

An Illusory Consensus behind GMO Health Assessment

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Abstract

Prominent scientists and policymakers assert with confidence that there is no scientific controversy over the health effects of genetically modified organisms (GMOs)—that genetically modified crops currently in commercial use and those yet to be commercialized are inherently safe for human consumption and do not have to be tested. Those who disagree are cast as “GMO deniers.” This article examines scientific reviews and papers on GMOs, compares the findings of professional societies, and discusses the treatment of scientists who have reported adverse effects in animal feeding experiments. This article concludes by exploring the role that politics and corporate interests have had in distorting an honest inquiry into the health effects of GMO crops.

Keywords

expertise, methodologies, methods, politics, power, governance, academic disciplines and traditions, GMOs, genetically modified crops, health assessment, conflict of interest, scientific controversy

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Introduction

This article is written in three parts. First, I examine the scientific literature through the systematic reviews of animal feeding experiments and the findings of professional societies on the health assessment of genetically modified (genetically modified organism [GMO]) crops. Second, I discuss the reception among segments of the scientific community of two high-visibility published research papers that found adverse effects in animal feeding studies. Third, I discuss the implications of my analysis for how people should understand the current state of science regarding the health assessment of GMOs as well as how it informs science, technology, and society (STS) studies.

The scientific literature on the health effects of GMO crops falls into three clusters. One group of authors (cluster 1) states that there is no need for testing GMO products, as long as you know the proteins coded by the transferred genes and the host organisms. The transgenic products are considered as safe or safer than traditional hybrid crops or other non-transgenic methods.

Another group of authors (cluster 2) makes as strong a claim that each GMO product must be tested for a variety of possible effects. They assert that science cannot, a priori, claim that a product of genetic modification is safe without undertaking a testing program that includes multiyear and multigenerational tests in animals fed on the transgenic crop. Finally, a third group of scientific authors (cluster 3) asserts in their published articles that some GMO crops, when fed to animals, have exhibited harmful effects compared to non-GMO controls, and these results should draw attention to human health concerns.

As an example of cluster 1 scientists, Richard Roberts (2004), Nobel Laureate in Physiology or Medicine, wrote, “hundreds of studies and tests have been done on GMO safety and we have seen no scientific evidence that GMOs are inherently more dangerous than crops produced by traditional plant breeding.” Nicolia et al. (2014) wrote in their review of genetic engineering crop safety research, “We have reviewed the scientific literature on GE crop safety for the last 10 years that catches the scientific consensus matured since GE plants became widely cultivated worldwide, and we can conclude that the scientific research conducted so far has not detected any significant hazard directly connected with the use of GM crops.” Peter Lachman (1999) of the British Academy of Medical Sciences stated, “There is no experimental evidence nor any plausible mechanism by which the process of genetic modification can make plants hazardous to human

beings.” He dismisses the allergenicity mechanism or the use of antibiotic resistance markers in the GMO as beside the point. Regarding allergenicity, Lachman argued, since we know the allergen before we transplant the gene, it is to be expected that it would be allergenic in the new plant. It is not a new risk. Concerning antibiotic resistant genes, Lachman (1999, 69) noted, “The practice of leaving antibiotic resistant markers in the GM plant . . . is a hypothetical risk that antibiotic resistance could spread to gut flora.” Lachman called an end to the scientific controversy in 1999 before it barely began.

Gro Harlem Brundtland (Wilson and Highfield 2002), World Health Organization (WHO) Director General, stated that the available evidence shows that GM foods are “not likely to present human health risks” and therefore “these foods may be eaten.” Jacques Diouf (2002), Food and Agriculture Organization (FAO) Director General, announced that current scientific research confirms the safety of GM food. And Norman Borlaug (2014), Nobel Laureate, said to a packed hall consisting of researchers and food scientists in Nairobi, “There is no evidence to indicate that biotechnology is dangerous. After all, mother nature has been doing this kind of thing for God knows how long.”

Both skeptics and non-skeptics of GMOs purport to debunk the myths of their opponents. *Popular Science* magazine cited as an illustration GM apples in its article “Core Truths: 10 common GMO claims debunked.” After interviewing nearly a dozen scientists, *Popular Science* reported (Borel 2014) that consumers should not have much to fear about GMOs. In contrast, a 123-page monograph published in Earth Open Source (Antoniou, Robinson, and Fagan 2012) debunked the myths of GMO advocates. Each side of the debate uses the term “myth” pejoratively against an opponent to describe allegedly false claims, false logic, or a biased interpretation of science. A *National Geographic* story (Achenbach 2015) connected GMO skeptics to climate change deniers. What does the actual science tell us about the health assessment of GMOs?

Systematic Reviews

To gain some understanding of how the safety issues were addressed in the scientific literature, I did a search in *PubMed* and *Web of Science* for systematic reviews of GMO health effects from 2008 to 2014, which examined animal feeding studies. Eight reviews published in refereed publications were found. The conclusions of the reviewers were distributed across my three clusters. The first review (Maghari and Ardekani 2011) noted, “Many scientific data indicate that animals fed by GM crops have been harmed or

even died. Rats exposed to transgenic potatoes or soya had abnormal young sperm; cows, goats, buffalo, pigs and other livestock grazing on Bt-maize, GM cottonseed and certain biotech corn showed complications including early deliveries, abortions, infertility and also many died.”

A second review (Domingo and Bordonaba 2011) found, “. . . the number of studies specifically focused on safety assessment of GM plants is still limited. However, it is important to remark that for the first time, a certain equilibrium in the number of research groups suggesting, on the basis of their studies, that a number of varieties of GM products (mainly maize and soybeans) are as safe and nutritious as the respective conventional non-GM plant, and those raising still serious concerns, was observed. Moreover, it is worth mentioning that most of the studies demonstrating that GM foods are as nutritional and safe as those obtained by conventional breeding, have been performed by biotechnology companies or associates, which are also responsible of [sic] commercializing these GM plants.” According to the reviewers, there is still a lively controversy over the health effects of GMOs.

After commenting on the small number of available studies, a third review (Dona and Arvanitouannis 2009) reported, “The results of most of the rather few studies conducted with GM foods indicate that they may cause hepatic, pancreatic, renal, and reproductive effects and may alter hematological, biochemical, and immunologic parameters the significance of which remains unknown. The above results indicate that many GM foods have some common toxic effects. Therefore, further studies should be conducted in order to elucidate the mechanism dominating this action.”

A fourth review (Snell et al. 2012) concluded, “Results from all the 24 studies do not suggest any health hazards and, in general, there were no statistically significant differences within parameters observed. However, some small differences were observed, though these fell within the normal variation range of the considered parameters and thus had no biological or toxicological significance The studies reviewed present evidence to show that GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed.” The authors acknowledged there were statistically significant differences between GMO and non-GMO crops in some parameters that were not health related. This raises the question of whether the crops are “substantially equivalent.”

