roundup Ready crops, he was subjected to a vicious smear campaign.[17]

Séralini believed the researchers Claude Allègre, Axel Kahn, and Marc Fellous, chair of the French Association of Plant Biotechnologies (AFBV), were behind the defamation and intimidation campaign. He sued Fellous for libel, arguing that the campaign had damaged his reputation, reducing his opportunities for work and his chances of getting funding for research.[17]

During the trial, it emerged that Fellous, who presented himself as a "neutral" scientist without personal interests and accused GMO critics of being "ideological" and "militant", owned patents through a company based in Israel. The company sells patents to GM corporations such as Aventis. Séralini's lawyer showed that other AFBV members also had links with agribusiness companies.[17]

The court found in Séralini's favour. The judge ordered Fellous to pay costs of 4,000 Euros, plus one Euro in compensation (as requested by Séralini).[17]

In September 2012 the attacks on Séralini escalated to unprecedented levels after he and his research colleagues published a study showing that rats fed over a two-year period with Monsanto's GM maize NK603 and very low levels of the Roundup herbicide it is engineered to tolerate suffered severe organ damage. They also showed a clear trend of increased rates of tumours and premature death.[18]

Many of Séralini's attackers had links with the GM industry or with organizations with vested interests in the public acceptance of GM technology. These links and vested interests went undeclared in media articles that quoted them.[19,20]

Yet more criticism of the study came from government agencies that had previously given opinions that this or other GM foods were safe, such as the European Food Safety Authority (EFSA).[21,22] In 2003 EFSA had issued an opinion that the GM maize was safe,[23] leading to its approval for commercialization by the EU authorities.

EFSA had also previously argued that 90-day feeding trials were sufficient to see even chronic (long-term) toxic effects and that even these short tests were not always necessary.[24] Indeed, EFSA had approved the GM maize as safe on the basis of just such a 90-day trial conducted by Monsanto.[23] Yet the first tumours in Séralini's experiment only showed up four months into the study, a month after Monsanto's 90-day trial ended. In addition, severe organ (especially liver, kidney and pituitary gland) damage linked to consumption of the GM maize and Roundup herbicide was noted during the second year of the feeding trial period.[18]

Séralini's study clearly showed that 90-day tests are inadequate to see chronic effects. So for EFSA to accept that the study had any validity would have been equivalent, as the French Member of the European Parliament Corinne Lepage said, to "cutting off the branch on which the agency has sat for years".[25]

A statement attacking the study by the French Academy of Sciences was strongly challenged by an eminent member of the Academy, Paul Deheuvels. Deheuvels said the statement was written and rushed out by a small lobby within the Academy without consulting the wider membership. Surprisingly, he himself was not consulted, even though the criticisms of Séralini's study focused heavily on the statistical aspects and he was the Academy's only statistician, so it would have been expected for him to be consulted.[26]

Deheuvels said the Academy's statement was equivalent to an arbitrary act of state and that its main criticisms of the study were "ridiculous" and examples of "rash judgement, with no solid foundation". Deheuvels had examined Séralini's study and the raw data on the tumour findings, and concluded that it was clear that there was a problem with GM maize and Roundup.[26]

Deheuvels concluded, "This case shows the pressures that are applied to manipulate the Academy, and to transform it into a lobbying tool. It is no longer the science that speaks, but the wallet!"[26]

Dr A. Wallace Hayes, the editor-in-chief of Food and Chemical Toxicology, the journal that published Séralini's study, was subjected to a long campaign from pro-GM scientists, demanding that he retract it.[19] In November 2013, over a year after the study had been published, Hayes retracted it.[27] The reasons he gave for the retraction were scientifically unjustified and unprecedented in scientific publishing. A full analysis of Séralini's study, and of the scientific and ethical aspects of the retraction and the implications for public health, is in Chapter 3.

### Manuela Malatesta

In 2002 and 2003, an Italian scientist, Manuela Malatesta, published her team's research showing that mice fed Monsanto's GM soy showed disturbed liver, pancreas and testes function. The researchers found abnormally formed structures in liver cells, which indicated increased metabolism and potentially altered patterns of gene expression.[28,29,30,31]

According to an interview with Malatesta in "The World According to Monsanto", the documentary film exposé by the French investigative journalist Marie-Monique Robin, the researcher was advised by her colleagues not to publish her findings, but went ahead anyway. As a result, she was forced out of her job at the University of Urbino, where she had worked for over ten years, and could not obtain funding to follow up her studies. With the support of a colleague, she found a post at another university. Reflecting on the advice of her colleagues not to publish her findings, Malatesta said: "They were right. I lost everything: my laboratory, my research team. I had to begin again from scratch at another university."[32,33]

## Emma Rosi-Marshall

In 2007 Emma Rosi-Marshall and her team published research showing that GM Bt maize material got into streams in the American Midwest and when fed to non-target insects, had toxic effects. In a laboratory feeding study, the researchers fed Bt maize material to the larvae of the caddis fly, an insect that lives near streams. The larvae that fed on the Bt maize debris grew half as fast as those that ate debris from non-GM maize. Caddis flies fed high concentrations of Bt maize pollen died at more than twice the rate of those fed non-Bt pollen.[34]

Rosi-Marshall was subjected to vociferous criticism from GM proponents, who said her paper was "bad science". They complained that the study did not follow the type of protocol usual for toxicological studies performed for regulatory purposes, using known doses – even though such protocols are extremely limited and are increasingly coming under fire from independent scientists for being unable to reliably detect risks (see Chapter 2). Rosi-Marshall replied that her study allowed the caddis flies to eat as much as they wanted, as they would in the wild.[3]

The critics also objected that laboratory findings did not give accurate information about real field conditions. Rosi-Marshall responded that only in the laboratory is it possible to control conditions tightly enough to allow firm conclusions.

Henry I. Miller, of the pro-free market think tank, the Hoover Institution, co-authored an opinion piece in which he called the publication of Rosi-Marshall's study an example of the "anti-science bias" of scientific journals. He accused the authors of scientific "misconduct" – a serious charge. According to Miller, the authors' main crime was failing to mention in their paper another study that concluded that Bt maize pollen did not affect the growth or mortality of filter-feeding caddis flies.[35] Rosi-Marshall responded that she had not cited these findings because they had not been peer-reviewed and published at the time and because they focused on a different type of caddis fly, with different feeding mechanisms from the insects in her study.[3]

Rosi-Marshall and her co-authors stand by their study. In a statement, they said, "The repeated, and apparently orchestrated, ad hominem and unfounded attacks by a group of genetic engineering proponents has done little to advance our understanding of the potential ecological impacts of transgenic corn."[3]

## Arpad Pusztai

In August 1998 the GM debate changed forever with the broadcast of a current affairs documentary on British television about GM food safety. The programme featured a brief but revealing interview with the internationally renowned scientist Dr Arpad Pusztai about his UK government-funded research into GM food safety testing procedures. Pusztai talked of his findings that GM potatoes had harmed the health of laboratory rats. Rats fed GM potatoes showed excessive growth of the lining of the gut similar to a pre-cancerous condition and toxic effects in multiple organ systems.

Pusztai had gone public with his findings prior to publication for reasons of public interest, particularly as the research had been funded by British taxpayers. He gave his television interview with the full backing of his employers, the Rowett Institute in Scotland. After the interview he was congratulated by the Rowett's director, Professor Philip James, for handling the questions so well.[36]

However, within days, the UK Government, the Royal Society, and the Rowett launched a vitriolic campaign to sack, silence and ridicule Dr Pusztai. He was suspended by the Rowett, his research team was disbanded, and his data were confiscated. He was forced to sign a gagging order banning him from speaking about his experiments under threat of legal action. His telephone calls and emails were diverted. He was subjected to a campaign of vilification and misrepresentation by pro-GM scientific bodies and individuals in an attempt to discredit him and his research.[36,37,38,39,40,41]

What caused the Rowett's turnaround? It was later reported that there had been a phone call from Monsanto to the then US president Bill Clinton, from Clinton to the then UK prime minister Tony Blair, and from Blair to the Rowett.[36,40] This shows that the decision to smear and discredit Pusztai's study was based on politics, not science, and was aimed at protecting the GMO industry.

Misrepresentations of Pusztai's research were circulated by GM proponents. These continue to be repeated today and include claims that:

- No GM potatoes were fed at all
- The GM potatoes expressed a protein that even in its natural form would have been toxic to rats (in fact, Pusztai chose this particular protein because it was toxic to insects but proven non-toxic to mammals)
- The experiment lacked proper controls.

These claims can be refuted simply by reading the study. It was also alleged that the GM potatoes were never intended for human consumption, a claim that Pusztai strongly contended.[42] Pusztai's paper subsequently passed peer-review by a larger-than-usual team of reviewers (only one out of six opposed publication[43]) and was published in The Lancet.[44]

Criticisms of the study design are particularly unsound because it was reviewed and passed by the Scottish Office, winning a £1.6 million grant over 28 other competing designs. According to Pusztai, it was also passed by the Biotechnology and Biological Sciences Research Council (BBSRC), the UK's main public biotechnology funding body.[36] Even Pusztai's critics have not suggested that he did not follow the study design as it was approved. And if his study design really had lacked proper controls, the Scottish Office and possibly the BBSRC would have faced serious questions.

Interestingly, T. J. Higgins, one of the critics who claimed that Pusztai's experiment lacked proper controls,[45] had previously co-authored and published with Pusztai a study on GM peas with exactly the same design.[46] The difference between this study and Pusztai's GM potato study was the result: the pea study had concluded that the GM peas were as safe as non-GM peas, whereas the potato study had found that the GM potatoes were unsafe. Higgins did not criticize this study, which he co-authored; nor did he withdraw his name from the publication.[47]

Many "opinion pieces" published in the scientific literature claim that Pusztai's study was flawed and an example of bad science that should be dismissed.[48] But crucially, they offer no new experimental data, which is the only valid way to counter Pusztai's findings. Other studies in the peer-reviewed literature continue to cite the study as valid.[49,50]

### Ignacio Chapela

In 2001 biologist Ignacio Chapela and his co-researcher David Quist tested native varieties of Mexican maize and found that they had been contaminated by GM genes. The findings were especially concerning because Mexico is the biological centre of origin for maize. It has numerous varieties adapted to different localities and conditions, which form the genetic reservoir for breeders seeking to develop new varieties. Mexico had banned the planting of GM maize out of concern for these native varieties. The GM contamination came from US maize imports.

Chapela started talking to various government officials, who, he felt, needed to know. As his findings were approaching publication in the journal Nature, events took a sinister turn. Chapela was put into a taxi and taken to an empty building in Mexico City, where a senior government official threatened him and his family. Chapela had the impression that he was trying to prevent him from publishing his findings.[51,36,52]

Chapela and Quist went ahead with publication.[53] Immediately, a virulent smear campaign against Chapela and the research was launched, with most of the attacks appearing on a pro-GM website called AgBioWorld. The attacks were spearheaded by two people called Mary Murphy and Andura Smetacek. Murphy and Smetacek accused Chapela of being more of an activist than a scientist. Smetacek suggested that Chapela's study was part of an orchestrated campaign in collusion with "fear-mongering activists (Greenpeace, Friends of the Earth)".[36]

The journal Science commented on the smear campaign, noting the "widely circulating anonymous emails" accusing Chapela and Quist of "conflicts of interest and other misdeeds".[54] Some scientists were alarmed at the personal nature of the attacks. "To attack a piece of work by attacking the integrity of the workers is a tactic not usually used by scientists," wrote one.[55]

Investigative research by Jonathan Matthews of GMWatch and the journalist Andy Rowell traced Murphy's attacks to an email address owned by Bivings Woodell. Bivings Woodell was part of the Bivings Group, a PR company with offices in Washington, Brussels, Chicago and Tokyo. Bivings developed "internet advocacy" campaigns for corporations and had assisted Monsanto with its internet PR since 1999, when the biotech company identified that the internet had played a significant part in its PR problems in Europe.[36,56]

Attempts to uncover the identity of Murphy and Smetacek led nowhere, leading the environmental journalist George Monbiot to write an article about the affair entitled, "The fake persuaders: Corporations are inventing people to rubbish their opponents on the internet".[56]

The aim of the smear campaign was to bully the editor of the journal that published the paper, Nature, into retracting it. In response, the editor, Philip Campbell, published a statement saying, "The evidence available is not sufficient to justify the publication of the original paper."[57] This is often mistakenly taken to be a retraction, but it is not. Campbell later confirmed, "The paper was not formally retracted by Nature or the authors".[57] The paper stands as a valid and citable source.

In a trend that has become typical of episodes of manufactured outrage aimed at casting doubt on research that is critical of GMOs, no data or analyses were produced by Chapela and Quist's attackers to counter the researchers' main finding of GM contamination in the samples they tested.

The main findings of Chapela and Quist's paper were later confirmed by other researchers, though samples collected from different areas have produced different results, as is to be expected. Sampling conducted by the Mexican government in 2003 found GM contamination in 0.96% of seed samples from farmers' fields,[58] but a different team of researchers testing different samples reported no GM contamination in 2005.59

A paper published in 2009[60] also reported GM contamination, though an analysis by authors from a GM testing company concluded that there was insufficient evidence of contamination in these particular samples.[61]

A separate study of Mexican farmers' maize seeds published in 2009 found contamination with GM Bt insecticidal toxins and herbicide-tolerant proteins in 3.1% and 1.8% of samples, respectively. As in Chapela's investigation, the spread of GM seeds from the US was thought to be responsible for the contamination.[62]

## Conclusion

The GM crop industry restricts access to its products by independent researchers, so their effects on human and animal health and the environment cannot be properly investigated. Agreements between GMO seed companies and some universities do not apply universally, are still restrictive, and crucially, are controlled by the industry. The research climate for independent researchers is unfavourable and there is no evidence that it is improving.

Independent researchers who do publish papers containing data that is not supportive of GMOs are attacked by the industry and by pro-GMO groups and individuals. This has had a chilling effect on the debate about GM crops and has com promised scientific progress in understanding their effects.

## References


1. Wendel J. With 2000+ global studies confirming safety, GM foods among most analyzed subjects in science. Genetic Literacy Project. http://bit.ly/1bjhPQG. Published October 8, 2013.
2. Diels J, Cunha M, Manaia C, Sabugosa-Madeira B, Silva M. Association of financial or professional conflict of interest to research outcomes on health risks or nutritional assessment studies of genetically modified products. Food Policy. 2011;36:197–203.
3. Waltz E. Battlefield. Nature. 2009;461:27–32. doi:10.1038/461027a.
4. Waltz E. Under wraps – Are the crop industry's strong-arm tactics and close-fisted attitude to sharing seeds holding back independent research and undermining public acceptance of transgenic crops? Nat Biotechnol. 2009;27(10):880–882. doi:10.1038/nbt1009-880.
5. Scientific American. Do seed companies control GM crop research? http://www.scientificamerican.com/article.cfm?id=do-seed-companies-control-gm-crop-research. Published July 20, 2009.
6. Pollack A. Crop scientists say biotechnology seed companies are thwarting research. New York Times. http://www.nytimes.com/2009/02/20/business/20crop.html. Published February 19, 2009.
7. Waltz E. Monsanto relaxes restrictions on sharing seeds for research. Nat Biotechnol. 2010;28:996. doi:10.1038/nbt1010-996c.
8. Johnson N. Food for bots: Distinguishing the novel from the knee-jerk in the GMO debate. Grist. 2013. Available at: http://grist.org/food/dodging-argument-bot-crossfire-to-revisit-some-gm-research-controversies/.
9. Carman JA, Vlieger HR, Ver Steeg LJ, et al. A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. J Org Syst. 2013;8:38–54.
10. Monsanto. 2011 Monsanto technology/stewardship agreement (limited use license). 2010. Available at: http://thefarmerslife.files.wordpress.com/2012/02/scan_doc0004.pdf.
11. GMOJudyCarman. How easy is it for researchers to access the materials for GM biosafety research? http://gmojudycarman.org/how-easy-is-it-for-researchers-to-access-the-materials-for-gm-biosafety-research/. Published September 1, 2013.
12. Carman J. Accessing GM seeds and non-GM isolines for GMO safety research [personal email communication]. 2014.
13. Vlieger H. Letter to the editor of Grist (unpublished). http://www.gmwatch.org/index.php/news/archive/2013/15027. Published August 24, 2013.
14. Séralini GE. Tous Cobayes! Flammarion; 2012.
15. Lotter D. The genetic engineering of food and the failure of science – Part 2: Academic capitalism and the loss of scientific integrity. Int Jrnl Soc Agr Food. 2008;16:50–68.
16. Séralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
17. GM Free Cymru. Independent GM researcher wins court victory for defamation [press release]. http://www.gmwatch.org/latest-listing/1-news-items/12815. Published January 19, 2011.
18. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
19. Matthews J. Smelling a corporate rat. Spinwatch. http://bit.ly/184fwif. Published December 11, 2012.
20. Sourice B. OGM: La guerre secrète pour décrédibiliser l'étude Séralini [The covert war to discredit Séralini's study]. Rue 89/Le Nouvel Observateur. http://blogs.rue89.nouvelobs.com/de-interet-conflit/2012/11/12/ogm-la-guerre-secrete-pour-decredibiliser-letude-seralini-228894. Published November 12, 2012.
21. European Food Safety Authority (EFSA). Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2910.
22. European Food Safety Authority (EFSA). Final review of the Séralini et al. (2012a) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2986.
23. European Food Safety Authority (EFSA). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from herbicide-tolerant genetically modified maize NK603, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (QUESTION NO EFSA-Q-2003-002): Opinion adopted on 25 November 2003. EFSA J. 2003;2003(9):1–14.
24. European Food Safety Authority (EFSA) GMO Panel Working Group on Animal Feeding Trials. Safety and nutritional assessment of GM plants and derived food and feed: The role of animal feeding trials. Food Chem Toxicol. 2008;46:S2-70. doi:10.1016/j.fct.2008.02.008.
25. Lepage C. OGM: l'EFSA a manqué à une déontologie élémentaire [GMOs: EFSA breaches basic ethical code]. Le Nouvel Observateur. http://bit.ly/QWjizy. Published October 7, 2012.
26. Guyon C. Académie des sciences: le scandale des OGM [French Academy of Sciences: The GMO scandal]. Rebelle-Santé. 2013;(153). Available at: http://gmoseralini.org/french-academy-of-sciences-the-gmo-scandal/.
27. Elsevier. Elsevier announces article retraction from Journal Food and Chemical Toxicology. 2013. Available at: http://www.elsevier.com/about/press-releases/research-and-journals/elsevier-announces-article-retraction-from-journal-food-and-chemical-toxicology#sthash.VfY74Y24.dpuf.
28. Vecchio L, Cisterna B, Malatesta M, Martin TE, Biggiogera M. Ultrastructural analysis of testes from mice fed on genetically modified soybean. Eur J Histochem. 2004;48:448-54.

29. Malatesta M, Caporaloni C, Gavaudan S, et al. Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. Cell Struct Funct. 2002;27:173–80.
30. Malatesta M, Caporaloni C, Rossi L, et al. Ultrastructural analysis of pancreatic acinar cells from mice fed on genetically modified soybean. J Anat. 2002;201:409–15.
31. Malatesta M, Biggiogera M, Manuali E, Rocchi MBL, Baldelli B, Gazzanelli G. Fine structural analyses of pancreatic acinar cell nuclei from mice fed on genetically modified soybean. Eur J Histochem. 2003;47:385–388.
32. Robin MM. The World According to Monsanto [film]. 2008.
33. Robin MM. Extrait: Le Monde selon Monsanto (2). Le Nouvel Observateur/Rue89. http://www.rue89.com/2008/02/16/extrait-le-monde-selon-monsanto-2#sdendnote4sym. Published February 16, 2008.
34. Rosi-Marshall EJ, Tank JL, Royer TV, et al. Toxins in transgenic crop byproducts may affect headwater stream ecosystems. Proc Natl Acad Sci USA. 2007;104:16204-8. doi:10.1073/pnas.0707177104.
35. Miller HI, Morandini P, Ammann K. Is biotechnology a victim of anti-science bias in scientific journals? Trends Biotechnol. 2008;26:122–5.
36. Rowell A. Don't Worry, It's Safe to Eat. London, UK: Earthscan Ltd; 2003.
37. Pusztai A. Home page. 2003. Available at: http://www.freenetpages.co.uk/hp/a.pusztai/.
38. GM-FREE magazine. Why I cannot remain silent: Interview with Dr Arpad Pusztai. 1999;1. Available at: http://gmwatch.org/index.php?option=com_content&view=article&id=13856.
39. Powerbase. Arpad Pusztai. 2009. Available at: http://www.powerbase.info/index.php/Arpad_Pusztai.
40. Rowell A. The sinister sacking of the world's leading GM expert – and the trail that leads to Tony Blair and the White House. Daily Mail. http://www.gmwatch.org/latest-listing/42-2003/4305. Published July 7, 2003.
41. Verhaag B. Scientists Under Attack [film]. Mercurymedia; 2009. Available at: http://www.scientistsunderattack.com/.
42. Pusztai A. Regarding "Response to GM myths"/Dr Roger Morton to AgBioView - 12/12/00 [email]. 2000. Available at: http://www.gmwatch.org/latest-listing/39-2000/9016.
43. Enserink M. The Lancet scolded over Pusztai paper. Science. 1999;286.
44. Ewen SW, Pusztai A. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet. 1999;354:1353-4. doi:10.1016/S0140-6736(98)05860-7.
45. Higgins TJ. "Disturbing" GM findings were not based on sound science. Canberra Times. http://www.gmwatch.org/latest-listing/1-news-items/3781. Published June 4, 2005.
46. Pusztai A, Grant G, Bardocz S, et al. Expression of the insecticidal bean a-amylase inhibitor transgene has minimal detrimental effect on the nutritional value of peas fed to rats at 30% of the diet. J Nutr. 1999;129:1597–1603.
47. Pusztai A. Comment on T. J. Higgins' attack. 2005. Available at: http://gmwatch.org/index.php/news/archive/2005/3781.
48. Martinelli L, Karbarz M, Siipi H. Science, safety, and trust: the case of transgenic food. Croat Med J. 2013;54:91-6.
49. Malatesta M, Boraldi F, Annovi G, et al. A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008;130:967–977.
50. Domingo JL. Toxicity studies of genetically modified plants: a review of the published literature. Crit Rev Food Sci Nutr. 2007;47:721-33. doi:10.1080/10408390601177670.
51. BBC Radio 4. Seeds of trouble. 2002.
52. BBC Newsnight. Row over GM crops – Mexican scientist tells Newsnight he was threatened because he wanted to tell the truth. 2002.
53. Quist D, Chapela IH. Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico. Nature. 2001;414:541-543. doi:10.1038/35107068.
54. Mann C. Has GM corn "invaded" Mexico? Science. 2002;295(5560):1617–1619.
55. Kinderlerer J. Regarding AgBioView: Chapela and Mexican corn, China, New Zealand support up, Lomborg, Peanut map [listserv post]. 2001.
56. Monbiot G. The fake persuaders. The Guardian (UK). http://www.monbiot.com/archives/2002/05/14/the-fake-persuaders/. Published May 14, 2002.
57. Campbell P. Editorial. Nature. 2002;416:600.
58. Serratos-Hernández J-A, Gómez-Olivares J-L, Salinas-Arreortua N, Buendía-Rodríguez E, Islas-Gutiérrez F, de-Ita A. Transgenic proteins in maize in the Soil Conservation area of Federal District, Mexico. Front Ecol Environ. 2007;5(5):247-252. doi:10.1890/1540-9295(2007)5[247:TPIMIT]2.0.CO;2.
59. Ortiz-Garcia S, Ezcurra E, Schoel B, Acevedo F, Soberon J, Snow AA. Absence of detectable transgenes in local landraces of maize in Oaxaca, Mexico. Proc Natl Acad Sci. 2005;102:18242.
60. Pineyro-Nelson A, Van Heerwaarden J, Perales HR, et al. Transgenes in Mexican maize: molecular evidence and methodological considerations for GMO detection in landrace populations. Mol Ecol. 2009;18:750-61. doi:10.1111/j.1365-294X.2008.03993.x.
61. Schoel B, Fagan J. Insufficient evidence for the discovery of transgenes in Mexican landraces. Mol Ecol. 2009;18:4143-4; discussion 4145-50. doi:10.1111/j.1365-294X.2009.04368.x.
62. Dyer GA, Serratos-Hernández JA, Perales HR, et al. Dispersal of transgenes through maize seed systems in Mexico. PLoS ONE. 2009;4(5):e5734. doi:10.1371/journal.pone.0005734.

# 2.3 Myth: The Nicolia review compiles 1,700+ studies showing that GMOs are safe

# Truth: The review suffers from important omissions, fails to show GMOs are safe, and provides evidence of risk for some GMOs

## Myth at a glance

A review by Nicolia and colleagues is widely cited to argue that over 1,700 studies show GM foods and crops are safe. However, the studies cited in the Nicolia review and supplementary materials, taken as a whole, do not show that GMOs are safe.

The majority of the articles in the list of 1,700 are irrelevant or tangential to assessing the safety of commercialized GM foods and crops for human and animal health and the environment.

The list includes some studies that are relevant to GMO safety but which show actual or potential hazards of the GMO to health or the environment. The Nicolia review authors ignore or dismiss these findings without sound scientific justification. They also ignore evidence contradicting key assumptions upon which regulators have based their conclusions that GMOs are safe.

Nicolia and colleagues omit important studies that demonstrate hazards related to GMOs and ignore major controversies over the interpretation of scientific findings on GMOs.

The authors use unscientific justifications for ignoring or dismissing important papers, including their arbitrary decision to include only studies published in the ten years since 2002.

Assembling large but questionable lists of studies supposedly providing evidence of the safety of GMOs has become common practice by GMO proponents. In the long term it will have a corrosive effect on public trust in science.

A review by Nicolia and colleagues, "An overview of the last 10 years of genetically engineered crop safety research",[1] is widely cited[2,3] to argue that over 1,700 studies show genetically modified (GM) foods and crops are safe. The list of 1,700 studies, which the authors provide in supplementary materials to their main review paper, is a collection of publications on many different aspects of GMO (genetically modified organism) research and commercialization.

The following analysis of the Nicolia review and the 1,700 publications listed in the supplementary materials is intended to investigate whether these claims are justified. This analysis is not exhaustive, but focuses on the most important aspects of the review. However, even this level of investigation reveals many shortcomings in the Nicolia review and supports the conclusion that it fails to provide convincing evidence of the safety of GMO foods and crops. Details are presented below.

## Overview of problems with the Nicolia review

### 1. Nicolia and colleagues include many studies that are largely irrelevant to assessing the safety for health and the environment of commercialized GMOs or GMOs in the commercialization pipeline

Studies that could address the vital question of long-term impacts of GM foods on human and animal health would typically consist of long-term rodent feeding studies, similar to those performed to support regulatory authorization of pesticide active ingredients. In such a study, one group of animals would be fed a GM diet and the control group an equivalent non-GM diet, in which the GM ingredients are replaced with isogenic (with the same genetic background) non-GM ingredients. The experiment would last for 1-2 years.

Few such long-term studies have been carried out on GMOs. Of these few, most were conducted by researchers independent of the GM industry, after the GMO in question was already in the food supply (post-commercialization): in other words, they were not required for regulatory approval and risk assessment. The rodent feeding studies routinely performed by industry to support regulatory authorization of their products generally last for a maximum of 90 days, a subchronic period that is too short to reveal long-term effects.

Long-term animal studies should be followed by systematic post-commercialization monitoring, in which products containing the GMO are labelled as such and consumers monitored for human health impacts such as allergies, chronic toxicity, carcinogenicity, reproductive and developmental toxicity, and teratogenicity. These impacts cannot, by definition, be studied in short 90-day toxicity tests in rodents.

Yet no post-commercialization monitoring studies in humans have ever been performed for any GMO, despite mounting evidence of adverse effects on animal health (see below).

Studies that could help address the question of the safety of GMOs for the environment include those in which beneficial and non-target insects are exposed to GM insecticidal crops, investigations of the environmental toxicity of the herbicides used with GM crops, and studies of the effects of GM crop cultivation on soil microbial life, non-target insects, and other wildlife.

Only a relatively small proportion of the studies cited in the Nicolia review and supplementary list of 1,700 papers attempt to address these questions.

The rest of the studies cited in the Nicolia review are simply irrelevant or tangential to investigation of the safety of GM foods and crops. Irrelevant categories of studies include the following (examples of studies included in the review and supplementary materials are referenced):

i. **Animal production studies, often performed by GM companies on their own products**.[4,5] These do not examine in detail the health impacts of GM feed but look at aspects of animal production of interest to the food and agriculture industry, such as weight gain and milk production. While such studies provide the agriculture industry with useful information about whether an animal fed on the GMO will survive to slaughter age and deliver an acceptable meat or dairy product, they are usually short-term in comparison to the animal's natural lifespan and provide no detailed information about the health of the animal. Many of these studies are performed on animals such as cows, fish, and chickens. The digestive systems and metabolic functioning of these animals differ significantly from those of humans. Thus these studies are unlikely to provide useful information on human health risks.

ii. **Opinion and advocacy pieces promoting the use of the concept of substantial equivalence in risk assessment**.[6,7,8] These papers do not provide any original data. Therefore they contribute nothing new to the safety debate. The concept of substantial equivalence was originated by the GM industry and inserted into GMO regulations worldwide, largely through the efforts of the industry-funded International Life Sciences Institute (ILSI). It remains controversial and has been challenged by many independent scientists and experts. The Nicolia review omits this criticism and thus falsely claims "consensus" on the use of the concept (see below for a full discussion of this topic).

iii. **Opinion pieces and reviews of safety assessment approaches and regulations relating to GMOs**. Many of these articles are written by GMO proponents and promote the view that GMOs are safe and adequately regulated[8,9] or promote industry-friendly approaches to safety assessment.[10] While Nicolia and colleagues' supplementary list includes articles that are critical of GMO regulation and assessment,[11] the criticisms put forth by the authors of these articles do not make their way into the text of the Nicolia review paper. However, the scientific answer to both sides of this debate is that opinions are not data, and the papers in this category fail to provide any data.

iv. **Studies on experimental GM crops that have never been commercialized**.[12,13] Some of these studies give important information about the imprecise and unpredictable nature of GM technology because they show unintended differences between the GM crop and the non-GM parent[13] or toxic effects in animals exposed to the GM crop.[12] However, because each GM transformation event is different, the findings of such studies are not useful in assessing the safety of the GMOs already in our food and feed supplies. Considerations of relevance apart, Nicolia and colleagues fail to address the safety questions raised by such studies.

v. **Studies on consumer perceptions of GM foods**.[14] Such studies are of special interest to those who wish to overcome public resistance to GMOs, but provide no new data and are therefore irrelevant to assessing GMO safety.

In conclusion, the above categories of studies cited by Nicolia and colleagues offer no hard data that can help answer the important question of whether commercialized or soon-to-be commercialized GMOs are safe.

## 2. Nicolia and colleagues omit from their list, or from their discussion, important studies that find risks and toxic effects from GMOs

Nicolia and colleagues admit in their review that they "selected" studies for inclusion, though they do not disclose their selection criteria. Many relevant studies are simply omitted from their list of 1,700 publications. Others are included in the list of 1,700 studies and/or in the references to the main review paper, but then the authors ignore their findings in the review. This is in spite of the fact that these findings are seminal to any discussion of GMO safety.[15,16,17,18,19,20,21,22]

In some cases, omissions are due to their arbitrary 10-year cut-off date. By choosing to focus on only the last 10 years of scientific research, the authors "select out" important early studies that found toxic effects in animals fed GM crops, including Ewen and Pusztai (1999)[23] and Fares and El-Sayed (1998).[24] There is no defensible scientific reason for excluding these studies.

Pro-GMO lobbyists often claim in online forums that these studies have been "debunked". But empirical findings of harm can only be challenged by replicating and extending the study and getting a different result. No one has attempted to replicate any study that has found toxic effects from a GM food, so the findings reported in these studies stand.

Those who claim that the studies are "bad science" and not worthy of replicating must clarify their criteria for "good" and "bad" studies and apply the criteria equally to studies that find harm from GMOs and studies concluding GMOs are safe.

Since the publication of the early papers excluded from the Nicolia review, the GM industry and its allies have gained increasing control over scientific research and publication, making it increasingly difficult for independent researchers to conduct and publish research critical of GMOs.[25,26] Therefore by restricting their review to research conducted later than 2002, Nicolia and colleagues bias their findings in favour of a false conclusion of GMO safety.

There is no valid scientific reason for excluding critical studies carried out in the late 1990s and early 2000s, especially as many focus on GMOs that are more widely grown today than when the studies were carried out. For example, the area of GM Bt insecticidal crops planted has increased since that time.

Even in a climate hostile to critical GMO research, independent researchers have managed to publish some papers that report toxic or allergenic effects from GMO diets after 2002. Nicolia and colleagues include some of these studies in their supplementary list of 1,700, but then ignore the results reported in those papers in their main review paper. An example is a multigenerational study that found rats fed GM Bt maize over three generations suffered damage to liver and kidneys and alterations in blood biochemistry.[21] A study that showed allergenic effects from GM peas[27] is omitted even from the supplementary list.

An even more glaring omission in Nicolia and colleagues' review (though included in the supplementary list) is the detailed research of Manuela Malatesta, which found toxic effects, including more acute signs of ageing in the liver, in mice fed GM soy over a long-term period.[16,17,18,19,20]

Malatesta's experiments represent some of the very few long-term animal feeding studies on commercialized GMOs. The seminal role of her research was made clear in a report issued by the French food safety agency ANSES[28,29] on Professor Gilles-Eric Séralini's long-term study, which found toxic effects in rats fed a GM maize and very small amounts of Roundup herbicide.[30]

Like EFSA in Europe, ANSES is responsible in France for issuing opinions on the food safety of GMOs, including the GM maize that Séralini found toxic. In its report, ANSES criticized Séralini's study (thus validating its own prior verdict that the GM maize was safe), yet nevertheless called for more long-term studies on GMOs.

ANSES had conducted its own literature search for long-term feeding studies on a glyphosate-tolerant GMO (which make up over 80% of all commercialized GMOs[31]) that were comparable with Séralini's. It had found just two studies: Malatesta's 2008 report on her research, which found toxic effects,[19] and a study that was only available in Japanese.[32] So out of three long-term studies on glyphosate-tolerant GM crops identified by ANSES, two showed evidence of toxicity and the findings of the third cannot be verified by the international scientific community. ANSES concluded that there was a "lack of studies on the potential effects of long-term exposure to various glyphosate-based formulations" and a "limited number of studies that have addressed the long-term effects of consuming GMOs".[29]

The fact that even a regulatory body that was engaged in dismissing the Séralini study recognized the importance of Malatesta's work underlines the lack of scientific justification for Nicolia and colleagues' omission of this research from their discussion of GMO safety.

Nicolia and colleagues omit even from their supplementary list a study that directly contradicts a fundamental claim of safety for GM Bt insecticidal crops. Approvals of GM Bt crops worldwide are based on the assumption that Bt toxin is degraded in the mammalian digestive tract. However, this study by Canadian researchers found Bt toxins circulating in the blood of non-pregnant and pregnant women and in the blood supply to their foetuses.[33,34,35,36] While this paper did not demonstrate that the Bt toxin came from GM crops, one key point is inescapable: Bt toxin is not fully degraded in the digestive tract. This finding places all approvals of GM Bt crops in question.

### 3. Nicolia and colleagues dismiss empirical evidence of toxicity from GM foods by citing non-peer-reviewed opinion pieces

Professor Gilles-Eric Séralini's group at the University of Caen, France, re-analyzed data from industry studies. They found signs of toxicity in the liver and kidneys of rats fed GM Bt maize and Roundup-tolerant maize for only 90 days.[37,38] A follow-up study tested these findings – and regulators' claims that the maize was safe – by feeding the Roundup tolerant GM maize NK603 and very low doses of Roundup herbicide for the extended period of 2 years. This was the most detailed long-term animal feeding study ever performed on a GM food. The study (Séralini et al, 2012) found dramatically increased levels of severe liver and kidney damage and hormonal disturbances in the rats fed NK603 GM maize and/or very low doses of Roundup. Additional unexpected observations were an increased incidence of tumours and premature death in most treatment groups.[30]

After a concerted campaign of attack by industry-linked lobbyists,[39] the study was retracted over a year after publication by the journal that published it, Food and Chemical Toxicology, for unscientific reasons that were condemned by hundreds of scientists in public statements and published articles.[40,41,42,43,44,45] In one case, a former member of the journal's editorial board wrote a letter to the editor opposing the retraction.[46]

Nevertheless, at the time of the writing of the Nicolia review, the paper was part of the scientific literature. Unlike most of the studies that feature in the review, it offers rare empirical data on the long-term effects of consumption of a GM food and its associated pesticide. Even if an extremely conservative view were taken of the Séralini study and the data on tumours and mortality were dismissed due to the relatively low number of animals used (dedicated cancer studies normally require larger numbers of animals), this would not provide a reason to dismiss the toxicological data on organ damage and hormonal disturbances. These findings are solidly based and statistically significant.

The scientifically valid way for Nicolia and colleagues to challenge Séralini's results would be to cite other toxicological studies in which the same GMO and associated pesticide were fed to animals over a long-term period and found not to cause the toxic effects observed by Séralini's group. However, no such studies exist, since Séralini's study was the first and only one of its kind to date on this particular GM maize.

In cavalier fashion, Nicolia and colleagues dismiss the findings of this pioneering study, as well as the findings of other studies on GMO toxicity by Séralini's team,[37,38] as being "of no significance" – without providing a scientifically defensible definition of "significance".

They base their conclusion not on empirical data, reasoned scientific argument, or even peer-reviewed papers. Instead, their only evidence is four non-peer-reviewed opinion pieces.

Of the four articles, two are opinions of the European Food Safety Authority,[47,48] the agency that previously issued favorable verdicts regarding the safety of these same GMOs,[49,50] leading to their approval for food and feed use in Europe. So in dismissing the Séralini group's findings, EFSA was effectively defending its own position, as the former French environment minister Corinne Lepage has pointed out.[51]

In addition, many EFSA staff and experts have conflicts of interest with the industries whose products the agency is supposed to regulate. This has been pointed out over many years by Members of the European Parliament[52,53] and the European Court of Auditors,[54] as well as civil society organisations.[52,53] The European Parliament even withheld its approval of EFSA's budget for the financial year ending 2010, largely out of concern over the industry-related conflicts of interest of its experts and staff.[55]

In an attempt to deal with this persistent criticism, EFSA instituted a new independence policy.[56] But that did not appear to solve EFSA's problems. A 2013 report by Corporate Europe Observatory found that over half of the agency's experts who give opinions on the safety of GMOs, food contaminants, and additives had conflicts of interest with industry.[57]

Thus EFSA's opinion pieces on the Séralini study can be discounted not only because they are not peer-reviewed and lack empirical evidence that contradicts Séralini's data, but also because EFSA has conflicts of interest that prevent it from considering this matter impartially.

The third opinion piece cited by Nicolia and colleagues to dismiss the Séralini group's findings is a self-published article on an agbiotech website written by two GMO proponents, Wayne Parrott and Bruce Chassy.[58] It contains factual inaccuracies and spurious arguments, including a claim that Dr Arpad Pusztai's research on GM potatoes "bypassed" peer review, when in fact it passed an unusually stringent peer review process[59] before being published in The Lancet.[23]

Parrott and Chassy also suggest that all studies finding harm from GM foods must be replicated by other researchers before they can be taken seriously. But they do not apply the same critical standard to studies that conclude GMO safety, even though most such studies are conducted by or for the same companies that hope to market the GMO concerned and are therefore subject to bias.[60]

Parrott and Chassy place the burden of proof of harm on publicly funded researchers to prove beyond doubt that the GMO is harmful – a level of proof that current scientific methods cannot provide. Science does not "prove": it provides evidence that assists the evolution of scientific understanding of a topic. Parrott and Chassy's partisan demand also flies in the face of internationally accepted biosafety rules and European laws on GMOs, which place the burden of proof of safety on the company that intends to market the GMO.[61,62] Even the US's notoriously weak biotech policy states that the responsibility to ensure the safety of any GM food lies with the technology developer.[63]

The fourth opinion piece cited by Nicolia and colleagues is a comment article by François Houllier, president of the French research group INRA.[64] Houllier offers no rigorous scientific analysis detailing why Séralini's research should not be taken seriously. He briefly refers to common criticisms of the study, but fails to mention that they have been addressed by the study's authors,[65] as well as many others.[53,66,67,68,69,70,71,42,72]

Indeed, the focus of Houllier's article is not the scientific methodology used by Séralini, but complaints about Séralini's media campaign and the effect of anti-GMO activists' actions on the public image of GMOs. These arguments have nothing to do with the science. Notably, however, Houllier's article concludes with a call for more and better research on GM crop safety – a conclusion that is shared by Séralini's team and many other scientists, especially those who work independently from corporations.

Thus Nicolia and colleagues attempt to refute Séralini's peer-reviewed original research without offering any empirical scientific evidence that challenges its findings. Instead they cite non-peer-reviewed opinion pieces containing inaccuracies and unsubstantiated personal views. This tactic is not justified by normal scientific standards, though it is commonly used in attempts to suppress critical research on GMOs.

### 4. As evidence of GMO safety, Nicolia and colleagues cite animal feeding studies that are too short to show long-term health effects

The longest studies cited are 90-day studies on rodents, which are the longest toxicological tests that the industry generally carries out.[73,74] In light of Séralini's and Malatesta's work, cited above, it is clear that 90-day studies are insufficient.

Short-term studies are useful for ruling out acute toxicity, but do not provide valid evidence regarding the long-term safety of GMOs. Effects that take a long time to show up, such as cancer, severe organ damage, compromised reproductive capacity, teratogenicity, and premature death, can be reliably detected only in long-term and multigenerational studies. Nicolia and colleagues seem unaware of this limitation of 90-day studies.

### 5. Nicolia and colleagues ignore the problem of non-substantial equivalence of GM crops and falsely claim a consensus on this hotly contested topic

GM approvals worldwide are based on the assumption by industry and regulators that, if a GMO is substantially equivalent to its closest non-GM relative, based on measurements of the levels of a few basic components such as protein, carbohydrate, and fat, then it does not need rigorous safety testing.

More detailed analyses, particularly cutting-edge molecular profiling investigations, often show that GM crops are not substantially equivalent to the non-GM comparator, revealing that the assumption of substantial equivalence is false. Yet Nicolia and colleagues completely overlook this issue.

Because of their chosen date range, Nicolia and colleagues omit a 1996 compositional analysis by Monsanto authors revealing that (contrary to these authors' claim) the company's GM glyphosate-tolerant soybean is not substantially equivalent to the non-GM isogenic comparator crop. The level of trypsin inhibitor, a major allergen, was significantly increased in the GM soybean.[75]

A study which is too recent to be included in the Nicolia review compared the nutritional composition of GM, industrially grown non-GM, and organic soybean lines. The study found that GM soybeans, claimed to be substantially equivalent to non-GM comparators by industry and regulators, could, with 100% accuracy, be differentiated from non-GM. It was also reported that the GM soybeans contained high levels of glyphosate, whereas no such residues were present in the non-GM or organic soybeans. Also the nutritional profile of organic soybeans was superior,[76] though no comparisons with organic crops are made in the regulatory process for GM crops.

While Nicolia and colleagues could not have included this study in their review, there is no excuse for ignoring the principle that any scientifically based assessment of equivalence would take into account the residues of the pesticide that the GM crop is engineered to be grown with.

Another revealing study that did fall within Nicolia and colleagues' chosen date range is included in the supplementary list of 1,700 studies but is not discussed in the review. The study found that a commercialized GM maize, MON810, had a markedly different profile of proteins compared with the isogenic non-GM counterpart when grown under the same conditions.[77] Such differences can result in unexpected toxicity or allergenicity. Another compositional analysis showing that the GM crop tested was not substantially equivalent to the non-GM comparator crop[78] was similarly ignored in the review, though included in the supplementary list of 1,700 studies.

As well as ignoring evidence that specific GM crops are not substantially equivalent to their isogenic non-GM comparators, Nicolia and colleagues incorrectly claim that there is a "consensus" about the validity of the concept of substantial equivalence in risk assessment. To justify this claim, they cite two papers[6,7] co-authored by Esther Kok,[6] an affiliate of the GM industry-funded group, the International Life Sciences Institute (ILSI), and Harry Kuiper, who during that time was head of EFSA's GMO Panel. Kuiper was also was a long-time affiliate of ILSI, including after starting work at EFSA.[79]

This choice of authority is problematic and serves to illustrate the lack of consensus around the substantial equivalence concept. The independent research organization Testbiotech documented evidence showing that Kok collaborated, via ILSI, with GMO companies and with EFSA's Kuiper to promote the industry-friendly concept of substantial equivalence and insert it into EU regulations on GMOs.[79] Testbiotech and the civil society organization Corporate Europe Observatory asserted that this collaboration may have violated EU rules on EFSA's independence. They filed a complaint with the EU Ombudsman against EFSA about the legacy of GM industry-crafted rules that Kuiper was allowed to build at the agency.[80] A Member of the European Parliament, Bart Staes, also raised a Parliamentary question on the issue with the EU Commission.[81]

The Ombudsman ruled against Testbiotech's complaint on a technicality, because it related to events before the current EFSA rules on conflicts of interest were put into place and thus at the time there were no rules for EFSA to violate.[82] However, in this ruling the Ombudsman failed to address the fact that EU regulations in place since 2002 require EFSA experts to act independently.[83]

The concept of substantial equivalence has been heavily criticized and challenged from the beginning by independent scientists because it has never been scientifically or legally defined.[30,38,79,84,85,86,87,88] In practice, there can be substantial compositional differences in the GMO compared with the non-GM comparator crop, but the GMO developer company still declares the GMO as "equivalent" and the regulators accept the designation.

Nicolia and colleagues admit that the literature on substantial equivalence is mostly composed of papers produced by GMO companies, but fail to draw the obvious conclusion that only an appearance of consensus has been generated due to the dominance in the literature of this biased group of authors.

In 2013 the EU passed a regulation establishing criteria for the EU for equivalence in compositional analyses of GMOs,[89] but these will not be applied to GMOs already approved or even to those in the approvals pipeline. According to the biologist Dr Frederic Jacquemart, president of the civil society group Inf'OGM and a member of France's High Council for Biotechnology, no GMO that has been already approved in Europe or that is in the pipeline for approval would meet the criteria for equivalence.[90]

The criteria established by EU law are limited in applicability, since they do not define criteria for equivalence relevant to toxicology studies. Thus the current situation, in which significant differences are often found in GM-fed animals but are dismissed by the industry and/or regulators as not biologically meaningful,[38,91] will continue.

Nicolia and colleagues' claim of consensus on the concept of substantial equivalence is not consistent with the facts. It remains a contentious issue.

## 6. Nicolia and colleagues include animal feeding studies funded by the GM developer company, without acknowledging the problem of funding bias

Nicolia and colleagues do not acknowledge funding bias in industry-led animal feeding studies. For example, included in Nicolia and colleagues' supplementary list of 1,700 papers are Monsanto's rat feeding studies on its GM maize products, which concluded the maize varieties were safe.[73,74,92] Nicolia and colleagues do not discuss the findings of these studies, but simply accept the Monsanto authors' conclusions of safety, which have proved controversial. Statistical re-analyses of the data by industry-independent scientists revealed signs of toxicity to multiple organ systems of GM maize-fed rats, particularly to the liver and kidney.[38,91,93]

Nicolia and colleagues' approach, with its indiscriminate treatment of a long list of studies, contrasts strikingly with the discriminating approach of two other peer-reviewed literature reviews. These focused on and evaluated those studies which specifically examine the food safety and nutritional value of GM foods on the basis of primary experimental evidence. These studies came to quite different conclusions from those of Nicolia and colleagues regarding the safety of GM foods.

The first of these reviews, by Domingo and colleagues (2011), focused on animal feeding studies on GMOs. The authors found that studies reporting that GMOs were safe were mostly carried out by researchers affiliated with the GMO developer company wishing to commercialize the GMO, whereas papers that raised "sometimes serious concerns" were authored by scientists independent of industry.[15]

While Nicolia and colleagues cite this paper, they omit to mention this important conclusion. Instead they only cite Domingo and colleagues' incidental remark that industry has improved its record on "transparency" by publishing the results of its animal feeding studies in peer-reviewed journals – a point that is of secondary importance to the food safety of GMOs.

A second review examined studies on human and animal health risks of GMOs and looked more closely at the question of funding bias. The review confirmed Domingo and colleagues' observation, finding that studies by authors with financial or professional conflicts of interest with the GMO industry[60] were strongly associated with conclusions that the GMO tested is as safe and/or nutritious as the non-GM comparator. This review was completely ignored by Nicolia and colleagues, being omitted even from their supplementary list of 1,700 studies.

### 7. Nicolia and colleagues misrepresent the scientific evidence and the debate on microRNAs, with the result that risks and uncertainties are downplayed

In recent years, an issue that has proven as controversial as substantial equivalence is regulators' failure to assess the risks of microRNAs (miRNAs) in GMOs. MicroRNAs are small RNA messenger molecules that regulate gene expression, resulting in silencing (switching off) gene function.

A study (Zhang et al. 2011) found that plant miRNAs survived cooking and degradation in the digestive tract, were found in the blood and tissues of mammals that had eaten them, and were biologically active in those mammals, affecting gene expression and the functioning of important processes in the body. While not on GM plants, the study showed that miRNAs from plants could exercise a direct physiological effect on humans and animals that eat them, crossing not only the species barrier but the barrier separating the plant and animal kingdoms.[94]

Nicolia and colleagues discuss the results of Zhang and colleagues and other papers on the same topic, but conclude reassuringly that "RNA in general" has a "history of safe use", since it is a normal component of the diet. However, this argument fails to acknowledge the major differences in structure and function of RNA molecules that are produced in the cells of an organism. It also ignores the fact that consumers are exposed to novel miRNAs when they eat certain GMOs.

GMOs are being engineered to make novel miRNA molecules that have never before been in the food supply, such as molecules that can kill insects or silence gene function. These GM miRNA molecules emphatically do not have a "history of safe use".

The conclusion of Nicolia and colleagues only addresses the chemical nature of RNA. It is not just the chemical nature of RNA that poses risks or induces the intended effect, but the instructions or information that the RNA molecule contains – in other words, what it can do.

Professor Jack Heinemann, a molecular biologist with expertise regarding miRNA risks and an author of peer-reviewed studies on the topic,[95,96] commented: "There is no basis for extrapolating the safety of novel dsRNA [double-stranded RNA, a type of miRNA] molecules from the history of safe use of dsRNA molecules in the cells of plants, animals, fungi and microorganisms that we eat.

"This is the key distinction: the adverse effects that might arise from dsRNA are determined by the actual sequence of nucleotides in the molecule (sequence-determined risks) and not the chemical nature of RNA. While there are also sequence-independent risks that should not be ignored, there is a difference between the sequence of novel dsRNA molecules in GM crops and those in nature, and that is why arguments about all dsRNAs being safe are dangerously flawed."[97]

A 2011 study by Heinemann and colleagues refutes the "history of safe use" argument with the example of a Monsanto GM maize engineered to resist the corn rootworm pest. The corn rootworm has always eaten maize roots and maize roots contain RNA, including forms of dsRNA. However, when Monsanto introduces a novel dsRNA of a specific sequence into the cells of the plant, the corn rootworm eating that RNA dies. The rootworm's long history of using conventional maize as a source of food does not protect it from the toxic effects of the novel dsRNA.[95]

Heinemann and colleagues emphasized that it is not valid to conclude that miRNA in a GM plant is as safe as miRNA molecules that might be present in non-GM crops that have long been in the human diet.

For example, rice has a long history of safe use in the human diet. If rice produced a miRNA that was toxic, it would have been screened out of our diets thousands of years ago. The authors commented that the safe use of a conventional plant with miRNAs does not extend to its GM counterpart any more than a scrapie-infected animal is as safe as a healthy animal.[95] Chemically, there is no difference between the two animals, since both healthy and scrapie-infected animals contain the protein that prions, the infectious agent for scrapie, are made of (PrP). What makes one animal sick and the other healthy is the difference in the way the protein is folded. If it is misfolded, the animal will be scrapie-infected. The form of the protein determines its function – and the difference in function will determine whether the animal lives a healthy life or dies prematurely of a serious illness.

Nicolia and colleagues include Heinemann's 2011 study containing the corn rootworm example[95] in their list of 1,700 studies, but ignore its findings in their review.

Even if Nicolia and colleagues failed to read the paper, they should be aware of the risks of GM crops engineered to contain dsRNA molecules, since a media controversy had erupted around the topic as early as September 2012. The debate followed the publication by Heinemann and colleagues of a report on the potential health risks of a GM wheat engineered to produce dsRNA molecules, which is being developed by the Australian research institute CSIRO.[98]

Such was the resulting public concern that the Science Media Centre felt it necessary to publish quotes from scientists dismissing Heinemann and colleagues' report.[99] Unlike Heinemann, however, the quote-providers had never published papers in scientific journals on the topic of miRNA risks. They also had major undeclared conflicts of interest with the GMO industry, as reported by GMWatch.[100]

Nicolia and colleagues' conclusion that miRNA molecules in GM plants have a "history of safe use" cannot be justified on the basis of current evidence, and their failure to address the scientific controversy around the topic is difficult to justify by any objective standards.

### 8. Nicolia and colleagues ignore important findings of adverse environmental and agronomic impacts from GMOs

Impacts neglected in the Nicolia review include toxic effects of GM Bt crops on non-target organisms, the spread of glyphosate-resistant superweeds, the GM contamination of native varieties of plants, and the effects on monarch butterflies of the spread of glyphosate-tolerant GM crops.

In line with their common practice in other areas of their paper, Nicolia and colleagues include in this section studies documenting adverse environmental and agronomic impacts of GM crops in their list of 1,700 articles,[31,101,102,103] but then ignore the findings in their review paper. This practice serves to inflate the number of studies that they claim document the safety of GMOs, catalogued in their list of 1,700 articles, while failing to disclose the fact that these papers actually document adverse effects.

Examples include studies confirming GM contamination of native Mexican maize varieties,[104,105] an issue of concern and debate even today, because Mexico is the genetic centre of origin for maize; and a study concluding that the spread of glyphosate-tolerant GM crops and consequent over-use of glyphosate herbicides has caused intense selection pressure, resulting in the evolution of many resistant weeds.[31]

Omitted even from their list of 1,700 articles is a 2012 study that was highly critical of GM herbicide-tolerant crops. The study found that "Agricultural weed management has become entrenched in a single tactic – herbicide-resistant crops – and needs greater emphasis on integrated practices that are sustainable over the long term". The study's authors were not optimistic about the industry's response to herbicide-resistant weeds – engineering crops to resist multiple herbicides, since "crops with stacked herbicide resistance are likely to increase the severity of resistant weeds… these crops will facilitate a significant increase in herbicide use, with potential negative consequences for environmental quality." The researchers concluded that "The short-term fix provided by the new traits will encourage continued neglect of public research and extension in integrated weed management."[106]

Nicolia and colleagues' treatment of the toxic effects of GM Bt crops on non-target organisms is an extreme example of biased and misleading reporting. They claim, "The literature considering the effects on biodiversity of non-target species (birds, snakes, non-target arthropods, soil macro and microfauna) is large and shows little or no evidence of the negative effects of GE crops."

But they only reach this conclusion by ignoring some important papers and misrepresenting the evidence in others. Assisted by their 10-year cut-off date, they misleadingly report a major scientific controversy around the effects of Bt toxins on non-target organisms.

The controversy began in the mid-1990s, when studies by a team led by Dr Angelika Hilbeck showed that Bt toxins of microbial and GM Bt plant origin caused lethal effects in the larvae of the green lacewing, a beneficial insect to farmers, when administered directly or via prey into their gut using a protocol that ensured ingestion.[107,108,109] A 2009 study by a different team also led by Hilbeck (Schmidt and colleagues, 2009) found that Bt toxins caused increased mortality in the larvae of another beneficial insect, the ladybird, even at the lowest concentration tested.[101] Ladybirds are useful to farmers because they devour pests such as aphids and disease-causing fungi.

Based on this study and over 30 others, in 2009 Germany banned the cultivation of Monsanto's GM Bt maize MON810,[110] which contains one of the Bt toxins that Hilbeck's team found to be harmful to non-target insects.[101]

Nicolia and colleagues included the Hilbeck ladybird study[101] in their list of 1,700 articles, but ignored it in their main review paper.

Rebuttal studies were carried out, apparently to disprove the findings of Hilbeck's teams and undermine the scientific basis of the German ban. These studies affirmed the safety of Bt toxins for lacewings[111,112,113] and ladybirds.[114,115,116] The authors of the rebuttal experimental study on ladybirds (Alvarez-Alfageme and colleagues, 2011) found no ill effects on ladybird larvae fed on Bt toxins and said that the "apparent harmful effects" found by Schmidt and colleagues were due to "poor study design and procedures".[114]

Nicolia and colleagues included several of these rebuttal studies in their list of 1,700. However, they failed to cite follow-up studies by Hilbeck and colleagues that proved that the rebuttal studies were poorly designed and executed. Hilbeck and colleagues demonstrated that changes in the testing protocols were the underlying reasons for failing to find the same results in the rebuttal studies for both non-target organisms: the green lacewing and the ladybird.

In one follow-up study, Hilbeck and colleagues showed that the lacewings in the rebuttal study could not have ingested the Bt toxins in the form provided by the researchers, coated onto moth eggs, as their mouthparts are formed in such a way as to make ingestion impossible.[110] This is equivalent to testing an orally administered drug for side-effects by applying it to the skin, ensuring that none of the human subjects actually swallows the drug.

For years, the US and EU regulatory agencies accepted these inadequate studies as valid evidence of safety to non-target organisms until the US EPA finally admitted that the study protocol was unsuited to lacewings. In other words, this supposed biosafety test was incapable of detecting toxic effects even when they occurred. However, the EPA did not retrospectively give credit to studies that had ensured the proper ingestion of the Bt toxin or reconsider its verdict of safety for lacewings. Instead the EPA chose to continue to ignore these inconvenient findings and simply suggested that this inconveniently susceptible species be replaced in future testing programs with an insect that Hilbeck's team had already found to be insensitive to Bt toxins. The EU's EFSA, for its part, has not recognized the inadequacy of these biosafety tests in any of its opinions to date.[110]

Hilbeck and colleagues also did further experiments[110,117] to test the claims of the authors of the rebuttal experimental study on ladybird larvae (Alvarez-Alfageme and colleagues, 2011[114]). Again, the results of the rebuttal study were shown to be the consequence of their altered and inadequate protocols. Alvarez-Alfageme's team only dosed the ladybird larvae with Bt toxins in sugar solution once per 24-hour period in each of the four larval stages and then allowed them to recover by feeding them normal food. Schmidt and colleagues, on the other hand, had exposed the larvae continuously over 9–10 days[101] – a different and arguably more environmentally realistic scenario.

Hilbeck and colleagues repeated Alvarez-Alfageme's methodology – and found that the water in the sugar solution in which the Bt toxin had been fed completely evaporated after a few hours, making it unlikely that the larvae in Alvarez-Alfageme's experiment had, as claimed, even ingested the Bt toxin. When Hilbeck and colleagues made the Bt toxins available continuously in a way that the ladybird larvae could access, a lethal effect on the larvae was found.[117]

In a commentary on the controversy, Hilbeck and colleagues criticized the confrontational tone, unscientific elements, and "concerted nature" of the three studies that attacked Schmidt's initial findings. The authors noted that the "dogmatic 'refutations'" and "deliberate counter studies" that routinely appear in response to peer-reviewed results on potential harm from GMOs were also a feature of the debate on risks of tobacco, asbestos, the controversial plastic food packaging chemical bisphenol A, and mobile phones.[110]

Hilbeck and colleagues also criticized the "double standards" that led EFSA to apply excessive scrutiny to papers that draw attention to the risks of GM crops while overlooking obvious deficiencies in studies that assert the safety of GM crops.[110]

Unaccountably, Nicolia and colleagues omit the two confirmatory empirical studies by Hilbeck's team[110,117] even from their list of 1,700 studies, though they fall within their chosen date range. They entirely ignore the scientific demolition by Hilbeck's team of the flawed rebuttal studies.

Instead Nicolia and colleagues conclude the debate on GM Bt crops' effects on non-target arthropods by citing two reviews with favorable conclusions on Bt crop safety. The first, by Gatehouse and colleagues, conceded that "some negative effects do occur in predatory arthropods and parasitoids following exposure to GM crops and/or the insecticidal proteins they express". However, Gatehouse and colleagues convinced themselves of the desirability of GM insecticidal crops by assuming that they were replacing systems reliant on chemical insecticides: "The relatively few negative effects that have been recorded are invariably substantially less than would have occurred under traditional pesticide-reliant regime".[118]

Gatehouse and colleagues failed to take into account such vital factors as the number of farmers who grow crops using no or minimal pesticides in agroecological or integrated pest management systems; the highly variable use of pesticides in years of light or heavy pest pressure; the increasing resistance of pests to GM Bt crops and the emergence of secondary pests, forcing farmers to return to chemical insecticides; and the routine use of insecticidal seed treatments even on GM Bt crop seeds, which are aimed at dealing with the pests not controlled by Bt toxins.

Crucially, Gatehouse and colleagues do not cite any data directly comparing the ecological impacts of planting GM Bt crops with the impacts of any alternative pest management regime. They simply choose as the comparator for Bt crops a "pesticide-reliant regime". Gatehouse and colleagues do not define this worst-case regime or analyze how typical it is in the context of usual farming practices – a serious omission, given that in the mid-1990s, before the advent of GM Bt insecticidal maize, less than a third of all US maize had any insecticides applied to it.[119] On the basis of the undefined "pesticide-reliant regime", Gatehouse and colleagues conclude that GM Bt crops are the lesser of the two evils.[118]

One meta-analysis of studies on the effects of GM Bt crops on non-target invertebrates used fields with no insecticide applications as the comparator – and reached a conclusion on Bt crops diametrically opposed to that of Gatehouse and colleagues. The meta-analysis demonstrated a significant reduction of non-target invertebrates in Bt maize varieties expressing the Cry1Ab protein generally, and for MON810 maize (the sole GM maize currently being grown commercially in Europe) specifically, compared with fields with no insecticides applied. When non-GM fields were sprayed with insecticides, there was a higher invertebrate abundance in Cry1Ab maize generally, but not in MON810.[120] This shows that for GM crops generally and for MON810 specifically, opposite conclusions can be reached from the same evidence base, depending on which comparator is used.

One lesson that can be drawn from this meta-analysis is that deciding which questions to address in scientific research should not be left to scientists alone, and certainly not to biotechnology and agrochemical multinationals. This role belongs to society as a whole, based on its environmental protection and food production goals.

The second review cited by Nicolia and colleagues to dismiss GM Bt crops' effects on non-target arthropods is by Shelton and colleagues and was published in 2009.[121]

Unfortunately for the credibility of the Nicolia review, Shelton and colleagues relied heavily on the studies discussed above, which used methodologies that Hilbeck and colleagues subsequently exposed as flawed and inadequate.[110] By giving the final word on this issue to Shelton and colleagues and failing to address the followup experiments by Hilbeck's team, Nicolia and colleagues misrepresent the state of scientific knowledge and its surrounding controversy.

### 9. Nicolia and colleagues sidestep the debate about monarch butterflies

Monarch butterflies are viewed as an important indicator species against which to gauge the impacts of GM crops on the numerous non-target insect species that live in the agricultural environment where GM crops are used. Yet Nicolia and colleagues ignore the scientific debate about the effects of GM crops on monarch butterflies, which has concluded badly for GMO proponents.

An initial laboratory study by Losey and colleagues conducted in 1999, outside Nicolia and colleagues' chosen date range, found that monarch butterfly larvae exposed to GM Bt maize (Event Bt11) pollen suffered higher mortality rates than larvae exposed to non-GM pollen.[122] Losey's study was criticized for using allegedly unrealistic doses of Bt pollen, but a follow-up study by Jesse and Obrycki (2000, also outside Nicolia and colleagues' date range) using realistic doses also found lethal effects from Bt176 and Bt11 maize pollen.[123]

A different team of researchers (Hellmich and colleagues, 2001) did further experiments and found significant growth inhibition and increased mortality in monarch larvae exposed to two out of four types of purified Bt toxin (Cry1Ab and Cry1Ac). However, the only Bt maize pollen that consistently negatively affected monarch larvae was from Bt176 maize, a variety that was withdrawn by the GM industry after it had already been cultivated for several years. The authors criticized the findings of Jesse and Obrycki on the grounds that the pollen on which the larvae were fed may have been contaminated with maize anthers, since maize anthers contain much higher concentrations of Bt toxin than does the pollen. The authors questioned whether monarch larvae in field conditions would be exposed to fractured anthers or could consume whole anthers.[124]

Jesse and Obrycki followed up with further experiments, published in 2004, within Nicolia and colleagues' date range. Nevertheless, Nicolia and colleagues excluded these studies from their list. Jesse and Obrycki's followup studies found a consistent trend of increased mortality when monarch larvae were exposed to Bt11 maize pollen and anthers naturally deposited on milkweed plants within a field. The researchers observed monarch larvae feeding on anthers that had become stuck to milkweed plants with moisture from rain and dew, confirming that monarch larvae are exposed to anthers. The researchers noted that "anthers do not represent experimental contamination as suggested by Hellmich and co-authors… but are a potential source of Bt toxin that needs to be considered". They concluded that increases in mortality of monarch larvae in Bt maize fields due to the deposition of transgenic Bt anthers and pollen on milkweed "could harm monarch populations".[125]

A review of the scientific literature on GM Bt crops and monarch butterflies (also not included in Nicolia and colleagues' list) concluded with regard to Jesse and Obrycki's 2004 study that while the trend observed did not meet the confidence level usually accepted in ecological studies, the results showed that "multiple year field studies are needed to quantify the potential effects of wide scale planting of Bt maize on monarch larvae, and that it is important to examine within-field mortality resulting from deposition of maize tissues that include pollen and anthers."[126]

A study of chronic exposure by Dively and colleagues (2004), included in Nicolia and colleagues' supplementary list but not addressed in their review paper, found that 23.7% fewer monarch larvae exposed to pollen of the Bt maize varieties Bt11 and MON810 survived to adult stage than larvae exposed to non-Bt maize pollen. However, Dively and colleagues minimized the importance of these findings, concluding that Bt maize would only cause 0.6% additional mortality in monarch populations.[127]

The debate over the effects of GM Bt maize pollen on monarch butterflies should have at least led Nicolia and colleagues to conclude that there is no consensus on the safety of Bt crops to non-target organisms, instead of claiming, as they did, that there was "little or no evidence" of "negative effects".

The scientific debate on whether Bt crops do or do not harm monarchs took a different direction in 2012–13 after worrying new facts emerged. This time, it was not Bt crops that were named as the culprit, but the increased use of glyphosate herbicide due to the spread of GM glyphosate-tolerant crops.

First, the monarch census for the winter of 2012-13 found that the population of North American monarch butterflies over-wintering in Mexico was at the lowest level ever measured, with a 59% decline over the previous year. The cause of the sharp drop in population was named by insect ecologist and founder of the conservation program Monarch Watch Orley R. "Chip" Taylor as the spread of glyphosate-tolerant GM crops and the resulting over-use of glyphosate herbicides. The glyphosate spraying had killed the milkweed that was the prime food source for monarchs.[128]

Second, Taylor's view was confirmed by a peer-reviewed study (Pleasants and Oberhauser, 2012) – absent from Nicolia and colleagues' list of 1,700. The study found a 58% decline in milkweeds in the US Midwest and an 81% decline in monarch butterfly populations in the Midwest from 1999 to 2010. This loss occurred in parallel with the increased planting of GM glyphosate-tolerant maize and soybeans and consequent increased use of glyphosate herbicide to control weeds, including milkweed. Pleasants and Oberhauser conclude that a loss of agricultural milkweeds is a major contributor to the decline in the monarch population.[129]

An entirely unaddressed question to date remains what effect stacked multiple-GM-trait Bt insecticidal and herbicide-tolerant crops will have on the few monarch larvae that remain in the Midwest. These crops, for instance Smartstax maize, contain unprecedentedly high levels of several Bt toxins.[130]

Nicolia and colleagues' review does not even mention monarch butterflies. However, their list of 1,700 studies does contain a 2002 article on Bt crops and monarchs by Gatehouse and colleagues, which concluded that the commercial large-scale cultivation of Bt maize hybrids did not pose "a significant risk" to monarch populations.[131]

In summary, Nicolia and colleagues selectively cite the literature on the impact of GM Bt crops on monarch butterflies and fail to consider the recent compelling research findings showing negative effects on monarch habitats of GM glyphosate-tolerant crops.

## 10. Nicolia and colleagues fail to demonstrate consensus on GMO safety and themselves acknowledge that there is "intense debate" regarding the safety of GMOs

Though their expressed aim is to "catch the scientific consensus" on GMO safety, Nicolia and colleagues, unlike those who cite the Nicolia review to promote GMOs, do not conclude that there is a consensus on the topic. Instead they accurately note that there is "intense debate". Given this admission, it is inappropriate for GMO proponents to use the Nicolia review as evidence of scientific consensus regarding the safety of GMOs.

However, Nicolia and colleagues also claim, "The scientific research conducted so far has not detected any significant hazard directly connected with the use of GM crops." In making this claim, they are ignoring or discounting a large and growing body of evidence of harm from peer-reviewed research papers (discussed above), including papers cited in their list of 1,700 articles.

In 2013 nearly 300 international scientists signed a joint statement saying that there is "No scientific consensus on GMO safety" and that some existing studies "give serious cause for concern".[132]

## 11. Nicolia and colleagues make unsubstantiated claims

Many claims made by Nicolia and colleagues are unsubstantiated. For example, they state that GM crops could be an "important tool" in producing healthy food with reduced environmental impacts and inputs, but offer no explanation as to how this can be achieved or evidence in support of this claim.

They also claim that the EU Commission report, "A decade of EU-funded GMO research", concluded that GM plants do not pose higher risks than conventionally bred plants. But the EU Commission report contains very little actual evidence evaluating whether GM foods are safer or more risky than non-GM foods. A few animal feeding studies were carried out and cited in the report, but none were on commercialized GM crops. In fact, these studies found unexpected problems with the GM food tested (see Myth 3.4).

Therefore claims that the report shows that GM plants are no riskier than non-GM foods are not evidence-based and are contrary to the small amount of toxicological data gathered by the studies performed under this research programme.

## Historical background: The "big list of studies" tactic

The Nicolia review is the latest of several similar long lists of studies collated by GMO proponents and purporting to prove that GMOs are safe. Just like the Nicolia review, however, these lists of studies do not prove the safety of GMOs and in fact provide evidence of actual or potential hazards and omit findings of harm.

Another much-promoted list is on the Biofortified website.[133] Yet another list of 600+ hundred studies collected by "GMO Pundit" David Tribe is claimed to "document the general safety and nutritional wholesomeness of GM foods and feeds."[134]

But closer examination of Tribe's list reveals:

- Most of the studies cited are not safety studies on GM foods. In other words, they do not examine in detail the health effects in animals fed GM foods. Some are compositional studies that compare the levels of certain major nutrients, such as fat or protein, in a GM crop with levels in a non-GM crop. Others are feed conversion studies that measure how efficiently a livestock animal converts GM feed into a food product, such as meat or milk, over a short-term period.[135]
- Some are short-term studies performed by industry, which are not long enough to reliably detect long-term health effects.[73]
- Many of the studies, on examination of the actual data, turn out to show problems with GM foods. These include unintended differences in a GM food compared with the non-GM counterpart and harmful effects in animal feeding trials.[38,23,24]

The Biofortified list suffers from similar problems. As is clear from the analysis above, the Nicolia review falls into the same pattern of disingenuous use of scientific research to support misleading claims.

In the field of pro-GMO lobbying, the Nicolia review has taken the place of the Snell review of 24 supposedly long-term animal feeding studies documenting the safety and nutritional wholesomeness of GM foods.[136] The Snell review, however, suffers from serious shortcomings, which are discussed in detail in Myth 3.1.

## Conclusion

Nicolia and colleagues' list of 1,700 articles does not show that GM foods and crops are safe and in fact provides evidence that some GMOs are unsafe. The majority of the articles are irrelevant or tangential to assessing the safety of commercialized GM foods and crops for human and animal health or for the environment. They include opinion and advocacy pieces on GMO regulation and safety assessment, animal production studies of interest to the agriculture industry, and studies on consumer perception of GM foods. Many of the articles demonstrate that there is no scientific consensus on the safety, efficacy or desirability of GM technology in food production.

Claims that the list of studies compiled by Nicolia and colleagues shows GMO safety rely for their persuasiveness on the assumption that no one will have the time to read the studies cited or notice the omissions.

Given the economic incentives at work in the GMO field, there is an understandable tendency among GM proponents to artificially inflate the evidence purporting to show that GMOs are safe. However, misrepresenting scientific studies to shore up a conclusion that is not justified by the data is unethical and will in the long term be corrosive to public trust in science.

Evidence-based debate is the lifeblood of science and is fulfilling for sincere scientists on both sides of a controversy, because it furthers the evolution of scientific knowledge. However, it should not be necessary to expend time and energy countering misleading claims made in the scientific literature that appear to be intended to further interests other than the evolution of scientific knowledge.

It takes few words and little effort to make a misleading claim, but many more words, time, and effort to counter such a claim. That much is demonstrated by this analysis, which, although long, is far from comprehensive and deals only with a few of the many misleading claims and serious omissions of Nicolia and colleagues' review.

The presence in the scientific literature of papers such as the Nicolia review represents a failure of the peer review process. Each time the authors cited a specific paper to support a claims or conclusions, the editors and peer reviewers should have asked them to identify the relevant supporting empirical data (derived from actual testing using appropriate methodologies), justifying the inclusion of the citation.

Traditionally, this is the standard of evidence upon which scientific debate is based. When editors and peer reviewers accept less, the result is that a publication enters the scientific literature that fails to meet minimum acceptable academic standards.