The fifth scientific review was published by the European Food Safety Association (EFSA 2014). Like many agency reviews, it typically is prepared by a scientific panel and has many scientific reviewers commenting on drafts before it is released. “The EFSA GMO panel concludes that the proposed uses of MON 87769 soybean oil in foods will not result in intakes

of stearidonic acid (SDA) with diverse effects and that the other changes in the dietary fatty acid pattern are unlikely to have negative nutritional consequences for humans. The EFSA GMO panel notes that the quantitative dietary estimates described here would have to be revisited if the oil produced by the soybean MON 87769 were to be extensively used in food products not considered in this assessment, for example as dietary supplements or to modify animal feed products.”

A sixth review (Bawa and Anilakumar 2013), covering a range of health, environmental, and social issues, found, “As the health effects are unknown, many people prefer to stay away from these foods” and “not much is known about their long-term effects on human beings.” The authors conclude by saying, “One has to agree that there are many opinions about scarce data on the potential health risks of GM food crops, even though these should have been tested for and eliminated before their introduction.”

The seventh review (Magana-Gomez and Calderon de la Barca 2008) reported, “The most common result [of animal feeding experiments] has been that there were no effects at the macroscopic level; however, organelles and other subcellular structures are clearly affected, as shown at ultramicroscopic levels.” They also noted that there are no standardized methods for evaluating GM foods and the “necessity of testing GM crops case by case has been established.”

The eighth and final review (Zhang and Shi 2011) focused on the question: do GM crops affect animal reproduction? The authors concluded, “It appears that there are no adverse effects of GM crops on many species of animals in acute and short-term feeding studies, but serious debates of effects of long-term and multigenerational feeding studies remain.” Other scientists (de Vendômois et al. 2010) concur on the need for long-term studies. “Lifetime studies for laboratory animals consuming GMOs must be performed, by contrast to what is done today, like the two-year long tests on rats for some pesticides or some drugs. Such tests could be associated to transgenerational, reproductive or endocrine research studies.”

One cannot read these systematic reviews and conclude that the science on health effects of GMOs has been resolved within the scientific community (see Table 1; Newman 2013). The eight reviewers made different choices about the endpoints they evaluated, the journal articles selected in their review (although there was considerable overlap), how they weighted the importance of individual studies, and how they interpreted the weight of evidence on the findings of health effects. These differences in methodology help to account for the variation in their findings.

Table 1. Eight Reviews on the Health Effects of GMOs.

Journal Review	Main Point
Maghari, B. M., and A. M. Ardekani. 2011. "Genetically Modified Foods and Social Concerns." <i>Avicenna Journal of Medical Biotechnology</i> 3 (3): 109-17 (July–September).	Many scientific data indicate that animals fed by GM crops have been harmed or even died. Rats exposed to transgenic potatoes or soya had abnormal young sperm. Cows, goats, buffalo, pigs, and other livestock grazing on Bt-maize, GM cottonseed, and certain biotech corn showed complications including early deliveries, abortions, infertility, and also many died.
Domingo, J. L., and J. G. Bordonaba. 2011. "A Literature Review on the Safety Assessment of Genetically Modified Plants." <i>Environment International</i> 37 (4): 734-42.	Most products have been found nutritionally safe, although the majority of the studies were associated with the industry producers.
Dona, A., and I. S. Arvanitouannis. 2009. "Health Risks of Genetically Modified Foods." <i>Critical Reviews in Food Science and Nutrition</i> 49 (2): 164-75.	The results of most studies with GM foods indicate that they may cause some common toxic effects such as hepatic, pancreatic, renal, or reproductive effects and may alter the hematological, biochemical, and immunological parameters.
Snell, C., A. Bernheim, J.-B. Berge, Marcel Kuntzd, Gérard Pascale, Alain Parisf, and Agnès E. Ricrochb. 2012. "Assessment of the Health Impact of GM Plant Diets in Long-term and Multigenerational Animal Feeding Trials: A Literature Review." <i>Food & Chemical Toxicology</i> 50 (3-4): 1134-48.	The studies reviewed present evidence to show that GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed.
EFSA (European Food Safety Authority). 2014. "Scientific Opinion on Application (EFSA-GMO-UK-2009-76) for the Placing on the Market of Soybean MON 87769." <i>EFSA Journal</i> 12 (5): 3644-85.	The majority of animal feeding experiments did not indicate clinical effects or histopathological abnormalities in organs or tissues of exposed animals. In some cases, adverse effects were noted but were difficult to interpret due to shortcomings in the studies.

(continued)

Table I. (continued)

Journal Review	Main Point
Bawa, A. S., and K. R. Anilakumar. 2013. "Genetically Modified Foods: Safety, Risks and Public Concerns—A Review." <i>Journal of Food Science & Technology</i> 50 (6): 1035-46.	As health effects of GMOs are unknown, many people prefer to stay away from these foods. In addition, not much is known about their long-term effects on human beings.
Magana-Gomez, J. A., and A. M. Calderon de la Barca. 2008. "Risk Assessment of Genetically Modified Crops for Nutrition and Health." <i>Nutrition Reviews</i> 67 (1): 1-16.	The most common result [of animal feeding experiments] has been that there were no effects at the macroscopic level; however, organelles and other subcellular structures are clearly affected, as shown at ultramicroscopic levels. There are no standardized methods for evaluating GM foods and the necessity of testing GM crops case by case has been established.
Zhang, W., and F. Shi. 2011. "Do Genetically Modified Crops Affect Animal Reproduction? A Review of the Ongoing Debates." <i>Animal</i> 5 (7): 1048-59.	There were no adverse effects of GM crops for many species of animals in acute or short-term feeding studies, but serious debate still surrounds long-term and multigenerational feeding studies. Long-term multigenerational feeding studies are clearly necessary to further investigate this issue.

Allergenicity

It has been confirmed without great surprise to plant geneticists that allergenic proteins can be transferred via their DNA from one plant to another. A laboratory experiment transferred a gene from a peanut to a soybean and demonstrated that people with peanut allergies showed allergenic responses to the transgenic soybean (Nordlee et al. 1996). Such products, where known allergens are transferred from one food to another that is allergen free, would not be permitted, certainly not without labeling.

What is less well understood is whether a non-allergenic protein in one food type can be transferred via its genes to another food type and become allergenic. Some scientists took it for granted that the transferred protein would behave as it did in its parental crop.

Testing for allergenicity without testing food on people can present some problems. Animal feeding studies do not provide the best assessment of human allergens. Animal immune systems are not always a good model for humans. Nevertheless, animal studies can reveal changes in proteins in transgenic crops. A food fed to mice in the original crop without immune responses can show allergenic responses when fed to mice in the transgenic crop. This is an important indicator that the protein was modified. When a gene is moved from one crop to another, this effect has been known to occur. Genes may be fungible (genes from one organism can be transferred and expressed in the cells of another, even across dissimilar species), but their products are not always identical.

This was learned in Australia from an experiment performed at the national research organization Commonwealth Scientific and Industrial Research Organisation. A decadelong research project focuses on developing genetically modified peas with pesticide resistance. Scientists (Campbell et al. 2011) took a gene from the common bean (*Phaseolus vulgaris*) that synthesized a protein capable of killing sea weevil pests and transferred it to the pea (*Pisum sativum*). The protein tested in the bean does not cause an allergic reaction in mice or humans. But after the protein was expressed in the pea, it was learned that its structure was modified slightly. When the gene for the protein was transferred to peas, the structural change in the protein could be responsible for its unanticipated immune effects in mice.

Scientists are not entirely sure why a transplanted gene undergoes a protein modification. The term “post translational modification” is used to describe the protein change. It cannot be assumed that a naturally occurring protein will be identical to a protein produced in a GM plant, suggesting that each protein transfer must be tested for allergenicity.

It is now well understood that genes do not always encode a fixed three-dimensional protein structure. The term “intrinsically disordered protein” has been introduced to describe proteins that lack a fixed three-dimensional structure. It has been reported that 33 percent of eukaryotic proteins contain disordered segments (Ward et al. 2004). Also, intrinsically unstructured proteins have been connected to a number of diseases. What has not been studied is whether GMOs, through posttranslational modification, have a higher frequency of proteins containing disordered segments.

Developmental biologist Stuart Newman (2009, 27) discusses the uncertainties of transplanting new genes into a plant’s genome. “Throwing an entirely new component into a plant’s biological mix can potentially change the hundreds to thousands of potentially toxic molecules every plant is

capable of manufacturing GM transgenesis can inadvertently induce extensive scrambling of the genome.”

Lee et al. (2013) repeated the bean–pea experiment and reached very different results. They found that transgenic alpha-amylase inhibitor peas, chickpeas, and cowpeas as well as non-transgenic beans were all allergenic in a species of mice. If that is corroborated, then the issue of posttranslational modification of transgenes for allergenicity has to be reevaluated. Until that is investigated, it remains uncertain whether allergenicity is an emergent property of transgenic plants.

Professional Societies

Another approach for gauging whether there is scientific consensus over the health effects of GMOs is to consult the opinion of professional associations. For many in the United States, the soundest advice about scientific or medical matters is provided by the National Academies of Science (NAS) because their studies are performed by carefully chosen scientific panels that offer their interpretation of the best published science. In 2004, the NAS published the *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects*. Among the findings of the report was, “All evidence evaluated to date indicates that unexpected and unintended compositional changes arise with all forms of genetic modification, including genetic engineering. Whether such compositional changes result in unintended health effects is dependent upon the nature of the substances altered and the biological consequences of the compounds. To date, no adverse health effects attributed to genetic engineering have been documented in the human population” (NAS 2004, 8).

The Academy report supports safety assessment of foods that have undergone compositional changes. “The committee recommends that compositional changes that result from all genetic modification in food, including genetic engineering, undergo an appropriate safety assessment. The extent of an appropriate safety assessment should be determined prior to commercialization” (NAS 2004, 8).

Because the addition of a foreign gene into a food substance is not considered a food additive, according to the 1992 Food and Drug Administration (FDA) policy, the product does not have to meet the standard of safety for chemical food additives, namely, reasonable certainty that no harm will result from intended uses of consumption. “There is no burden on the food manufacturer to demonstrate the safety of food products that are not food additives” (NAS 2004, 131). The NAS report provides a pre- and

post-market framework for assessing the safety of GMOs on a case-by-case basis.

The FDA has classified GM foods as “generally regarded as safe” known as “GRAS” and has a reporting mechanism but not a mandatory testing policy (Druker 2015). According to the NAS (2004, 8), “All evidence evaluated to date indicates that unexpected and unintended compositional changes arise with all forms of genetic modification, including genetic engineering To date, no adverse health effects attributed to genetic engineering have been documented in the human population.”

Even as the NAS asserts its confidence in the safety of transgenic foods, it recommends pre-market assessment of all new food prior to commercialization, but emphasizes that the policy to assess products should not be based exclusively on their methods of breeding (NAS 2004, 9). The Academy also acknowledges “there remain sizable gaps in our ability to identify compositional changes that result from genetic modification of organisms intended for food” (NAS 2004, 15).

The British Medical Association (BMA) issued its first statement on GMOs in 1999 when it advised that there should be a moratorium on the commercial planting of GM crops. The BMA report titled *The Impact of Genetic Modification on Agriculture, Food and Health* warned that “any adverse effects from GMOs are likely to be irreversible. As we cannot yet know whether there are any serious risks to the environment or human health, the precautionary principle [when a product or policy is suspected of causing harm, even in the absence of scientific consensus and definitive evidence of risk, the burden of proof is to demonstrate that it is not harmful before taking action.] should apply.” An updated report by the BMA in 2004 expressed less concern about the health risks of current GMOs. “The potential for GM foods to cause harmful health effects is very small However, safety concerns cannot, as yet, be dismissed completely on the basis of information currently available” (BMA 2004, 3). The report also noted that “the few robust studies that have looked for health effects have been short term and specific. There is a lack of evidence-based research with regard to medium and long-term effects on health and the environment.”

In 2003, BMA (Scotland) welcomed a report of the Scottish Parliament that the risk assessment of GMOs was flawed. BMA (Scotland) testified that “There is insufficient evidence to show whether or not there are potential health risks from exposure to Genetically Modified Organisms (GMOs). The only way to try and answer this question is to actually look in a systematic way for adverse effects on human health” (BMA 2003).

The Indiana State Medical Association and the Illinois State Medical Society introduced resolutions to the American Medical Association (AMA) supporting Federal legislation and/or regulations to require labeling of food with genetically engineered (GE) ingredients. As of 2012, the AMA Council of Delegates did not support mandatory labeling of GMOs without evidence of material differences between bioengineered foods and their traditional counterparts. The AMA Council affirmed that no long-term health effects have been detected from the use of transgenic crops and GM foods. The Council and the AMA do support mandatory pre-market systematic safety assessments of bioengineered foods in lieu of a voluntary notification policy and the development and validation of additional techniques for the detection and assessment of unintended effects (AMA 2012).

The American Public Health Association, the American Nurses Association, the Illinois Public Health Association, and the California State Medical Association have passed resolutions calling for labeling of GE food.