## References


1. Nicolia A, Manzo A, Veronesi F, Rosellini D. An overview of the last 10 years of genetically engineered crop safety research. Crit Rev Biotechnol. 2013:1-12. doi:10.3109/07388551.2013.823595.
2. Bailey P. GMOs are nothing to fear. US News & World Report. http://www.usnews.com/opinion/articles/2013/11/04/scientific-evidence-doesnt-show-gmos-are-harmful. Published November 4, 2013.
3. Wendel J. With 2000+ global studies confirming safety, GM foods among most analyzed subjects in science. Genetic Literacy Project. http://bit.ly/1bjhPQG. Published October 8, 2013.
4. Taylor M, Hartnell G, Lucas D, Davis S, Nemeth M. Comparison of broiler performance and carcass parameters when fed diets containing soybean meal produced from glyphosate-tolerant (MON 89788), control, or conventional reference soybeans. Poult Sci. 2007;86(12):2608-2614. doi:10.3382/ps.2007-00139.
5. Bakke-McKellep AM, Sanden M, Danieli A, et al. Atlantic salmon (Salmo salar L.) parr fed genetically modified soybeans and maize: Histological, digestive, metabolic, and immunological investigations. Res Vet Sci. 2008;84:395-408.
6. Kok EJ, Keijer J, Kleter GA, Kuiper HA. Comparative safety assessment of plant-derived foods. Regul Toxicol

Pharmacol. 2008;50:98-113. doi:10.1016/j.yrtph.2007.09.007.
7. Kok EJ, Kuiper HA. Comparative safety assessment for biotech crops. Trends Biotechnol. 2003;21:439–444.
8. Chassy BM. Food safety evaluation of crops produced through biotechnology. J Am Coll Nutr. 2002;21(3 Suppl):166S-173S.
9. Konig A, Cockburn A, Crevel RW, et al. Assessment of the safety of foods derived from genetically modified (GM) crops. Food Chem Toxicol. 2004;42:1047-88. doi:10.1016/j.fct.2004.02.019.
10. International Life Sciences Institute (ILSI). Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology, prepared by a task force of the ILSI International Food Biotechnology Committee. Compr Rev Food Sci Food Saf. 2004;3:38–104.
11. Freese W, Schubert D. Safety testing and regulation of genetically engineered foods. Biotechnol Genet Eng Rev. 2004:299-324.
12. Kroghsbo S, Madsen C, Poulsen M, et al. Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. Toxicology. 2008;245:24-34. doi:10.1016/j.tox.2007.12.005.
13. Poulsen M, Kroghsbo S, Schroder M, et al. A 90-day safety study in Wistar rats fed genetically modified rice expressing snowdrop lectin Galanthus nivalis (GNA). Food Chem Toxicol. 2007;45:350-63. doi:10.1016/j.fct.2006.09.002.
14. Magnusson MK, Koivisto Hursti U-K. Consumer attitudes towards genetically modified foods. Appetite. 2002;39(1):9-24. doi:10.1006/appe.2002.0486.
15. Domingo JL, Bordonaba JG. A literature review on the safety assessment of genetically modified plants. Env Int. 2011;37:734–742.
16. Malatesta M, Caporaloni C, Gavaudan S, et al. Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. Cell Struct Funct. 2002;27:173–80.
17. Malatesta M, Caporaloni C, Rossi L, et al. Ultrastructural analysis of pancreatic acinar cells from mice fed on genetically modified soybean. J Anat. 2002;201:409–15.
18. Malatesta M, Biggiogera M, Manuali E, Rocchi MBL, Baldelli B, Gazzanelli G. Fine structural analyses of pancreatic acinar cell nuclei from mice fed on genetically modified soybean. Eur J Histochem. 2003;47:385–388.
19. Malatesta M, Boraldi F, Annovi G, et al. A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008;130:967–977.
20. Vecchio L, Cisterna B, Malatesta M, Martin TE, Biggiogera M. Ultrastructural analysis of testes from mice fed on genetically modified soybean. Eur J Histochem. 2004;48:448-54.
21. Kilic A, Akay MT. A three generation study with genetically modified Bt corn in rats: Biochemical and histopathological investigation. Food Chem Toxicol. 2008;46:1164–70. doi:10.1016/j.fct.2007.11.016.
22. Dona A, Arvanitoyannis IS. Health risks of genetically modified foods. Crit Rev Food Sci Nutr. 2009;49:164–75. doi:10.1080/10408390701855993.
23. Ewen SW, Pusztai A. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet. 1999;354:1353-4. doi:10.1016/S0140-6736(98)05860-7.
24. Fares NH, El-Sayed AK. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. Nat Toxins. 1998;6:219-33.
25. Waltz E. Battlefield. Nature. 2009;461:27–32. doi:10.1038/461027a.
26. Waltz E. Under wraps – Are the crop industry's strong-arm tactics and close-fisted attitude to sharing seeds holding back independent research and undermining public acceptance of transgenic crops? Nat Biotechnol. 2009;27(10):880–882. doi:10.1038/nbt1009-880.
27. Prescott VE, Campbell PM, Moore A, et al. Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenicity. J Agric Food Chem. 2005;53:9023–30. doi:10.1021/jf050594v.
28. ANSES (French Agency for Food Environmental and Occupational Health & Safety). Avis de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail relatif à l'analyse de l'étude de Séralini et al. (2012) "Long term toxicity of a ROUNDUP herbicide and a ROUNDUP-tolerant genetically modified maize."; 2012. Available at: http://www.anses.fr/en/content/anses-highlights-weaknesses-study-s%C3%A9ralini-et-al-recommends-new-research-long-term-effects.
29. ANSES (French Agency for Food Environmental and Occupational Health & Safety). Opinion concerning an analysis of the study by Séralini et al. (2012) "Long term toxicity of a ROUNDUP herbicide and a ROUNDUP-tolerant genetically modified maize." 2012. Available at: http://www.anses.fr/sites/default/files/files/BIOT2012sa0227EN.pdf.
30. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
31. Duke SO, Powles SB. Glyphosate-resistant crops and weeds: Now and in the future. AgBioForum. 2009;12(3&4):346–357.
32. Sakamoto Y, Tada Y, Fukumori N, et al. [A 104-week feeding study of genetically modified soybeans in F344 rats]. Shokuhin Eiseigaku Zasshi J Food Hyg Soc Jpn. 2008;49:272-82.
33. Aris A, Leblanc S. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Reprod Toxicol. 2011;31.
34. Aris A. Response to comments from Monsanto scientists on our study showing detection of glyphosate and Cry1Ab in blood of women with and without pregnancy. Reprod Toxicol. 2012;33:122-123.
35. Aris, A. Reply to letter to the editor: Response to "Food Standards Australia New Zealand's" comments. Reprod Toxicol. 2012;33:403–404.
36. Aris, A. Reply to letter to the editor: Response to Bayer CropScience's position on the findings of glufosinate and its metabolite. Reprod Toxicol. 2011;32:496–497.

37. Séralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
38. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
39. Matthews J. Smelling a corporate rat. Spinwatch. http://bit.ly/184fwif. Published December 11, 2012.
40. Institute of Science in Society. Open letter on retraction and pledge to boycott Elsevier. 2013. Available at: http://www.i-sis.org.uk/Open_letter_to_FCT_and_Elsevier.php#form. Accessed February 19, 2014.
41. EndScienceCensorship.org. Statement: Journal retraction of Séralini GMO study is invalid and an attack on scientific integrity. 2014. Available at: http://www.endsciencecensorship.org/en/page/Statement#.UwUSP14vFY4.
42. Schubert D. Science study controversy impacts world health. U-T San Diego. http://www.utsandiego.com/news/2014/jan/08/science-food-health/. Published January 8, 2014.
43. Portier CJ, Goldman LR, Goldstein BD. Inconclusive findings: Now you see them, now you don't! Environ Health Perspect. 2014;122(2).
44. European Network of Scientists for Social and Environmental Responsibility (ENSSER). Journal's retraction of rat feeding paper is a travesty of science and looks like a bow to industry: ENSSER comments on the retraction of the Séralini et al. 2012 study. 2013. Available at: http://bit.ly/1cytNa4.
45. AFP. Mexican scientists criticise journal's retraction of study on GMO. terra.cl. http://bit.ly/1jVl1HZ ; English translation available at: http://gmwatch.org/index.php/news/archive/2013/15225. Published December 18, 2013.
46. Roberfroid M. Letter to the editor. Food Chem Toxicol. 2014;65:390. doi:10.1016/j.fct.2014.01.002.
47. European Food Safety Authority (EFSA). EFSA reaffirms its risk assessment of genetically modified maize MON863 [press release]. Eur Food Saf Auth. 2007. Available at: http://www.efsa.europa.eu/en/press/news/gmo070628.htm.
48. European Food Safety Authority (EFSA). Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2910.
49. European Food Safety Authority (EFSA). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from herbicide-tolerant genetically modified maize NK603, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (QUESTION NO EFSA-Q-2003-002): Opinion adopted on 25 November 2003. EFSA J. 2003;2003(9):1–14.
50. European Food Safety Authority (EFSA). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from insect-protected genetically modified maize MON 863 and MON863 x MON 810, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (Question No EFSA-Q-2003-121) Opinion adopted on 2 April 2004. EFSA J. 2004;2004(50):1–25.
51. Lepage C. OGM: l'EFSA a manqué à une déontologie élémentaire [GMOs: EFSA breaches basic ethical code]. Le Nouvel Observateur. http://bit.ly/QWjizy. Published October 7, 2012.
52. Holland N, Robinson C, Harbinson R. Conflicts on the menu: A decade of industry influence at the European Food Safety Authority (EFSA). Brussels, Belgium: Corporate Europe Observatory and Earth Open Source; 2012. Available at: http://earthopensource.org/files/pdfs/Conflicts_on_the_menu_report/Conflicts_on_the_menu_report_English.pdf.
53. Robinson C, Holland N, Leloup D, Muilerman H. Conflicts of interest at the European Food Safety Authority erode public confidence. J Epidemiol Community Health. 2013;67:717–720.
54. European Court of Auditors. Management of conflict of interest in selected EU agencies: Special report no. 15. Luxembourg; 2012.
55. European Parliament. Report on discharge in respect of the implementation of the budget of the European Food Safety Authority for the financial year 2010 (C7-0286/2011 – 2011/2226(DEC)). Committee on Budgetary Control; 2012. Available at: http://www.europarl.europa.eu/document/activities/cont/201204/20120404ATT42587/20120404ATT42587EN.pdf.
56. European Food Safety Authority (EFSA). Policy on independence and scientific decision-making processes of the European Food Safety Authority. 2011. Available at: http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf.
57. Corporate Europe Observatory. Unhappy meal: The European Food Safety Authority's independence problem. 2013. Available at: http://corporateeurope.org/sites/default/files/attachments/unhappy_meal_report_23_10_2013.pdf.
58. Parrott W, Chassy BM. Is this study believable? Examples from animal studies with GM foods. 2009. Available at: http://web.archive.org/web/20130405195129/http://agribiotech.info/details/Is%20This%20Study%20Believable%20V6%20final%2002%20print.pdf.
59. Rowell A. Don't Worry, It's Safe to Eat. London, UK: Earthscan Ltd; 2003.
60. Diels J, Cunha M, Manaia C, Sabugosa-Madeira B, Silva M. Association of financial or professional conflict of interest to research outcomes on health risks or nutritional assessment studies of genetically modified products. Food Policy. 2011;36:197–203.
61. European Parliament and Council. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Off J Eur Communities. 2001:1–38.
62. European Parliament and Council. Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Off J Eur Union. 2003;268:1–23.
63. US Food and Drug Administration (FDA). Biotechnology consultation agency response letter BNF No. 000001. 1995.

Available at: http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/Submissions/ucm161129.htm.
64. Houllier F. Biotechnology: Bring more rigour to GM research. Nature. 2012;491(7424):327-327. doi:10.1038/491327a.
65. Séralini GE, Mesnage R, Defarge N, et al. Answers to critics: Why there is a long term toxicity due to NK603 Roundup-tolerant genetically modified maize and to a Roundup herbicide. Food Chem Toxicol. 2013;53:461-8.
66. Bardocz S, Clark EA, Ewen SW, et al. Seralini and science: an open letter. Independent Science News. http://bit.ly/11NhFKw. Published October 2, 2012.
67. Deheuvels P. Étude de Séralini sur les OGM: Pourquoi sa méthodologie est statistiquement bonne [Seralini study on GMOs: Why the methodology is statistically sound]. Le Nouvel Observateur. http://www.gmwatch.org/component/content/article/14294. Published October 9, 2012.
68. Deheuvels P. L'étude de Séralini sur les OGM, pomme de discorde à l'Académie des sciences [The Seralini GMO study - A bone of contention at the Academy of Sciences]. Le Nouvel Observateur. http://www.gmwatch.org/latest-listing/51-2012/14336. Published October 19, 2012.
69. Saunders P. Excess cancers and deaths with GM feed: The stats stand up. Sci Soc. 2012. Available at: http://www.i-sis.org.uk/Excess_cancers_and_deaths_from_GM_feed_stats_stand_up.php.
70. Robinson C [ed.], GMOSeralini.org. 2013. http://www.gmoseralini.org.
71. Heinemann J. Letter to the editor. Food Chem Toxicol. 2013;53:427.
72. Meyer H, Hilbeck A. Rat feeding studies with genetically modified maize – a comparative evaluation of applied methods and risk assessment standards. Environ Sci Eur. 2013;25(33). Available at: http://www.enveurope.com/content/pdf/2190-4715-25-33.pdf.
73. Hammond B, Dudek R, Lemen J, Nemeth M. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food Chem Toxicol. 2004;42:1003-14. doi:10.1016/j.fct.2004.02.013.
74. Hammond B, Lemen J, Dudek R, et al. Results of a 90-day safety assurance study with rats fed grain from corn rootworm-protected corn. Food Chem Toxicol. 2006;44:147-60. doi:10.1016/j.fct.2005.06.008.
75. Padgette SR, Taylor NB, Nida DL, et al. The composition of glyphosate-tolerant soybean seeds is equivalent to that of conventional soybeans. J Nutr. 1996;126:702-16.
76. Bøhn T, Cuhra M, Traavik T, Sanden M, Fagan J, Primicerio R. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. Food Chem. 2014;153:207–215. doi:10.1016/j.foodchem.2013.12.054.
77. Zolla L, Rinalducci S, Antonioli P, Righetti PG. Proteomics as a complementary tool for identifying unintended side effects occurring in transgenic maize seeds as a result of genetic modifications. J Proteome Res. 2008;7:1850-61. doi:10.1021/pr0705082.
78. Jiao Z, Si XX, Li GK, Zhang ZM, Xu XP. Unintended compositional changes in transgenic rice seeds (Oryza sativa L.) studied by spectral and chromatographic analysis coupled with chemometrics methods. J Agric Food Chem. 2010;58:1746-54. doi:10.1021/jf902676y.
79. Then C, Bauer-Panskus A. European Food Safety Authority: A playing field for the biotech industry. TestBiotech; 2010. Available at: http://www.testbiotech.de/en/node/431.
80. Corporate Europe Observatory (CEO). Independence of EFSA's GMO risk assessment challenged [press release]. 2012. Available at: http://corporateeurope.org/pressreleases/2012/independence-efsas-gmo-risk-assessment-challenged.
81. Staes B. European Ombudsman asks for an explanation of the EFSA's rules and procedures: Parliamentary question for written answer to the Commission, Rule 117, Bart Staes (Verts/ALE). 2012. Available at: http://bit.ly/17S7eLx.
82. O'Reilly E. Decision of the European Ombudsman closing his inquiry into complaint 622/2012/ANA against the European Food Safety Authority (EFSA). 2013. Available at: http://www.testbiotech.org/sites/default/files/0622-2012-ANA-S2013-184815.pdf.
83. European Parliament and Council. Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. 2002. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32002R0178:en:NOT.
84. Levidow L, Murphy J, Carr S. Recasting "substantial equivalence": Transatlantic governance of GM food. Sci Technol Hum Values. 2007;32:26–64.
85. Millstone E, Brunner E, Mayer S. Beyond "substantial equivalence." Nature. 1999;401:525–6. doi:10.1038/44006.
86. Pusztai A. Genetically modified foods: Are they a risk to human/ animal health? Actionbioscience.org. 2001. Available at: http://www.actionbioscience.org/biotech/pusztai.html.
87. Pusztai A, Bardocz S. GMO in animal nutrition: Potential benefits and risks. In: Mosenthin R, Zentek J, Zebrowska T, eds. Biology of Nutrition in Growing Animals. Vol 4. Elsevier Limited; 2006:513–540. Available at: http://www.sciencedirect.com/science/article/pii/S1877182309701043.
88. Lotter D. The genetic engineering of food and the failure of science – Part 1: The development of a flawed enterprise. Int Jrnl Soc Agr Food. 2008;16:31–49.
89. European Parliament and Council. Commission implementing regulation (EU) no. 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Off J Eur Union. 2013. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF.
90. Jacquemart F. Personal communication [email]. 2013.
91. De Vendomois JS, Cellier D, Velot C, Clair E, Mesnage R, Séralini GE. Debate on GMOs health risks after statistical findings in regulatory tests. Int J Biol Sci. 2010;6:590-8.
92. Hammond BG, Dudek R, Lemen JK, Nemeth MA. Results of a 90-day safety assurance study with rats fed grain from

corn borer-protected corn. Food Chem Toxicol. 2006;44:1092-9. doi:10.1016/j.fct.2006.01.003.
93. Séralini GE, Cellier D, de Vendomois JS. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
94. Zhang L, Hou D, Chen X, et al. Exogenous plant MIR168a specifically targets mammalian LDLRAP1: Evidence of cross-kingdom regulation by microRNA. Cell Res. 2012;22(1):107-126. doi:10.1038/cr.2011.158.
95. Heinemann JA, Kurenbach B, Quist D. Molecular profiling – a tool for addressing emerging gaps in the comparative risk assessment of GMOs. Env Int. 2011;37:1285-93. doi:10.1016/j.envint.2011.05.006.
96. Heinemann J, Agapito-Tenfen SZ, Carman J. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. Environ Int. 2013;55:43–55.
97. GMWatch. New paper on dsRNA type GMOs - Q&A with the authors. http://www.gmwatch.org/index.php/news/archive/2013/14699. Published March 22, 2013.
98. Heinemann J. Evaluation of risks from creation of novel RNA molecules in genetically engineered wheat plants and recommendations for risk assessment. Centre for Integrated Research in Biosafety, University of Canterbury, New Zealand; 2012.
99. Science Media Centre New Zealand. Concern over Australian GM wheat – experts respond. 2012. Available at: http://www.sciencemediacentre.co.nz/2012/09/12/concern-over-australian-gm-wheat-experts-respond/.
100. GMWatch. Science Media Centre touts sales pitch as science. 2013. Available at: http://gmwatch.org/latest-listing/52-2013/14718.
101. Schmidt JE, Braun CU, Whitehouse LP, Hilbeck A. Effects of activated Bt transgene products (Cry1Ab, Cry3Bb) on immature stages of the ladybird Adalia bipunctata in laboratory ecotoxicity testing. Arch Env Contam Toxicol. 2009;56(2):221-8. doi:10.1007/s00244-008-9191-9.
102. Zwahlen C, Hilbeck A, Howald R, Nentwig W. Effects of transgenic Bt corn litter on the earthworm Lumbricus terrestris. Mol Ecol. 2003;12:1077-86.
103. Pilcher CD, Rice ME, Obrycki JJ. Impact of transgenic Bacillus thuringiensis corn and crop phenology on five nontarget arthropods. Environ Entomol. 2005;34(5):1302-1316. doi:10.1603/0046-225X(2005)034[1302:IOTBTC]2.0.CO;2.
104. Dyer GA, Serratos-Hernández JA, Perales HR, et al. Dispersal of transgenes through maize seed systems in Mexico. PloS One. 2009;4(5):e5734. doi:10.1371/journal.pone.0005734.
105. Pineyro-Nelson A, Van Heerwaarden J, Perales HR, et al. Transgenes in Mexican maize: molecular evidence and methodological considerations for GMO detection in landrace populations. Mol Ecol. 2009;18:750-61. doi:10.1111/j.1365-294X.2008.03993.x.
106. Mortensen DA, Egan JF, Maxwell BD, Ryan MR, Smith RG. Navigating a critical juncture for sustainable weed management. BioScience. 2012;62(1):75-84.
107. Hilbeck A, Moar WJ, Pusztai-Carey M, Filippini A, Bigler F. Toxicity of Bacillus thuringiensis CryIAb toxin to the predator Chrysoperla carnea (Neuroptera: Chrysopidae). Environ Entomol. 1998;27(5):1255-1263.
108. Hilbeck A, Moar WJ, Pusztai-Carey M, Filippini A, Bigler F. Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator Chrysoperla carnea. Entomol Exp Appl. 1999;91:305–316.
109. Hilbeck A, Baumgartner M, Fried PM, Bigler F. Effects of transgenic Bt corn-fed prey on immature development of Chrysoperla carnea (Neuroptera: Chrysopidae). Environ Entomol. 1998;27(2):480–487.
110. Hilbeck A, Meier M, Trtikova M. Underlying reasons of the controversy over adverse effects of Bt toxins on lady beetle and lacewing larvae. Environ Sci Eur. 2012;24(9). doi:10.1186/2190-4715-24-9.
111. Dutton A, Klein H, Romeis J, Bigler F. Uptake of Bt-toxin by herbivores feeding on transgenic maize and consequences for the predator Chrysoperla carnea. Ecol Entomol. 2002;27:441–447.
112. Dutton A, Klein H, Romeis J, Bigler F. Prey-mediated effects of Bacillus thuringiensis spray on the predator Chrysoperla carnea in maize. Biol Control. 2003;26(2):209-215. doi:10.1016/S1049-9644(02)00127-5.
113. Romeis J, Dutton A, Bigler F. Bacillus thuringiensis toxin (Cry1Ab) has no direct effect on larvae of the green lacewing Chrysoperla carnea (Stephens) (Neuroptera: Chrysopidae). J Insect Physiol. 2004;50(2-3):175-183. doi:10.1016/j.jinsphys.2003.11.004.
114. Alvarez-Alfageme F, Bigler F, Romeis J. Laboratory toxicity studies demonstrating no adverse effects of Cry1Ab and Cry3Bb1 to larvae of Adalia bipunctata (Coleoptera: Coccinellidae): the importance of study design. Transgenic Res. 2011;20:467-479.
115. Rauschen S. A case of "pseudo science"? A study claiming effects of the Cry1Ab protein on larvae of the two-spotted ladybird is reminiscent of the case of the green lacewing. Transgenic Res. 2010;19:13-6. doi:10.1007/s11248-009-9301-0.
116. Ricroch A, Berge JB, Kuntz M. Is the German suspension of MON810 maize cultivation scientifically justified? Transgenic Res. 2010;19:1-12. doi:10.1007/s11248-009-9297-5.
117. Hilbeck A, McMillan JM, Meier M, Humbel A, Schlaepfer-Miller J, Trtikova M. A controversy re-visited: Is the coccinellid Adalia bipunctata adversely affected by Bt toxins? Environ Sci Eur. 2012;24(10). doi:10.1186/2190-4715-24-10.
118. Gatehouse AMR, Ferry N, Edwards MG, Bell HA. Insect-resistant biotech crops and their impacts on beneficial arthropods. Philos Trans R Soc B Biol Sci. 2011;366(1569):1438-1452. doi:10.1098/rstb.2010.0330.
119. Perkins JH. Integrated pest management, biofuels, and a new Green Revolution: A case study of the American Midwest. In: Peshin R, Dhawan AK, eds. Integrated Pest Management: Volume 2: Dissemination and Impact. Integrated Pest Management. Springer; 2009:581–627.
120. Marvier M, McCreedy C, Regetz J, Kareiva P. A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. Science. 2007;316:1475-7. doi:10.1126/science.1139208.

121. Shelton AM, Naranjo SE, Romeis J, et al. Setting the record straight: a rebuttal to an erroneous analysis on transgenic insecticidal crops and natural enemies. Transgenic Res. 2009;18:317-22. doi:10.1007/s11248-009-9260-5.
122. Losey JE, Rayor LS, Carter ME. Transgenic pollen harms monarch larvae. Nature. 1999;399:214. doi:10.1038/20338.
123. Jesse LCH, Obrycki JJ. Field deposition of Bt transgenic corn pollen: Lethal effects on the monarch butterfly. J Oecologia. 2000;125:241–248.
124. Hellmich RL, Siegfried BD, Sears MK, et al. Monarch larvae sensitivity to Bacillus thuringiensis-purified proteins and pollen. Proc Natl Acad Sci. 2001;98(21):11925-11930. doi:10.1073/pnas.211297698.
125. Jesse LCH, Obrycki JJ. Survival of experimental cohorts of monarch larvae following exposure to transgenic Bt corn pollen and anthers. In: Oberhauser KS, Solensky MJ, eds. The Monarch Butterfly: Biology and Conservation. Ithaca, NY: Cornell University Press; 2004:69–75.
126. Oberhauser KS, Rivers ERL. Monarch butterfly (Danaus plexippus) larvae and Bt maize pollen: a review of ecological risk assessment for non-target species. AgBiotechNet. 2003;5:1-7.
127. Dively GP, Rose R, Sears MK, et al. Effects on monarch butterfly larvae (Lepidoptera: Danaidae) after continuous exposure to Cry1Ab-expressing corn during anthesis. Env Entomol. 2004;33:1116-1125.
128. Conniff R. Tracking the causes of sharp decline of the monarch butterfly. Yale Environment 360. http://e360.yale.edu/feature/tracking_the_causes_of_sharp__decline_of_the_monarch_butterfly/2634/. Published April 1, 2013.
129. Pleasants JM, Oberhauser KS. Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population. Insect Conserv Divers. 2013;6:135–144.
130. Then C. Expression of Bt toxins in "SmartStax": Analyses of Stilwell & Silvanovich, 2007 and Phillips, 2008: Report number MSL0021070 and Sub-Report ID: 61026.05. Testbiotech; 2011. Available at: http://www.testbiotech.de/sites/default/files/SmartStax_Expression_data_Testbiotech.pdf.
131. Gatehouse AMR, Ferry N, Raemaekers RJM. The case of the monarch butterfly: a verdict is returned. Trends Genet TIG. 2002;18(5):249-251.
132. European Network of Scientists for Social and Environmental Responsibility (ENSSER). Statement: No scientific consensus on GMO safety. 2013. Available at: http://www.ensser.org/increasing-public-information/no-scientific-consensus-on-gmo-safety/.
133. Biofortified.org. Studies for GENERA. 2014. Available at: http://www.biofortified.org/genera/studies-for-genera/.
134. Tribe D. 600+ published safety assessments on GM foods and feeds. GMOPundit. 2007. Available at: http://gmopundit.blogspot.co.uk/2007/06/150-published-safety-assessments-on-gm.html.
135. Calsamiglia S, Hernandez B, Hartnell GF, Phipps R. Effects of corn silage derived from a genetically modified variety containing two transgenes on feed intake, milk production, and composition, and the absence of detectable transgenic deoxyribonucleic acid in milk in Holstein dairy cows. J Dairy Sci. 2007;90(10):4718-23.
136. Snell C, Aude B, Bergé J, et al. Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Food Chem Toxicol. 2012;50:1134-48.

# 3. Health hazards of GM foods

*"The argument advanced… for the safety of GM food is false… Yes, the DNA of all living organisms is made up of just four nucleosides, and yes, virtually all proteins are made up from just 20 amino acids. But this does not imply that everything containing these basic building blocks is without risk to human beings. The same units, arranged in different ways, are contained in the smallpox virus, bubonic plague and influenza, deadly nightshade and other poisonous plants, creatures such as poisonous jellyfish, scorpions, deadly snakes, sharks – and people who talk absolute nonsense."*

– G. D. W. Smith, Fellow of the Royal Society, professor of materials, Oxford University, UK[1]

*"Most studies with GM foods indicate that they may cause hepatic, pancreatic, renal, and reproductive effects and may alter haematological [blood], biochemical, and immunologic parameters, the significance of which remains to be solved with chronic toxicity studies."*

– Artemis Dona, Department of Forensic Medicine and Toxicology, University of Athens Medical School, Greece, and Ioannis S. Arvanitoyannis, University of Thessaly School of Agricultural Sciences, Greece[2]

## References

1. Smith GDW. Is GM food good for you? Letter to the editor of the Sunday Times [unpublished]. 2004.
2. Dona A, Arvanitoyannis IS. Health risks of genetically modified foods. Crit Rev Food Sci Nutr. 2009;49:164–75. doi:10.1080/10408390701855993.

# 3.1 Myth: GM foods are safe to eat

## Truth: Studies show that GM foods can be toxic, allergenic, or have unintended nutritional changes

### Myth at a glance

Peer-reviewed studies have found that GM foods can have unintended toxic and allergenic effects and altered nutritional value. Such effects have even been found in industry's own studies carried out in support of regulatory authorization.

Most animal feeding studies on GMOs are short-term or medium-term in length – too short to show long-term (chronic) effects such as organ failure, cancer, or reproductive problems.

What is needed are long-term and multi-generational studies on GMOs to see if the signs of toxicity commonly reported in shorter studies develop into serious disease. But such studies are not required by government regulators anywhere in the world.

Industry and regulators often dismiss findings of toxicity in animal feeding trials on GMOs by claiming they are "not biologically significant" or "not biologically relevant". However, these terms have never been properly defined in the context of animal feeding trials with GMOs and are scientifically meaningless.

There are three possible sources of adverse health effects from GM foods:

- The GM transformation process may produce mutagenic effects that can disrupt or alter gene structure, disturb normal gene regulatory processes, or cause effects at other levels of biological structure and function. These effects can result in unintended changes in composition, including new toxins or allergens and/or disturbed nutritional value
- The GM gene product – for example, the Bt toxin in GM insecticidal crops – may be toxic or allergenic
- Changes in farming practices linked to the use of a GMO may result in toxic residues – for example, higher levels of crop contamination with the herbicide Roundup are an inevitable result of using GM Roundup Ready crops.

Evidence presented below and in Chapters 4 and 5 suggests that problems are arising from all three sources.

## Unintended changes in composition

GM crops have been shown to have a different composition to their non-GM counterparts (see Myth 2.1) even when the two crops are grown under the same conditions, at the same time and in the same location – meaning that the changes are not due to different environmental factors but to the genetic modification.

Altered nutritional value is of concern for two reasons: first, because it could directly affect the health of the animal or human being that eats the food through providing an excess or shortage of certain nutrients; and second, because it is an indicator that the GM process has altered biochemical processes in the plant. This could be a clue that other unexpected and as yet unidentified changes have also occurred that might impact human or animal health, such as altered toxicity or allergenicity.

## Toxic effects and signs of toxicity in laboratory and farm animal feeding studies with GMOs

Feeding studies on laboratory and farm animals show that GM foods can be toxic or allergenic. In these studies, a GM diet was fed to one group of animals and a non-GM diet was fed to a control group. The studies found signs of toxicity or actual toxic effects in the GM-fed animals, meaning that the GM foods tested were more toxic or allergenic than the non-GM foods.

Of the findings listed below, some are from experiments conducted by independent academic researchers and others by GM industry employees or contractors.

### Severe organ damage and increased rates of large tumours and mortality

Rats fed Monsanto's GM maize NK603 and tiny amounts of Roundup herbicide, which the maize is engineered to tolerate, over a long-term two-year period developed severe liver and kidney damage, disturbance to pituitary gland function, and hormonal disruption. Additional unexpected findings included increased rates of large palpable tumours and premature death in some treatment groups.[1]

This study came under heavy attack by pro-GM critics and was retracted by the journal that published it, over a year after it had passed peer review and appeared in print. However, the retraction was condemned as invalid by hundreds of scientists worldwide.[2,3] A full discussion of this study and its retraction can be found below (Myth 3.2).

### Altered blood biochemistry, multiple organ damage, and potential effects on male fertility

Rats fed the GM Bt maize MON810: Ajeeb YG (a variety developed by Monsanto for the Egyptian market) for 45 and 91 days showed differences in organ and body weights and in blood biochemistry, compared with rats fed the non-GM parent variety grown side-by-side in the same conditions. The authors noted that the changes could indicate "potential adverse health/toxic effects", which needed further investigation.[4]

Histopathological investigations by the same group of researchers found toxic effects in multiple organs in rats fed the GM Bt maize for 91 days. Effects included abnormalities and fatty degeneration of liver cells, congestion of blood vessels in kidneys, and excessive growth and necrosis (death) of intestinal structures called villi. Examination of the testes revealed necrosis and desquamation (shedding) of the spermatogonial cells that are the foundation of sperm cells and thus of male fertility.[5]

## Stomach lesions and unexplained mortality

Rats fed GM tomatoes over a 28-day period developed stomach lesions (sores or ulcers).[6,7] There was unexplained high mortality in GM-fed rats: seven out of 40 rats fed GM tomatoes died within two weeks of the start of the experiment.[8] This tomato, Calgene's Flavr Savr, was the first commercialized GM food. The study, commissioned by Calgene itself, was never peer-reviewed and published and was only forced into the public domain by a lawsuit brought by a public interest group, the Alliance for Bio-Integrity, against the US Food and Drug Administration (FDA).[9]

The director of the FDA's Office of Special Research Skills concluded that Calgene's data fell short of "a demonstration of safety" or a "demonstration of reasonable certainty of no harm",[10] the typical standard expected of foods.

A "repeat" study performed by Calgene found lesions in non-GM fed animals as well as GM-fed animals. However, the study was not in reality a repeat but used tomatoes that had been prepared in a different way, which could affect the results, as noted by Fred Hines, the FDA pathologist. Hines concluded that Calgene had not provided enough data to justify its claim that the lesions seen across all the experiments were "incidental" and not due to the GM tomato.[6]

These studies and their implications have been discussed in detail in peer-reviewed articles by Dr Arpad Pusztai, a leading expert in animal feeding studies, and his research colleagues.[8,11] Pusztai concluded, "The FDA's conclusion that Flavr Savr presented no more dangers to consumers than ordinary tomatoes does not ... appear to rest on good science and evidence which could stand up to critical examination."[11]

## Immune response and allergic reaction

Mice fed GM peas engineered with an insecticidal protein (alpha-amylase inhibitor) from beans showed a strong, sustained immune reaction against the GM protein. Mice developed antibodies against the GM protein and an allergic-type inflammation response (delayed hypersensitivity reaction). Also, the mice fed on GM peas developed an immune reaction to chicken egg white protein. The mice did not show immune or allergic-type inflammation reactions to either non-GM beans naturally containing the insecticide protein, to egg white protein fed with the natural protein from the beans, or to egg white protein fed on its own.[12]

The findings showed that the GM insecticidal protein acted as a sensitizer, making the mice susceptible to developing immune reactions and allergies to normally non-allergenic foods.[12] This is called immunological cross-priming.

The fact that beans naturally containing the insecticidal protein did not cause the effects seen with the peas that expressed the GM insecticidal protein indicated that the immune responses of the mice to the GM peas were caused by changes in the peas brought about by the genetic engineering process. In other words, the insecticidal protein was changed by the GM process so that it behaved differently in the GM peas compared with its natural form in the non-GM beans – and the altered protein from the GM peas stimulated a potent immune response in the mice.[12]

T. J. Higgins, one of the researchers on the original study, subsequently co-authored a second, more recent study,[13] which he claimed[14,15] resolved concerns raised by the first study.[12]

But this claim is unfounded, as the two studies used markedly different methodologies to evaluate immune reactions. In the first study (Prescott and colleagues, 2005), the food was fed to the mice intragastrically (into the stomach), an approximation of human dietary exposure; then the mice were tested for allergic reactions.[12]

In the second study (Lee and colleagues, 2013), the GM and non-GM test proteins were first injected into the abdomen of the mice (intraperitoneal immunization) or introduced into their noses (intranasal immunization). Only after this procedure were the mice fed intragastrically with GM peas and non-GM beans containing the test proteins. Then the mice were tested for allergic sensitization. The result: both GM peas and non-GM beans were found to be equally allergenic.[13]

However, these allergic reactions to both the GM and non-GM test proteins are not surprising, because the mice had already been immunologically pre-sensitized to these products by the intraperitoneal and intranasal immunization procedures conducted prior to their being fed these products.

Therefore the second study (Lee and colleagues, 2013)[13] does not contradict or disprove the the allergenic potential of the protein in the GM peas found in the first study[12] in any way. Instead, the second study (Lee and colleagues, 2013)[13] shows that it is possible to induce an allergic response to either GM peas or non-GM beans by pre-immunizing the mice to the proteins in a way that is very different from the usual way an animal or human is exposed to a food.

## Immune disturbances

Young and old mice fed GM Bt maize for periods of 30 and 90 days respectively showed a marked disturbance in immune system cells and in biochemical activity. An increase of serum cytokines (protein molecules involved in immune response) after Bt maize feeding was also found, an effect associated with allergic and inflammatory responses.[16]

A study in rats fed GM Bt rice for 28 or 90 days found a Bt-specific immune response in the non-GM-fed control group as well as the GM-fed groups. The researchers concluded that the immune response in the control animals was due to their inhaling particles of the powdered Bt toxin-containing feed consumed by the GM-fed group. They recommended that for future tests involving Bt crops, GM-fed and control groups should be kept separate.[17] This indicates that animals can be sensitive to small amounts of GM proteins, so even low levels of contamination of conventional crops with GMOs could be harmful to health.

### Enlarged lymph nodes and immune disturbances

Mice fed for five consecutive generations with GM herbicide-tolerant triticale (a wheat/rye hybrid) showed enlarged lymph nodes and increased white blood cells, as well as a significant decrease in the percentage of T lymphocytes in the spleen and lymph nodes and of B lymphocytes in lymph nodes and blood, in comparison with controls fed with non-GM triticale.[18] T and B lymphocytes are white blood cells involved in immunity.

### Disturbed liver, pancreas and testes function

Mice fed GM soy showed disturbed liver, pancreas and testes function. The researchers found abnormally formed nuclei and nucleoli (structures within the nuclei) in liver cells, which indicates increased metabolism and potentially altered patterns of gene expression.[19,20,21]

### Liver ageing

Mice fed GM soy over a long-term (24-month) period showed changes in the expression of proteins relating to hepatocyte (liver cell) metabolism, stress response, and calcium signalling, indicating more acute signs of ageing in the liver, compared with the control group fed non-GM soy.[22]

### Disturbed enzyme functioning in kidney and heart

Rabbits fed GM soy showed enzyme function disturbances in kidney and heart.[23]

### Higher density of uterine lining

Female rats fed GM soy for 15 months showed significant changes in the uterus and ovaries compared with rats fed organic non-GM soy or a non-soy diet. The number of corpora lutea, structures that secrete sex hormones and are involved in establishing and maintaining pregnancy, was increased only in the GM soy rats compared with the organic soy-fed and non-soy-fed rats. The density of the epithelium (lining of the uterus) was higher in the GM soy-fed group than the other groups, meaning that there were more cells than normal.

Certain effects on the female reproductive system were found with organic soy as well as GM soy when compared with the non-soy diet, leading the authors to conclude that there was also a need for further investigation into the effects of soy-based diets (whether GM or non-GM) on reproductive health.[24]

### Severe stomach inflammation and heavier uteri

A feeding study in pigs fed a mixed diet containing GMO soy and maize over an average commercial lifespan of 22.7 weeks found that the GM-fed pigs had more severe stomach inflammation than pigs fed an equivalent non-GM diet and 25% heavier uteri, which could be an indicator of pathology.[25] GM-fed pigs had a higher rate of severe stomach inflammation, 32% for GM-fed pigs compared to 12% for non-GM-fed. The severe stomach inflammation was worse in GM-fed males compared with non-GM fed males by a factor of 4.0, and in GM-fed females compared with non-GM fed females by a factor of 2.2.

GMO proponents claimed that non-GM-fed pigs had more cases of mild and moderate inflammation than GM-fed pigs and that therefore the GM diet had a protective effect.[26] However, this claim collapses when it is considered that many GM-fed pigs were moved up from the "mild" and "moderate" categories into the "severe" inflammation category, leaving fewer pigs in the "mild" and "moderate" categories.

The Australia/New Zealand GMO regulator FSANZ argued: "The authors have not provided convincing evidence that stomach inflammation was present. The stomach data, as presented, do not support the authors' interpretation and conclusions because… The presence of 'inflammation' was determined by visual appearance (reddening) only, without any microscopic (histological) confirmation. This is not considered a reliable method for establishing the presence of true inflammation, because it relies solely on the colour of the tissue which can vary for many reasons."[27]

The lead researcher on the study, Dr Judy Carman, replied: "FSANZ suggest that the reddening may not be due to inflammation without suggesting what else it may be due to.

"Furthermore, the veterinarian that assessed the stomach inflammation in our pigs has many years of training and experience with pigs and other animals, including years of experience in assessing inflammation in those animals. In contrast, we are not aware that anyone in FSANZ has any training or experience in assessing stomach inflammation in pigs. In fact, we are not aware that anyone in FSANZ has any clinical experience whatsoever, either as a medical doctor or as a veterinarian. Therefore, FSANZ is commenting well outside of its area of expertise.

"In essence, FSANZ is saying that a veterinarian (or doctor) cannot determine if an animal (or human) has inflammation of a tissue such as a foot or an eye or anything else, without cutting out a sample of the affected tissue and sending it to a laboratory for histology. This is absurd.

"Also, while FSANZ want histology for this feeding study, they do not want it for feeding studies conducted by the GM industry. In fact, FSANZ does not require any feeding studies to be conducted on any GM crop whatsoever before they assess the crop to be safe to eat."[28]

### Liver and kidney toxicity

A review of 19 studies (including industry's own studies submitted to regulators in support of applications to commercialize GM crops) on mammals fed with commercialized GM soy and maize that are already in our food and feed chain found consistent signs of toxicity in the liver and kidneys. Such effects may mark the onset of chronic disease, but longer-term studies would be required to assess this more thoroughly. Such long-term feeding trials on GMOs are not required by regulators anywhere in the world.[29]

In a separate study, the same research group, led by Professor Gilles-Eric Séralini at the University of Caen, France, re-analyzed Monsanto's own rat feeding trial data, submitted to obtain approval in Europe for three commercialized GM Bt maize varieties, MON863, MON810, and NK603. Séralini's team concluded that the maize varieties caused signs of toxicity in liver and kidneys. They stated that while the findings may have been due to the pesticides specific to each variety, genetic engineering could not be excluded as the cause.[30] The data suggest that approval of these GM maize varieties should be withdrawn because they are not substantially equivalent to non-GM maize and may be toxic.

As a result of their findings, Séralini's team decided to replicate and extend Monsanto's study on GM maize NK603.[31] Whereas Monsanto had ended its study after just 90 days, Séralini's experiment ran for two years.[1] The results are described in Myth 3.2.

### Changed level of fats in blood and signs of liver and kidney toxicity

Rats fed insecticide-producing MON863 Bt maize had different growth rates and higher levels of certain fats (triglycerides) in their blood compared with rats fed the control diet. They also showed changes in liver and kidney function, which could have been early indicators of disease. This study was a re-analysis of Monsanto's rat feeding trial data on its own GM maize. The authors of the re-analysis stated that the findings did not allow a conclusion that MON863 maize is safe. They added that long-term studies were needed to investigate the consequences of these effects.[32]

### Toxic effects on liver and kidneys and altered blood biochemistry

Rats fed GM Bt maize over three generations showed damage to liver and kidneys and alterations in blood biochemistry.[33]

### Enlarged liver

Rats fed a Monsanto GM oilseed rape (canola) over four weeks developed enlarged livers, often a sign of toxicity. The US FDA allowed Monsanto to do another experiment, this time comparing the GM canola with a range of eight different canola varieties, thus widening the range of variation and obscuring any effects of feeding the GM canola. This allowed Monsanto to conclude that the canola was as safe as other canola varieties.[34]

### Disturbances in digestive system and changes to liver and pancreas

Female sheep fed Bt GM maize over three generations showed disturbances in the functioning of the digestive system, while their lambs showed cellular changes in the liver and pancreas.[35]

### Excessive growth in the lining of the gut

Rats fed GM potatoes for only ten days showed excessive growth of the lining of the gut similar to a pre-cancerous condition, as well as toxic effects in multiple organ systems.[36,37]

### Intestinal abnormalities

Mice fed a diet of GM Bt potatoes or non-GM potatoes spiked with natural Bt toxin protein isolated from bacteria over two weeks showed abnormalities in the cells and structures of the small intestine, compared with a control group of mice fed non-GM potatoes. The abnormalities were more marked in the Bt toxin-fed group.[38]

This study shows that the GM Bt potatoes caused mild damage to the intestines. It also shows that Bt toxin protein is not harmlessly broken down in digestion, as GM proponents claim, but survives in a functionally active form in the small intestine and can cause damage to that organ.[38]

### Altered blood biochemistry and gut bacteria, and immune response

Rats fed GM rice for 90 days had a higher water intake as compared with the control group fed the non-GM isogenic (genetically the same, except for the genetic modification) line of rice. The GM-fed rats showed differences in blood biochemistry and gut bacteria, as well as an immune response. Organ weights of female rats fed GM rice were different from those fed non-GM rice. The authors claimed that none of the differences were "adverse", but they did not define what they meant by "adverse". Even if they had defined it, the only way to know if such changes are adverse is to extend the length of the study, which was not done. The authors conceded that the study "did not enable us to conclude on the safety of the GM food".[39]

### Altered gut bacteria and organ weights

Rats fed GM Bt rice for 90 days developed significant differences as compared with rats fed the non-GM isogenic line of rice. The GM-fed group had 23% higher levels of coliform bacteria in their gut and there were differences in organ weights between the two groups, namely in the adrenals, testes and uterus.[40]

### Less efficient feed utilization and digestive disturbance

A feeding trial in which salmon were fed Monsanto's GM Bt maize MON810 revealed less efficient feed utilization, with reduced ability to digest protein and minerals, compared with salmon fed non-GM maize. Also, a localized immune response was observed in the intestines of the GM-fed fish. The analyses were conducted after 33 and 97 days of feeding.[41]

Fish are not considered relevant to assessing health risks in humans, as they have a different metabolism and digestive system. However, GMO proponents use studies in fish to claim that GM foods are as safe and nutritional for human and animal consumption as their non-GM counterparts.[42] Thus by their standards, it is acceptable to cite a study in fish as indicating risk.

## Masking statistical significance through the concept of "biological relevance"

Study findings such as those described above have made it increasingly difficult for GM proponents to claim that there are no differences between the effects of GM foods and their non-GM counterparts. Clearly, there are.

To sidestep this problem, GM proponents have shifted their argument to claim that statistically significant effects are not "biologically relevant".

The concept of lack of biological relevance has been heavily promoted by the industry-funded group, the International Life Sciences Institute (ILSI), and affiliates to argue against regulatory restrictions on toxic chemicals.[43] But increasingly, it is invoked by authors defending the safety of GM crops[42] to argue that statistically significant observable effects in GM-fed animals are not important.

However, this argument is scientifically indefensible. Biological relevance with respect to changes brought about by GM foods has never been properly defined.

Most feeding trials on GM foods, including those carried out by industry to support applications for GM crop commercialization, are not long-term but short- or medium-term studies of 30–90 days. These studies are too short to determine whether changes in animals fed a GM diet are biologically relevant or not.

In order to determine whether changes seen in these short- to medium-term studies are biologically relevant, the researchers would have to:

- Define in advance what "biological relevance" means with respect to effects found from feeding GM crops
- Extend the study duration from short- or medium-term to a long-term period. In the case of rodent studies, this would be two years – the major part of their lifespan[29]
- Examine the animals closely to see how any changes found in short- or medium-term studies progress – for example, they may disappear or lead to disease or premature death
- Analyze the biological relevance of the changes in light of the researchers' definition of the term
- Carry out additional reproductive and multigenerational studies to determine effects on fertility and future generations.

Since these steps are not followed in cases where statistically significant effects are dismissed as not "biologically relevant", assurances of GM food safety founded on this line of argument are baseless.

In parallel with asserting lack of "biological relevance", a trend has grown of claiming that statistically significant effects of GM feed on experimental animals are not "adverse".[39] Again, however, the term "adverse" is not defined and the experiments are not extended to check whether any changes seen are the first signs of disease. So the term is technically meaningless.

GMO proponents should cease attempting to mask findings of statistically significant effects from GM crops through the use of poorly defined and scientifically indefensible concepts.

## Misuse of "biological relevance" places public health at risk: Monsanto GM maize study

In 2007 a team led by Professor Gilles-Eric Séralini published a new analysis of a rat feeding study conducted by Monsanto with one of its GM maize varieties.

The maize, called MON863, was approved for food and feed use in Europe in 2005–2006.[44] The Monsanto study was used to gain regulatory authorization for the maize, but it could not be scrutinized by independent scientists and the public because the raw data were kept hidden on claimed grounds of commercial confidentiality. Only after a court action in Germany forced disclosure of Monsanto's data could Séralini and colleagues conduct their analysis.[32]

Séralini's team found that according to Monsanto's own data, rats fed GM maize over a 90-day period had signs of liver and kidney toxicity. Also, the GM-fed rats had statistically significant differences in weight from those fed non-GM maize control diets. The GM-fed females had higher concentrations of certain fats in their blood. Excretion of some minerals was disturbed in GM-fed males.[32]

However, the statistically significant effects found in Monsanto's study were dismissed by the European Food Safety Authority (EFSA) in its favourable safety assessment of the maize. Without evidence, EFSA claimed that these effects were not "biologically meaningful".[45,46] Both EFSA and the Monsanto-sponsored scientists cited differences in response to the GM feed between male and female animals, implying that toxic effects should be the same in both sex groups before they could be taken seriously.[29,47,48,49] This is scientifically indefensible, since some substances, especially those with hormone-disrupting properties, are known to have different effects on males and females.[50,51]

Séralini and colleagues commented on the dangerous trend of dismissing statistically significant effects by claiming lack of biological relevance in a 2011 review of the scientific literature assessing the safety of GM crops, stating: "The data indicating no biological significance of statistical effects in comparison to controls have been published mostly by [GM crop developer] companies from 2004 onwards, and at least 10 years after these GMOs were first commercialized round the world". Séralini's team called the trend a matter of "grave concern".[29]

### EFSA responds to criticism over use of "biological relevance"

After being subjected to years of criticism by independent scientists and a member of the European Parliament over its use of "biological relevance",[52,29,53] in 2011 EFSA finally issued an Opinion on the relationship between statistical significance and biological relevance.[54]

But EFSA's Opinion fails to give a rigorous scientific or legal definition of what makes a statistically significant finding "biologically relevant" or not. Instead, it allows industry to come to its own conclusion on whether changes found in an experiment are "important", "meaningful", or "may have consequences for human health". These are vague concepts for which no measurable or objectively verifiable endpoints are defined. Thus they are a matter of opinion, not science.

Moreover, the lack of a sound definition of biological relevance means that regulators have no strong scientific or legal grounds to disagree with industry's claim that a statistically significant finding is not biologically relevant. This, in effect, makes the GMO impossible to regulate.

The conclusions of the EFSA Opinion are not surprising, given that it is authored[54] by several current or former affiliates of the industry-funded group, the International Life Sciences Institute (ILSI), including Harry Kuiper[55] (also then the chair of EFSA's GMO panel), Josef Schlatter, and Susan Barlow.[56,57] ILSI is funded by GM crop developer/agrochemical companies, including Monsanto.[58] Allowing ILSI affiliates to write EFSA's scientific advice on how to assess the safety of GM foods and crops is akin to allowing a student to write his or her own examination paper or allowing scientists to review their own papers submitted for publication.

## Masking statistical significance through the concept of "normal variation"

Studies often find statistically significant differences in the composition of GM foods compared with their non-GM counterparts. Studies also find statistically significant differences in animals fed a GM crop variety compared with animals fed the non-GM comparator variety.

However, GMO proponents consistently dismiss these statistically significant differences by claiming that they are "within the normal range of biological variation".

This claim was made by Snell and colleagues in their review of animal feeding studies on GMOs. The review included some of the studies summarized in this report, which found significant differences in the GM-fed animals. In spite of this, the reviewers (in some cases reflecting the opinion of the authors of the original studies) used the concept of normal variation to conclude that "GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed".[42]

It is scientifically unjustifiable to dismiss statistically significant changes in the GM-fed animals on the basis that they are within the normal range of variation. GMO proponents define the "normal range of variation" by collecting so-called "historical control data" from the control animals in many different studies carried out at different times, using different experimental conditions and measurement methods. The result is a set of numbers that vary widely, which appears to be the GM proponents' objective. By using a dataset with such an unjustifiably wide range of variation, GM proponents are able to hide the differences in the animals fed the GMO under test and the non-GM control in the "noise" introduced by the irrelevant data.

However, there is no scientific justification for gathering disparate "historical control data" into the same dataset, and even less justification for comparing this sham dataset to the GMO of interest. On the contrary, this practice runs counter to the aim of scientific experiments, which are designed to minimise variables. According to rigorous scientific practice, in any single experiment, the scientist manipulates just one variable in order to test its effect. In this way, any changes observed can be traced to a probable single cause.

The scientific approach in an animal feeding trial designed to find out if a GMO is safe to eat is to ensure that the GMO is the single manipulated variable. One group of animals, the "treated" group, should be fed a diet containing the GMO. Another group, the control group, should be fed a similar diet, with the only difference being that it has not been subject to the genetic modification. All conditions of the experiment outside the GM component of the treated group's diet must be the same. Within this tightly controlled setup, any changes seen in the treated group are likely to be caused by the GM feed.

Therefore in any experiment to discover the effects of a GMO in an animal feeding trial, the most valid comparator is the control group within that same experiment, known as the concurrent control. This is because the animals in other "historical" experiments will be subject to many variables, such as differences in diet and contaminants in food, water and bedding, laboratory conditions, and animal genetics. Restricting comparisons to the concurrent control group should be the rule in experiments commissioned by the GM industry in support of regulatory authorization.

## Limitation of many feeding studies on GM foods

A limitation of many feeding studies on GM foods conducted by industry and independent researchers alike is that they use a non-GM comparator other than the isogenic non-GM parent.

In evaluating the importance of this shortcoming in various studies, it is necessary to consider the aim of the study. Feeding studies performed for regulatory purposes are supposed to reveal whether a GM crop is toxicologically different from the same crop without the genetic modification. Such studies should therefore involve feeding the test animals with the GM crop and the controls with the same amount of the non-GM isogenic variety, which has the same genetic background without the genetic modification. To minimize variables, the two crops should be grown in the same location and conditions at the same time.

However, the GM industry often does not carry out its feeding studies in this way. It does not restrict itself to the non-GM isogenic variety as the comparator. Instead it introduces a number of non-GM diets consisting of a range of distantly related non-GM crops grown in different locations and conditions and at different times.[31,59] This has the effect of obscuring any effects from feeding the GM diet amongst the "noise" of irrelevant diets.

Many independent studies on GM foods suffer from the same limitation, though for a different reason. The reason in this case is that researchers find it difficult to access GM seeds of a specific variety and the non-GM isogenic comparator, because the GM companies restrict access to these research materials.[60,61]

Nonetheless, it is important to put this limitation in its proper perspective. Industry studies conducted for regulatory authorizations should be required to use (but often do not) the specific GM variety under test and the non-GM isogenic comparator grown at the same time under the same conditions, because this is the only way to ascertain whether unintended changes have been introduced into the crop by the genetic modification process. It is the purpose of the regulatory safety assessment to find this out.

A study that does not observe these restrictions cannot answer that particular question. But it can answer other questions.

For example, a study comparing the effects of feeding Roundup Ready soy versus feeding a non-GM soy variety with different background genetics and grown in different environmental conditions provides information regarding the relative toxicity of the two soy varieties. It can show whether the GM soy is "substantially equivalent" to the non-GM soy, or not. But if the GM soy diet is found to be more toxic than the non-GM soy diet, the study will not be able to identify the genetic modification as the cause of the increased toxicity. It will not reveal whether the toxic effects observed from consumption of the GM crop feed arise from the GM transformation process, from Roundup herbicide residues, from compositional differences arising from the different background genetics, from the different environmental conditions in which the crop was grown, or from a combination of two or more of these factors. Further experiments would have to be carried out to answer these questions.

### Double standards used in evaluating studies that find risk versus studies that conclude safety

The much-cited review of animal feeding studies with GMOs by Snell and colleagues concluded that GM foods were safe. However, many of the reviewed studies had the limitation that the non-GM comparator crop was not the isogenic or near-isogenic variety. This limitation was common to studies that concluded the GM food tested was safe and those that raised concerns. But in an example of the double standards that are often applied to studies that find a GMO is safe versus studies that raise concerns, Snell and colleagues accepted at face value the conclusions of safety while rejecting as unreliable the findings of risk and harm.[42]

## Regulators do not require long-term tests on GMOs

In order to detect health effects caused over time in humans eating GM foods, long-term (chronic) animal feeding trials are needed. But currently, no long-term tests on GM crops or foods are required by regulatory authorities anywhere in the world. Reproductive and multigenerational tests, which are necessary to reveal any effects of GM crops or foods on fertility and future generations, are also not required.[29]

This contrasts with the testing requirements for pesticides, which are far more stringent. Before a pesticide can be approved for use, it must undergo long-term two-year and reproductive tests on mammals.[32] Yet GM foods escape such testing, in spite of the fact that virtually all commercialized GM foods are engineered either to contain an insecticide or to tolerate being sprayed with large amounts of herbicide, so they are likely to contain significant amounts of pesticides (herbicides are technically pesticides).

The longest tests that are routinely conducted on GM foods for regulatory assessments are 90-day rodent feeding trials. In Europe, even these were not compulsory[29] until 2013, when a new law was passed.[62] Such 90-day rodent trials are only medium-term (subchronic) tests that correspond to around seven years in human terms, based on the three-year average life expectancy of the Sprague-Dawley rat[63] and the current life expectancy of a human in the UK.[64] They are too short to show long-term effects such as organ damage or cancer.[65] In addition, too few animals are used in these industry tests to reliably detect harmful effects.

In spite of these serious shortcomings, statistically significant harmful effects have been found even in industry's own 90-day rodent feeding trials. The most common effects observed are signs of toxicity in the liver and kidney, which are the major detoxifying organs and often the first to show evidence of chronic disease.[29]

These observations are consistently interpreted by GM proponents and regulators as "not biologically significant" or as "within the range of normal variation". But as explained above, these claims are not science-based.

## Stacked-trait crops are less rigorously tested than single-trait crops

Most GM crops currently on the market and in the approvals pipeline are not single-trait crops but stacked-trait crops. "Stacked-trait" means that several GM traits are combined in one seed. For example, GM SmartStax maize has eight GM traits: six for insect resistance (Bt toxins) and two for tolerance to different herbicides.

Biotech companies have resorted to developing multi-trait crops because of the failure of single traits. For example (see Chapter 5):

- Pests have developed resistance to single Bt toxins
- Bt crops have been attacked by secondary insect pests
- Weeds have become resistant to glyphosate, the herbicide that most GM crops are engineered to tolerate.

Stacked-trait GM crops pose more risk than single-trait crops because of the possibility of unexpected interactions between the different GM genes introduced into the crop – and between the multiple introduced GM genes and the genes of the host plant. There is also the risk of combined effects resulting from interactions between multiple toxins and biologically active compounds that may be produced in the plant as a result of the introduction of multiple genes. Interactions with residues of pesticides used in conjunction with the GM crop add another dimension of complexity. In short, the addition of multiple traits to a single crop increases the risk of unexpected harmful effects.

However, stacked-trait GM crops are even less rigorously tested for possible health effects than single-trait GM crops. Since 2013 Europe has required 90-day toxicological testing in rats for single-trait GM crops, but not for stacked-trait crops. The European Food Safety Authority (EFSA) maintains that it can assess the toxicity of the final stacked-trait crop by looking at industry test findings on the single-trait crops that were used to develop it.[66]

This stance is based on a series of simplistic assumptions, not on empirical evidence. It fails to look at the actual effects of the combined mutational effects and the mixed transgenes and their products within the crop.

## Antibiotic resistance genes could produce "superbugs"

An additional cause for concern regarding GM food safety is the potential presence of antibiotic resistant "marker" genes in the GM crop. These genes are included in the GM gene cassette to enable genetic engineers to see whether the GM gene of interest has been successfully integrated into the DNA the cells of the host plant. When an antibiotic is added to the plant cells, only those cells that have successfully integrated the GM gene cassette into their DNA will survive. If the antibiotic resistance marker gene is physically linked to the GM gene of interest, it remains in the final GM crop that is commercialized.

In an in vitro study (laboratory study not performed in living animals or humans), GM Bt maize DNA was found to survive processing and was detected in the digestive fluids of sheep. This raises the possibility that the antibiotic resistance gene in the maize could be incorporated into the DNA of gut bacteria, an example of horizontal gene transfer.[67] If the antibiotic resistance gene transferred to a pathogenic bacterial species, this could result in antibiotic-resistant disease-causing bacteria ("superbugs") in the gut.

## What tests should GM crop developers do to ensure that they are safe to eat?

The following tests are the minimum that should be carried out in order to ensure that a GM food is safe to eat.

1. A full range of "omics" molecular profiling analyses should be carried out (genomics, transcriptomics, proteomics, and metabolomics). Profiling of siRNA (gene-silencing RNA) and microRNA (miRNA) molecules should be conducted, to look for intended and unintended changes brought about by the genetic engineering process. Unlike regular RNA molecules, which code for proteins, miRNA molecules regulate gene expression.

These "omics" profiling tests must be done on the GMO and the isogenic non-GMO grown at same location and time, in order to highlight the presence of potential toxins, allergens, and compositional/nutritional disturbances caused by the GM transformation. There must be no spurious use of non-isogenic controls, as is often done by industry in tests conducted for regulatory purposes.

2. Long-term feeding studies should be carried out in an appropriate laboratory animal species. The studies should include:

- Comparison of the GMO with isogenic non-GMO only.
- At least three doses of the GMO and any relevant agrochemicals, including a physiologically relevant dose to which a population could be exposed.
- Three parallel arms of investigation addressing toxicity, carcinogenicity, and multigenerational effects.
- Toxicokinetics analysis of the pesticide, to find out what happens to it once it enters the body of an animal or human that consumes it. This includes how and where it travels in the body, how it breaks down and into what, how efficiently it is excreted, and to what extent and where it bioaccumulates. The entire pesticide formulation as sold and used

must be tested; and in the case of pesticide-producing GM plants, the pesticide isolated from the GM plant must be tested as well as the entire GM plant.

- Comprehensive anatomical, histological (microscopic examination of body tissues), physiological, and biochemical analysis of organs, blood, and urine.
- Molecular profiling of selected organs from test animals to evaluate effects on gene expression, proteins, metabolites, and RNA interference, which could underlie any negative health effects observed.

If a herbicide-tolerant GM crop is being tested, then the herbicide must be tested both alone and in combination with the GM crop (sprayed on during cultivation according to normal practice). The full commercial formulations of herbicides should be tested, as they are sold and used. This study design enables the effects of the GMO to be distinguished from the effects of the herbicide and enables the researchers to determine if the GMO, the herbicide, or a combination of the two are at the basis of any negative health effects observed.

If a pesticide-expressing crop is being tested (e.g. a Bt crop), the pesticide product (e.g. Bt toxin) isolated from the GM crop must be toxicologically tested, as well as testing the whole Bt crop given in feed. It is not adequate to test Bt toxin protein produced from bacteria, which is the current practice of industry in its applications for regulatory authorization. Bt toxin produced from bacteria is only equivalent to the Bt toxin produced in the GM crop in terms of the amino acid sequence. It is not equivalent in terms of the post-translational modifications – the chemical modifications that occur to the protein in the new host organism as an indirect result of the GM gene transfer. Any post-translational modifications to the Bt toxin in bacteria will be markedly different from those in the plant or even completely absent. This is because bacteria lack the ability to perform the post-translational modifications that higher organisms like plants are capable of.

If the Bt toxin is tested only by feeding the whole GM plant and toxicity is found, it is not possible to know if the cause is the Bt toxin, or some novel toxin produced in the plant as a result of the mutagenic effects of the GM process, or the two combined. Hence there is a need to test the Bt toxin isolated from the GM plant as well as the whole Bt crop in order to understand the source of any toxicity.

It is also possible to test the same Bt toxin produced from GM bacteria, in addition. This enables the researchers to determine if any toxicity is due to the post-translational modifications brought about specifically in the GM plant as a result of the genetic engineering process.

3. Following on from the animal feeding studies, the following should be carried out:

- Farm animal toxicity study along the same lines as the laboratory animal feeding studies.
- Long-term dose escalation trials in human volunteers.

## Conclusion

Contrary to frequent claims that there is no evidence of dangers to health from GM foods and crops, peer-reviewed studies have found potential signs of toxicity and actual harmful effects on the health of laboratory and farm animals fed GMOs. These include toxic and allergenic effects.

Most animal feeding studies on GMOs have only been short-term or medium-term in length. While GM proponents claim that the observed harmful effects on health are not "biologically relevant" or "adverse", such claims are scientifically unjustifiable, as these terms have not been properly defined with respect to GMOs.

What is needed are long-term and multi-generational studies on GMOs to see if the changes found in short- and medium-term studies, which are suggestive of harmful health effects, develop into serious disease, premature death, or reproductive or developmental effects. Such studies are not required by regulators anywhere in the world.

## References


1. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
2. EndScienceCensorship.org. Statement: Journal retraction of Séralini GMO study is invalid and an attack on scientific integrity. 2014. Available at: http://www.endsciencecensorship.org/en/page/Statement#.UwUSP14vFY4.
3. Institute of Science in Society. Open letter on retraction and pledge to boycott Elsevier. 2013. Available at: http://www.i-sis.org.uk/Open_letter_to_FCT_and_Elsevier.php#form.
4. Gab-Alla AA, El-Shamei ZS, Shatta AA, Moussa EA, Rayan AM. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(9):1117–1123.
5. El-Shamei ZS, Gab-Alla AA, Shatta AA, Moussa EA, Rayan AM. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(10):684–696.
6. Hines FA. Memorandum to Linda Kahl on the Flavr Savr tomato (Pathology Review PR–152; FDA Number FMF–000526): Pathology Branch's evaluation of rats with stomach lesions from three four-week oral (gavage) toxicity studies (IRDC Study Nos. 677–002, 677–004, and 677–005) and an Expert Panel's report. US Department of Health & Human Services; 1993. Available at: http://www.biointegrity.org/FDAdocs/17/view1.html.
7. Pusztai A. Witness Brief – Flavr Savr tomato study in Final Report (IIT Research Institute, Chicago, IL 60616 USA) cited by Dr Arpad Pusztai before the New Zealand Royal Commission on Genetic Modification. 2000. Available at: http://www.gmcommission.govt.nz/.
8. Pusztai A. Can science give us the tools for recognizing possible health risks of GM food? Nutr Health. 2002;16:73-84.
9. US District Judge Colleen Kollar-Kotelly. Alliance for Bio-Integrity v Shalala (No. 98-1300 D.D.C.). 2000. Available at: http://bit.ly/MnQV0x.
10. Scheuplein RJ. Memorandum: Response to Calgene amended petition. 1993. Available at: http://www.biointegrity.org/FDAdocs/11/view1.html.
11. Pusztai A, Bardocz S, Ewen SWB. Genetically modified foods: Potential human health effects. In: D'Mello JPF, ed. Food Safety: Contaminants and Toxins. Wallingford, Oxon: CABI Publishing; 2003:347–372. Available at: http://www.leopold.iastate.edu/sites/default/files/events/Chapter16.pdf.
12. Prescott VE, Campbell PM, Moore A, et al. Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenicity. J Agric Food Chem. 2005;53:9023–30. doi:10.1021/jf050594v.
13. Lee RY, Reiner D, Dekan G, Moore AE, Higgins TJV, Epstein MM. Genetically modified alpha-amylase inhibitor peas are not specifically allergenic in mice. PloS One. 2013;8:e52972. doi:10.1371/journal.pone.0052972.
14. Higgins TJ. Presentation at the GMSAFOOD conference, Vienna, Austria, 6-8 March 2012 [video]. 2012. Available at: http://www.youtube.com/watch?v=yKda722clq8.
15. Higgins TJ. GMSAFOOD project press conference [video]. 2012. Available at: http://www.youtube.com/watch?v=gHUKE_luMR8.
16. Finamore A, Roselli M, Britti S, et al. Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. J Agric Food Chem. 2008;56:11533–39. doi:10.1021/jf802059w.
17. Kroghsbo S, Madsen C, Poulsen M, et al. Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. Toxicology. 2008;245:24-34. doi:10.1016/j.tox.2007.12.005.
18. Krzyzowska M, Wincenciak M, Winnicka A, et al. The effect of multigenerational diet containing genetically modified triticale on immune system in mice. Pol J Vet Sci. 2010;13:423-30.
19. Malatesta M, Biggiogera M, Manuali E, Rocchi MBL, Baldelli B, Gazzanelli G. Fine structural analyses of pancreatic acinar cell nuclei from mice fed on genetically modified soybean. Eur J Histochem. 2003;47:385–388.
20. Malatesta M, Caporaloni C, Gavaudan S, et al. Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. Cell Struct Funct. 2002;27:173–80.
21. Vecchio L, Cisterna B, Malatesta M, Martin TE, Biggiogera M. Ultrastructural analysis of testes from mice fed on genetically modified soybean. Eur J Histochem. 2004;48:448-54.
22. Malatesta M, Boraldi F, Annovi G, et al. A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008;130:967–977.
23. Tudisco R, Lombardi P, Bovera F, et al. Genetically modified soya bean in rabbit feeding: Detection of DNA fragments and evaluation of metabolic effects by enzymatic analysis. Anim Sci. 2006;82:193–199. doi:10.1079/ASC200530.

24. Brasil FB, Soares LL, Faria TS, Boaventura GT, Sampaio FJ, Ramos CF. The impact of dietary organic and transgenic soy on the reproductive system of female adult rat. Anat Rec Hoboken. 2009;292:587–94. doi:10.1002/ar.20878.
25. Carman JA, Vlieger HR, Ver Steeg LJ, et al. A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. J Org Syst. 2013;8:38–54.
26. Lynas M. GMO pigs study – more junk science. marklynas.org. 2013. Available at: http://www.marklynas.org/2013/06/gmo-pigs-study-more-junk-science/.
27. Food Standards Australia New Zealand (FSANZ). Response to a feeding study in pigs by Carman et al. 2013. Available at: http://www.foodstandards.gov.au/consumer/gmfood/Pages/Response-to-Dr-Carman%27s-study.aspx.
28. Carman J. Response to FSANZ [personal email communication]. 2014.
29. Séralini GE, Mesnage R, Clair E, Gress S, de Vendômois JS, Cellier D. Genetically modified crops safety assessments: Present limits and possible improvements. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-10.
30. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
31. Hammond B, Dudek R, Lemen J, Nemeth M. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food Chem Toxicol. 2004;42:1003-14. doi:10.1016/j.fct.2004.02.013.
32. Séralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
33. Kilic A, Akay MT. A three generation study with genetically modified Bt corn in rats: Biochemical and histopathological investigation. Food Chem Toxicol. 2008;46:1164–70. doi:10.1016/j.fct.2007.11.016.
34. US Food and Drug Administration (FDA). Biotechnology consultation note to the file BNF No 00077. Office of Food Additive Safety, Center for Food Safety and Applied Nutrition; 2002. Available at: http://bit.ly/ZUmiAF.
35. Trabalza-Marinucci M, Brandi G, Rondini C, et al. A three-year longitudinal study on the effects of a diet containing genetically modified Bt176 maize on the health status and performance of sheep. Livest Sci. 2008;113:178–190. doi:10.1016/j.livsci.2007.03.009.
36. Ewen SW, Pusztai A. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet. 1999;354:1353-4. doi:10.1016/S0140-6736(98)05860-7.
37. Pusztai A, Bardocz S. GMO in animal nutrition: Potential benefits and risks. In: Mosenthin R, Zentek J, Zebrowska T, eds. Biology of Nutrition in Growing Animals.Vol 4. Elsevier Limited; 2006:513–540. Available at: http://www.sciencedirect.com/science/article/pii/S1877182309701043.
38. Fares NH, El-Sayed AK. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. Nat Toxins. 1998;6(6):219-33.
39. Poulsen M, Kroghsbo S, Schroder M, et al. A 90-day safety study in Wistar rats fed genetically modified rice expressing snowdrop lectin Galanthus nivalis (GNA). Food Chem Toxicol. 2007;45:350-63. doi:10.1016/j.fct.2006.09.002.
40. Schrøder M, Poulsen M, Wilcks A, et al. A 90-day safety study of genetically modified rice expressing Cry1Ab protein (Bacillus thuringiensis toxin) in Wistar rats. Food Chem Toxicol. 2007;45:339-49. doi:10.1016/j.fct.2006.09.001.
41. Gu J, Krogdahl A, Sissener NH, et al. Effects of oral Bt-maize (MON810) exposure on growth and health parameters in normal and sensitised Atlantic salmon, Salmo salar L. Br J Nutr. 2013;109:1408-23. doi:10.1017/S000711451200325X.
42. Snell C, Aude B, Bergé J, et al. Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Food Chem Toxicol. 2012;50:1134-48.
43. Tyl RW, Crofton K, Moretto A, Moser V, Sheets LP, Sobotka TJ. Identification and interpretation of developmental neurotoxicity effects: a report from the ILSI Research Foundation/Risk Science Institute expert working group on neurodevelopmental endpoints. Neurotoxicol Teratol. 2008;30:349-81. doi:10.1016/j.ntt.2007.07.008.
44. GMO Compass. MON863. 2006. Available at: http://www.gmo-compass.org/eng/gmo/db/53.docu.html.
45. European Food Safety Authority (EFSA). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from insect-protected genetically modified maize MON 863 and MON863 x MON 810, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (Question No EFSA-Q-2003-121) Opinion adopted on 2 April 2004. EFSA J. 2004;2004(50):1–25.
46. European Food Safety Authority (EFSA) GMO Panel. Opinion of the scientific panel on genetically modified organisms on a request from the Commission related to the notification (reference C/DE/02/9) for the placing on the market of insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. EFSA J. 2004;2004:1-25.
47. Doull J, Gaylor D, Greim HA, Lovell DP, Lynch B, Munro IC. Report of an Expert Panel on the reanalysis by of a 90-day study conducted by Monsanto in support of the safety of a genetically modified corn variety (MON 863). Food Chem Toxicol. 2007;45:2073-85. doi:10.1016/j.fct.2007.08.033.
48. European Food Safety Authority (EFSA). EFSA review of statistical analyses conducted for the assessment of the MON 863 90-day rat feeding study. Parma, Italy; 2007.
49. European Food Safety Authority (EFSA) GMO Panel. Statement of the Scientific Panel on Genetically Modified Organisms on the analysis of data from a 90-day rat feeding study with MON 863 maize. Parma, Italy; 2007.
50. Takeuchi T, Tsutsumi O. Serum bisphenol A concentrations showed gender differences, possibly linked to androgen levels. Biochem Biophys Res Commun. 2002;291:76-8. doi:10.1006/bbrc.2002.6407.
51. Laviola G, Gioiosa L, Adriani W, Palanza P. D-amphetamine-related reinforcing effects are reduced in mice exposed prenatally to estrogenic endocrine disruptors. Brain Res Bull. 2005;65:235-40. doi:10.1016/j.brainresbull.2004.11.015.
52. Hilbeck A, Meier M, Römbke J, Jänsch S, Teichmann H, Tappeser B. Environmental risk assessment of genetically

modified plants - concepts and controversies. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-13.
53. Breyer H. EFSA definition of "biological relevance" in connection with GMO tests: Written question by Hiltrud Breyer (Verts/ALE) to the Commission. 2008. Available at: http://bit.ly/M6UFyn.
54. European Food Safety Authority (EFSA). Scientific opinion: Statistical significance and biological relevance. EFSA J. 2011;9:2372.
55. International Life Sciences Institute (ILSI). Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology, prepared by a task force of the ILSI International Food Biotechnology Committee. Compr Rev Food Sci Food Saf. 2004;3:38–104.
56. International Life Sciences Institute (ILSI). Risk assessment of genotoxic carcinogens task force. Brussels, Belgium; 2011. Available at: http://bit.ly/1i8n8qk.
57. Constable A, Barlow S. Application of the margin of exposure approach to compounds in food which are both genotoxic and carcinogenic: Summary report of a workshop held in October 2008 organised by the ILSI Europe Risk Assessment of Genotoxic Carcinogens in Food Task Force. Brussels, Belgium: ILSI Europe; 2009. Available at: http://www.ilsi.org.ar/administrador/panel/newsletter/news27/moe_ws_report.pdf.
58. Corporate Europe Observatory. The International Life Sciences Institute (ILSI), a corporate lobby group. 2012. Available at: http://corporateeurope.org/sites/default/files/ilsi-article-final.pdf.
59. Hammond B, Lemen J, Dudek R, et al. Results of a 90-day safety assurance study with rats fed grain from corn rootworm-protected corn. Food Chem Toxicol. 2006;44:147-60. doi:10.1016/j.fct.2005.06.008.
60. Lotter D. The genetic engineering of food and the failure of science – Part 2: Academic capitalism and the loss of scientific integrity. Int Jrnl Soc Agr Food. 2008;16:50–68.
61. Scientific American. Do seed companies control GM crop research? http://www.scientificamerican.com/article.cfm?id=do-seed-companies-control-gm-crop-research. Published July 20, 2009.
62. European Parliament and Council. Commission implementing regulation (EU) no. 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Off J Eur Union. 2013. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF.
63. SAGE Research Labs. Sprague-Dawley outbred rat. 2014. Available at: http://www.sageresearchlabs.com/research-models/outbred-rats/sprague-dawley-outbred-rat.
64. World Health Organization. Life expectancy by country. 2013. Available at: http://apps.who.int/gho/data/node.main.688?lang=en.
65. Séralini GE, de Vendomois JS, Cellier D, et al. How subchronic and chronic health effects can be neglected for GMOs, pesticides or chemicals. Int J Biol Sci. 2009;5:438-43.
66. European Food Safety Authority Panel on Genetically Modified Organisms (GMO). Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. EFSA J. 2011;9:2150.
67. Duggan PS, Chambers PA, Heritage J, Michael Forbes J. Fate of genetically modified maize DNA in the oral cavity and rumen of sheep. Br J Nutr. 2003;89:159–66. doi:10.1079/BJN2002764.

## 3.2 Myth: The Séralini (2012) study was bad science and no conclusions can be drawn from it

## Truth: The Séralini study is the most detailed and thorough study ever done on a GM food and its associated pesticide

### Myth at a glance

A study published in 2012 found that a Monsanto GM Roundup-tolerant maize and very low levels of the Roundup herbicide it was engineered to be grown with caused severe organ damage and hormonal disruption in rats fed over a long-term period of two years. Unexpected additional findings were increased rates of large palpable tumours and premature death in some treatment groups.

Starting from just hours after publication, the paper was viciously attacked as "bad science" by pro-GM scientists and commentators. Over a year after it had passed peer review and was published, the journal editor appeared to succumb to the continued pressure and retracted the paper. Scientists worldwide condemned the move as an "act of scientific censorship" and as unjustified on scientific and ethical grounds.

The study, carried out by a team led by Professor Gilles-Eric Séralini, based at the University of Caen, France, remains to date the most detailed and thorough study ever carried out on a GM food crop.

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The study was carried out by a team led by Professor Gilles-Eric Séralini, based at the University of Caen, France.

### Why this study?

Séralini designed his two-year rat feeding study[1] as a direct follow-up of Monsanto's short 90-day rat feeding trial on the same GM NK603 maize, which the company had conducted to support its application for regulatory authorization. Monsanto published the results of its trial in 2004,[2] the same year that the maize was authorized in the EU.

Differences were found in the GM-fed rats, but the Monsanto authors dismissed the findings as not related to the GM maize and as not "biologically meaningful".[2] The European Food Safety Authority (EFSA) agreed with Monsanto, claiming that the differences were "of no biological significance" and that the maize was as safe as non-GM maize.[3]

Séralini's team obtained Monsanto's raw data and re-analyzed it. They found signs of liver and kidney toxicity in the GM-fed rats, publishing their findings in a peer-reviewed journal in 2009.[4]

Séralini carried out his 2012 study on NK603 maize and Roundup[1] to see whether these initial findings of potential toxicity really were of no biological significance, as Monsanto and EFSA claimed, or whether they developed into serious disease.

The overall experimental design was similar to Monsanto's, in order to make the two experiments comparable. The differences were that Séralini's experiment:

- Was longer (two years to Monsanto's 90 days) and far more detailed in scope
- Included three rather than two doses (as Monsanto had used) of the GM maize feed
- Measured a larger number of bodily functions
- Was designed to separate out the effects of the GM maize from those of the Roundup herbicide it is engineered to tolerate. This was the first study on a GM crop to distinguish effects in this way.