The professional toxicologists also issued a policy statement in 2003 through the Society of Toxicology with a perspective akin to cluster 1 scientists, “The available scientific evidence indicates that the potential adverse health effects arising from biotechnology-derived foods are not different in nature from those created by conventional breeding practices for plant, animal, or microbial enhancement, and are already familiar to toxicologists.” However, it also added, “Methods have not yet been developed by which whole foods (as compared with single chemical components) can be fully evaluated for safety. Progress also needs to be made in developing definitive methods for the identification and characterization of protein allergens, and this is currently a major focus of research.” And while rather optimistic about the safety of existing GMOs, the report of the Society makes it clear that the methods to test the food and the passive reporting system are deficient. “The level of safety of current (“biotechnology-derived”) BD foods to consumers appears to be equivalent to that of traditional foods. Verified records of adverse health effects are absent, although the current passive reporting system would probably not detect minor or rare adverse effects, nor can it detect a moderate increase in common effects such as diarrhea. However, this is no guarantee that all future genetic modifications will have such apparently benign and predictable results. A continuing evolution of toxicological methodologies and regulatory strategies will be necessary to ensure that this level of safety is maintained” (Society of Toxicology 2003).

The American Academy of Environmental Medicine (AAEM), an organization formed in 1965 largely made up of MDs who identify themselves as clinical ecologists, a medical specialty not recognized by more traditional

medical associations, issued a policy statement on GMOs acknowledging adverse impacts of animal studies (AAEM 2009). “[S]everal animal studies indicate serious health risks associated with GM food consumption including infertility, immune dysregulation, accelerated aging, dysregulation of genes associated with cholesterol synthesis, insulin regulation, cell signaling, and protein formation, and changes in the liver, kidney, spleen and gastrointestinal system. There is more than a casual association between GM foods and adverse health effects.” In contrast, the Royal Society of Canada (RSC) concluded that GMOs pose no inherent risk. While not unduly concerned about GMO health effects based on 2001 evidence, the RSC (2001, 48) questioned the nature of the evidence in its statement “that regulatory requirements related to toxicological assessment of GM food appeared to be ad hoc and provided little guidance either as to when specific studies would be required or what types of studies would be most informative. The [RSC] Panel was unaware of any validated study protocols currently available to assess the safety of GM food in their entirety (as opposed to food constituents) in a biological and statistically meaningful manner.” Among its recommendations, the RSC (2001, 50) Panel called upon federal officials in Canada to establish “clear criteria regarding when and what types of toxicological studies are required to support the safety of novel constituents derived from transgenic plants.”

The conclusions of the chosen group of professional associations mirror the disparity found in the systematic reviews. Medical and scientific societies have reached their consensus positions by selecting the studies each deems credible and important and by preferentially weighing the evidence those studies provide, even as some societies question the reliability or sufficiency of those studies. It is not unusual for expert panels to differ in their conclusions and advice. Building on the work of Erving Goffman, science studies scholars have applied the metaphor of dramaturgy, where science advisory panels engage in a type of performance, to understand the factors that determine how information gets presented to the public (front stage) and which conclusions get negotiated in the back rooms (back stage). The study of GMO science panels provides fertile ground for such an analysis (Hilgartner 2000).

Individual Studies

Thus far, I have identified twenty-six studies in the scientific literature that have reported adverse effects or uncertainties of GMOs fed to animals (Table 2). In this section, I shall focus on two of those published studies

Table 2. Articles Citing Adverse Effects or Uncertainties on the Health Effects of GMOs.

- Fares, N. H., and A. K. El-Sayed. 1998. "Fine Structure Changes in the Ileum of Mice Fed on Endotoxin-treated Potatoes and Transgenic Potatoes." *Natural Toxins* 6 (6): 219-33.
- Ewen, S. W. B., and A. Pusztai. 1999. "Effects of Diets Containing Genetically Modified Potatoes Expressing *Galanthus nivalis* Lectin on Rat Small Intestine." *Lancet* 354 (9187): 1353-54.
- Birch, A. N. E., I. E. Geoghegan, M. E. N. Majerus, J. W. McNicol, C. A. Hackett, A. M. R. Gatehouse, and J. A. Gatehouse. 1999. "Tri-trophic Interactions Involving Pest Aphids, Predatory 2-spot Ladybirds and Transgenic Potatoes Expressing Snowdrop Lectin for Aphid Resistance." *Molecular Breeding* 5 (1): 75-83.
- Malatesta, M., C. Caporaloni, S. Gavaudan, M. B. L. Rocchi, S. Serafini, C. Tiberi, and G. Gazzanelli. 2002. "Ultrastructural Morphometrical and Immunocytochemical Analysis of Hepatocyte Nuclei from Mice Fed on Genetically Modified Soybean." *Cell Structure Function* 27 (5): 173-80.
- Malatesta, M., C. Caporaloni, L. Rossi, S. Battistelli, M. B. L. Rocchi, F. Tonucci, and G. Gazzanelli. 2002. "Ultrastructural Analysis of Pancreatic Acinar Cells from Mice Fed on Genetically Modified Soybean." *Journal of Anatomy* 201 (5): 409-15.
- Malatesta, M., M. Biggiogera, E. Manuali, M. B. L. Rocchi, B. Baldelli, and G. Gazzanelli. 2003. "Fine Structural Analyses of Pancreatic Acinar Cell Nuclei from Mice Fed on Genetically Modified Soybean." *European J. Histochemistry* 47 (4): 385-99.
- Pryme, I. F., and Rolf Lembcke. 2003. "In Vivo Studies on Possible Health Consequences of Genetically Modified Food and Feed—with Particular Regard to Ingredients Consisting of Genetically Modified Plant Materials." *Nutrition and Health* 17 (1): 1-8.
- Vecchio, L., B. Cisterna, M. Malatesta, T. Martin, and B. Biggiogera. 2004. "Ultrastructural Analysis of Testes from Mice Fed on Genetically Modified Soybean." *European Journal of Histochemistry* 48 (4): 449-54.
- Prescott, V. E., P. M. Campbell, A. Moore, J. Mattes, M. E. Rothenberg, P. S. Foster, T. J. Higgins, and S. P. Hogan. 2005. "Transgenic Expression of Bean Alpha-amylase Inhibitor in Peas Results in Altered Structure and Immunogenicity." *Journal of Agriculture Food & Chemistry* 53 (23): 9023-30.
- Tudisco, R., F. Lombardi, F. Bovera, D. d'Angelo, M. I. Cutrignelli, V. Mastellone, V. Terzi, L. Avallone, and F. Infascelli. 2006. "Genetically Modified Soy Bean in Rabbit Feeding: Detection of DNA Fragments and Evaluation of Metabolic Effects by Enzymatic Analysis." *Animal Science* 82 (2): 193-99.
- Ermakova, I. V. 2006. "Genetically Modified Soy Leads to the Decrease of Weight and High Mortality of Rat Pups of the First Generation. Preliminary Studies." *EcosInform* 1:4-9. (in Russian)
- Sagstad, A., M. Sanden, Ø. Haugland, A. C. Hansen, P. A. Olsvik, and G. I. Hemre. 2007. "Evaluation of Stress- and Immune-response Biomarkers in Atlantic Salmon for Different Levels of Bt Maize." *Journal of Fish Diseases* 30 (4): 201-12.

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Table 2. (continued)

- Seralini, G.-E., D. Cellier, and J. S. de Vendomois. 2007. "New Analysis of Rat Feeding Study with GM Maize Reveals Signs of Hepatorenal Toxicity." *Archives of Environmental Contaminant Toxicology* 52 (4): 596-602.
- Malatesta, M., F. Boraldi, G. Annovi, Beatrice Baldelli, Serafina Battistelli, Marco Biggiogera, and Daniela Quaglino. 2008. "A Long-term Study on Female Mice Fed on a Genetically Modified Soybean: Effects on Liver Ageing." *Histochemistry Cell Biology* 130 (5): 967-77.
- Finamore, A., M. Roselli, S. Britti, G. Monastra, R. Ambra, A. Turrini, and E. Mengheri. 2008. "Intestinal and Peripheral Immune Response to MON810 Maize Ingestion to Weaning and Old Mice." *Journal of Agriculture Food & Chemistry* 56 (23): 11533-39.
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- Trabalza-Marinucci, M., E. Chiaradia, G. Brandi, C. Rondini, L. Avellini, C. Giammarini, S. Costarelli, G. Acuti, C. Orlandi, and G. Filippini. 2008. "A Three Year Longitudinal Study on the Effects of a Diet Containing Genetically Modified Bt176 Maize on the Health Status and Performance on Sheep." *Livestock Science* 113 (2-3): 178-90.
- Sissener, N. H., M. Sanden, A. M. Bakke, A. Krogdahl, and G. I. Hemre. 2009. "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* 294 (1-2): 108-17.
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in order to provide an in-depth analysis of the receptivity of their work by the scientific community.

The animal feeding study that created the largest media response was published in the *Lancet* in 1999. No one in the field of medicine needs an introduction to this journal, which began publication in 1823 and has a Journal Impact Factor of 39. The article in question was authored by Stanley Ewen, Department of Pathology at the University of Aberdeen and Arpad Pusztai, Rowett Research Institute in Aberdeen. Rowett is largely a government-funded research institute focusing on animal and human nutrition. They fed GM potatoes to rats and observed damage to their intestines and immune systems.

Pusztai is an internationally recognized expert on lectins, plant-protective proteins with insecticidal properties. He had published about 300 scientific papers, including two in *Nature*, and published two books: he was coeditor of *Lectins: Biomedical Perspectives* (Taylor and Francis; Pusztai and Bardocz 1995) and coauthor of *Handbook of Plant Lectins* (John Wiley; van Damme et al. 1998).

Pusztai reported that the Rowett Institute had a major research collaboration with a pharmaceutical company. According to the contract with Rowett, the company had intellectual property rights on all research at the institute pertaining to lectins in the human gut, even research the company did not fund. The company was interested in the role lectins might play in the prevention of gut damage in chemoradiation therapy. Pusztai noted, "So, everything which we did in this field belonged to them," including his GM potato research (2002a, 80).

The story began in 1995 when the Scottish Office of Agriculture, Environment and Fisheries Department (SOAEFD) reported funding for a new research program on evaluating the safety of GM crops. According to

Pusztai, there were no peer-reviewed studies on the safety of GM crops at the time. He submitted a fifty-page proposal. It was among twenty-eight proposals, which were eventually whittled down to eight that were sent out for peer review. Pusztai's proposal was accepted and he was awarded 1.6 million pounds for doing the study. There were three research units involved: the Scottish Crop Research Institute (SCRI), the University of Durham's Department of Biology, and the Rowett Institute.

Pusztai reported that Rowett had a profit-sharing agreement with Axis-Genetics, which financed the development of the GM potato. If the potato were eventually commercialized, Rowett would share the profits. Pusztai (2002a, 85) wrote, "We thought that GM potatoes would be ok because it's a great idea."

In a talk he delivered on May 7, 1999, to the British Hungarian Fellowship in South Kensington, UK, Pusztai said that he believed that GM potatoes were destined for a commercial market, and he thought that they should be tested to know whether they were safe to eat. They had two transgenic genetic lines of potatoes with insecticidal lectin genes from the snowdrop (*Galanthus nivalis*). At the time Pusztai (2002b, 74) wrote "there are many opinions on the safety of GM food but very few data published in peer reviewed journals."

The Nature of the Experiment

Pusztai and his team decided to study a transgenic potato with a gene from a white-flowering, spring blooming Eurasian plant called a snowdrop. They chose a gene that coded for a lectin protein. The snowdrop species selected was *G. nivalis*. The lectin gene is called *G. nivalis* agglutinin or GNA. The idea of genetically modifying plants for insect resistance was in the air at the time. There were experiments underway in the late 1990s for encoding GNA in wheat so the crop would be resistant to grain aphids (Stogar et al. 1999).

Pusztai stated his hypothesis for the experiment, "It was thought that comparison of the histological parameters of the gut of rats fed potato diets containing either GM potatoes, or non-GM potatoes with or without being supplemented with GNA should give a clear indication whether GNA gene insertion had affected the nutritional and physiological impact of potatoes on the mammalian gut" (Ewen and Pusztai 1999a).

Pusztai and his group chose to incorporate the snowdrop lectin into the potato because they believed it would not cause a health problem for the animals. They had done experiments where freestanding GNA proteins

were introduced into the rats' diet without adverse effects. Pusztai (2002a, 70) wrote that he had experimental assurances that GNA was a safe lectin and the gene coding it a safe gene. He also published a study of transgenic peas fed to rats and reported "that the nutritional value of diets containing transgenic or parent peas was remarkably similar" and were "without major harmful effects on their growth, metabolism and health" (Pusztai et al. 1999, 1603, 1597).

Pusztai's study used two transgenic potato lines that were developed at the Scottish Research Institute, each with a lectin gene from snowdrop. They had four experimental groups of male nineteen-day-old rats, believing that any adverse effects would likely show up in younger animals (Pryme and Lembcke 2003).

GM and non-GM potatoes came from the same field site. Each of the two GM potato lines was fed to separate groups of rats, and another group was fed the parental non-GMO potato spiked with the GNA protein. There were also controls fed the standard rat feed. Ewen and Pusztai (1999a) wrote, "We compared the histological indices of the gut of rats fed potato diets containing GM potatoes, non-GM potatoes, or non-GM potatoes supplemented with GNA, to find out whether GNA gene insertion had affected the nutritional and physiological impact of potatoes on the mammalian gut."

Two commentators noted in their 2003 publication *Nutrition and Health* "Pusztai's studies . . . are remarkable in that the experimental conditions were varied and several ways were found by which to demonstrate possible health effects of GM-foods" (Pryme and Lembcke 2003).

In 1998, Dr. Pusztai accepted an interview on a program titled *World in Action*. He said that his group had observed adverse changes to the intestines and immune systems of rats fed GM potatoes. He also said that "If I had the choice I would certainly not eat it [GM potatoes]" and that "I find it's very unfair to use our fellow citizens as guinea pigs" (Randerson 2008). For a short time, the Rowett Institute was proud of Pusztai's media attention. But soon thereafter, the institute suspended Pusztai and used misconduct procedures to seize his data. His contract was not renewed, and while suspended he was banned from speaking publicly and thereafter forced to retire.