## The methodology

Séralini's study[1] tested the long-term effects of Monsanto's GM NK603 maize, which is engineered to survive being sprayed with Roundup herbicide, and Roundup, both separately and in combination.

The study used 200 rats divided into ten groups, each of ten males and ten females. The GM maize alone was tested on three groups at 11%, 22% and 33% of the total diet. GM maize that had been sprayed with Roundup in the field was tested on three groups in the same proportions. Roundup alone, given in drinking water at three different doses, was tested on three groups. The lowest dose corresponded to the level of contamination that can be found in some tap water, the intermediate dose to the maximum level permitted in the USA in animal feed, and the highest dose to half the strength of Roundup as used in agriculture. Controls were fed a diet containing 33% non-GM maize and plain drinking water.

## The findings in brief – and their implications

Séralini's findings were alarming. Both GM maize NK603 and Roundup caused serious kidney and liver damage and an increased and earlier development of large palpable tumours, leading to an increased rate of mortality. The first tumours only appeared four months into the study, one month after Monsanto's test had ended, and peaked at 18 months. Many toxic effects found in the GM maize-treated groups were also found in the Roundup-treated groups, indicating that the two substances had similar toxic effects.[1]

These serious effects had not shown up in Monsanto's 90-day test[2] simply because it was too short. Chronic diseases like organ damage and tumours take time to develop and become obvious.[5]

An objective analysis of Séralini's study would conclude that long-term chronic toxicity and carcinogenicity studies are needed on all GM foods and complete commercial pesticide formulations before they are commercialized.

## The findings in detail

### Toxicological effects

The main findings were multiple organ damage in rats fed the GM maize, whether or not the crop had been sprayed with Roundup, and independently, in rats fed low levels of Roundup in drinking water.

Statistical analysis was conducted on the biochemical measurements of blood and urine samples taken at 15 months, the latest time point when at least 90% of the rats were still alive in each treatment group. Statistically significant damage was found to mammary tissues, liver, kidneys, and pituitary glands of the rats fed the GM maize grown with and without Roundup, and in the rats given Roundup alone in drinking water.

The main objective of the study was to see if the signs of liver and kidney toxicity seen in Monsanto's 90-day investigation vanished or escalated into serious health problems over an extended period of two years. The study found that the signs of liver and kidney toxicity seen at 90 days did indeed escalate into serious organ damage and failure over a two-year period. Thus the main objective of the study was comprehensively met.

### Mortality and tumours

Unexpectedly, both the timing and rate of mortality and tumour growth were affected by the treatments.

Mortality reflected both spontaneous deaths and euthanasia due to tumours that impeded functions such as breathing, nutrition, and digestion. Spontaneous deaths accounted for most male mortality, while euthanasia accounted for most female mortality during the study.

Male and female rats responded differently to the GM maize and Roundup treatments. Whereas 30% of control males and 20% of control females died before the mean survival time, up to 50% of males and 70% of females died prematurely in some groups containing GM maize. However, the rate of mortality did not increase proportionately with the treatment dose, reaching a threshold at the lowest dose (11%) or, for some groups, the mid dose (22%) of GM maize, both with and without Roundup spraying during treatment.

In males, the maximum difference between treatment groups and controls was five times more deaths occurring during the 17th month in the group consuming 11% GM maize, and in females six times greater mortality during the 21st month on the 22% GM maize diet with and without Roundup. In the female treatment groups, there were two to three times more deaths compared with controls by the end of the experiment, and these occurred earlier. Females were more sensitive to the presence of Roundup in drinking water than males, as evidenced by a shorter lifespan. The most common causes of death were linked to large mammary tumours in females, and liver and kidney damage in males.

Three types of tumours were reported: non-regressive palpable tumours (NRPTs), small internal tumours, and metastatic (spreading to other parts of the body) tumours. As with mortality, tumour incidence appeared to vary between male and female animals. Small internal tumours accounted for most tumours in males, and roughly half of those in females, although the proportion varied among treatments. NRPTs in female rats were largely mammary tumours. Metastatic tumours were rare.

None of the treatments affected incidence of small internal or metastatic tumours, but all treatments increased NRPTs as compared to the controls. Furthermore, NRPTs began to occur earlier in treated than in control rats. For male and female animals, respectively, the first NRPT occurred at about 700 and 400 days in controls, compared with 100 and 200-300 days in GM maize treatments, and at around 530–600 and 200–400 days in Roundup-dosed water treatments.

While this was not a carcinogenicity study but a chronic toxicity study, tumour occurrence is relevant for two reasons. First, researchers are required to report tumours even in toxicity studies, according to the chronic toxicity protocol set by the Organization for Economic Cooperation and Development (OECD).[6] Second, some types of tumours may indicate metabolic dysfunctions to be explored in further studies.

Nonetheless, of pivotal importance to GMO safety testing is the timing of the tumour onset. The first NRPTs were detected at 4 and 7 months for male and female rats respectively, with most tumours occurring after 18 months. This illustrates the futility of relying on 90-day feeding trials to detect potential risks from chronic exposure to GMOs and their associated pesticides.

### Hormonal effects

Both GM NK603 maize and Roundup significantly and independently disrupted hormonal regulation. Substances that do this are known as endocrine disruptors. Séralini's team suggested possible avenues through which this might happen.

The GM trait inserted into NK603 maize causes the over-expression of a key enzyme that would otherwise be suppressed by glyphosate. The GM version of the enzyme is unaffected by glyphosate, meaning that the GM plant can survive despite being sprayed with glyphosate herbicide.

However, in its original, unmodified state, this enzyme catalyzes the first step in the shikimic acid pathway, a major metabolic trunk with many outcomes. One of those outcomes is the production of the metabolites, caffeic and ferulic acids, which may inhibit the growth of tumours. Ferulic acid is also known to modulate estrogenic activity in mammals and the growth of most mammary tumours is dependent on estrogen. Séralini and colleagues suggested in their paper that the reduced levels of caffeic and ferulic acid found in GM NK603 maize could have contributed to the observed trend of increased tumour occurrence, and specifically to the increased incidence of mammary tumours.

In addition to possible downstream metabolic impacts from the GM trait, it is also necessary to account for the independent effect of glyphosate. Roundup, which may be present as a residue in the sprayed GM maize treatments as well as in the dosed water treatments, is known to disrupt aromatase. This enzyme, also known as estrogen synthetase, catalyzes the conversion of androgen to estrogen. Roundup has further been shown in studies cited by Séralini's team to impact upon androgen and estrogen receptors, and to act as an endocrine disruptor of sex hormones.

Furthermore, in studies carried out in vitro (laboratory experiments not performed in living animals or humans), glyphosate has been shown to act as an estrogen substitute capable of stimulating the growth of estrogen-dependent breast cancer cells at very low doses.[7] This may be a contributing factor to the more rapid growth of mammary tumours in the Roundup treatment groups.

Thus both the GM maize and the Roundup herbicide it relies upon had toxic effects on the mammalian physiology in a gender-specific way. In other words, the effects on males were different from the effects on females.

Treatment responses recorded in this study were non-linear, meaning that the effect did not increase in proportion to the dose. They appeared to be more reflective of a threshold-type response. For example, incidence of NRPTs in female rats was uniform across all three doses of Roundup in drinking water. This would suggest that even the lowest dose was high enough to meet the threshold for a full response. Endocrine disruptor effects can act at extremely low concentrations and can be non-linear.[8] This may explain why mortality appeared to be higher in male rats fed a diet containing 11% GM maize than a diet containing 22% or 33% GM maize.

The findings of the study challenge the central premise of GM, namely that it is feasible to insert a GM gene to confer a single specific trait without compromising the expression of other apparently unrelated traits.

## Study "a bomb"

Séralini's study was called "a bomb" by Corinne Lepage, a French Member of the European Parliament and France's former minister for the environment. Lepage explained that the study exposed the weakness of industry studies conducted for regulatory authorization.[9] The GM maize had previously been judged safe by regulators around the world, including the European Food Safety Authority (EFSA),[3] on the basis of a short 90-day study by Monsanto.[2]

If the study were taken seriously, it could cause the collapse of the GMO industry worldwide and of the regulatory systems that have approved GM foods as safe since the 1990s.

As an example of the study's power, seven expert witnesses tried but failed to rebut it in a court case brought by Greenpeace Asia against the Philippines government. The court ruled in Greenpeace's favour and banned the release of GM Bt brinjal (eggplant/aubergine) on precautionary grounds.[10]

## Campaign to discredit the study

Within hours of the study's release,[1] it came under sustained attack from pro-GM lobbyists and scientists. Leading the campaign to discredit the study was the UK's Science Media Centre,[11] an organization that defends and promotes GM technology and has taken funding from GMO companies like Monsanto and Syngenta.[12,13]

Séralini's critics soon turned their attention to trying to get the journal that had published the study to retract it. Many of the critics had undisclosed conflicts of interest with the GM industry or industry-funded lobby groups, or with organizations with vested interests in public acceptance of GM technology.[14,15]

The study was also dismissed by regulatory agencies, including the European Food Safety Authority (EFSA).[16,17,18,19] However, these were the same agencies that had previously approved this or other GM foods as safe. For example, in 2003 EFSA had issued an opinion that GM NK603 maize was as safe as non-GM maize,[3] an opinion that had served as the basis for its authorization in Europe for use in food and feed.

EFSA had also previously argued that 90-day feeding trials were sufficient to see even chronic (long-term) toxic effects, adding that even these short tests were not always necessary.[20] Yet the first tumours in Séralini's experiment had only shown up four months into the study, a full month after a 90-day trial would have ended.[1] Séralini's study showed that 90-day tests are inadequate to see chronic effects. So for EFSA to accept that the study had any validity would have been equivalent, as the French Member of the European Parliament and former minister for the environment Corinne Lepage said, to "cutting off the branch on which the agency has sat for years".[21]

The French Academy of Sciences issued a statement attacking Séralini's study, but it was strongly challenged by an eminent member of the Academy, Paul Deheuvels (see Myth 2.2, "Gilles-Eric Séralini", for details).[22]

## Criticisms misrepresent the study

The main criticisms levelled at Séralini's study are addressed on a website, gmoseralini.org, set up by scientists and citizens who were concerned that important findings were being buried. Séralini's team has also replied to the critics in the pages of the journal that published their original research.[23]

The criticisms rely on a misrepresentation of the study – that it was a flawed carcinogenicity (cancer) study. In fact it was a long-term (chronic) toxicity study, as is made clear in the title and introduction.[1] Criticizing the study on these grounds is equivalent to criticizing a cat for not being a dog. It is simply an irrelevance, apparently introduced in order to distract from the main findings of the study, which were toxicological in nature and included severe organ damage and hormonal disturbances.

## The "too few rats" criticism

The criticism levelled against the statistical aspect of Séralini's study is that the numbers of rats in the experiments (ten per sex per group) were too small to draw any conclusions about tumours. The critics claimed that given the relatively low numbers of rats and the tendency of the Sprague-Dawley strain of rat to develop tumours spontaneously, the dramatic increase in large palpable tumours in treated groups of rats was only due to random variation and not to the effects of the GM maize and Roundup herbicide.[11]

However, Séralini's study was not a carcinogenicity study, for which larger groups of rats are generally used. It was a chronic toxicity study that unexpectedly found an increase in tumour incidence. The number of rats used was appropriate for a chronic toxicity study.[24] For example, the chronic toxicity protocol set by the Organisation for Economic Cooperation and Development for industry testing of chemicals recommends that 20 rats per sex per group be used, but stipulates that only 50% (10 per sex per group) need to be analyzed for blood and urine chemistry.[6] This is the same number that Séralini used in total, so his experiment yielded the same amount of data as the OECD chronic toxicity studies that form the basis for authorization of thousands of chemicals worldwide.

In addition, the fact that Séralini analyzed 100% of the animals in his study means that he avoided the selection bias introduced by the OECD practice of allowing only 50% of the animals to be analyzed.

The eminent statistician and member of the French Academy of Sciences Paul Deheuvels has defended the statistical aspects of Séralini's study, including the numbers of rats used. Deheuvels argues that larger numbers of rats (typically 50 per sex per group) are only needed in cancer studies that test the safety of a substance for regulatory assessments. The larger numbers are designed to avoid false negative error, in which a toxic effect exists but is missed because too few rats are used to reliably show it.[25]

Deheuvels's point is confirmed by the OECD guideline 116 on how to carry out carcinogenicity and chronic toxicity studies, which states that the purpose of using higher numbers of animals is "in order to increase the sensitivity of the study".[26] Lack of sensitivity of study design was not an issue with Séralini's investigation, since a dramatic increase in tumour incidence was seen in the treated groups of rats, despite the relatively small size of the groups. Deheuvels said this provided strong evidence that the GM maize and Roundup tested were indeed toxic.[25]

Peter Saunders, emeritus professor of mathematics at King's College London, agreed with Deheuvels that the fact Séralini had used smaller groups "makes the results if anything more convincing, not less". Saunders explained: "Using a smaller number of rats actually made it less likely to observe any effect. The fact that an effect was observed despite the small number of animals made the result all the more serious."[27]

## The "wrong strain of rat" criticism

Séralini was also criticized for using the Sprague-Dawley strain of rat, which the critics claimed is unusually prone to tumours.[11] The reasoning is that the rats could have got tumours anyway, even without being exposed to GM NK603 maize and Roundup.

But this criticism is absurd. The Sprague-Dawley (SD) rat is a standard strain for long-term chronic toxicity experiments like Séralini's, as well as carcinogenicity experiments.[28] Monsanto used the SD rat in its chronic toxicity, carcinogenicity, and reproductive toxicity rat feeding studies on glyphosate, the main ingredient of Roundup herbicide, which it conducted in support of regulatory authorisation.[29,30]

If the SD rat was the wrong strain for Séralini to use, then it was the wrong strain in all these other studies, too, and market authorizations for the thousands of chemicals and GM foods that were authorized on the basis of these studies would have to be revoked.

Monsanto also used the SD rat in its 90-day study on GM NK603 maize.[2] Séralini chose the same strain in order to make his experiment comparable with Monsanto's. If he had used a different strain of rat, he undoubtedly would have been criticized for failing to make his experiment comparable with Monsanto's.

It has been argued that the SD rat is acceptable for carcinogenicity studies using large numbers of animals but not for studies using smaller numbers due to its "tumour-prone" nature. However, as we have pointed out, Séralini's study was not a carcinogenicity study, but a chronic toxicity study that unexpectedly found an increase in tumour incidence.

In fact, there is every reason to doubt claims that the SD rat is especially tumour-prone. The SD rat is about as prone to developing cancerous tumours as humans living in industrialized countries, as is shown by data from the Ramazzini Institute in Italy, which specialises in carcinogenicity research and uses this strain of rat.[31]

And while tumours are not necessarily cancerous, the tumour incidence in control animals in Séralini's experiment was consistent with data on human cancer incidence in the UK. In Séralini's study, 30% of female control animals developed tumours,[1] and the lifetime risk of developing cancer in the UK (excluding non-melanoma skin cancer) is 37% for females and 40% for males.[32] It should also be noted that only one of the ten male control animals in Séralini's experiment developed a tumour and that was very late in life.[1]

## Support from scientists

Séralini's study was supported by hundreds of independent scientists from across the world in a series of petitions, letters, and articles.[33,34,35,36,37,38,39]

Two public interest scientific research groups condemned the double standards whereby regulatory authorities relentlessly criticized Séralini's study for perceived weaknesses in methodology, yet accepted at face value far weaker studies carried out by the GMO industry as proof of the products' safety.[36,40]

While no research study is perfect and all are limited in scope, Séralini's study is the most carefully designed, thorough, and detailed to date on a GM food.

## The retraction

Over a year after Séralini's study had passed peer review and was published in the Elsevier journal Food and Chemical Toxicology (FCT), Dr A. Wallace Hayes, the editor-in-chief of the journal, apparently gave in to pressure and retracted the paper.[41] The retraction followed a non-transparent post-publication second review process by anonymous persons of unknown professional competence using undisclosed terms of reference.[42] It also followed the appointment of a former Monsanto scientist, Richard E. Goodman, to the journal's editorial board.[43]

The reasons given by Hayes for retracting the study appear to be unprecedented in the history of scientific publishing. According to the Committee on Publication Ethics (COPE), of which FCT is a member,[44] retraction is reserved for cases of unreliable findings due to honest error, misconduct, redundant publication or plagiarism, and unethical research.[45]

None of these criteria applied to the Séralini paper, as Hayes conceded in a letter to Professor Séralini. Hayes stated that an examination of Séralini's raw data had revealed "no evidence of fraud or intentional misrepresentation" and results presented were "not incorrect".[42]

Hayes added that the retraction was solely based on the "inconclusive" nature of the outcomes concerning rates of tumour incidence and mortality, based on the relatively low number of animals and the strain of rat used.[42]

In a later statement, Hayes appeared to contradict his previous statement that the results were "not incorrect". He now claimed that the paper was an example of unreliable findings due to "honest error". He wrote: "The data are inconclusive, therefore the claim (i.e. conclusion) that Roundup Ready maize NK603 and/or the Roundup herbicide have a link to cancer is unreliable… it is the entire paper, with the claim that there is a definitive link between GMO and cancer that is being retracted."[46]

However, this is a misrepresentation of Séralini's paper. The authors did not claim that the GM maize NK603 and/or Roundup herbicide have a "link to cancer", let alone a "definitive link". In fact, the word "cancer" is not even used in the paper and the authors specified in their introduction that the study was not designed as a carcinogenicity study.[1]

Moreover, it is unacceptable to retract an entire paper on the grounds of the perceived inconclusiveness of some of its findings. The chronic toxicity findings – the organ damage and hormonal disruption – are solidly based and statistically significant, and have not been challenged by Hayes. Yet these findings have been removed from the record based on the perceived inconclusiveness of a part of the study's findings – the rates of tumours and mortality.

## Scientists condemn retraction

The retraction was condemned by scientists worldwide, many of whom derided the very notion that a scientific study should produce “conclusive” results.

Professor Jack Heinemann of the Centre for Integrated Research in Biosafety in New Zealand applied Hayes’s criterion of conclusiveness to several revolutionary and pivotal studies in the history of science.

Heinemann found that among the studies that would have to be retracted on grounds of “inconclusiveness” were two pioneering papers by the Nobel Prize winners James Watson and Francis Crick, describing the structure of DNA and how it might replicate. Watson and Crick expressed important qualifications of their data, which were only confirmed by a further study five years later. Nonetheless, as of the time of publication these findings were acknowledged to be inconclusive.

Heinemann concluded that in science, getting less than definitive results is “not uncommon” and that such findings must be allowed to stand the test of time and further research.[47]

David Schubert, a professor with the Salk Institute for Biological Studies in the USA, commented on the purported rationale for the retraction, “The editors claim the reason was that ‘no definitive conclusions can be reached.’ As a scientist, I can assure you that if this were a valid reason for retracting a publication, a large fraction of the scientific literature would not exist.”[48]

Schubert added, “The major criticisms of the Séralini manuscript were that the proper strain of rats was not used and their numbers were too small. Neither criticism is valid. The strain of rat is that required by the FDA for drug toxicology, and the toxic effects were unambiguously significant.”[48]

The European Network of Scientists for Social and Environmental Responsibility (ENSSER) said in a statement that the retraction violates the “standards of good science”, adding, “‘Conclusive’ results are rare in science, and certainly not to be decided by one editor and a secret team of persons using undisclosed criteria and methods. Independent science would cease to exist if this were to be an accepted mode of procedure.”[49]

ENSSER denounced the lack of transparency about how the decision to retract the paper was reached, noting, “In a case like this, where many of those who denounced the study have long-standing, well-documented links to the GM industry and, therefore, a clear interest in having the results of the study discredited, such lack of transparency … is inexcusable, unscientific and unacceptable. It raises the suspicion that the retraction is a favour to the interested industry, notably Monsanto.”[49]

A group of Mexican scientists also criticized Hayes for giving in to “pressure” from multinational companies to retract the study. Elena Alvarez-Buylla, a member of the Union of Scientists Committed to Society (UCCS), said the retraction “has no scientific basis and is in response to pressures from multinational companies that market GM crops.”[50]

Three researchers writing in the scientific journal Environmental Health Perspectives stated that the retraction of any paper on grounds of inconclusiveness "has adverse implications on the integrity of the concept of the peer-review process as the critical foundation of unbiased scientific inquiry" and marks "a significant and destructive shift in management of the publication of controversial scientific research".[51]

The retraction was condemned as an "act of scientific censorship" by 181 scientists on the website endsciencecensorship.org.[52] Some of the scientists authored an article on the website explaining why the retraction was not justified ethically or scientifically. They noted that insofar as definitive conclusions exist in science, "they tend to be found in fields that have been studied for many years. For example, there is a definite conclusion that gravity exists on earth, but no journal would be interested in publishing such known facts. Scientific publications are about new knowledge and new data. This hardly ever arrives accompanied by 'definitive conclusions'."[53]

In a separate initiative, over 1,340 scientists pledged to boycott Elsevier over the retraction on the website of the Institute of Science in Society.[54]

The French MEP Corinne Lepage commented that the purpose of the retraction was to shut down the possibility of long-term studies on GMOs forever. She said, "The study by Gilles-Eric Séralini should not have happened. But it did happen. Now it must be as if it had never happened."[55]

## Conclusion

The Séralini study is the most in-depth study ever carried out on a GM food and its associated pesticide.

The attacks on the study and its subsequent retraction by the editor of the journal that published it have been widely condemned by scientists as commercially motivated, based on misrepresentations of the study, and not scientifically justified. The editor's purported rationale for retraction – inconclusiveness of some aspects of the study – is not credible, since lack of conclusiveness is common in scientific studies.

Also, the main findings of the study, consisting of the organ damage and hormonal disruption, are statistically significant and are not disputed by the journal editor. Nevertheless the entire study has been retracted on the basis of the alleged inconclusiveness of some of its findings – the rates of tumour incidence and mortality.

Any uncertainties and questions raised by the study's findings can only be resolved by further long-term studies.

In the meantime, GM NK603 maize and Roundup should be withdrawn from the market, as they have not been proven to be safe over the long term and the study by Séralini and colleagues provides evidence that they are not safe.

## References


1. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
2. Hammond B, Dudek R, Lemen J, Nemeth M. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food Chem Toxicol. 2004;42:1003-14. doi:10.1016/j.fct.2004.02.013.
3. European Food Safety Authority (EFSA). Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from herbicide-tolerant genetically modified maize NK603, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (QUESTION NO EFSA-Q-2003-002): Opinion adopted on 25 November 2003. EFSA J. 2003;2003(9):1–14.
4. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
5. Séralini GE, de Vendomois JS, Cellier D, et al. How subchronic and chronic health effects can be neglected for GMOs, pesticides or chemicals. Int J Biol Sci. 2009;5:438-43.
6. Organisation for Economic Cooperation and Development (OECD). OECD guideline no. 452 for the testing of chemicals: Chronic toxicity studies: Adopted 7 September 2009. 2009. Available at: http://bit.ly/LxJT1Z.
7. Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol. 2013. doi:10.1016/j.fct.2013.05.057.
8. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012;33(3):378-455. doi:10.1210/er.2011-1050.
9. Lepage C. OGM: Une étude et une démarche historiques [GMOs: A study and a historical approach]. Huffington Post. http://huff.to/10Jp0PP. Published September 24, 2012.
10. Republic of the Philippines Court of Appeals, Manila, Former Special 13th Division. Greenpeace Southeast Asia et al. vs Environmental Management Bureau of the Dept of Environment and Natural Resources et al. CA-G.R. SP No. 00013: Resolution. Manila, Philippines; 2013:10.
11. Science Media Centre. Expert reaction to GM maize causing tumours in rats [press release]. http://bit.ly/163wOg6. Published September 19, 2012.
12. Powerbase. Science Media Centre. 2014. Available at: http://www.powerbase.info/index.php/Science_Media_Centre.
13. Science Media Centre. Funding. 2012. Available at: http://bit.ly/11sRAzV.
14. Matthews J. Smelling a corporate rat. Spinwatch. http://bit.ly/184fwif. Published December 11, 2012.
15. Sourice B. OGM: La guerre secrète pour décrédibiliser l'étude Séralini [The covert war to discredit Séralini's study]. Rue 89/Le Nouvel Observateur. http://blogs.rue89.nouvelobs.com/de-interet-conflit/2012/11/12/ogm-la-guerre-secrete-pour-decredibiliser-letude-seralini-228894. Published November 12, 2012.
16. European Food Safety Authority (EFSA). Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2910.
17. European Food Safety Authority (EFSA). Final review of the Séralini et al. (2012a) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2986.
18. Haut Conseil des Biotechnologies Comité Scientifique (France). Avis en réponse à la saisine du 24 septembre 2012 relative à l'article de Séralini et al (Food and Chemical Toxicology, 2012). 2012. Available at: http://bit.ly/ZODCdn.
19. ANSES (French Agency for Food Environmental and Occupational Health & Safety). Opinion concerning an analysis of the study by Séralini et al. (2012) "Long term toxicity of a ROUNDUP herbicide and a ROUNDUP-tolerant genetically modified maize." 2012. Available at: http://www.anses.fr/sites/default/files/files/BIOT2012sa0227EN.pdf.
20. European Food Safety Authority (EFSA) GMO Panel Working Group on Animal Feeding Trials. Safety and nutritional assessment of GM plants and derived food and feed: The role of animal feeding trials. Food Chem Toxicol. 2008;46:S2-70. doi:10.1016/j.fct.2008.02.008.
21. Lepage C. OGM: l'EFSA a manqué à une déontologie élémentaire [GMOs: EFSA breaches basic ethical code]. Le Nouvel Observateur. http://bit.ly/QWjizy. Published October 7, 2012.
22. Guyon C. Académie des sciences: le scandale des OGM [French Academy of Sciences: The GMO scandal]. Rebelle-Santé. 2013;(153). Available at: http://gmoseralini.org/french-academy-of-sciences-the-gmo-scandal/.
23. Séralini GE, Mesnage R, Defarge N, et al. Answers to critics: Why there is a long term toxicity due to NK603 Roundup-tolerant genetically modified maize and to a Roundup herbicide. Food Chem Toxicol. 2013;53:461-8.
24. GMOSeralini.org. Criticism: Séralini used too few animals to draw any conclusions.; 2013. Available at: http://gmoseralini.org/criticism-seralini-used-too-few-animals/.
25. Deheuvels P. Étude de Séralini sur les OGM: Pourquoi sa méthodologie est statistiquement bonne [Seralini study on GMOs: Why the methodology is statistically sound]. Le Nouvel Observateur. http://www.gmwatch.org/component/content/article/14294. Published October 9, 2012.
26. Organisation for Economic Cooperation and Development (OECD). Guidance document 116 on the conduct and design of chronic toxicity and carcinogenicity studies, supporting test guidelines 451, 452 and 453: 2nd edition: Environment directorate joint meeting of the chemicals committee and the working party on chemicals, pesticides and biotechnology. 2012.
27. Saunders P. Excess cancers and deaths with GM feed: The stats stand up. Sci Soc. 2012. Available at: http://www.i-sis.org.uk/Excess_cancers_and_deaths_from_GM_feed_stats_stand_up.php.

28. Meyer H, Hilbeck A. Rat feeding studies with genetically modified maize - a comparative evaluation of applied methods and risk assessment standards. Environ Sci Eur. 2013;25(33). Available at: http://www.enveurope.com/content/pdf/2190-4715-25-33.pdf.
29. Rapporteur member state Germany. Monograph on glyphosate: Glyphosate: Annex B-5: Toxicology and metabolism: Full Report Glyphosat 05: Volume 3-1_Glyphosat_05.pdf. German Federal Agency for Consumer Protection and Food Safety (BVL); 1998. Available at: http://bit.ly/12Af5cm.
30. Rapporteur member state Germany. Monograph on glyphosate: Glyphosate: Annex B-5: Toxicology and metabolism: Vol 3-1 Glyphosat 04. German Federal Agency for Consumer Protection and Food Safety (BVL); 1998. Available at: http://bit.ly/QwOnPA.
31. Soffritti M, Belpoggi F, Degli Esposti D. Cancer prevention: The lesson from the lab. In: Biasco G, Tanneberger S, eds. Cancer Medicine at the Dawn of the 21st Century: The view from Bologna. Bologna: Bononia University Press; 2006:49–64. Available at: http://www.ramazzini.it/ricerca/pdfUpload/Cancer%20Medicine%2049-64_2006.pdf.
32. Sasieni PD, Shelton J, Ormiston-Smith N, Thomson CS, Silcocks PB. What is the lifetime risk of developing cancer?: The effect of adjusting for multiple primaries. Br J Cancer. 2011;105:460-5. doi:10.1038/bjc.2011.250.
33. Bardocz S, Clark EA, Ewen SW, et al. Seralini and science: an open letter. Independent Science News. http://bit.ly/11NhFKw. Published October 2, 2012.
34. Andalo C, Chercheuse AHS, Atlan A, Auclair D, Austerlitz F, Barot S. Science et conscience [Science and conscience]. Le Monde. http://bit.ly/ZEtOUM. Published November 14, 2012.
35. Heinemann J. Letter to the editor. Food Chem Toxicol. 2013;53:427.
36. European Network of Scientists for Social and Environmental Responsibility (ENSSER). Questionable biosafety of GMOs, double standards and, once again, a “shooting-the-messenger” style debate. Berlin, Germany; 2012. Available at: http://bit.ly/SHCfvm.
37. GMOSeralini.org. What was the reaction to the study? Available at: http://gmoseralini.org/faq-items/what-was-the-reaction-to-the-study-2/.
38. Agence France Presse. OGM: Séralini publie une liste de soutien de 193 scientifiques internationaux. 20minutes.fr. http://bit.ly/11LJlk8. Published November 16, 2012.
39. Battaglia D. Kritische Gentech-Forschung: “Hier geht es um viel Geld” [Crucial GM research: “This is about large sums of money”]. Tages Woche. http://www.gmwatch.org/index.php/news/archive/2012/14458. Published November 2, 2012.
40. Then C. The European Food Safety Authority: Using double standards when assessing feeding studies: A Testbiotech background. Munich, Germany; 2012. Available at: http://www.testbiotech.de/node/725.
41. Elsevier. Elsevier announces article retraction from Journal Food and Chemical Toxicology. 2013. Available at: http://www.elsevier.com/about/press-releases/research-and-journals/elsevier-announces-article-retraction-from-journal-food-and-chemical-toxicology#sthash.VfY74Y24.dpuf.
42. Hayes AW. Letter to Professor GE Séralini. 2013. Available at: http://www.gmwatch.org/files/Letter_AWHayes_GES.pdf.
43. Robinson C, Latham J. The Goodman affair: Monsanto targets the heart of science. Earth Open Source Indep Sci News. 2013. Available at: http://bit.ly/1hC69y4.
44. Committee on Publication Ethics (COPE). Members: Food and Chemical Toxicology. 2014. Available at: http://publicationethics.org/members/food-and-chemical-toxicology.
45. Committee on Publication Ethics (COPE). Retraction guidelines. 2009. Available at: http://publicationethics.org/files/retraction%20guidelines.pdf.
46. Hayes AW. Food and Chemical Toxicology editor-in-chief, A. Wallace Hayes, publishes response to Letters to the Editors. 2013. Available at: http://www.elsevier.com/about/press-releases/research-and-journals/food-and-chemical-toxicology-editor-in-chief,-a.-wallace-hayes,-publishes-response-to-letters-to-the-editors#sthash.tTW2LCGq.dpuf.
47. Heinemann J. Let’s give the scientific literature a good clean up. Biosafetycooperative.newsvine.com. 2013. Available at: http://bit.ly/1aeULiB.
48. Schubert D. Science study controversy impacts world health. U-T San Diego. http://www.utsandiego.com/news/2014/jan/08/science-food-health/. Published January 8, 2014.
49. European Network of Scientists for Social and Environmental Responsibility (ENSSER). Journal’s retraction of rat feeding paper is a travesty of science and looks like a bow to industry: ENSSER comments on the retraction of the Séralini et al. 2012 study. Berlin, Germany; 2013. Available at: http://bit.ly/1cytNa4.
50. AFP. Mexican scientists criticise journal’s retraction of study on GMO. terra.cl. http://bit.ly/1jVl1HZ ; English translation available at: http://gmwatch.org/index.php/news/archive/2013/15225. Published December 18, 2013.
51. Portier CJ, Goldman LR, Goldstein BD. Inconclusive findings: Now you see them, now you don’t! Environ Health Perspect. 2014;122(2).
52. EndScienceCensorship.org. Statement: Journal retraction of Séralini GMO study is invalid and an attack on scientific integrity. 2014. Available at: http://www.endsciencecensorship.org/en/page/Statement#.UwUSP14vFY4.
53. Antoniou M, Clark EA, Hilbeck A, et al. Reason given for retraction – inconclusiveness – is invalid. 2014. Available at: http://www.endsciencecensorship.org/en/page/retraction-reason#.Uweb4l4vFY4.
54. Institute of Science in Society. Open letter on retraction and pledge to boycott Elsevier. 2013. Available at: http://www.i-sis.org.uk/Open_letter_to_FCT_and_Elsevier.php#form.
55. European Parliament. Séralini au Parlement Européen (28/11/2013) - Elsevier retire l’étude sur les OGM.; 2013. Available at: http://www.youtube.com/watch?v=4VSqeKd7M9k&feature=youtu.be; Partial English translation of French transcript available at: http://gmwatch.org/index.php/news/archive/2014/15271.

# 3.3 Myth: Many long-term studies show GM is safe

# Truth: Few long-term studies have been carried out, but some show unexpected toxic effects

## Myth at a glance

Some GMO proponents and scientists say that many long-term animal feeding studies have concluded GM foods are safe. But this claim is not accurate. Few long-term and in-depth studies have been carried out and several studies that have been carried out have found toxic effects.

A review by Snell and colleagues purporting to present long-term studies showing long-term safety is misleading, with double standards being used to dismiss findings of harm while findings of safety are accepted at face value.

Some GMO proponents and scientists say that many long-term animal feeding studies have concluded GM foods are safe. But this claim is not accurate. Few long-term and in-depth studies have been carried out and several studies that have been carried out have found toxic effects. An analysis of one genuinely long-term study and a review purporting to examine long-term studies on GMOs follows.

## The Séralini study

This study, covered in detail in Myth 3.2 above, found that a Monsanto GM Roundup-tolerant maize and tiny amounts of the Roundup herbicide it was engineered to be grown with caused severe organ damage and hormonal disruption in rats fed over a long-term period of two years. Unexpected additional findings were increased rates of large palpable tumours and premature death in some treatment groups.[1]

The study was retracted by the journal that published it for reasons that cannot be scientifically or ethically justified (see Myth 3.2 above).

The extreme shortage of long-term studies on GM foods was emphasized by two of France's national regulatory agencies, the HCB (High Council for Biotechnology) and ANSES (the French national food safety agency), in their critiques[2,3] of the Séralini 2012 study.[1] ANSES noted that it had conducted a search for long-term animal feeding studies on GMOs and their associated pesticides that were comparable with Séralini's study – and found only two.[3,4] One, by Manuela Malatesta's group in Italy, found health problems in mice fed GM soybeans (see also Myth 3.1).[5] The other is only available in Japanese and cannot be evaluated by the international scientific community.[6]

## The Snell review

A review by Snell and colleagues (2011) purports to examine the health impacts of GM foods as revealed by long-term and multi-generational studies. The Snell review concludes that the GM foods examined are safe.[7] However, this cannot be justified from the data presented in the review.

Some of the studies examined by Snell and colleagues are not even toxicological studies that look at health effects. Instead they are so-called animal production studies that look at aspects of interest to food producers, such as feed conversion (the amount of weight the animal puts on relative to the amount of food it eats)[8] or milk production in cows.[9]

Several of the studies examined are not long-term studies, in that they do not follow the animal over anything approaching its natural lifespan. For example, Snell and colleagues categorized a 25-month feeding study with GM Bt maize in dairy cows by Steinke and colleagues[9] as a long-term study. But although most dairy cows are sent to slaughter at four to five years old because their productivity and commercial usefulness decreases after that age, a cow's natural lifespan is 17–20 years. A 25-month study in dairy cows is equivalent to around eight years in human terms. So from a toxicological point of view, Steinke's study is not long-term and could at most be described as medium-term (subchronic).

Similarly, Snell and colleagues categorized a seven-month study in salmon[10] as long-term. But a farmed salmon lives for between 18 months and three years before being killed and eaten and a wild salmon can live for seven to eight years. Snell and colleagues also categorized as long-term some studies in chickens lasting 35[11] and 42 days,[8] even though a chicken's natural lifespan is between seven and 20 years, depending on breed and other factors. So again, these are not long-term studies.

Moreover, in Steinke's study, nine cows from the treatment group and nine from the control group – half of the 18 animals in each group – fell ill or proved infertile, for reasons that were not investigated or explained. In a scientifically unjustifiable move, these cows were simply removed from the study and replaced with other cows. No analysis is presented to show whether the problems that the cows suffered had anything to do with either of the two diets tested.[9]

It is never acceptable to replace animals in a feeding experiment. For this reason alone, this study[9] is irrelevant to an assessment of health effects from GM feed and Snell and colleagues should not have included it in their analysis.

Many of the studies reviewed are on animals that have a very different digestive system and metabolism to humans and are so are not considered relevant to assessing human health effects. These include studies on broiler chickens, cows, sheep, and fish.

Some of the studies reviewed did in fact find toxic effects in the GM-fed animals, but these were dismissed by Snell and colleagues. For example, findings of damage to liver and kidneys and alterations in blood biochemistry in rats fed GM Bt maize over three generations[12] are dismissed, as are the findings of Manuela Malatesta's team, of abnormalities in the liver, pancreatic, and testicular cells of mice fed on GM soy,[13,14,15,5] in both cases on the basis that the researchers used a non-isogenic soy variety as the non-GM comparator. This was unavoidable, given the refusal of GM seed companies to release their patented seeds to independent researchers.[16]

An objective assessment of Malatesta's findings would have concluded that while the results do not show that GM soy was more toxic than the non-GM isogenic variety (because the isogenic variety was not used), they do show that GM herbicide-tolerant soy was more toxic than the wild-type soybean tested, either because of the herbicide used, or the effect of the genetic engineering process, or the different environmental conditions in which the two soy types were grown, or a combination of two or more of these factors.

In an extraordinary move, Snell and colleagues offered as the main counter to Malatesta's experimental findings a poster presentation offering no new or existing data and with no references, presented at a Society of Toxicology conference[17] by two employees of the chemical industry consultancy firm Exponent.[18] Though at first glance the reference given by Snell and colleagues has the appearance of a peer-reviewed paper, it is not. An abstract of the presentation was also published by the Society of Toxicology in its collection of conference proceedings.[19]

Presentations given at conferences are not usually subjected to the scrutiny given to peer-reviewed publications. They certainly do not carry sufficient weight to counter original research findings from laboratory animal feeding experiments with GM foods, such as Malatesta's. This is particularly true when they do not base their argument on hard data, as in the case of this opinion piece.

## Snell and colleagues use double standards

Snell and colleagues dismiss studies findings of risk on the basis that the researchers did not use the non-GM isogenic comparator, while accepting findings of safety in studies with the same methodological weakness.

They also accept as proof of GMO safety some studies in which the number of animals is not stated,[6] meaning that it is not possible to analyze the statistics to see if the findings are statistically significant (and therefore meaningful).

Other studies accepted by Snell and colleagues as proof of GMO safety include some with such small group sizes (for example, of six animals) that no conclusions can be drawn from them.[11]

It is educational to recall how critics of Séralini's 2012 study[1] claimed that his groups of ten animals per sex per group were too small to draw any conclusions.[20] Though this allegation is incorrect according to the standards of the Organization for Economic Cooperation and Development for chronic toxicity studies, which requires that only ten animals per sex per group are analyzed for blood and urine chemistry,[21] it is clear that studies using sample sizes of only six animals cannot be used to claim safety for GM foods.

As a result of these double standards, Snell and colleagues' review is fatally biased and no conclusions can be drawn from it.

## Russian long-term studies not followed up

Two long-term multigenerational studies conducted by Russian researchers found worrying results but were never followed up. On the contrary, at least one of the research studies was deliberately suppressed.

This was a multigenerational study in rats by the researcher Irina Ermakova. The study found decreased fertility in rats and decreased weight gain and increased mortality in pups, in groups fed GM Roundup-tolerant soy.[22,23]

Ermakova never had the chance to publish her findings in full in an international journal. Instead her work was subjected to a deceptive and highly irregular review process by the editor of the journal Nature Biotechnology. She was sent a dummy proof of what she thought was going to be her article, complete with her byline as author.[24] However, the article as published was very different. It was an attack on her work by four pro-GM critics.

Contrary to the ethics of scientific publishing, the critics' conflicts of interest with the GM crop industry went undisclosed by the journal.[25] Also Ermakova was not shown their criticisms before the article was published, so she did not have a chance to defend herself in the same issue of the journal.[26]

Ermakova's treatment at the hands of the editor of Nature Biotechnology and the four pro-GM scientists attracted condemnation from scientists[27] and in the media.[28,29,30]

Harvey Marcovitch, director of the Committee on Publication Ethics (COPE), which sets ethical standards for academic journals, commented, "This is a type of publication which I have never encountered." He said that while reading it he was struck by "some surprising things". He was unwilling to speculate as to what exactly happened: "Either the editor was trying out a new form of experimentation, in which not everything went according to plan, or there was indeed a conspiracy or whatever one wants to call it."[28]

Nevertheless, the journal editor kept his job and Ermakova was deprived of any chance of ever publishing her work in an international journal.

In a separate experiment that was only reported in the Russian media and not published in a peer-reviewed journal, Russian biologist Alexey V. Surov and his team fed three generations of hamsters different diets (one without soy, one with non-GM soy, one with GM soy, and the final one with higher amounts of GM soy). By the third generation, the pups from the fourth group suffered a high mortality rate and most of the adults lost the ability to reproduce.[31]

It is not possible to judge the quality of Ermakova's or Surov's studies because neither study has been published in full in an international journal. The studies should be repeated to confirm or refute the reported findings.

## Conclusion

Few long-term and in-depth studies have been carried out on GM foods and several studies that have been carried out have found toxic effects. A review by Snell and colleagues purporting to present long-term studies showing long-term safety is misleading, with double standards being used to dismiss findings of harm while accepting at face value findings of safety. A Russian long-term study that produced concerning results was suppressed and has not been followed up.

There is no evidence that commercialized GM foods are safe to eat over the long term and conversely there is some evidence that they are not safe.

## References


1. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221–4231.
2. Haut Conseil des Biotechnologies Comité Scientifique (France). Avis en réponse à la saisine du 24 septembre 2012 relative à l'article de Séralini et al (Food and Chemical Toxicology, 2012). 2012. Available at: http://bit.ly/ZODCdn.
3. ANSES (French Agency for Food Environmental and Occupational Health & Safety). Opinion concerning an analysis of the study by Séralini et al. (2012) "Long term toxicity of a ROUNDUP herbicide and a ROUNDUP-tolerant genetically modified maize." 2012. Available at: http://www.anses.fr/sites/default/files/files/BIOT2012sa0227EN.pdf.
4. ANSES (French Agency for Food Environmental and Occupational Health & Safety). ANSES highlights the weaknesses of the study by Séralini et al., but recommends new research on the long-term effects of GMOs. 2012. Available at: http://www.anses.fr/en/content/anses-highlights-weaknesses-study-s%C3%A9ralini-et-al-recommends-new-research-long-term-effects.
5. Malatesta M. A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008;130:967–977.
6. Sakamoto Y, Tada Y, Fukumori N, et al. [A 104-week feeding study of genetically modified soybeans in F344 rats]. Shokuhin Eiseigaku Zasshi J Food Hyg Soc Jpn. 2008;49:272–82.
7. Snell C, Aude B, Bergé J, et al. Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Food Chem Toxicol. 2012;50:1134–48.
8. Brake J, Faust MA, Stein J. Evaluation of transgenic event Bt11 hybrid corn in broiler chickens. Poult Sci. 2003;82:551–9.
9. Steinke K, Guertler P, Paul V, et al. Effects of long-term feeding of genetically modified corn (event MON810) on the performance of lactating dairy cows. J Anim Physiol Anim Nutr Berl. 2010;94:e185–93. doi:10.1111/j.1439-0396.2010.01003.x.
10. Sissener NH, Sanden M, Bakke AM, Krogdahl A, Hemre GI. A long term trial with Atlantic salmon (Salmo salar L.) fed genetically modified soy; focusing general health and performance before, during and after the parr–smolt transformation. Aquaculture. 2009;2009:108–117.
11. Flachowsky G, Aulrich K, Böhme H, Halle I. Studies on feeds from genetically modified plants (GMP) – Contributions to nutritional and safety assessment. Anim Feed Sci Technol. 2007;133:2–30.
12. Kilic A, Akay MT. A three generation study with genetically modified Bt corn in rats: Biochemical and histopathological investigation. Food Chem Toxicol. 2008;46:1164–70. doi:10.1016/j.fct.2007.11.016.
13. Malatesta M, Biggiogera M, Manuali E, Rocchi MBL, Baldelli B, Gazzanelli G. Fine structural analyses of pancreatic acinar cell nuclei from mice fed on genetically modified soybean. Eur J Histochem. 2003;47:385–388.
14. Malatesta M, Caporaloni C, Gavaudan S, et al. Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. Cell Struct Funct. 2002;27:173–80.
15. Vecchio L, Cisterna B, Malatesta M, Martin TE, Biggiogera M. Ultrastructural analysis of testes from mice fed on genetically modified soybean. Eur J Histochem. 2004;48:448–54.
16. Waltz E. Under wraps – Are the crop industry's strong-arm tactics and close-fisted attitude to sharing seeds holding back independent research and undermining public acceptance of transgenic crops? Nat Biotechnol. 2009;27(10):880–882. doi:10.1038/nbt1009-880.
17. Williams AL, DeSesso JM. Genetically-modified soybeans: A critical evaluation of studies addressing potential changes associated with ingestion; Abstract 1154, Poster Board 424, Safety Concerns of Food and Natural Products. 2010. Available at: http://www.exponent.com/files/Uploads/Documents/news%20and%20features/SOT%20Presentation%20Handout_draft.pdf.
18. Williams AL, Watson RE, DeSesso JM. Developmental and reproductive outcomes in humans and animals after glyphosate exposure: A critical analysis. J Toxicol Environ Health Part B. 2012;15:39–96.
19. Williams AL, DeSesso JM. Genetically-modified soybeans: A critical evaluation of studies addressing potential changes associated with ingestion; Abstract 1154. The Toxicologist. 2010;114:246.

20. GMOSeralini.org. Criticism: Séralini used too few animals to draw any conclusions. 2013. Available at: http://gmoseralini.org/criticism-seralini-used-too-few-animals/.
21. Organisation for Economic Cooperation and Development (OECD). OECD guideline no. 452 for the testing of chemicals: Chronic toxicity studies: Adopted 7 September 2009. 2009. Available at: http://bit.ly/LxJT1Z.
22. Ermakova I. Genetically modified soy leads to the decrease of weight and high mortality of rat pups of the first generation. Preliminary studies. Ecosinform. 2006;1:4–9.
23. Ermakova I. [Influence of soy with gene EPSPS CP4 on the physiological state and reproductive function of rats in the first two generations]. Contemp Probl Sci Educ. 2009;5:15–20.
24. Nature Biotechnology. Supplementary materials 1: Email correspondence between Nature Biotechnology and Irina Ermakova; and Supplementary materials 2: Galley proof for Irina Ermakova. 2007. Available at: http://www.nature.com/nbt/journal/v25/n12/extref/nbt1207-1359-S1.pdf.
25. Marshall A. GM soybeans and health safety – a controversy reexamined. Nat Biotechnol. 2007;25:981–987.
26. Ermakova IV. GM soybeans – revisiting a controversial format. Nat Biotechnol. 2007;25:1351–1360.
27. Ermakova I, John B, Ho MW, et al. Letters to the editor. Nat Biotechnol. 2007;25:1351–1360.
28. Fischer R. The excommunication of a heretic. WOZ. http://www.gmwatch.org/latest-listing/46-2007/5861-the-excommunication-of-a-heretic. Published November 13, 2007.
29. Latham J, Wilson A. What is Nature Biotechnology good for? Indep Sci News. 2007. Available at: http://independentsciencenews.org/health/nature-biotechnology/.
30. John B. Journal editor admits involvement in Ermakova "set-up." GM-Free Cymru. 2007. Available at: http://www.gmfreecymru.org/pivotal_papers/involvement_ermakova.htm.
31. Domnitskaya M. Russia says genetically modified foods are harmful. Voice of Russia. http://english.ruvr.ru/2010/04/16/6524765.html. Published April 16, 2010.

# 3.4 Myth: EU research shows GM foods are safe
# Truth: EU research shows evidence of harm from GM foods

## Myth at a glance

Research on GM foods commissioned by the European Union (EU) is often claimed to conclude that GM foods are safe. This is a misrepresentation of this research project, most of which was not designed to examine the safety of specific GM foods.

Three animal feeding studies from the project that did examine the safety of a GM food raise concerns, including differences in organ weights and immune responses in the GM-fed animals. These findings should be followed up in long-term studies.

An EU research project is often cited as providing evidence for GM crop and food safety. Those who have cited the project in this way include:

- The GM industry lobby group ISAAA[1]
- Jonathan Jones, a British Monsanto-connected scientist[2,3]
- Nina Fedoroff,[4] former science and technology adviser to US secretary of state Hillary Clinton
- Máire Geoghegan-Quinn, European Commissioner for research, innovation and science.[5]

However, the report based on this project, "A decade of EU-funded GMO research"[6], presents no data that could provide such evidence – for example, from long-term feeding studies in animals.

Indeed, the project was not even designed to test the safety of any single GM food, but to focus on "the development of safety assessment approaches".[6] In fact, taxpayers would be entitled to ask why the Commission spent 200 million Euros of public money[6] on a research project that failed to address this most pressing of questions about GM foods.

In the SAFOTEST section of the report, which is dedicated to GM food safety, only five published animal feeding studies are referenced.[7,8,9,10,11]

Two of these studies were carried out with a GM rice expressing a protein known to be toxic to mammals, in order to ascertain that the methodology used was sensitive enough to detect toxicity of a comparable level.[7,8]

None of the studies tested a commercialized GM food; none tested the GM food for long-term effects beyond the medium-term period of 90 days; all found differences in the GM-fed animals, which in some cases were statistically significant; and none concluded on the safety of the GM food tested, let alone on the safety of GM foods in general. Therefore the EU research project provides no evidence that could support claims of safety for any single GM food or of GM crops in general.

It is difficult to work out from the EU report how many studies were completed, what the findings were, and how many studies were published in peer-reviewed journals, because the authors of the report often fail to reference specific studies to back up their claims. Instead, they randomly list references to a few published studies in each chapter of the report and leave the reader to guess which statements refer to which studies.

In some cases it is unclear whether there is any published data to back up the report's claims. For example, a 90-day feeding study on hamsters is said to show that "the GM potato is as safe as the non-GM potato", but no reference is given to any published study or other source of data, so there is no way of verifying the claim.

An analysis of the three SAFOTEST studies that fed a GMO not previously known to be toxic is below.

## Poulsen and colleagues (2007)[10]

A feeding trial in rats fed a GM insect-resistant rice found significant differences in the GM-fed group as compared with the control group fed the non-GM parent line of rice. Differences included a markedly higher water intake by the GM-fed group, as well as differences in blood biochemistry, immune response, and gut bacteria. Organ weights of female rats fed GM rice were different from those fed non-GM rice. Commenting on the differences, the authors said, "None of them were considered to be adverse". But they added that this 90-day study "did not enable us to conclude on the safety of the GM food."[10]

In reality, a 90-day study is too short to show whether any changes found are "adverse" (giving rise to identifiable illness). Yet no regulatory body anywhere in the world requires GM foods to be tested for longer than this subchronic (medium-term) period of 90 days.

The study also found that the composition of the GM rice was different from that of the non-GM parent, in spite of the fact that the two rice lines were grown side-by-side in the same conditions. This is clear evidence that the GM transformation process had disrupted gene structure and/or function in the GM variety, making it substantially non-equivalent to the non-GM line.

## Schrøder and colleagues (2007)[11]

A study in rats fed GM Bt rice found significant differences in the GM-fed group of rats as compared with the group fed the non-GM isogenic (with the same genetic background but without the genetic modification) line of rice. These included differences in the distribution of gut bacterial species – the GM-fed group had 23% higher levels of coliform bacteria. There were also differences in organ weights between the two groups, namely in the adrenals, testes and uterus. The authors concluded that due to the study design, any toxicological findings "most likely will derive from unintended changes introduced in the GM rice and not from toxicity of Bt toxin" in its natural, non-GM form.[11]

The study found that the composition of the GM rice was different from that of the non-GM isogenic variety in levels of certain minerals, amino acids, and total fat and protein content.[11] The authors dismissed these differences on the basis that they were within the range reported for all varieties of rice in the literature. However, comparing the GM rice to genetically distinct, unrelated rice varieties is scientifically flawed and irrelevant. It serves only to mask the effects of the GM process.

Despite this flawed approach, the level of one amino acid, histidine, was found to be markedly higher in the GM rice compared with the non-GM isogenic variety and outside the variability range for any rice.[11] Does this matter? No one knows, as the required investigations have not been carried out. However, in other studies on rats, an excess of histidine caused rapid zinc excretion[12] and severe zinc deficiency.[13]

In addition, the level of the fatty acid, stearic acid, was below the value reported in the literature for any rice[11] and therefore the rice cannot be considered substantially equivalent to non-GM rice.

## Kroghsbo and colleagues (2008)[8]

A study in rats fed GM Bt rice (this study in addition contained a group of rats fed GM rice expressing the known mammalian toxin mentioned above) found a Bt-specific immune response in the non-GM-fed control group as well as the GM-fed groups. This unexpected finding led the researchers to conclude that the immune response in the control animals must have been due to their inhaling particles of the powdered Bt toxin-containing feed consumed by the GM-fed group. The researchers recommended that for future tests on Bt crops, GM-fed and control groups should be kept in separate rooms or with separate air handling systems.[8]

## Conclusion

The EU research project provides no evidence that commercialized GM foods are safe to eat and was not designed to provide such evidence. Instead, it was designed to develop methodologies to test GM food safety.

The three SAFOTEST studies examined above do not provide evidence of safety for GM foods and crops. On the other hand, they provide evidence that:

- Over a decade after GM foods were released into the food and feed supplies, regulators still have not agreed on methods of assessing them for safety
- The GM foods tested were markedly different in composition from their non-GM counterparts – probably due to the mutagenic or epigenetic (producing changes in gene function) effects of the GM process
- The GM foods tested caused unexpected, potentially adverse effects in GM-fed animals that should be investigated further in long-term tests
- The authors were not able to conclude that the GM foods tested were safe.

## References


1. International Service for the Acquisition of Agri-biotech Applications (ISAAA). EC report on "A Decade of EU-Funded GMO Research" describes "tailored" bioenergy crop research project. Crop Biotech Update. 2010. Available at: http://bit.ly/12AjVpL.
2. Doward J. Scientist leading GM crop test defends links to US biotech giant Monsanto. The Guardian. http://bit.ly/10k54vC. Published July 18, 2010.
3. Jones JD. The cost of spurning GM crops is too high. The Guardian (UK). http://bit.ly/MpSIil. Published July 21, 2011.
4. Fedoroff NV. Engineering food for all. New York Times. http://nyti.ms/K4Hufn. Published August 18, 2011.
5. European Commission. Commission publishes compendium of results of EU-funded research on genetically modified crops. Brussels, Belgium; 2010. Available at: http://europa.eu/rapid/pressReleasesAction.do?reference=IP/10/1688.
6. European Commission Directorate-General for Research and Innovation, Biotechnologies, Agriculture, Food. A decade of EU-funded GMO research (2001–2010). Brussels, Belgium; 2010.
7. Poulsen M, Schrøder M, Wilcks A, et al. Safety testing of GM-rice expressing PHA-E lectin using a new animal test design. Food Chem Toxicol Int J Publ Br Ind Biol Res Assoc. 2007;45(3):364-377. doi:10.1016/j.fct.2006.09.003.
8. Kroghsbo S, Madsen C, Poulsen M, et al. Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. Toxicology. 2008;245:24-34. doi:10.1016/j.tox.2007.12.005.
9. Knudsen I, Poulsen M. Comparative safety testing of genetically modified foods in a 90-day rat feeding study design allowing the distinction between primary and secondary effects of the new genetic event. Regul Toxicol Pharmacol. 2007;49(1):53-62. doi:10.1016/j.yrtph.2007.07.003.
10. Poulsen M, Kroghsbo S, Schroder M, et al. A 90-day safety study in Wistar rats fed genetically modified rice expressing snowdrop lectin Galanthus nivalis (GNA). Food Chem Toxicol. 2007;45:350-63. doi:10.1016/j.fct.2006.09.002.
11. Schrøder M, Poulsen M, Wilcks A, et al. A 90-day safety study of genetically modified rice expressing Cry1Ab protein (Bacillus thuringiensis toxin) in Wistar rats. Food Chem Toxicol. 2007;45:339-49. doi:10.1016/j.fct.2006.09.001.
12. Freeman RM, Taylor PR. Influence of histidine administration on zinc metabolism in the rat. Am J Clin Nutr. 1977;30:523-7.
13. Wensink J, Van den Hamer CJ. Effect of excess dietary histidine on rate of turnover of 65Zn in brain of rat. Biol Trace Elem Res. 1988;16:137-50. doi:10.1007/BF02797098.

# 3.5 Myth: Those who claim that GM foods are unsafe are being selective with the data, since many other studies show safety

# Truth: Studies that claim safety for GM crops are more likely to be industry-linked and therefore biased

## Myth at a glance

GM proponents claim that those who claim GM foods are unsafe are being selective with the data, since many other studies show they are safe.

But two comprehensive reviews of the scientific literature show that industry-linked studies are more likely to conclude that the GM food being tested is safe, whereas independent studies are more likely to raise concerns.

A comprehensive review of studies on the health risks and nutritional value of GM crops found that if a study on GMOs involves an industry scientist, it will invariably find no problem with the GMO.

This pattern of industry bias and advocacy science has been well documented in the case of other products, such as tobacco and pharmaceutical drugs.

The bias of industry-sponsored or industry-linked studies on the safety of hazardous products is well documented. Each time industry-linked studies are compared with studies on the same product from the independent (non-industry-linked) scientific literature, the same verdict is reached: industry studies are more likely to conclude that the product is safe.

The best known example is tobacco industry studies, which successfully delayed regulation for decades by manufacturing doubt and controversy about the negative health effects of smoking and passive smoking.[1] Studies sponsored by the pharmaceutical and mobile phone industry have also been shown to be more likely to portray their products in a favourable light than non-industry-funded studies.[2,3,4]

The case of GM crops is no different. Reviews of the scientific literature on the health risks of GM foods demonstrate that industry-linked studies are more likely to conclude that the GM food tested is safe, whereas independent studies are more likely to raise concerns:

- A review of 94 published studies on health risks and nutritional value of GM crops found that they were much more likely to reach favourable conclusions when the authors were affiliated with the GM industry than when the authors had no industry affiliation. In the studies where there was such a conflict of interest, 100% (41 out of 41) reached a favourable conclusion on GMO safety. The remaining 53 papers, in which none of the authors had professional ties to the biotech industry, were split: 39 concluded safety, 12 found problems, and two had neutral conclusions.[5] This was a highly statistically significant difference: the probability of it happening by chance was less than one in 1,000. This finding suggests that if a study on GMOs involves an industry scientist, it will invariably find no problem with the GMO.

- A literature review of GM food safety studies found about an equal number of research groups suggesting that GM foods were safe and groups raising serious concerns. However, most studies concluding that GM foods are as nutritious and safe as non-GM counterparts were performed by the companies responsible for developing the GMO or associates.[6]

In spite of the fact that industry-linked studies are biased in favour of conclusions of safety, approvals for GM crops are based solely on industry studies.

*"In a study involving 94 articles selected through objective criteria, it was found that the existence of either financial or professional conflict of interest was associated [with] study outcomes that cast genetically modified products in a favourable light."*
– Johan Diels, CBQF/Escola Superior de Biotecnologia da Universidade Católica Portuguesa, Portugal, and colleagues[5]

## Conclusion

A comprehensive review of the scientific literature on the health risks and nutritional wholesomeness of GM foods found that studies in which authors had a financial or professional conflict of interest with the GMO industry were more likely to conclude that the GMO was as safe and nutritional as the non-GM food tested.

## References

1. Michaels D. Doubt is Their Product: How Industry's Assault on Science Threatens Your Health. Oxford University Press; 2008.
2. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. Br Med J. 2003;326:1167. doi:10.1136/bmj.326.7400.1167.
3. Baker CB, Johnsrud MT, Crismon ML, Rosenheck RA, Woods SW. Quantitative analysis of sponsorship bias in economic studies of antidepressants. Br J Psychiatry. 2003;183:498–506.
4. Huss A, Egger M, Hug K, Huweiler-Müntener K, Röösli M. Source of funding and results of studies of health effects of mobile phone use: Systematic review of experimental studies. Environ Health Perspect. 2007;115:1–4.
5. Diels J, Cunha M, Manaia C, Sabugosa-Madeira B, Silva M. Association of financial or professional conflict of interest to research outcomes on health risks or nutritional assessment studies of genetically modified products. Food Policy. 2011;36:197–203.
6. Domingo JL, Bordonaba JG. A literature review on the safety assessment of genetically modified plants. Env Int. 2011;37:734–742.

# 3.6 Myth: GM foods are safe for human consumption

# Truth: The few studies that have been conducted on humans show problems

## Myth at a glance

GM proponents claim that GM foods are extensively tested and have been found safe for people to eat. But this is false. GM foods are not properly tested for safety for human consumption before they are released for sale.

The few published studies that have directly tested the safety of GM foods for human consumption found potential problems but were not followed up.

All GM crops should be tested in long-term studies on human volunteers prior to commercialization.

GM foods should be labelled as such and post-commercialization monitoring of populations consuming these foods should be carried out.

GM proponents claim that GM foods are extensively tested and have been found safe for people to eat. But this is false. GM foods are not properly tested for safety for human consumption before they are released for sale.[1,2] The only published studies that have directly tested the safety of GM foods for human consumption found potential problems but were not followed up. Findings include the following:

- In a study on human volunteers fed a single GM soybean meal, intact GM DNA was found to survive processing and was detected in the digestive tract. There was also evidence for the presence of intact GM gene units in the digesta (food undergoing digestion) of some of the subjects and of horizontal gene transfer of the glyphosate herbicide-tolerance GM gene to gut bacteria.[3,4] Horizontal gene transfer is a process by which DNA is transferred from one organism to another through mechanisms other than reproduction.
- In a study in humans testing immune response to wild-type non-GM soybeans and GM soybeans, skin test results from 49 patients showed that 13 had immune responses to non-GM soybeans and eight to GM soybeans. One of the experimental subjects showed an immune response to GM soy but not to non-GM soy. GM soy was found to contain a protein that was different from the protein in non-GM soy.[5] Most allergies are to proteins. This study does not show that GM soy is more allergenic than non-GM soy, but it does show that GM foods could cause new allergies that are not predictable from analysis of a person's immune response to non-GM versions of the same food.
- A GM soy variety modified with a gene from Brazil nuts was found to react with antibodies present in blood serum taken from people known to be allergic to Brazil nuts.

Based on current immunological knowledge, this observation indicates that this soy variety would produce an allergic reaction in people allergic to Brazil nuts.[6]

- A study conducted in Canada detected significant levels of the insecticidal protein, Cry1Ab, circulating in the blood of pregnant and non-pregnant women and in the blood supply to foetuses.[7] This insecticidal protein is present in GM Bt crops as well as in insecticidal sprays used in chemically-based and organic farming. How the Bt toxin protein got into the blood (whether through food or another exposure route) is unclear. The validity of the detection method used was disputed by Monsanto,[8] but Monsanto's objections have been answered by the authors of the original study.[9] The study raises questions as to why GM Bt crops are being commercialized widely without investigating the fate and potential effects of Bt toxin in humans.

## Conclusion

The above studies show potential problems from GM food consumption and should be followed up with further research. All GM crops should be tested in long-term studies on human volunteers prior to commercialization. In the absence of such testing, GM foods and crops should not be commercialized.

GM foods should be labelled as such in all countries and post-commercialization monitoring of populations consuming these foods should be carried out.

## References


1. Freese W, Schubert D. Safety testing and regulation of genetically engineered foods. Biotechnol Genet Eng Rev. 2004:299-324.
2. Pusztai A, Bardocz S. GMO in animal nutrition: Potential benefits and risks. In: Mosenthin R, Zentek J, Zebrowska T, eds. Biology of Nutrition in Growing Animals.Vol 4. Elsevier Limited; 2006:513–540. Available at: http://www.sciencedirect.com/science/article/pii/S1877182309701043.
3. Netherwood T, Martin-Orue SM, O'Donnell AG, et al. Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. Nat Biotechnol. 2004;22:204–209. doi:10.1038/nbt934.
4. Heritage J. The fate of transgenes in the human gut. Nat Biotechnol. 2004;22:170-2. doi:10.1038/nbt0204-170.
5. Yum HY, Lee SY, Lee KE, Sohn MH, Kim KE. Genetically modified and wild soybeans: an immunologic comparison. Allergy Asthma Proc. 2005;26:210-6.
6. Nordlee JA, Taylor SL, Townsend JA, Thomas LA, Bush RK. Identification of a Brazil-nut allergen in transgenic soybeans. N Engl J Med. 1996;334:688-92. doi:10.1056/NEJM199603143341103.
7. Aris A, Leblanc S. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Reprod Toxicol. 2011;31.
8. Goldstein DA, Dubelman S, Grothaus D, G. Hammond BG. Comment: Aris and Leblanc "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada." Reprod Toxicol. 2012;33:120-121.
9. Aris A. Response to comments from Monsanto scientists on our study showing detection of glyphosate and Cry1Ab in blood of women with and without pregnancy. Reprod Toxicol. 2012;33:122-123.

## 3.7 Myth: No one has ever been made ill by a GM food

## Truth: There is no scientific evidence to support this claim

### Myth at a glance

GMO proponents claim that millions of Americans have been eating GM foods in the United States without ill effects. But this is an anecdotal, scientifically untenable assertion, as no epidemiological studies to look at GM food effects on the general population have ever been conducted. Also, GM foods are not labelled in the US, so there is no way of tracking their consumption and linking any suspected ill effects back to them. It is a case of "don't look, don't find".

In two cases, outbreaks of illness were linked to GM technology: the case of a food supplement, L-tryptophan, produced with GM bacteria; and the case of StarLink, a GM maize that was reported to cause allergic reactions. Both cases involved denial and cover-ups by the responsible authorities.

GMO proponents claim that millions of people have been eating GM foods in the United States without ill effects. But this is an anecdotal and scientifically untenable assertion, as no epidemiological studies to look at GM food effects on the general population have ever been conducted. Also, GM foods are not labelled in the US, so there is no way of tracking their consumption. It is a case of "don't look, don't find".

Under the conditions existing in the US, any health effects from a GM food would have to meet very specific and unusual conditions before they would be noticed. They would have to:

- Occur soon after eating a food that was known to be GM – in spite of its not being labelled – so that the consumer could establish a causal correlation between consumption and the harmful effect. Increases in diseases like cancer, which has a long latency period, would not be traceable to a GM food
- Cause symptoms that are different from common diseases. If GM foods caused a rise in common diseases like allergies, diabetes, or cancer, nobody would know what caused the rise
- Be dramatic and obvious to the naked eye or to the consumer of the GM food. No one examines a person's body tissues with a microscope for harm after they eat a GM food. But just this type of examination is needed to give early warning of problems such as pre-cancerous changes.

In addition, health effects would have to be recorded and reported by a centralized body that the public knew about and that could collate data as it came in and identify correlations. No such monitoring body is in place.

Moderate or slow-onset health effects of GM foods could take decades to become apparent through epidemiological studies, just as it took decades for the damaging effects of trans fats (another type of artificial food) to be recognised. Slow-poison effects from trans fats have caused millions of premature deaths across the world.[1]

Similarly, harm from chronic low-dose exposure to endocrine (hormone) disruptive chemicals, including pesticides, may not show up in the short to medium term but could lead to devastating illness in the long term.[2]

To detect important but subtle effects on health, or effects that take time to appear (chronic effects), long-term controlled studies on large populations would be needed.

## Two outbreaks of illness linked to GM technology

Two high-profile cases have emerged in which a GM food was suspected of causing illness in people. In both cases, industry and regulators denied that genetic engineering was the cause, but an examination of the evidence gives no such reassurance.

### L-tryptophan

In 1989 in the US, a food supplement, L-tryptophan, produced using GM bacteria, was found to be toxic, killing 37 people and disabling over 1500 others.[3,4,5] The resulting disease was named eosinophilia myalgia syndrome (EMS). Symptoms included an overproduction of white blood cells called eosinophils, severe myalgia (muscle pain), and in some cases, paralysis.

The L-tryptophan that affected people was traced back to a single source, a Japanese company called Showa Denko. In July 1990, a study published in the Journal of the American Medical Association mentioned that Showa Denko had introduced a new genetically engineered bacterium, called Strain V, in December 1988, a few months before the main epidemic hit.[5]

There was debate about whether the toxin's presence in the L-tryptophan was due to genetic engineering or to Showa Denko's sloppy manufacturing processes. The company had made changes to its carbon filtration purification process before the toxic contaminant was discovered.

However, the authors of a 1990 study sponsored by the US Centers for Disease Control pointed out that blaming a failure in the carbon filtration process does not answer the question of how the toxin got into the product in the first place.[6] This was a novel toxin that was not found in other companies' L-tryptophan products. The authors of the study noted that the new GM bacterial strain introduced by the manufacturer before the outbreak "may have produced larger quantities" of the toxin than earlier strains.[6]

One of the study's co-authors, Dr Michael Osterholm, an epidemiologist at the Minnesota

> *"No exposure assessment [of GM foods] has been done, as far as we know. In the States, where the GM plants have been introduced, no one really knows who is eating what. Without that information, we have to ask what the risk assessment is based on. If subtle changes were being caused to people's health by GM plants, we would not know. What is worse, we would not have any way of detecting those changes, because we do not know where we are starting from and we do not know what the exposure level is. If GM products were acutely toxic, we would obviously know, but we accept that they are not acutely toxic. If, however, they were causing subtle changes at the level of allergy and so on – common things – we would not know. If thalidomide had caused cleft palate instead of a rather obvious [and unusual] malformation, the likelihood is that we still would not know about it, because cleft palate is a common condition. If one starts changing the rate of instance of common conditions, and one does not know the starting point and there is no exposure data, one cannot know whether something is causing a problem."*
> – C. Vyvyan Howard, medically qualified toxicopathologist, University of Liverpool, UK (now at the School of Biomedical Sciences, University of Ulster, Northern Ireland)[15]

Department of Health, commented in a press article that the new bacterial strain "was cranked up to make more L-tryptophan and something went wrong. This obviously leads to that whole debate about genetic engineering."[7]

Following Osterholm's comment, a number of press articles appeared, voicing doubts about the safety of genetic engineering. The US FDA took on the role of exonerating genetic engineering from blame for the EMS epidemic. An article in Science magazine quoted FDA official Sam Page as saying that Osterholm was "propagating hysteria". Tellingly, Page added (our emphasis), "The whole question: Is there any relation to genetic engineering? is premature – *especially given the impact on the industry*".[8]

Osterholm countered: "Anyone who looks at the data comes to the same conclusion [that there may be a link with genetic engineering]… I think FDA doesn't want it to be so because of the implications for the agency."[8]

James Maryanski, FDA biotech policy coordinator, blamed the EMS epidemic on Showa Denko's changes to the purification process.[9] Maryanski also said that genetic engineering could not have been solely or even chiefly responsible for EMS because cases of the illness had been reported for several years before Showa Denko introduced its genetically engineered bacterial Strain V in December 1988.[10]

However, a study published in 1994 shows that this argument is misleading. Showa Denko had named its bacterial strain "V" because there had been four previous strains of the bacterium. Over a period of years, Showa Denko had progressively introduced more genetic modifications into the bacteria used in its manufacturing process. It began using Strain V in December 1988, shortly before the EMS main outbreak in 1989.[3] But according to lawyers who took on the cases of EMS sufferers, it had begun using its first genetically modified strain, Strain II, as long ago as 1984.[11] This timescale means that Showa Denko's genetically engineered bacteria could have been responsible for the EMS epidemic.

The FDA responded to the crisis by claiming that all L-tryptophan was dangerous and temporarily banning all L-tryptophan from sale.[12] But a study sponsored by the Centers for Disease Control concluded that this was not the case, since out of six manufacturers of L-tryptophan, only Showa Denko's product was clearly associated with illness.[13]

If Showa Denko's L-tryptophan were produced today, it would have to be assessed for safety, since it was derived from GM bacteria. However, since this L-tryptophan was greater than 99% pure, devoid of DNA, and the suspected novel toxin was present at less than 0.1% of the final marketed product, it would be passed as substantially equivalent to the same substance obtained from non-GM organisms. So the same tragedy would result.[14]

### StarLink maize

In 2000 in the US, people reported allergic reactions, some of them severe, to maize products. A GM Bt maize called StarLink was found to have contaminated the food supply. Regulators had allowed StarLink to be grown for animal feed and industrial use but had not approved it for human food because of suspicions that the Bt insecticidal protein it contained, known as Cry9C, might cause allergic reactions.

The number of people who reported allergic reactions to maize products is not known because there is no centralized reporting system. The US Food and Drug Administration (FDA) analyzed the reports it received and asked the US Centers for Disease Control (CDC) to investigate just 28 cases that met its criteria. The CDC carried out tests on blood serum taken from these people but concluded that the findings did not provide evidence that the allergic reactions were associated with the Cry9C protein.[16]

However, there were problems with the CDC investigation, many of which were identified by the researchers themselves. For example, the control group of serum was obtained from blood samples taken before the 1996 release of StarLink. Yet this serum showed a more dramatic allergic response to Cry9C than did the serum from people who had reported allergic reactions to StarLink.[16] The researchers stated that this is common in samples that have been frozen and stored, as the control samples had been. But they expressed no concern that this would skew the results towards a false conclusion of no effect from StarLink. Neither did they replace the problem control samples with more reliable ones – for example, samples freshly taken from people who were unlikely to have been exposed to StarLink.

CDC's test and findings were reviewed by a panel convened by the US Environmental Protection Agency (EPA) – which criticized them on several grounds. The panel pointed out that the CDC researchers had isolated the Cry9C protein from E. coli bacteria rather than from StarLink maize. So the protein tested would have been different from the Cry9C protein suspected of causing allergic reactions.[17] Specifically, the Cry9C protein from E.

coli bacteria would have lacked sugar molecules, which would have been attached through a process called glycosylation to the same protein derived from maize. Glycosylation can be crucial in eliciting an allergic reaction. CDC's use of the incorrect protein invalidates its analysis and conclusions.

The seriousness of CDC's error in using E. coli-derived rather than maize-derived Cry9C protein is illustrated by a study on GM peas containing an insecticidal protein from beans. The study found marked changes in the pattern of sugar molecules (glycosylation) on the insecticidal protein expressed in the GM peas, as compared with its native form in beans. The authors concluded that this change in the nature and structure of the sugar molecules was the reason why the GM insecticidal protein caused immune and allergic-type inflammation reactions in mice.[18]

This case shows that it is necessary to derive the GM protein being studied from the GM crop rather than an unrelated source, as sugar molecule patterns will differ and the potential to cause immune and allergic reactions could vary significantly between the two.

The EPA panel also criticised the CDC test for its lack of proper controls and questioned the methodology and sensitivity of the test used. The EPA panel concluded, "The test, as conducted, does not eliminate StarLink Cry9C protein as a potential cause of allergic symptoms". The panel's verdict was that there is a "medium likelihood" that the Cry9C protein is an allergen.[17]

The company that developed StarLink, Aventis, withdrew the variety in 2000.[19] However, in an example of the impossibility of recalling a GMO once it has been released, StarLink was still being detected in samples gathered from Saudi Arabian markets in 2009 and 2010.[20]

## Conclusion

Claims that no one has been made ill by a GM crop or food have no scientific basis, since no epidemiological studies have been carried out. Also, GM foods are not labelled in the US, the country where most such foods are eaten, so patterns of consumption cannot be traced and linked to any ill effects. However, the cases of L-tryptophan produced with GM bacteria and GM StarLink maize give cause for concern.

## References


1. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. N Engl J Med. 2006;354:1601–13.
2. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012;33(3):378-455. doi:10.1210/er.2011-1050.
3. Mayeno AN, Gleich GJ. Eosinophilia-myalgia syndrome and tryptophan production: A cautionary tale. Trends Biotechnol. 1994;12:346-52.
4. US Congress House Committee on Government Operations: Human Resources and Intergovernmental Relations Subcommittee. FDA's regulation of the dietary supplement L-tryptophan: Hearing before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, House of Representatives, One Hundred Second Congress, first session, July 18, 1991. Washington, DC, USA: US GPO; 1992. Available at: http://catalog.hathitrust.org/Record/003481988.
5. Slutsker L, Hoesly FC, Miller L, Williams LP, Watson JC, Fleming DW. Eosinophilia-myalgia syndrome associated with exposure to tryptophan from a single manufacturer. JAMA. 1990;264:213-7.
6. Belongia EA, Hedberg CW, Gleich GJ, et al. An investigation of the cause of the eosinophilia-myalgia syndrome associated with tryptophan use. N Engl J Med. 1990;323:357-65. doi:10.1056/NEJM199008093230601.