Pusztai wrote that the Rowett Institute had a major research program with a pharmaceutical company, which funded many of the projects on lectins in the human gut. "So everything we did in this field belonged to the company, so the GM potato project also belonged to the company The company was interested in a way to use lectins for the prevention of gut

damage in chemo-radiation therapy In a sense we were sold to them [the company]—lock, stock and barrel The company, in fact, disowned us, in order to avoid bad publicity” (2002a, 80).

Because the data were likely held by his colleague Stanley Ewen, Rowett could not restrict its publication. The results of the study were varied and complex. The principal conclusions were published in *The Lancet* on October 16, 1999. In brief, the authors reported that the rats fed on the GM diet, compared to controls, grew less well, exhibited unusual changes in their tissue, and were found to have immune problems, which did not occur when the rats were fed free GNA lectin proteins.

The authors suggested that some of the adverse effects they observed were possibly a result of the transformation of the potato with the transgene and was not a consequence of the lectins per se. The two lines of the GM potatoes derived from the same transformation event exhibited some different effects. The authors surmised that genes are inserted into different positions in the potato chromosome and in some placements may interfere with the plant’s own gene expression.

A scientific committee of the Royal Society of London told Pusztai that his results were obtained by poor experimentation, bad design, and wrong conclusions. According to *The Guardian* and the journal *Science as Culture*, Pusztai responded, “Supposedly in my previous 270 papers, some 40 of them with the same design and methodology, I was scientifically alright, but then suddenly I had a mental breakdown” (Randerson 2008, 18; Pusztai 2002a). There were 919 media stories published from 1998 through early 2015 on the Pusztai affair without conclusive evidence of why his experiment was allegedly deficient.

Criticisms

There were two stages of criticisms of Pusztai’s work: the prepublication review and the post-publication review. In the former, there was a review of the methodology of the proposal and there were six members of the Scottish Royal Society who looked at a range of documents prior to publication at the request of the head of Rowett. There were also six reviewers for *The Lancet*. The post-publication criticisms came immediately after *The Lancet* article was published. Prior to publication, *The Guardian* wrote that Professor Peter Lachmann, British immunologist, Emeritus professor at the University of Cambridge, and Fellow of the Royal Society, phoned the editor of *The Lancet* and threatened him if he published the Pusztai paper (Flynn and Gillard 1999). Lachmann confirmed that he made the call but

denied that he threatened the editor. Lachmann was an author of the Royal Society's 1998 highly favorable report on GMOs.

A widely reported story line goes as follows: in 1999, Lachmann tried to persuade the editor of *The Lancet* not to publish Árpád Pusztai's research on the adverse effects of GM potatoes on rats on the grounds that it was not sound science. *The Lancet*'s editor, Richard Horton, received what he described as an aggressive phone call from Lachmann. Dr. Horton said he was called at his office in central London on the morning of Wednesday October 13, two days before the *Lancet* published the paper by Pusztai.

Dr. Horton, editor of *The Lancet* since 1995, said the phone call began in a "very aggressive manner." He said he was called "immoral" and accused of publishing Dr. Pusztai's paper, which he "knew to be untrue." Toward the end of the call, Dr. Horton said the caller told him that if he published the Pusztai paper, it would "have implications for his personal position" as editor. *The Lancet* is owned by Reed Elsevier, one of Europe's largest scientific publishing houses (Flynn and Gillard 1999). Lachmann's own account of the Pusztai affair can be found in *Panic Nation* (2005). He categorically denies making the threat to Richard Horton.

When *The Lancet* received the manuscript from Ewen and Pusztai, it was sent to six referees, whereas the usual peer review has two to three referees. Five of the six referees recommended the paper for publication, while one referee was strongly against publication. In addition, that referee transgressed a long-standing norm of the journal to keep reviews to the editor confidential by disclosing his negative review to the press. *The Lancet* published the article despite the pressures to do otherwise. The attacks against Pusztai were unrelenting. He and Ewen responded to a number of his critics in *The Lancet* (Ewen and Pusztai 1999b). Pusztai left Rowett and periodically has commented on the incident. To this date, no one has made an effort to replicate his study. The episode left Pusztai's otherwise distinguished career in shambles.

The Séralini Case

The second most highly publicized study was led by Gilles-Eric Séralini, a professor of molecular biology at the University of Caen in Normandy, France. He is the founder and president of the scientific advisory board of the nonprofit Committee of Research and Independent Information on Genetic Engineering (CRIIGEN), an association that was in the public record. Funding from CRIIGEN was acknowledged in Séralini's papers.

In 2009, Séralini and eight other authors published a paper in the *International Journal of Biological Sciences* that discussed the relevant criteria

that should be used to evaluate GMOs. Their paper raised questions about what regulatory agencies use to undertake risk assessments involving mammalian feeding experiments of GMOs (Séralini et al. 2009). By that time Monsanto had been undertaking short-term tests (ninety days) on certain GMO food products. The authors considered the current criteria to be fostering false negative results because of sample size and statistical design. Referring to some experiments that found adverse effects from GMOs the authors stated, “These GM-linked effects are then considered as signs of toxicity in the ninety-days, not proofs of toxicity” (Séralini et al. 2009, 442).

The authors proposed new tests of increased duration and larger number of rats in order to increase the sensitivity or resolution power of the tests. “We call for more serious standardized tests such as those used for pesticides or drugs, on at least three mammalian species tested for at least three months, employing larger sample sizes and up to one and two years before commercialization” (Séralini et al. 2009, 442). Long-term tests were not popular with industry because of the time and expense. Ironically, when Séralini undertook such tests, his published results drew considerable criticism.

In 2012, Séralini headed a study on the long-term toxicity of the herbicide *Roundup* (Monsanto’s trade name for a glyphosate-based herbicide) and *Roundup* tolerant GM maize. The scientific group was interested in evaluating the health effects of *Roundup*, which consisted of the herbicide glyphosate and other additives called adjuvants, as well as the GM crop that was made herbicide tolerant from the transgenes (GM maize NK603). In prior feeding experiments, some showed effects and some showed no effects for both *Roundup* and the GM plant. The group used the Organisation for Economic Co-operation and Development (OECD) Guideline 408 but went beyond it. They were very clear in their paper that they were not using a carcinogenesis protocol, which requires fifty rats per group. They used ten rats per group that were fed three doses of the GMO. They found that *Roundup* delivered to rats at concentrations below officially set safety limits “induce severe hormone-dependent mammary, hepatic and kidney disturbances” (Séralini et al. 2012, 4230). Female rats developed large mammary tumors more often than and before controls. Liver congestion and necrosis were between 2.5 and 5.5 times higher in treated males than controls. Males showed four times more palpable tumors than controls. Most of the adverse effects were kidney related. Séralini et al. reported adverse effects for the GM maize alone, for *Roundup* alone, and for GM maize with *Roundup* residues.

The paper was published on line September 19, 2012, and within a very short time letters of criticism began flooding the journal. They charged Séralini with conflict of interest because of his association with the non-profit CRIIGEN. He was criticized for using too few animals, the wrong strain of rats, for violating protocols of a carcinogen study, and for using poor statistics. Séralini had to deal with about fifty points of criticism.

A few months later, Editor-in-chief A. Wallace Hayes wrote an editorial on the review process for manuscripts submitted to *Food and Chemical Toxicology*. It covered some broad themes such as conflict of interest, selection of peer reviewers, post-publication review including letters to the editor, and responses to comments by the authors. It is everything you would expect from a transparent editor-in-chief discussing the manuscript review process. Hayes only gets specific in the first sentence. "Manuscripts submitted to *Food and Chemical Toxicology* (FCT), such as the Seralini et al September 2012 publication, are subjected to a rigorous peer review process." (The accent aigu was omitted from Séralini's name.) In selecting out the Séralini et al. paper in the editorial, it appears to the reader that the editor-in-chief stands behind the judgment of the peer review process, particularly with this article. That's what makes the next stage of this case much more difficult to understand.

Séralini and his colleagues (2013) wrote an eight-page response to the critical letters attacking their 2012 publication. They began with two points of clarification about their study. First, they said that their study is the first long-term detailed research on mammals exposed to a highly diluted pesticide in its total formulation with adjuvants. In other words, they were not testing simply the active ingredient glyphosate. The adjuvants are added in the formulation because they make the herbicide more effective. Secondly, they noted that their work is not the final word on toxicological effects of GM maize (NK603 and *Roundup*). They noted that their research is the first step in studying long-term health effects of GMOs that should be replicated independently. Séralini was criticized for not following OECD guidelines in doing such experiments, but as he pointed out, there are no such guidelines for *in vivo* studies of GMO toxicity. He was criticized for using too few animals. His response was that ten animals in each sex group was recommended by OECD in 1981. People criticized him because he did not use the protocols for a carcinogen study. He responded that his study was not a carcinogen study but rather a long-term, full toxicological study. Nevertheless, he was required to report any lesions or tumors, which he did. He was criticized for the type of rats he used and the low number and for how he presented the data, which, critics said, placed too much emphasis

on tumors. He was brought to task for claiming *Roundup* was an endocrine disruptor, while studies reported glyphosate had not shown hormonal effects. The criticisms included a finding of breach of ethics for letting the rat tumors grow too large when the rats should have been euthanized. They even charged him with conflicts of interest. Séralini et al. responded to about forty-five individual criticisms, taking them point-by-point. He responded to the criticism that no adverse effects have been observed in farm animals or humans.

Some critics have emphasized that no adverse effects have been reported on either farm animals or in the human population of the USA who have consumed an unknown mixture GMO crop derived food. Such claims are scientifically unsound for the following reasons. First, it is important to note that there have been neither epidemiological studies of the human population nor monitoring of farm animals in an attempt to correlate any ill-health observed with the consumption of a given GM crop. Second, it should be recalled that farm animals are not reared to live for the entire duration of their natural life-span, and thus usually do not live long enough to develop long-term chronic diseases, which contrasts with the rats in our life-long experiment. If any studies in lactating cows are conducted, biological analyses performed are far less complete than those done in regulatory tests using rodents including in our study. Third, as there is no labeling of GMO food and feed in the USA, the amount consumed is unknown, and no “control group” exists. Thus, without a clear traceability or labeling, no epidemiological survey can be performed. (Séralini et al. 2013, 481)

It is rare in scientific publishing to find such a preponderance of criticism directed at a peer-reviewed publication and equally as rare to find such an extensive and detailed response to the criticism—seven published pages.

With pressure building on the journal editorial staff from strident letters, some declaring fraud in the Séralini et al. paper, in late fall 2013 the editor-in-chief requested that Séralini retract the paper. As told by Séralini et al.,

On 19 November, 2013, the editor-in-chief requested the retraction of our study while recognizing that the data were not incorrect and that there was no misconduct and no fraud or intentional misinterpretation in our complete raw data—an unusual or even unprecedented action in scientific publishing. The editor argued that no conclusions could be drawn because we studied 10 rats per group over 2 years, because they were Sprague Dawley rats, and because the data were inconclusive on cancer. Yet this was known at the time of submission of our study. Our study was however never intended

to be a carcinogenicity study. We never used the word ‘cancer’ in our paper. (2014, 13)

Several months after Séralini refused to retract his paper, an unsigned editorial was published in the journal early in 2014 issuing a retraction notice for the paper. While unsigned, the editorial was presumably authored or approved by the editor-in-chief. The retraction editorial stated that the editor-in-chief requested from the corresponding author the permission to review the raw data. The editor-in-chief commended Séralini for “his commitment to the scientific process.” What followed was probably unprecedented in the history of science publishing. First, the editor-in-chief supplied his justification for the retraction.

Unequivocally, the Editor-in-Chief found no evidence of fraud or intentional misrepresentation of the data. However, there is a legitimate cause for concern regarding both the number of animals in each study group and the particular strain selected. The low number of animals had been identified as a cause for concern during the initial review process, but the peer-review decisions ultimately weighed that the work still had merit despite its limitations. A more in-depth look at the raw data revealed that no definitive conclusions can be reached with this small sample size regarding the role of either NK603 or glyphosate in regards to overall mortality or tumor incidence. Given the known high incidence of tumors in the Sprague-Dawley rats, normal variability cannot be excluded as the cause of the higher mortality and incidence observed in the treated groups. Ultimately, the results presented while not incorrect are inconclusive, and therefore do not reach the threshold of publication for *Food and Chemical Toxicology*. The retraction is only on the inconclusiveness of this one paper. (FCT 2014, 244)

One might ask whether a paper’s “lack of definitive results” is a justification for retraction. Some of Séralini’s supporters cited the retraction guidelines of the Committee on Publication Ethics (COPE 2009) to answer this question. COPE has four conditions for justifying a retraction. “Journal editors should consider retracting a publication if: (1) they have clear evidence that the findings are unreliable, either as a result of misconduct (e.g. data fabrication) or honest error (e.g. miscalculation or experimental error); (2) the findings have previously been published elsewhere without proper cross referencing, permission or justification (i.e. cases of redundant publication); (3) it constitutes plagiarism; (4) it reports unethical research.” There is nothing close to the justification “lack of definitive

results.” The International Committee of Medical Journal Editors (ICMJE) is another well-respected journal publication organization that provides guidelines for all journals and requirements for its members on publication ethics. ICMJE links retraction of articles to scientific misconduct, which they consider (but is not necessarily limited to) data fabrication and data falsification including deceptive manipulation of images and plagiarism. They refer to COPE’s recommendations on retraction or expressions of concern (ICMJE 2013, 7).