7. Garrett L. Genetic engineering flaw blamed for toxic deaths. Newsday. August 14, 1990:C-1.
8. Roberts L. L-tryptophan puzzle takes new twist. Science. 1990;249(4972):988.
9. Jacobs P. Cornucopia of biotech food awaits labeling. Los Angeles Times. http://articles.latimes.com/2000/jan/31/news/mn-59543. Published January 31, 2000.
10. Crist WE. Toxic L-tryptophan: Shedding light on a mysterious epidemic – Background information. 2005. Available at: http://www.responsibletechnology.org/gmo-dangers/health-risks/L-tryptophan/background-information.
11. Crist WE. Toxic L-tryptophan: Shedding light on a mysterious epidemic – Contaminants. 2005. Available at: http://responsibletechnology.org/gmo-dangers/health-risks/L-tryptophan/contaminants.
12. Cimons M. FDA expands L-tryptophan recall, cites a major risk: Health: The action applies to even small dosages: Nineteen people have died of a blood disorder linked to the dietary supplement. Los Angeles Times. http://lat.ms/NAzzw8. Published March 23, 1990.
13. Kilbourne EM, Philen RM, Kamb ML, Falk H. Tryptophan produced by Showa Denko and epidemic eosinophilia-myalgia syndrome. J Rheumatol Suppl. 1996;46:81-8; discussion 89-91.
14. Antoniou M. Genetic pollution. Nutr Ther Today. 1996;6:8–11.
15. Howard CV. GM crops inquiry: Testimony of Prof C. Vyvyan Howard to the Scottish Parliament Health and Community Care Committee, meeting no. 31, 27 November 2002. 2002. Available at: http://archive.scottish.parliament.uk/business/committees/historic/health/or-02/he02-3102.htm.
16. Centers for Disease Control and Prevention (CDC). Investigation of human health effects associated with potential exposure to genetically modified corn: A report to the US Food and Dug Administration. 2001. Available at: www.cdc.gov/nceh/ehhe/cry9creport/pdfs/cry9creport.pdf.
17. FIFRA Scientific Advisory Panel. A set of scientific issues being considered by the Environmental Protection Agency regarding assessment of additional scientific information concerning StarLinkTM corn. SAP Report No. 2001-09. Arlington, Virginia: US Environmental Protection Agency (EPA); 2001.
18. Prescott VE, Campbell PM, Moore A, et al. Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenicity. J Agric Food Chem. 2005;53:9023–30. doi:10.1021/jf050594v.
19. Carpenter JE, Gianessi LP. Agricultural biotechnology: Updated benefit estimates. National Center for Food and Agricultural Policy; 2001. Available at: http://ucbiotech.org/biotech_info/PDFs/Carpenter_2001_Updated_Benefits.pdf.
20. Elsanhoty RM, Al-Turki AI, Ramadan MF. Prevalence of genetically modified rice, maize, and soy in Saudi food products. Appl Biochem Biotechnol. 2013. doi:10.1007/s12010-013-0405-x.

## 3.8 Myth: GM Bt insecticidal crops only harm insects and are harmless to animals and people

## Truth: GM Bt insecticidal crops pose hazards to people and animals that eat them

### Myth at a glance

Many GM crops are engineered to produce the insecticide Bt toxin. Regulators have approved GM Bt crops on the assumption that the insecticidal toxin they contain is the same as the natural form of Bt toxin, a substance produced by the soil-dwelling bacterium Bacillus thuringiensis.

Natural Bt is used as an insecticidal spray in chemically-based and organic farming, and is claimed to have a history of safe use and to only affect certain types of insect. Regulators assume that GM Bt crops must also be harmless to humans and other mammals.

But these assumptions are incorrect. Natural Bt toxin is different from the Bt toxins produced in GM crops and behaves differently in the environment. GM Bt plants express the pesticide in every cell throughout their life, so that the plants themselves become a pesticide. Even natural Bt has never intentionally been part of the human diet and cannot be claimed to have a history of safe use.

Animal feeding experiments with GM Bt crops have revealed toxic effects and a laboratory study showed toxic effects on human cells tested in vitro. Bt toxins and Bt crop pollen and debris have toxic effects on non-target and beneficial organisms.

Contrary to claims by the GM industry and regulators, Bt toxin does not reliably break down in the digestive tract. Bt toxin proteins have been found circulating in the blood of pregnant women and in the blood supply to their foetuses.

Regulatory approvals of GM Bt crops worldwide have been granted on the basis of poorly designed and interpreted experiments and false assumptions.

Bacillus thuringiensis (Bt) is a natural soil-dwelling bacterium that produces a protein complex called Bt toxin. Some types of Bt toxin possess selective insecticide properties: that is, they will specifically kill certain crop pests such as caterpillars. Therefore Bt toxin has been used for decades as an insecticidal spray in chemically-based and organic farming. Genetic engineers have engineered Bt toxin into GM crops so that they produce their own form of this insecticide.

Regulators have approved GM Bt crops largely on the assumption that the GM Bt toxin is the same as the natural Bt toxin, which they say has a history of safe use. They conclude that GM crops engineered to contain Bt insecticidal protein must also be harmless. However, this assumption and conclusion are incorrect.

## Bt toxin in GM plants is not the same as natural Bt toxin

The Bt toxin expressed by GM Bt plants is different from natural Bt, both in terms of its structure and its mode of action.[1] Structurally, there is at least a 40% difference between the toxin in Bt176 maize (formerly commercialized in the EU, now withdrawn) and natural Bt toxin.[2] The US Environmental Protection Agency, in its review of the commercialized Monsanto GM maize MON810, said it produced a "truncated" version of the protein – in other words, a much shorter form of the protein that is different from the natural form.[3]

Such changes in a protein can mean that it has very different environmental and health effects. First, the GM Bt toxin loses its selectivity and can kill non-target insects including beneficial predators. Second, GM Bt toxin can have unsuspected negative health impacts on people or animals that eat a crop containing it. The protein may be more toxic or allergenic than the natural form of the protein.

Even tiny changes in a protein can completely change its properties. For example, soybeans can be genetically engineered to tolerate a herbicide that would normally kill them by changing a gene that gives rise to a protein differing from the natural protein by just two amino acids.[4] As researchers at the Centre for Integrated Research in Biosafety in New Zealand pointed out in a submission to the Australia/New Zealand GMO regulator FSANZ on the regulatory assessment of this soybean,[5] a change even of a single amino acid can radically change the properties of proteins, which in turn can result in changed behaviour of a plant.[6,7]

In some cases, not even an amino acid change is necessary to alter the characteristics of a protein. Differences in the sequence of the DNA base units in a gene can change the properties of the resulting protein without altering the amino acid sequence.[8] Changes in the three-dimensional shape of the protein alone can turn harmless proteins into toxins,[9,10] as demonstrated by the prion protein causing the "mad cow disease" BSE.[11]

Natural Bt toxin also has a very different mode of action from the Bt toxin produced in GM plants. Natural Bt is not a toxin but a protoxin. That means it only becomes toxic when subjected to certain conditions, such as when made into a solution and broken down by enzymes in the gut of the insect that eats it.

In the environment, natural Bt breaks down rapidly in daylight soon after it is sprayed, so it is unlikely to find its way into animals or people that eat the crop. With GM Bt crops, in contrast, the Bt toxin is present in every cell of the plant in pre-activated form.[1,12] The plant itself becomes a pesticide, and people and animals who eat the plant are eating a pesticide.

## Bt toxin does not only affect insect pests

GMO proponents claim that the Bt toxin engineered into GM Bt crops only affects the target pests and is harmless to mammals, including people or animals that eat the crops.[13] All regulatory approvals of GM Bt crops are based on this assumption and no regulatory body has ever required human toxicity studies to be carried out.

However, these assumptions about the safety of GM Bt crops are constantly being challenged by new evidence.

In an in vitro study (laboratory experiment not carried out in living animals or humans), genetically engineered Bt toxins were found to be toxic to human cells. One type of Bt toxin killed human cells, albeit at the relatively high dose of 100 parts per million. The findings showed that GM Bt toxin is not specific to insect pests and does affect human cells, contrary to claims from the GM lobby and regulators.[14]

In vitro studies may not accurately reflect what happens in a living human or animal that eats GM Bt crops, so they must be followed up with in vivo studies performed on living animals, and then on humans. However, it is unacceptable that Bt toxins were never even subjected to basic and inexpensive in vitro tests before they were released into the food and feed supply.

Some feeding studies in mammals have been performed with GM Bt crops and have found adverse effects, such as:

- Toxic effects or signs of toxicity in the small intestine, liver, kidney, spleen, pancreas[15,16,17,18,19]
- Disturbances in the functioning of the digestive system[17,19]
- Increased or decreased weight gain compared with controls[15,20]
- Male reproductive organ damage[19]
- Blood biochemistry disturbances[20]
- Immune system disturbances.[21]

Laboratory studies in mice found that genetically engineered Bt toxin produces a potent immune response when delivered into the stomach by intragastric administration (a method considered similar to human dietary exposure), or injected into the abdomen (intraperitoneal immunization).[22,23] The Bt toxin protein was found to bind to the mucosal surface of the small intestine of the mice, an effect that could lead to changes in the physiological status of the intestine.[24] The Bt toxin protein also enhanced the immune response of the mice to other substances.[25]

GM Bt crops and the Bt toxins they are engineered to contain have been found to have toxic effects on butterflies and other non-target insects,[26,27,28] beneficial pest predators,[29,30,31,32,33,34] bees,[35] aquatic organisms,[36,37] and beneficial soil organisms[38] (see Myths 2.3, 5.3).

Toxic effects associated with GM Bt crops may be due to one or more of the following causes:

- The Bt toxin as produced in the GM crop

- New toxins produced in the Bt crop by the GM process, and/or
- Residues of herbicides or chemical insecticides used on the Bt crop. Many Bt crops have added herbicide-tolerant traits,[39] making it likely that herbicide residues will be found on them.

In-depth toxicological research would have to be carried out in order to identify which factors are responsible.

## Bt toxin protein may not be broken down harmlessly in the digestive tract

GMO proponents claim that the Bt toxin insecticidal protein in GM plants is broken down in the digestive tract and so cannot get into the blood or body tissues to cause toxic effects beyond the digestive system. But this claim has been shown to be false by several studies:

- A study in cows found that Bt toxins from GM maize MON810 were not completely broken down in the digestive tract.[40]
- A study simulating human digestion found that the Bt toxin protein was highly resistant to being broken down in realistic stomach acidity conditions and still produced an immune response.[41]
- A survey conducted in Canada found Bt toxin protein circulating in the blood of pregnant and non-pregnant women and the blood supply to foetuses.[42,43] Whether the Bt toxin originated from GM crops or elsewhere is not known. But wherever it came from, it clearly did not break down fully in the digestive tract.

## How selective are the Bt toxins in GM crops?

Monsanto argues that Bt toxins only affect a certain class of insects and are non-toxic to mammals, including humans.[44] However, Bt toxins have been found to have toxic effects on non-target organisms other than insect pests – including mammals.

For example, in one study, Bt toxins were found to be toxic to the blood of mice.[45] This was not a feeding study with Bt crops, so the findings do not tell us whether GM Bt crops are toxic to the blood of mice. Instead the Bt toxins were fed to the mice in the form of spore crystals containing individual Bt toxins Cry1Aa, Cry1Ab, Cry1Ac, and Cry2A obtained from genetically engineered Bt bacteria. Different GM Bt crops are engineered to express these Bt toxins. The Bt toxins caused red blood cells of the mice to rupture, albeit they were fed at high doses.[45]

This is of concern because Bt toxins exercise their toxic effects in target pests in a similar fashion, by rupturing the cells of the gut, causing the insect to die from starvation or septicaemia due to the gut contents, including pathogenic bacteria, leaking out into the body. This study showed that the assumption that Bt toxins are non-toxic to mammals is questionable, as the Bt toxins in the genetically engineered spore crystal form tested were toxic to the blood of mice, a species of mammal.[45]

Also, a wide range of external factors can influence the selectivity and toxicity of Bt toxin proteins. These include interaction with infectious disease agents, nematodes (roundworms, many of which are parasitic), gut bacteria, and other Bt toxins.[46]

It cannot even be assumed that the natural Bt toxin used in insecticidal sprays is safe for those applying it or exposed to it immediately after spraying. In farm workers, exposure to Bt sprays was found to lead to allergic skin sensitization and immune responses.[47] An immune response to Bt toxin was found in the blood serum of 23–29% of Danish greenhouse workers in a respiratory health study.[48]

## Regulatory assessment of Bt crops flawed

Some of the safety tests carried out for regulatory approvals of Bt crops, such as investigation of allergenic, nutritional, and immunological properties, are not carried out with the Bt toxin protein as expressed in the GM plant. Instead, tests are carried out on a "surrogate" Bt toxin protein derived from genetically engineered E. coli bacteria,[49] as GM companies find it too difficult and expensive to extract enough Bt toxin from the GM crop itself.

The problem with this is that the protein that is expressed in a plant will be different in structure, conformation and stability from the protein expressed in a bacterium. Thus it is scientifically invalid to draw conclusions about the safety or digestibility of a protein in a GM plant on the basis of experiments on a protein produced in E. coli bacteria, even if the two proteins are coded for by the same gene.[49]

This fundamental flaw in the regulatory process could partly be addressed by long-term animal feeding trials with the whole GM plant, which would contain the actual protein that people and animals eat. Although the 90-day animal feeding trials that are routinely carried out by GM developer companies are not long enough to identify the full range of potential toxic effects from GM crops, studies of even this short duration and less performed by both industry and independent scientists have revealed worrying health effects.[15,16,18,50,19,20] Unfortunately, these effects are routinely dismissed.

Another problem is that the 90-day animal feeding trial required in Europe for single-trait GM crops does not apply to stacked-trait GM crops, many of which incorporate multiple Bt insecticidal traits. Instead, regulators assess the safety of the stacked-trait crop on the basis of the company's animal feeding trials on the single-trait varieties that were cross-bred to create the stacked-trait crop. This process is scientifically invalid, as unintended changes can result from the process of combining the traits into the stacked-trait crop and the total Bt toxin content will be higher than in single-trait Bt crops.

## Conclusion

Studies on GM Bt crops show that Bt toxin is not specific to a narrow range of insect pests but can affect a wide variety of non-target organisms. Taken together, the studies on GM Bt crops and natural Bt toxin raise the possibility that eating GM crops containing Bt toxin may cause toxic effects to multiple organ systems or allergic reactions and/or sensitize people to other food substances.

## References


1. Székács A, Darvas B. Comparative aspects of Cry toxin usage in insect control. In: Ishaaya I, Palli SR, Horowitz AR, eds. Advanced Technologies for Managing Insect Pests. Dordrecht, Netherlands: Springer; 2012:195–230.
2. Séralini GE, Mesnage R, Clair E, Gress S, de Vendômois JS, Cellier D. Genetically modified crops safety assessments: Present limits and possible improvements. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-10.
3. Freese W, Schubert D. Safety testing and regulation of genetically engineered foods. Biotechnol Genet Eng Rev. 2004:299-324.
4. Food Standards Australia New Zealand (FSANZ). Application A1018 - Food derived from High Oleic Acid Soybean Line DP-305423-1 – Safety assessment report supporting document 1. Canberra, Australia; 2009. Available at: http://www.foodstandards.gov.au/code/applications/documents/A1018%20High%20oleic%20GM%20soybean%20AR%20SD11.pdf.
5. Kurenbach B, Coray DS, Heinemann JA, Catchpole RJ, Turner LA. Submission II on the assessment report for Application A1018 food derived from high oleic acid soybean DP-DP-305423-1-1. Centre for Integrated Research in Biosafety; 2009. Available at: http://www.inbi.canterbury.ac.nz/Documents/submissions/A1018%20submission%20II.pdf.
6. Doyle MR, Amasino RM. A single amino acid change in the enhancer of zeste ortholog CURLY LEAF results in vernalization-independent, rapid flowering in Arabidopsis. Plant Physiol. 2009;151:1688-97. doi:10.1104/pp.109.145581.
7. Hanzawa Y, Money T, Bradley D. A single amino acid converts a repressor to an activator of flowering. Proc Natl Acad Sci U A. 2005;102:7748-53. doi:10.1073/pnas.0500932102.
8. Kimchi-Sarfaty C, Oh JM, Kim IW, et al. A "silent" polymorphism in the MDR1 gene changes substrate specificity. Science. 2007;315:525-8. doi:10.1126/science.1135308.
9. Bucciantini M, Giannoni E, Chiti F, et al. Inherent toxicity of aggregates implies a common mechanism for protein misfolding diseases. Nature. 2002;416:507-11. doi:10.1038/416507a.
10. Ellis RJ, Pinheiro TJ. Medicine: danger--misfolding proteins. Nature. 2002;416:483-4. doi:10.1038/416483a.
11. Caughey B, Baron GS. Prions and their partners in crime. Nature. 2006;443:803-10. doi:10.1038/nature05294.
12. Li H, Buschman LL, Huang F, Zhu KY, Bonning B, Oppert BA. Resistance to Bacillus thuringiensis endotoxins in the European corn borer. Biopestic Int. 2007;3:96–107.
13. GMO Compass. Environmental safety: insects, spiders, and other animals. 2006. Available at: http://www.gmo-compass.org/eng/safety/environmental_safety/169.effects_gm_plants_insects_spiders_animals.html.
14. Mesnage R, Clair E, Gress S, Then C, Székács A, Séralini G-E. Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide. J Appl Toxicol. 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22337346.
15. Séralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Arch Environ Contam Toxicol. 2007;52:596–602.
16. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
17. Trabalza-Marinucci M, Brandi G, Rondini C, et al. A three-year longitudinal study on the effects of a diet containing genetically modified Bt176 maize on the health status and performance of sheep. Livest Sci. 2008;113:178–190. doi:10.1016/j.livsci.2007.03.009.
18. Fares NH, El-Sayed AK. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. Nat Toxins. 1998;6(6):219-33.
19. El-Shamei ZS, Gab-Alla AA, Shatta AA, Moussa EA, Rayan AM. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(10):684–696.
20. Gab-Alla AA, El-Shamei ZS, Shatta AA, Moussa EA, Rayan AM. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(9):1117–1123.
21. Finamore A, Roselli M, Britti S, et al. Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. J Agric Food Chem. 2008;56:11533–39. doi:10.1021/jf802059w.
22. Vázquez-Padrón RI, Moreno-Fierros L, Neri-Bazan L, de la Riva GA, Lopez-Revilla R. Intragastric and intraperitoneal administration of Cry1Ac protoxin from Bacillus thuringiensis induces systemic and mucosal antibody responses in mice. Life Sci. 1999;64:1897-912.
23. Vázquez-Padrón RI, Moreno-Fierros L, Neri-Bazan L, Martinez-Gil AF, de-la-Riva GA, Lopez-Revilla R. Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from Bacillus thuringiensis HD 73 in mice. Braz J Med Biol Res. 2000;33:147-55.
24. Vázquez-Padrón RI, Gonzales-Cabrera J, Garcia-Tovar C, et al. Cry1Ac protoxin from Bacillus thuringiensis sp. kurstaki HD73 binds to surface proteins in the mouse small intestine. Biochem Biophys Res Commun. 2000;271:54-8. doi:10.1006/bbrc.2000.2584.
25. Vázquez-Padron RI, Moreno-Fierros L, Neri-Bazan L, De La Riva GA, Lopez-Revilla R. Bacillus thuringiensis Cry1Ac protoxin is a potent systemic and mucosal adjuvant. Scand J Immunol. 1999;49:578-84.
26. Losey JE, Rayor LS, Carter ME. Transgenic pollen harms monarch larvae. Nature. 1999;399:214. doi:10.1038/20338.
27. Jesse LCH, Obrycki JJ. Field deposition of Bt transgenic corn pollen: Lethal effects on the monarch butterfly. J Oecologia. 2000;125:241–248.
28. Lang A, Vojtech E. The effects of pollen consumption of transgenic Bt maize on the common swallowtail, Papilio machaon L. (Lepidoptera, Papilionidae). Basic Appl Ecol. 2006;7:296–306.

29. Hilbeck A, Baumgartner M, Fried PM, Bigler F. Effects of transgenic Bt corn-fed prey on immature development of Chrysoperla carnea (Neuroptera: Chrysopidae). Environ Entomol. 1998;27(2):480–487.
30. Hilbeck A, McMillan JM, Meier M, Humbel A, Schlaepfer-Miller J, Trtikova M. A controversy re-visited: Is the coccinellid Adalia bipunctata adversely affected by Bt toxins? Environ Sci Eur. 2012;24(10). doi:10.1186/2190-4715-24-10.
31. Hilbeck A, Meier M, Trtikova M. Underlying reasons of the controversy over adverse effects of Bt toxins on lady beetle and lacewing larvae. Environ Sci Eur. 2012;24(9). doi:10.1186/2190-4715-24-9.
32. Hilbeck A, Moar WJ, Pusztai-Carey M, Filippini A, Bigler F. Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator Chrysoperla carnea. Entomol Exp Appl. 1999;91:305–316.
33. Marvier M, McCreedy C, Regetz J, Kareiva P. A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. Science. 2007;316:1475-7. doi:10.1126/science.1139208.
34. Lövei GL, Arpaia S. The impact of transgenic plants on natural enemies: A critical review of laboratory studies. Entomol Exp Appl. 2005;114:1–14. doi:10.1111/j.0013-8703.2005.00235.x.
35. Ramirez-Romero R, Desneux N, Decourtye A, Chaffiol A, Pham-Delègue MH. Does Cry1Ab protein affect learning performances of the honey bee Apis mellifera L. (Hymenoptera, Apidae)? Ecotoxicol Environ Saf. 2008;70:327–333.
36. Rosi-Marshall EJ, Tank JL, Royer TV, et al. Toxins in transgenic crop byproducts may affect headwater stream ecosystems. Proc Natl Acad Sci USA. 2007;104:16204-8. doi:10.1073/pnas.0707177104.
37. Bøhn T, Traavik T, Primicerio R. Demographic responses of Daphnia magna fed transgenic Bt-maize. Ecotoxicology. 2010;19:419-30. doi:10.1007/s10646-009-0427-x.
38. Castaldini M, Turrini A, Sbrana C, et al. Impact of Bt corn on rhizospheric and soil eubacterial communities and on beneficial mycorrhizal symbiosis in experimental microcosms. Appl Env Microbiol. 2005;71:6719-29. doi:10.1128/AEM.71.11.6719-6729.2005.
39. GMO Compass. Maize. 2014. Available at: http://www.gmo-compass.org/eng/gmo/db/.
40. Paul V, Guertler P, Wiedemann S, Meyer HH. Degradation of Cry1Ab protein from genetically modified maize (MON810) in relation to total dietary feed proteins in dairy cow digestion. Transgenic Res. 2010;19:683-9. doi:10.1007/s11248-009-9339-z.
41. Guimaraes V, Drumare MF, Lereclus D, et al. In vitro digestion of Cry1Ab proteins and analysis of the impact on their immunoreactivity. J Agric Food Chem. 2010;58:3222-31. doi:10.1021/jf903189j.
42. Aris A, Leblanc S. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Reprod Toxicol. 2011;31.
43. Aris A. Response to comments from Monsanto scientists on our study showing detection of glyphosate and Cry1Ab in blood of women with and without pregnancy. Reprod Toxicol. 2012;33:122-123.
44. Betz FS, Hammond BG, Fuchs RL. Safety and advantages of Bacillus thuringiensis-protected plants to control insect pests. Regul Toxicol Pharmacol. 2000;32:156-73. doi:10.1006/rtph.2000.1426.
45. Mezzomo BP, Miranda-Vilela AL, de Souza Freire I, et al. Hematotoxicity of Bacillus thuringiensis as spore-crystal strains Cry1Aa, Cry1Ab, Cry1Ac or Cry2Aa in Swiss albino mice. J Hematol Thromb Dis. 2013;1. Available at: http://esciencecentral.org/journals/JHTD/JHTD-1-104.pdf.
46. Then C. Risk assessment of toxins derived from Bacillus thuringiensis - synergism, efficacy, and selectivity. Env Sci Pollut Res Int. 2010;17:791-7. doi:10.1007/s11356-009-0208-3.
47. Bernstein IL, Bernstein JA, Miller M, et al. Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides. Environ Health Perspect. 1999;107:575–582.
48. Doekes G, Larsen P, Sigsgaard T, Baelum J. IgE sensitization to bacterial and fungal biopesticides in a cohort of Danish greenhouse workers: the BIOGART study. Am J Ind Med. 2004;46:404-7. doi:10.1002/ajim.20086.
49. Pusztai A, Bardocz S. Potential health effects of foods derived from genetically modified plants: What are the issues? Penang, Malaysia: Third World Network; 2011.
50. Ewen SW, Pusztai A. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet. 1999;354:1353-4. doi:10.1016/S0140-6736(98)05860-7.

# 3.9 Myth: Myth: GM foods are rigorously assessed for their ability to cause allergic reactions

## Truth: No thorough allergenicity assessment is conducted on GM foods

### Myth at a glance

The public is told that GM foods are no more likely to cause allergic reactions than non-GM foods and that they are fully assessed for allergenicity. But this is untrue. Genetic engineering can create novel proteins that have no history of safe use in food, raising the potential for allergic reactions.

The absence of reliable methods for allergenicity testing and the lack of rigour in current allergy assessments mean that it is impossible to reliably predict whether a GMO will prove to be allergenic.

If a GMO did prove to be allergenic, it would be almost impossible to find out, as no post-commercialization monitoring is carried out anywhere in the world.

Most food allergies are caused by a reaction to a protein in a food. The DNA of an organism contains instructions for making proteins. Genetic engineering changes the DNA of a food, and the altered DNA can in turn create new proteins. GM foods could create new allergies in two ways: the new proteins could cause allergic reactions (be allergens) themselves, or the new proteins could sensitize people to existing food proteins.

The website GMO Compass, which is run by the public relations firm Genius GmbH, claims that GM plants pose no greater risk than new varieties of crops obtained through conventional breeding, or the importation of new exotic foods, which can also result in new allergens appearing in the diet.[1]

But independent scientists disagree. A 2003 review states that compared with conventional breeding, GM has a "greater potential to introduce novel proteins into the food supply" and increase the likelihood of allergic reactions.[2]

A study on humans confirmed the potential for GM to create novel and potentially allergenic proteins. One of the experimental subjects showed an immune response to GM soy but not to non-GM soy. GM soy was found to contain at least one protein that was different from the profile of proteins present in the non-GM variety.[3] The study did not show that GM soy is more allergenic than non-GM soy, but it did show that a GM food can unexpectedly cause an allergic reaction in a person who is not allergic to the food in its non-GM form.

## The EU system for assessing GM foods for allergenicity

Under European law, GM foods must be assessed for their potential to cause allergies before they are allowed onto the market. Proponents claim that any potentially allergenic GM foods are likely to be caught by these regulatory checks. The GMO Compass website calls these assessments "rigorous" and adds, "If a GM plant is found to contain a potential allergen, its chances of receiving approval in the EU are slim to none."[1]

But in reality, the European regulatory process, though stronger than the US process, has no rigorous system for assessing the allergenic potential of GM foods. This is largely because reliable scientific tests to predict allergenicity have not been developed.

The process that EU regulators use to assess the allergenicity of GM foods[1,4] is based on a system proposed in 2001 by the Food and Agriculture Organization (FAO) of the United Nations and the World Health Organization (WHO). This system was actually designed by two GM industry-funded groups, the International Life Sciences Institute (ILSI) and the International Food Biotechnology Council (IFBC), as the FAO/WHO freely states.[5]

The process begins with a comparison of the protein that the GM plant is designed to produce with known allergenic proteins. Depending on the outcome of this initial assessment, further investigations can include:

- Tests to see if the new protein reacts with the blood serum of sensitive individuals
- Artificial stomach tests to see if the protein is broken down easily. If it is, it is thought unlikely to be an allergen
- Animal feeding trials.[1]

## Why the allergy assessment process is ineffective

The EU's allergy assessment is unlikely to reliably predict whether a GM food will cause allergic reactions.

The most important reason is that the new protein that is assessed in the regulatory process is normally not the protein as expressed in the whole GM plant. Instead, it is what is known as a surrogate protein. This surrogate protein is isolated from sources such as GM E. coli bacteria or occasionally, a different plant species.[6] This is scientifically unjustifiable because the protein can change as a result of the genetic engineering process and according to the organism within which it is expressed – as in the case of StarLink maize (Myth 3.7).

In other words, the same GM gene introduced into a GM plant and into E. coli bacteria can produce proteins that can have very different effects on the people and animals that eat them. Plants and bacteria process newly synthesized proteins in different ways. In particular, the GM plant protein will undergo a process known as "post-translational modification" and will thus possess added sugar molecules ("glycosylation"). So even though the amino acid sequences of the GM plant and GM E. coli proteins may be identical, their functions and allergenic potential can be quite different.

Other reasons why the allergenicity decision tree model is unsatisfactory include:

*"There is more than a casual association between GM foods and adverse health effects. There is causation as defined by Hill's Criteria in the areas of strength of association, consistency, specificity, biological gradient, and biological plausibility. The strength of association and consistency between GM foods and disease is confirmed in several animal studies... Multiple animal studies show significant immune dysregulation, including upregulation of cytokines [protein molecules involved in immune responses] associated with asthma, allergy, and inflammation."*
– American Academy of Environmental Medicine[11]

- A comparison of the new protein in the GM food with the database of known allergens will not detect new allergens.
- Blood serum tests are problematic because allergenic sensitization is an allergen-specific process. So unless the transgenic protein expressed in the GM food is already a common allergen, there is unlikely to be a single sensitized person in the world whose blood serum would react with it.[2]
- Blood serum tests are not useful in detecting uncommon allergens – substances that few people are allergic to[2] – since it is unlikely that serum samples will be taken from these few people.
- A phenomenon known as cross-reactivity can make it difficult to identify from blood serum testing which specific protein out of several is the allergen.[2]
- The artificial stomach tests carried out for regulatory purposes are performed under unrealistic conditions. Levels of acidity and digestive enzymes are much higher than would be present in the digestive systems of individuals who would consume the GM food. This makes it likely that the new GM protein will be broken down into fragments that are too small to be potent allergens. In real life, however, the levels of acidity and digestive enzymes in people's stomachs vary according to age, health status, length of time since they ate their last meal, and other factors. One study found that under the standard conditions used in artificial stomach tests, one of the insecticidal proteins commonly present in GM Bt crops was broken down. But when the researchers adjusted the acidity and enzymes to more realistic levels, the insecticidal protein was highly resistant to being broken down. The authors called for regulatory tests to be carried out in "more physiologically relevant" conditions of lower acidity and enzyme levels.[7]

One review concluded that the allergenicity assessment might be useful in assessing GM foods containing a known allergenic protein, but that assessing proteins of unknown allergenicity is "more problematic" and "the predictive value of such an assessment is unknown".[2] Another review agreed that the standard tests were "not always conclusive", especially when the organism from which the GM gene is taken has no history of dietary use or has unknown allergenicity.[8]

The current allergy assessment system is not reliable because it relies heavily on in vitro tests (laboratory experiments in non-living systems, such as the blood serum and artificial stomach tests). Unfortunately, however, an effective alternative does not yet exist. In vivo tests (tests on living organisms such as animals or humans) are useful for detecting nutritional or toxicological effects of foods, but no reliable animal testing methods have yet been established for allergenicity testing of foods.[9,2,8,10]

The main problem is that the immune systems of humans and animals are different, so it is difficult to predict human allergenicity from animal responses. The most reliable assessment of allergenicity of a GM food would be to test the food prior to commercialization, on large numbers (around 5,000) of human volunteers. The large numbers avoid false negative results (where an allergenic effect exists but is missed because too few subjects are used) and provide statistical power.

In the absence of pre-market tests on humans, at present the only reliable approach to assessing the allergenicity of GMOs would be post-commercialization monitoring. Consumers would have to be clearly informed when they ate the new GMO and would be asked to report any adverse effects to designated authorities.

Such post-commercialization assessments are not required in any country. In countries such as the US and Canada, where GM foods are not labelled, the likelihood that allergenicity would be linked to a GMO is extremely low, unless it caused acute allergic reactions in a large portion of the population.

## Studies on GM foods confirm existing allergy assessments are inadequate

Studies on GM foods confirm that current allergy assessments are inadequate to detect new allergens created by the genetic engineering process.

In a study on mice fed GM peas containing an insecticidal protein from beans, mice showed antibody immune reactions and allergic-type inflammatory responses to the GM protein and chicken egg white protein when it was fed to them with the GM peas.[12]

The mice did not show antibody immune reactions and allergic-type inflammatory responses to beans that naturally contain the insecticidal protein or to egg white protein when it was fed with the natural insecticidal protein obtained from beans. They also did not have an immune response to the egg white protein when it was fed on its own.[12]

These outcomes show that the GM insecticidal protein made the mice more susceptible to developing allergic-type inflammatory reactions to foods eaten with the GM food. This is called immunological cross-priming.

The results indicated that the reaction of the mice to the GM peas was caused by changes brought about by the genetic engineering process. The normally non-immunogenic and non-allergenic insecticidal protein naturally produced in beans was altered in structure and/or function when engineered into peas, in particular in the addition to the protein of sugar molecules (glycosylation) via post-translational modification processes, becoming a potent immunogen (substance that produces an immune response) and allergen.[12]

This was not a regulatory test and tests such as this are not required to be carried out for the regulatory assessment of GM foods. The allergenicity of the GM peas would likely not have been spotted by the EU's screening process because the natural, non-GM version of the bean insecticidal protein is not a known allergen. Because of this, blood serum from sensitized individuals would not have been available for regulatory serum tests.

Overall, the study shows that GM foods can contain new allergens and cause new allergic reactions – and that the GMO's allergenicity is unlikely to be detected using the current allergy assessment process.

Other studies confirm the inadequacy of the current allergy assessment process:

- A study on a commercialized GM insecticidal maize, MON810, showed that the GM plant's proteins were markedly altered compared with those in the non-GM counterpart. Unexpected changes included the appearance of a new form of the protein zein, a known allergen, which was not present in the non-GM maize variety. A number of other proteins were present in both their natural forms and in truncated and lower molecular mass forms.[13] These findings suggest major disruptions in gene structure and function in this GM crop. The EU's allergy assessment failed to pick up these changes and failed to detect the presence of the newly created allergen.
- A GM soy variety modified with a gene from Brazil nuts was found to be capable of producing an allergic reaction in people who are allergic to Brazil nuts. The researchers had genetically engineered the Brazil nut gene into the soy in order to increase its nutritional value. When they tested the effect of this GM soy on blood serum from people allergic to Brazil nuts, they found that the serum produced an allergic response to the soy. Through scratch tests on skin, they confirmed that people allergic to Brazil nuts were allergic to the modified soybean.[14] This study is often cited by GM proponents as evidence of the effectiveness of regulatory processes in identifying allergenic foods before they reach the marketplace. But this is untrue. As with the GM peas study,[12] this was not a regulatory test and tests such as this are not required to be carried out for the regulatory assessment of GM foods in any country.

## Conclusion

The absence of reliable methods for allergenicity testing and the lack of rigour in current allergy assessments mean that it is impossible to reliably predict whether a GMO will prove to be allergenic. If a GMO did prove to be allergenic, it would be almost impossible to find out, as no post-commercialization monitoring is carried out anywhere in the world.

## References


1. GMO Compass. The allergy check. 2006. Available at: http://bit.ly/LWmnNR.
2. Bernstein JA, Bernstein IL, Bucchini L, et al. Clinical and laboratory investigation of allergy to genetically modified foods. Env Health Perspect. 2003;111:1114-21.
3. Yum HY, Lee SY, Lee KE, Sohn MH, Kim KE. Genetically modified and wild soybeans: an immunologic comparison. Allergy Asthma Proc. 2005;26:210-6.
4. European Food Safety Authority Panel on Genetically Modified Organisms (GMO). Guidance document for the risk assessment of genetically modified plants and derived food and feed. EFSA J. 2006;99:1–100.
5. Food and Agriculture Organization (FAO) and World Health Organization. Decision tree approach to the evaluation of

the allergenicity of genetically modified foods. In: Evaluation of Allergenicity of Genetically Modified Foods: Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, 22–25 January 2001. Rome, Italy: Food and Agriculture Organization of the United Nations (FAO); 2001:5–15; 25–27.

6. Friends of the Earth. Could GM foods cause allergies? A critique of current allergenicity testing in the light of new research on transgenic peas. London, UK; 2006.
7. Guimaraes V, Drumare MF, Lereclus D, et al. In vitro digestion of Cry1Ab proteins and analysis of the impact on their immunoreactivity. J Agric Food Chem. 2010;58:3222-31. doi:10.1021/jf903189j.
8. Penninks AH, Knippels LM. Determination of protein allergenicity: studies in rats. Toxicol Lett. 2001;120:171-80.
9. Pusztai A, Bardocz S, Ewen SWB. Genetically modified foods: Potential human health effects. In: D'Mello JPF, ed. Food Safety: Contaminants and Toxins. Wallingford, Oxon: CABI Publishing; 2003:347–372. Available at: http://www.leopold.iastate.edu/sites/default/files/events/Chapter16.pdf.
10. Pusztai A. Genetically modified foods: Are they a risk to human/ animal health? Actionbioscience.org. http://www.actionbioscience.org/biotech/pusztai.html. Published June 2001.
11. American Academy of Environmental Medicine. Genetically modified foods. 2009. Available at: http://www.aaemonline.org/gmopost.html.
12. Prescott VE, Campbell PM, Moore A, et al. Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenicity. J Agric Food Chem. 2005;53:9023–30. doi:10.1021/jf050594v.
13. Zolla L, Rinalducci S, Antonioli P, Righetti PG. Proteomics as a complementary tool for identifying unintended side effects occurring in transgenic maize seeds as a result of genetic modifications. J Proteome Res. 2008;7:1850-61. doi:10.1021/pr0705082.
14. Nordlee JA, Taylor SL, Townsend JA, Thomas LA, Bush RK. Identification of a Brazil-nut allergen in transgenic soybeans. N Engl J Med. 1996;334:688-92. doi:10.1056/NEJM199603143341103.

## 3.10 Myth: GM animal feed poses no risks to animal or human health

## Truth: GM feed affects the health of animals and may affect the humans who eat their products

### Myth at a glance

It has often been claimed that GM DNA and proteins in GM animal feed are broken down in the animals' digestive tracts and are not detectable in the final food product. However, GM DNA present in animal feed has been detected in the milk and meat that people eat.

GM feed has been found to negatively affect the health of animals that eat it.

Other research shows that small molecules called microRNAs in any plants that are eaten, including GM plants, could have a direct physiological effect on human and animal consumers.

For all these reasons, meat, eggs, and dairy products from GM-fed animals should be labelled.

Most GM crops go into animal feed. In countries where GM foods have to be labelled, meat, eggs, and dairy products from GM-fed animals are exempt from labelling.

Is the absence of labelling justified? Historically, regulators and some sectors of the food industry have claimed that GM molecules – DNA and proteins – are broken down in the animals' digestive tracts and are not detectable in the final food product.[1,2] For example, in 2007 the European Food Safety Authority (EFSA) claimed: "After ingestion, a rapid degradation into short DNA or peptide fragments is observed in the gastrointestinal tract of animals and humans. To date, a large number of experimental studies with livestock have shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals like broilers, cattle, pigs or quails."[2]

However, such claims have been shown to be false by the following study findings, some of which were published before EFSA issued its statement:

- GM DNA present in animal feed was detected in milk sold on the Italian market, though the authors of the study said it was unclear whether the source of the GM DNA was ingestion by the animal or external contamination.[3]
- GM DNA in feed was taken up by the animals' organs and detected in the meat and fish that people eat.[4,5,6,7]

- Insecticidal Bt toxin proteins were found circulating in the blood of pregnant and non-pregnant women and the blood supply to foetuses.[8,9] It is not known if the Bt toxin proteins originated from GM Bt crops or from Bt sprays used in chemically-based and organic agriculture. Similarly, the exposure route (dietary or inhalation) is not known. However, the study shows that the assumption that Bt toxin proteins are broken down in the mammalian digestive tract and are unable to reach the blood and organs is false.
- GM feed was found to affect the health of animals that eat it. GM DNA from soy was detected in the blood, organs, and milk of goats. An enzyme, lactic dehydrogenase, was found at significantly raised levels in the heart, muscle, and kidneys of young goats fed GM soy.[10] This enzyme leaks from damaged cells during immune reactions or injury, so high levels may indicate such problems. It is not possible to tell from this study whether this effect was due to the presence of GM DNA in the feed or some other aspect of the GM crop, such as changes in a protein in the crop or residues of the pesticides sprayed on the growing crop.

After it became widely known that the evidence does not support claims that GM DNA is not detectable in the final product, in 2012 the UK Food Standards Agency (FSA) conceded: "It is… possible that DNA fragments derived from GM plant materials may occasionally be detected in animal tissues, in the same way that DNA fragments derived from non-GM plant materials can be detected in these same tissues."[11]

However, the FSA's statement appears to be a gross understatement in light of a 2013 study in humans which showed that DNA fragments large enough to carry complete genes can avoid degradation in the digestive tract and pass from food into the blood.[12] This study was not on GM foods but its findings would apply equally to GM and non-GM foods.

The stretches of plant DNA were complete enough to enable the researchers to identify the plants that the human subjects ate, such as soy, maize, and oilseed rape. The researchers even found that one of the blood serum samples had a higher concentration of plant DNA than human DNA.[12]

The highest concentrations of plant DNA were found in people with inflammatory diseases such as inflammatory bowel disease and Kawasaki disease, an autoimmune disease in which the blood vessels become inflamed.[12]

It should be noted that the presence of intact genes in the circulation does not imply that they are functioning (expressing). Several steps would need to happen for this to take place, namely:

1. Uptake by cells
2. Integration into the host cell DNA
3. In the case of a plant-derived gene, integration in a location and orientation that would allow a host promoter to switch on the gene and make it express (plant promoters are highly inefficient in animals and humans).

It can be concluded that the chances of expression are low. The most plausible adverse health consequence would result from intact genes being taken up by bacteria and expressed.
If there are intact genes in the blood of the consumer, this implies that there are intact

genes in the gut, which could then be taken up by bacteria and expressed. This needs to be investigated experimentally.

Nevertheless, it has been shown that another type of DNA molecule ingested in food can affect animals that eat them. MicroRNAs (miRNAs, a type of double-stranded RNA molecule that is involved in the regulation of many genes) of plants were found in the blood of humans and animals that had eaten them. In experiments on mice, microRNAs from rice plants that the mice had eaten were found to be biologically active, affecting gene expression and the functioning of important processes in the body.[13]

While this study was not carried out with GM plants, it showed that any plants that are eaten, including GM plants, could have a direct physiological effect on human and animal consumers.[13] The study suggested that the saying, "You are what you eat", may have some scientific credibility.

Many GM crops are being tested and are in the pipeline for regulatory approval that are engineered to express novel miRNA sequences, either to impose control on host plant genes or to act as insecticides. Regulators have not assessed these products adequately.[14]

Does any of this matter? The UK Food Standards Agency would conclude that it does not, since "food from animals fed on authorized GM crops is considered to be as safe as food from animals fed on non-GM crops."[11]

However, this claim has been shown to be false by the animal feeding studies discussed earlier in this chapter. The studies show that a diet containing GM crops can damage the health of animals. Therefore there could also be risks to the humans that eat products derived from unhealthy GM-fed animals.

## Conclusion

The argument that meat, eggs, and dairy products from GM-fed animals do not need to carry a GM label cannot be scientifically justified, since in some cases those products may contain GM DNA and could even be materially changed as a result of the animals' consumption of GMOs. In addition, some GM crops have been shown to have toxic effects on laboratory and farm animals, so consumers eating meat and dairy products from animals raised on GM crops may be eating sick animals.

## References


1. Mann A. Stores retreat on GM feed. The Scottish Farmer. http://bit.ly/163z8Uj. Published April 18, 2013.
2. European Food Safety Authority (EFSA). EFSA statement on the fate of recombinant DNA or proteins in meat, milk and eggs from animals fed with GM feed. 2007. Available at: http://www.efsa.europa.eu/en/efsajournal/doc/744.pdf.
3. Agodi A, Barchitta M, Grillo A, Sciacca S. Detection of genetically modified DNA sequences in milk from the Italian market. Int J Hyg Env Health. 2006;209:81–8. doi:10.1016/j.ijheh.2005.08.005.
4. Mazza R, Soave M, Morlacchini M, Piva G, Marocco A. Assessing the transfer of genetically modified DNA from feed to animal tissues. Transgenic Res. 2005;14:775–84. doi:10.1007/s11248-005-0009-5.
5. Sharma R, Damgaard D, Alexander TW, et al. Detection of transgenic and endogenous plant DNA in digesta and tissues of sheep and pigs fed Roundup Ready canola meal. J Agric Food Chem. 2006;54:1699–1709. doi:10.1021/jf052459o.
6. Chainark P, Satoh S, Hirono I, Aoki T, Endo M. Availability of genetically modified feed ingredient: investigations of ingested foreign DNA in rainbow trout Oncorhynchus mykiss. Fish Sci. 2008;74:380–390.

7. Ran T, Mei L, Lei W, Aihua L, Ru H, Jie S. Detection of transgenic DNA in tilapias (Oreochromis niloticus, GIFT strain) fed genetically modified soybeans (Roundup Ready). Aquac Res. 2009;40:1350–1357.
8. Aris A, Leblanc S. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Reprod Toxicol. 2011;31.
9. Aris A. Response to comments from Monsanto scientists on our study showing detection of glyphosate and Cry1Ab in blood of women with and without pregnancy. Reprod Toxicol. 2012;33:122-123.
10. Tudisco R, Mastellone V, Cutrignelli MI, et al. Fate of transgenic DNA and evaluation of metabolic effects in goats fed genetically modified soybean and in their offsprings. Animal. 2010;4:1662–1671. doi:10.1017/S1751731110000728.
11. Food Standards Agency (UK). GM material in animal feed. 2013. Available at: http://www.food.gov.uk/policy-advice/gm/gmanimal#.UXw5SoJAtY4.
12. Spisak S, Solymosi N, Ittzes P, et al. Complete genes may pass from food to human blood. PLOS ONE. 2013;8(7):e69805.
13. Zhang L, Hou D, Chen X, et al. Exogenous plant MIR168a specifically targets mammalian LDLRAP1: Evidence of cross-kingdom regulation by microRNA. Cell Res. 2012;22(1):107-126. doi:10.1038/cr.2011.158.
14. Heinemann J, Agapito-Tenfen SZ, Carman J. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. Environ Int. 2013;55:43–55.

# 3.11 Myth: Genetic engineering will deliver more nutritious crops

## Truth: No GM crop that is more nutritious than its non-GM counterpart has been commercialized and GM is not needed for good nutrition

### Myth at a glance

GM proponents have long claimed that genetic engineering will deliver healthier and more nutritious "biofortified" crops. However, no such nutritionally enhanced GM foods are available in the marketplace.

In some cases, GM foods have been found to be less nutritious than their non-GM counterparts, due to unexpected effects of the genetic engineering process.

The much-hyped GM golden rice, which is claimed to be able to alleviate vitamin A deficiency in developing countries, is still not ready for the market and at the time of writing had not yet undergone toxicological testing.

Cheap and safe solutions to deficiencies of vitamin A and other nutrients are available now and only lack the modest funding needed to roll out more widely.

GM proponents have long claimed that genetic engineering will deliver healthier and more nutritious "biofortified" crops. However, no such nutritionally enhanced GM foods are available in the marketplace.

On the contrary, in some cases, GM foods have been found to be less nutritious than their non-GM counterparts, due to unexpected effects of the genetic engineering process (see Myth 2.1).[1,2]

## GM golden rice: More hype than hope?

The best-known attempt to nutritionally improve a crop by genetic engineering is beta-carotene-enriched GM "golden rice".[3,4] Beta-carotene can be converted by the human body to vitamin A. The crop is intended for use in poor countries in the Global South, where vitamin A deficiency causes blindness, illness, and deaths. However, despite over a decade's worth of headlines hyping golden rice as a miracle crop, it is still not available in the marketplace.

GM proponents blame excessive regulation and anti-GM activists for delaying the commercialization of golden rice. Bjørn Lomborg, author of The Skeptical Environmentalist, wrote an article in February 2013 stating that golden rice had been delayed for 12 years by "relentless opposition to GM foods" from "rich, well-meaning Westerners", during which time "about 8 million children worldwide died from vitamin A deficiency".[5]

But the real reasons for the delay in deploying golden rice are basic research and development problems. The first golden rice variety had insufficient beta-carotene content and would have had to be consumed in kilogram quantities per day to provide the required daily vitamin A intake.[3] As a result, a new GM rice variety had to be developed with higher beta-carotene content.[4]

Also, the process of backcrossing golden rice with varieties that perform well in farmers' fields in order to ensure a viable product has taken many years.[6,7] A 2008 article in the journal Science said that there was still a "long way to go" in the process of backcrossing golden rice lines into the Indica varieties that perform well in Asian farmers' fields and are favoured by the Asian market.[6]

After the publication of Lomborg's article and another by the Observer newspaper's science editor Robin McKie,[8] in February 2013 the International Rice Research Institute (IRRI), the body responsible for the rollout of GM golden rice, felt it necessary to issue a statement contradicting the claims that golden rice was (a) already available and (b) proven effective. On the latter the IRRI said: "It has not yet been determined whether daily consumption of golden rice does improve the vitamin A status of people who are vitamin A deficient and could therefore reduce related conditions such as night blindness," adding that studies would need to be conducted in order to find this out.[9]

All in all, the IRRI expected that it "may take another two years or more" for GM golden rice to be available to farmers.[9]

Clearly, anti-GM activists and excessive regulation are not responsible for the long delay in the deployment of GM golden rice.

## Human trials carried out before toxicological safety testing

At the time of writing, golden rice had not been subjected to basic toxicological testing in animals – testing that is required by the European regulatory system for all GMOs before they can be authorized for human consumption.[10] Nevertheless this GM rice was fed to human subjects (adults[11] and children[12]) in experiments conducted by researchers from Tufts University, Boston, MA.

It is important to note that these were not safety studies to look for any effects on health, but efficacy tests to see whether the human subjects assimilated sufficient beta-carotene and converted it to vitamin A. Thus these trials did not reflect the intended conditions of regular consumption of golden rice by the target malnourished population.

The trial in adults involved feeding a single serving of golden rice to healthy human subjects. Butter was given with the rice to enable uptake of the beta-carotene from the digestive tract.[11] Yet in real-life conditions, golden rice would only be effective if it were consumed regularly. And malnourished people are by definition not healthy and are highly unlikely to have access to fat (oil or butter) to eat with their rice to allow its effective assimilation.

The feeding of GM golden rice to human subjects, especially young children, in the absence of prior animal toxicological testing was condemned by international scientists as a breach of medical ethics and the Nuremberg Code, which was established after World War II to prevent a repeat of inhumane Nazi experiments on people.[13]

## Breaches of medical ethics and Chinese law

In 2012 a further controversy arose when the journal Nature reported that neither the children on whom the rice was tested, nor their parents or their schoolteachers, knew it was genetically modified. Lack of informed consent to the trial is another serious breach of medical and scientific ethics.[14]

In the row that followed, the Chinese Centre for Disease Control and Prevention (CDC) conducted an investigation into the trial. The CDC investigation revealed discrepancies over the details of the trial. For example, there was confusion over the amount of GM rice the children ate during the study period.[14,12] The affair culminated in three officials being sacked for violating Chinese laws and ethical regulations.[14]

## Solutions to vitamin A deficiency already available

Inexpensive and effective methods of combating vitamin A deficiency have long been available. The World Health Organization's (WHO) long-standing project to combat vitamin A deficiency uses supplements where necessary, but centres on education and development programmes. These programmes encourage mothers to breastfeed and teach people how to grow carrots and leafy vegetables in home gardens – two inexpensive, effective, and widely available solutions.

Beta-carotene is one of the commonest molecules in nature, being found in abundance in green leafy plants and fruits. There is no need to engineer beta-carotene into rice.

The WHO says its programme has "averted an estimated 1.25 million deaths since 1998 in 40 countries."[15] According to WHO malnutrition expert Francesco Branca, these approaches are, for now, more promising approaches to combating vitamin A deficiency than golden rice.[6]

Vitamin A supplementation enjoys broad support. A review published in the British Medical Journal assessed 43 studies involving 200,000 children and found deaths were cut by 24% if children were given the vitamin. The researchers estimated that giving vitamin A supplements to children under the age of five in developing countries could save 600,000 lives a year. They concluded, "Vitamin A supplements are highly effective and cheap to produce and administer."[16,17]

If the resources that have been poured into developing golden rice had been put into such proven programmes, thousands of children and adults could have been saved. As the food writer Michael Pollan wrote in an article for the New York Times entitled “The great yellow hype”, “These ridiculously obvious, unglamorous, low-tech schemes are being tried today, and according to the aid groups behind them, all they need to work are political will and money.”[18]

Pollan suggested that the real value of golden rice lies in its usefulness as a public relations strategy to boost the tarnished image of the biotechnology industry. Pollan wrote that golden rice seemed not so much a solution to vitamin A deficiency as a solution “to the public-relations problem of an industry that has so far offered consumers precious few reasons to buy what it’s selling – and more than a few to avoid it.”[18]

## Purple cancer-fighting tomato

The John Innes Centre (JIC) in the UK has developed a purple tomato engineered to contain high levels of anthocyanin antioxidants, which, like many other antioxidants, have cancer-preventing properties. The JIC announced the development of the tomato in 2008 in a press release headlined, “Purple tomatoes may keep cancer at bay”.[19] Professor Cathie Martin, who led the research, published an article in the press entitled, “How my purple tomato could save your life”.[20]

These claims were based on the results of a preliminary small-scale feeding study on cancer-susceptible mice, which found that those fed with the purple tomato had an extended lifespan, measured against control groups fed non-GM tomatoes and a standard rodent diet.[21] Yet as one of the researchers pointed out, the study did not test for possible toxicity, so “We’re far from considering a human trial”.[22]

Meanwhile, anthocyanins are available in abundance in many common fruits and vegetables, including raspberries, blackberries, blueberries, bilberries, blood oranges, red cabbage, red onions, and aubergine (eggplant).

The JIC’s Cathie Martin has argued that tomatoes are consumed by people who might not normally consume many fruits and vegetables.[20] It is questionable, however, whether people who are so conservative in their food choices would eat a tomato that looks, in the words of one journalist, “like a cross between an orange and a black pudding”[23] – let alone a tomato that in most countries will carry a GM label.

In 2010, a year after the JIC announced its purple GM tomato, Italian researchers announced a non-GM tomato with higher-than-usual levels of the antioxidant lycopene.[24] Lycopene, like anthocyanin, has anti-cancer properties.

For anyone who wants to derive their anthocyanins from tomatoes instead of the many fruits and vegetables rich in these substances, a non-GM purple tomato with high levels of anthocyanins and vitamin C has been developed.[25] In contrast with the JIC’s GM tomato, the non-GM tomatoes received little publicity.

Overall it is important to note that the cancer-prevention properties of antioxidants results from the total level consumed rather than due to the special properties of any one antioxidant. So the benefits of antioxidants can best be achieved with a diet containing a variety of fruits and vegetables. A GM crop engineered with a particular antioxidant offers nothing that cannot be achieved through consumption of natural products rich in antioxidants.

## "Biofortified" crops are not a solution to hunger

Most "biofortified" crops, whether produced through GM or conventional breeding, target the poor and hungry in the Global South and focus on one or two nutrients, such as Vitamin A or iron. Even if we assume that GM can produce more crops with high levels of one or two nutrients, some important topics need to be addressed before concluding that biofortifying crops by whatever means is a sensible approach to malnutrition:

- Malnourished people are hungry not because of a lack of biofortified crops, but because they lack the money to buy food and the access to land on which to grow it. This type of poverty is often due to political conflicts in the country. Another cause is ill-advised development programmes that, in return for foreign loans and investment, have forced countries to convert farmland from growing food for people into growing cash crops for export. These are political and economic problems that cannot be solved by offering a biofortified crop, for which the grower will need to be paid. People who have no money to buy basic food will certainly be unable to buy a biofortified food that has taken millions in investment funds to develop.
- Malnourished people are not usually deficient in just one or two nutrients, but in many. Focusing on a crop that can deliver one or two nutrients is unhelpful because a balance of nutrients is needed for proper absorption. For example, in order to absorb vitamin A, people need to have enough fat in their diet. This problem would need to be addressed before they could benefit from vitamin A-enriched food.
- Manipulating nutrients in food is controversial and risky. Dosage is difficult to control and certain nutrients may be needed by one person, yet be excessive and potentially dangerous for the next. Overdosing on vitamin A has been linked in some studies to an increased risk of birth defects[26,27] and cancer.[28] Also, nutritional theory is a fast-moving discipline, with today's desirable nutrient becoming tomorrow's suspect ingredient.[29]

## Non-GM biofortified crops are already available

If we assume that biofortified foods are a desirable approach to malnutrition, plenty of non-GM crop varieties are available now that do not present the risks and uncertainties of genetic engineering (see Chapter 6).

In addition, there are ways of adding nutrients to people's diets that do not involve the considerable expense and timespan of crop breeding. These include a rice fortified with iron and vitamins, which has been reported in a preliminary study to have caused dramatic falls in anaemia and vitamin B1 deficiency in children.[30]

## Conclusion

While GM proponents claim that GM can provide nutritionally enhanced (biofortified) foods, no such GM foods are available on the market.

The most widely publicized example of a GM nutritionally enhanced food, golden rice, has swallowed millions of dollars in research and development money. Yet it has not undergone proper toxicological testing and, after more than a decade, is still not ready for the market. In contrast, tried, tested, and inexpensive means of preventing and curing vitamin A deficiency are successful when applied but under-utilized due to lack of funding.

Aspirational claims of nutritionally enhanced GM crops are a dangerous distraction from the real causes of hunger, which are poverty and a lack of access to land on which to grow food.

If society decides that nutritionally enhanced foods are an important route to food security, it need not wait for expensive GM "solutions". Conventional plant breeding has already successfully and safely produced many such biofortified foods.

## References


1. Lappé M, Bailey B, Childress C, Setchell KDR. Alterations in clinically important phytoestrogens in genetically modified herbicide-tolerant soybean. J Med Food. 1999;1:241–245.
2. Jiao Z, Si XX, Li GK, Zhang ZM, Xu XP. Unintended compositional changes in transgenic rice seeds (Oryza sativa L.) studied by spectral and chromatographic analysis coupled with chemometrics methods. J Agric Food Chem. 2010;58:1746-54. doi:10.1021/jf902676y.
3. Ye X, Al-Babili S, Kloti A, et al. Engineering the provitamin A (beta-carotene) biosynthetic pathway into (carotenoid-free) rice endosperm. Science. 2000;287:303-5.
4. Paine JA, Shipton CA, Chaggar S, et al. Improving the nutritional value of Golden Rice through increased pro-vitamin A content. Nat Biotechnol. 2005;23:482-7. doi:10.1038/nbt1082.
5. Lomborg B. The deadly opposition to genetically modified food. Slate. http://slate.me/ZUgOWB. Published February 17, 2013.
6. Enserink M. Tough lessons from Golden Rice. Science. 2008;230:468–471.
7. Sharma A. Golden Rice still at development stage. The Financial Express (India). http://bit.ly/10Jsfqw. Published November 23, 2006.
8. McKie R. After 30 years, is a GM food breakthrough finally here? The Observer. http://bit.ly/10k62If. Published February 2, 2013.
9. International Rice Research Institute (IRRI). Clarifying recent news about Golden Rice. http://bit.ly/Z6ohSq. Published February 21, 2013.
10. European Parliament and Council. Commission implementing regulation (EU) no. 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Off J Eur Union. 2013. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF.
11. Tang G, Qin J, Dolnikowski GG, Russell RM, Grusak MA. Golden Rice is an effective source of vitamin A. Am J Clin Nutr. 2009;89:1776-83. doi:10.3945/ajcn.2008.27119.
12. Tang G, Hu Y, Yin SA, et al. Beta-carotene in Golden Rice is as good as beta-carotene in oil at providing vitamin A to children. Am J Clin Nutr. 2012. doi:10.3945/ajcn.111.030775.
13. Hooper M, Schubert D, Goodwin B, et al. Tufts University involvement in Golden Rice feeding trials. Letter from scientists and experts to Professor Robert Russell, Professor Emeritus, Friedman School of Nutrition Science and Policy, Tufts University School of Medicine. 2009. Available at: http://www.i-sis.org.uk/SPUCTGM.php.
14. Qiu J. China sacks officials over Golden Rice controversy. Nature. 2012. Available at: http://www.nature.com/news/china-sacks-officials-over-golden-rice-controversy-1.11998.
15. World Health Organization (WHO). Micronutrient deficiencies: Vitamin A deficiency. 2011. Available at: http://www.who.int/nutrition/topics/vad/en/index.html. Accessed January 1, 1915.
16. Mayo-Wilson E, Imdad A, Herzer K, Yakoob MY, Bhutta ZA. Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. Br Med J. 2011;343:d5094. doi:10.1136/bmj.d5094.
17. BBC News. Vitamin A pills "could save thousands of children." http://www.bbc.co.uk/news/health-14666287. Published August 27, 2011.

18. Pollan M. The way we live now: The great yellow hype. The New York Times Magazine. http://bit.ly/Lb7J9m. Published March 4, 2001.
19. John Innes Centre. Purple tomatoes may keep cancer at bay.http://bit.ly/NAwtZ6. Published October 26, 2008.
20. Martin C. How my purple tomato could save your life. Mail Online. http://bit.ly/10JsmlO. Published November 8, 2008.
21. Butelli E, Titta L, Giorgio M, et al. Enrichment of tomato fruit with health-promoting anthocyanins by expression of select transcription factors. Nat Biotechnol. 2008;26:1301-8. doi:10.1038/nbt.1506.
22. Catholic University of Campobasso. Purple tomatoes: The richness of antioxidants against tumors. Esciencenews.com. http://bit.ly/13CoYpN. Published October 26, 2008.
23. Philpott M. What the papers say. BBC News. http://news.bbc.co.uk/1/hi/northern_ireland/7692560.stm. Published October 27, 2008.
24. Knowles M. Italian producers unveil "supertomato." Fruitnet.com. http://bit.ly/1oLKL7t. Published July 5, 2010.
25. CBS News. Purple tomatoes may fight cancer, other diseases. http://on.wfmy.com/L7aB5Z. Published December 3, 2011.
26. Ross CA. Vitamin A. In: Coates PM, Betz JM, Blackman MR, et al., eds. Encyclopedia of Dietary Supplements. 2nd ed. London and New York: Informa Healthcare; 2010:115–120.
27. Ross A. Vitamin A and carotenoids. In: Shils M, Shike M, Ross A, Caballero B, Cousins R, eds. Modern Nutrition in Health and Disease. 10th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2006:351-75.
28. Mondul AM, Watters JL, Männistö S, et al. Serum retinol and risk of prostate cancer. Am J Epidemiol. 2011;173(7):813-821. doi:10.1093/aje/kwq429.
29. BBC News. Vitamins "may shorten your life." http://news.bbc.co.uk/1/hi/7349980.stm. Published April 16, 2008.
30. Foster P. Fortified rice to save millions of lives each year. The Telegraph. http://bit.ly/KIKT3g. Published May 14, 2009.

# 4. Health hazards of Roundup and glyphosate

Over 80% of all GM crops are engineered to tolerate one or more herbicides.[1] Herbicide-tolerant soybeans are the most widely grown GM crop, going from 17% percent of US soybean acreage in 1997 to 93% in 2013.[2]

The most widely grown GM crop is Roundup Ready (RR) soy,[1] which is engineered to tolerate Roundup herbicide, the presumed "active ingredient" of which is glyphosate. The RR gene enables farmers to spray the field liberally with herbicide. All plant life is killed except the crop.

The widespread adoption of GM RR soy in North and South America has led to substantial increases in the use of Roundup and other glyphosate herbicides.[3,4]

GM RR crops do not break down glyphosate herbicide, but absorb it into their tissues. Some of the glyphosate is broken down (metabolized) into a substance called aminomethylphosphonic acid (AMPA). Both glyphosate and AMPA remain in the plant and are eaten by people and animals. As documented below, both are toxic.

As well as being used on GM RR crops, Roundup is increasingly used as a desiccant on grain crops to dry them before harvest, making the grains easier to harvest and store without rotting. The herbicide is also widely used by municipal authorities on roads, railway lines, parks, and other public places, and by home gardeners.

## References


1. James C. Global status of commercialized biotech/GM crops: 2012. ISAAA; 2012. Available at: http://www.isaaa.org/resources/publications/briefs/44/download/isaaa-brief-44-2012.pdf.
2. USDA Economic Research Service. Recent trends in GE adoption. 2013. Available at: http://www.ers.usda.gov/data-products/adoption-of-genetically-engineered-crops-in-the-us/recent-trends-in-ge-adoption.aspx#.UzgPocfc26w.
3. Benbrook C. Impacts of genetically engineered crops on pesticide use in the US – The first sixteen years. Environ Sci Eur. 2012;24.
4. Binimelis R, Pengue W, Monterroso I. Transgenic treadmill: Responses to the emergence and spread of glyphosate-resistant johnsongrass in Argentina. Geoforum. 2009;40:623–633.

## 4.1 Myth: Roundup is a safe herbicide with low toxicity to animals and humans

## Truth: Roundup has never been tested or assessed for long-term safety for regulatory purposes but independent studies show it is highly toxic to animals and humans

### Myth at a glance

Claims that Roundup is safe are misleading. Independent studies show that glyphosate, the presumed active ingredient of Roundup, is toxic. Commercial glyphosate herbicide formulations contain extra added ingredients (adjuvants) and are more toxic than glyphosate alone.

Toxic effects of glyphosate and Roundup include disruption of hormonal systems and beneficial gut bacteria, damage to DNA, developmental and reproductive toxicity, birth defects, cancer, and neurotoxicity.

Roundup and other glyphosate herbicide formulations have never been tested or assessed for long-term safety for regulatory purposes. Only glyphosate alone was tested. Even the industry tests on glyphosate alone revealed toxic effects, including malformations.

The endocrine disruptive effects of glyphosate and Roundup are most worrying, as they manifest at very low doses and can lead to ill health when exposure takes place over long periods of time.

The GMO industry claims that glyphosate is non-toxic to animals and humans because they lack the shikimate biochemical pathway present in plants. This is false, as glyphosate also affects other pathways that are present in animals and humans.

Claims that the Roundup used on GM Roundup Ready crops replaces more toxic herbicides are misleading. The toxicity of Roundup and glyphosate has been underestimated, and the failure of Roundup Ready technology due to resistant weeds has resulted in farmers using mixtures of herbicides to control weeds. The industry has responded by developing GM crops that tolerate other, potentially even more toxic herbicides, such as 2,4-D, an ingredient of Agent Orange.

Roundup, the herbicide used on most GM crops, is often claimed to be safe by industry-linked sources.[1] But these claims are based on outdated and largely unpublished studies on the isolated ingredient glyphosate, commissioned by manufacturers in support of their application for regulatory authorization.[1] The regulatory tests focus only on glyphosate because it is presumed to be the "active ingredient" in Roundup.

The problem with testing glyphosate alone is that Roundup and other commercial glyphosate herbicide formulations have been found in studies to be far more toxic than the isolated supposed "active ingredient" glyphosate. This is logical, since the added ingredients in commercial herbicide formulations, called adjuvants, are included specifically to increase the toxicity of the supposed "active ingredient" to the weeds.

Even glyphosate alone has been found to be more toxic than claimed by industry and regulators, based on data from industry's own studies.[2]

Roundup and other formulations as sold and used have never been tested by industry for long-term toxicity for regulatory purposes prior to being marketed. Neither have regulators required that the formulations be tested at low, realistic doses over long periods of time to see whether they are endocrine (hormone) disruptors.

It has been left to independent scientists to carry out toxicity studies on the formulations after they were released onto the market – and after millions of people have been exposed. The results are concerning. Toxic effects found in these studies include disruption of hormonal systems, damage to DNA, developmental and reproductive toxicity, malformations, cancer, and neurotoxicity.

## Key studies showing toxic effects of glyphosate and Roundup

Studies in human cell lines in vitro and in animals, as well as in human epidemiological and clinical studies, have shown that Roundup and glyphosate have serious toxic effects. In many cases effects are seen at realistic exposure levels. Below are some of the findings.

### Adjuvants in Roundup are toxic and increase toxicity of glyphosate

The added ingredients (adjuvants) in Roundup are themselves toxic[3] and increase the toxicity of glyphosate by enabling it to penetrate plant and animal cells more easily, making it more bioavailable.[4,5,6]

Adjuvants are widely found in the environment, so people and animals are likely to be exposed to them. For example, the half-life of the Roundup adjuvant POEA (21–42 days) is longer than that of glyphosate alone (7–14 days) in aquatic environments.[7]

### Roundup more toxic than glyphosate

In an in vitro study, eight out of nine major pesticides tested in vitro in their complete formulations, including Roundup, were up to 1,000 times more toxic to human cells than their isolated active ingredients. This increased toxicity of the complete formulation compared with the active ingredient alone was found to be a general principle of pesticide toxicology.[8]

This principle has been confirmed by experiments in living mammals. An in vivo study in pigs showed that the adjuvant POEA and commercial glyphosate herbicide formulations were toxic and lethal to the pigs, whereas glyphosate alone had no such effects.[9] An in vivo study in rats showed that POEA and Roundup formulations containing POEA were more toxic than glyphosate alone.[10]

## Damage to DNA

Glyphosate herbicides altered cell cycle checkpoints in sea urchin embryos by interfering with the DNA repair machinery. Cell cycle dysfunction was seen from the first cell division in the sea urchin embryos.[11,12,13,14] The failure of cell cycle checkpoints is known to lead to genomic instability and cancer in humans.

Glyphosate and its main metabolite AMPA have been found to cause irreversible damage to DNA in human cells in vitro and in mice in vivo.[15,16] Such damage to DNA may increase the risk of cancer and birth defects. AMPA damaged DNA in human cells in vitro at doses of 2.5-7.5mM and caused breaks in chromosomes at 1.8mM.[16]

An in vitro study showed that irradiation corresponding to a few minutes of sun exposure greatly amplified the DNA-damaging effects of glyphosate on mammalian cells. The glyphosate metabolite AMPA proved even more damaging, provoking cellular toxic effects from 0.5 ppb, a low environmentally relevant dose that can be found in European rivers and even in drinking water. The effects were even greater when glyphosate was mixed with other pesticides (the so-called "cocktail effect"), including atrazine. The authors concluded that "the Directive Standards for Pesticides in Drinking Water should be re-evaluated according to these underestimated factors of risk".[17]

Glyphosate and Roundup caused DNA damage in human mouth cells in vitro after a single 20-minute exposure at much lower doses than those used in agriculture. Roundup was much more toxic than glyphosate alone. The study showed that in principle, people who are exposed to Roundup through inhalation (as in South American soy-producing countries) could suffer DNA damage. With both glyphosate and Roundup, DNA damage occurred at concentrations below those required to cause cell damage, suggesting that the DNA damage was caused directly by these substances instead of being an indirect result of cell toxicity.[18]

Glyphosate and Roundup caused damage to DNA and chromosomes in the bone marrow of mice in vivo and in human cells in vitro. Roundup was only slightly more toxic than glyphosate.[19]

Roundup caused mutations in the DNA of fruit flies.[20] Roundup increased the frequency of DNA adducts (cancer-causing chemicals that link to DNA), which can mark the onset of cancer, in the liver and kidneys of mice.[21]

Genetic damage was found in soybean workers exposed to pesticides, glyphosate herbicides among them, in Brazil.[22]

Ecuadorian people exposed to aerial glyphosate herbicide spraying showed a higher degree of DNA damage in blood cells than a control population. The researchers ruled out tobacco, alcohol, non-prescription drugs and asbestos as causes. None of the individuals had used or been exposed to other herbicides or pesticides when the samples were taken. The study also found acute poisoning reactions to the glyphosate herbicide spraying, including intestinal pain and vomiting, diarrhoea, fever, heart palpitations, headaches, dizziness, numbness, insomnia, burning eyes, blurred vision, difficulty in breathing, and skin rash.[23]

## Endocrine (hormone) disruption

Laboratory studies on animals and in vitro experiments on human cells indicate that glyphosate herbicides and glyphosate alone are endocrine disruptive chemicals (EDCs). Endocrine disruption can cause cancer, birth defects, and other reproductive and developmental problems.

The endocrine-disruptive effect of glyphosate and its commercial formulations is their most worrying toxic effect. This is because EDCs do not function like normal poisons, where a higher dose gives greater toxicity. Instead they exert their effects at very low doses and exposure over long periods of time can lead to severe ill health.[24] Often, endocrine disruptive effects are seen at lower doses but not at higher doses.[24,25]

Study findings include the following:

- Glyphosate herbicide altered hormone levels in female catfish and decreased egg viability. The study concluded that the herbicide is harmful to catfish reproduction.[26] Roundup disrupted production of the steroid hormone progesterone in mouse cells.[27] Glyphosate herbicide was a potent EDC in rats, causing disturbances in reproductive development after exposure during puberty.[28]
- In an in vitro experiment in human cells, glyphosate herbicides prevented the action of androgens, the masculinizing hormones, at levels up to 800 times lower than glyphosate residue levels allowed in some GM crops used for animal feed in the USA. DNA damage was found in human cells treated with glyphosate herbicides at these levels. Glyphosate herbicides disrupted the action and formation of estrogens, the feminizing hormones. The first toxic effects were found at the low dose of 5 ppm and the first endocrine disruption at 0.5 ppm – 800 times less than the 400 ppm level authorized for some animal feeds.[29]
- Roundup herbicide at environmentally relevant exposure levels (down to 0.00023% glyphosate dilution of the commercial formulation) caused the dysregulation of large numbers of genes in human breast cancer cells grown in the laboratory in vitro. Of the 1,550 genes analyzed, expression of 680 was either increased or decreased. Roundup was able to replace and work synergistically with estrogen, which is required for growth of the breast cancer cells. This demonstrates the strong potential endocrine disruptive potential of glyphosate in this hormonal system. The authors commented, "There remains an unclear pattern of very complex events following exposure of human cells to low levels of glyphosate, but events surrounding the altered levels of expression of only three genes… out of the entire battery tested, are both complicated and potentially damaging to adult and fetal cells."[30]

- Glyphosate alone increased the proliferation of estrogen-dependent breast cancer cells by estrogenic mechanisms in vitro.[31]
- An in vivo study of Roundup administered to rats in drinking water diluted to 50ng/L glyphosate equivalence – half of the level permitted in drinking water in the EU[32] and 14,000 times lower than that permitted in drinking water in the USA[33] – resulted in severe organ damage and a trend of increased incidence of mammary tumours in female animals over a 2-year period of exposure.[34] This type of non-linear endocrine disruptive effect of glyphosate and Roundup is not taken into account in safety evaluations, resulting in exposures to the public that could lead to severe illness and reproductive and developmental problems.

### Malformations and reproductive and developmental toxicity

A study on the reproductive effects of Roundup on male and female offspring of rats exposed during pregnancy and lactation found significant adverse effects at non-maternally toxic doses. Findings in male offspring included a decrease in sperm number and daily sperm production during adulthood, an increase in the percentage of abnormal sperms, a dose-related decrease in serum testosterone level at puberty, and sperm cell degeneration. The authors noted that Roundup had been found in other experiments to inhibit steroidogenesis (formation of steroid hormones) in vitro by disrupting the expression of a regulatory protein, but glyphosate did not, indicating that at least one other component of the formulation is required to disrupt steroidogenesis.[35]

A study of farming families in Ontario, Canada found a higher than normal rate of late miscarriages and premature births associated with male glyphosate herbicide exposure.[36] Monsanto claimed in non-peer-reviewed articles that the association for glyphosate was weak and not statistically significant.[37,38] But in the study, the odds ratios (a statistical measure of a possible link) were 1.5 for an association between glyphosate herbicide exposure and miscarriage and 2.4 between glyphosate herbicide exposure and premature birth. 1.5 is near the lower limit but 2.4 is fairly strong. Both indicate an association.

Studies on glyphosate alone commissioned by industry in support of regulatory authorization showed that it caused malformations in rabbits and rats. These effects were not only found at high maternally toxic doses but also at lower doses. Statistical significance was not always achieved at lower doses, perhaps because too few animals were used. Germany, the "rapporteur" member state for glyphosate, responsible for liaising between industry and the EU authorities during the approval process, dismissed the findings, using unscientific reasoning and practices.[2]

Roundup and glyphosate tested alone caused malformations in chicken and frog embryos at doses far below those used in agricultural spraying. Malformations were of a similar type as those reported in human populations exposed to Roundup spraying in GM soy-producing regions of South America. Glyphosate itself was responsible for the malformations in the chicken and frog embryos, rather than the adjuvants in the commercial formulation.[39]

The study identified the mechanism of toxicity as interference with the retinoic acid signalling pathway. This pathway is present in higher animals and affects gene expression. When disrupted, it can result in the development of malformations.[39] This finding countered claims or implications by industry authors that glyphosate is non-toxic to animals on the supposed grounds that its sole mechanism of toxicity is the shikimate biochemical pathway, which plants have but animals lack.[40]

Roundup was found to cause skeletal malformations in rat foetuses after the mothers were dosed during pregnancy. The authors observed that the findings were not due to poisoning of the mother (maternal toxicity) and concluded that Roundup had a direct toxic effect on the foetuses. They also noted that the Roundup formulation was more toxic than glyphosate alone.[41]

Glyphosate herbicide caused malformations in tadpoles, even at concentrations that caused low mortality.[42]

An epidemiological study carried out in California showed a modest association between Roundup exposure and anencephaly, a type of neural tube birth defect or malformation of the structures of the developing brain and spinal cord, in which part of the skull and brain are missing.[43,44]

The authors found that the association was present using one type of analytical model (a multiple pesticide model), but not with another (a single pesticide model). The authors did not show the data in which they applied either model. But Table 2 of their publication reveals modest associations between glyphosate and neural tube defects for both the single pesticide and multiple pesticide models – with an odds ratio (OR, a statistical measure of a possible link) of 1.5 for both. For the hierarchical model they found an OR of 1.4. Their criteria for significant effects were that the OR should be greater than or equal to 1.4 and the lower limit of the confidence interval (CI) should be greater than or equal to 0.9.[44] The OR requirement is met for glyphosate and neural tube defects using both models, but both models deliver CIs that are just below the cut-off: 0.8.

These results could reasonably be interpreted as indicating a modest association between glyphosate herbicide exposure, neural tube defects, and anencephaly.

This finding is consistent with findings in frog and chicken embryos[39] and rats,[41] which also linked glyphosate/Roundup exposure to impaired development of the structures of the central nervous system. It is also consistent with findings of industry studies on the effects of glyphosate alone in rats, in which the observed malformations included "reduced ossification of one or more cranial centres".[45] These malformations involving the structures of the central nervous system are consistent with descriptions of retinoic acid-induced malformations in the literature.[2,46]

## Cancer

In a laboratory study, Roundup was found to promote cancerous tumour growth in the skin of mice.[47] An epidemiological study of pesticide applicators in the USA found that exposure to glyphosate herbicide was associated with higher incidence of multiple myeloma, a type of blood cancer.[48] Epidemiological studies conducted in Sweden found that exposure to glyphosate herbicide was linked with a higher incidence of non-Hodgkin's lymphoma, another type of blood cancer.[49,50,51]

The EU's 2002 review of industry studies on glyphosate claimed "no evidence" of carcinogenicity (ability to cause cancer).[1] But two long-term studies on rats indicating possible carcinogenic effects already existed at this time. These long-term studies on rats were conducted in 1979–1981 and 1988–1990.[52] The rats received relatively low doses of glyphosate per day in the first study and higher doses in the second. The first study found an increase in tumours in the testes of rats fed glyphosate, but the same effect was not found in the second test using the higher doses. On this basis, glyphosate was excluded from the carcinogenic category of chemicals.[52,41]

However, this move was based on outdated and incorrect assumptions about toxicology. Cancers can be triggered by the endocrine disruptive effects of a chemical, which can occur at extremely low doses. As explained above, EDCs can have more potent endocrine disruptive effects at lower doses than higher doses. Sometimes a disruptive effect seen at the lower dose is not seen at all at a higher dose.[24]

Low-dose effects cannot be predicted by effects at higher doses, such as are tested in regulatory tests performed on pesticides, including glyphosate. Regulatory tests do not require low doses to be tested for possible endocrine disrupting effects.[25] Therefore the findings of the long-term cancer studies on rats discussed above[52] should be re-evaluated in light of up-to-date scientific knowledge.

## Neurotoxicity

A toxicological study on rats found that glyphosate depleted the neurotransmitters serotonin and dopamine.[53] It is not clear from the published study whether the test substance was pure glyphosate or a complete commercial formulation. Glyphosate was also found to injure rat brain cells tested in vivo.[54]

An epidemiological study carried out in Minnesota, USA found that the children of pesticide applicators exposed to glyphosate herbicides had an increased incidence of neurobehavioral disorders, including ADHD (attention deficit hyperactivity disorder). The finding suggested that glyphosate herbicide impacts neurological development.[55]

A clinical case study described how a man[56] who was exposed to glyphosate herbicide developed the neurological disorder Parkinson's disease. A separate case study involving a woman[57] found the same result, though in this case it is not clear if the exposure was to glyphosate alone or a complete formulation, as the exposure took place in a factory that manufactured herbicides.[57]

An in vitro study suggested a mechanism through which glyphosate could cause Parkinson's disease: glyphosate alone was found to induce programmed cell death and degradation leading to death in PC12 cells – human cells that serve as an experimental model for nerve cells.[58]

## Negative effects on gut bacteria

An in vitro study carried out to investigate the rise in botulism disease in cattle in the past 10–15 years found that glyphosate and Roundup were toxic to beneficial gut bacteria that inhibit the growth of the botulism-causing bacterium Clostridium botulinum, but non-toxic to the botulism-causing bacteria themselves. In short, glyphosate and Roundup favoured the growth of botulism-causing Clostridium botulinum bacteria. The authors concluded that ingestion of Roundup residues in cattle feed could predispose cattle to falling ill with botulism.[59]

In a separate in vitro study on strains of bacteria found in the gut of poultry, most of the pathogenic bacteria tested were highly resistant to Roundup, but most of the beneficial gut bacteria tested were found to be moderately to highly susceptible. The researchers documented the antibiotic damage done to beneficial bacteria in the gut by very low concentrations of Roundup, which allowed the overgrowth of serious pathogens such as Clostridium botulinum, Salmonella spp, and E. coli. These would otherwise be kept in check by the beneficial bacteria that were wiped out by the Roundup residues in feed.[60]

The authors concluded that the ingestion of Roundup-contaminated feed could be a significant factor predisposing poultry to diseases caused by Clostridium botulinum. It could also explain the now widespread contamination of poultry products with pathogenic Salmonella and E. coli strains of bacteria, which can make human consumers ill.[60]

### Metal chelating effect

Glyphosate chelates (binds to) essential nutrient metals, including manganese, magnesium, iron, zinc, and calcium, making them unavailable to plants sprayed with the herbicide[61,62] and thus to the people and animals that eat the plants. A German-Egyptian team of researchers found that all cows tested from Danish dairy farms excreted glyphosate in their urine. Unexpectedly low levels of manganese and cobalt were observed in all animals, which the authors said could be explained due to the strong metal chelating effect of glyphosate. Potential signs of liver and kidney toxicity were also found in the cows, which were consistent with the findings of rodent feeding studies with GM glyphosate-tolerant plants.[63]

This effect could cause human and animal deficiencies in the nutrient metals affected, indirectly impacting their health.

## Reviews of health effects of Roundup spraying in South America

In South America a public health crisis has emerged around the spraying of Roundup herbicide on GM Roundup Ready soy, which is often carried out from the air. The spray drifts into people's homes, schools, food crops, and watercourses. It has been blamed for widespread serious health problems.

A report commissioned by the provincial government of Chaco, Argentina, found that the rate of birth defects increased fourfold and rates of childhood cancers tripled in only a decade in areas where rice and GM soy crops are heavily sprayed. The report noted that problems centred on "transgenic crops, which require aerial and ground spraying with agrochemicals"; glyphosate herbicides were named as chemicals of concern.[64]

A review of studies on the health effects of glyphosate and Roundup, as well as other pesticides used with GMOs, in human and animal model systems concluded that the precautionary principle was not being observed with regard to the GMO herbicide-tolerant agricultural model. The authors concluded, "It will not be possible to devise a sustainable agriculture that satisfies social needs if man does not begin to prioritize policies that enhance environmental and food security over the interests of private agrochemical industries and markets."[65]

A non-peer-reviewed report by Argentine physicians and scientists, based on clinical data, detailed acute and chronic health effects in people associated with increased cultivation of GM soy and exposure to the spraying of glyphosate herbicides. Health effects included increased incidence of birth defects (including in young mothers), miscarriages, and cancers in children and young people as well as adults. Also noted were increased incidence of difficulty conceiving, genetic damage (which can lead to cancer and birth defects); increased cases of toxic liver disease, neurological developmental problems in children, kidney failure, respiratory problems, and allergies. DNA damage was also found in people exposed to spraying.[66]

The physicians commented that they had been serving the same populations for over 25 years, but the recent trends were unusual and linked to a systemic increase in the spraying of pesticides.[66]

## Roundup link with modern diseases suggested

A review published in 2013 (Samsel and Seneff, 2013) hypothesized a mechanism by which glyphosate herbicides could be contributing to modern human diseases that are on the increase worldwide. The authors focused especially on celiac disease and gluten intolerance, but also drew potential links between glyphosate toxicity and a broader range of diseases, such as ADHD (attention deficit hyperactivity disorder), autism, Alzheimer's disease, infertility, birth defects, and cancer.[67]

The review cited glyphosate's known ability to disrupt gut bacteria and to suppress the activity of the cytochrome P450 (CYP) family of enzymes, which play an important role in detoxifying harmful chemicals. The authors concluded that glyphosate enhances the damaging effects of other foodborne chemical residues and environmental toxins.[67]

If this potential pathway to modern diseases is confirmed by further research, it highlights the industry's failure to consider any mechanism of glyphosate toxicity other than the shikimate pathway, which plants have but humans and animals do not.[40] In a second review, Samsel and Seneff pointed out that gut bacteria have this pathway and are susceptible to glyphosate toxicity, with the resulting disruptions in gut bacteria potentially impacting human and animal health. In addition, the authors noted glyphosate's ability to chelate essential nutrient metals, making them unavailable to human and animal consumers, thus potentially affecting their health.[68]

## Roundup linked to chronic kidney disease

An epidemic of chronic kidney disease in farming regions of Sri Lanka and other countries has been linked in a study to exposure to Roundup. The study's authors propose that glyphosate becomes highly toxic to the kidney when it mixes with "hard" water or heavy metals like arsenic and cadmium, either naturally present in the soil or added in the form of fertilizers. Hard water contains metals such as calcium, magnesium, strontium and iron, along with carbonate, bicarbonate, sulphate and chlorides. Glyphosate chelates or binds to these substances and carries them to the kidneys, resulting in the destruction of tissue.[69]

The study prompted the Sri Lankan government to order a ban on glyphosate herbicides.[70] Under pressure from the plantation sector, the ban was subsequently watered down to a restriction in areas where chronic kidney disease was most serious[71] and later rescinded.

It is noteworthy that kidney problems were also observed in laboratory animals that received Roundup in water over a long-term 2-year period.[34]

## Courts rule Roundup not safe – Brazil seeks to ban it

Claims that Roundup and glyphosate are safe for human health and the environment have been overturned in courts in the US[72] and France. The French court forced Monsanto to withdraw advertising claims that Roundup is biodegradable and leaves the soil clean after use.[73]

In 2014 in Brazil, the Federal Public Prosecutor requested the Justice Department to suspend the use of glyphosate herbicides, the most widely used herbicides in the country. The Prosecutor ordered the National Health Surveillance Agency (ANVISA) to re-evaluate the toxicity of glyphosate, along with eight other pesticide active ingredients suspected of causing damage to human health and the environment.[74]

## Arguments that Roundup replaces more toxic herbicides are false

GMO proponents often argue that Roundup has replaced more toxic herbicides and that GM Roundup Ready (RR) crops therefore reduce the toxic burden on humans and the environment. But this is false. GM RR crops have not only increased the use of glyphosate herbicides but have also increased the use of other, potentially even more toxic herbicides, due to the spread of glyphosate-resistant weeds (see Myth 5.2). Farmers can no longer control weeds with glyphosate alone and add other herbicides to their spray mix.

Also, as we have seen, the presumed safety of Roundup is a marketing claim that does not reflect the scientific facts.

## Health risks of other herbicides used with GM crops

As the spread of glyphosate-resistant weeds makes Roundup Ready GM crop technology obsolete, industry is developing crops that resist other herbicides, either in addition to, or instead of, glyphosate. The health risks of these other herbicides need to be considered in any evaluation of the relevant herbicide-tolerant GM crops.

For example, the GM seed and agrochemical company Dow is seeking USDA approval of GM corn and soybeans resistant to 2,4-D, an ingredient of Agent Orange. The USDA has given a positive opinion on the applications, though final approval of the 2,4-D crops is being strongly opposed by health professionals and groups such as the Center for Food Safety.[75]

Exposure to 2,4-D has been linked in studies to genetic damage,[76,77,78] endocrine disruption,[76,79,80] reduced sperm count,[81] reproductive problems,[82] birth defects,[83] Parkinson's disease,[84] and harmful impacts on brain development.[85,86]

Scientists warn that widespread cultivation of 2,4-D resistant soybeans alone would trigger a substantial increase in the use of 2,4-D, damage to non-target crops through drift, and the inevitable spread of 2,4-D-resistant weeds.[87]

## Conclusion

Claims of safety for Roundup are misleading. Many independent studies show that the complete formulations as sold and used are much more toxic than glyphosate alone, though even glyphosate alone has been found to be toxic.

Toxic effects of Roundup and glyphosate found in studies include disruption of hormonal systems and beneficial gut bacteria, damage to DNA, developmental and reproductive toxicity, malformations, cancer, and neurotoxicity.

Roundup and other glyphosate formulations have never been tested or assessed for long-term safety for regulatory purposes, as only the isolated supposed "active ingredient" glyphosate was tested by industry in long-term studies. In addition, the "cocktail" effect of increased toxicity created when glyphosate is mixed with other pesticides has never been tested for regulatory purposes. This is in spite of the fact that people and animals are exposed not to single chemicals but to chemical mixtures.

Industry claims that glyphosate is non-toxic to animals and humans because they lack the shikimate biochemical pathway present in plants. But this claim is false. There are other pathways through which glyphosate and its commercial formulations can have toxic effects on animals and humans. Glyphosate and Roundup have been found to interfere with the retinoic acid signalling pathway, which affects gene expression in animals and humans. When disrupted, it can result in the development of malformations. Glyphosate and Roundup negatively affect gut bacteria that are vital to the healthy functioning of the immune system. Glyphosate is a chelator of essential nutrient metals, making them unavailable to the plant and therefore to the consumer. Glyphosate and Roundup are endocrine disruptors, an effect that can lead to multiple health problems during development and adult life.

The endocrine disruptive effects are most worrying, as they manifest at very low doses and can lead to ill health when exposure takes place over long periods of time.

Even industry studies on glyphosate alone show ill effects on laboratory animals, including malformations (birth defects). These effects were dismissed by regulators using unscientific reasoning.

Claims that the Roundup used on GM Roundup Ready crops replaces even more toxic herbicides are misleading. First, the toxicity of Roundup has been underestimated. And second, the failure of Roundup Ready technology due to resistant weeds has resulted in the industry developing GM crops that tolerate other, potentially even more toxic herbicides, such as 2,4-D, an ingredient of Agent Orange.

## References


1. European Commission Health & Consumer Protection Directorate-General. Review report for the active substance glyphosate. 2002. Available at: http://bit.ly/HQnkFj.
2. Antoniou M, Habib MEM, Howard CV, et al. Teratogenic effects of glyphosate-based herbicides: Divergence of regulatory decisions from scientific evidence. J Env Anal Toxicol. 2012;S4:006. doi:10.4172/2161-0525.S4-006.
3. Bradberry SM, Proudfoot AT, Vale JA. Glyphosate poisoning. Toxicol Rev. 2004;23:159–167.
4. Benachour N, Séralini GE. Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells. Chem Res Toxicol. 2009;22:97–105. doi:10.1021/tx800218n.
5. Haefs R, Schmitz-Eiberger M, Mainx HG, Mittelstaedt W, Noga G. Studies on a new group of biodegradable surfactants for glyphosate. Pest Manag Sci. 2002;58:825-33. doi:10.1002/ps.539.
6. Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini GE. Differential effects of glyphosate and Roundup on human placental cells and aromatase. Env Health Perspect. 2005;113:716-20.
7. Giesy JP, Dobson S, Solomon KR. Ecotoxicological risk assessment for Roundup herbicide. Rev Env Contam Toxicol. 2000;167:35–120.
8. Mesnage R, Defarge N, de Vendomois JS, Séralini GE. Major pesticides are more toxic to human cells than their declared active principles. BioMed Res Int. 2014;2014. doi:10.1155/2014/179691.
9. Lee H-L, Kan C-D, Tsai C-L, Liou M-J, Guo H-R. Comparative effects of the formulation of glyphosate-surfactant herbicides on hemodynamics in swine. Clin Toxicol Phila Pa. 2009;47(7):651-658. doi:10.1080/15563650903158862.
10. Adam A, Marzuki A, Abdul Rahman H, Abdul Aziz M. The oral and intratracheal toxicities of ROUNDUP and its components to rats. Vet Hum Toxicol. 1997;39(3):147-151.
11. Marc J, Mulner-Lorillon O, Belle R. Glyphosate-based pesticides affect cell cycle regulation. Biol Cell. 2004;96:245-9. doi:10.1016/j.biolcel.2003.11.010.
12. Bellé R, Le Bouffant R, Morales J, Cosson B, Cormier P, Mulner-Lorillon O. Sea urchin embryo, DNA-damaged cell cycle checkpoint and the mechanisms initiating cancer development. J Soc Biol. 2007;201:317–27.
13. Marc J, Mulner-Lorillon O, Boulben S, Hureau D, Durand G, Bellé R. Pesticide Roundup provokes cell division dysfunction at the level of CDK1/cyclin B activation. Chem Res Toxicol. 2002;15(3):326-31.
14. Marc J, Bellé R, Morales J, Cormier P, Mulner-Lorillon O. Formulated glyphosate activates the DNA-response checkpoint of the cell cycle leading to the prevention of G2/M transition. Toxicol Sci. 2004;82:436-42. doi:10.1093/toxsci/kfh281.
15. Mañas F, Peralta L, Raviolo J, et al. Genotoxicity of glyphosate assessed by the Comet assay and cytogenic tests. Env Toxicol Pharmacol. 2009;28:37–41.
16. Mañas F, Peralta L, Raviolo J, et al. Genotoxicity of AMPA, the environmental metabolite of glyphosate, assessed by the Comet assay and cytogenetic tests. Ecotoxicol Env Saf. 2009;72:834-7. doi:10.1016/j.ecoenv.2008.09.019.
17. Roustan A, Aye M, De Meo M, Di Giorgio C. Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation products before and after photoactivation. Chemosphere. 2014;108:93-100. doi:10.1016/j.chemosphere.2014.02.079.
18. Koller VJ, Furhacker M, Nersesyan A, Misik M, Eisenbauer M, Knasmueller S. Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Arch Toxicol. 2012;86:805–813. doi:10.1007/s00204-012-0804-8.
19. Bolognesi C, Bonatti S, Degan P, et al. Genotoxic activity of glyphosate and its technical formulation Roundup. J Agric Food Chem. 1997;45:1957–1962.
20. Kale PG, Petty BT, Walker S, et al. Mutagenicity testing of nine herbicides and pesticides currently used in agriculture. Env Mol Mutagen. 1995;25:148-53.
21. Peluso M, Munnia A, Bolognesi C, Parodi S. 32P-postlabeling detection of DNA adducts in mice treated with the herbicide Roundup. Env Mol Mutagen. 1998;31:55-9. doi:10.1002/(SICI)1098-2280(1998)31:1<55::AID-EM8>3.0.CO;2-A.
22. Benedetti D, Nunes E, Sarmento M, et al. Genetic damage in soybean workers exposed to pesticides: evaluation with the comet and buccal micronucleus cytome assays. Mutat Res. 2013;752:28-33. doi:10.1016/j.mrgentox.2013.01.001.
23. Paz-y-Miño C, Sánchez ME, Arévalo M, et al. Evaluation of DNA damage in an Ecuadorian population exposed to glyphosate. Genet Mol Biol. 2007;30:456–460.
24. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012;33(3):378-455. doi:10.1210/er.2011-1050.
25. Vom Saal FS, Akingbemi BT, Belcher SM, et al. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. Reprod Toxicol. 2007;24:131-8. doi:10.1016/j.reprotox.2007.07.005.
26. Soso AB, Barcellos LJG, Ranzani-Paiva MJ, et al. Chronic exposure to sub-lethal concentration of a glyphosate-based herbicide alters hormone profiles and affects reproduction of female Jundiá (Rhamdia quelen). Environ Toxicol Pharmacol. 2007;23:308–313.

27. Walsh LP, McCormick C, Martin C, Stocco DM. Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression. Env Health Perspect. 2000;108:769-76.
28. Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide Glyphosate alters testosterone levels and testicular morphology. Arch Toxicol. 2010;84:309-317.
29. Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology. 2009;262:184-91. doi:10.1016/j.tox.2009.06.006.
30. Hokanson R, Fudge R, Chowdhary R, Busbee D. Alteration of estrogen-regulated gene expression in human cells induced by the agricultural and horticultural herbicide glyphosate. Hum Exp Toxicol. 2007;26:747-52. doi:10.1177/0960327107083453.
31. Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol. 2013. doi:10.1016/j.fct.2013.05.057.
32. Council of the European Union. Council directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. Off J Eur Communities. 1998. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF.
33. US Environmental Protection Agency (EPA). Basic information about glyphosate in drinking water. 2014. Available at: http://water.epa.gov/drink/contaminants/basicinformation/glyphosate.cfm#four.
34. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
35. Dallegrave E, Mantese FD, Oliveira RT, Andrade AJ, Dalsenter PR, Langeloh A. Pre- and postnatal toxicity of the commercial glyphosate formulation in Wistar rats. Arch Toxicol. 2007;81:665–73. doi:10.1007/s00204-006-0170-5.
36. Savitz DA, Arbuckle T, Kaczor D, Curtis KM. Male pesticide exposure and pregnancy outcome. Am J Epidemiol. 1997;146:1025-36.
37. Monsanto. Backgrounder: Glyphosate and reproductive outcomes. 2004. Available at: http://www.monsanto.com/products/documents/glyphosate-background-materials/gly_reprooutcomes_bkg.pdf.
38. Monsanto. Backgrounder: Response to "Glyphosate toxic and Roundup worse." 2006. Available at: http://www.monsanto.com/products/documents/glyphosate-background-materials/response_isis_apr_06.pdf.
39. Paganelli A, Gnazzo V, Acosta H, López SL, Carrasco AE. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling. Chem Res Toxicol. 2010;23:1586–1595. doi:10.1021/tx1001749.
40. Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regul Toxicol Pharmacol. 2000;31:117-65. doi:10.1006/rtph.1999.1371.
41. Dallegrave E, Mantese FD, Coelho RS, Pereira JD, Dalsenter PR, Langeloh A. The teratogenic potential of the herbicide glyphosate-Roundup in Wistar rats. Toxicol Lett. 2003;142:45-52.
42. Lajmanovich RC, Sandoval MT, Peltzer PM. Induction of mortality and malformation in Scinax nasicus tadpoles exposed to glyphosate formulations. Bull Env Contam Toxicol. 2003;70:612–618. doi:10.1007/s00128-003-0029-x.
43. Rull RP, Ritz B, Shaw GM. Neural tube defects and maternal residential proximity to agricultural pesticide applications. Epidemiology. 2004;15:S188.
44. Rull RP, Ritz B, Shaw GM. Neural tube defects and maternal residential proximity to agricultural pesticide applications. Am J Epidemiol. 2006;163:743-53. doi:10.1093/aje/kwj101.
45. Rapporteur member state Germany. Monograph on glyphosate: Glyphosate: Annex B-5: Toxicology and metabolism: Vol 3-1 Glyphosat 04. German Federal Agency for Consumer Protection and Food Safety (BVL); 1998. Available at: http://bit.ly/QwOnPA.
46. Lammer EJ, Chen DT, Hoar RM, et al. Retinoic acid embryopathy. N Engl J Med. 1985;313:837–41. doi:10.1056/NEJM198510033131401.
47. George J, Prasad S, Mahmood Z, Shukla Y. Studies on glyphosate-induced carcinogenicity in mouse skin: A proteomic approach. J Proteomics. 2010;73:951–64. doi:10.1016/j.jprot.2009.12.008.
48. De Roos AJ, Blair A, Rusiecki JA, et al. Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study. Env Health Perspect. 2005;113:49-54.
49. Hardell L, Eriksson M. A case-control study of non-Hodgkin lymphoma and exposure to pesticides. Cancer. 1999;85:1353–60. doi:10.1002/(SICI)1097-0142(19990315)85:6<1353::AID-CNCR19>3.0.CO;2-1.
50. Hardell L, Eriksson M, Nordstrom M. Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies. Leuk Lymphoma. 2002;43:1043-9.
51. Eriksson M, Hardell L, Carlberg M, Akerman M. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. Int J Cancer. 2008;123:1657-63. doi:10.1002/ijc.23589.
52. International Programme on Chemical Safety. Environmental health criteria 159: Glyphosate. 1994. Available at: http://www.inchem.org/documents/ehc/ehc/ehc159.htm.
53. Anadón A, del Pino J, Martínez MA, et al. Neurotoxicological effects of the herbicide glyphosate. Toxicol Lett. 2008;180S:S164.
54. Astiz M, de Alaniz MJ, Marra CA. Effect of pesticides on cell survival in liver and brain rat tissues. Ecotoxicol Env Saf. 2009;72:2025-32. doi:10.1016/j.ecoenv.2009.05.001.
55. Garry VF, Harkins ME, Erickson LL, Long-Simpson LK, Holland SE, Burroughs BL. Birth defects, season of conception, and sex of children born to pesticide applicators living in the Red River Valley of Minnesota, USA. Env Health Perspect. 2002;110 Suppl 3:441-9.
56. Barbosa ER, Leiros da Costa MD, Bacheschi LA, Scaff M, Leite CC. Parkinsonism after glycine-derivate exposure. Mov Disord. 2001;16:565–568.
57. Wang G, Fan XN, Tan YY, Cheng Q, Chen SD. Parkinsonism after chronic occupational exposure to glyphosate. Park Relat Disord. 2011;17:486-7. doi:10.1016/j.parkreldis.2011.02.003.
58. Gui YX, Fan XN, Wang HM, Wang G, Chen SD. Glyphosate induced cell death through apoptotic and autophagic mechanisms. Neurotoxicol Teratol. 2012;34(3):344–349.

59. Krüger M, Shehata AA, Schrödl W, Rodloff A. Glyphosate suppresses the antagonistic effect of Enterococcus spp. on Clostridium botulinum. Anaerobe. 2013;20:74–78.
60. Shehata AA, Schrodl W, Aldin AA, Hafez HM, Kruger M. The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. Curr Microbiol. 2012. doi:10.1007/s00284-012-0277-2.
61. Huber DM. What about glyphosate-induced manganese deficiency? Fluid J. 2007:20–22.
62. Zobiole LHS, de Oliveira RS, Huber DM, et al. Glyphosate reduces shoot concentrations of mineral nutrients in glyphosate-resistant soybeans. Plant Soil. 2010;328:57–69.
63. Krüger M, Schrödl W, Neuhaus J, Shehata AA. Field investigations of glyphosate in urine of Danish dairy cows. J Env Anal Toxicol. 2013;3(5). doi:http://dx.doi.org/10.4172/2161-0525.1000186.
64. Comision Provincial de Investigación de Contaminantes del Agua. Primer informe [First report]. Resistencia, Chaco, Argentina; 2010. Available at: http://www.gmwatch.org/files/Chaco_Government_Report_Spanish.pdf ; English translation at http://www.gmwatch.org/files/Chaco_Government_Report_English.pdf.
65. Lopez SL, Aiassa D, Benitez-Leite S, et al. Pesticides used in South American GMO-based agriculture: A review of their effects on humans and animal models. In: Fishbein JC, Heilman JM, eds. Advances in Molecular Toxicology. Vol 6. New York: Elsevier; 2012:41–75.
66. Vazquez MA, Nota C. Report from the 1st national meeting of physicians in the crop-sprayed towns, Faculty of Medical Sciences, National University of Cordoba, August 27–28 2010, University Campus, Cordoba. Cordoba, Argentina: Faculty of Medical Sciences, National University of Cordoba; 2011. Available at: http://www.reduas.fcm.unc.edu.ar/report-from-the-first-national-meeting-of-physicians-in-the-crop-sprayed-towns/.
67. Samsel A, Seneff S. Glyphosate's suppression of cytochrome P450 enzymes and amino acid biosynthesis by the gut microbiome: Pathways to modern diseases. Entropy. 2013;15:1416-1463.
68. Samsel A, Seneff S. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. Interdiscip Toxicol. 2013;6(4):159-184. doi:10.2478/intox-2013-0026.
69. Jayasumana C, Gunatilake S, Senanayake P. Glyphosate, hard water and nephrotoxic metals: Are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka? Int J Environ Res Public Health. 2014;11(2):2125-2147. doi:10.3390/ijerph110202125.
70. Chavkin S. Sri Lanka bans Monsanto herbicide citing potential link to deadly kidney disease. Center for Public Integrity. http://www.publicintegrity.org/2014/03/13/14418/sri-lanka-bans-monsanto-herbicide-citing-potential-link-deadly-kidney-disease. Published March 13, 2014.
71. Kirinde C. Dangerous weedicide: No total ban. Sunday Times (Sri Lanka). http://www.sundaytimes.lk/140323/news/dangerous-weedicide-no-total-ban-90193.html. Published March 23, 2014.
72. Attorney General of the State of New York CF and PB. In the matter of Monsanto Company, respondent. Assurance of discontinuance pursuant to executive law § 63(15). New York, NY, Nov. False advertising by Monsanto regarding the safety of Roundup herbicide (glyphosate). 1996. Available at: http://www.mindfully.org/Pesticide/Monsanto-v-AGNYnov96.htm.
73. Agence France Presse. Monsanto fined in France for "false" herbicide ads. http://www.organicconsumers.org/articles/article_4114.cfm. Published January 26, 2007.
74. Gottems L. Ministério Público quer proibir uso do glifosato [Public proescutor seeks to ban use of glyphosate]. Agrolink. http://bit.ly/1kbDStx ; English translation at http://bit.ly/QVv4AE. Published March 25, 2014.
75. Center for Food Safety. "Agent Orange" crops would trigger massive increase in use of toxic pesticide 2,4-D. 2014. Available at: http://bit.ly/PFDHyM.
76. Garry VF, Tarone RE, Kirsch IR, et al. Biomarker correlations of urinary 2,4-D levels in foresters: genomic instability and endocrine disruption. Environ Health Perspect. 2001;109(5):495-500.
77. Zeljezic D, Garaj-Vrhovac V. Chromosomal aberrations, micronuclei and nuclear buds induced in human lymphocytes by 2,4-dichlorophenoxyacetic acid pesticide formulation. Toxicology. 2004;200(1):39-47. doi:10.1016/j.tox.2004.03.002.
78. Arias E. Cytogenetic effects of short- and long-term exposure of chick embryos to the phenoxyherbicide 2,4-D. Environ Mol Mutagen. 2007;48(6):462-466. doi:10.1002/em.20301.
79. Lin N, Garry VF. In vitro studies of cellular and molecular developmental toxicity of adjuvants, herbicides, and fungicides commonly used in Red River Valley, Minnesota. J Toxicol Env Health A. 2000;60:423-39.
80. Meulenberg EP. A new test to identify endocrine disruptors using sex hormone-binding globulins from human serum. Eur J Lipid Sci Technol. 2002;104(2):131-136. doi:10.1002/1438-9312(200202)104:2<131::AID-EJLT131>3.0.CO;2-0.
81. Swan SH, Kruse RL, Liu F, et al. Semen quality in relation to biomarkers of pesticide exposure. Environ Health Perspect. 2003;111(12):1478-1484.
82. Cavieres MF, Jaeger J, Porter W. Developmental toxicity of a commercial herbicide mixture in mice: I. Effects on embryo implantation and litter size. Environ Health Perspect. 2002;110(11):1081-1085.
83. Schreinemachers DM. Birth malformations and other adverse perinatal outcomes in four U.S. wheat-producing states. Environ Health Perspect. 2003;111(9):1259-1264.
84. Tanner CM, Ross GW, Jewell SA, et al. Occupation and risk of parkinsonism: A multicenter case-control study. Arch Neurol. 2009;66(9):1106-1113. doi:10.1001/archneurol.2009.195.
85. Bortolozzi A, Duffard R, de Duffard AME. Asymmetrical development of the monoamine systems in 2,4-dichlorophenoxyacetic acid treated rats. Neurotoxicology. 2003;24(1):149-157.
86. Bortolozzi AA, Evangelista De Duffard AM, Duffard RO, Antonelli MC. Effects of 2,4-dichlorophenoxyacetic acid exposure on dopamine D2-like receptors in rat brain. Neurotoxicol Teratol. 2004;26(4):599-605. doi:10.1016/j.ntt.2004.04.001.
87. Mortensen DA, Egan JF, Maxwell BD, Ryan MR, Smith RG. Navigating a critical juncture for sustainable weed management. BioScience. 2012;62(1):75-84.

## 4.2 Myth: Strict regulations ensure we are only exposed to safe levels of Roundup

## Truth: So-called "safe" levels of Roundup may not be safe after all

### Myth at a glance

It is often claimed that regulations protect us from unsafe pesticide exposures. But the effects on animals and humans of eating increased amounts of Roundup residues in GM Roundup Ready (RR) crops have not been investigated. On the contrary, since the introduction of GM RR crops, regulators have changed safety rules to allow higher levels of glyphosate residues into the food and feed chain. So people and animals that eat GM RR crops are eating potentially toxic herbicide residues.

The supposedly safe levels of glyphosate set by regulators have never been tested to find out if they really are safe to consume over the long term. Also, the safety limits were set for glyphosate alone, not the complete herbicide formulations as sold and used – yet many studies show that the formulations containing added ingredients (adjuvants) are more toxic than glyphosate alone.

Even glyphosate alone was found to cause toxic effects in vitro (laboratory non-animal studies) at a level permitted in drinking water in the EU and the US, though these findings would need to be confirmed in vivo (animal experiments).

GM crops have increased the use of glyphosate and thus people's exposure to it, presenting a risk that has not been adequately considered in regulatory assessments.

GM herbicide-tolerant crops are designed to survive being sprayed with large doses of herbicide that would kill a non-GM crop. The most widely grown GM crop is Roundup Ready (RR) soy,[1] the majority of which is grown in South America and is used for animal feed in intensive livestock operations in Europe and other industrialized countries. Inevitably, RR crops contain far higher levels of Roundup residues than have previously formed part of our diet.[2]

It is often claimed that regulations protect us from unsafe pesticide exposures. But in fact the effects on animals and humans of eating increased amounts of Roundup residues in GM RR crops have not been investigated. On the contrary, since the introduction of GM RR crops, regulators have changed safety rules to allow higher levels of glyphosate residues into the food and feed chain – without any experimental evidence to show that these higher levels of exposure are indeed safe.

For example, after the 1996 commercialization of GM RR soy, EU regulators raised the allowed maximum residue limit (MRL) for glyphosate in imported soy 200-fold, from 0.1 mg/kg to 20 mg/kg.[3] The UK government said this was necessary to accommodate the new farm practice of using glyphosate as a desiccant to dry crops before harvest, making grains or beans easier to gather and store without rotting.[3] This is no doubt true, but it also conveniently coincided with the introduction of RR soy.

Indeed, a 1994 report of the Joint FAO/WHO Meetings on Pesticide Residues (JMPR) indirectly admitted that GM soy was a factor in the need for the higher limit. The JMPR meeting appears to have been the source of the recommendation for the new higher residue limit. In its report, the JMPR recommended the higher limit of 20 mg/kg for soybeans. The JMPR said the change was needed not only due to glyphosate's use as a desiccant before harvest, but also to accommodate "sequential application of glyphosate in the crop".[4] This practice is only possible with GM RR soy, as it would kill non-GM soy.

In a 1999 press interview, Malcolm Kane, who had just retired as head of food safety at UK supermarket chain Sainsbury's, confirmed that the European regulators raised the residue limit to "satisfy the GM companies" and smooth the path for GM soy to enter the food and feed market. Kane added, "One does not need to be an activist or overtly anti-GM to point out that herbicide-resistant crops come at the price of containing significant chemical residues of the active chemical in the commercial weedkiller."[3]

Recent analysis has found that GM RR plants can accumulate up to 100 mg/kg of glyphosate.[5] Some animal feed plants are authorized by the international food standards body Codex Alimentarius to accumulate up to 500 mg/kg.[6]

## How safe are "safe" levels?

The maximum residue limit (MRL) set by regulators for glyphosate in some food and feed crops in the EU is 20 mg/kg.[7] The "acceptable daily intake" of glyphosate is set at 0.3 mg per kg of bodyweight per day (written as 0.3 mg/kg bw/d).[8]

Are these levels safe? There is strong reason for doubt. This is because:

- These supposedly safe levels of glyphosate consumption have never been tested to find out if they really are safe to consume over the long term. Instead, the supposed safe levels are extrapolated from industry tests using very high, poisonous doses. This is not valid because some toxins, especially those that disrupt the hormonal system (endocrine disruptors) are known to be more toxic at low doses than higher doses, so safe levels cannot be extrapolated from effects at higher doses.[9]
- The safety limits were set for glyphosate alone, not the complete herbicide formulations as sold and used (this limitation of the regulatory process applies to all pesticides in all countries worldwide). The complete formulations contain adjuvants, which have been shown to be toxic in themselves and to increase the toxicity of glyphosate to human cells

in vitro (non-animal laboratory studies).[10] Studies in rats carried out by independent scientists show that the complete formulations are toxic at levels deemed safe by regulators for the isolated ingredient glyphosate.[11,12,13]

- In vitro studies in human cells show that glyphosate-based herbicide formulations are far more toxic than glyphosate alone. This principle was true for eight of nine pesticides tested – the formulations were up to 1,000 times more toxic.[14] Thus safe levels set for glyphosate are not adequate for ensuring the safety of the formulations.
- Feeding studies in pigs[15] and rats[16] directly comparing the toxicity of formulations with glyphosate alone found that the formulations were far more toxic.
- Industry tests on glyphosate alone revealed toxic effects below the levels that regulators claimed showed no toxic effect – but these results were ignored or dismissed by regulators in setting the supposedly safe levels. Thus even the "safe" levels set for glyphosate are questionable.[11]
- A study in Daphnia magna (a type of water flea often used as an experimental model for environmental toxicity) demonstrated that chronic exposure to glyphosate and a commercial formulation of Roundup resulted in reproductive problems, including reduced fertility and increased abortion rate, at environmental concentrations of 0.45-1.35 mg/l: that is, in some cases below accepted environmental tolerance limits set in the US (0.7 mg/l). A reduced body size of juveniles was observed at an exposure of 0.05 mg/l.[17] The study authors commented that their findings were in sharp contrast to worldwide regulatory assumptions, which were strongly influenced by old studies by Monsanto claiming that glyphosate is virtually non-toxic in Daphnia magna.[18]
- Glyphosate, its metabolite AMPA, and especially the commercial formulation Roundup have been found to be toxic in vitro, in some cases at extremely low levels.[19,20,21] Roundup damages and kills human cells at levels below those used in agriculture[22] and at residual levels to be expected in food and feed derived from Roundup-treated crops.[19] Roundup is a potent endocrine disruptor, disturbing hormonal function in human cells vitro at concentrations up to 800 times lower than permitted levels in some food and feed crops.[23]

## Levels of glyphosate found in GM soy are higher than those causing cancer cells to proliferate in vitro

In an in vitro study, glyphosate alone acted as an estrogen substitute in human hormone-dependent breast cancer cells, stimulating their growth at minute concentrations as low as 10(-12) M. The toxic effect peaked at the higher dose of 10(-9) M and then decreased at still higher concentrations.[24] This is an example of a non-linear dose-response: the toxic effect did not increase in a straight line in proportion to the dose but instead decreased as the dose increased. This type of response is typical of endocrine disrupting chemicals (EDCs), chemicals that disturb hormone functioning.[9]

The results indicated that low and environmentally relevant concentrations of glyphosate possessed estrogenic activity. The study also found that there was an additive estrogenic effect between glyphosate and genistein, a phytoestrogen (plant estrogen) in soybeans. The authors concluded that their results needed further study in animals.[24]

The most toxic dose in this experiment, 10(-9) M, equals 169ng/L or 169 ppb (parts per billion) glyphosate; 10(-12) M equals 0.169ng/L or 169 ppt (parts per trillion). Although 169 ppb glyphosate is above the EU maximum permitted level for drinking water – currently set at 100ng/L or 100ppb for any one pesticide active ingredient[25] – clear estrogenic effects were also observed at progressively lower concentrations down to 10(-12) M,[24] a concentration which falls within permitted levels in the EU.

In other words, glyphosate caused estrogenic effects and induced cancer cells to proliferate in vitro at a level permitted in drinking water in the EU.

How do these levels compare with the levels of glyphosate residues found in GM soy in a recent analysis? The researchers analyzed the composition of GM glyphosate-tolerant soybeans, industrially grown non-GM soybeans, and organic soybeans. They found that the GM soybeans contained high residues of glyphosate and its toxic metabolite AMPA (mean of 3.3 and 5.7 mg/kg, respectively), but industrially grown non-GM soybeans and organic soybeans contained neither chemical.[2]

Monsanto itself had previously called these levels of glyphosate "extreme". It is clear that since the widespread cultivation of GM glyphosate-tolerant soybeans, "extreme" levels of glyphosate have become the new norm.[18]

Taking the figure of 3.3 mg/kg of glyphosate in the GM soybeans (excluding the AMPA), this is equivalent to 3.3 ppt (parts per thousand) or 3,300,000 ppb (parts per billion). This is a staggering 19,500-fold higher concentration than the 10(-9) M level found toxic in the in vitro experiment and 19,500,000-fold higher than the 10(-12) M level, also found to have estrogen-mimicking effects.[24] In short, the level of glyphosate in the soy was well above that found to have estrogenic effects on the breast cancer cells in vitro.

## In vitro versus in vivo studies

Findings of toxicity from in vitro experiments involving cells grown in tissue culture need to be confirmed in animal studies (in vivo). This is because in the current state of scientific knowledge we cannot fully understand from in vitro studies how the same toxin would affect a living mammal. Nevertheless, findings of toxicity in studies carried out in vitro should not be ignored (as regulators and industry all too often do), but should be treated as indicators of the need for further studies in animals. Such animal studies should test environmentally relevant low doses of the complete pesticide formulation over long periods of time, mirroring human exposures.

### Qualifications and questions

When evaluating the importance of these findings, a number of qualifications and unresolved questions need to be considered.

Most importantly, we do not know how much of the glyphosate in the soy is absorbed by the human or animal consumer when present at these levels in food or feed. Since so little is required to have an estrogenic effect in vitro, it is possible that enough can be taken up and accumulate in the body to have hormone-disrupting effects, including stimulation of estrogen-dependent breast cancer growth. But we do not know that for certain because there are major gaps in our knowledge regarding the absorption, accumulation and excretion rates of glyphosate and AMPA.

The amounts of glyphosate found in the urine of EU citizens in a survey conducted by Friends of the Earth[26] may be biologically significant and have a hormone-disruptive effect, especially as exposure takes place over long periods. Again, no one knows for certain.

Although the mean levels found in the soy of 3.3 mg/kg for glyphosate and 5.7 mg/kg for AMPA[2] are below the maximum residue limit set for soy in Europe (20 mg/kg glyphosate), that does not mean that these levels are safe to consume. Also, the official limit does not take into account the increased toxicity of the complete commercial formulations, including adjuvants, over the isolated active ingredient. As stated above, the formulations have not been tested for long-term toxicity.

We conclude from these results, taken together, that people who eat food products from GM Roundup Ready crops are eating amounts of these substances that may have toxic – particularly endocrine disruptive – effects. Further animal testing would be necessary to confirm or refute this possibility.

## People and animals are widely exposed to glyphosate

Glyphosate-based herbicides are not only used by farmers. They are also widely used in non-farm environments to control weeds – for example, on roadsides and railway lines and in parks and school grounds, as well as by home gardeners. So even city-dwellers' exposure to glyphosate can be significant. In agricultural areas where GM glyphosate-resistant crops are grown, exposure is likely to increase exponentially.

Unsurprisingly, glyphosate and its metabolite AMPA are widely found in the environment and in the bodies of people and animals. Study findings include:

- Glyphosate and its toxic metabolite AMPA were found in over 75% of the air and rain samples tested from the Mississippi Delta agricultural region in 2007. The researchers noted that the widespread presence of glyphosate was due to the cultivation of GM glyphosate-tolerant crops.[27]
- Glyphosate and AMPA were frequently detected in streams in the American Midwest during the growing season.[28]
- In a monitoring programme in Denmark, glyphosate and AMPA were washed out of the root zone of some types of soil and into drainage water in average concentrations that exceeded the EU permitted limit for drinking water (0.1 μg/l).[29,30]
- Glyphosate was found circulating in the blood of non-pregnant women living in Canada. The amounts of glyphosate detected ranged from undetectable to 93.6 ng/ml (93.6μg/L), with an average of 73.6ng/ml (73.6μg/L).[31] Worryingly, this is well within the range

of glyphosate concentration found in vitro to have endocrine disruptive effects on the estrogen hormone system,[24] which can lead to slow-onset disease upon long-term exposure and adverse reproductive and developmental effects in offspring.[9]

- In an in vitro study modelling human exposures, 15% of administered glyphosate crossed the human placental barrier and entered the foetal compartment.[32] The study showed that the placental barrier in mammals does not protect the unborn foetus from glyphosate exposures.
- Laboratory testing commissioned by two civil society organizations found levels of glyphosate in American women's breast milk of 76 μg/L to 166 μg/L – that is, 760 to 1600 times higher than the EU permitted level in drinking water. These levels were, however, less than the 700 μg/L maximum contaminant level (MCL) for glyphosate in drinking water in the US. Tests on the women's urine found maximum glyphosate levels over 8 times higher than those found in the urine of Europeans[33] (see next item below). These high levels raise the question of whether glyphosate bioaccumulates in our bodies. If it does, then so-called safe levels are meaningless, since the glyphosate could build up to dangerous levels even if daily exposures are low.
- In laboratory testing commissioned by Friends of the Earth, glyphosate and AMPA were found in the urine of respectively 44% and 36% of European city dwellers. Levels detected varied but the highest levels of glyphosate and AMPA were respectively 1.8 μg/L and 2.6 μg/L.[34]
- Urinary levels of glyphosate were 1.6 ppb in farming fathers and 1.5 ppb in non-farming fathers. For farming mothers, levels were 1.1 ppb, and for non-farming mothers, 1.2 ppb. For children of farmers, the levels were 1.9 ppb, and for children of non-farming families, the glyphosate urinary levels were 2.5 ppb. Urinary burdens in non-farm children were slightly higher than those in farm children. The authors suggested that this was because of the widespread use of glyphosate in non-farm areas, such as in home gardens.[35]
- Glyphosate was found in the urine of cows, humans, and rabbits. Cows kept in a GM-free area had significantly lower glyphosate concentrations in urine than cows in conventional livestock systems. Glyphosate was also detected in the intestines, liver, muscles, spleen and kidney of slaughtered cows. Glyphosate levels were significantly higher in urine of humans who ate non-organic food, compared with those who ate mostly organic food. Chronically ill people showed significantly higher glyphosate residues in their urine than healthy people.[36]

Are these levels dangerous? No one knows, as the necessary testing of presumed safe "acceptable daily intake" levels has not been done in animals; and neither have the complete herbicide formulations as sold and used been tested at realistic exposure levels.

There is cause for concern and sound justification for applying the precautionary principle at the individual and societal levels to minimize exposure until direct experimentation testing the acceptable daily intake has been evaluated in long-term feeding studies.

## People and animals are not protected by current regulations

An analysis of glyphosate's current approval in the EU and in the US suggests that the "acceptable daily intake" (ADI) level, the level of exposure that is deemed safe for humans over a long period of time, is inaccurate and dangerously high.[11]

Regulators calculate the ADI on the basis of industry studies submitted to the regulators in support of the application for the chemical's approval. The figure used to set the ADI is the highest dose at which no adverse effect is found (the No Observed Adverse Effect Level or NOAEL), which is also lower than the lowest dose that has a toxic effect (the Lowest Observed Adverse Effect Level or LOAEL). The ADI is derived by dividing this figure by 100, to allow a safety margin.[11]

The current EU[8] and Australasian[37] ADI for glyphosate is 0.3 mg/kg bw/d.

But this ADI has been shown to be inaccurate and potentially dangerously high by two independent rat feeding studies on Roundup. The studies found that:

- Roundup was a potent endocrine disruptor and caused disturbances in the reproductive development of rats when the exposure was performed during the puberty period. Adverse effects, including delayed puberty and reduced testosterone production, were found at all dose levels, including the LOAEL of 5 mg/kg bw/d.[12]
- Glyphosate herbicide caused damage to rats' liver cells that the researchers said was probably "irreversible" at a dose of just 4.87 mg/kg bw/d.[13]

These studies did not find a safe or "no effect" level (NOAEL). Even the lowest dose tested produced a toxic effect and no further experiments were done with lower doses to establish the NOAEL. A reasonable estimate of the NOAEL based on these studies might be 2.5 mg/kg of body weight – though this level would have to be tested in long-term studies, using the complete formulation, to gain more certainty. Then, applying the 100-fold safety factor, the ADI should be 0.025 mg/kg bw/d – 12 times lower than the level for glyphosate currently in force in the EU.[11]

Even if only the industry studies are considered, the current ADI should still be lower. An objective analysis of these studies results in a more objectively accurate ADI of 0.1 mg/kg bw/d, one-third of the current ADI.[11]

It should be borne in mind, however, that since glyphosate herbicides are known to have endocrine disrupting properties, they may be toxic at far lower doses than this. This possibility has not been explored in regulatory tests. If the very low levels found to be disrupt hormones in an independent study in vitro[24] were found to do the same in vivo, then no safe dose could be claimed and glyphosate herbicides would have to be banned. The extremely low dose toxicity of Roundup found in Professor Gilles-Eric Séralini's two-year rat feeding study[38] is a testament to this possibility.

### Wildlife not protected by recommended application rates

There is evidence that Roundup spray rates recommended by manufacturers do not protect amphibians. A study in a natural setting found that Roundup application at the rate recommended by the manufacturer eliminated two species of tadpoles and nearly exterminated a third species, resulting in a 70% decline in the species richness of tadpoles. Contrary to common belief, the presence of soil does not reduce the chemical's effects.[39] Further experiments with lower concentrations, well within levels to be expected in the environment, still caused 40% amphibian mortality.[40]

## Conclusion

GM Roundup Ready (RR) soy is the most widely grown GM crop. It is engineered to tolerate being sprayed with Roundup herbicide, based on the chemical glyphosate. The majority of GM RR soy goes into animal feed for intensive livestock feedlots in Europe and other industrialized countries. Widespread planting of GM RR soy in North and South America has led to large increases in the amount of glyphosate herbicide used. Regulators have responded by raising the allowed maximum residue limit of glyphosate in crops eaten by people and animals. GM RR soy has been found to contain high levels of glyphosate residues, above those found to cause cancer cells to multiply in vitro. People and animals that eat GM RR crops are eating potentially toxic and endocrine disruptive amounts of herbicide residues.

Claims by regulators and industry that these levels of Roundup are safe are based on industry studies on glyphosate alone. Regulators' interpretation of these industry studies is open to question, as some of the studies showed toxic effects below the level claimed by regulators to show no effect. Effects found in animal studies and studies on human cells grown under laboratory conditions include cell death and damage, damage to DNA, disruption of hormones, birth defects, and cancer. Some of these effects have been found at levels far below those used in agriculture and corresponding to low levels of residues in food and feed. The added ingredients in Roundup (adjuvants) increase the toxicity of glyphosate, and the main metabolite of glyphosate, AMPA, is also toxic.

The risk of increased exposure to Roundup residues due to the presence of GM RR crops in our food and feed supply has not been adequately considered in regulatory assessments.

## References


1. James C. Global status of commercialized biotech/GM crops: 2012. ISAAA; 2012. Available at: http://www.isaaa.org/resources/publications/briefs/44/download/isaaa-brief-44-2012.pdf.
2. Bøhn T, Cuhra M, Traavik T, Sanden M, Fagan J, Primicerio R. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. Food Chem. 2013. doi:10.1016/j.foodchem.2013.12.054.
3. Poulter S. Pesticide safety limit raised by 200 times "to suit GM industry." Daily Mail. http://www.connectotel.com/gmfood/dm210999.txt. Published September 21, 1999.
4. Food and Agriculture Organization (FAO). Pesticide residues in food – 1994: FAO plant production and protection paper 127. Report of the joint meeting of the FAO panel of experts on pesticide residues in food and the environment and the WHO expert group on pesticide residues, Rome, 19–28 September. Rome, Italy; 1994. Available at: http://bit.ly/LSeBaB.
5. Testbiotech. Spraying with glyphosate leaves high levels of residue in soybeans. Munich, Germany; 2013. Available at: http://www.testbiotech.org/sites/default/files/Testbiotech_Glyphosate_Argentinia.pdf.

6. Codex Alimentarius. Pesticide residues in food and feed: 158 Glyphosate. Food and Agriculture Organization and World Health Organization; 2013. Available at: http://www.codexalimentarius.net/pestres/data/pesticides/details.html?id=158.
7. European Union. EU pesticides database. 2014. Available at: http://ec.europa.eu/sanco_pesticides/public/?event=homepage.
8. European Commission Health & Consumer Protection Directorate-General. Review report for the active substance glyphosate. 2002. Available at: http://bit.ly/HQnkFj.
9. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012;33(3):378-455. doi:10.1210/er.2011-1050.
10. Mesnage R, Bernay B, Seralini GE. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology. 2013;313(2–3):122-8. doi:10.1016/j.tox.2012.09.006.
11. Antoniou M, Habib MEM, Howard CV, et al. Teratogenic effects of glyphosate-based herbicides: Divergence of regulatory decisions from scientific evidence. J Env Anal Toxicol. 2012;S4:006. doi:10.4172/2161-0525.S4-006.
12. Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide Glyphosate alters testosterone levels and testicular morphology. Arch Toxicol. 2010;84:309-317.
13. Benedetti AL, Vituri C de L, Trentin AG, Domingues MA, Alvarez-Silva M. The effects of sub-chronic exposure of Wistar rats to the herbicide Glyphosate-Biocarb. Toxicol Lett. 2004;153:227–32. doi:10.1016/j.toxlet.2004.04.008.
14. Mesnage R, Defarge N, de Vendomois JS, Séralini GE. Major pesticides are more toxic to human cells than their declared active principles. BioMed Res Int. 2014;2014. doi:10.1155/2014/179691.
15. Lee H-L, Kan C-D, Tsai C-L, Liou M-J, Guo H-R. Comparative effects of the formulation of glyphosate-surfactant herbicides on hemodynamics in swine. Clin Toxicol Phila Pa. 2009;47(7):651-658. doi:10.1080/15563650903158862.
16. Adam A, Marzuki A, Abdul Rahman H, Abdul Aziz M. The oral and intratracheal toxicities of ROUNDUP and its components to rats. Vet Hum Toxicol. 1997;39(3):147-151.
17. Cuhra M, Traavik T, Bøhn T. Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna. Ecotoxicology. 2013;22:251-62. doi:10.1007/s10646-012-1021-1.
18. Bøhn T, Cuhra M. How “extreme levels” of Roundup in food became the industry norm. Indep Sci News. 2014. Available at: http://www.independentsciencenews.org/news/how-extreme-levels-of-roundup-in-food-became-the-industry-norm/.
19. Benachour N, Séralini GE. Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells. Chem Res Toxicol. 2009;22:97–105. doi:10.1021/tx800218n.
20. Benachour N, Sipahutar H, Moslemi S, Gasnier C, Travert C, Séralini GE. Time- and dose-dependent effects of Roundup on human embryonic and placental cells. Arch Env Contam Toxicol. 2007;53:126–33. doi:10.1007/s00244-006-0154-8.
21. Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini GE. Differential effects of glyphosate and Roundup on human placental cells and aromatase. Env Health Perspect. 2005;113:716-20.
22. Mesnage R, Clair E, Gress S, Then C, Székács A, Séralini G-E. Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide. J Appl Toxicol. 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22337346.
23. Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology. 2009;262:184-91. doi:10.1016/j.tox.2009.06.006.
24. Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol. 2013. doi:10.1016/j.fct.2013.05.057.
25. Council of the European Union. Council directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. Off J Eur Communities. 1998. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF.
26. Friends of the Earth Europe. Human contamination by glyphosate. Brussels, Belgium; 2013. Available at: http://www.foeeurope.org/sites/default/files/press_releases/foee_4_human_contamination_glyphosate.pdf.
27. Majewski MS, Coupe, R. H., Foreman WT, Capel PD. Pesticides in Mississippi air and rain: A comparison between 1995 and 2007. Env Toxicol Chem. 2014. doi:10.1002/etc.2550.
28. Coupe RH, Kalkhoff SJ, Capel PD, Gregoire C. Fate and transport of glyphosate and aminomethylphosphonic acid in surface waters of agricultural basins. Pest Manag Sci. 2011;68:16–30. doi:10.1002/ps.2212.
29. Kjaer J, Olsen P, Ullum M, Grant R. Leaching of glyphosate and amino-methylphosphonic acid from Danish agricultural field sites. J Environ Qual. 2005;34(2):608-620.
30. Kjær J, Olsen P, Barlebo HC, et al. The Danish Pesticide Leaching Assessment Programme: Monitoring results 1999–2003: 2004. Available at: http://pesticidvarsling.dk/monitor_uk/2003.html.
31. Aris A, Leblanc S. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Reprod Toxicol. 2011;31.
32. Poulsen MS, Rytting E, Mose T, Knudsen LE. Modeling placental transport: Correlation of in vitro BeWo cell permeability and ex vivo human placental perfusion. Toxicol Vitro. 2009;23:1380–6. doi:10.1016/j.tiv.2009.07.028.
33. Honeycutt Z, Rowlands H. Glyphosate testing report: Findings in American mothers’ breast milk, urine and water. 2014. Available at: http://www.momsacrossamerica.com/glyphosate_testing_results.
34. Hoppe HW. Determination of glyphosate residues in human urine samples from 18 European countries (sponsor: BUND, FoE). Bremen, Germany: Medical Laboratory Bremen; 2013. Available at: http://www.foeeurope.org/sites/default/files/glyphosate_studyresults_june12.pdf.
35. Curwin BD, Hein MJ, Sanderson WT, et al. Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in Iowa. Ann Occup Hyg. 2007;51:53–65. doi:10.1093/annhyg/mel062.

36. Krüger M, Schledorn P, Schrödl W, Hoppe HW, Lutz W, Shehata AA. Detection of glyphosate residues in animals and humans. J Env Anal Toxicol. 2014;4(2). doi:10.4172/2161-0525.1000210.
37. Food Standards Australia New Zealand (FSANZ). Assessment of glyphosate residues for A1021: Supporting document 2. Canberra, Australia; 2010. Available at: http://www.foodstandards.gov.au/code/applications/documents/A1021%20GM%20Maize%20AppR%20SD2%20Glyphosate%20residues%20FINAL.pdf.
38. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
39. Relyea RA. The impact of insecticides and herbicides on the biodiversity and productivity of aquatic communities. Ecol Appl. 2005;15:618–627.
40. Relyea RA, Schoeppner NM, Hoverman JT. Pesticides and amphibians: the importance of community context. Ecol Appl. 2005;15:1125–1134.

# 5. GM crops – impacts on the farm and environment

*"Over the past decade, corporate and government managers have spent millions trying to convince farmers and other citizens of the benefits of genetically modified (GM) crops. But this huge public relations effort has failed to obscure the truth: GM crops do not deliver the promised benefits; they create numerous problems, costs, and risks; and … consumers and foreign customers alike do not want these crops. It would be too generous even to call GM crops a solution in search of a problem: These crops have failed to provide significant solutions, and their use is creating problems – agronomic, environmental, economic, social, and (potentially) human health problems."*

– National Farmers Union of Canada[1]

GM crops are promoted on the claimed basis that they give higher yields, reduce pesticide use, and benefit farmers and the environment. But independent studies either contradict these claims or show them to be inflated.

GM crops were not designed to give higher yields and generally yield no higher than the non-GM parent crop: in some cases yield is reduced. And GM crop technology is already failing under the onslaught of herbicide-resistant superweeds and pests resistant to the Bt toxin engineered into crops. These failures mean increasing costs to farmers and harm to the environment.

On-farm and environmental impacts of GM crops are not limited to the effects of the GM crop itself. They also include the effects of the pesticide that the crop is engineered to contain or to tolerate during cultivation. Research shows that negative impacts are occurring from all these sources.

Some of these impacts also occur with non-GM crops grown under chemically-based agricultural systems. So GMO proponents may obscure the negative effects of GM crops by comparing them with crops grown in chemically-based agricultural systems and concluding that GM crops have less harmful impacts.

But this is to compare one unsustainable agricultural system with another. A more meaningful comparison, and one that would help advance agricultural technology, would be to compare GM with agroecological or integrated pest management (IPM) systems. Many farmers outside the certified organic sector already use agroecological and IPM methods. This progressive trend should be encouraged. Instead, it is being delayed by the false hope offered by GM agriculture, which is only serving to prolong dependence on pesticides and fertilizers.

Below we address some of the common arguments used to promote GM crops.

## References

1. National Farmers Union of Canada. GM crops: Not needed on the Island. Recommendations of the National Farmers Union to the Prince Edward Island legislature's standing committee on agriculture, forestry, and the environment. Charlottetown, PEI, Canada; 2005. Available at: http://www.nfu.ca/sites/www.nfu.ca/files/PEI%20GMO%20BRIEF%20TWENTY%20SEVEN%20FINAL.pdf.

# 5.1 Myth: GM crops increase yield potential

## Truth: GM crops do not increase yield potential – and in some cases decrease it

### Myth at a glance

GM has not increased the yield potential of crops. Though yield increases were seen in major crops in the twentieth century, these were due to improvements in conventional breeding, and not to GM traits.

High yield is a complex genetic trait based on multiple gene functions and cannot be genetically engineered into a crop.

Data comparing agricultural productivity for staple crops in the United States and Western Europe shows that Europe's mostly non-GM production produces better yields with less pesticide than the US's mostly GM production.

Contrary to claims that Europe's refusal to embrace GM is causing it to fall behind the US, the data show that the reverse is true: the US, with its mostly GM production, is falling behind Europe in terms of productivity and sustainability.

The funding and research that are currently poured into GM crop research and development should be redirected toward approaches that are proven effective in improving crop yields, including conventional plant breeding as well as the use of agroecological practices.

If GM cannot increase yields even in the US, where high-input, irrigated, heavily subsidized commodity farming is the norm, it is irresponsible to assume that it would improve yields in the Global South, where farmers may literally bet their farms and livelihoods on a crop.

GM crops are often claimed to give higher yields than naturally bred varieties. But the data do not support this claim. At best, GM crops have not performed consistently better than their non-GM counterparts, with GM soybeans giving lower yields in university-based trials.[1,2]

Controlled field trials comparing GM and non-GM soy production suggested that 50% of the drop in yield was due to the disruption in gene function caused by the GM transformation process.[2] Similarly, field tests of Bt maize hybrids showed that they took longer to reach maturity and produced up to 12% lower yields than their non-GM counterparts.[3] And trials of canola varieties in Australia conducted by the Grains Research and Development Council found that yields were 0.7 tonnes per hectare for GM and 0.8 tonnes per hectare for non-GM.[4]

In 2009, in an apparent attempt to counter criticisms of lower yields from its GM soy, Monsanto released its new generation of supposedly high-yielding GM soybeans, RR2 Yield®. RR2 Yield is an elite high-yielding soy variety with a new version of the GM Roundup tolerance gene inserted. But a study carried out in five US states involving 20 farm managers who planted RR2 soybeans in 2009 concluded that the new varieties "didn't meet their [yield] expectations".[5] In June 2010 the state of West Virginia launched an investigation of Monsanto for false advertising claims that RR2 soybeans gave higher yields.[6] This was part of a broader anti-trust investigation of Monsanto by the US Justice Department, which was, however, quietly closed in 2012 without reporting on its findings.[7]

A US Department of Agriculture (USDA) report of 2002 acknowledged the absence of yield gain from GM crops, stating, "GE [genetically engineered] crops available for commercial use do not increase the yield potential of a variety. In fact, yield may even decrease.... Perhaps the biggest issue raised by these results is how to explain the rapid adoption of GE crops when farm financial impacts appear to be mixed or even negative."[8]

An updated USDA report in 2014 stated, "Over the first 15 years of commercial use, GE seeds have not been shown to increase yield potentials of the varieties. In fact, the yields of herbicide-tolerant [HT] or insect-resistant seeds may be occasionally lower than the yields of conventional varieties if the varieties used to carry the HT or Bt genes are not the highest yielding cultivars, as in the earlier years of adoption."[9]

This should not surprise us. GM crops were not designed to increase yield: the vast majority of GM crops are engineered to tolerate herbicides and/or to contain an insecticide. The

*"Over the first 15 years of commercial use, GE seeds have not been shown to increase yield potentials of the varieties. In fact, the yields of herbicide-tolerant [HT] or insect-resistant seeds may be occasionally lower than the yields of conventional varieties if the varieties used to carry the HT or Bt genes are not the highest yielding cultivars, as in the earlier years of adoption."*
– US Department of Agriculture[9]

*"Commercial GE crops have made no inroads so far into raising the intrinsic or potential yield of any crop. By contrast, traditional breeding has been spectacularly successful in this regard; it can be solely credited with the intrinsic yield increases in the United States and other parts of the world that characterized the agriculture of the twentieth century."*
– Doug Gurian-Sherman, former biotechnology advisor to the US Environmental Protection Agency (EPA) and senior scientist at the Union of Concerned Scientists[10]

yield of a GM crop depends on the genetic background of the non-GM plants into which the GM traits are inserted. Yield is a complex trait that is the product of many genes working together. Much depends on the agronomic practices used, such as conserving and building soil fertility and structure. High yield cannot be conferred by the manipulation of one or a few genes, as occurs in genetic engineering.

## Failure to yield

The definitive study to date on GM crops and yield is "Failure to yield", by Dr Doug Gurian-Sherman, senior scientist at the Union of Concerned Scientists and former biotechnology adviser to the US Environmental Protection Agency. The study, based on peer-reviewed research and official USDA data, was the first to tease out the contribution of genetic engineering to yield performance from the gains made through conventional breeding.[10] It is important to bear in mind when evaluating the yield performance of GM crops that GMO companies insert their proprietary GM genes into the best-performing conventionally bred varieties.

The study also differentiated between intrinsic and operational yield.[10] Intrinsic or potential yield is the highest yield that can be achieved when crops are grown under ideal conditions. In contrast, operational yield is obtained under field conditions, when environmental factors such as pests and stress result in yields that are less than ideal. Genes that improve operational yield reduce losses from such factors.

The study found that GM technology has not raised the intrinsic yield of any crop. The intrinsic yields of corn and soybeans rose during the twentieth century, but this was not as a result of GM traits, but due to improvements brought about through traditional breeding.[10]

The study found that GM soybeans did not increase operational yields, either. GM maize increased operational yields only slightly, mostly in years of heavy infestation with the European corn borer pest. GM Bt maize offered little or no advantage when infestation with European corn borer was low to moderate, even when compared with conventional maize that was not treated with insecticides.[10]

This interpretation is shared by the USDA report of 2014, which noted that while GM crops have not been shown to increase yield potential, "by protecting the plant from certain pests, GE crops can prevent yield losses to pests, allowing the plant to approach its yield potential."[9]

"Failure to yield" concluded, "Commercial GE crops have made no inroads so far into raising the intrinsic or potential yield of any crop. By contrast, traditional breeding has been spectacularly successful in this regard; it can be solely credited with the intrinsic yield increases in the United States and other parts of the world that characterized the agriculture of the twentieth century."[10]

## Non-GM farming produces higher yields with less pesticide

A peer-reviewed study led by researchers from the University of Canterbury, New Zealand, confirmed the conclusions of "Failure to yield". The study analyzed data on agricultural productivity in the United States and Western Europe over the last 50 years, focusing on the staple crops of maize, canola, and wheat. It found that the US's mostly GM production was lowering yields and increasing pesticide use compared to Western Europe's mostly non-GM production.[11]

The yield reduction found in the US relative to Europe may be due in part to technology choices beyond GM plants themselves, because even non-GM wheat yield improvements in the US are poor in comparison to Europe. Therefore the mostly non-GM agricultural system of Western Europe shows more promise of meeting future food needs than does the GM-based US system.[11]

The study found that both herbicide and insecticide use is increasing in the US relative to Western Europe. Hence the agricultural system of Western Europe appears to be reducing chemical inputs and thus is becoming more sustainable than that of the US, without sacrificing yield gains.

Commenting on the finding, lead author Professor Jack Heinemann said, "The US and US industry have been crowing about the reduction in chemical insecticide use with the introduction of Bt [GM insecticidal] crops. And at face value, that's true. They've gone to about 85% of the levels that they used in the pre-GE era. But what they don't tell you is that France went down to 12% of its previous levels. France is the fourth biggest exporter of corn in the world, one of the biggest exporters of wheat, and it's only 11% of the size of the US.

"So here is a major agroecosystem growing the same things as the US, corn and wheat, and it's reduced chemical insecticide use to 12% of 1995 levels. This is what a modern agroecosystem can do. What the US has done is invented a way to use comparatively more insecticide… [US use] should be down to 12% too!"[12]

Heinemann was prompted to carry out the study by a claim from a British economics professor that Europe was falling behind the US in agricultural productivity because of its avoidance of GM. Heinemann and his team found that the data showed that completely the opposite is true: "Europe has learned to grow more food per hectare and use fewer chemicals in the process. The American choices in biotechnology [GM] are causing it to fall behind Europe in productivity and sustainability."[13]

## Conclusion

GM has not increased the yield potential of crops. Though yield increases were seen in major crops in the twentieth century, these are due to improvements from conventional breeding, and not to the introduction of GM traits. High yield is a complex genetic trait with multiple coordinated gene functions at its basis that cannot be genetically engineered into a crop.

Data comparing agricultural productivity in the United States and Western Europe shows that Europe's mostly non-GM production produces better yields with less pesticide than the US's mostly GM production. Contrary to claims that Europe's refusal to embrace GM is causing it to fall behind the US, the data show that the reverse is true: the US, with its mostly GM production for staple crops, is falling behind Europe in terms of productivity and sustainability.

The funding and research that are currently poured into GM crop research and development should be redirected toward approaches that are proven effective in improving crop yields, including conventional plant breeding as well as the use of agroecological practices. These are by far the most efficient, affordable, and widely practised methods of improving yield.

If GM cannot increase yields even in the US, where high-input, irrigated, heavily subsidized commodity farming is the norm, it is irresponsible to assume that it would improve yields in the Global South, where farmers may literally bet their farms and livelihoods on a crop.

## References


1. Benbrook C. Evidence of the magnitude and consequences of the Roundup Ready soybean yield drag from university-based varietal trials in 1998: Ag BioTech InfoNet Technical Paper Number 1. Sandpoint, Idaho; 1999. Available at: http://www.mindfully.org/GE/RRS-Yield-Drag.htm.
2. Elmore RW, Roeth FW, Nelson LA, et al. Glyphosate-resistant soyabean cultivar yields compared with sister lines. Agron J. 2001;93:408-412.
3. Ma BL, Subedi KD. Development, yield, grain moisture and nitrogen uptake of Bt corn hybrids and their conventional near-isolines. Field Crops Res. 2005;93:199-211.
4. Bennett H. GM canola trials come a cropper. WA Business News. http://www.wabusinessnews.com.au/en-story/1/69680/GM-canola-trials-come-a-cropper. Published January 16, 2009.
5. Kaskey J. Monsanto facing "distrust" as it seeks to stop DuPont (update 3). Bloomberg. http://www.bloomberg.com/apps/news?pid=newsarchive&sid=aii_24MDZ8SU. Published November 10, 2009.
6. Gillam C. Virginia probing Monsanto soybean seed pricing. West Virginia investigating Monsanto for consumer fraud. Reuters. http://www.reuters.com/article/idUSN2515475920100625. Published June 25, 2010.
7. Khan L. How Monsanto outfoxed the Obama administration. Salon.com. http://www.salon.com/2013/03/15/how_did_monsanto_outfox_the_obama_administration/. Published March 15, 2013.
8. Fernandez-Cornejo J, McBride WD. The adoption of bioengineered crops. Agricultural Economic Report No. 810. Washington, DC: US Department of Agriculture; 2002. Available at: http://www.ers.usda.gov/publications/aer810/aer810.pdf.
9. Fernandez-Cornejo J, Wechsler S, Livingston M, Mitchell L. Genetically engineered crops in the United States. Washington, DC: US Department of Agriculture; 2014. Available at: http://www.ers.usda.gov/publications/err-economic-research-report/err162.aspx#.U0P_qMfc26x.
10. Gurian-Sherman D. Failure to yield: Evaluating the performance of genetically engineered crops. Cambridge, MA: Union of Concerned Scientists; 2009. Available at: http://www.ucsusa.org/assets/documents/food_and_agriculture/failure-to-yield.pdf.
11. Heinemann JA, Massaro M, Coray DS, Agapito-Tenfen SZ, Wen JD. Sustainability and innovation in staple crop production in the US Midwest. Int J Agric Sustain. 2013:1–18.
12. Richardson J. Study: Monsanto GMO food claims probably false. Salon.com. 2013. Available at: http://www.salon.com/2013/06/27/study_monsanto_gmo_food_claims_probably_false_partner/.
13. University of Canterbury. GM a failing biotechnology in modern agro-ecosystems [press release]. 2013. Available at: http://www.gmwatch.org/index.php/news/rss/14802.

# 5.2 Myth: GM crops decrease pesticide use
# Truth: GM crops increase pesticide use

## Myth at a glance

GM crops are claimed by proponents to reduce pesticide use (the term "pesticide" includes herbicides, which technically are pesticides). But this is untrue. GM herbicide-tolerant crops have led to massive increases in herbicide use. The vast majority of these crops are engineered to be used with glyphosate-based herbicides such as Roundup.

The small reduction in the use of chemical insecticide sprays due to GM Bt insecticidal crops is swamped by the large increase in herbicide use due to GM herbicide-tolerant crops.

Since GM crops were introduced in the US, overall pesticide use has increased by an estimated 183 million kg (404 million pounds), or about 7%, compared with the amount that would have been used if the same acres had been planted to non-GM crops.

The widespread use of herbicide-tolerant crops has led to the rapid spread of herbicide-resistant superweeds. As a result, farmers have to spray more herbicide, or mixtures of herbicides, to try to control the weeds.

The area of US cropland infested with glyphosate-resistant weeds expanded to a massive 61.2 million acres in 2012. In some areas, farmland has had to be abandoned or farmers have had to resort to pulling weeds by hand.

This "chemical treadmill" model of farming is unsustainable and especially impractical for farmers in the Global South, who cannot afford expensive chemical inputs to control resistant weeds.

GM crops are claimed by proponents to reduce pesticide use (the term "pesticide" includes herbicides, which technically are pesticides). But this is untrue. Herbicide-tolerant crops have been developed specifically to depend upon agrochemicals and have extended the market for these chemicals. Far from weaning agriculture away from environmentally damaging chemicals, GM technology has prolonged and extended the chemically-based agricultural model.

The increased adoption of GM Roundup Ready crops, especially soy, has been accompanied by massive increases in the use of glyphosate herbicides worldwide.[1,2,3,4,5,6]

## North America

A report by agronomist Dr Charles Benbrook based on US Department of Agriculture data looked at the effects on pesticide use of the first sixteen years of GM crop cultivation in the United States, from 1996 to 2011. Benbrook analyzed the impact of the six major GM pest-management traits on pesticide use. The crops taken into account were herbicide-tolerant maize, soybeans, and cotton; Bt maize targeting the European corn borer and corn rootworm; and Bt cotton targeting Lepidopteran insects (butterflies and moths).[2]

The report found that GM herbicide-tolerant crops have led to a 239 million kilogram (527 million pound) increase in herbicide use in the United States between 1996 and 2011, while Bt crops have reduced chemical insecticide spray use by 56 million kilograms (123 million pounds). Overall pesticide use increased by an estimated 183 million kg (404 million pounds), or about 7%, compared with the amount that would have been used if the same acres had been planted to non-GM crops.[2]

Herbicide-tolerant soybeans accounted for 70% of the total increase across the three herbicide-tolerant crops. Rising reliance on glyphosate accounted for most of this increase.[2]

Moreover, GM herbicide-tolerant soy is increasing the use of herbicides over time, whereas non-GM soy is decreasing herbicide use, clearly showing that GM soy is not sustainable. In 1996 GM herbicide-tolerant soy needed 0.30 pounds per acre less herbicide than non-GM soy. But in 2011 the cultivation of GM herbicide-tolerant soy needed 0.73 pounds per acre more herbicide than non-GM soy.[2]

This data is unsurprising, since the pesticide industry is the GM seed industry.[7] It is in its interest to produce seeds that are dependent on pesticides.

Two major factors are driving the upward trend in herbicide use on herbicide-tolerant acres compared to acres planted to non-GM crops: incremental reductions in the application rate of herbicides other than glyphosate applied to non-GM crops and the rapid spread of glyphosate-resistant weeds. The first factor is driven by the pesticide industry trend of selling more potent herbicides effective at lower rates of application.