In their response to the retraction, Séralini and his colleagues (2014b) argued that post hoc standards for papers that have found adverse findings of GMOs are far higher than the standards for papers that have found no differences between GMOs and parental plants. Monsanto-funded studies using similar strains and numbers of mice were not retracted because of deficient methods. When a Monsanto study found differences in multiple organ functions between the GM and non-GM feeding groups, they dismissed the differences as not biologically meaningful (Hammond et al. 2004).

A former member of the editorial board of FCT wrote a letter to the editor that was published in the journal. “I feel ashamed about your resent decision to retract Séralini’s paper previously accepted for publication after a full review process, which I tend to believe, had been performed seriously as usual for a journal of high quality like FCT. I also feel ashamed because your decision gives support for those who argue and even claim that scientific research (especially in biosciences) is less and less independent and more and more subject to industry pressure. Your decision can be interpreted as a will to eliminate scientific information that does not help support industrial interests is, in my view, unacceptable” (Roberfroid 2014, 390). This raises the question of whether conflict of interest could be a factor in how the GMO health studies are executed and interpreted. In another unusual event, after Séralini’s paper was retracted by *Food & Chemical Toxicology*, it was republished by 2014 in *Environmental Sciences Europe* (Séralini et al. 2012).

GMO Conflict of Interest

It has been well established in social science research that in some fields there is a funding effect in science from corporate sponsorship of research. That means that corporate-funded science tends to produce results that are consistent with corporate financial interests. The effect has been found in tobacco research, drug studies, and to a lesser extent in chemical health and

safety studies (Bekelman, Li, and Gross 2003; Bourgeois 2010; Krimsky 2005). I found three papers on conflicts of interest (COIs) and GMOs. The first paper, authored by a group of researchers in Portugal and published in the journal *Food Policy* (Diels et al. 2011), undertook a systematic review of the scientific literature drawing from the *Medline* and *Web of Science* databases starting with 3,626 references on GMOs and winnowing those down to ninety-four articles that meet their criteria. Their main finding was that papers where COIs were identified showed a tendency to produce outcomes favorable to the commercial interests of the stakeholders. They found one of the forty-four papers with a COI was unfavorable toward GMOs while eight of the thirty-five with no COI were unfavorable toward GMOs. This means that without a COI, there was a 23 percent chance of reaching an unfavorable conclusion and with a COI only a 2 percent chance.

The second paper was a published commentary that focused on conflicts of interest of those criticizing Séralini's papers (Séralini et al. 2014). The authors note that a new assistant editor of biotechnology joined the journal *Food and Chemical Toxicology* after Séralini's article was published and that this assistant editor previously worked for Monsanto for seven years. The authors interpret the decision to retract their paper a little over a year after it was appropriately refereed grew out of the role of the new assistant editor who had a conflict of interest as a former employee of Monsanto.

A third paper discussed the conflicts of interest at the European Food Safety Authority (EFSA), a weak counterpart to the US FDA since it issues advisories to members of the European Union. According to its website, "The European Food Safety Authority (EFSA) [an independent European agency funded by the EU budget that operates separately from the European Commission, European Parliament and EU Member States] is the keystone of European Union (EU) risk assessment regarding food and feed safety . . . EFSA provides independent scientific advice and clear communication on existing and emerging risks" (EFSA). The agency reviewed the Séralini et al. publication and published the results in the *EFSA Journal* in 2012. EFSA found the study to be "inadequately designed, analysed" and discounted Séralini's response to critics concluding that the study is of "insufficient scientific quality for safety assessments."

Robinson et al. (2013) argued that the EFSA has been rife with conflicts of interest. For example, the chair of EFSA's management board had a long-standing relationship with the industry funded International Life Sciences Institute (ILSI). They claim that in 2010 more than half of the EFSA experts on the GMO panel had financial conflicts of interest. The agency had been cited by the Ombudsman for failing to manage conflicts of interest and

despite changes still has not distanced itself from ILSI and thus does not represent an independent review of S eralini's work. Among the points raised by Robinson et al. is that when differences are found between GMOs and non-GMO counterparts, several authors, including those funded by industry, dismiss the findings as being within the normal range of variation and are not biologically relevant. "An EFSA opinion allows industry to define biological relevance on a case-by-case basis" (Robinson et al. 2013, 2).

Conclusion

I began this article with the testimonials from respected scientists that there is literally no scientific controversy over the health effects of GMOs. My investigation into the scientific literature tells another story. I found twenty-six animal feeding studies that have shown adverse effects or animal health uncertainties (Table 2). The eight review articles were mixed in their assessment of the health effects of GMOs (Table 1). The analysis of how two respected scientists were treated so poorly by the scientific community over their peer-reviewed work raises questions about likely political and ideological influences in the science. I could find no comparable case in the history of science where someone's published and peer-reviewed work was retracted because it was not definitive. Comparable works that found GMOs equivalent to their non-GMO parental strain were not retracted for the same reason since they too were not definitive. It has been argued that the weight of evidence is favorable to the hypothesis that the current family of commercialized GMOs is safe to humans and animals because there is a preponderance of articles establishing that point. In risk assessment, the number of studies that reveal a risk can be more significant than a larger number of studies that do not. Imagine a hundred flights to test a new aircraft. Ninety-five prove safe. Five flights produce electrical problems, failed landing gear, and a wing collapse. Does one just negate the five flights and go with the weight of evidence? Those five flights are very significant, perhaps because the aircraft was pushed beyond standard flight operations but within its design limits.

When there is a controversy about the risk of a consumer product, instead of denying the existence of certain studies, the negative results should be replicated to see if they hold up to rigorous testing. This point was made by the 300 scientists who signed a joint statement that was published in *Environmental Sciences Europe*. The statement "does not assert that GMOs are unsafe or safe. Rather the statement concludes that the scarcity and

contradictory nature of the scientific evidence published to date prevents conclusive claims of safety, or lack of safety, of GMOs” (Hilbeck et al. 2015, 1). David Schubert, professor at the Salk Institute, summarized the state of affairs of the GMO controversy as follows: “To me, the only reasonable solution is to require that all GM plant products be tested for long-term toxicity and carcinogenicity before being brought to market” (2002, 969). Until the twenty-six studies, or at least the best of them, are replicated and shown to be false positives, we have an obligation to treat these studies with respect and concern. My results have broad implications for the study of scientific and medical controversies, whether climate change, endocrine disruptors, statins, or mercury preservatives in vaccines. STS scholarship is best accomplished when it approaches a controversial issue systemically and includes a deep analysis of the primary science, a review of the function of professional societies, an analysis of the peer review process of journals, a study of the political climate and its impact on science and on federal regulatory agencies which set policy, the media’s role in shaping public understanding or misunderstanding, and the role that financial interests play in scientific risk analysis. All of these factors are brought into play in the GMO debate, about which I have argued that the putative consensus about the inherent safety of transgenic crops is premature.

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