The area of US cropland infested with glyphosate-resistant weeds expanded to 61.2 million acres in 2012, according to a survey conducted by Stratus Agri-Marketing. Nearly half of all US farmers interviewed reported that glyphosate-resistant weeds were present on their farm in 2012, up from 34% of farmers in 2011. The survey also indicates that the rate at which glyphosate-resistant weeds are spreading is gaining momentum; increasing 25% in 2011 and 51% in 2012.[8,9]

## South America

The same trend of increasing herbicide use has been found in South America since the introduction of GM herbicide-tolerant soy. In Argentina, as the area planted to GM herbicide-tolerant soy increased from 0.4 million hectares in 1996/97 to 14.1 million hectares in 2003/04, the volume of glyphosate applied to soybeans increased from 0.82 million kg in 1996/97 to 45.86 million kg in 2003/04. Between 1999 and 2003 the volume of glyphosate applied to soy increased by 145% (figures are from the Argentine crop

> *"Herbicide-resistant crop technology has led to a 239 million kilogram (527 million pound) increase in herbicide use in the United States between 1996 and 2011, while Bt crops have reduced insecticide applications by 56 million kilograms (123 million pounds). Overall, pesticide use increased by an estimated 183 million kgs (404 million pounds), or about 7%."*
> – Dr Charles Benbrook, Centre for Sustaining Agriculture and Natural Resources, Washington State University, in a study based on US Department of Agriculture data[2]

> *"The promise was that you could use less chemicals and produce a greater yield. But let me tell you none of this is true."*
> – Bill Christison, president of the US National Family Farm Coalition[28]

protection industry association, CASAFE, as no official government data are available).[3]

These increases in herbicide use are to be expected, given the expansion in area planted to GM herbicide-tolerant soy in that period. However, as in North America, each year, farmers have had to apply more glyphosate per hectare than the previous year to achieve weed control. The average rate of glyphosate application on soy increased steadily from 1.14 kg/hectare in 1996/97 to 1.30 kg/hectare in 2003/04.[3]

Increasing rates of herbicide use per hectare over time has also been found in Brazil. In the state of Rio Grande do Sul, where GM soy was first planted illegally in 1998, use of glyphosate increased 85% between 2000 and 2005, while the area of soy cultivation increased by only 30.8%, according to the Brazilian Institute of the Environment (IBAMA).[10]

## Glyphosate-resistant superweeds

The widespread use of Roundup Ready crops has led to over-reliance on a single herbicide – glyphosate, commonly sold as Roundup. This has resulted in the rapid spread of glyphosate-resistant weeds in regions where GM crops are planted.[1,11] Resistant weeds include pigweed,[12] ryegrass,[13] and marestail.[14]

The International Survey of Herbicide Resistant Weeds' website lists 28 glyphosate-resistant weeds around the world.[15]

When resistant weeds first appear, farmers often use more glyphosate herbicide to try to control them. But as time passes, no amount of glyphosate herbicide is effective.[11,12] Farmers are forced to resort to potentially even more toxic herbicides and mixtures of herbicides, including 2,4-D (an ingredient of the Vietnam defoliant Agent Orange) and dicamba.[1,13,14,16,17,18,19,20]

Some US farmers are going back to more labour-intensive methods like ploughing – and even pulling weeds by hand.[21] In Georgia in 2007, 10,000 acres of farmland were abandoned

## Herbicide-tolerant crops undermine sustainable agriculture

> *"Agricultural weed management has become entrenched in a single tactic – herbicide-resistant crops – and needs greater emphasis on integrated practices that are sustainable over the long term. In response to the outbreak of glyphosate-resistant weeds, the seed and agrichemical industries are developing crops that are genetically modified to have combined resistance to glyphosate and synthetic auxin herbicides. This technology will allow these herbicides to be used over vastly expanded areas and will likely create three interrelated challenges for sustainable weed management. First, crops with stacked herbicide resistance are likely to increase the severity of resistant weeds. Second, these crops will facilitate a significant increase in herbicide use, with potential negative consequences for environmental quality. Finally, the short-term fix provided by the new traits will encourage continued neglect of public research and extension in integrated weed management."*
>
> – David A. Mortensen, professor of weed and applied plant ecology, Penn State University, and colleagues[1]

after being overrun by glyphosate-resistant pigweed.[22] One report said the resistant pigweed in the Southern US was so tough that it broke farm machinery.[23]

Another report said of the Roundup Ready system, "This silver bullet of American agriculture is beginning to miss its mark."[24] As glyphosate-resistant weeds undermine the Roundup Ready farming model, Monsanto has taken the extraordinary step of paying farmers to spray other herbicides to supplement Roundup.[20,21]

## How are superweeds created?

Many glyphosate-resistant weeds appear through what is known as selection pressure. Only those weeds that survive being sprayed with glyphosate herbicides pass on their genes, leading to a steady increase in glyphosate-resistant plants in the weed population.

There is also a second route through which glyphosate-resistant weeds develop: GM crops can pass on their genes for herbicide tolerance to wild or cultivated non-GM relatives. GM canola has been found to pass on its glyphosate-tolerance genes to related wild plants such as wild mustard, turning them into difficult-to-control superweeds. The GM herbicide-tolerance gene was shown to persist in these weed populations over a period of six years.[25]

GM canola itself has also become a weed. Feral canola populations have acquired resistance to all of the main herbicides used in Canada,[26] making it difficult and expensive to control "volunteer" canola in soy and maize fields. Feral herbicide-resistant canola has also become a problem in sugar beet fields in the US, where canola seeds are reported to be deposited by defecation from geese migrating from Canada.[27]

## The GM industry "solution" to superweeds: More herbicides

The industry's solution to the glyphosate-tolerant superweeds crisis has been first, to aggressively market pre-mixed herbicide products to farmers; and second, to develop stacked-trait GM crop varieties that are resistant to multiple herbicides. These stacked-trait crops enable farmers to spray mixtures of herbicides freely, instead of having to apply them carefully in order to spare crops.[19] Simple logic indicates that this will increase the amount of herbicide applied to any given field.

The chemical and GM seed company Dow has applied to the US government to release its multi-herbicide-tolerant GM soybean, engineered to tolerate being sprayed with glyphosate, glufosinate, and 2,4-D,[29] and a 2,4-D-tolerant maize.[30]

Weed scientists warn that such multi-herbicide-tolerant crops will cause an increase in 2,4-D use, trigger an outbreak of still more intractable weeds resistant to both glyphosate and 2,4-D, and undermine sustainable approaches to weed management.[1]

In fact, weed species already exist that are resistant to dicamba,[31] to 2,4-D,[32] and to multiple herbicides.[33] They could be termed stacked-trait superweeds.

Most stacked-trait superweeds emerge through selection pressure, where only those weeds that can tolerate a herbicide survive to pass on their genes. Others emerge through cross-pollination of GM herbicide-tolerant crops within the crop species or with wild relatives. Stacked-trait multi-herbicide-resistant oilseed rape (canola) plants have already appeared as a result of cross-pollination between GM crops engineered to tolerate different herbicides. The plants are considered weeds because they grow and spread despite the fact that they are not deliberately planted. As early as 1998, oilseed rape plants were found that tolerated up to three different herbicides.[34]

A Canadian government study showed that after just 4–5 years of commercial growing, GM oilseed rape engineered to tolerate different single herbicides had cross-pollinated to create stacked-trait "escaped" plants resistant to up to three herbicides, posing a serious problem for farmers.[26,18]

## Conclusion

GM herbicide-tolerant crops have led to massive increases in herbicide use (herbicides are a class of pesticide). The small reduction in the use of chemical insecticide sprays due to GM Bt insecticidal crops is swamped by the large increase in herbicide use due to GM herbicide-tolerant crops.

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## References


1. Mortensen DA, Egan JF, Maxwell BD, Ryan MR, Smith RG. Navigating a critical juncture for sustainable weed management. BioScience. 2012;62(1):75-84.
2. Benbrook C. Impacts of genetically engineered crops on pesticide use in the US – The first sixteen years. Environ Sci Eur. 2012;24. doi:10.1186/2190-4715-24-24.
3. Benbrook CM. Rust, resistance, run down soils, and rising costs – Problems facing soybean producers in Argentina. Technical Paper No 8. AgBioTech InfoNet; 2005. Available at: http://www.greenpeace.org/raw/content/international/press/reports/rust-resistence-run-down-soi.pdf.
4. Pengue W. El glifosato y la dominación del ambiente. Biodiversidad. 2003;37. Available at: http://www.grain.org/biodiversidad/?id=208.
5. MECON (Ministerio de Economia Argentina). Mercado argentino de fitosanitarios – Año 2001. 2001. Available at: http://bit.ly/1eqMudL.
6. CASAFE. Mercado Argentino de productos fitosanitarios 2012. 2012. Available at: http://www.casafe.org/pdf/estadisticas/Informe%20Mercado%20Fitosanitario%202012.pdf.
7. Howard P. Visualizing consolidation in the global seed industry: 1996–2008. Sustainability. 2009;1:1266-1287.
8. Fraser K. Glyphosate resistant weeds – intensifying. Guelph, Ontario, Canada: Stratus Ag Research; 2013. Available at: http://stratusresearch.com/blog/glyphosate-resistant-weeds-intensifying/.
9. Farm Industry News. Glyphosate-resistant weed problem extends to more species, more farms. http://farmindustrynews.com/ag-technology-solution-center/glyphosate-resistant-weed-problem-extends-more-species-more-farms. Published January 29, 2013.
10. Zanatta M. Avanço da soja transgênica amplia uso de glifosato. Valor Econômico. 2007. Available at: http://www.seagri.ba.gov.br/noticias.asp?qact=view&exibir=clipping¬id=9931.
11. Nandula VK, Reddy KN, Duke SO, Poston DH. Glyphosate-resistant weeds: Current status and future outlook. Outlooks Pest Manag. 2005;16:183–187.
12. Syngenta. Syngenta module helps manage glyphosate-resistant weeds. Delta Farm Press. http://deltafarmpress.com/syngenta-module-helps-manage-glyphosate-resistant-weeds. Published May 30, 2008.
13. Robinson R. Resistant ryegrass populations rise in Mississippi. Delta Farm Press. 2008. Available at: http://deltafarmpress.com/resistant-ryegrass-populations-rise-mississippi.
14. Johnson B, Davis V. Glyphosate resistant horseweed (marestail) found in 9 more Indiana counties. Pest Crop. 2005. Available at: http://extension.entm.purdue.edu/pestcrop/2005/issue8/index.html.
15. Heap I. International Survey of Herbicide Resistant Weeds: Weeds resistant to EPSP synthase inhibitors (G/9) by species and country. weedscience.org. 2014. Available at: http://www.weedscience.org/summary/MOA.aspx?MOAID=12.
16. Nice G, Johnson B, Bauman T. A little burndown madness. Pest & Crop. http://extension.entm.purdue.edu/pestcrop/2008/issue1/index.html. Published March 7, 2008.
17. Nice G, Johnson B. Fall applied programs labeled in Indiana. Pest Crop. 2006;(23). Available at: http://extension.entm.purdue.edu/pestcrop/2006/issue23/table1.html.
18. Randerson J. Genetically-modified superweeds "not uncommon." New Sci. 2002. Available at: http://www.newscientist.com/article/dn1882-geneticallymodified-superweeds-not-uncommon.html.
19. Kilman S. Superweed outbreak triggers arms race. Wall Street Journal. http://biolargo.blogspot.com/2010/06/round-up-weed-killer-and-acquired.html. Published June 4, 2010.
20. Brasher P. Monsanto paying farmers to increase herbicide use. Des Moines Register. http://bit.ly/az3fSo. Published October 19, 2010.
21. Neuman W, Pollack A. US farmers cope with Roundup-resistant weeds. New York Times. http://www.nytimes.com/2010/05/04/business/energy-environment/04weed.html?pagewanted=1&hp. Published May 3, 2010.
22. Caulcutt C. "Superweed" explosion threatens Monsanto heartlands. France 24. http://www.gmwatch.org/index.php/news/archive/2009/10923. Published April 19, 2009.
23. Osunsami S. Killer pig weeds threaten crops in the South. http://abcnews.go.com/WN/pig-weed-threatens-agricultureindustryovertaking-fields-crops/story?id=8766404&page=1. Published October 6, 2009.
24. Gustin G. Roundup's potency slips, foils farmers. St. Louis Post-Dispatch. http://www.soyatech.com/news_story.php?id=19495. Published July 25, 2010.
25. Warwick SI, Legere A, Simard MJ, James T. Do escaped transgenes persist in nature? The case of an herbicide resistance transgene in a weedy Brassica rapa population. Mol Ecol. 2008;17:1387-95. doi:10.1111/j.1365-

294X.2007.03567.x.
26. Knispel AL, McLachlan SM, Van Acker RC, Friesen LF. Gene flow and multiple herbicide resistance in escaped canola populations. Weed Sci. 2008;56:72–80.
27. Hart M. Farmer to farmer: The truth about GM crops [film]. http://gmcropsfarmertofarmer.com/film.html. 2011.
28. Christison B. Family farmers warn of dangers of genetically engineered crops. In Motion Magazine. http://www.inmotionmagazine.com/genet1.html. Published July 29, 1998.
29. Gillam C. Dow launches multi-herbicide tolerant GM soybean. Reuters. http://bit.ly/qBR9a5. Published August 22, 2011.
30. Kimbrell A. “Agent Orange” corn: Biotech only winner in chemical arms race as herbicide resistant crops fail. Huffington Post. http://www.huffingtonpost.com/andrew-kimbrell/agent-orange-corn-biotech_b_1291295.html. Published February 22, 2012.
31. Rahman A, James TK, Trolove MR. Chemical control options for the dicamba resistant biotype of fathen (Chenopodium album). N Z Plant Prot. 2008;61:287–291.
32. Heap I. International Survey of Herbicide Resistant Weeds: Weeds resistant to synthetic auxins (O/4) by species and country. 2014. Available at: http://weedscience.org/Summary/MOA.aspx?MOAID=24.
33. Martin H. Herbicide resistant weeds. Ontario Ministry of Agriculture, Food and Rural Affairs; 2013. Available at: http://www.omafra.gov.on.ca/english/crops/facts/01-023.htm.
34. Downey RK. Gene flow and rape – the Canadian experience. In: Lutman PJW, ed. Gene Flow and Agriculture: Relevance for Transgenic Crops. Vol 72. British Crop Protection Council Symposium Proceedings; 1999:109–116. Available at: http://cat.inist.fr/?aModele=afficheN&cpsidt=1171731.

## 5.3 Myth: GM Bt crops reduce insecticide use

## Truth: GM Bt crops change the way in which insecticides are used

### Myth at a glance

GM proponents claim that GM Bt crops reduce insecticide use, as farmers do not have to spray chemical insecticides.

But GM Bt crops do not reduce or eliminate insecticides. They simply change the type of insecticide and the way in which it is used – from sprayed on, to built in. The amount of Bt toxin expressed in the plant is generally far greater than the amount of chemical pesticide displaced.

The most optimistic claim for reduced pesticide (herbicide and insecticide) use from GM crops, from an industry consultancy source, is 6.9% globally. In contrast with this small reduction, in France by 2009, herbicide use was down to 82% and insecticide use was down to 12% of 1995 levels – without the use of GM crops.

Far from being safe insecticides, the Bt toxins expressed in GM Bt crops harm beneficial and non-target insects. The high levels of Bt toxin expressed in stacked-trait GM crops like SmartStax maize have not been tested to see if they are safe to eat.

Pests are rapidly evolving resistance to the Bt toxins in GM Bt crops. Even when Bt toxins are effective in killing the target pest, secondary pests that are not controlled by Bt toxins are moving into the ecological niche. Both developments are forcing a return to chemical insecticides.

Attempts to delay pest resistance to Bt crops by planting refuges of non-Bt crops have not been completely successful, both because refuge recommendations have not been enforced and because refuges are not working as planned.

It is not valid to measure insecticide use only by the amount of insecticide sprayed onto the growing crop. Increasingly insecticides are applied to seeds before planting and to soil.

When evaluating the impact of GM Bt crops on insecticide use, a more useful comparator than chemically-grown non-GM crops would be non-GM crops under organic or integrated pest management, where insecticide use is reduced or eliminated.

GM proponents claim that GM Bt crops reduce insecticide use, as farmers do not have to spray chemical insecticides. But this claim does not stand up to analysis, for several reasons. The first and most important is that the GM Bt gene turns the plant itself into an insecticide. The GM insecticide is present in active form in every part of the crop, including the parts that people and animals eat. So Bt crops do not reduce or eliminate insecticides. They simply change the type of insecticide and the way in which it is used – from sprayed on, to built in.

What is more, the amount of insecticide produced by the plant is in many cases far more than the amount of chemical insecticide spray that is displaced. This is confirmed by data collected by the agronomist Dr Charles Benbrook from industry documents on Bt toxin expression levels in GM Bt plants submitted for regulatory purposes.[1] Benbrook's findings were as follows.

### GM Bt maize targeting the European corn borer

Bt maize events targeting the European corn borer (ECB) produce nearly as much or more Bt toxin per hectare (ha) than the average rate of chemical insecticides applied on a hectare planted to non-Bt maize for ECB control (about 0.15 kgs insecticide per ha; 0.13 pounds/acre in 2010):

- MON810 produces 0.2 kg/ha of Bt toxin
- Bt11 produces 0.28 kg/ha
- MON 89034 produces two Bt toxin proteins totalling 0.62 kg/ha
- TC1507 produces the least amount of Bt toxin – 0.1 kg/ha.[1]

### GM Bt maize targeting the corn rootworm

Every Bt maize hectare planted in recent years targeting the corn rootworm (CRW) expresses substantially greater volumes of Bt toxin than the approximately 0.2 kg of insecticides applied on the average hectare for corn rootworm control (0.19 pounds/acre):

- MON88017 expresses 0.62 kg/ha of Bt toxin
- DAS 59122–7 expresses two Bt toxin proteins totalling 2.8 kg/ha, 14-fold more than the chemical insecticides displaced.[1]

### SmartStax maize

SmartStax GM maize synthesizes six Bt toxin proteins, three targeting the ECB, and three the CRW. Total Bt toxin protein production is estimated at 4.2 kg/ha (3.7 pounds/acre), 19 times the average conventional insecticide rate of application in 2010.[1]

This high level of Bt toxin expressed in GM plants has never been tested to see whether it is safe to eat over the long term in animals or humans.

Claims that GM Bt crops reduce or eliminate insecticides invariably fail to take these plant-produced pesticides into account.

## Reduction in chemical insecticides from Bt crops unspectacular

Let's ignore for a moment the fact that Bt crops generally produce more insecticides than the chemical sprays displaced and only consider the claimed reduction in chemical insecticide sprays due to Bt crops.

This reduction is based on the assumption that farmers who grow Bt crops do not also spray chemical insecticides. Even if that assumption were true, the resulting reduction in chemical insecticide use due to GM Bt crops is an unspectacular 56 million kilograms (123 million pounds) over the first sixteen years of GM crop cultivation in the US.[1]

This small reduction is swamped by the massive estimated 183 million kg (404 million pounds) increase in pesticide use resulting from the adoption of GM herbicide-tolerant crops. This means that overall pesticide use has increased by 7% due to the introduction of GM crops.[1]

Even the modest reduction in chemical insecticides attributed to GM Bt crops has proved temporary and unsustainable, due to the emergence of pests resistant to Bt toxin (see below).

Moreover, there is a question mark over whether Bt crops can even be said to have reduced chemical insecticide use in view of the facts that most corn seed – Bt and non-Bt – is now coated in toxic neonicotinoid pesticides (see below) and farmers plagued with Bt toxin-resistant pests are returning to harmful soil-applied insecticides.[2,3]

## Pesticide use number crunching

In his 2012 paper discussed above, Benbrook calculated that overall pesticide use (including herbicides) increased by 7% in the US due to the introduction of GM crops.[1]

The most optimistic claim for reduced pesticide use (including herbicides) from GM crops, in a 2006 paper by a consultancy firm to the GM industry, P G Economics, and based on "farm-level impact data" from an unnamed source, is 6.9% globally.[4]

In contrast with this small (unvalidated) reduction, by 2007 France reduced both herbicide use (to 94% of 1995 levels) and chemical insecticide use (to 24% of 1995 levels). By 2009 herbicide use was down to 82% and insecticide use was down to 12% of 1995 levels. Similar trends were found in Germany and Switzerland. These benefits were achieved without the use of GM crops.[5]

These progressive trends do not have to mean a severe drop in yield or farmer income. A 2011 study by French government scientists found that pesticide use could be reduced by 30% through adoption of integrated agriculture techniques, with only a small reduction in production (96.3% of the current level) and without impacting farm income.[6] GM crops were not part of the equation in this study.

## Resistant pests are making GM Bt technology obsolete

Insect pests quickly adapt to tolerate pesticides, especially when under constant exposure to the insecticide. The Bt toxin engineered into GM Bt crops are no exception. GM Bt insecticidal crops express the Bt toxin in every cell for their entire lifetime, constantly exposing pests to the toxin. This is different from the traditional use of natural Bt as a spray, where targeted pests are only exposed for a brief period before the Bt breaks down in daylight and the toxin is only activated within the insect's gut.

Exposing pests to a pesticide for long periods of time inevitably speeds up the emergence of resistant pests, since selective pressure eliminates all but the most resistant pests, which then reproduce and pass on their resistance genes.

For this reason, GM Bt crop technology sometimes enjoys short-term success in controlling pests but is soon undermined by the emergence of pests resistant to the toxin.[7,8,9] In 2011 a paper was published showing that corn rootworms in some areas of the US were already resistant to two of the three available Bt toxins that previously controlled them. Fields in the corn belt were sustaining severe damage.[10,11] Bt-resistant rootworm populations have been reported in Iowa[10,12] and Illinois.[13,14]

Entomologist Elson Shields of Cornell University commented on the evolution of pests resistant to Bt toxin in GM plants, "The insect will win. Always bet on the insect if there is not a smart deployment of the trait."[11]

## Refuge recommendations ignored

By "smart deployment of the trait", Shields was referring to the refuge concept. From the time GM Bt technology was introduced, scientists and even the US EPA have recommended that farmers plant "refuges" of non-Bt crops alongside the Bt crops as a resistance management strategy to delay the emergence of Bt-resistant pests.

The idea is that the non-Bt crop acts as a refuge where Bt-susceptible pests can survive, ensuring the existence of a population of Bt-susceptible pests to mate with any Bt-resistant pests that survive in the adjacent field where the Bt crop is under cultivation. It is assumed that the Bt-susceptible pest population will dilute out the Bt-resistant population that survives in the Bt crop, assuring that the predominant population is Bt-susceptible.

However, these recommendations were watered down by the EPA itself, which started out arguing for 50% refuges but ended up accepting voluntary 20% refuges. Even these, in practice, were widely ignored.[11,3] The result has been widespread Bt resistance in the corn rootworm.[10]

## Refuge concept breaking down

Refuges may be less effective than believed. A study on rootworm resistance found that refuges were redundant in the case of substantial Bt-resistant rootworm populations, as the pests were able to live and reproduce in Bt maize fields. The study concluded, "Even with resistance management plans in place, sole reliance on Bt crops for management of agriculture pests will likely hasten the evolution of resistance in some cases."[10]

Also, the effectiveness of refuges relies on the Bt crops expressing doses of Bt toxin that are high enough to kill pests, and the non-Bt refuges remaining free from Bt toxin-expressing genes. But cross-pollination between GM Bt and non-Bt maize has been found to cause "low to moderate" Bt toxin levels in the refuge plants,[15] making refuges less effective.

## Bt crops are the opposite of integrated pest management

Integrated pest management (IPM) is a successful and respected approach to minimizing pesticide use. It is widely practised by farmers who are not prepared to give up pesticides entirely.

A central principle of IPM is avoiding the evolution of pest resistance to insecticides. Resistance is caused by continuous exposure to the pesticide. Only those pests that survive the exposure end up reproducing and passing on their genes, leading to the rapid emergence of a resistant pest population. IPM requires that insecticides are only sprayed when needed – when pest infestation has reached a critical point of damage to the plant. That way, the pests do not get a chance to become resistant and the pesticide's effectiveness is preserved.

GM Bt crops, with their permanently active pesticides built into every cell, are incompatible with the IPM approach.

## Bt crops harm natural enemies of pests

Indiscriminate use of insecticides does not only kill pests, but also the natural enemies of the pests, the beneficial predators. Pests are generally far more resilient than their predators and recover from insecticide spraying more quickly. Therefore spraying insecticides, while effective in the short term, soon leads to rapid surges in pest populations, which are no longer kept in check by their natural enemies.

This process is well documented by Professor Robert van den Bosch of the University of California, one of the developers of integrated pest management, in his book, The Pesticide Conspiracy.[16] Van den Bosch concluded that pesticides do not control pests, but create them.

Bt crops are no exception to this rule. Contrary to claims by GMO promoters, the pesticides built into Bt crops are not restricted to insect pests but also affect beneficial predators (see Myth 5.4). For example, the rootworms that are killed by the Bt toxins in GM crops are beetles, and are related to many beneficial insects, such as ladybirds, which can then become collateral damage.[3,17] In 2012, scientists at Cornell University found that rootworm Bt toxin is likely to be harming several important species of beneficial beetles in GMO corn.18 It has been established that Bt toxins harm ladybirds.[17]

Destruction of beneficial pest predators, combined with rising resistance to Bt toxins in the pests themselves, will result in pest proliferation. This in turn enables GMO seed developer companies to sell more and different pesticidal GMOs and accompanying chemical sprays.

## Secondary pests move in on GM Bt crops

Nature abhors a vacuum. So even when Bt toxin succeeds in controlling the target pest, secondary pests move into the ecological niche. For instance, in the US, the Western bean cutworm has increased significantly in GM Bt maize fields.[19] In China and India, Bt cotton was initially effective in suppressing the target pest, the bollworm. But secondary pests that are resistant to Bt toxin, especially mirids and mealy bugs, soon took its place.[20,21,22,23,24,25]

Two studies from China show that GM Bt cotton is already failing under the onslaught of secondary pests:

- A study of 1,000 farm households in five provinces found that farmers noticed a substantial increase in secondary pests after the introduction of Bt cotton. The researchers found that the initial reduction in pesticide use in Bt cotton cultivars was "significantly lower than that reported in research elsewhere" and that "more pesticide sprayings are needed over time to control emerging secondary pests" such as aphids, spider mites, and lygus bugs. In addition, a quarter of the farmers thought Bt cotton yielded less than non-GM varieties. Close to 60% said that overall production costs had not decreased, due to the higher price of Bt cotton seed.[26]
- Field trials conducted over ten years in northern China show that mirid bugs have increased in cotton and multiple other crops, in proportion to a regional increase in Bt cotton adoption. The researchers' analyses show that "Bt cotton has become a source of mirid bugs and that their population increases are related to drops in [chemical] insecticide use in this crop." Mirid bug infestation of other food crops (Chinese dates, grapes, apples, peaches, and pears) also increased in proportion to the regional planting area of Bt cotton.[27]

### Do GM Bt crops have lowered defence against non-target pests?

GM plants' vulnerability to secondary pests may be explained by the findings of a study examining aphid attacks on Bt cotton. The study found increased numbers of aphid pests on Bt cotton compared with non-Bt cotton. The authors suggested that this may have been due to the Bt cotton plants' reduced levels of certain protective substances that non-Bt cotton plants produce to defend themselves against a variety of pests. This would have left the Bt cotton plants vulnerable to secondary pests such as aphids, which are not killed by the Bt toxin in the crop.[28]

## GM Bt cotton farmers don't always give up insecticides

GM proponents often assume that farmers who adopt Bt crops give up chemical insecticides – but this is not necessarily the case. Tabashnik (2008) reported that while bollworms have evolved resistance to a type of Bt toxin in GM cotton, this has not caused widespread crop failure because "insecticides have been used from the outset" to control the pest.[9] So claims of reductions in insecticide use from Bt crop adoption are unreliable unless there is evidence that the farmer does not use chemical insecticides.

Moreover, most Bt crops currently commercialized or in the pipeline have added herbicide tolerance traits and so are likely to be grown with the application of herbicides.[29] It is with good reason that one independent scientist has called GM crops "pesticide plants".[30]

## Hidden chemical insecticides in GM Bt maize

Studies claiming reductions in insecticide use due to Bt crops have previously focused on insecticides that are applied to the soil or sprayed onto the plant after it has begun to grow. They may neglect to mention a different, potentially environmentally destructive type of pesticide: those that are applied to the seed before it sprouts.

According to a study by US entomologists, all commercially available rootworm-directed GM Bt maize seed is now treated before it is planted with the controversial chemical insecticides known as neonicotinoids.[31]

In this case, GM Bt crops have not reduced or eliminated chemical insecticide sprays. Instead there has been a shift in the type of insecticides used. Where insecticides used to be applied to the plant while it is growing, now they are applied to the seed before planting.

Dr Doug Gurian-Sherman, senior scientist at the Union of Concerned Scientists, commented that neonicotinoid treatments on Bt maize seed aim to kill the insect pests that are not well controlled by Bt toxins. Ironically, prior to the introduction of Bt maize, Gurian-Sherman says a substantial amount of maize was grown without the use of insecticides. For example, maize rotated with soybeans from year to year usually needed little or no insecticide treatment, and only 5–10% of maize was sprayed for corn borers.[32]

Neonicotinoids are systemic insecticides, meaning that they spread throughout all tissues of the crop plant as it grows and are even present in the pollen and nectar. Like the Bt toxin engineered into GM plants, neonicotinoids differ from sprayed insecticides in that they are persistently present in the growing plant and always active. Because of this long exposure period, pests are more likely to develop resistance to them, and non-target and beneficial insects are more likely to be exposed, too.

Neonicotinoids are toxic to a wide variety of beneficial creatures, including some that help protect crops.[33,34] They have highly toxic effects even at very low doses when the exposure time is prolonged.[35] The rise in the use of neonicotinoid seed treatments has been implicated in bee die-off and colony collapse.[36,37] Bees living near agricultural fields have been found to be exposed by multiple routes, including contaminated wild flowers growing near fields, and neonicotinoids have been found in dead bees.[37]

In addition to the use of insecticidal seed treatments, some seed and pesticide companies are now recommending a return to the use of soil-applied insecticides in an attempt to combat the spread of Bt toxin-resistant pests in Bt maize.[1]

The chief – seemingly the only – concern of defenders of GM Bt crop technology is the volume of insecticide applied as sprays after planting. If that volume decreases, they consider that Bt crops reduce insecticide use. But they are not reporting the whole story. The case of neonicotinoid seed treatments shows that it is necessary to consider other types of insecticide applications, how toxic the insecticides are (based on peer-reviewed research, not industry data), how they behave and persist in the environment, and the acreage over which they are applied.[32]

Given the extreme toxicity of neonicotinoids to bees and other beneficial organisms, their high degree of persistence and spread,[37] and the vast acreage over which they are applied, it is questionable whether Bt crop technology has had a beneficial effect on insecticide use.

## Conclusion

Claims that GM Bt crops reduce insecticide use fail to take into account the fact that the GM Bt crop is itself an insecticide. The amount of Bt toxin expressed in the plant is generally far greater than the amount of chemical pesticide displaced.

Far from being safe insecticides, the Bt toxins expressed in GM Bt crops harm beneficial and non-target insects. The high levels of Bt toxin expressed in stacked-trait GM crops like SmartStax maize have not been tested to see if they are safe to eat.

Pests are rapidly evolving resistance to the Bt toxins in GM Bt crops. Even when Bt toxins are effective in killing the target pest, secondary pests that are not controlled by Bt toxins are moving into the ecological niche. Both developments are forcing a return to chemical insecticide sprays.

Attempts to delay pest resistance to GM Bt crops by planting refuges of non-Bt crops have not been completely successful, both because refuge recommendations have not been enforced and because refuges are not working as planned.

It is not valid to measure insecticide use only by the amount of insecticide sprayed onto the growing crop. Increasingly insecticides are applied to seeds before planting and to soil.

When evaluating the impact of GM Bt crops on insecticide use, a more useful comparator than chemically-grown non-GM crops would be non-GM crops under organic or integrated pest management, where insecticide use is reduced or eliminated. This would quickly make clear which farming methods can best reduce insecticide use while maximizing yield and farmer incomes.

## References


1. Benbrook C. Impacts of genetically engineered crops on pesticide use in the US – The first sixteen years. Environ Sci Eur. 2012;24. doi:10.1186/2190-4715-24-24.
2. Jongeneel S. Expect more soil insecticide used with Bt hybrids. Agprofessional.com. http://www.agprofessional.com/news/Expect-more-soil-insecticide-used-with-Bt-hybrids-200626161.html. Published March 29, 2013.
3. Gurian-Sherman D. New science sounds the alarm about destructive beetles on GMO corn. Civil Eats. http://civileats.com/2014/03/20/new-science-sounds-the-alarm-about-destructive-beetles-on-gmo-corn/. Published March 20, 2014.
4. Brookes G, Barfoot P. Global impact of biotech crops: Socio-economic and environmental effects in the first ten years of commercial use. AgBioForum. 2006;9:139–151.
5. Heinemann JA, Massaro M, Coray DS, Agapito-Tenfen SZ, Wen JD. Sustainability and innovation in staple crop production in the US Midwest. Int J Agric Sustain. 2013:1–18.
6. Jacquet F, Butault JP, Guichard L. An economic analysis of the possibility of reducing pesticides in French field crops. Ecol Econ. 2011;70(9):1638–1648.
7. Rensburg JBJ. First report of field resistance by the stem borer, Busseola fusca (Fuller) to Bt-transgenic maize. Afr J Plant Soil. 2007;24:147-151.
8. Huang F, Leonard BR, Wu X. Resistance of sugarcane borer to Bacillus thuringiensis Cry1Ab toxin. Entomol Exp Appl. 2007;124:117-123.
9. Tabashnik BE, Gassmann AJ, Crowder DW, Carriere Y. Insect resistance to Bt crops: Evidence versus theory. Nat Biotechnol. 2008;26:199–202. doi:10.1038/nbt1382.
10. Gassmann AJ, Petzold-Maxwell JL, Keweshan RS, Dunbar MW. Field-evolved resistance to Bt maize by Western corn

rootworm. PLoS ONE. 2011;6:e22629. doi:10.1371/journal.pone.0022629.
11. Keim B. Voracious worm evolves to eat biotech corn engineered to kill it. Wired.com. 2014. Available at: http://www.wired.com/2014/03/rootworm-resistance-bt-corn/.
12. Associated Press. Monsanto shares slip on bug-resistant corn woes. Bloomberg Businessweek. http://www.businessweek.com/ap/financialnews/D9PDS5KO0.htm. Published August 29, 2011.
13. Gray M. Western corn rootworm resistance to Bt corn confirmed in more Illinois counties. Aces News. http://www.aces.uiuc.edu/news/stories/news5903.html. Published April 7, 2014.
14. Gillam C. GMO corn failing to protect fields from pest damage – report. Reuters. http://www.reuters.com/article/2013/08/28/usa-gmo-corn-rootworm-idUSL2N0GT1ED20130828. Published August 28, 2013.
15. Chilcutt CF, Tabashnik BE. Contamination of refuges by Bacillus thuringiensis toxin genes from transgenic maize. Proc Natl Acad Sci USA. 2004;101:7526-9. doi:10.1073/pnas.0400546101.
16. Van Den Bosch R. The Pesticide Conspiracy. University of California Press; 1978.
17. Hilbeck A, McMillan JM, Meier M, Humbel A, Schlaepfer-Miller J, Trtikova M. A controversy re-visited: Is the coccinellid Adalia bipunctata adversely affected by Bt toxins? Environ Sci Eur. 2012;24(10). doi:10.1186/2190-4715-24-10.
18. Stephens EJ, Losey JE, Allee LL, DiTommaso A, Bodner C, Breyre A. The impact of Cry3Bb Bt-maize on two guilds of beneficial beetles. Agric Ecosyst Environ. 2012;156:72–81.
19. Dorhout DL, Rice ME. Intraguild competition and enhanced survival of western bean cutworm (Lepidoptera: Noctuidae) on transgenic Cry1Ab (MON810) Bacillus thuringiensis corn. J Econ Entomol. 2010;103:54–62.
20. Pearson H. Transgenic cotton drives insect boom. Nature. 2006. doi:10.1038/news060724-5.
21. Wang S, Just DR, Pinstrup-Andersen P. Bt-cotton and secondary pests. Int J Biotechnol. 2008;10:113–121.
22. Goswami B. Making a meal of Bt cotton. Infochange. 2007. Available at: http://infochangeindia.org/other/features/making-a-meal-of-bt-cotton.html?Itemid=.
23. Ashk GKS. Bt cotton not pest resistant. The Times of India. http://timesofindia.indiatimes.com/Chandigarh/Bt_cotton_not_pest_resistant/articleshow/2305806.cms. Published August 24, 2007.
24. The Economic Times (India). Bug makes meal of Punjab cotton, whither Bt magic? http://www.gmwatch.org/latest-listing/46-2007/7640. Published September 2, 2007.
25. Rohini RS, Mallapur CP, Udikeri SS. Incidence of mirid bug, Creontiades biseratense (Distant) on Bt cotton in Karnataka. Karnataka J Agric Sci. 2009;22:680–681.
26. Zhao JH, Ho P, Azadi H. Benefits of Bt cotton counterbalanced by secondary pests? Perceptions of ecological change in China. Env Monit Assess. 2010;173:985-94. doi:10.1007/s10661-010-1439-y.
27. Lu Y, Wu K, Jiang Y, et al. Mirid bug outbreaks in multiple crops correlated with wide-scale adoption of Bt cotton in China. Science. 2010;328:1151-4. doi:10.1126/science.1187881.
28. Hagenbucher S, Wackers FL, Wettstein FE, Olson DM, Ruberson JR, Romeis J. Pest trade-offs in technology: Reduced damage by caterpillars in Bt cotton benefits aphids. Proc Biol Sci. 2013;280:20130042. doi:10.1098/rspb.2013.0042.
29. GMO Compass. Maize. 2014. Available at: http://www.gmo-compass.org/eng/gmo/db/.
30. Séralini GE, Mesnage R, Clair E, Gress S, de Vendômois JS, Cellier D. Genetically modified crops safety assessments: Present limits and possible improvements. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-10.
31. Leslie TW, Biddinger DJ, Mullin CA, Fleischer SJ. Carabidae population dynamics and temporal partitioning: Response to coupled neonicotinoid-transgenic technologies in maize. Env Entomol. 2009;38:935-43.
32. Gurian-Sherman D. Genetically engineered crops in the real world – Bt corn, insecticide use, and honey bees. The Cornucopia Institute. http://www.cornucopia.org/2012/01/genetically-engineered-crops-in-the-real-world-bt-corn-insecticide-use-and-honey-bees/. Published January 13, 2012.
33. Kunkel BA, Held DW, Potter DA. Lethal and sublethal effects of bendiocarb, halofenozide, and imidacloprid on Harpalus pennsylvanicus (Coleoptera: Carabidae) following different modes of exposure in turfgrass. J Econ Entomol. 2001;94(1):60-67.
34. Rogers MA, Krischik VA, Martin LA. Effect of soil application of imidacloprid on survival of adult green lacewing, Chrysoperla carnea (Neuroptera: Chrysopidae), used for biological control in greenhouse. Biol Control. 2007;42(2):172–177.
35. Tennekes HA. The significance of the Druckrey-Kupfmuller equation for risk assessment--the toxicity of neonicotinoid insecticides to arthropods is reinforced by exposure time. Toxicology. 2010;276:1-4.
36. Pettis JS, Vanengelsdorp D, Johnson J, Dively G. Pesticide exposure in honey bees results in increased levels of the gut pathogen Nosema. Naturwissenschaften. 2012;99:153-8. doi:10.1007/s00114-011-0881-1.
37. Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. Multiple routes of pesticide exposure for honey bees living near agricultural fields. PLoS ONE. 2012;7:e29268. doi:10.1371/journal.pone.0029268.

# 5.4 Myth: GM Bt crops only affect target pests and their relatives

# Truth: GM Bt crops are not specific to pests but affect a range of organisms

## Myth at a glance

The Bt toxins engineered into GM Bt crops are not specific to target pests and close relatives but can negatively affect a range of non-target organisms, including beneficial insects that help protect crops, beneficial soil organisms, and mammals.

GMO proponents claim that Bt crops only affect target pests and their close relatives. Regulators have uncritically accepted this claim and allowed the commercialization of Bt crops with a minimum of oversight. But research studies show that the claim is false.

## GM Bt crops harm non-target and beneficial organisms

GM Bt insecticide-producing crops have been found to have toxic effects on non-target insect populations when Bt crop fields are compared with insecticide-free fields.[1] Non-target insects that are adversely affected by Bt crops include monarch[2,3] and swallowtail butterflies,[4] and beneficial pest predators such as ladybirds[5,6] and lacewings[7] (see Myth 2.3).

Bt crops have been found to have more negative than positive impacts on the natural enemies of crop pests.[8] Bt toxin has been found to negatively impact bee learning behaviour, interfering with the bees' ability to find nectar sources for food.[9]

GM crops containing Bt toxins have had toxic effects on mammals in animal feeding studies[10,11,12,13,14] (see Myth 3.1).

## GM Bt crops negatively impact soil organisms

Mycorrhizal fungi benefit plants by colonizing their roots, helping them take up nutrients, resist disease, and tolerate drought. A study comparing Bt and non-Bt maize found a lower level of mycorrhizal colonization in the roots of GM Bt maize plants. Residues of Bt maize plants, ploughed under at harvest and kept mixed with soil for up to four months, suppressed soil respiration (carbon dioxide production), markedly altered bacterial communities, and reduced mycorrhizal colonization.[15] A separate field study on Bt maize residues ploughed into soil after harvest confirmed that Bt toxin resisted breakdown and persisted in soil for months.[16]

Arbuscular mycorrhizal fungi (AMF) are beneficial fungi that penetrate the root cells of the host plant. GM Bt maize was found to have decreased arbuscular mycorrhizal fungi (AMF) colonization of roots, compared with non-GM maize.[17,18]

## Bt crops harm aquatic organisms

A study conducted in Indiana, USA found that Bt insecticide released from GM Bt maize was polluting 25% of streams tested.[19] GM Bt maize biomass is toxic to aquatic organisms.[20] Water fleas (an organism often used as an indicator of environmental toxicity) fed GM Bt maize showed toxic effects including reduced fitness, higher mortality, and impaired reproduction.[21]

## Conclusion

The Bt toxins engineered into GM Bt crops are not specific to target pests and close relatives but can negatively affect a range of non-target organisms, including beneficial insects that help protect crops, beneficial soil organisms, and mammals.

## References


1. Marvier M, McCreedy C, Regetz J, Kareiva P. A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. Science. 2007;316:1475-7. doi:10.1126/science.1139208.
2. Losey JE, Rayor LS, Carter ME. Transgenic pollen harms monarch larvae. Nature. 1999;399:214. doi:10.1038/20338.
3. Jesse LCH, Obrycki JJ. Field deposition of Bt transgenic corn pollen: Lethal effects on the monarch butterfly. J Oecologia. 2000;125:241–248.
4. Lang A, Vojtech E. The effects of pollen consumption of transgenic Bt maize on the common swallowtail, Papilio machaon L. (Lepidoptera, Papilionidae). Basic Appl Ecol. 2006;7:296–306.
5. Schmidt JE, Braun CU, Whitehouse LP, Hilbeck A. Effects of activated Bt transgene products (Cry1Ab, Cry3Bb) on immature stages of the ladybird Adalia bipunctata in laboratory ecotoxicity testing. Arch Env Contam Toxicol. 2009;56(2):221-8. doi:10.1007/s00244-008-9191-9.
6. Hilbeck A, McMillan JM, Meier M, Humbel A, Schlaepfer-Miller J, Trtikova M. A controversy re-visited: Is the coccinellid Adalia bipunctata adversely affected by Bt toxins? Environ Sci Eur. 2012;24(10). doi:10.1186/2190-4715-24-10.
7. Hilbeck A, Moar WJ, Pusztai-Carey M, Filippini A, Bigler F. Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator Chrysoperla carnea. Entomol Exp Appl. 1999;91:305–316.
8. Lövei GL, Arpaia S. The impact of transgenic plants on natural enemies: A critical review of laboratory studies. Entomol Exp Appl. 2005;114:1–14. doi:10.1111/j.0013-8703.2005.00235.x.
9. Ramirez-Romero R, Desneux N, Decourtye A, Chaffiol A, Pham-Delègue MH. Does Cry1Ab protein affect learning performances of the honey bee Apis mellifera L. (Hymenoptera, Apidae)? Ecotoxicol Environ Saf. 2008;70:327–333.
10. De Vendomois JS, Roullier F, Cellier D, Séralini GE. A comparison of the effects of three GM corn varieties on mammalian health. Int J Biol Sci. 2009;5:706–26.
11. Gab-Alla AA, El-Shamei ZS, Shatta AA, Moussa EA, Rayan AM. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(9):1117–1123.
12. El-Shamei ZS, Gab-Alla AA, Shatta AA, Moussa EA, Rayan AM. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). J Am Sci. 2012;8(10):684–696.
13. Séralini GE, Clair E, Mesnage R, et al. [RETRACTED:] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-4231.
14. Séralini GE, Mesnage R, Clair E, Gress S, de Vendômois JS, Cellier D. Genetically modified crops safety assessments: Present limits and possible improvements. Environ Sci Eur. 2011;23. doi:10.1186/2190-4715-23-10.
15. Castaldini M, Turrini A, Sbrana C, et al. Impact of Bt corn on rhizospheric and soil eubacterial communities and on beneficial mycorrhizal symbiosis in experimental microcosms. Appl Env Microbiol. 2005;71:6719-29. doi:10.1128/AEM.71.11.6719-6729.2005.
16. Zwahlen C, Hilbeck A, Gugerli P, Nentwig W. Degradation of the Cry1Ab protein within transgenic Bacillus thuringiensis corn tissue in the field. Mol Ecol. 2003;12:765-75.
17. Cheeke TE, Pace BA, Rosenstiel TN, Cruzan MB. The influence of fertilizer level and spore density on arbuscular mycorrhizal colonization of transgenic Bt 11 maize (Zea mays) in experimental microcosms. FEMS Microbiol Ecol. 2011;75:304-12. doi:10.1111/j.1574-6941.2010.01013.x.
18. Cheeke TE, Rosenstiel TN, Cruzan MB. Evidence of reduced arbuscular mycorrhizal fungal colonization in multiple

lines of Bt maize. Am J Bot. 2012;99:700–707. doi:10.3732/ajb.1100529.
19. Tank JL, Rosi-Marshall EJ, Royer TV, et al. Occurrence of maize detritus and a transgenic insecticidal protein (Cry1Ab) within the stream network of an agricultural landscape. PNAS. 2010. doi:10.1073/pnas.1006925107.
20. Rosi-Marshall EJ, Tank JL, Royer TV, et al. Toxins in transgenic crop byproducts may affect headwater stream ecosystems. Proc Natl Acad Sci USA. 2007;104:16204-8. doi:10.1073/pnas.0707177104.
21. Bøhn T, Traavik T, Primicerio R. Demographic responses of Daphnia magna fed transgenic Bt-maize. Ecotoxicology. 2010;19:419-30. doi:10.1007/s10646-009-0427-x.

## 5.5 Myth: GM has enabled the adoption of environmentally friendly no-till farming

## Truth: GM has had little impact on the adoption of no-till farming, and no-till with GM herbicide-tolerant crops is not environmentally friendly

### Myth at a glance

GMO proponents claim that GM herbicide-tolerant crops, notably GM Roundup Ready (RR) crops, are environmentally friendly because they allow farmers to adopt the no-till system of cultivation. No-till farming avoids ploughing in order to conserve soil and water. It is claimed to reduce carbon dioxide emissions by sequestering more carbon in the soil.

In no-till cultivation of GM herbicide-tolerant crops, farmers try to control weeds through herbicide applications rather than mechanically, by ploughing.

However, USDA data show that the introduction of GM crops did not significantly increase no-till adoption.

A study comparing the environmental impact of GM RR and non-GM soy found that once the ecological damage caused by herbicides is taken into account, the negative environmental impact of GM soy is greater than that of non-GM soy in both no-till and tillage systems. Also, the adoption of no-till raised the negative environmental impact level, whether the soy was GM RR or non-GM.

No-till fields do not sequester more carbon than ploughed fields when carbon sequestration at soil depths greater than 30 cm is taken into account.

Claims of environmental benefits from no-till herbicide-tolerant farming systems are unjustified.

GMO proponents claim that GM herbicide-tolerant crops, notably GM Roundup Ready (RR) crops, are environmentally friendly because they allow farmers to adopt the no-till system of cultivation. No-till farming avoids ploughing in order to conserve soil and water. It is claimed to reduce carbon dioxide emissions by sequestering more carbon in the soil.

In no-till cultivation of GM herbicide-tolerant crops, farmers try to control weeds through herbicide applications rather than mechanically, by ploughing.

There are several problems with the inflated claims made for the environmental benefits of this farming system, which are detailed below.

## GM is not needed to practise no-till

No-till or low-till farming can be – and is – practised in chemically-based non-GM and agroecological farming. Farmers do not have to adopt GM crops or use herbicides to practise no-till.

## GM has not significantly increased the adoption of no-till

The vast majority of no-till and low-till adoption in the US occurred before GM crops came onto the market and rates of adoption have stagnated since, according to a US Department of Agriculture report. The report says that adoption of no-till and low-till for soybeans grew from 25% of the soybean acreage in 1990 to 48% in 1995, the 5-year period previous to the introduction of GM herbicide-tolerant soybeans. Growth of no-till and low-till increased further in 1996, the year herbicide-tolerant soybeans were introduced, but then stagnated to 50–60% in the following years.[1]

Biotechnology expert Dr Doug Gurian-Sherman of the Union of Concerned Scientists commented on the findings: "Roundup Ready crops have made no-till easier, but so have no-till seed drills, and Farm Bill incentives that went into effect in 1986. If you actually look at the additional adoption of no-till after 1996, it is only a few per cent in corn, almost nothing in cotton, and a little more in soy (maybe 5 to 10% of acres). So contrary to the widespread myth, the data do not support a major role of GM crops in the increase in no-till over the past few decades."[2]

## Claims of environmental benefits for no-till with GM are misleading

Claims of environmental benefits for GM herbicide-tolerant crops with no-till cultivation are misleading. One study compared the environmental impacts of growing GM RR and non-GM soy, using an indicator called Environmental Impact Quotient (EIQ). EIQ assesses the negative environmental impacts of the use of pesticides and herbicides on farm workers, consumers and ecology (fish, birds, bees and other beneficial insects).

The study found that in Argentina, the negative environmental impact of GM soy was higher than that of non-GM soy in both no-till and tillage systems, because of the herbicides used. These are broad-spectrum in nature – that is, they kill all plants except GM plants engineered to tolerate them. Also, the adoption of no-till raised the EIQ, whether the soy was GM RR or non-GM. The main reason for the increase in herbicides used in no-till systems was the spread of glyphosate-resistant superweeds.[3]

The spread of herbicide-resistant superweeds has undermined the GM no-till model of farming, forcing farmers back to ploughing and even pulling weeds by hand.[4]

### No-till farming does not sequester more carbon

Chemically-based agriculture is a major contributor to climate change, producing over 20% of greenhouse gas emissions.[5] GMO proponents claim that soil in no-till systems sequesters (stores) more carbon than ploughed soil, preventing the carbon from being released into the atmosphere as the greenhouse gas carbon dioxide and thus helping to mitigate climate change.

However, a comprehensive review of the scientific literature found that no-till fields sequester no more carbon than ploughed fields when carbon sequestration at soil depths greater than 30 cm is taken into account. Studies claiming to find carbon sequestration benefits from no-till only measure carbon sequestration down to a depth of about 30 cm and so do not give an accurate picture.[6]

## Conclusion

Claims of environmental benefits from no-till farming with GM crops are misleading and unjustified. No-till farming can be and is practised by chemically-based non-GM and agroecological growers and it is not necessary to grow GM crops to practise it. The introduction of GM crops has not significantly increased no-till adoption.

No-till farming with GM herbicide-tolerant crops is not environmentally friendly. A study carried out in Argentina found that the negative environmental impact of GM soy was higher than that of non-GM soy in both no-till and tillage systems, because of the herbicides used. No-till fields also do not sequester more carbon than ploughed fields when soil depths greater than 30 cm are taken into account.

## References


1. Fernandez-Cornejo J, McBride WD. The adoption of bioengineered crops. Agricultural Economic Report No. 810. Washington, DC: US Department of Agriculture; 2002. Available at: http://www.ers.usda.gov/publications/aer810/aer810.pdf.
2. Gurian-Sherman D. Comment on: Science, dogma and Mark Lynas. The Equation. http://blog.ucsusa.org/science-dogma-and-mark-lynas. Published January 24, 2013.
3. Bindraban PS, Franke AC, Ferrar DO, et al. GM-related sustainability: Agro-ecological impacts, risks and opportunities of soy production in Argentina and Brazil. Wageningen, the Netherlands: Plant Research International; 2009. Available at: http://bit.ly/Ink59c.
4. Neuman W, Pollack A. US farmers cope with Roundup-resistant weeds. New York Times. http://www.nytimes.com/2010/05/04/business/energy-environment/04weed.html?pagewanted=1&hp. Published May 3, 2010.
5. Intergovernmental Panel on Climate Change (IPCC). Working Group III: Mitigation. A Report of Working Group III of the Intergovernmental Panel on Climate Change. Geneva, Switzerland; 2001. Available at: http://www.ipcc.ch/ipccreports/tar/wg3/index.php?idp=21.
6. Baker JM, Ochsner TE, Venterea RT, Griffis TJ. Tillage and soil carbon sequestration – What do we really know? Agric Ecosyst Environ. 2007;118:1–5.

# 5.6 Myth: Roundup is a benign herbicide that makes life easier for farmers

## Truth: Roundup causes soil and plant problems that negatively impact yield

### Myth at a glance

Roundup and other glyphosate herbicides are not benign but have negative effects on soil and crops, some of which impact plant health and yield.

Glyphosate increases the incidence and severity of infection with Fusarium fungus, which is especially serious as Fusarium can harm humans and livestock.

Glyphosate binds (chelates) essential metal nutrients in the soil, making them unavailable to plants and impacting yield.

Glyphosate has been found to impair nitrogen fixation in plants and to impact yield in drought conditions.

Seed and agrochemical companies are marketing various "techno-fixes" to address these problems, tying farmers to a chemical treadmill.

GM Roundup Ready (RR) crops are marketed on the basis that Roundup is a safe herbicide that simplifies weed control and makes the farmer's life easier. But recent studies show that Roundup and glyphosate can accumulate in plants, have negative effects on soil organisms, and harm the growth and health even of soy plants that are genetically engineered to tolerate it. These effects may be partly responsible for yield decline (see Myth 5.1) and disease outbreaks found in GM Roundup Ready soy and maize.

## Glyphosate causes or exacerbates plant diseases

Manufacturers claim that glyphosate kills plants by inhibiting an enzyme necessary for plant growth. But research shows that glyphosate has another way of killing plants: it makes the plant more susceptible to disease, potentially leading to the plant's death from the disease. Spraying glyphosate on a plant is, according to US agronomist Michael McNeill, "like giving it AIDS".[1]

One possible mechanism for this process is suggested in a study on GM RR soybeans. The study found that once glyphosate is applied to the plant, it accumulates in the plant tissues and then is released into soil through the roots. There, it stimulates the growth of certain

> *"When you spray glyphosate on a plant, it's like giving it AIDS."*
> – Michael McNeill, agronomist and farm consultant, Iowa[1]

fungi, notably Fusarium, a fungus that causes wilt disease and sudden death syndrome in soy plants.[2] Other studies confirm the link between glyphosate applications and increased infection of plants with Fusarium.[3,4,5,6,7,8]

Fusarium is of especial concern because it does not only affect plants. It produces toxins that can enter the food chain and harm humans and livestock.[9] In pigs, Fusarium-contaminated feed is a reproductive toxin[10] and increases stillbirths.[11]

Glyphosate has also been shown to increase the incidence and severity of other fungal diseases in plants, including take-all in wheat[12] and Corynespora root rot in soy.[13]

In an attempt to combat soil-borne diseases such as Fusarium, in 2011 Monsanto marketed its new Roundup Ready 2 Yield soy seed with a proprietary fungicide/insecticide coating.[14] Such chemical treadmills are profitable for seed and chemical companies, but are costly to farmers and add to the toxic burden borne by humans, animals and the environment.

## Glyphosate makes nutrients unavailable to plants

Glyphosate binds (chelates) vital nutrients such as iron, manganese, zinc, and boron in the soil, preventing plants from taking them up.[15,16,17,18] So GM soy plants treated with glyphosate have lower levels of essential nutrients and reduced growth, compared with GM and non-GM soy controls not treated with glyphosate.[19,20] Lower nutrient uptake may partly account for the increased susceptibility of GM soy to disease,[2] as well as its lower yield.[3] It could also have implications for humans and animals that eat the crop, as it is less nutritious.

## Glyphosate impairs nitrogen fixation

The yield decline in GM RR soy may be partly due to glyphosate's negative impact on nitrogen fixation, a process that is vital to plant growth and depends on the beneficial relationship between the soy plants and nitrogen-fixing bacteria. In a greenhouse study of young RR soy plants, glyphosate delayed nitrogen fixation and reduced the growth of roots and sprouts, resulting in yield declines of up to 30%. In field studies, glyphosate had no such effect on GM RR soybean when there was adequate soil water throughout the growing season. However, glyphosate decreased biomass and seed yields in drought conditions.[21] Other studies have also linked glyphosate with impaired nitrogen fixation in plants.[22,23]

The mechanism of impaired nitrogen fixation in GM RR soybeans may be explained by a field study finding that glyphosate enters the root nodules and negatively affects the soil bacteria responsible for nitrogen fixation. Glyphosate inhibits root development, reducing root nodule biomass by up to 28%. It also reduces by up to 10% an oxygen-carrying protein, leghemoglobin, which helps bind nitrogen in soybean roots.[24]

To counter such problems, GMO seed and agrochemical companies have begun to market a "techno-fix" in the form of nitrogen-fixing bacterial inoculants, which are either applied to soy seed before sale or to the soil after sowing. The companies claim that this will increase yield potential.[25] However, a soybean inoculant evaluation trial conducted in Iowa concluded, "none of the inoculants resulted in a significant yield increase over the non-inoculated plots".[26] Inevitably, the costs of such treatments are borne by farmers.

## Conclusion

Roundup and other glyphosate herbicides are not benign but have negative effects on soil and crops, some of which impact plant health and yield. Glyphosate's link with Fusarium infection is especially serious as this fungus can harm humans and livestock. Seed and agrochemical companies are marketing various "techno-fixes" to address these problems, tying farmers to a chemical treadmill.

## References


1. Dodge J. Expert: GMOs to blame for problems in plants, animals. Boulder Weekly. http://www.boulderweekly.com/article-6211-expert-gmos-to-blame-for-problems-in-plants-animals.html. Published August 11, 2011.
2. Kremer RJ. Glyphosate affects soybean root exudation and rhizosphere microorganisms. Int J Anal Environ Chem. 2005;85:1165–1174.
3. Johal GS. Glyphosate effects on diseases of plants. Eur J Agron. 2009;31:144–152.
4. Johal GS, Rahe JE. Effect of soilborne plant-pathogenic fungi on the herbicidal action of glyphosate on bean seedlings. Phytopathology. 1984;74:950-955.
5. Sanogo S, Yang XB, Scherm H. Effects of herbicides on Fusarium solani f. sp. glycines and development of sudden death syndrome in glyphosate-tolerant soybean. Phytopathology. 2000;90:57-66. doi:10.1094/PHYTO.2000.90.1.57.
6. University of Missouri. MU researchers find fungi buildup in glyphosate-treated soybean field. 2000. Available at: http://web.archive.org/web/20130625073438/http://www.biotech-info.net/fungi_buildup.html.
7. Kremer RJ, Means NE. Glyphosate and glyphosate-resistant crop interactions with rhizosphere microorganisms. Eur J Agron. 2009;31:153–161.
8. Fernandez MR, Zentner RP, Basnyat P, Gehl D, Selles F, Huber D. Glyphosate associations with cereal diseases caused by Fusarium spp. in the Canadian prairies. Eur J Agron. 2009;31:133–143.
9. Food Standards Agency (UK). About mycotoxins. 2013. Available at: http://www.food.gov.uk/policy-advice/mycotoxins/about/#Fusariumtoxins.
10. Alm H, Brussow KP, Torner H, et al. Influence of Fusarium-toxin contaminated feed on initial quality and meiotic competence of gilt oocytes. Reprod Toxicol. 2006;22(1):44-50. doi:10.1016/j.reprotox.2005.11.008.
11. Diaz-Llano G, Smith TK. Effects of feeding grains naturally contaminated with Fusarium mycotoxins with and without a polymeric glucomannan mycotoxin adsorbent on reproductive performance and serum chemistry of pregnant gilts. J Anim Sci. 2006;84(9):2361-6. doi:10.2527/jas.2005-699.
12. Huber DM. Managing nutrition to control plant disease. Landbauforsch Volkenrode. 2007;57(4):313–322.
13. Huber DM. Association of severe Corynespora root rot of soybean with glyphosate-killed giant ragweed. Phytopathology. 2005;95:S45.
14. Monsanto. Get soybean and corn crops off to a good start in 2011 with Acceleron® seed treatment products. http://bit.ly/1ndlWoq. Published February 7, 2011.
15. Cakmak I, Yazici A, Tutus Y, Ozturk L. Glyphosate reduced seed and leaf concentrations of calcium, manganese, magnesium, and iron in non-glyphosate resistant soybean. Eur J Agron. 2009;31:114–119.
16. Neumann G, Kohls S, Landsberg E, Stock-Oliveira Souza K, Yamada T, Romheld V. Relevance of glyphosate transfer to non-target plants via the rhizosphere. J Plant Dis Prot. 2006;20:963–969.
17. Huber DM. What about glyphosate-induced manganese deficiency? Fluid J. 2007:20–22.
18. Bott S, Tesfamariam T, Candan H, Cakmak I, Römheld V, Neumann G. Glyphosate-induced impairment of plant growth and micronutrient status in glyphosate-resistant soybean (Glycine max L.). Plant Soil. 2008;312(1-2):185-194. doi:10.1007/s11104-008-9760-8.
19. Zobiole LH, de Oliveira RS, Visentainer JV, Kremer RJ, Bellaloui N, Yamada T. Glyphosate affects seed composition in glyphosate-resistant soybean. J Agric Food Chem. 2010;58:4517-22. doi:10.1021/jf904342t.
20. Zobiole LHS, de Oliveira RS, Huber DM, et al. Glyphosate reduces shoot concentrations of mineral nutrients in

glyphosate-resistant soybeans. Plant Soil. 2010;328:57–69.

21. King CA, Purcell LC, Vories ED. Plant growth and nitrogenase activity of glyphosate-tolerant soybean in response to foliar glyphosate applications. Agron J. 2001;93:179–186.
22. De María N, Becerril JM, García-Plazaola JI, Hernandez A, De Felipe MR, Fernandez-Pascual M. New insights on glyphosate mode of action in nodular metabolism: Role of shikimate accumulation. J Agric Food Chem. 2006;54(7):2621-2628. doi:10.1021/jf058166c.
23. Bellaloui N, Reddy KN, Zablotowicz RM, Mengistu A. Simulated glyphosate drift influences nitrate assimilation and nitrogen fixation in non-glyphosate-resistant soybean. J Agric Food Chem. 2006;54(9):3357-3364. doi:10.1021/jf053198l.
24. Reddy KN, Zablotowicz RM. Glyphosate-resistant soybean response to various salts of glyphosate and glyphosate accumulation in soybean nodules. Weed Sci. 2003;51:496–502.
25. Dekalb. Increase soybean yield potential with inoculants, protect with seed treatments. 2010. Available at: http://www.dekalb.ca/_uploads/documents/Agronomic_Information/SoybeanArchive/increase_soybean_yield.pdf.
26. Iowa State University Soybean Extension and Research Program. Seed inoculation. 2007. Available at: http://extension.agron.iastate.edu/soybean/production_seedinoc.html.

## 5.7 Myth: GM crops help biodiversity

## Truth: The herbicides used with GM crops harm biodiversity

### Myth at a glance

The UK government-funded Farm Scale Evaluations (FSEs) looked at the effects on farmland wildlife of the cultivation of four GM herbicide-tolerant crops, compared with non-GM crops grown under intensive chemically-based management.

The results for sugar beet and oilseed rape showed that GM herbicide-tolerant crop management reduced weeds and weed seeds and therefore would damage farmland wildlife.

For maize the results showed GM crop management to be better for wildlife than conventional chemically intensive management. However, the conventional weed control used the toxic herbicide atrazine, which was banned in Europe before the FSE results were published.

The outcome of the FSEs was that all but one of the GM crops tested were worse for biodiversity than non-GM crops grown under intensive chemically-based management. No GM crops were subsequently commercially planted in the UK.

In the late 1990s in the UK, concerns were expressed that the use of GM herbicide-tolerant crops might have an indirect impact on farmland biodiversity by reducing weeds in arable fields and field margins. Farmland birds, such as the skylark, were already badly affected by intensive arable production.

In the early 2000s the UK government decided to fund open field trials (the Farm Scale Evaluations or FSEs) to test the effects of GM crop management compared with conventional chemically intensive non-GM crop management. It appointed a consortium of research institutions to carry out the research over four years. The following GM crops were grown:

- Roundup Ready sugar beet and fodder beet
- Glufosinate ammonium-tolerant winter oilseed rape (canola)
- Glufosinate ammonium-tolerant spring oilseed rape
- Glufosinate ammonium-tolerant fodder maize (in which the whole crop was made into silage and fed to dairy cattle).[1]

> *"The commercialization of GM beet and oilseed rape could be disastrous for birds. The government is committed to reversing bird declines and has promised to ban GM crops if they damage the environment. The Farm Scale Evaluations show that two GM crops harm the environment and ministers now have no choice but to refuse their approval."*
> – Dr Mark Avery, director of conservation at the UK's Royal Society for the Protection of Birds (RSPB) and member of the UK government's Science Review Panel[12]

The researchers investigated whether the changes in weed management associated with herbicide-tolerant GM crops would reduce weed levels and have wider impacts on farmland biodiversity.[1] The direct toxic effects of herbicides on wildlife were not studied.

Each field was divided in half, with one half planted with a non-GM variety managed according to the farmer's normal practice, and the other half planted with a GM herbicide-tolerant variety.

The results for beet and oilseed rape showed that GM herbicide-tolerant crop management significantly reduced weeds and weed seeds and therefore would further damage farmland wildlife.[1,2,3,4,5,6,7,8,9]

For maize the results showed GM herbicide-tolerant crop management to be better for wildlife than conventional chemically intensive management.[1,2,3,4,5,6,7,8,9] However, this was because the conventional weed control used the highly toxic herbicide atrazine. Before the results of the FSEs were published, atrazine was banned in Europe.[10]

A more useful comparator for the GM herbicide-tolerant maize would have been maize grown in an organic or integrated pest management (IPM) system, which eliminate or reduce herbicide use. In the EU, this is not a purely idealistic notion. A 2009 European Directive asks member states to implement national plans to adopt integrated pest management and alternative approaches in order to reduce pesticide use.[11]

After the results of the FSEs were published the UK government announced that it would not approve the GM oilseed rape or sugar beet applications for commercial growing, but would approve the glufosinate-tolerant GM maize, known as Chardon LL. However, within a few weeks, the developer company Bayer (formerly Aventis) announced that it would not be commercializing this GM maize variety in the UK. The outcome was that no GM crops were approved for UK cultivation.[10]

## Conclusion

The overall outcome of the FSEs was that the management of all but one of the GM herbicide-tolerant crops tested were more damaging to farmland wildlife than the management of non-GM crops grown under a conventional chemically intensive system. GM maize was only found better for wildlife because the non-GM comparator was grown with the toxic herbicide atrazine.

## References


1. DEFRA. Managing GM crops with herbicides: Effects on farmland wildlife. Farmscale Evaluations Research Consortium and the Scientific Steering Committee; 2005. Available at: http://bit.ly/P8ocOW.
2. Hawes C, Haughton AJ, Osborne JL, et al. Responses of plants and invertebrate trophic groups to contrasting herbicide regimes in the Farm Scale Evaluations of genetically modified herbicide-tolerant crops. Philos Trans R Soc Lond B Biol Sci. 2003;358:1899-913. doi:10.1098/rstb.2003.1406.
3. Roy DB, Bohan DA, Haughton AJ, et al. Invertebrates and vegetation of field margins adjacent to crops subject to contrasting herbicide regimes in the Farm Scale Evaluations of genetically modified herbicide-tolerant crops. Philos Trans R Soc Lond B Biol Sci. 2003;358:1879-98. doi:10.1098/rstb.2003.1404.
4. Brooks DR, Bohan DA, Champion GT, et al. Invertebrate responses to the management of genetically modified herbicide-tolerant and conventional spring crops. I. Soil-surface-active invertebrates. Philos Trans R Soc Lond B Biol Sci. 2003;358:1847-62. doi:10.1098/rstb.2003.1407.
5. Heard MS, Hawes C, Champion GT, et al. Weeds in fields with contrasting conventional and genetically modified herbicide-tolerant crops. II. Effects on individual species. Philos Trans R Soc Lond B Biol Sci. 2003;358:1833-46. doi:10.1098/rstb.2003.1401.
6. Firbank LG. Introduction: The farm scale evaluations of spring-sown genetically modified crops. Phil Trans R Soc Lond. 2003;358:1777–1778.
7. Bohan DA, Boffey CW, Brooks DR, et al. Effects on weed and invertebrate abundance and diversity of herbicide management in genetically modified herbicide-tolerant winter-sown oilseed rape. Proc Biol Sci. 2005;272:463-74. doi:10.1098/rspb.2004.3049.
8. BBC News. Q&A: GM farm-scale trials. http://news.bbc.co.uk/2/hi/science/nature/3194574.stm. Published March 9, 2004.
9. Amos J. GM study shows potential "harm." BBC News. http://news.bbc.co.uk/1/hi/sci/tech/4368495.stm. Published March 21, 2005.
10. Friends of the Earth. Press briefing: Government to publish the final results of the farm scale evaluations of genetically modified crops: Winter oilseed rape. London, UK; 2004. Available at: http://www.foe.co.uk/sites/default/files/downloads/government_to_publish_the.pdf.
11. European Parliament and Council. Directive 2009/128/EC of 21 October 2009 establishing a framework for Community action to achieve the sustainable use of pesticides. Off J Eur Union. 2009:71–84.
12. Brown A, Ross T. Two GM crops are "worse for wildlife." The Independent (UK). http://www.mindfully.org/GE/2003/Trials-Threat-Wildlife16oct03.htm. Published October 16, 2003.

# 5.8 Myth: GM crops bring economic benefits to farmers

## Truth: Economic impacts of GM crops on farmers are mixed and depend on many factors

### Myth at a glance

The economic impacts of GM crops on farmers are variable and depend on complex factors.

Well-controlled studies giving reliable data are rare.

Consolidation in the seed market has led to steep increases in the price of GM seed as compared with non-GM seed.

The question of economic impacts of GM crops on farmers is complex and a thorough examination is beyond the scope of this report. Results vary and depend on many factors, including:

- The crops and agricultural practices that the adoption of the GM crop is being compared with (for example, subsistence farming, or high-yielding non-GM varieties of the same crop).
- GM crop adopter and non-adopter characteristics, as described by Fernandez-Cornejo and colleagues in a report for the US Department of Agriculture. The authors explain that these two populations cannot be compared in a controlled scientific manner from survey data, since adopters and non-adopters may be systematically different from each other – for example, in management ability.[1] Glenn Davis Stone noted that this same confounding factor applies to some studies claiming economic benefits to farmers in India who adopted GM Bt cotton.[2]
- Cultivation bias, which Stone defines as resulting from seeds that are relatively costly, or for which the farmer has high expectations, being planted in preferred locations and given greater care and expense than other seeds. Stone found that this applied to GM Bt cotton in India and has not been properly controlled for in many studies on the economic impacts of the crop.[2]

Additional factors affecting economic impacts include:

- Suitability of the crop for local conditions
- Access to irrigation
- Climate
- Cost of seed

> *"Farm financial impacts [of adopting GM crops] appear to be mixed or even negative."*
> – J. Fernandez-Cornejo, W. D. McBride, "The adoption of bioengineered crops", US Department of Agriculture[3]

- Pest and disease prevalence
- Cost of weed and pest management
- Subsidies and incentives offered by governments or corporations
- Availability of markets for the crop.

The following studies give an overview of the issue.

### Fernandez-Cornejo and colleagues (2014)

This report on the adoption of GM crops in the US concluded, "The profitability of GE seeds for individual farmers depends largely on the value of the yield losses mitigated and the associated pesticide and seed costs. GE adoption tends to increase net returns if the value of yield losses mitigated plus the pesticide savings exceeds the additional GE seed costs… The impacts of GE crop adoption vary by crop and technology. Most studies show that adoption of Bt cotton and Bt corn is associated with increased net returns… However, some studies of Bt corn show that profitability is strongly dependent on pest infestation levels. The impact of HT seeds (for corn, cotton, and soybeans) on net returns depends on many factors."[1]

### Fernandez-Cornejo and McBride (2002)

This report on farm-level economic impacts of adopting GM crops found that they were "mixed or even negative". The report, mostly based on data from USDA surveys, found that adoption of herbicide-tolerant maize had a positive effect on net returns, but the effect was negative for Bt maize. GM soybeans had no effect either way.[3]

### Gómez-Barbero and Rodríguez-Cerezo (2006)

This review for the European Commission of the economic impact of the main GM crops worldwide found that herbicide-tolerant soybeans had a negative effect on US farmers' income. But the same crop brought income gains to Argentine farmers, due to lower prices for GM seed in that country.[4]

Why do US farmers adopt GM soy if it brings no financial gain? The authors suggested that the reason may be simpler weed control,[4] though the data cited to back up this claim pre-date the explosion of herbicide-resistant superweeds that have caused management challenges for farmers (see Myth 5.2).

The review found that GM Bt cotton in China had produced economic gains for farmers, mostly because of reduced expenditure on pesticide sprays. GM Bt cotton in India was claimed to provide economic benefits, though with considerable "local variability".[4]

However, many studies on GM Bt cotton in India suffer from the confounder of uncontrolled-for GM crop adopter/non-adopter variables described by Fernandez-Cornejo[1] and Stone[2] and from the cultivation bias described by Stone.[2]

In addition, many of these studies were carried out before the full impact of pest resistance and emergence of secondary pests had been experienced by Chinese and Indian farmers (see Myth 5.3).

### Morse and colleagues (2005)

This study found that GM Bt cotton in India produced better profit margins for farmers than non-GM cotton. However, the authors pointed out that these benefits will only be sustained if pests do not evolve resistance to Bt cotton.[5] Recent studies suggest that they are already evolving resistance (see Myth 5.3). These findings appear to be confirmed by a leaked advisory from the Indian government that blamed the failure of GM Bt cotton for the spate of farmer suicides across the subcontinent. The advisory stated, "Cotton farmers are in a deep crisis since shifting to Bt cotton. The spate of farmer suicides in 2011–12 has been particularly severe among Bt cotton farmers." The advisory said that Bt cotton's success had only lasted five years. Since then, yields had fallen and pest attacks had increased: "In fact cost of cotton cultivation has jumped... due to rising costs of pesticides. Total GM Bt cotton production in the last five years has reduced."[6]

## Importance of information that is independent of industry

Some who claim that GM crops bring economic benefits to farmers cite upbeat reports written by Graham Brookes and Peter Barfoot, the directors of a private consultancy firm called PG Economics, which has GM and agrochemical firms as its primary clients.[7] Generally, PG Economics' reports are commissioned by GM firms or industry lobby groups such as Agricultural Biotechnology in Europe,[8] the membership of which consists of GM seed companies.[9]

Agronomist Dr Charles Benbrook has published a detailed critique of what he termed PG Economics' "creative – and highly questionable – methodological strategies" in calculating pesticide use on GM crops. These strategies included using data from partly or entirely industry-sponsored sources in preference to widely accepted data from the US government and projecting an increase in the total rate of herbicide application on non-GM crop acres, despite the trend in favour of low-dose herbicides.[10]

Most of PG Economics' reports are not peer-reviewed and rely heavily on industry data. Some are published in a peer-reviewed journal – the Journal of Agrobiotechnology Management & Economics,[11] otherwise known as AgBioForum.[12] AgBioForum is funded by the Illinois-Missouri Biotechnology Alliance (IMBA).[13] The IMBA states that its purpose is "to fund biotechnology research... directed at expanding the volume of profitable businesses in the US food and agricultural sector".[14] The IMBA has been funded since 1997 by the US

Department of Agriculture. Its grant-funded status was obtained with the help of Richard Mahoney, who was at the time the CEO of Monsanto.[15]

## Rising cost of GM seed and decreased seed choice

An important factor in assessing the economic impact of GM crops is the cost of seed. In the US, where GM firms dominate the seed market, a 2009 report documented that prices for GM seeds increased dramatically compared with prices for non-GM and organic seeds. This cut average farm incomes for US farmers growing GM crops. The $70 per bag price set for RR2 soybeans for 2010 was twice the cost of conventional seed and reflected a 143% increase in the price of GM seed since 2001.[16]

Farmers have little choice but to tolerate such price hikes because of consolidation within the seed industry. In other words, the GM industry dictates which seed varieties are available. In 2008, 85% of GM maize patents and 70% of non-maize GM plant patents in the US were owned by the top three seed companies: Monsanto, DuPont, and Syngenta. Even these three companies are not independent of each other but increasingly network to cross-license GM seed traits.[17]

The largest of the big three companies is Monsanto. In 2010 Monsanto raised its prices for its RR2 soybeans and SmartStax maize seeds so steeply that the US Department of Justice launched (but never completed) an investigation into the consolidation of agribusiness firms that has led to anti-competitive pricing and monopolistic practices. Farmers actively gave evidence against Monsanto and other seed companies.[18,19]

## Conclusion

The economic impacts of GM crops on farmers are variable and depend on complex factors. Well-controlled studies giving reliable data are rare. However, consolidation in the seed market has led to steep increases in the price of GM seed as compared with non-GM seed.

## References


1. Fernandez-Cornejo J, Wechsler S, Livingston M, Mitchell L. Genetically engineered crops in the United States. Washington, DC: US Department of Agriculture; 2014. Available at: http://www.ers.usda.gov/publications/err-economic-research-report/err162.aspx#.U0P_qMfc26x.
2. Stone GD. Constructing facts: Bt cotton narratives in India. Econ Polit Wkly. 2012;47(38):62-70.
3. Fernandez-Cornejo J, McBride WD. The adoption of bioengineered crops. Agricultural Economic Report No. 810. Washington, DC: US Department of Agriculture; 2002. Available at: http://www.ers.usda.gov/publications/aer810/aer810.pdf.
4. Gómez-Barbero M, Rodríguez-Cerezo E. Economic impact of dominant GM crops worldwide: A review. European Commission Joint Research Centre: Institute for Prospective Technological Studies; 2006. Available at: http://ftp.jrc.es/EURdoc/eur22547en.pdf.
5. Morse S, Bennett RM, Ismael Y. Genetically modified insect resistance in cotton: Some farm level economic impacts in India. Crop Prot. 2005;24:433–440.
6. Haq Z. Ministry blames Bt cotton for farmer suicides. Hindustan Times. http://bit.ly/IrPRRZ. Published March 26, 2012.
7. PG Economics. Who we are. 2013. Available at: http://www.pgeconomics.co.uk/who-we-are.php.
8. Brookes G, Barfoot P. Co-existence of GM and non GM arable crops: the non GM and organic context in the EU. Dorchester, UK: PG Economics; 2004.
9. Gate2Biotech. 2014. Available at: http://www.gate2biotech.com/agricultural-biotechnology-in/.
10. Benbrook CM. Impacts of genetically engineered crops on pesticide use in the United States: The first

thirteen years. Washington, DC: The Organic Center; 2009. Available at: http://www.organic-center.org/reportfiles/13Years20091126_FullReport.pdf.
11. Brookes G. Global impact of biotech crops: Environmental effects, 1996–2008. AgBioForum. 2010;13(1):76–94.
12. AgBioForum (The Journal of Agrobiotechnology Management & Economics). Home page [website]. 2013. Available at: http://www.agbioforum.org/.
13. AgBioForum (The Journal of Agrobiotechnology Management & Economics). Welcome [website]. 2013. Available at: http://www.agbioforum.org/welcome.htm.
14. Illinois-Missouri Biotechnology Alliance (IMBA). Home page. 2010. Available at: http://www.imba.missouri.edu/.
15. Illinois-Missouri Biotechnology Alliance (IMBA). History. 2010. Available at: http://www.imba.missouri.edu/index.php?region=3.
16. Benbrook CM. The magnitude and impacts of the biotech and organic seed price premium. Washington, DC: The Organic Center; 2009. Available at: http://www.organic-center.org/reportfiles/Seeds_Final_11-30-09.pdf.
17. Howard P. Visualizing consolidation in the global seed industry: 1996–2008. Sustainability. 2009;1:1266-1287.
18. Neuman W. Rapid rise in seed prices draws US scrutiny. New York Times. http://www.nytimes.com/2010/03/12/business/12seed.html?_r=1. Published March 11, 2010.
19. Kirchgaessner S. DOJ urged to complete Monsanto case. Financial Times. http://www.ft.com/cms/s/0/6327dfda-a3ef-11df-9e3a-00144feabdc0.html. Published August 9, 2010.

## 5.9 Myth: GM crops increase farmer choice
## Truth: GM-adopting countries have reduced farmer choice

### Myth at a glance

It is often claimed that the adoption of GM crops by a country increases farmer choice.

But countries that have adopted GM seeds have decreased seed choices. Consolidation in the seed market has led to the big seed companies, which are heavily invested in patented GM technology, withdrawing high-performing competing non-GM seeds from the market. This trend has been documented in the US, Brazil, and India.

A study on farmer seed choices in Europe found that the GM-adopting country, Spain, had fewer seed choices on offer to farmers than non-GM adopting countries. Moreover, GM-adopting countries, including the US, had no yield advantage.

It is often claimed that the adoption of GM crops by a country increases farmers' choice of which seeds to plant. But this claim is not supported by evidence and on the contrary, there is evidence that once a country adopts GM crops, seed choice decreases.

This happens because a few companies own a large proportion of the seed market.[1] These companies are heavily invested in patented GM technology and have been able to restrict the availability of competing non-GM seed or withdraw it altogether from the market.

For example, a 2011 media report said that seed companies had responded to farmer concern about the high price and less than impressive performance of GM seed by withdrawing a non-GM variety of maize that gave higher yields. The report added that the companies are raising the prices of herbicides used by non-GM farmers to artificially increase the cost of non-GM production.[2]

In India, non-GM cotton seeds have been withdrawn from the market.[3,4,5] The same process has happened for non-GM soybean seeds in Brazil, forcing farmers to buy GM seed, as reported by Pierre Patriat, the president of APROSMAT, the association of seed producers of Mato Grosso. Patriat said that the trend threatens seed and food sovereignty and security.[6]

Similarly in the US, farmers disillusioned with GM crops are unable to return to planting non-GM seeds because they are not available in the marketplace, as reported in British farmer Michael Hart's documentary film, Farmer to Farmer.[7]

The result of these developments is that farmers are forced into dependency on the GM industry. Such reports expose claims that GM crops increase "farmer choice" – and that countries that do not adopt GMOs have reduced choice – as disingenuous.

## Choice of seed decreases in GM-adopting country

GMO proponents' claims that farmers in countries that do not adopt GM crops have fewer seed options were tested in a research study on European countries with differing degrees of GM adoption. The study found that far from offering greater farmer choice, adoption of GM crops was accompanied by decreasing seed choice. Along with the increasing adoption of GM crops in Spain, the GM maize-adopting country in the study, came a decline in farmers' seed choices. In the non-adopting European countries, farmers had more maize varieties available to them today than they had in the 1990s, despite restricting GM varieties. Moreover, there was no yield advantage in GM-adopting countries, even when the analysis was extended to the US.[8]

## Conclusion

Countries that have adopted GM crops have seen seed choice decrease. Seed market consolidation has led to competing high-performing non-GM seed varieties being withdrawn from the market, restricting farmer choice.

## References


1. Howard P. Visualizing consolidation in the global seed industry: 1996–2008. Sustainability. 2009;1:1266-1287.
2. Roseboro K. Iowa organic farmer says non-GMO corn outperforms GMO. The Organic & Non-GMO Report. http://www.non-gmoreport.com/articles/april2011/organicnongmocornoutperformsgmo.php. Published April 1, 2011.
3. Roseboro K. Scientist: GM technology has exacerbated pesticide treadmill in India. The Organic & Non-GMO Report. http://www.non-gmoreport.com/articles/february2012/gmtechnologypesticideindia.php. Published February 1, 2010.
4. Aaronson T. The suicide belt. Columbia City Paper. http://www.gmfreecymru.org.uk/documents/suicidebelt.html. Published November 10, 2009.
5. Disappearing non-GM cotton – ways forward to maintain diversity, increase availability and ensure quality of non-GM cotton seed. Karnataka, India: Research Institute of Organic Agriculture (FiBL); 2011. Available at: http://www.fibl.org/fileadmin/documents/en/news/2011/ProceedingNationalWorkshop_DisappearingNon-GMCotton.pdf.
6. Patriat P. Speech delivered at the association of seed producers of Mato Grosso, on May 11, 2011 at the soy industry conference SEMEAR 2011 in Sao Paulo, Brazil. GMWatch. 2012. Available at: http://www.gmwatch.org/latest-listing/1-news-items/14092.
7. Hart M. Farmer to farmer: The truth about GM crops [film]. http://gmcropsfarmertofarmer.com/film.html. Published 2011.
8. Hilbeck A, Lebrecht T, Vogel R, Heinemann JA, Binimelis R. Farmer's choice of seeds in four EU countries under different levels of GM crop adoption. Environ Sci Eur. 2013;25(1):12. doi:10.1186/2190-4715-25-12.

# 5.10 Myth: GM crops can "coexist" with non-GM and organic crops

## Truth: Co-existence means widespread contamination of non-GM and organic crops

### Myth at a glance

"Coexistence" of GM with non-GM conventionally farmed and organic crops inevitably results in GM contamination of the non-GM and organic crops. This removes choice from farmers and consumers, forcing everyone to produce and consume crops that are potentially GM-contaminated into the indefinite future.

GM contamination cannot be recalled. On the contrary, since GMOs are living organisms, they are likely to persist and proliferate.

There have been numerous GM contamination events since GMOs were first released, since the GMO industry cannot control the spread of its patented GM genes. These contamination events have cost the food and GMO industry and the US government millions of dollars in lost markets, legal damages and compensation schemes for producers, and product recalls.

GMO industry representatives used to claim that GM contamination of non-GM crops would not occur and that farmers' and consumers' choice would be preserved.[1] After it became clear that this was false, the GMO industry shifted the argument to lobbying for "co-existence" of GM, non-GM conventionally farmed, and organic crops. It argued that farmers should be able to choose to plant GM crops if they wish and implied that no serious problems would be caused for non-GM and organic farmers.[2]

But experience has shown that the arrival of GM crops in a country removes choice. "Coexistence" rapidly results in widespread contamination of non-GM crops, resulting in lost markets. Contamination occurs through cross-pollination, spread of GM seed by farm machinery, and inadvertent mixing during storage. Farmers are gradually forced to grow GM crops or have their non-GM crops contaminated.

Scientific surveys confirm that GM contamination is unavoidable once GM crops are grown in a region. For example, GM herbicide-tolerant oilseed rape (canola) seed can persist and remain viable in soil for years. GM herbicide-resistant "volunteers" – plants that were not deliberately planted but are the result of the shedding of seeds from GM crops previously grown in the field – were found growing ten years after the GM oilseed rape crop had been planted.[3] GM herbicide-resistant oilseed rape was found to be thriving in the wild in North Dakota, often far from areas of agricultural production. GM genes were present in 80% of the wild canola plants found.[4,5]

## Who is liable for GM contamination?

In countries where legal liability for GM contamination is clearly established, GM crop cultivation has become severely restricted. In Germany, a law has been passed making farmers who grow GM crops liable for economic damages to non-GM and organic farmers resulting from GM contamination.[6,7] The planting of GM crops in the country rapidly declined and had been abandoned by 2012.[8] The fact that farmers who previously chose to grow GM crops have ceased to do so because they could be held liable for damages is clear evidence that coexistence is impossible.

The GM seed industry also knows it cannot contain or control its GM genes. In 2011, after years of industry lobbying, the EU dropped its policy of zero tolerance of animal feed with unapproved GMOs, allowing contamination of up to 0.1%.[9,10,11] In doing so, it granted industry release from liability for damages resulting from GM contamination with up to 0.1% of GM crop varieties ("Low Level Presence") that are under evaluation but not yet approved in the EU.[9]

In the US, the courts have recognized that GM crops are likely to contaminate non-GM crops. Two court rulings temporarily reversed US Department of Agriculture (USDA) approvals for the commercial planting of GM sugar beet and GM alfalfa. The courts ordered the USDA to halt the planting of the GM crops until it had completed an environmental impact statement (EIS) on the environmental and economic effects of contamination of non-GM crops.[12]

In the case of GM sugar beet, the USDA defied the court order and allowed farmers to continue planting the crop while it worked on the EIS. In the case of GM alfalfa, USDA completed an EIS in which it admitted that cross-contamination with non-GM alfalfa could occur and that the economic interests of non-GM growers could be harmed. But, bowing to heavy lobbying from the GM industry, USDA "deregulated" GM alfalfa, an action that superseded the court ruling and allowed planting of the crop without restriction.[12]

## GM contamination has had severe economic consequences

GM contamination of crops has had severe economic consequences, threatening the livelihoods of farmers who receive premiums for growing organic and GM-free crops and blocking export markets to countries with strict regulations on GMOs.

Examples of GM contamination events include:

- In 2011 an unauthorized GM Bt pesticidal rice, Bt63, was found in baby formula and rice noodles on sale in China.[13] Contaminated rice products were also found in Germany,[14] Sweden,[15] and New Zealand, where the discovery led to product recalls.[16] GM Bt rice has not been shown to be safe for human consumption. Bt63 contamination of rice imports into the EU was still being reported in 2012.[17]

- In 2006 an unapproved experimental GM rice, grown for only one year in experimental plots, was found to have contaminated the US rice supply and seed stocks.[18] Contaminated rice was found as far away as Africa, Europe, and Central America. In 2007 US rice exports were down 20% from the previous year as a result of the GM contamination.[19] In 2011 the company that developed the GM rice, Bayer, agreed to pay $750 million to settle lawsuits brought by 11,000 US farmers whose rice crops were contaminated.[20] A court ordered Bayer to pay $137 million in damages to Riceland, a rice export company, for loss of sales to the EU.[21]
- In 2009 an unauthorized GM flax called CDC Triffid contaminated Canadian flax seed supplies, resulting in the collapse of Canada's flax export market to Europe.[22,23]
- In Canada, contamination from GM oilseed rape has made it virtually impossible to cultivate organic non-GM oilseed rape.[24]

## GM contamination: The learning process

*"OK, we know that cross-pollination will occur but we've got thirty years of experience to say we know how far pollen will travel. And therefore what we've done is we'll grow a GM crop at a distance away from a non-GM crop, so the people that want non-GM can buy non-GM, and the people that want GM can buy GM. The two will not get mixed up. Everybody will have the right to choose."*
– Paul Rylott, seed manager for Aventis CropScience (now Bayer), BBC television broadcast, 2000[1]

*"GM farming cannot 'coexist' in Europe without either accepting widespread GM contamination of non-GM crops or major changes to farming practices."*
– Friends of the Earth Europe, 2006[33]

*"If some people are allowed to choose to grow, sell and consume GM foods, soon nobody will be able to choose food, or a biosphere, free of GM. It's a one way choice, like the introduction of rabbits or cane toads to Australia; once it's made, it can't be reversed."*
– Roger Levett, specialist in sustainable development, 2008[34]

*"The AC21 [USDA Advisory Committee on Biotechnology and 21st Century Agriculture] has wrestled with identifying and quantifying actual economic losses to farmers resulting from unintended presence of GE material in their crops… There are… clear data that some consignments of identity-preserved and organic commodities have been tested and found to contain GE material in amounts that exceed contractual requirements or de facto market standards. Such rejected shipments pose problems for those farmers whose loads have been rejected."*
– USDA Advisory Committee on Biotechnology and 21st Century Agriculture, 2012[35]

- Organic maize production in Spain has dropped as the acreage of GM maize production has increased, due to contamination by cross-pollination with GM maize.[25]
- In 2000 GM StarLink maize, produced by Aventis (now Bayer CropScience), was found to have contaminated the US maize supply. StarLink had been approved for animal feed but not for human consumption. The discovery led to recalls of StarLink-contaminated food products across the US, spreading to Europe, Japan, Canada, and other countries. Costs to the food industry are estimated to have been around $1 billion.[26] One study estimated that the StarLink incident resulted in $26 million to $288 million in lost revenue for producers in market year 2000/2001.[27] In addition, the US government bore indirect costs of between $172 and $776 million through the USDA's Loan Deficiency Payments Program, which offers producers short-term loans and direct payments if the price of a commodity crop falls below the loan rate.[28] Aventis paid $110 million to farmers who brought a class action suit against the company[29] and spent another $110 million buying back StarLink-contaminated maize.[18] Researchers estimated that the presence of StarLink in the food supply caused a 6.8% drop in the price of maize, lasting for one year.[30]

As no official body keeps records of GM contamination incidents, Greenpeace and Genewatch UK have stepped into the gap with their GM Contamination Register.[31] In the years 2005–2007 alone, 216 contamination incidents were recorded in the database.[32]

## Conclusion

"Coexistence" of GM with non-GM and organic crops inevitably results in GM contamination of the non-GM and organic crops. This removes choice from farmers and consumers, forcing everyone to produce and consume crops that are potentially GM-contaminated into the indefinite future.

GM contamination cannot be recalled. On the contrary, since GMOs are living organisms, they are likely to persist and proliferate.

There have been numerous GM contamination events since GMOs were first released, since the GMO industry cannot control the spread of its patented GM genes. These contamination events have cost the food and GMO industry and the US government millions of dollars in lost markets, legal damages and compensation schemes for producers, and product recalls.

## References


1. Rylott P. Matter of Fact [television broadcast]. BBC2 Eastern Region. October 12, 2000.
2. SCIMAC (Supply Chain Initiative on Modified Agricultural Crops. GM crop co-existence in perspective. 2006. Available at: http://sbc.ucdavis.edu/old_files/25542.pdf.
3. D'Hertefeldt T, Jørgensen RB, Pettersson LB. Long-term persistence of GM oilseed rape in the seedbank. Biol Lett. 2008;4:314–317.
4. Gilbert N. GM crop escapes into the American wild. Nature. 2010. Available at: http://www.nature.com/news/2010/100806/full/news.2010.393.html.
5. Black R. GM plants "established in the wild." BBC News. http://www.bbc.co.uk/news/science-environment-10859264. Published August 6, 2010.
6. Bhattacharya S. German farmers to be liable for GM contamination. New Sci. 2004. Available at: http://www.newscientist.com/article/dn6729-german-farmers-to-be-liable-for-gm-contamination.html.
7. Hogan M, Niedernhoefer D. German court upholds GMO planting curbs. Reuters. http://uk.reuters.com/article/2010/11/24/us-germany-gmo-idUSTRE6AN55420101124. Published November 24, 2010.
8. Friends of the Earth Europe. GM crops irrelevant in Europe. 2013. Available at: http://www.stopthecrop.org/sites/

default/files/content/attachments/foee_factsheet_feb_2013_gmcrops_irrelevant_in_europe.pdf.
9. European Commission. Commission Regulation (EU) No 619/2011 of 24 June 2011 laying down the methods of sampling and analysis for the official control of feed as regards presence of genetically modified material for which an authorisation procedure is pending or the authorisation of which has expired. Off J Eur Union. 2011:9–15.
10. Doward J. GM crops to be allowed into Britain under controversial EU plans. The Observer. http://www.guardian.co.uk/environment/2011/feb/06/genetically-modified-crops-uk. Published February 6, 2011.
11. ENDS Europe. EU states back 0.1% GM contamination limit. 2011. Available at: http://www.endseurope.com/25650/eu-states-back-01-gm-contamination-limit.
12. Waltz E. Industry exhales as USDA okays glyphosate resistant alfalfa. Nat Biotechnol. 2011;29:179–181.
13. Greenpeace. Children and infants in China at risk of eating food contaminated by illegal GE rice. http://www.greenpeace.org/eastasia/press/releases/food-agriculture/2011/ge-rice-baby-food/. Published April 20, 2011.
14. Greenpeace and GeneWatch UK. Germany finds unauthorised genetically modified (Bt63) rice noodles. GM Contamination Register. http://bit.ly/1nEKmEO. Published June 15, 2011.
15. Greenpeace and GeneWatch UK. Sweden finds unauthorised genetically modified (Bt63) rice. GM Contamination Register. http://bit.ly/1kXDCSP. Published June 27, 2011.
16. New Zealand Food Safety Authority (NZFSA). Unauthorised GM rice product found and withdrawn. http://www.foodsafety.govt.nz/elibrary/industry/Unauthorised_Rice-Zealand_Food.htm. Published July 30, 2008.
17. Eurofins. New regulations concerning GMO rice from China. Eurofins Food Testing Newsletter No. 38. http://www.eurofins.de/food-analysis/information/food-testing-newsletter/food-newsletter-38/gmo-rice-from-china.aspx. Published March 2012.
18. Blue EN. Risky business: Economic and regulatory impacts from the unintended release of genetically engineered rice varieties into the rice merchandising system of the US. Greenpeace; 2007. Available at: http://www.greenpeace.org/raw/content/international/press/reports/risky-business.pdf.
19. Reuters. Mexico halts US rice over GMO certification. http://www.gmwatch.org/latest-listing/1-news-items/3625. Published March 16, 2007.
20. Harris A, Beasley D. Bayer agrees to pay $750 million to end lawsuits over gene-modified rice. Bloomberg. http://www.bloomberg.com/news/2011-07-01/bayer-to-pay-750-million-to-end-lawsuits-over-genetically-modified-rice.html. Published July 2, 2011.
21. Fox JL. Bayer's GM rice defeat. Nat Biotechnol. 2011;29(473). Available at: http://www.nature.com/nbt/journal/v29/n6/full/nbt0611-473c.html.
22. Dawson A. CDC Triffid flax scare threatens access to no. 1 EU market. Manitoba Cooperator. http://www.manitobacooperator.ca/2009/09/17/cdc-triffid-flax-scare-threatens-access-to-no-1-eu-market/. Published September 17, 2009.
23. Dawson A. Changes likely for flax industry. Manitoba Cooperator. http://www.gmwatch.org/component/content/article/11541. Published September 24, 2009.
24. Organic Agriculture Protection Fund Committee. Organic farmers seek Supreme Court hearing. 2007. Available at: http://bit.ly/1iGdQla.
25. Binimelis R. Coexistence of plants and coexistence of farmers: Is an individual choice possible? J Agric Environ Ethics. 2008;21:437–457.
26. Macilwain C. US launches probe into sales of unapproved transgenic corn. Nature. 2005;434(423). Available at: http://www.nature.com/nature/journal/v434/n7032/full/nature03570.html.
27. Schmitz TG, Schmitz A, Moss CB. The economic impact of StarLink corn. Agribusiness. 2005;21(3):391–407.
28. United States Government Accountability Office (GAO). Genetically engineered crops: Agencies are proposing changes to improve oversight, but could take additional steps to enhance coordination and monitoring: Report to the Committee on Agriculture, Nutrition, and Forestry, US Senate. Washington, DC; 2008. Available at: http://www.gao.gov/assets/290/283060.pdf.
29. Arasu KT. US farmers reach $110 million StarLink settlement. Reuters. February 7, 2003.
30. Carter C, Smith A. Estimating the market effect of a food scare: The case of genetically modified StarLink corn. Rev Econ Stat. 2007;89(3).
31. Greenpeace and GeneWatch UK. GM contamination register. 2014. Available at: http://www.gmcontaminationregister.org/index.php?content=ho.
32. Greenpeace and GeneWatch UK. GM contamination register report 2007. Amsterdam, The Netherlands: Greenpeace International; 2008. Available at: http://www.greenpeace.org/international/Global/international/planet-2/report/2008/2/gm-contamination-register-2007.pdf.
33. Friends of the Earth Europe. Contaminate or legislate? European Commission policy on "coexistence." Brussels, Belgium; 2006. Available at: http://www.foeeurope.org/sites/default/files/press_releases/contaminate_or_legislate%5B1%5D.pdf.
34. Levett R. Choice: Less can be more. Food Ethics. 2008;3(3):11.
35. USDA Advisory Committee on Biotechnology and 21st Century Agriculture (AC21). Enhancing coexistence: A report of the AC21 to the Secretary of Agriculture. Washington, DC; 2012. Available at: http://www.usda.gov/documents/ac21_report-enhancing-coexistence.pdf.

# 5.11 Myth: Horizontal gene transfer from GM crops into bacteria or higher organisms is unlikely or of no consequence

# Truth: GM genes can escape into the environment by horizontal gene transfer with potentially serious consequences

## Myth at a glance

Horizontal gene transfer (HGT) is the movement of genetic material between unrelated species through a mechanism other than reproduction.

It is often claimed that HGT from GM crops into bacteria, animals, or humans is unlikely or of no consequence. But independent scientists have warned that GM genes could escape from GM crops into other organisms through HGT.

HGT from plants into other plants or animals does appear to be a low-frequency event.

However, the routes of HGT that are most likely to occur are DNA uptake by bacteria in the environment or the digestive tract. There is good evidence that the latter has already happened in the intestinal bacteria of humans who eat GM soy.

Other scenarios involving HGT by the pathogenic bacterium A. tumefaciens or by viruses are less probable. But given the wide distribution of GM crops and their intended use over decades, even low probabilities translate into a high likelihood that HGT events will occur. It is just a matter of time.

The negative impacts and risks associated with HGT must be taken into account in considering the overall biosafety of any GM crop.

Most GM contamination incidents occur through cross-pollination, contamination of seed stocks, or failure to segregate GM from non-GM crops after harvest. But for years, scientists have warned that GM genes could also escape from GM crops into other organisms through what is known as horizontal gene transfer (HGT). HGT is the movement of genetic material between individuals through a mechanism other than reproduction. Those individuals could be of the same or a different species. Reproduction, in contrast, is known as vertical gene transfer because the genes are passed down through the generations from parent to offspring within a species or closely related species.

Based on very limited experimental data, HGT from plants into bacteria or multicellular organisms (plants, animals, or fungi) is believed to be rare, although HGT is acknowledged to occur frequently between different species of bacteria and more rarely between higher species by certain mechanisms. The EU-supported website GMO Compass states that HGT from plants to bacteria "can only be demonstrated under optimized laboratory conditions."[1]

Gijs Kleter, a member of the European Food Safety Authority's (EFSA) GMO Panel and for some years an affiliate of the GMO industry-funded group ILSI,[2] is among those who have argued that if HGT occurs from commercialized GM plants into gut bacteria, this is unlikely to pose a risk to health.[3]

There are several mechanisms through which HGT can occur, some of which are more likely than others. HGT via some of these mechanisms occurs easily and frequently in nature. The consequences of HGT from GM crops are potentially serious, yet have not been adequately taken into account by regulators.

The basic mechanisms by which HGT could occur are:

- Uptake of GM DNA by bacteria
- Uptake of GM DNA from the digestive tract into the tissues of the organism
- Transmission of GM DNA via pathogenic bacteria, such as Agrobacterium tumefaciens. The capacity of A. tumefaciens to introduce foreign DNA into plants is often exploited by genetic engineers to introduce GM genes into plants
- Gene transfer by viruses.

The following sections outline these mechanisms and provide a perspective on the frequency at which these events can occur, as well as their potential impacts.

## DNA uptake by bacteria

Bacteria are promiscuous. They are always exchanging DNA and taking up DNA from their environment. Some of this environmentally acquired DNA can be incorporated into their genome and may be expressed. There are two scenarios in which DNA uptake by bacteria could result in HGT of GM genes.

The first scenario is the transfer of GM DNA from GM food into intestinal bacteria. DNA from a GM plant is released into the intestinal tract of the consumer during digestion. Contrary to frequent claims, GM DNA is not always broken down in digestion and can survive in sufficiently large fragments to contain intact genes that are potentially biologically active (see Myths 3.6, 3.10).

Bacteria of many different species are present in the digestive tract, some of which can take up DNA from their environment and incorporate it into their own DNA. In the case of GMOs, this could be problematic. For example, if the GM plant contained a gene for antibiotic resistance, the bacterium could incorporate that antibiotic resistance gene into its genome and thereby become resistant to the antibiotic. If the bacteria in question happened to be pathogenic (disease-causing), this process would create an antibiotic-resistant pathogen – a "superbug".

The transfer of GM genes from food to intestinal bacteria has been documented in a study on humans. The study found that the intestinal bacteria of a person whose diet included soy carried sequences unique to the GM soy that was part of their diet.[4]

The second scenario in which DNA uptake by bacteria could result in HGT of GM genes is the transfer of GM DNA to soil and aquatic bacteria. Cultivation of transgenic crops leads to the degradation of GM plant material in the environment, liberating GM genes into soil and bodies of water. Every cubic centimetre of soil contains thousands of different species of bacteria, only a small percentage of which have been identified and characterized. Bacteria are abundant in bodies of water, as well. Some soil bacteria are known to take up free DNA that may be present in the soil, incorporating the DNA into their genomes.[5] This could result in the transfer of GM genes to natural soil bacterial populations. Based on limited currently available data, this type of event is thought to be extremely rare.[6] However, it has been shown that GM DNA can persist in soil at detectable levels for at least a year,[7] increasing the likelihood of HGT.

We only know the identities and characteristics of a small fraction of the soil bacteria that could potentially take up GM DNA from their environment.[5] Furthermore, if the uptake of a GM gene, for example for antibiotic resistance, were to give the bacterium a survival or growth advantage, this would allow it to outcompete other bacterial strains in the presence of antibiotics widely used in agriculture and medicine. Therefore, this initial rare event could escalate and result in significant environmental and health outcomes.[8]

## DNA uptake during digestion of GM foods

A study in mice demonstrated that foreign DNA present in food can be transferred from the digestive tract to the bloodstream of animals that eat the food. This foreign DNA was also found in white blood cells and in the cells of many other tissues of the mice.[9] In another investigation, foreign DNA in a diet fed to pregnant mice was found in the organs of their foetuses and newborn offspring. The foreign DNA was believed to have reached the foetus through the placenta.[10]

It has also been shown that GM DNA in animal feed can be taken up in the organs of the animals that eat it and can be detected in the meat and fish that people eat.[11,12,13,14,15]

Most of the GM DNA in food is fragmented before it reaches the blood or tissues, so any genes present would not be able to express and reprogramme the host organism's cells. However, a few copies of GM DNA large enough to contain the sequence of a full and functional gene are likely to be present in the digestive tract and can be taken up into the blood at low frequency. A study in humans (not involving GM foods) showed that meal-derived DNA fragments large enough to carry complete genes entered the circulatory system. In some of the human blood samples studied the relative concentration of plant DNA was higher than the human DNA. The researchers were even able to identify individual plant varieties eaten by the human subjects from the DNA sequences present in the blood.[16]

Once the GM DNA, potentially carrying genes, is in the blood, it can then be transported to the cells of the body's tissues or organs.[9] When taken up by a cell, a GM gene could be integrated into the DNA of the cell, causing either direct mutation of a host gene function or reprogramming the host cell to produce the protein for which that GM gene codes, or both.

At present, this scenario is speculative. Although it is possible to detect GM DNA in the tissues of animals that consume GM feed, no research has been published that shows that the GM DNA is integrated and expressed in the tissues of those organisms. Neither has it been shown that the relatively small amount of GM DNA in the GM gene unit is in itself more dangerous than the large quantities of non-GM DNA found in the tissues. While toxic effects have been found from feeding GM diets to animals, it is not likely that GM DNA in itself is the culprit. The culprit is far more likely to be the novel proteins and downstream small molecule metabolites produced by the GM DNA and the overall GM transformation process, and/or the pesticides engineered into or applied to the GM crop.

If expression of the GM DNA in the tissues of animals and humans that eat GM foods did occur, it would most likely not occur frequently. In order to find out whether such expression events do occur, it would be necessary to conduct very large-scale studies – though finding a suitable experimental design would be challenging. Although such events may be infrequent, the widespread and long-term consumption of GMOs by humans and animals could mean that even infrequent events have important biosafety consequences.

## Horizontal gene transfer by Agrobacterium tumefaciens

Agrobacterium tumefaciens (A. tumefaciens) is a pathogenic soil bacterium often used to introduce GM genes into plants.

The introduction of GM genes into plants by infection with A. tumefaciens is carried out by exploiting a Ti plasmid – a small circular molecule of DNA that is naturally found in A. tumefaciens. When A. tumefaciens infects a plant, the Ti plasmid is introduced into the plant cells. Parts of the Ti plasmid may then insert themselves into the DNA of the plant and result in plant tumours, called crown gall.

Genetic engineers have adapted this natural but pathogenic process in order to introduce foreign DNA into plants and thereby produce GM crops. First, the naturally occurring genes of the Ti plasmid in the region that can insert into host plant cell DNA are removed and replaced with the GM gene of choice. The now genetically modified Ti plasmid is then introduced into A. tumefaciens, which in turn is used to infect plant cells. Once inside the plant cell, some of the genetically modified Ti plasmid can insert into the host plant cells' DNA, thereby permanently altering the genetic makeup of the infected cells.

Although A. tumefaciens is a convenient way of introducing new genes into plants, it can also serve as a vehicle for HGT from the GM plant to other species. This can happen via two mechanisms.

First, residual A. tumefaciens carried in a GM plant could infect plants of other species, thereby carrying the GM gene(s) from the intentionally genetically modified plant into other plants. A. tumefaciens can serve as a vehicle for HGT to hundreds of species of plants, since it can infect a wide range of plant species.

The second mechanism creates the risk that A. tumefaciens could pass GM genes on to an even wider range of species, including, but not limited to, plants. It consists of certain types of fungi functioning as intermediate hosts in the transfer of transgenes from GM A. tumefaciens to other organisms.

A study (Knight and colleagues, 2010) found that under conditions found in nature, A. tumefaciens introduced DNA into a species of disease-causing fungi that is known to infect plants. The study also found that GM DNA sequences in the A. tumefaciens were incorporated into the DNA of the fungi. In other words, the A. tumefaciens was genetically engineering the fungi.[17]

The authors concluded that in cases where a GM plant is infected with fungi, A. tumefaciens in the GM plant could infect the fungi, introducing GM genes into the fungi.[17] Many fungi have a wide host range and could therefore pass the GM genes onto a range of other plants.

Genetic engineers had previously assumed that A. tumefaciens only infects plants. But this study showed that it can infect fungi, a different class of organism. The study stated, "A. tumefaciens may be able to [genetically] transform non-plant organisms such as fungi in nature, the implications of which are unknown."[17] The authors pointed out[17] that A. tumefaciens is already known to genetically modify human cells in the laboratory.[18]

One of the study's co-authors, Andy Bailey, a plant pathologist at the University of Bristol, UK, said, "Our work raises the question of whether [A. tumefaciens's] host range is wider than we had thought – maybe it's not confined only to plants after all."[19]

The implications of this research are that GM gene(s), once introduced by A. tumefaciens into a GM crop and released into the environment, could then be introduced into an organism outside the plant kingdom – in this case, a fungus – and genetically modify it. This would be an uncontrolled and uncontrollable process, with unpredictable consequences.

## Implications of horizontal gene transfer through A. tumefaciens

Could A. tumefaciens transfer GM genes from a GM plant to another organism under realistic farming conditions? The answer depends on whether any A. tumefaciens carrying GM genes remains in the GM crop that is planted in open fields. Genetic engineers use antibiotics to try to remove the A. tumefaciens from the GM plant after the initial GM transformation process is complete in the laboratory. But this process has been found to be unreliable and incomplete:

- A study on GM brassicas, potatoes and blackberries found that the use of three antibiotics failed to completely remove A. tumefaciens. Instead, the A. tumefaciens contamination levels increased from 12 to 16 weeks after the GM transformation process and the A. tumefaciens was still detected six months after transformation.[20]
- A study on GM conifers found that residual A. tumefaciens remained in the trees 12 months after the genetic transformation but were not detected after this time in the same plants.[21]

However, these experiments only examined the first GM plant clones. In the GM development process, such GM clones go through a long process of back-crossing and propagation with the best-performing non-GM or GM plant relatives in order to try to produce a GM plant that performs well in the field and expresses the desired traits. The important question is whether A. tumefaciens carrying GM genes survives this back-crossing and propagation process and remains in the final GM plant that is commercialized.

To the best of our knowledge there have been no studies to assess whether any A. tumefaciens remains in the final commercialized GM plant. This question should be answered before a GM variety is commercialized, in order to avoid unwanted consequences that could be caused by residual A. tumefaciens in the final GM plant. Examples of consequences that should be excluded are the transfer of insecticidal properties to bacteria, or of herbicide tolerance to other crops or wild plants. The study by Knight and colleagues (2010) discussed above shows that the introduction of GM genes into crop plants could have consequences to organisms outside the plant kingdom, through the mechanism of infection by fungi carrying A. tumefaciens, which in turn carry GM genes.[17]

The consequences of such HGT for human and animal health and the environment are not predictable based on current knowledge, but are potentially serious. The health and environmental risk assessment for any GM variety must demonstrate that the GM plants have been completely cleared of GM A. tumefaciens before they are approved for commercialization.

## Gene transfer by viruses

Viruses are efficient at transferring genes from one organism to another and in effect are able to carry out HGT. Scientists have made use of this capacity to create viral gene transfer vectors that are frequently used in research to introduce GM genes into other organisms. Such vectors based on plant viruses have also been developed to generate GM crops, though no crops produced with this approach have been commercialised to date.[22,23]

The viral vectors that are used to generate GM crops are designed to prevent the uncontrolled transfer of genetic material. However, because the long time period during which virally engineered crops would be propagated in the environment, and the large numbers of humans and livestock that would be exposed to this GM genetic material, there is a real, though small, risk that unintended modifications could occur that could lead to virus-mediated HGT – with unpredictable effects.

Another potential risk of virus-mediated HGT comes from GM crops engineered to contain a virus gene, in particular those carrying information for a viral "coat" protein. This is done in an attempt to make the crop resist infection and damage by the "wild" virus from which the viral GM gene was derived. However, it has been suggested that if a GM crop containing a viral gene of this type was infected by the wild virus, this may result in exchange of genetic material between the GM viral gene in the plant and the infecting virus, through a process known as recombination. This can potentially result in a new, more potent ("virulent") strain of virus.[24,25]

The reasons for these concerns are as follows:

- The GM viral gene will be present in every cell of the crop. As a result, the large-scale cultivation of such a viral GM gene-containing crop will result in an extremely high concentration of particular viral genes in fields.
- It has been suggested that this provides an unprecedented opportunity for genetic recombination events to take place between an infecting virus and GM viral genes in the crop, thereby increasing the risk of new, mutated, and potentially more virulent strains of virus being produced.[25] Such viral mutation with increased virulence has been shown to occur under laboratory conditions.[26,27]

To date only two GM crops engineered with genes from viruses have been commercialized: a variety of squash grown in the US[28] and Mexico,[29] and papaya cultivated in Hawaii.[30] There are no reports of any investigations to see if any new viral strains have arisen by recombination in these two crops.

Interestingly, and quite unexpectedly, although the GM squash was resistant to viral infection, it was found to be prone to bacterial wilt disease following attack by beetles.[31,32]

## Conclusion

HGT from plants into other plants or animals appears to be a low-frequency event. The methods of HGT that are most likely to occur are DNA uptake by bacteria in the environment or the digestive tract. There is good evidence that the latter has already happened in the intestinal bacteria of humans who eat GM soy.

Other scenarios involving HGT by A. tumefaciens or by viruses are less probable. However, given the extremely wide distribution of GM crops and their intended use over decades, even low probabilities translate into the likelihood that HGT events could occur.

Therefore the negative impacts and risks associated with HGT must be taken into account in considering the overall biosafety of any GM crop.

## References


1. GMO Compass. Gene transfer to microorganisms. 2006. Available at: http://www.gmo-compass.org/eng/safety/environmental_safety/167.gene_transfer_microorganisms.html.
2. Then C, Bauer-Panskus A. European Food Safety Authority: A playing field for the biotech industry. Munich, Germany: Testbiotech; 2010. Available at: http://www.testbiotech.de/en/node/431.
3. Kleter GA, Peijnenburg AACM, Aarts HJM. Health considerations regarding horizontal transfer of microbial transgenes present in genetically modified crops. J Biomed Biotechnol. 2005;2005(4):326-352. doi:10.1155/JBB.2005.326.
4. Netherwood T, Martin-Orue SM, O'Donnell AG, et al. Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. Nat Biotechnol. 2004;22:204–209. doi:10.1038/nbt934.
5. Pontiroli A, Simonet P, Frostegard A, Vogel TM, Monier JM. Fate of transgenic plant DNA in the environment. Env Biosaf Res. 2007;6:15-35. doi:10.1051/ebr:2007037.
6. Brigulla M, Wackernagel W. Molecular aspects of gene transfer and foreign DNA acquisition in prokaryotes with regard to safety issues. Appl Microbiol Biotechnol. 2010;86:1027-41. doi:10.1007/s00253-010-2489-3.
7. Lerat S, Gulden RH, Hart MM, et al. Quantification and persistence of recombinant DNA of Roundup Ready corn and soybean in rotation. J Agric Food Chem. 2007;55:10226-31. doi:10.1021/jf072457z.
8. Heinemann JA, Traavik T. Problems in monitoring horizontal gene transfer in field trials of transgenic plants. Nat Biotechnol. 2004;22:1105-9. doi:10.1038/nbt1009.
9. Schubbert R, Renz D, Schmitz B, Doerfler W. Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA. Proc Natl Acad Sci USA. 1997;94:961-6.
10. Schubbert R, Hohlweg U, Renz D, Doerfler W. On the fate of orally ingested foreign DNA in mice: chromosomal association and placental transmission to the fetus. Mol Gen Genet. 1998;259:569-76.

11. Mazza R, Soave M, Morlacchini M, Piva G, Marocco A. Assessing the transfer of genetically modified DNA from feed to animal tissues. Transgenic Res. 2005;14:775–84. doi:10.1007/s11248-005-0009-5.
12. Sharma R, Damgaard D, Alexander TW, et al. Detection of transgenic and endogenous plant DNA in digesta and tissues of sheep and pigs fed Roundup Ready canola meal. J Agric Food Chem. 2006;54:1699–1709. doi:10.1021/jf052459o.
13. Chainark P, Satoh S, Hirono I, Aoki T, Endo M. Availability of genetically modified feed ingredient: investigations of ingested foreign DNA in rainbow trout Oncorhynchus mykiss. Fish Sci. 2008;74:380–390.
14. Ran T, Mei L, Lei W, Aihua L, Ru H, Jie S. Detection of transgenic DNA in tilapias (Oreochromis niloticus, GIFT strain) fed genetically modified soybeans (Roundup Ready). Aquac Res. 2009;40:1350–1357.
15. Tudisco R, Mastellone V, Cutrignelli MI, et al. Fate of transgenic DNA and evaluation of metabolic effects in goats fed genetically modified soybean and in their offsprings. Animal. 2010;4:1662–1671. doi:10.1017/S1751731110000728.
16. Spisak S, Solymosi N, Ittzes P, et al. Complete genes may pass from food to human blood. PLOS ONE. 2013;8(7):e69805.
17. Knight CJ, Bailey AM, Foster GD. Investigating Agrobacterium-mediated transformation of Verticillium albo-atrum on plant surfaces. PLoS ONE. 2010;5:13684. doi:10.1371/journal.pone.0013684.
18. Kunik T, Tzfira T, Kapulnik Y, Gafni Y, Dingwall C, Citovsky V. Genetic transformation of HeLa cells by Agrobacterium. Proc Natl Acad Sci USA. 2001;98:1871-6. doi:10.1073/pnas.041327598.
19. Marshall T. Bacteria spread genes to fungi on plants. Planet Earth Online. http://planetearth.nerc.ac.uk/news/story.aspx?id=853. Published October 27, 2010.
20. Barrett C, Cobb E, McNicol R, Lyon G. A risk assessment study of plant genetic transformation using Agrobacterium and implications for analysis of transgenic plants. Plant Cell Tissue Organ Cult. 1997;47:135–144.
21. Charity JA, Klimaszewska K. Persistence of Agrobacterium tumefaciens in transformed conifers. Env Biosaf Res. 2005;4:167-77.
22. Gleba Y, Marillonnet S, Klimyuk V. Engineering viral expression vectors for plants: the “full virus” and the “deconstructed virus” strategies. Curr Opin Plant Biol. 2004;7:182-8. doi:10.1016/j.pbi.2004.01.003.
23. Gleba Y, Klimyuk V, Marillonnet S. Viral vectors for the expression of proteins in plants. Curr Opin Biotechnol. 2007;18:134-41. doi:10.1016/j.copbio.2007.03.002.
24. Hull R. Detection of risks associated with coat protein transgenics. In: Foster GD, Taylor SC, eds. Methods in Molecular Biology: Plant Virology Protocols: From Virus Isolation to Transgenic Resistance. Vol 81. Totowa, NJ: Humana Press Inc. 1998:574–555.
25. Kleiner K. Fields of genes. New Sci. 1997. Available at: http://www.gene.ch/gentech/1997/Jul-Aug/msg00573.html.
26. Nowak R. Disaster in the making. New Sci. 2001;169(2273):4–5.
27. Jackson RJ, Ramsay AJ, Christensen CD, Beaton S, Hall DF, Ramshaw IA. Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox. J Virol. 2001;75:1205-10. doi:10.1128/JVI.75.3.1205-1210.2001.
28. US Department of Agriculture Animal and Plant Health Inspection Service (APHIS). Environmental assessment for Upjohn Company/Asgrow Seed Company petition for determination of non-regulated status for CZW-3 squash. Washington, DC; 1996.
29. Acatzi A, Magaña J, Moles C, Peña C, Castillo M. Detection and quantification of GM maize varieties in Mexican imports. Mexico City, Mexico; 2008. Available at: http://gmoglobalconference.jrc.ec.europa.eu/2008/Presentations/Galvez%20-%20presentation.pdf.
30. Gonsalves D. Transgenic papaya in Hawaii and beyond. AgBioForum. 2004;7:36–40.
31. Sasu MA, Ferrari MJ, Du D, Winsor JA, Stephenson AG. Indirect costs of a nontarget pathogen mitigate the direct benefits of a virus-resistant transgene in wild Cucurbita. Proc Natl Acad Sci USA. 2009;106:19067-71. doi:10.1073/pnas.0905106106.
32. Leonard A. Transgenic squash super-weeds gone wild. Salon.com. http://www.salon.com/2009/10/28/transgenic_squash_super_weeds_gone_wild/. Published October 28, 2009.

# 5.12 Myth: GM will deliver climate-ready crops

## Truth: Conventional breeding outstrips GM in delivering climate-ready crops

### Myth at a glance

Tolerance to extreme weather conditions and resistance to the pests and diseases that often accompany them are complex traits that cannot be inserted into plants through genetic engineering. Claimed GM successes in this respect are actually conventionally bred plants with added GM traits for herbicide tolerance or to produce Bt insecticidal toxins.

Conventional breeding is far ahead of genetic engineering in delivering climate-ready crop varieties that often have additional useful qualities such as pest- and disease-resistance.

Only part of the solution to climate change lies in plant genetics. The other part lies in climate-resilient agriculture based on proven agroecological techniques, such as building the soil to conserve water and planting a diversity of crops.

Climate change is often used as a reason to claim that we need GM crops.[1] But the evidence suggests that the solutions to climate change do not lie in GM. This is because tolerance to extreme weather conditions such as drought and flooding – and resistance to the pests and diseases that often accompany them – are complex traits. That means they are the product of many genes working together in ways we do not yet fully understand. Such complex genetic traits cannot be delivered through GM.

Where a GM crop is claimed to possess complex traits, they have generally been achieved through conventional breeding, not GM. After the complex trait is developed through conventional breeding, simple GM traits such as pest resistance or herbicide tolerance are added to the conventionally bred crop to represent the "inventive step" necessary to enable the GMO developer company to patent it.

While the resulting crop is often claimed as a GM success, this is untrue. It is a success of conventional breeding with added GM traits. The GM traits do not contribute to the agronomic performance of the crop but make the crop the property of a GMO company and (in the case of herbicide tolerance) keep farmers dependent on chemical inputs sold by the same company.

### Hollow promises vs. existing solutions

GMO developer companies have promised for years that GM would deliver climate-ready crops that would help humankind survive climate change. But these promises have proved hollow.

Some thought the breakthrough had finally come in December 2011, when the US Department of Agriculture (USDA) deregulated Monsanto's drought-tolerant maize variety, DroughtGard MON87460.[2] It was hailed as the first commercialized GM maize variety designed to tolerate drought.[3] But the USDA, in its assessment of the crop, noted that many non-GM maize varieties on the market are at least as effective as Monsanto's engineered maize variety in managing water use.[4]

According to calculations based on Monsanto's own data by Dr Doug Gurian-Sherman of the Union of Concerned Scientists, DroughtGard GM maize has at best delivered around a 1% US nationwide increase in yield under moderate drought conditions only,[5] whilst conventional breeding coupled with improved agronomy and agroecological practices have provided a 1% year-on-year yield benefit.[5,6]

This is to be expected, given that GM crops are developed by adding GM traits to the best conventionally bred varieties.

Meanwhile, conventional breeding, sometimes helped by marker assisted selection, has outstripped GM in producing numerous climate-ready crops.

Examples include:

- Maize varieties that yield well in drought conditions,[7] including some developed for farmers in Africa[8,9,10,11,12]
- Cassava that gives high yields in drought conditions and resists disease[13]
- Climate-adapted, high-yield sorghum varieties developed for farmers in Mali[14]
- Beans resistant to heat, drought, and disease[15,16]
- Pearl millet, sorghum, chickpea, pigeon pea and groundnut varieties that tolerate drought and high temperatures[17]
- Rice varieties bred to tolerate drought, flood, disease, and saline (salty) soils[18]
- Drought-resistant rice that yields up to 30% higher than other local varieties in Uganda[19]
- Flood-tolerant rice varieties developed for Asia[20,21]
- Over 2,000 indigenous rice varieties variously adapted to environmental fluctuations and resistant to pests and diseases, registered by Navdanya, an NGO based in New Delhi, India[22]
- Tomato varieties developed by Nepali farmers that tolerate extreme heat and resist disease.[23]

These are just a few examples among many. GMWatch keeps a database of non-GM breeding successes on its website.[24]

## Genetics not the whole solution

Only a part of the solution to climate change lies in plant genetics. Insofar as genetics is the solution, humanity will continue to rely on the same source that GMO developer companies mine for their germplasm – the hundreds of thousands of locally adapted seed varieties developed and conserved over centuries by farmers worldwide. These varieties are our living germplasm bank.

That part of the solution that lies beyond plant genetics is found in proven effective agroecological farm management techniques, such as building organic matter into the soil to conserve water, water conservation and management, planting a diversity of crops, rotating crops, and choosing the right plant for the conditions.

## Conclusion

Tolerance to extreme weather conditions and resistance to the pests and diseases that often accompany them are complex genetic traits with multiple gene functions at their basis. These complex traits cannot be inserted into plants through genetic engineering, which is limited to manipulating one or a few genes. Claimed GM successes in this respect are actually conventional breeding successes with added GM traits for herbicide tolerance or to produce Bt insecticidal toxins. These GM traits do not contribute to the agronomic performance of the crop under adverse weather conditions.

Conventional breeding is far ahead of genetic engineering in delivering climate-ready crop varieties that often have additional useful qualities such as pest- and disease-resistance.

Only part of the solution to climate change lies in plant genetics. The other part lies in climate-resilient agriculture based on proven agroecological techniques, such as building the soil to conserve water and planting a diversity of crops.

## References


1. Gray L. GM foods "could feed growing population during climate change." The Telegraph (UK). http://tgr.ph/nnywRL. Published January 22, 2009.
2. Abbott C. U.S. approves Monsanto drought-tolerant GM corn. Reuters. http://reut.rs/KyB8pX. Published December 22, 2011.
3. Marshall A. Drought-tolerant varieties begin global march. Nat Biotechnol. 2014;32(308). doi:10.1038/nbt.2875.
4. Voosen P. USDA looks to approve Monsanto's drought-tolerant corn. New York Times. http://nyti.ms/mQtCnq. Published May 11, 2011.
5. Gurian-Sherman D. High and dry: Why genetic engineering is not solving agriculture's drought problem in a thirsty world. Cambridge, MA: Union of Concerned Scientists; 2012. Available at: http://www.ucsusa.org/assets/documents/food_and_agriculture/high-and-dry-report.pdf.
6. Yu T, Babcock BA. Are US corn and soybeans becoming more drought tolerant? Am J Agric Econ. 2010;92:1310-1323.
7. Gillam C. DuPont says new corn seed yields better in droughts. Reuters. http://reut.rs/Li0c5B. Published January 5, 2011.
8. Cocks T. Drought tolerant maize to hugely benefit Africa: Study. Reuters Africa. http://bit.ly/bPXW0p. Published August 26, 2010.
9. La Rovere R, Kostandini G, Tahirou A, et al. Potential impact of investments in drought tolerant maize in Africa. Addis Ababa, Ethiopia: CIMMYT; 2010. Available at: http://bit.ly/1mLExYQ.
10. Atser G. Ghanaian farmers get quality protein, drought-tolerant, and Striga-resistant maize varieties to boost production. Modern Ghana. http://bit.ly/LZolNL. Published April 2, 2010.
11. Khisa I. Drought tolerant maize varieties ready. The East African. http://www.www.theeastafrican.co.ke/news/Drought-tolerant-maize-varieties-ready/-/2558/2134334/-/yk6a9p/-/index.html. Published January 4, 2014.

12. Atser G. Nigeria releases two extra-early maturing white maize hybrids. modernghana.com. http://www.modernghana.com/news/482841/1/nigeria-releases-two-extra-early-maturing-white-ma.html. Published August 17, 2013.
13. International Institute of Tropical Agriculture (IITA). Farmers get better yields from new drought-tolerant cassava. http://bit.ly/L3s946. Published November 3, 2008.
14. Diarra ST. Resistant seed helps Mali farmers battling climate change. AlertNet. http://bit.ly/Li0AkE. Published January 11, 2011.
15. Yao S. ARS releases heat-tolerant beans. USDA Agricultural Research Service. http://www.ars.usda.gov/is/pr/2010/100630.htm. Published June 30, 2010.
16. USDA Agricultural Research Service. Help for the common bean: Genetic solutions for legume problems. Agric Res USDA. 2010; May-June. Available at: http://www.ars.usda.gov/is/ar/archive/may10/bean0510.htm.
17. International Crops Research Institute for the Semi-Arid Tropics (ICRISAT). ICRISAT develops climate change ready varieties of pearl millet, sorghum, chickpea, pigeonpea and groundnut. SeedQuest. http://bit.ly/KqvVoV. Published June 5, 2009.
18. Berthelsen J. A new rice revolution on the way? AsiaSentinel. http://bit.ly/Lzthdi. Published January 17, 2011.
19. Food and Agriculture Organization (FAO). Uganda: After decades of war, a new rice variety helps farmers resume their lives. http://www.fao.org/news/story/en/item/35606/icode/. Published October 2, 2009.
20. International Rice Research Institute (IRRI). Indian farmers adopt flood-tolerant rice at unprecedented rates. ScienceDaily. http://www.sciencedaily.com/releases/2010/09/100915151015.htm. Published September 15, 2010.
21. IRIN News. Philippines: Could flood-resistant rice be the way forward? http://www.irinnews.org/Report.aspx?ReportId=82760. Published February 5, 2009.
22. Commodity Online. GM and India's rice fields. http://www.rediff.com/money/2007/mar/02comod4.htm. Published March 2, 2007.
23. Giri A. Nepali farm develops disease, heat resistant tomato. OneIndiaNews. http://news.oneindia.in/2010/12/05/nepalifarm-develops-disease-resistant-tomatoes.html. Published December 5, 2010.
24. GMWatch. Non-GM successes. 2014. Available at: http://www.gmwatch.org/index.php/articles/non-gm-successes.

# 5.13 Myth: GM will solve the nitrogen crisis
## Truth: GM has not delivered nitrogen-efficient crops and better solutions are available

### Myth at a glance

The production and use of nitrogen fertilizer in chemically-based agriculture is energy-hungry, emits climate-damaging greenhouse gases, and causes water pollution.

The cost of nitrogen fertilizer is tied into the cost of natural gas, as the production process uses large amounts of this non-renewable fossil fuel. Prices have risen since 2009 and that trend will likely continue.

For years, the notion has been promoted that crops could be genetically engineered for high nitrogen use efficiency (NUE), so that they require less nitrogen fertilizer. But this remains an empty promise.

In contrast, conventional breeding has successfully delivered significant improvements in NUE in important crops.

Studies show that organic, low-input and sustainable farming methods are the key to nitrogen management. These methods could provide enough nitrogen to replace that derived from fossil fuels, with no additional agricultural land area required. Nitrogen pollution of water would also be greatly reduced.

Synthetic nitrogen fertilizer is used in GM farming, as in all chemically-based agriculture. There are many problems associated with its production and use. The production process uses large amounts of natural gas, a non-renewable fossil fuel.[1] Nitrogen fertilizer production can account for more than 50% of the total energy used in industrialized agriculture.[2]

Nitrogen fertilizer produces greenhouse gases at the time of manufacture and again when used on fields, giving off nitrous oxide, a greenhouse gas 300 times more potent than carbon dioxide.[3] Fertilizer-intensive agriculture is by far the largest source of human-created nitrous oxide emissions in the United States[3] and this is likely to be the case in any country where chemically-based agriculture is practised.

The profitability of farming is highly dependent on the cost of fertilizers and the cost of nitrogen fertilizer is tied to natural gas prices.[1] In Canada, a major producer country, the price of nitrogen fertilizer reached a record high in 2008 and after a brief drop in 2009, has continued to rise.[4] According to some analysts, peak gas, the point at which the maximum rate of gas extraction is reached and supplies enter terminal decline, is expected to arrive around 2020,[5] pushing up prices still more. Already the industry is ramping up expensive and environmentally damaging strategies, such as fracking, for improving the "efficiency" of natural gas extraction.

For all these reasons, agriculture cannot continue to depend on synthetic nitrogen fertilizer. Other ways of managing nitrogen must be found.

Some plants, including most legumes (the bean family of plants, which includes soy and peanuts), fix nitrogen directly from the air with the help of nitrogen-fixing bacteria associated with the plant's roots. But other crops, such as wheat and barley, cannot do this and need to be fed nitrogen through the soil.

For years, the notion has been promoted that genetic engineering can produce crops with high nitrogen use efficiency (NUE) that require less nitrogen fertilizer.[6,7]

But GM technology has not produced any commercially available NUE crops. In contrast, conventional breeding has successfully delivered significant improvements in NUE in a number of crops.[6] Estimates for wheat from France show an increase in NUE of 29% over 35 years,[8] and Mexico improved wheat NUE by 42% over 35 years.[9]

Studies show that organic, low-input and sustainable farming methods are the key to nitrogen management. Such methods include the planting of nitrogen-fixing legumes, either in rows as cover crops (crops planted to manage soil quality and fertility), or between the main crop rows, or in a crop rotation. This makes growth-promoting nitrogen available to other plants growing nearby at the same time or planted in subsequent cropping seasons. A study calculated that these methods could provide enough nitrogen to replace that derived from fossil fuels, with no additional agricultural land area required.[10]

Other study findings include:

- Planting legumes on severely degraded land in Brazil successfully fixed nitrogen in soil, restoring soil and ecosystem biodiversity in the process.[11]
- Maize/peanut intercropping (growing two or more crops in close proximity) increased soil nitrogen and other nutrients, increased the growth of beneficial soil bacteria, and was expected to promote plant growth, as compared with monoculture, in experiments carried out in China.[12]

Agroecological methods of managing nitrogen solve another major problem associated with the application of synthetic nitrogen fertilizer – loss of soil nitrogen though agricultural runoff. In the runoff process, nitrogen leaches from soil in the form of nitrate, polluting groundwater. It can get into drinking water supplies, threatening human and livestock health.

Agroecological, organic, low-input, and sustainable farming practices have been found to reduce soil nitrogen losses in the form of nitrate by between 59 and 62% compared with conventional farming practices.[13] The result was reduced nitrate pollution and better conservation of nitrogen in soil.

## Conclusion

For years, the notion has been promoted that crops could be genetically engineered for high nitrogen use efficiency (NUE), so that they require less nitrogen fertilizer. But this remains an empty promise.

In contrast, conventional breeding has successfully delivered significant improvements in NUE in important crops.

Studies show that organic, low-input and sustainable farming methods are the key to nitrogen management. These methods could provide enough nitrogen to replace that derived from fossil fuels, with no additional agricultural land area required. Nitrogen pollution of water would also be greatly reduced

## References


1. Funderburg E. Why are nitrogen prices so high? Ag News Views. 2001. Available at: http://www.noble.org/ag/soils/nitrogenprices/.
2. Woods J, Williams A, Hughes JK, Black M, Murphy R. Energy and the food system. Philos Trans R Soc Lond B Biol Sci. 2010;365:2991–3006. doi:10.1098/rstb.2010.0172.
3. US Environmental Protection Agency (EPA). Nitrous oxide. 2014. Available at: http://www.epa.gov/nitrousoxide/scientific.html.
4. Agriculture and Agri-Food Canada. Canadian farm fuel and fertilizer: Prices and expenses (March 2012). Mark Outlook Rep. 2012;4(1). Available at: http://bit.ly/1h2pqD0.
5. Mobbs P. In: Energy Beyond Oil. Trowbridge, Wiltshire, UK: Cromwell Press; 2005:54.
6. Gurian-Sherman D, Gurwick N. No sure fix: Prospects for reducing nitrogen fertilizer pollution through genetic engineering. Cambridge, MA; 2009. Available at: http://www.ucsusa.org/assets/documents/food_and_agriculture/no-sure-fix.pdf.
7. McAllister CH, Beatty PH, Good AG. Engineering nitrogen use efficient crop plants: the current status. Plant Biotechnol J. 2012;10(9):1011-1025. doi:10.1111/j.1467-7652.2012.00700.x.
8. Brancourt-Hulmel M, Doussinault G, Lecomte C, Bérard P, Le Buanec B, Trottet M. Genetic improvement of agronomic traits of winter wheat cultivars released in France from 1946 to 1992. Crop Sci. 2003;43(1):37–45. doi:10.2135/cropsci2003.3700.
9. Ortiz-Monasterio I, Sayre KD, Rajaram S, McMahon MA. Genetic progress in wheat yield and nitrogen use efficiency under four nitrogen rates. 1997. Available at: http://repository.cimmyt.org/xmlui/handle/10883/2316.
10. Badgley C, Moghtader J, Quintero E, et al. Organic agriculture and the global food supply. Renew Agric Food Syst. 2007;22:86–108.
11. Chaer GM, Resende AS, Campello EF, de Faria SM, Boddey RM, Schmidt S. Nitrogen-fixing legume tree species for the reclamation of severely degraded lands in Brazil. Tree Physiol. 2011;31(2):139-49. doi:10.1093/treephys/tpq116.
12. Zhang JE, Gao AX, Xu HQ, Luo MZ. [Effects of maize/peanut intercropping on rhizosphere soil microbes and nutrient contents]. Ying Yong Sheng Tai Xue Bao. 2009;20(7):1597-602.
13. Oquist KA, Strock JS, Mulla DJ. Influence of alternative and conventional farming practices on subsurface drainage and water quality. J Env Qual. 2007;36(4):1194-204. doi:10.2134/jeq2006.0274.

# 5.14 Myth: Myth: GM crops reduce energy use
# Truth: GM crops are energy-hungry

## Myth at a glance

Industrial chemically-based agriculture is heavily dependent on energy from fossil fuels, which are in decline. In spite of claims that GM crops will reduce energy consumption due to a decreased need for pesticides and ploughing, GM crops have increased overall pesticide use and the spread of herbicide-resistant superweeds has forced farmers back to ploughing and spraying greater quantities of complex mixtures of herbicides. Thus GM crops are energy-hungry.

Proven methods of reducing the amount of fossil energy used in farming include minimizing pesticides and fertilizer use, planting leguminous crops to fix nitrogen in the soil, using agroecological techniques to manage soil fertility and control pests, and favouring human labour over fossil fuel-dependent machinery.

In experiments in the US, energy inputs for organic animal and organic legume farming systems have been found to be 28% and 32% less than those of the conventional chemically-based system. Organic, low-input, and agroecological farming is well suited to the Global South, with yields doubling in one experiment simply from the introduction of composting.

In the US food system, to produce 1 kilocalorie of plant protein requires an input of about 2.2 kilocalories of fossil energy. The average fossil energy input for animal protein production is 25 kilocalories per 1 kilocalorie of protein produced – more than 11 times greater than that for grain protein production.[1,2] The major fossil energy inputs for grain, vegetable, and forage production include fertilizers, agricultural machinery, fuel, irrigation, and pesticides.[2]

There is widespread agreement that the energy consumption of agriculture must be radically reduced. Graham Brookes and Peter Barfoot, directors of PG Economics, a consultancy firm to the agrochemical and biotechnology industry, claim that GM crops can help to achieve that aim.[3] They cite savings in tractor fuel due to two factors:

- Less frequent herbicide or insecticide applications on GM crops
- The no-till farming method that is used in the cultivation of GM Roundup Ready crops. The idea is that because weeds are controlled with herbicides and not with ploughing, no-till reduces the number of tractor passes that farmers have to make across their fields.[3]

However, these claims do not stand up to scrutiny. Although no-till reduces tractor fuel use, this saving is cancelled out by the fossil fuel used in herbicide production. Data from Argentina comparing the energy used in growing GM Roundup Ready soy and non-GM soy confirm that, while no-till did reduce farm operations (tractor passes across the field), the production of GM soy required more energy in both no-till and tillage systems. The reason for the increase was the large amount of energy consumed in the production of herbicides (mostly Roundup) used on GM soy.[4]

In addition, GM crops lead to increased overall pesticide use, and the incidence of herbicide-resistant superweeds is rapidly increasing. Both trends undermine the utility of herbicide-tolerant crops in no-till (see Myths 5.2 and 5.5).

Proven methods of reducing the amount of fossil energy used in farming include minimizing the use of synthetic pesticides and fertilizers, maximizing the use of leguminous crops to fix nitrogen in the soil, switching from annual to perennial crops, limiting irrigation, using agroecological techniques to manage soil fertility and control pests, and replacing fossil-fuel-dependent machinery with human and animal labour and technologies to harness renewable energy.[5] Feeding livestock animals only on good-quality pasture instead of keeping them in intensive feedlots reduces energy inputs by about half.[2]

A study carried out at the Rodale Institute in the US found that energy inputs for organic animal and organic legume farming systems were 28% and 32% less than those of the conventional chemically-based system.[6]

Organic, low-input, and agroecological farming is well suited to the Global South. A study in Ethiopia, part-funded by the UN Food and Agriculture Organization (FAO), investigated the effect on the yields of seven cereal and two pulse crops of three different fertilization systems: compost, chemical fertilizer, and a control system with no inputs.[7]

The study found that compost applications doubled cereal crop grain yields in eight out of the nine crops tested, compared with the no-input control system. The use of compost also gave higher yields than the use of chemical fertilizer, though differences in the yields from compost and from chemical fertilizer were not as great as the differences between the use of compost and the control system. For sorghum and faba bean, the yields from the use of

*"We have tried to have more efficient farming, with fewer people, more machines and a greater dependency on pesticides, fertilizers, GM crops and energy, using 10 kilocalories to produce one kilocalorie [of food delivered to the consumer]. But that is only possible if there is cheap oil. The system basically is bankrupt, which is why we need to change it to a more modern, advanced system, which will create energy, rather than consume it, and is not dependent on fossil energy, but more on people and better science."*
– Dr Hans Herren, president of the Millennium Institute (Washington, DC, USA) and co-chair, International Assessment of Agricultural Knowledge, Science and Technology, (IAASTD), a UN-, World Bank-, and WHO-sponsored project on the future of farming involving more than 400 experts from across the world[9]

compost and chemical fertilizer were similar. But the yield difference for all the other crops was greater, with the yield from the compost treatment being always higher than that from the use of chemical fertilizer.[7]

The crops grown with compost had better resistance to pests and disease and there were fewer difficult weeds; soil fertility was also restored in this system.[7]

## Peak oil and gas mean GM crops are unsustainable

According to some analysts, peak oil – the point when the maximum rate of extraction is reached, after which production goes into terminal decline – has already arrived, with peak gas expected around 2020.[8] Peak oil and gas mark the end of chemically-based agriculture because nitrogen fertilizers are synthesized using large amounts of natural gas, and pesticides (including herbicides) are made from oil.

GMO firms constantly promise new GM crops that are not reliant on the chemical model of farming, but GM technology is simply not capable of creating the complex traits that would fulfil this promise, such as more efficient nitrogen utilization. Furthermore, GM companies are agrochemical companies. Their business model is built on increasing the use of chemical pesticides and fertilizers. The 80% of GM crops that are herbicide-tolerant are designed to be grown with high doses of fossil fuel-hungry herbicide. Many of the newest GM crops are engineered to tolerate several different herbicides (see Myth 5.2).

Agriculture cannot continue to depend on non-renewable and increasingly expensive external inputs. Future food production systems will reduce or eliminate pesticide use and rely on renewable biologically-based fertilizers – such as compost and animal manure – produced on the farm or locally.

## Conclusion

Claims that GM crops will reduce energy consumption due to a decreased need for pesticides and ploughing are incorrect. GM crops have increased overall pesticide use and the spread of herbicide-resistant superweeds has forced farmers back to ploughing and spraying even greater quantities of complex mixtures of herbicides. The production of herbicides uses large quantities of fossil energy. Thus GM crops are energy-hungry.

Proven methods of reducing the amount of fossil energy used in farming include minimizing pesticides and fertilizer use, planting leguminous crops to fix nitrogen in the soil, using agroecological techniques to manage soil fertility and control pests, and favouring human labour over fossil fuel-dependent machinery.

In experiments in the US, energy inputs for organic animal and organic legume farming systems have been found to be 28% and 32% less than those of the conventional chemically-based system. Organic, low-input, and agroecological farming is well suited to the Global South, with yields doubling in one experiment simply from the introduction of composting.

## References


1. Pimentel D, Doughty R, Carothers C, Lamberson S, Bora N, Lee K. Energy use in developing and developed crop production. In: Lal R, Hansen D, Uphoff N, Slack S, eds. Food security and environmental quality in the developing world. Boca Raton, FL: CRC Press; 2002:129–51.
2. Pimentel D, Pimentel M. Sustainability of meat-based and plant-based diets and the environment. Am J Clin Nutr. 2003;78(3):660S-663S.
3. Brookes G, Barfoot P. Global impact of biotech crops: Socio-economic and environmental effects in the first ten years of commercial use. AgBioForum. 2006;9:139–151.
4. Bindraban PS, Franke AC, Ferrar DO, et al. GM-related sustainability: Agro-ecological impacts, risks and opportunities of soy production in Argentina and Brazil. Wageningen, the Netherlands: Plant Research International; 2009. Available at: http://bit.ly/Ink59c.
5. Pimentel D, Pimentel M. Food, Energy and Society. Niwot, CO: University Press of Colorado; 1996. Available at: http://www.amazon.com/Food-Energy-Society-David-Pimentel/dp/0870813862.
6. Pimentel D, Hepperly P, Hanson J, Douds D, Seidel R. Environmental, energetic, and economic comparisons of organic and conventional farming systems. Bioscience. 2005;55:573–582.
7. Edwards S, Asmelash A, Araya H, Egziabher TBG. Impact of compost use on crop yields in Tigray, Ethiopia. Rome, Italy: Natural Resources Management and Environment Department, Food and Agriculture Organization of the United Nations; 2007.
8. Mobbs P. In: Energy Beyond Oil. Trowbridge, Wiltshire, UK: Cromwell Press; 2005:54.
9. Driver A. CropWorld Global 2011: Changing our global approach to farming. Farmers Guardian. http://bit.ly/LXmk2s. Published September 1, 2011.

# 6. Feeding the world

*"Something approaching a billion people are hungry, a number that's been fairly stable for more than 50 years, although it has declined as a percentage of the total population. 'Feeding the world' might as well be a marketing slogan for Big Ag, a euphemism for 'Let's ramp up sales,' as if producing more cars would guarantee that everyone had one. But if it worked that way, surely the rate of hunger in the United States would not be the highest percentage of any developed nation, a rate closer to that of Indonesia than of Britain. The world has long produced enough calories, around 2,700 per day per human, more than enough to meet the United Nations projection of a population of nine billion in 2050, up from the current seven billion. There are hungry people not because food is lacking, but because not all of those calories go to feed humans (a third go to feed animals, nearly 5% are used to produce biofuels, and as much as a third is wasted, all along the food chain)."*

– Mark Bittman, food writer for the New York Times, in an article, "How to feed the world"[1]

*"[GMOs] haven't actually proven anything yet in terms of increased yields, as far as any of the major food crops are concerned… I don't really see any proper use for GMOs, now or even in the future. I think that the solutions for problems with agricultural food security lie elsewhere – not in the seed or GMO seeds in particular… The fact of life is that right now, we produce enough food for 14 billion people. We lose a lot in pre- and post-harvest. In the developed countries in particular, we produce more food than is required. In developing countries, we under-produce and that's not because we need GMOs, that's because those countries have bad agronomic practices, farmers don't have the right information on when to plant and how to best manage their farms. It's an issue of more and better information to farmers in the developing countries."*

– Dr Hans Herren, president of the Millennium Institute (Washington, DC, USA) and co-chair, International Assessment of Agricultural Knowledge, Science and Technology, (IAASTD), a UN-, World Bank-, and WHO-sponsored project on the future of farming involving more than 400 experts from across the world[2]

*"A billion starve because the wrong food is produced in the wrong places by the wrong means by the wrong people – and once the food is produced, as the Food and Agriculture Organization of the UN (FAO) has pointed out, half of it is wasted. The UN demographers tell us that although human numbers are rising the percentage rise is going down and should reach zero by 2050 – so the numbers should level out. Nine and a half billion is as many as we will ever have to feed – and we already produce 50% more than will ever be needed. The task, then, is not to increase output, but to produce what we do produce (or even less) by means that are kinder to people, livestock, and wildlife, more sustainable, and more resilient."*
– Colin Tudge, biologist, three-time winner of the Glaxo/ABSW Science Writer of the Year Award, and co-founder of the Campaign for Real Farming[3]

*"Who wants to buy GM crops or GM-containing foods? Well, no one, actually. When was the last time you saw people protesting to demand the right to eat GM foods? Why would they, when essentially all of the GM land on the planet is sown to crops modified with just two traits – herbicide tolerance and Bt (endotoxins that target specific kinds of insect pests) – fitted to four industrial crops – corn, soy, canola, and cotton – none of which are directly human consumable? Despite all the tantalizing promises that GM proponents offer – in the pipeline, just around the corner – what has GM actually delivered? After 20+ years, governmental advocacy on an unprecedented scale, and billions of dollars of taxpayer funding in Canada alone, commercialized GM today consists almost entirely of just these two traits. A 'GM variety' is a conventionally bred variety that has been fitted with transgenes conveying either or both of herbicide tolerance and Bt. The remaining tens of thousands of genes in a modern crop variety – the ones conferring high yield, drought tolerance, and all other valued traits – are the result of conventional breeding – not GM."*
– Dr E. Ann Clark, retired professor, Plant Agriculture, University of Guelph, Ontario, Canada[4]

From the day they were launched, GM crops have been promoted as a way of increasing food production and of solving world hunger at a time when the population is expected to increase. But do they offer any real solutions? In this final chapter we examine some of the more common claims made about the role of GM crops in feeding the world.

## References


1. Bittman M. How to feed the world. New York Times. http://www.nytimes.com/2013/10/15/opinion/how-to-feed-the-world.html. Published October 14, 2013.
2. Sherman M. Q & A: Hans Herren on Sustainable Agriculture Solutions. GMO Inside. http://gmoinside.org/q-hans-herren-sustainable-agriculture-solutions/. Published April 9, 2014.
3. Tudge C. The founding fables of industrialized agriculture. Independent Science News. http://www.independentsciencenews.org/un-sustainable-farming/the-founding-fables-of-industrialised-agriculture/. Published October 30, 2013.
4. Clark EA. Reality check on "Overwhelming number of farmers favour the use of GE crops." GMWatch. http://gmwatch.org/index.php/news/archive/2014/15317. Published February 20, 2014.

# 6.1 Myth: Myth: GM crops are needed to feed the world's growing population

## Truth: GM crops are irrelevant to feeding the world

### Myth at a glance

The notion that GM crops are needed to feed the world's growing population is repeated everywhere.

But it is difficult to see how GM can contribute to solving world hunger. GM crops do not increase yield. Nor are there any GM crops that are better than non-GM crops at tolerating poor soils or challenging climate conditions.

Virtually all of the currently available GM crops are engineered for herbicide tolerance or to contain a pesticide, or both.

The two major GM crops, soy and maize, mostly go into animal feed for intensive livestock operations, biofuels to power cars, and processed human food – products for wealthy nations that have nothing to do with meeting the basic food needs of the poor and hungry.

Even if a GM crop were developed that did increase yield, this would not solve the problem of hunger. This is because the cause of hunger is not a shortage of food, but poverty and lack of access to land on which to grow food.

According to the UN Food and Agriculture Organization, we already produce more than enough food to feed the world's population and could produce enough with existing agricultural methods to feed 12 billion people.

A few GM crops have been specifically promoted as helping small-scale and poor farmers in Africa. However, the results were the opposite of what was promised and all these projects failed.

It is irresponsible to pressure poor farmers in the Global South into gambling their farms and livelihoods on risky and experimental GM crops when alternative farming models have proven effective.

The notion that GM crops are needed to feed the world's growing population is repeated everywhere by organizations, industry, governments, and individuals in favour of GMOs. But it is difficult to see how GM can contribute to solving world hunger when there are no GM crops available that increase intrinsic yield (see Myth 5.1). Nor are there any GM crops that are better than non-GM crops at tolerating poor soils or challenging climate conditions (see Myth 5.12).

Instead, virtually all of the currently available GM crops are engineered for herbicide tolerance or to contain a pesticide, or both.[1] The two major GM crops, soy and maize, mostly go into animal feed for intensive livestock operations, biofuels to power cars, and processed human food – products for wealthy nations that have nothing to do with meeting the basic food needs of the poor and hungry. GM corporations are answerable to their shareholders and are interested in profitable commodity markets, not in feeding the world.

Even if a GM crop did appear that gave higher yields than non-GM crops, this would not impact the problem of hunger. This is because the cause of hunger is not a lack of food, but a lack of access to food. According to the UN Food and Agriculture Organization, we already produce more than enough food to feed the world's population and could produce enough with existing agricultural methods to feed 12 billion people.[2] The problem is that the poor have no money to buy food and increasingly, no access to land on which to grow it. Hunger is a social, political, and economic problem, which GM technology cannot address. GM is a dangerous distraction from real solutions and claims that GM can help feed the world can be viewed as exploitation of the suffering of the hungry.

## GM crops for Africa: Catalogue of failure

A handful of GM crops have been promoted as helping small-scale and poor farmers in Africa. However, the results were the opposite of what was promised.

### GM sweet potato yielded poorly, lost virus resistance

The virus-resistant sweet potato has been a GM showcase project for Africa, generating global media coverage. Florence Wambugu, the Monsanto-trained scientist fronting the project, was proclaimed an African heroine and the saviour of millions, based on her claims that the GM sweet potato doubled output in Kenya. Forbes magazine even declared her one of a tiny handful of people around the globe who would "reinvent the future".[3]

Eventually it emerged that the claims being made for the GM sweet potato were untrue, with field trial results showing it to be a failure. The GM sweet potato was out-yielded by the non-GM control and succumbed to the virus it was designed to resist.[4,5]

In contrast, a conventional breeding programme in Uganda produced a new high-yielding variety that was virus-resistant and raised yields by roughly 100%. The Ugandan project achieved its goal in a fraction of the time – and at a fraction of the cost – of the GM project. The GM sweet potato project, over 12 years, consumed funding from Monsanto, the World Bank, and USAID to the tune of $6 million.[6]

### GM cassava lost virus resistance

The potential of genetic engineering to boost the production of cassava – one of Africa's staple foods – by defeating a devastating virus has been heavily promoted since the mid-1990s. It was even claimed that GM cassava could solve hunger in Africa by increasing yields as much as tenfold.[7]

But almost nothing appears to have been achieved. Even after it became clear that the GM cassava had suffered a major technical failure, losing resistance to the virus,[8] media stories continued to appear about its curing hunger in Africa.[9,10]

Meanwhile, conventional (non-GM) plant breeding has quietly produced a virus resistant cassava that is already proving successful in farmers' fields, even under drought conditions.[11]

### Bt cotton failed in Makhatini

> *"The [GM cotton] seed itself is doing poorly. Without irrigation, and with increasingly unpredictable rain, it has been impossible to plant the cotton. In 2005 T. J. Buthelezi, the man whose progress was hymned by Monsanto's vice-president not three years before, had this to say: 'My head is full – I don't know what I'm going to do. I haven't planted a single seed this season. I have paid Rand 6,000 (USD 820, GBP 420) for ploughing, and I'm now in deep debt.' T. J. is one of the faces trucked around the world by Monsanto to prove that African farmers are benefiting from GM technology."*
> – Raj Patel, "Making up Makhatini", in Stuffed and Starved[12]

Makhatini in South Africa was home to a showcase GM Bt cotton project for small-scale farmers.

The project began in 1997 and by 2001 there were an estimated 3,000 smallholder farmers cultivating Monsanto's Bt cotton – 90% of the total number of farmers on the Flats.[13] The high rate of adoption was influenced by the fact that the only source of credit available to farmers in the region was at that time a cottonseed and chemicals company called Vunisa. Vunisa was also the only cotton buyer and seller and heavily promoted Bt cotton.[6]

> *"We strongly object that the image of the poor and hungry from our countries is being used by giant multinational corporations to push a technology that is neither safe, environmentally friendly nor economically beneficial to us. We do not believe that such companies or gene technologies will help our farmers to produce the food that is needed in the 21st century. On the contrary, we think it will destroy the diversity, the local knowledge and the sustainable agricultural systems that our farmers have developed for millennia, and that it will thus undermine our capacity to feed ourselves."*
> – Statement signed by 24 delegates from 18 African countries to the UN Food and Agricultural Organization, 1998[18]

> *"If anyone tells you that GM is going to feed the world, tell them that it is not… To feed the world takes political and financial will."*
> – Steve Smith, head of GMO company Novartis Seeds UK (now Syngenta), at a public meeting on a proposed local GMO farm scale trial, Tittleshall, Norfolk, UK, 29 March 2000[19]

The area that was planted to Bt cotton under the project was disputed, with industry sources claiming 100,000 hectares but a survey team suggesting only 3,000.[6] Whatever the true figure, after its peak in 2001, the project rapidly went into steep decline.

The project failed due to adverse weather conditions, and most importantly, farmer indebtedness. A 2003 report calculated that crop failures left the farmers who had adopted the expensive Bt cotton with debts of $1.2 million.[6] Pest attacks on the crop were also reported, which forced farmers into buying costly insecticide sprays.[14]

In 2004, only 700 farmers delivered cotton at the Makhathini Cotton ginnery, down from the total of 3,000 farmers planting cotton in 2000 – equivalent to an 80% drop in farmers growing Bt cotton.[15]

According to a documentary film by the India-based Deccan Development Society, those farmers who still grew the crop after 2004 did so at a loss. They continued only because the South African government subsidized the project from public funds, the company that sold the cottonseed and bought the cotton was their only source of credit, and there was a guaranteed market for the cotton.[16]

A study published in 2006 concluded that the project did not generate sufficient income to generate a "tangible and sustainable socioeconomic improvement".[14]

A 2012 review reported that by the 2010–2011 growing season, the total number of farmers growing GM Bt cotton had shrunk even further, to just 200. The area planted to Bt cotton had shrunk to a minuscule 500 hectares – a decline of more than 90% from the area under cultivation during the period of Bt cotton's claimed success (1998–2000).[17]

Yields continued to vary widely according to rainfall levels, hovering within 10% of what they were before Bt cotton was introduced. Overall pest control costs remained significantly higher with Bt cotton (65% of total input costs) than with non-Bt cotton (42% of total input costs).[17]

The review concluded that the main value of Makhatini project appears to have been as a public relations exercise for GM proponents, providing "crucial ammunition to help convince other African nations to adopt GM crops". The author added that there was a "disconnect" between how the project was represented and "the realities faced by its cotton growers".[17]

### GM soy and maize project ends in ruin for poor farmers

A GM soy and maize farming project ended in disaster for poor black farmers in South Africa. The Eastern Cape government was criticized for its support of this so-called "Green Revolution" project, which was launched in 2003–2004. A research study by the Masifunde Education and Development Project Trust, together with Rhodes University, found that the programme had disastrous results for farmers.[20]

"We saw a deepening of poverty and people returning to the land for survival," said Masifunde researcher, Mercia Andrews. The study raised concerns about feeding schemes conducted on animals with "alarming results", including damage to internal organs. It presented evidence of weed and pest problems, contamination of crops with GM pollen, and the control exercised by big companies over local and global food systems as a result of patented seeds.[20]

## Conclusion

GM crops do not increase yield. Nor are there any GM crops that are better than non-GM crops at tolerating poor soils or challenging climate conditions. Thus it is difficult to see how GM can contribute to solving world hunger.

Virtually all of the currently available GM crops are engineered for herbicide tolerance or to contain a pesticide, or both.[1] The two major GM crops, soy and maize, mostly go into animal feed for intensive livestock operations, biofuels to power cars, and processed human food – products for wealthy nations that have nothing to do with meeting the basic food needs of the poor and hungry.

Even if a GM crop were developed that did increase yield, this would not solve the problem of hunger. This is because the cause of hunger is not a shortage of food, but poverty and lack of access to land on which to grow food. According to the UN Food and Agriculture Organization, we already produce more than enough food to feed the world's population and could produce enough with existing agricultural methods to feed 12 billion people. GM is a dangerous distraction from real solutions to hunger.

A few GM crops have been specifically promoted as helping small-scale and poor farmers in Africa. However, the results were the opposite of what was promised and all these projects failed.

It is irresponsible to pressure poor farmers in the Global South into gambling their farms and livelihoods on risky and experimental GM crops when alternative farming models have proven effective.

## References


1. James C. Global status of commercialized biotech/GM crops: 2012. ISAAA; 2012. Available at: http://www.isaaa.org/resources/publications/briefs/44/download/isaaa-brief-44-2012.pdf.
2. Ziegler J. Economic, social and cultural rights: The right to food. Report by the special rapporteur on the right to food, Mr Jean Ziegler, submitted in accordance with Commission on Human Rights Resolution 2000/25 (Geneva: UNECOSOC E/CN.4/2002/558). New York, NY: United Nations Economic and Social Council: Commission on Human Rights; 2002. Available at: http://repository.forcedmigration.org/pdf/?pid=fmo:5322.
3. Cook LJ. Millions served. Forbes. 2002. Available at: http://www.forbes.com/forbes/2002/1223/302.html.
4. Gathura G. GM technology fails local potatoes. The Daily Nation (Kenya). http://bit.ly/KPQPxL. Published January 29, 2004.
5. New Scientist. Monsanto failure. 2004;181(2433). Available at: http://bit.ly/MHPG9W.
6. deGrassi A. Genetically modified crops and sustainable poverty alleviation in Sub-Saharan Africa: An assessment of current evidence. Third World Network – Africa; 2003. Available at: http://allafrica.com/sustainable/resources/view/00010161.pdf.
7. Groves M. Plant researchers offer bumper crop of humanity. LA Times. http://articles.latimes.com/1997/dec/26/news/mn-2352. Published December 26, 1997.
8. Donald Danforth Plant Science Center. Danforth Center cassava viral resistance review update. 2006. Available at: http://bit.ly/1ry2DUC.
9. Greenbaum K. Can biotech from St. Louis solve hunger in Africa? St. Louis Post-Dispatch. http://bit.ly/L2MmG4. Published December 9, 2006.
10. Hand E. St Louis team fights crop killer in Africa. St Louis Post-Dispatch. http://www.gmwatch.org/index.php/news/archive/2006/5580. Published December 10, 2006.

11. International Institute of Tropical Agriculture (IITA). Farmers get better yields from new drought-tolerant cassava. http://bit.ly/L3s946. Published November 3, 2008.
12. Patel R. Making up Makhatini. In: Stuffed and Starved. London, UK: Portobello Books; 2007:153–158.
13. Falck-Zepeda J, Gruère G, Sithole-Niang I. Genetically modified crops in Africa: Economic and policy lessons from countries south of the Sahara. In: International Food Policy Research Institute (IFPRI); 2013:27–29. Available at: http://www.ifpri.org/sites/default/files/publications/oc75.pdf.
14. Hofs J-L, Fok M, Vaissayre M. Impact of Bt cotton adoption on pesticide use by smallholders: A 2-year survey in Makhatini Flats (South Africa). Crop Prot. 2006;25:984–988.
15. Pschorn-Strauss E. Bt cotton in South Africa: The case of the Makhathini farmers. Durban, South Africa: Biowatch South Africa; 2005. Available at: http://www.grain.org/article/entries/492-bt-cotton-in-south-africa-the-case-of-the-makhathini-farmers.
16. Community Media Trust and Deccan Development Society. A disaster in search of success: Bt cotton in Global South.; 2007.
17. Schnurr MA. Inventing Makhathini: Creating a prototype for the dissemination of genetically modified crops into Africa. Geoforum. 2012;43(4):784–792.
18. Paul H, Steinbrecher R. Hungry Corporations: Transnational biotech companies colonise the food chain. In: London, UK: Zed Books; 2003:3.
19. Monbiot G. Organic farming will feed the world. The Guardian (UK). http://www.monbiot.com/2000/08/24/organic-farming-will-feed-the-world/. Published August 24, 2000.
20. Jack M. GM project faces ruin. The New Age (South Africa). http://www.thenewage.co.za/21688-1008-53-GM_project_faces_ruin. Published June 28, 2011.

# 6.2 Myth: GM crops are vital to achieve food security
# Truth: Agroecological farming is the key to food security

## Myth at a glance

The IAASTD report on the future of farming was a four-year project involving over 400 scientists and experts from 80 countries and sponsored by the World Bank and four United Nations agencies. The report, which was endorsed by 58 governments, did not endorse GM crops, pointing to variable yields, safety concerns, and restrictive patents on seeds that could undermine food security in poorer countries. Instead the IAASTD report called for a shift to "agroecological" food production systems.

Findings from agricultural development projects in developing countries confirm that agroecological and organic farming methods can dramatically increase yields, boost food security, and help alleviate poverty. Instead of the side-effects brought by chemically-based farming, these methods bring side-benefits, such as reductions in pesticide poisonings and less environmental damage.

Criticisms of the patents on GM seeds have prompted calls for publicly funded development of "public good" GMOs. But it would be difficult to justify spending large sums of taxpayer money on speculative "solutions" to problems that could be solved using methods that are simpler, cheaper, and available now.

In 2008 the World Bank and four United Nations agencies completed a four-year study on the future of farming. Conducted by over 400 scientists and experts from 80 countries and endorsed by 58 governments, the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD) did not endorse GM crops as a solution to world hunger. The IAASTD report pointed out that yields of GM crops were "highly variable" and in some cases there were "yield declines". It added that there were lingering safety concerns over GM crops and that the patents attached to them could undermine seed saving and food security in developing countries.[1]

Asked at a press conference if GM crops were the answer to world hunger, IAASTD Director Professor Bob Watson (subsequently chief scientist at the UK food, environment and agriculture ministry Defra) said, "The simple answer is no."[2] The UK government is among the 58 governments that approved the IAASTD report.[1]

The IAASTD called for a shift to "agroecological" food production systems.[1] Examples of such systems documented in IAASTD and other sources include:

- Low-input, energy-saving practices that preserve and build soil, conserve water, and enhance natural pest resistance and resilience in crops: for example, crop rotation, intercropping, "push-pull" systems to control pests, and use of nitrogen fixing plants to enhance soil fertility
- Use of thousands of traditional varieties of major food crops which are naturally adapted to stresses such as drought, heat, harsh weather conditions, flooding, salinity, poor soil, and pests and diseases[3]
- Programmes that enable farmers to cooperatively preserve and improve traditional seeds
- Use of existing crops and their wild relatives in traditional breeding programmes to develop varieties with useful traits
- Use of safe techniques of modern biotechnology, such as marker assisted selection (MAS), to speed up traditional breeding.[4] Unlike GM technology, MAS can produce new varieties of crops with valuable complex traits such as enhanced nutrition and taste, high yield, and tolerance to drought, heat, salinity, and flooding.

## Dramatic yield increases from sustainable agriculture

Sustainable agriculture projects in the Global South and other developing regions have produced dramatic increases in yields and food security.[5,6,7,8,9,10]

Olivier De Schutter, UN special rapporteur on the right to food:

> *"Agroecology mimics nature not industrial processes. It replaces the external inputs like fertilizer with knowledge of how a combination of plants, trees and animals can enhance productivity of the land. Yields went up 214% in 44 projects in 20 countries in sub-Saharan Africa using agroecological farming techniques over a period of 3 to 10 years… far more than any GM crop has ever done."*[12]
>
> *"To feed 9 billion people in 2050, we urgently need to adopt the most efficient farming techniques available. Today's scientific evidence demonstrates that agroecological methods outperform the use of chemical fertilizers in boosting food production where the hungry live – especially in unfavorable environments. To date, agroecological projects have shown an average crop yield increase of 80% in 57 developing countries, with an average increase of 116% for all African projects. Recent projects conducted in 20 African countries demonstrated a doubling of crop yields over a period of 3–10 years. Conventional farming relies on expensive inputs, fuels climate change and is not resilient to climatic shocks. It simply is not the best choice anymore today. Agriculture should be fundamentally redirected towards modes of production that are more environmentally sustainable and socially just."*[13]

A 2008 United Nations report looked at 114 farming projects in 24 African countries and found that adoption of organic or near-organic practices resulted in yield increases averaging over 100%. In East Africa, a yield increase of 128% was found. The report concluded that organic agriculture can be more conducive to food security in Africa than chemically-based production systems, and that it is more likely to be sustainable in the long term.[8]

The System of Rice Intensification, known as SRI, is an agroecological method of increasing the productivity of irrigated rice by changing the management of plants, soil, water and nutrients. SRI is based on the cropping principles of reducing plant population, improving soil conditions and irrigation methods for root and plant development, and improving plant establishment methods. According to the SRI International Network and Resources Center (SRI-Rice) at Cornell University, the benefits of SRI have been demonstrated in over 50 countries. They include 20%–100% or more increased yields, up to a 90% reduction in required seed, and up to 50% water savings.[11]

These results serve as a reminder that plant genetics are only a part of the answer to food security. The other part is how crops are grown. Sustainable farming methods that preserve soil and water and minimize external inputs not only ensure that there is enough food for the current population, but that the land stays productive for future generations.

## Small farms are more efficient

Research confirms that future food security lies in the hands of small farmers. Small farms are more efficient than large ones, producing more crops per hectare of land.[14,15,16]

## Sustainable agriculture can reduce poverty

Studies based in Asia, Africa, Latin America and the Caribbean have found that organic and agroecological farming can combat poverty in an environmentally sustainable way:

- Farmers growing organic crops for export and domestic markets in Latin America and the Caribbean had higher incomes than a control group of farmers using chemically-based methods. Reasons included the lower cost of organic technologies; the substitution of labour and organic inputs for more expensive chemical inputs that often require access to credit; premiums paid for organic products; and the strong long-term relationships that organic farmers developed with buyers, which resulted in better prices. As a bonus, organic production was associated with positive effects on the health of farm workers. Concern about pesticide poisoning was an important factor in farmers' adoption of organic farming.[17]
- The income of farmers in China and India improved after they switched to organic systems and was greater than that of farmers using chemically-based methods. The study concluded that the promotion of organic agriculture among small farmers can contribute to poverty alleviation.[18]
- Certified organic farms in tropical Africa involved in production for export were more profitable than those involved in chemically-based export production. The result was decreased poverty and increased food security for farming communities, as people had

more money to buy food. Also, organic conversion brought increases in yield.[19]

- Organic systems in Africa were found to raise farm incomes as well as agricultural productivity. Reasons for the higher incomes included lower input costs, as expensive synthetic pesticides and fertilizers were not used; and use of local, inexpensive, and readily available technologies.[8]
- The agroecological "integrated rice-duck" system of using ducks and fish to control pests in rice paddies in Japan, China, India, the Philippines, and Bangladesh has cut labour costs for weeding, reduced pesticide costs, increased yields by up to 20%, and boosted farm incomes by up to 80%.[20,21]

## Who owns food?

Traditionally, most food crop seeds have not been owned by anyone. Farmers have been free to save seeds from one year's crop for the next year's crop. Around 1.4 billion people in the Global South rely on farm-saved seed for their livelihoods.[23]

But this ancient practice is being undermined, since the GM genes used in creating GM crops are patented and owned by GM companies. The patents forbid farmers from saving seed to plant the following year. They have to buy new seed each year.

While an increasing number of non-GM seeds are also being patented (in many cases by big GM companies such as Monsanto, Dupont, and Syngenta), GM seeds are easier to patent. The artificial genetic constructs used to develop GM seeds can be more clearly identified, the inventive step required for patenting is more obvious, and there are fewer legal grey areas.[24] So for the time being, at least, GM will remain the technology of choice for the seed multinationals. It is possible that if non-GM seeds ever become as easy to patent as GM seeds, GM technology will be confined to the dustbin of history.

In the US and Canada, the presence of a company's patented GM genes in a farmer's harvest has been used by GM companies, particularly Monsanto, as the basis for litigation against the farmer. Contamination from cross-pollination happens readily, so the harvests of many farmers who have not planted Monsanto seed have tested positive for GM genes and Monsanto has sued them for patent infringement. This has pushed many farmers into switching to buying Monsanto's seed, because then they are safer from litigation. Farmers' claims that they have not intentionally planted GM crops have not protected them from having to pay large cash settlements or damages as a result of civil lawsuits.[25]

Patented GM seeds transfer control of food production from farmers to seed companies. GM companies co-opt centuries of farmer knowledge that went into creating locally adapted and genetically diverse seed stocks by adding one GM gene on top of the collective creation of generations of farmers.

Patents also transfer control of the food supply from the Global South to developed countries in the Global North. This is because most patents on food crops are held by companies in developed countries in the North.[26] There is widespread concern in the Global South about the "biopiracy" of its genetic resources by the Global North, with the consequent loss of farmers' rights to save seed.

*"A key question for our scientists, and politicians to address, which we should have the courage to demand industry addresses too, is whether GM technology can and will co-exist in the global agricultural toolbox with other technologies, without destroying those other tools. Apart from more promise than delivery, and delivery of only private benefits like greater market share for their own chemical pesticides, GM has brought with it a marked narrowing of seed varieties available to farmers, a concentration of ownership of seed production and sales, and a concentration in ownership and control of the knowledge (intellectual property rights or IPRs) required for agricultural production.*

*"In 2002, the director of the Vietnamese government agricultural research centre told me that he could spend all of his annual R&D budget ($20 million, as I recall) just on lawyers, trying to sort out what materials his researchers could and could not use, and on licence fees for such IPRs, according to the IPR jungle which has grown on plant and crop materials and molecules. Is this kind of commercial restriction, and narrowing of diversity of agricultural innovation trajectories, helping such food-poor countries to gain food security?*

*"This concentration and narrowing, and the associated transformation of agriculture into industrialized monocrop production requiring more expensive and unsustainable inputs, which in turn ignores and externalizes entirely predictable pest and weed resistance, cannot be a sustainable technology. Nor does it seem that it could co-exist with other technologies in the so-called toolbox."*

– Professor Brian Wynne, ESRC Centre for Economic and Social Aspects of Genomics, Cesagen Lancaster University, UK[22]

Some GMO proponents believe that the answer to these problems is for "public good" GM crops to be developed using public funds.[27] But it is difficult to justify gambling taxpayer funds on speculative GM "solutions" to problems that can be solved using methods that are simpler, cheaper, and available now. Nor would any public or private entity have an incentive to fund the lengthy, expensive, and often inefficient process of GM crop development unless they owned a patent that would enable them to recoup their expenses and make a profit.

Patents have no place in the agricultural system. To protect the security of the food supply and to ensure food sovereignty for each nation, governments must establish policies that ensure that the control of food production remains in the hands of farmers.

## Conclusion

The IAASTD report on the future of farming did not endorse GM crops, pointing to variable yields, safety concerns, and restrictive patents on seeds that could undermine food security in poorer countries. Instead the IAASTD report called for a shift to "agroecological" food production systems.

Findings from agricultural development projects in the Global South and other developing regions confirm that agroecological and organic farming methods can dramatically increase yields, boost food security, and help alleviate poverty. Instead of the side-effects brought by chemically-based farming, these methods bring side-benefits, such as reductions in pesticide poisonings and less environmental damage.

Criticisms of the patents on GM seeds have prompted calls for publicly funded development of "public good" GMOs. But it would be difficult to justify spending large sums of taxpayer money on speculative "solutions" to problems that could be solved using methods that are simpler, cheaper, and available now.

## References


1. International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD). Agriculture at a crossroads: Synthesis report of the International Assessment of Agricultural Knowledge, Science and Technology for Development: A Synthesis of the Global and Sub-Global IAASTD Reports. Washington, DC, USA: Island Press; 2009. Available at: http://www.unep.org/dewa/agassessment/reports/IAASTD/EN/Agriculture%20at%20a%20Crossroads_Synthesis%20Report%20%28English%29.pdf.
2. Lean G. Exposed: The great GM crops myth. The Independent. http://www.independent.co.uk/environment/green-living/exposed-the-great-gm-crops-myth-812179.html. Published April 20, 2008.
3. National Research Council. Lost Crops of Africa. Volume I: Grains. Washington DC; 1996. Available at: http://www.nap.edu/catalog.php?record_id=2305.
4. Collard BC, Mackill DJ. Marker-assisted selection: An approach for precision plant breeding in the twenty-first century. Philos Trans R Soc Lond B Biol Sci. 2008;363:557-72. doi:10.1098/rstb.2007.2170.
5. Altieri MA. Applying agroecology to enhance the productivity of peasant farming systems in Latin America. Environ Dev Sustain. 1999;1:197–217.
6. Bunch R. More productivity with fewer external inputs: Central American case studies of agroecological development and their broader implications. Environ Dev Sustain. 1999;1:219–233.
7. Pretty J. Can sustainable agriculture feed Africa? New evidence on progress, processes and impacts. J Environ Dev Sustain. 1999;1:253–274. doi:10.1023/A:1010039224868.
8. Hine R, Pretty J, Twarog S. Organic agriculture and food security in Africa. New York and Geneva: UNEP-UNCTAD Capacity-Building Task Force on Trade, Environment and Development; 2008. Available at: http://bit.ly/KBCgY0.
9. Barzman M, Das L. Ecologising rice-based systems in Bangladesh. LEISA Mag. 2000;16. Available at: http://bit.ly/L2N71R.
10. Zhu Y, Chen H, Fan J, et al. Genetic diversity and disease control in rice. Nature. 17;406:718–722.
11. SRI International Network and Resources Center (SRI-Rice)/Cornell Univesity College of Agriculture and Life Sciences. Home page. 2014. Available at: http://sri.ciifad.cornell.edu/.
12. Leahy S. Africa: Save climate and double food production with eco-farming. IPS News. http://allafrica.com/stories/201103090055.html. Published March 8, 2011.
13. United Nations Human Rights Council. Eco-farming can double food production in 10 years, says new UN report [press release]. http://bit.ly/Lkfa9U. Published March 8, 2011.
14. Ünal FG. Small is beautiful: Evidence of an inverse relationship between farm size and yield in Turkey. Annandale-on-Hudson, NY: The Levy Economics Institute of Bard College; 2008. Available at: http://www.levyinstitute.org/pubs/wp_551.pdf.
15. Cornia G. Farm size, land yields and the agricultural production function: An analysis for fifteen developing countries. World Dev. 1985;13:513–34.
16. Heltberg R. Rural market imperfections and the farm size-productivity relationship: Evidence from Pakistan. World Dev. 1998;26(10):1807–1826.
17. International Fund for Agricultural Development (IFAD). The adoption of organic agriculture among small farmers in Latin America and the Caribbean: Thematic evaluation. Rome, Italy; 2003.
18. International Fund for Agricultural Development (IFAD). Organic agriculture and poverty reduction in Asia: China and India focus: Thematic evaluation. Rome, Italy; 2005.
19. Gibbon P, Bolwig S, Odeke M, Taylor A, Twarog S. Certified organic export production: Implications for economic welfare and gender equality among smallholder farmers in tropical Africa. New York and Geneva: United Nations Conference on Trade and Development; 2008.
20. Khan MA, Ahmed GJU, Magor NP, Salahuddin A. Integrated rice-duck: a new farming system for Bangladesh. In: Van Mele P, Ahmad S, Magor NP, eds. Innovations in Rural Extension: Case Studies from Bangladesh. Wallingford, Oxfordshire: CABI Publishing; 2005.
21. United Nations General Assembly Human Rights Council (16th session). Report submitted by the special rapporteur on the right to food, Olivier De Schutter. 2010.
22. Wynne B. Comment to Hickman, L., "Should the UK now embrace GM food?" The Guardian (UK). http://bit.ly/

zvNSpL. Published March 9, 2012.

23. United Nations Development Programme (UNDP). Human development report 1999. New York and Oxford; 1999. Available at: http://hdr.undp.org/sites/default/files/reports/260/hdr_1999_en_nostats.pdf.
24. Then C, Tippe R. Seed monopolists increasingly gaining market control: Applications and granting of patents in the sphere of animal and plant breeding in 2010. No Patents on Seeds; 2011. Available at: http://www.no-patents-on-seeds.org/sites/default/files/news/patente_report_2011_final_en.pdf.
25. Center for Food Safety. Monsanto vs. US farmers: November 2007 Update. Washington, DC and San Francisco, CA; 2007. Available at: http://bit.ly/KPLEh2.
26. Khor M. Intellectual Property, Biodiversity, and Sustainable Development. London, UK and Penang, Malaysia: Zed Books and Third World Network; 2002:9; 89.
27. Jones JD. The cost of spurning GM crops is too high. The Guardian (UK). http://bit.ly/MpSIil. Published July 21, 2011.

# 6.3 Myth: Anti-GMO activists in wealthy countries are keeping people in poor countries hungry by denying them GM crops

# Truth: The 2008 food crisis was not caused by a lack of GM crops but by the rush to biofuels

## Myth at a glance

The World Bank and the UN Food and Agriculture Organization (FAO) have identified the biofuels boom – not a lack of GM foods – as the main cause of the 2007–2008 food crisis and the ongoing rise in global food prices.

The FAO and other major international organizations have recommended that the leaders of the G20 countries remove their support for biofuels development in order to protect food supplies.

Vast tracts of agricultural land are now growing crops to fuel cars, not to feed people.

The same companies that produce GM seeds also produce feedstocks for biofuels. Therefore it appears that these companies are not motivated by a desire to feed the world but by a desire to make a profit.

Currently available GM crops are engineered to tolerate herbicides or to express insecticides. Neither trait is useful in addressing hunger.

Attempts to genetically engineer crops to address hunger in poor regions have ended in failure and farmer indebtedness.

The 2007–2008 global food crisis led to food riots around the world, as the escalating price of staple crops pushed food out of reach of the poor and hungry. GMO proponents have used the food crisis to claim that anti-GMO activists in the Global North are keeping the Global South hungry by creating unfounded fears about GM crops. GM crops, they claim, could help solve the hunger problem, if only the activists in affluent countries would stop interfering.

But in 2008 the World Bank and the UN Food and Agriculture Organization (FAO) identified the biofuels boom – not a lack of GM foods – as the main cause of the 2007–2008 food crisis.[1,2]

Biofuels are crops used for fuel. Vast tracts of cropland have been taken out of food production to grow biofuels for cars, funded by generous government subsidies. This has made food scarcer, pushing up costs.

Two years on in 2010, the food crisis had not abated. At a summit meeting, the leaders of the G20 countries requested the FAO, along with the Organization for Economic Cooperation and Development (OECD), the World Bank, the World Health Organization (WHO), and other international bodies to "develop options… on how to better mitigate and manage the risks associated with the price volatility of food and other agriculture commodities, without distorting market behaviour, ultimately to protect the most vulnerable."[3]

The FAO and its partner organizations responded with a report that was uncompromising in its conclusion that biofuels were a major threat to food security. The report recommended removing government support for their development: "G20 governments [should] remove provisions of current national policies that subsidize (or mandate) biofuels production or consumption… Failing a removal of support, G20 governments should develop contingency plans to adjust (at least temporarily) policies that stimulate biofuel production or consumption (in particular mandatory obligations) when global markets are under pressure and food supplies are endangered."[3]

In 2014 the World Bank's Food Price Watch publication reported a small 3% decline in the price of internationally traded food commodities between October 2013 and January 2014, but noted that "international prices are still not overly far from their historical peak" in August 2012.[4]

*"The agribusiness giants who have developed and patented genetically modified crops have long argued that their mission is to feed the world, rarely missing an opportunity to mention starving Africans. Their mission is, in fact, to make a profit. Land rights for small farmers, political stability, fairer markets, education and investment hold the key to feeding Africa but offer little prospect of increased profits.The climate crisis was used to boost biofuels, helping to create the food crisis; and now the food crisis is being used to revive the fortunes of the GM industry."*
– Daniel Howden, Africa correspondent, The Independent (UK)[9]

*"The cynic in me thinks that they're just using the current food crisis and the fuel crisis as a springboard to push GM crops back on to the public agenda. I understand why they're doing it, but the danger is that if they're making these claims about GM crops solving the problem of drought or feeding the world, that's bullshit."*
– Denis Murphy, head of biotechnology, University of Glamorgan, Wales[10]

## Biofuels couple food prices to petrochemical fuel prices

The growth of the biofuels industry has created a link between agriculture and fuel that never existed before. Previously, agricultural markets were driven only by food demands and were not linked to petroleum markets. But now they are tightly linked, because agriculture provides the crops that are used to make the biofuels alternative to petrochemical fuels. Four major food and feed crops – sugarcane, maize, wheat, and soy – are now used for biofuels feedstock. So the biofuels boom has coupled food prices to petrochemical fuel prices,[5] with the result that food prices will continue to rise as petroleum becomes scarcer and more expensive.

The same companies that produce GM seeds also produce feedstocks for biofuels.[6,7] We conclude that these companies are not motivated by a desire to feed the world but by a desire to make a profit.

## Food speculation and hunger

An additional cause of the food crisis is financial speculation in food commodity markets. This trend drives up prices for the crops that are traded internationally on a large scale, namely maize, wheat, and soy. One report on the topic concluded, "Food markets should serve the interests of people and not those of financial investors... Given that hunger still exists in the world, even small price increases that are driven by financial investment are scandalous. We must not allow food to become a purely financial asset."[8]

GM crops do not provide a solution to the problem of financial speculation in food markets.

## Currently available GM crops do not address hunger

Currently available GM crops are engineered to tolerate herbicides or to express insecticides. Neither trait is useful in addressing hunger. Attempts to genetically engineer crops to address hunger in poor regions have ended in failure and farmer indebtedness (see Myth 6.1). Golden rice, which is intended to alleviate vitamin A deficiency in developing countries, is still not ready for market after over a decade's worth of costly research and development work. It has not even been toxicologically tested to see if it is safe to eat.

## Conclusion

The World Bank and the UN Food and Agriculture Organization (FAO) have identified the biofuels boom – not a lack of GM foods – as the main cause of the 2007–2008 food crisis and the ongoing rise in global food prices. The FAO and other major international organizations have recommended that the leaders of the G20 countries remove their support for biofuels development in order to protect food supplies.

Vast tracts of agricultural land are now growing crops to fuel cars, not to feed people.

The same companies that produce GM seeds also produce feedstocks for biofuels. Therefore it appears that these companies are not motivated by a desire to feed the world but by a desire to make a profit.

Currently available GM crops are engineered to tolerate herbicides or to express insecticides. Neither trait is useful in addressing hunger. Attempts to genetically engineer crops to address hunger in poor regions have ended in failure and farmer indebtedness. Golden rice, which is intended to alleviate vitamin A deficiency in developing countries, is still not ready for market after over a decade's worth of costly research and development work. It has not even been toxicologically tested to see if it is safe to eat.

## References


1. Mitchell D. A note on rising food prices: Policy Research Working Paper 4682. Washington, DC, USA: The World Bank Development Prospects Group; 2008.
2. Food and Agriculture Organization (FAO). Soaring food prices: Facts, perspectives, impacts and actions required. In: Rome, Italy; 2008. Available at: http://www.fao.org/fileadmin/user_upload/foodclimate/HLCdocs/HLC08-inf-1-E.pdf.
3. Food and Agriculture Organization of the United Nations and others. Price volatility in food and agricultural markets: Policy responses. Policy Report including contributions by FAO, IFAD, IMF,OECD, UNCTAD, WFP, the World Bank, the WTO, IFPRI and the UN HLTF. Food and Agriculture Organization of the United Nations; 2011. Available at: http://ictsd.org/downloads/2011/05/finalg20report.pdf.
4. Cuesta J. Food price watch. Washington, DC, USA: World Bank; 2014. Available at: http://www.worldbank.org/content/dam/Worldbank/document/Poverty%20documents/FPW%20Feb%202014%20final.pdf.
5. World Bank. Food price watch. Washington, DC, USA; 2011. Available at: http://bit.ly/JZBHaQ.
6. The Bioenergy Site. Monsanto biofuels feedstock research extended. http://www.thebioenergysite.com/news/13514/monsanto-biofuels-feedstock-research-extended. Published November 5, 2013.
7. Syngenta. What Syngenta thinks about biofuels. 2013. Available at: http://www.syngenta.com/global/corporate/en/news-center/Pages/what-syngenta-thinks-about-full.aspx.
8. Henn M. The speculator's bread: What is behind rising food prices? EMBO Rep. 2011;12:296–301.
9. Howden D. Hope for Africa lies in political reforms. The Independent (UK). http://ind.pn/LsLp9O. Published September 8, 2008.
10. Lyons R. GM: It's safe, but it's not a saviour. Spiked Online. 2008. Available at: http://www.spiked-online.com/index.php?/site/article/5438/.

# 6.4 Myth: GM is needed to provide the crops that will enable us to survive the challenges ahead

# Truth: Non-GM breeding methods are more effective at creating crops with useful traits

## Myth at a glance

Conventional plant breeding continues to outperform GM in producing crops with useful traits such as tolerance to extreme weather conditions and poor soils, improved nutrient utilization, complex-trait disease resistance, and biofortification (enhanced nutritional value). Such traits are known as complex traits because they involve many genes working together in a precisely regulated way. They cannot be genetically engineered into crops.

The proof of this is the fact that the GMO lobby has been promising GM crops with desirable complex traits for 18 years – but today, almost all commercialized GMOs are engineered with one or both of just two simple traits: to tolerate herbicides or to contain an insecticide.

There are also GM virus-resistant papayas, but the virus resistance is a simple, not a complex trait, and a non-GM virus-resistant papaya is available.

Often, non-GM crops with complex desirable traits are wrongly claimed as GM successes. GM crops that do have such traits are generally conventional breeding successes with GM genes for herbicide tolerance or insect resistance added.

Conventional breeding has achieved its successes at a fraction of the cost of GM. In addition, GM is no quicker than conventional plant breeding and carries additional risks.

GM is not needed to enable us to feed the world and survive the challenges ahead. In fact the quality and efficacy of our food production system depends only partly on crop genetics. The other part of the equation is farming methods. What is needed are not just high-yielding, climate-ready, and disease-resistant crops, but productive, climate-ready, and disease-resistant agriculture.

Conventional breeding combined with agroecological farming methods can fulfil all our current and future food needs.

When people hear about "supercrops" such as flood-tolerant rice, drought-tolerant maize, salt-tolerant wheat, pest-resistant chickpeas, low-allergen peanuts, iron-rich beans, beta-carotene-enriched cassava, and heart-healthy soybeans, many automatically think of GM.

But all these improved crops have been created without GM. They are the products of conventional (natural) breeding, in some cases helped by marker assisted selection, or MAS. MAS, sometimes called precision breeding, is a largely uncontroversial branch of biotechnology that can speed up conventional breeding by identifying the presence of genes linked to the desired important traits in the new naturally bred plants. Thus MAS dramatically reduces the time taken to select the new crop variety. MAS does not involve inserting foreign genes into the DNA of a host plant and avoids the risks and uncertainties of genetic engineering. It is widely supported by environmentalists and organic farming bodies. Any concerns tend to focus on patent ownership of the seeds developed in this way.

Conventional breeding and MAS have succeeded where GM has failed in developing crops with useful traits such as tolerance to extreme weather conditions and poor soils, disease resistance, and enhanced nutritional value. Such properties are known as complex traits because they involve many genes working together in a precisely regulated way. Only conventional breeding methods, sometimes helped by MAS, are able to produce crops with the desired complex traits. In contrast, GM technology can only manipulate one or a few genes at a time and is unable to confer precise and integrated control of expression of GM genes. Therefore it is incapable of producing crops with desired complex traits, which rely on multiple genes working together.

In a few GM crops, such as GM virus-resistant papayas,[1,2] resistance to a particular virus has been conferred by inserting a single gene from the virus (virus coat protein gene). This process is known as "coat protein-mediated protection" and is akin to a vaccination in animals or humans.[3] But the more valuable and broadly resilient complex-trait disease resistance cannot be genetically engineered into a plant.

Conventional breeding and MAS use the many existing varieties of crops to create a diverse, flexible, and resilient crop base. GM technology offers the opposite – a narrowing of crop diversity and an inflexible technology that requires years and millions of dollars of investment for each new trait.[4,5]

Non-GM breeding successes usually gain minimal media coverage, in contrast with the often speculative claims of potential GM "miracles". Thanks to the huge public relations budgets of biotechnology companies, the GMO stories are broadcast far and wide – but have little grounding in fact.

While the GMO lobby has been promising GM crops with desirable traits such as tolerance to flood and drought, salty soils, or enhanced nutritional value for 18 years, it has failed to produce them. Today the vast majority of commercialized GMOs have one or both of just two traits: herbicide tolerance and pesticide expression.

Monsanto has released a drought-tolerant maize, but even the US Department of Agriculture admitted that it was no more effective than existing non-GM varieties.[6] Truly drought-tolerant agriculture depends on agronomic methods more than genetics – for example, incorporating plenty of organic matter into the soil so that it absorbs and retains water.

## The GM successes that never were

Many crops developed through conventional breeding, either alone or with assistance from marker assisted selection (MAS), are wrongly claimed as GM successes. These fall into three broad categories, as follows.

### 1. Conventionally bred crop with GM tweak

> *"Biotech traits by themselves are absolutely useless unless they can be put into the very best germplasm."*
> – Brian Whan, spokesman for Monsanto subsidiary InterGrain[7]

Typically, GM firms use conventional breeding, not GM, to develop crops with traits such as higher intrinsic yields or drought tolerance. They first obtain germplasm from the best varieties developed over years by farmers and breeders. Then they use conventional breeding and MAS to achieve the desired combination of complex traits. Finally, once they have developed a successful variety using conventional breeding, they use GM to engineer in the company's proprietary genes. This GM tweak, usually a herbicide-tolerant or insecticidal gene, adds nothing to the agronomic performance of the crop. But it does allow the company to patent and own the crop.

This process was mentioned in a news broadcast about Monsanto's 2010 buy-out of part of a Western Australia cereal breeding company, InterGrain. An InterGrain spokesman explained Monsanto's interest in his company: "A really important concept is that biotech traits by themselves are absolutely useless unless they can be put into the very best germplasm."[7]

An example of a GM product developed in this way is Monsanto's VISTIVE® soybean, which has been described as the first GM product with benefits for consumers. These low linolenic acid soybeans were designed to produce oil that would reduce unhealthy trans fats in processed food made from the oil. They were created by conventional breeding. But Monsanto turned them into a GM crop by adding a GM trait – tolerance to its Roundup herbicide.[8]

Interestingly, Iowa State University developed some even lower linolenic acid soybean varieties and did not add any GM traits to them.[9] Very little has been heard about them, compared with VISTIVE.

Another product of this type is Syngenta's Agrisure Artesian drought-tolerant maize. The crop was developed using non-GM breeding, but herbicide tolerant and insecticidal GM genes were subsequently added through genetic engineering.[10]

## 2. Conventionally bred crop without GM tweak – GM used as lab tool

In some cases, a crop is developed with the aid of GM as a laboratory research tool, but no GM genes are added. Nevertheless, such crops have been claimed to be GM successes. An example is flood-tolerant rice, which the UK government's former chief scientist, Sir David King, wrongly claimed as a triumph of genetic engineering.[11,12]

In fact, the two best-known flood-tolerant rice varieties – one of which was almost certainly the one that King referred to – are not GM at all. One variety was developed by a research team led by GMO proponent Pamela Ronald.[13] Ronald's team developed the rice using MAS as part of a natural breeding programme.[13,14] They used genetic engineering as a laboratory research tool first to identify the desired genes, and then to look for their presence in the plants obtained through natural cross-breeding. So the resulting rice is not genetically engineered but naturally bred.

Ronald does not appear to have tried to clear up the confusion around the non-GM status of this rice – quite the opposite, as she misleadingly referred to the MAS method of developing the rice as "sort of a hybrid between genetic engineering and conventional breeding".[15] While MAS can be used with both genetic engineering and conventional breeding, MAS is not a "hybrid" between the two. MAS uses molecular mapping methods to track genetic markers (specific regions of DNA) associated with certain traits of interest during the conventional breeding process. This enables the breeder to more quickly and precisely identify progeny that carry the traits of interest.

The website of University of California at Davis (UC Davis), where Ronald's laboratory is based, also misleadingly implied that her rice was genetically engineered, saying, "Her laboratory has engineered rice for resistance to diseases and flooding, which are serious problems of rice crops in Asia and Africa."[16] It would be more accurate to say that her team had bred the rice.

Another flood-tolerant rice created with "Snorkel" genes has also been claimed as a genetic engineering success. But the rice, which adapts to flooding by growing longer stems that prevent the crop from drowning, was bred by conventional methods and is entirely non-GM.[17]

Laboratory-based genetic modification and modern gene mapping methods were used to study a deepwater rice variety and identify the genes responsible for its flood tolerance trait. Three gene regions were identified, including one where the two "Snorkel" genes are located. MAS was used to guide the conventional breeding process by which all three flood tolerance gene regions were successfully combined in a commercial rice variety.[17]

Only conventional breeding and MAS could be used to generate the resulting flood-tolerant rice line. This is because it is beyond the ability of current genetic modification methods to transfer the genes and control switches for the flood-tolerance trait in a way that enables them to work properly.

### 3. Crop that has nothing to do with GM

In one high-profile case, a crop that had nothing to do with GM at all was claimed as a GM success. In a BBC radio interview, the UK government's former chief scientist, Sir David King, said that a big increase in grain yields in Africa was due to GM, when in fact it did not involve the use of GM technology.[18] Instead, the yield increase was due to a "push-pull" management system, an agroecological method of companion planting that diverts pests away from crop plants.[19] King later admitted to what he called an "honest mistake".[20]

King produced this example when under pressure to provide compelling reasons why GM crops are needed. But far from showing why we need to embrace GM, it shows the exact opposite – that we need to stop being distracted by GM and put funding and support behind proven effective non-GM solutions to urgent problems.

## Non-GM breeding successes show no need for GM

> *"The advantage of science is not in principle, for its own self – it's because it does something useful and valuable, that people want. If it is not supporting those particular objectives, I think we should take a much more sceptical view of it."*
> – Michael Meacher, former UK environment minister[21]

> *"A surge of media reports and rhetorical claims depicted genetically modified (GM) crops as a solution to the 'global food crisis' manifested in the sudden spike in world food prices during 2007–2008. Broad claims were made about the potential of GM technologies to tackle the crisis, even though the useful crops and traits typically invoked had yet to be developed, and despite the fact that real progress had in fact been made by using conventional breeding. The case vividly illustrates the instrumental use of food-crisis rhetoric to promote GM crops."*
> – Glenn Davis Stone, professor of anthropology and environmental studies, Washington University, St Louis; and Dominic Glover, then postdoctoral fellow in technology and agrarian development, Wageningen University, The Netherlands[22]

The following are just a few examples of conventionally bred crops with the types of traits that GMO proponents claim can only be achieved through genetic engineering. Many are already commercially available and making a difference in farmers' fields.

### Drought-tolerant and climate-ready

See Myth 5.12 for a list of non-GM breeding successes with enhanced drought-tolerant and climate-ready traits.

### Salt-tolerant

- Rice varieties that tolerate saline soils and other problems[23]
- Durum wheat that yields 25% more in saline soils than a commonly used variety[24,25]
- Indigenous crop varieties from India that tolerate saline soils, stored by the Indian seed-keeping NGO, Navdanya. Navdanya reported that it gave some of these seeds to farmers in the wake of the 2004 tsunami, enabling them to continue farming in salt-saturated soils in spite of scientists' warnings that they would have to abandon the land temporarily.[26]

### High-yield, pest-resistant, and disease-resistant

- High-yield, multi-disease-resistant beans for farmers in Central and East Africa[27]
- High-yield, disease-resistant cassava for Africa[28]
- Australian high-yield maize varieties targeted at non-GM Asian markets[29]
- Maize that resists the Striga parasitic weed pest and tolerates drought and low soil nitrogen, for African farmers[30]
- Maize that resists the grain borer pest[31]
- "Green Super-Rice" bred for high yield and disease resistance[23]

## GM "solution" to pest problem that's already solved by agroecology

Genetics, whether engineered or natural, are only part of the solution to pest problems. Sometimes they are just a distraction from existing agroecological solutions. For example, Rothamsted Research in the UK has conducted open field trials of wheat genetically engineered to produce a chemical that repels aphids. The chemical is present in natural form in some plants. Rothamsted presented the project, which swallowed £1.28 million of public funds,[54] as an environmentally friendly chemical-free way to control aphids.[55]

However, this was yet another GM "solution" to a problem that had already been solved by agroecological methods. Previously published long-term research, which included substantial input from Rothamsted Research, has shown that aphid populations in cereal crops can be successfully kept below the level at which they cause economic damage to the crop by planting strips of certain flowers around fields. These flowers attract native predators and parasites, such as parasitic wasps, ladybirds, lacewings, and hoverflies, which control the aphids.[56,57]

It is even questionable as to whether aphids in wheat are a real problem requiring new solutions. British farmer Peter Lundgren has pointed out that the trial was on spring wheat, for which aphid damage is negligible. For winter wheat, there are other existing non-GM solutions, ranging from chemical insecticides to agroecological methods,[58] such as those described above.

- High-yield soybeans that resist the cyst nematode pest[32]
- Aphid-resistant soybeans[33,34,35,36]
- High-yield tomato with sweeter fruit[37]
- High-yield, pest-resistant chickpeas[38]
- Sweet potato that is resistant to nematodes, insect pests and Fusarium wilt, a fungal disease[39]
- High-yield, high-nutrition, and pest-resistant "superwheat"[40]
- Habanero peppers with resistance to root-knot nematodes[41]
- Potatoes that resist late blight and other diseases[42,43,44,45,46,47,48]
- Potato that resists root-knot nematodes[49]
- Papayas that resist ringspot virus.[50] There is also a GM virus-resistant papaya,[1] which is claimed by GMO proponents to have saved Hawaii's papaya industry.[51] However, this claim is questionable. Though the GM papaya has dominated Hawaiian papaya production since the late 1990s, Hawaii's Department of Agriculture reportedly said that the annual yield of papayas in 2009 was lower than when the ringspot virus was at its peak.[52] An article in the Hawaiian press said that GM has not saved Hawaii's papaya industry, which has been in decline since 2002. The article cites as a possible reason for the decline the market rejection that has plagued GM papayas from the beginning.[53]

### Nutritionally fortified and health-promoting

- Soybeans containing high levels of oleic acid, reducing the need for hydrogenation, a process that leads to the formation of unhealthy trans fats[59]
- Beta-carotene-enriched orange maize, aimed at people suffering from vitamin A deficiency[60,61]
- Millet rich in iron, wheat abundant in zinc, and beta-carotene-enriched cassava[62]
- Purple potatoes containing high levels of the cancer-fighting antioxidants, anthocyanins[63,64]
- A tomato containing high levels of the antioxidant, lycopene, which has been found in studies to have the potential to combat heart attacks, stroke, and cancer[65]
- A purple tomato containing high levels of anthocyanins and vitamin C[66] (this story attracted only a fraction of the publicity gained by the John Innes Centre's GM purple "cancer-fighting" tomato[67,68,69])
- Low-allergy peanuts[70] (in a separate development, a process has been discovered to render ordinary peanuts allergen-free[71])

Nutritionally fortifying foods does not necessarily involve crop breeding. Adding nutrients is a popular and successful method to improve the nutritional quality of food. For example, an iron-fortified maize has been shown in a study to decrease anaemia in children.[72,73]

### Consumer appeal

A GM non-browning apple has gained a less than enthusiastic reception, notably from the apple industry, which fears it could damage markets.[74,75] Meanwhile, a non-GM version is already available.[76]

## Conventional breeding outstrips GM in delivering desirable traits

The GMO lobby uses promises of drought-resistant, salt-resistant, and biofortified crops to sell GM technology to politicians, the food industry, and the public. But these promises are empty. There are no commercialized GMOs that outperform non-GM crops in expressing these desirable traits. After 18 years of failed promises, virtually all commercialized GMOs have one or both of just two traits: herbicide tolerance and the production of a pesticide.[77]

## GM is no quicker than conventional breeding – but it is more expensive

> *"The assertion that GM is quicker than breeding is common, but false. The average time required to develop a non-vegetatively engineered crop is about the same as developing one produced through breeding."*
>
> – Doug Gurian-Sherman, biotechnology specialist at the Union of Concerned Scientists[78]

> *"The overall cost to bring a new biotech trait to the market between 2008 and 2012 is on average $136 million."*
>
> – Phillips McDougall, "The cost and time involved in the discovery, development and authorization of a new plant biotechnology derived trait: A consultancy study for Crop Life International"[79]

> *"Genetic engineering might be worth the extra cost if classical breeding were unable to impart such desirable traits as drought-, flood- and pest-resistance, and fertilizer efficiency. But in case after case, classical breeding is delivering the goods."*
>
> – Margaret Mellon and Doug Gurian-Sherman, Union of Concerned Scientists[5]

The plant breeder Major M. Goodman of North Carolina State University says that GM is no quicker than conventional breeding; on the contrary, GM involves additional steps. He concludes that on average, and provided there are no complications, there is a 10–15-year lag time between the discovery of a new, potentially useful transgene and seed sales to farmers – about the same as the time needed to breed a new variety of a sexually propagated non-GM crop.[4,80] The Bt insecticidal trait engineered into GM crops took 16 years to reach the market – and that figure did not include toxicity testing.[4]

Dr Doug Gurian-Sherman of the Union of Concerned Scientists commented: "The assertion that GM is quicker than breeding is common, but false. The average time required to develop a non-vegetatively engineered crop is about the same as developing one produced through breeding." He said that false claims about the speed of GM stem from "the notion that once a gene is found, it is simply a matter of putting it into a plant and running a few tests to see if it works properly."[78]

Gurian-Sherman explained, "In fact, years of backcrossing are needed to get rid of possible harmful mutations and epigenetic changes introduced through the tissue culture process used with GM. And backcrossing is also needed to transfer the trait into multiple elite crop varieties of many crops (for example, grains). Sometimes the original genetic construct turns out to cause problems. This happened for example with GM flood-tolerant rice, which showed breeding to be faster and more effective than GM. New regulatory sequences are found to be needed, or there are position effects that cause problems from the particular site of insertion in the plant genome."[78]

In addition, Gurian-Sherman said, years of field testing are needed to determine how well the trait responds in various and variable environments, regardless of whether the trait is developed through GM or breeding.[78]

Gurian-Sherman added, "When we look at actual examples, it has taken 10 to 15 years to develop a GM trait. And it is important to note that this is not an issue of delay due to regulatory requirements, as GM proponents are fond of asserting, but inherent in the limitations of the process."[78]

This timeline might be reduced in the case of plants that are vegetatively propagated, like apples and potatoes, since the crossing and backcrossing carried out with sexually propagated plants does not happen. Instead the genetic engineers insert the transgene and do some field testing to see that the transgenes function as hoped.

However, this shorter process also carries greater risks. Because there is no backcrossing or breeding of any kind, the GM apples or potatoes will always carry all of the changes that occurred during the engineering process, namely insertion-site mutations and effects and tissue culture-induced mutations and epigenetic changes. The GM varieties are put out into the field still carrying any GM-induced unintended changes.

Other than checking that the apple trees and the potatoes look normal and grow acceptably during a few years of field testing under highly managed conditions, the developer company does not look for any other types of changes, such as unexpected toxic or allergenic qualities.

As for the cost of GM versus non-GM plant breeding, an industry consultancy study put the cost of developing a GM trait and bringing it to market at $136 million. Out of that figure, only $35 million is spent on regulatory costs, the rest being taken up by basic research and development.[79] Even Monsanto admits that non-GM plant breeding is "significantly cheaper" than GM.[81]

The plant breeder Major M. Goodman of North Carolina State University said the cost of developing a single-gene GM trait was fifty times as much as the cost of developing an equivalent conventionally bred plant variety. Goodman called the cost of GM breeding a "formidable barrier" to its expansion.[4]

Time and cost are vital considerations for the Global South, where the need for crop varieties adapted to local conditions is urgent, yet farmers cannot afford expensive seeds and inputs.

## Conclusion

Conventional plant breeding continues to outperform GM in producing crops with useful traits, such as tolerance to extreme weather conditions and poor soils, complex-trait disease resistance, and enhanced nutritional value. Such properties are called complex traits because they involve many genes working together in a precisely regulated way. They cannot be genetically engineered into crops.

Often, non-GM crops with these desirable traits are wrongly claimed as GM successes. GM crops that do have such traits are generally conventional breeding successes with GM genes for herbicide tolerance or insect resistance added.

Conventional breeding has achieved its successes at a fraction of the cost of GM. In addition, GM is no quicker than conventional plant breeding and carries additional risks.

For 18 years the GMO lobby has been promising GM crops with desirable traits in order to sell GM technology to politicians, the food industry, and the public. But today, almost all commercialized GMOs have been modified with just two simple traits: to resist herbicides or produce their own pesticides.

GM is not needed to enable us to feed the world and survive the challenges ahead. In fact the quality and efficacy of our food production system depends only partly on crop genetics. The other part of the equation is farming methods. What is needed are not just high-yielding, climate-ready, and disease-resistant crops, but productive, climate-ready, and disease-resistant agriculture.

Conventional breeding combined with agroecological farming methods can fulfil all our current and future food needs.

## References


1. Gonsalves D. Transgenic papaya in Hawaii and beyond. AgBioForum. 2004;7(1 & 2):36–40.
2. Ferreira SA, Pitz KY, Manshardt R, Zee F, Fitch M, Gonsalves D. Virus coat protein transgenic papaya provides practical control of papaya ringspot virus in Hawaii. Plant Dis. 2002;86(2):101-105. doi:10.1094/PDIS.2002.86.2.101.
3. Fitch MMM, Manshardt RM, Gonsalves D, Slightom JL, Sanford JC. Virus resistant papaya plants derived from tissues bombarded with the coat protein gene of papaya ringspot virus. Nat Biotechnol. 1992;10(11):1466-1472. doi:10.1038/nbt1192-1466.
4. Goodman MM. New sources of germplasm: Lines, transgenes, and breeders. In: Martinez JM, ed. Memoria Congresso Nacional de Fitogenetica. Univ Autonimo Agr Antonio Narro, Saltillo, Coah, Mexico; 2002:28–41. Available at: http://www.cropsci.ncsu.edu/maize/publications/NewSources.pdf.
5. Mellon M, Gurian-Sherman D. The cost-effective way to feed the world. The Bellingham Herald. http://bit.ly/NvQoZd. Published June 20, 2011.
6. Voosen P. USDA looks to approve Monsanto's drought-tolerant corn. New York Times. http://nyti.ms/mQtCnq. Published May 11, 2011.
7. ABC Rural News Online. Monsanto and the WA government team up on grain breeding: Skye Shannon speaks with Brian Whan, Intergrain and Peter O'Keefe, Monsanto [Audio]. 2010.
8. PR Newswire. Cargill to process Monsanto's VISTIVE(TM) low linolenic soybeans. http://prn.to/KyIREy. Published October 4, 2005.
9. Iowa State University. Six new soybean varieties highlight progress in developing healthier oils at ISU. http://www.plantbreeding.iastate.edu/pdf/soybeanReleases11-08.pdf. Published 2008.

10. Ranii D. Drought-tough corn seed races to the finish line. newsobserver.com. http://bit.ly/KqA1xl. Published December 21, 2010.
11. Melchett P. Who can we trust on GM food? The Guardian (UK). http://www.guardian.co.uk/commentisfree/2008/dec/09/david-king-gm-crops. Published December 9, 2008.
12. Pendrous R. Europe's GM barrier is "starving the poor." FoodManufacture.co.uk. http://bit.ly/MpPw6m. Published June 13, 2011.
13. Xu K, Xu X, Fukao T, et al. Sub1A is an ethylene-response-factor-like gene that confers submergence tolerance to rice. Nature. 2006;442:705-8. doi:10.1038/nature04920.
14. Gunther M. Biotech and organic food: A love story. marcgunther.com. http://www.marcgunther.com/biotech-and-organic-food-a-love-story/. Published April 15, 2010.
15. Lebwohl B. Pamela Ronald has developed a more flood-tolerant rice. EarthSky. 2010. Available at: http://earthsky.org/food/pamela-ronald-has-developed-a-more-flood-tolerant-rice.
16. UC Davis. Ronald biography. 2006. Available at: http://indica.ucdavis.edu/ronald_bio/pamcv. Accessed January 1, 2012.
17. Hattori Y, Nagai K, Furukawa S, et al. The ethylene response factors SNORKEL1 and SNORKEL2 allow rice to adapt to deep water. Nature. 2009;460:1026–1030.
18. BBC Today Programme. David King interviewed by Sarah Montague. 2007.
19. Rothamsted Research Chemical Ecology Group. Push-pull habitat manipulation for control of maize stemborers and the witchweed Striga. Available at: http://bit.ly/1pST9I5.
20. Adam D. Eco Soundings: It's in the Mail. The Guardian (UK). http://www.guardian.co.uk/environment/2008/jul/30/1. Published July 30, 2008.
21. Meacher M. GM foods: Meacher on super tomatoes and trampled fields: Interview by David Thompson [TV broadcast]. BBC News. http://www.bbc.co.uk/news/uk-politics-17147649. Published February 24, 2012.
22. Stone GD, Glover D. Genetically modified crops and the "food crisis": discourse and material impacts. Dev Pract. 2011;21:509–516.
23. Berthelsen J. A new rice revolution on the way? AsiaSentinel. http://bit.ly/Lzthdi. Published January 17, 2011.
24. Sawahel W. Wheat variety thrives on saltier soils. SciDevNet. 2010. Available at: http://www.scidev.net/en/news/wheat-variety-thrives-on-saltier-soils.html.
25. Dean T. Salt tolerant wheat could boost yields by 25%. LifeScientist. http://lifescientist.com.au/content/biotechnology/news/salt-tolerant-wheat-could-boost-yields-by-25--583063808. Published March 12, 2012.
26. Davis R. Interview with Vandana Shiva. New Int. 2008. Available at: http://bit.ly/L3yhcA.
27. Ogodo O. Beans climb to new heights in Rwanda. SciDevNet. 2010. Available at: http://www.scidev.net/en/news/beans-climb-to-new-heights-in-rwanda.html.
28. AFP. "Rooting" out hunger in Africa – and making Darwin proud. Indep UK. 2010. Available at: http://www.independent.co.uk/life-style/health-and-families/rooting-out-hunger-in-africa--and-making-darwin-proud-2076547.html.
29. Queensland Country Life. New maize hybrids to target niche Asian markets. http://bit.ly/LZr89P. Published April 5, 2011.
30. Atser G. Ghanaian farmers get quality protein, drought-tolerant, and Striga-resistant maize varieties to boost production. Modern Ghana. http://bit.ly/LZolNL. Published April 2, 2010.
31. CIMMYT. Body blow to grain borer. CIMMYT E-News. 2007;14 May 2012. Available at: http://www.cimmyt.org/en/news-and-updates/item/body-blow-to-grain-borer.
32. Swoboda R. Cho[o]se high-yielding, SCN-resistant soybeans. Wallace's Farmer (Iowa, USA). http://bit.ly/1fCi7H2. Published November 7, 2007.
33. Diers B. Discovering soybean plants resistant to aphids and a new aphid. University of Illinois Extension. http://web.extension.illinois.edu/state/newsdetail.cfm?NewsID=15202. Published February 20, 2010.
34. Li Y, Hill CB, Carlson SR, Diers BW, Hartman GL. Soybean aphid resistance genes in the soybean cultivars Dowling and Jackson map to linkage group M. Mol Breed. 2007;19(1):25-34. doi:10.1007/s11032-006-9039-9.
35. Kim K-S, Hill CB, Hartman GL, Mian MAR, Diers BW. Discovery of soybean aphid biotypes. Crop Sci. 2008;48(3):923. doi:10.2135/cropsci2007.08.0447.
36. Hill CB, Kim K-S, Crull L, Diers BW, Hartman GL. Inheritance of resistance to the soybean aphid in soybean PI 200538. Crop Sci. 2009;49(4):1193. doi:10.2135/cropsci2008.09.0561.
37. Allen J. Single gene powers hybrid tomato plants. PlanetArk. http://www.planetark.com/enviro-news/item/57360. Published March 30, 2010.
38. Suszkiw J. Experimental chickpeas fend off caterpillar pest. USDA Agricultural Research Service News & Events. http://www.ars.usda.gov/is/pr/2009/090825.htm. Published August 25, 2009.
39. Clemson University. New not-so-sweet potato resists pests and disease. Bioscience Technology. http://bit.ly/LGHVlo. Published June 22, 2011.
40. Kloosterman K. Pest-resistant super wheat "Al Israeliano." greenprophet.com. http://www.greenprophet.com/2010/08/israel-super-wheat/. Published August 17, 2010.
41. Yao S. New pest-resistant habanero joins peck of ARS-created peppers. USDA Agricultural Research Service News & Events. http://www.ars.usda.gov/is/pr/2009/090922.htm. Published September 22, 2009.
42. Clarke A. Conventional potato varieties resist PCN and blight. Farmers Wkly. 2014. Available at: http://www.fwi.co.uk/articles/09/04/2014/144089/conventional-potato-varieties-resist-pcn-and-blight.htm.
43. Potato Council (UK). Toluca. British Potato Variety Database. 2014. Available at: http://varieties.potato.org.uk/

display_description.php?variety_name=Toluca.
44. Wragg S. Elm Farm 2010: Blight-resistant spuds could lower carbon levels. Farmers Weekly Interactive. http://bit.ly/LsRjb2. Published January 11, 2010.
45. Suszkiw J. ARS scientists seek blight-resistant spuds. USDA Agricultural Research Service. http://www.ars.usda.gov/is/pr/2010/100603.htm. Published June 3, 2010.
46. Shackford S. Cornell releases two new potato varieties, ideal for chips. Chronicle Online. http://www.news.cornell.edu/stories/Feb11/NewPotatoes.html. Published February 21, 2011.
47. Fowler A. Sárpo potatoes. The Guardian. http://www.theguardian.com/lifeandstyle/2012/jan/13/alys-fowler-sarpo-potatoes. Published January 13, 2012.
48. White S, Shaw D. The usefulness of late-blight resistant Sarpo cultivars – A case study. ISHS Acta Hortic. 2009;834. Available at: http://www.actahort.org/members/showpdf?booknrarnr=834_17.
49. Suszkiw J. Scientists use old, new tools to develop pest-resistant potato. USDA Agricultural Research Service. http://www.ars.usda.gov/is/ar/archive/apr09/potato0409.htm. Published March 31, 2009.
50. Siar SV, Beligan GA, Sajise AJC, Villegas VN, Drew RA. Papaya ringspot virus resistance in Carica papaya via introgression from Vasconcellea quercifolia. Euphytica. 2011;181(2):159–168.
51. Summers J. GM halo effect: Can GM crops protect conventional and organic farming? Genetic Literacy Project. http://www.geneticliteracyproject.org/2014/01/09/gm-papaya-halo-effect/#.U2Kp3ccowsk. Published January 9, 2014.
52. Chan K. War of the papayas. ChinaDaily.com. http://bit.ly/LQT67d. Published September 8, 2011.
53. Hao S. Papaya production taking a tumble. The Honolulu Advertiser. http://bit.ly/LzDZRb. Published March 19, 2006.
54. GM Freeze. Rothamsted's GM wheat – "A step backwards for farming" [press release]. http://www.gmfreeze.org/news-releases/187/. Published March 29, 2012.
55. Rothamsted Research. Rothamsted GM wheat trial. 2014. Available at: http://www.rothamsted.ac.uk/our-science/rothamsted-gm-wheat-trial.
56. Powell W, A'Hara SA, Harling R, et al. Managing biodiversity in field margins to enhance integrated pest control in arable crops ("3-D Farming" Project): Project report no. 356 part 1. Home-Grown Cereals Authority (HGCA); 2004. Available at: http://archive.hgca.com/document.aspx?fn=load&media_id=1496&publicationId=1820.
57. Hickman JM, Written SD. Use of Phelia tanacetifolia strips to enhance biological control of aphids by overfly larvae in cereal fields. J Econ Entomol. 1996;89(4):832-840.
58. Lundgren P. GM wheat in the UK? No thanks! PeterLundgren.co.uk. http://www.peterlundgren.co.uk/2012/03/03/gm-wheat-in-the-uk-no-thanks-6/. Published March 3, 2012.
59. Suszkiw J. New soybeans bred for oil that's more heart-healthy. USDA Agricultural Research Service News & Events. http://www.ars.usda.gov/is/pr/2010/100916.htm. Published September 16, 2010.
60. Li S, Nugroho A, Rocheford T, White WS. Vitamin A equivalence of the beta-carotene in beta-carotene–biofortified maize porridge consumed by women? Am J Clin Nutr. 2010;92(5):1105-1112. doi:10.3945/ajcn.2010.29802.
61. HarvestPlus. Scientists find that "orange" maize is a good source of vitamin A. HarvestPlus.org. http://bit.ly/L2PxNV. Published September 7, 2010.
62. Anderson T. Biofortified crops ready for developing world debut. SciDev.Net. http://bit.ly/MAkMg7. Published November 17, 2010.
63. BBC News. "Healthy" purple potato goes on sale in UK supermarkets. http://www.bbc.co.uk/news/uk-scotland-11477327. Published October 6, 2010.
64. Watson J. Purple spud will put you in the pink. Scotland on Sunday. http://scotlandonsunday.scotsman.com/uk/Purple-spud-will-put-you.4841710.jp. Published January 3, 2009.
65. Knowles M. Italian producers unveil "supertomato." Fruitnet.com. http://bit.ly/1oLKL7t. Published July 5, 2010.
66. CBS News. Purple tomatoes may fight cancer, other diseases. http://archive.digtriad.com/news/health/article/202115/8/Purple-Tomatoes-May-Fight-Cancer-Other-Diseases. Published December 3, 2011.
67. John Innes Centre. Purple tomatoes may keep cancer at bay. http://bit.ly/NAwtZ6. Published October 26, 2008.
68. Martin C. How my purple tomato could save your life. Mail Online. http://bit.ly/10JsmlO. Published November 8, 2008.
69. Derbyshire D. Purple "super tomato" that can fight against cancer. Daily Mail. http://www.athena-flora.eu/florapress/4-Purple_Tomatoes_International_press_clip/UK/daily%20mail_UK.pdf. Published October 27, 2008.
70. Asian News International. Low-allergy peanuts on the anvil. OneIndiaNews. http://bit.ly/Li7xlV. Published June 8, 2010.
71. North Carolina A&T State University School of Agricultural and Environmental Sciences. N.C. A&T food scientist develops process for allergen-free peanuts. EurekAlert. http://bit.ly/LQVQBE. Published July 23, 2007.
72. Ogodo O. Iron-fortified maize cuts anaemia rates in children. SciDev.Net. http://bit.ly/LRAFl7. Published May 31, 2007.
73. Andang'o PE, Osendarp SJ, Ayah R, et al. Efficacy of iron-fortified whole maize flour on iron status of schoolchildren in Kenya: a randomised controlled trial. Lancet. 2007;369:1799-806. doi:10.1016/S0140-6736(07)60817-4.
74. Pollack A. That fresh look, genetically buffed. New York Times. http://www.nytimes.com/2012/07/13/business/growers-fret-over-a-new-apple-that-wont-turn-brown.html?_r=2&smid=tw-nytimesdining&seid=auto&. Published July 12, 2012.
75. Charles D. This GMO apple won't brown. Will that sour the fruit's image? NPR.org. 2014. Available at: http://www.npr.org/blogs/thesalt/2014/01/08/260782518/this-gmo-apple-wont-brown-will-that-sour-the-fruits-image.
76. The Organic & Non-GMO Report. Washington State University develops non-GMO, non-browning apple alternative. http://www.non-gmoreport.com/articles/february2014/wsu-develops-non-gmo-non-browning-apple-alternative.php.

Published January 31, 2014.
77. James C. Global status of commercialized biotech/GM crops: 2012. ISAAA; 2012. Available at: http://www.isaaa.org/resources/publications/briefs/44/download/isaaa-brief-44-2012.pdf.
78. GMWatch. Is GM quicker than conventional breeding? http://www.gmwatch.org/index.php/news/archive/2013-2/15227. Published December 23, 2013.
79. Phillips McDougall. The cost and time involved in the discovery, development and authorisation of a new plant biotechnology derived trait: A consultancy study for Crop Life International. Pathhead, Midlothian; 2011.
80. Goodman MM, Carson ML. Reality vs. myth: Corn breeding, exotics, and genetic engineering. In: Proc. of the 55th Annual Corn & Sorghum Research Conference. Vol 55. Chicago, IL; 2000:149–72.
81. Lloyd T. Monsanto's new gambit: Fruits and veggies. Harvest Public Media. http://bit.ly/LQTNxp. Published April 8, 2011.

# Conclusion

The introduction of GM crops and foods represents an unprecedented development in the history of agriculture. Never before has the nature of the food supply and the manner in which crops are grown been so fundamentally altered in such a short period of time. This change will affect the lives of all people on earth for many years to come.

Advances in agriculture are to be welcomed if they can contribute to a more sustainable, secure and fair production system and help solve the problem of world hunger and malnutrition. GM crops and foods have been consistently promoted as a way to produce higher yields with less inputs, reduce pesticide use, make farming easier and more profitable, produce more nutritious foods, and meet the challenges of climate change.

But the evidence that has emerged since their introduction in 1996 paints a very different picture. Scientific research and real-world farming experience shows that GM crops have not delivered on the promises above. They have not increased yields or sustainably reduced toxic chemical inputs. They have presented farmers with the new challenges of controlling herbicide-resistant superweeds and Bt toxin-resistant super-pests. GM crops are no less dependent on artificial fertilizers than any other chemically grown crop. They are not as safe to eat as conventionally bred crop varieties. They provide no solution to the major challenges of our time: climate change, the energy crisis, and world hunger.

## Why has GM failed to deliver on its promises?

The GM approach treats genes as isolated units of information with predictable outcomes. But this approach is flawed. Gene organization within the DNA of any organism is not random and gene function is a complex, interconnected, and coordinated network, consisting of layer upon layer of molecular systems.

GM is based on an outdated understanding of genetics and is destined to fail. It is beyond the ability of GM to deliver anything but the simplest of properties such as single-gene herbicide tolerance. GM is simply not up to the task of delivering safe, productive, and resilient food production systems.

Our modern understanding of genetics tells us that we need to take a holistic "systems biology" approach in crop development that preserves gene organization and regulation, rather than disrupting it, as GM does. The way to safely and effectively generate crops with complex desirable properties such as higher yield, drought tolerance, and disease resistance is through natural breeding, augmented where useful by marker assisted selection.

Given the fundamental technical and conceptual flaws of the GM approach to crop and food development, we should not be surprised to find that it has failed to deliver on any of its promises and has delivered foods that are not safe to eat.

## Why do farmers plant GM crops?

The GMO lobby's trump card in responding to these arguments is to ask: If GMOs are as unimpressive and problematic as we suggest, why do so many farmers in so many countries plant them?

The simple answer is that while some farmers do plant GM crops, the vast majority do not. Non-GM farming is by far the dominant model. Industry figures from 2013 show that 18 million farmers grow GM crops in 27 countries worldwide: that's less than 1% of the farming population. Around 92% of all GMOs are grown in just six countries, and these countries mainly grow just four GM crops: soy, maize, oilseed rape (canola) and cotton. Eighty-eight percent of arable land across the globe remains GM-free.[1]

What is more, in 2014, industry figures revealed that GM crop planting had fallen in industrialized countries for the first time since the technology was commercialized in 1996. Clive James, head of the industry group ISAAA, admitted that the industry now sees the developing world as the target for GMO industry expansion.[2]

As the evidence and case studies presented in this report make clear, it is irresponsible to use farmers in the developing world as guinea pigs for experimental GM crops that the majority of people do not want to eat.

## Time to move on

For two decades, GM proponents have dominated the political and media discussion on food and agriculture. Many of our agricultural research institutes and universities accept GMO industry funding and obligingly pursue a narrow GM-focused agenda, at the expense of proven effective agroecological solutions that focus on improving soil quality and maintaining crop diversity and health. Pro-GMO propaganda has even made its way into school and college curricula.

Yet the public, the vast majority of whom do not want to eat GM foods, is unconvinced. It has become common for pro-GMO lobbyists to try to shut down resistance to GM food and agriculture by saying that the debate is over, that science has shown that GMOs are safe and beneficial, and that it is time to move on and accept them.

We agree with only one aspect of this argument. It is indeed time to move on, but in the opposite direction to the one promoted by the GMO proponents. The scientific evidence presented in this report shows that the hypothetical benefits of GM crops and foods are not worth the known risks.

It is time to face up to what the evidence tells us about GMOs and stop pretending that GMOs can do anything that non-GM agriculture and good farming can't do far better, at a fraction of the cost, and without the restrictions attached to patent ownership. In fact, patents represent the single area in which GM crops and foods outstrip non-GM. If it ever becomes as easy to patent a non-GM crop as it is to patent a GM crop, it is likely that GM crops and foods will be consigned to the dustbin of history. Agricultural genetic engineering is not a smart or useful enough technology to succeed on its own merits. It is of interest to multinational companies and their government allies as a route to patent ownership of the food and feed supplies.

Once this fact has become clear to citizens and policy-makers, we hope they will throw resources and funding behind the safe, sustainable, and equitable agriculture that the world needs.

## References


1. Friends of the Earth. *Who benefits from GM crops? An industry built on myths*. Amsterdam, The Netherlands; 2014. Available at: http://www.foeeurope.org/sites/default/files/publications/foei_who_benefits_from_gm_crops_2014.pdf.
2. Kaskey J. Modified crop plantings fall in industrialized nations. *Bloomberg*. http://www.bloomberg.com/news/2014-02-13/modified-crop-plantings-fall-in-industrialiez-nations.html. Published February 13, 2014.

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