EXHIBIT B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF VERMONT

GROCERY MANUFACTURERS ASSOCIATION, SNACK FOOD ASSOCIATION, INTERNATIONAL DAIRY FOODS ASSOCIATION, and NATIONAL ASSOCIATION OF MANUFACTURERS, Plaintiffs, v. WILLIAM H. SORRELL, in his official capacity as the Attorney General of Vermont, PETER E. SHUMLIN, in his official capacity as Governor of Vermont; TRACY DOLAN, in her official capacity as Commissioner of the Vermont Department of Health; and JAMES B. REARDON, in his official capacity as Commissioner of the Vermont Department of Finance and Management, Defendants.	Case No. 5:14-cv-117

DECLARATION OF DR. MICHAEL ANTONIOU

1. I, Michael Antoniou, make this declaration pursuant to Federal Rule of Evidence 702. My *curriculum vitae* is attached as Exhibit 1 to this declaration.

2. In preparing to make this declaration, I have reviewed the text of Vermont's Act 120, Plaintiffs' Amended Complaint, Plaintiffs' Motion for a Preliminary Injunction (including the Declaration of Dr. Alan McHughen in support of that motion), and numerous scientific and technical studies related to genetically engineered ("GE") food, as discussed in greater detail below.

Expert Background and Qualifications

3. I am a molecular geneticist with extensive experience in genetic engineering, the

organization and regulation of gene expression, and gene expression systems, including gene therapy. I am currently a Reader (the equivalent of a full Professor) in Molecular Genetics in the Department of Medical and Molecular Genetics at King's College London, Faculty of Life Sciences and Medicine.

4. I received a B.A. in Biochemistry from the University of Oxford in 1977, and earned my Ph.D. from the University of Reading in 1980. I then conducted post-doctoral research in the Tumor Biology Laboratory at the University of Nebraska, and in the Laboratory of Gene Structure and Expression at the National Institute for Medical Research (London, U.K.). Prior to my tenure at King's College London, I was a Senior Lecturer at the United Medical and Dental Schools of Guy's and St. Thomas's Hospital, London.

5. My general background is in basic molecular biology, researching the organization of genes within DNA and their regulation in mammalian systems. Over the years my research has employed, and continues to employ, genetically engineered ("GE") bacteria, yeast, mammalian tissue culture cells, viruses and mice.

6. Among my discoveries are potent gene regulatory elements that can function specifically in muscle cells and, alternatively, in all cell types. In the latter case, the discovery of what we have designated as "ubiquitous chromatin opening elements" ("UCOEs") has led to a number of patents on which I am an inventor. UCOE-based gene expression platforms are industry-award winning systems that have provided unprecedented reproducibility and stability in gene function. UCOE-based gene expression systems have not only proven valuable research tools, but have also entered commercial use within the biomanufacturing sector for the production of therapeutic protein products.

7. My discoveries have also made significant contributions to the field of gene

therapy. A gene medicine designed and developed in my laboratory for targeting the red blood cell disorders thalassemia and sickle cell disease will be entering clinical trials with my collaborators in Italy in 2015. UCOE-based gene medicines are being successfully developed by myself and numerous research groups around the world to target many different conditions.

8. The insertion of the foreign genetically engineered gene unit into plants is fundamentally similar to what occurs in animal cells, albeit using different gene delivery systems. In addition, the mechanisms of gene control in plants and animals are fundamentally similar, as are the expected and unexpected consequences of genetic engineering. Thus, my overall experience with GE technologies and the regulation of gene expression qualifies me to critically evaluate genetic engineering in plants and scientific studies regarding GE plants.

9. In addition, within the last 18 months I have embarked on my own research program to evaluate the health risks of GE crops and their associated pesticides using "molecular profiling" methods (e.g., looking at gene-expression patterns, protein spectrum composition, and small molecule composition) within organs of animals.

10. I have been called on over the years to critically evaluate and offer technical comments and advice on GE crop developments, especially with respect to their health risks, by non-government organizations and politicians, both within the U.K. and abroad.

11. In 2003 I was a member of the Science Review Panel chaired by the U.K. Government's Chief Scientists. The Science Review Panel was tasked with scrutinizing the scientific literature dealing with GE crop and food health risks and their environmental impact. The published reports of the Science Review Panel formed part of the U.K. Government's "GM Nation?" public exercise and debate.

12. I am co-author of a book entitled "GMO Myths and Truths: An evidence-based

examination of the claims made for the safety and efficacy of genetically modified crops and foods."[1] This book and the references therein have been referred to by the State of Vermont in support of its Act 120 GE food labelling legislation.

The Production of Genetically Engineered Plants

13. A gene is a sequence of DNA that causes cells to produce, or "express," particular proteins. Alternatively, genes can also express molecules of RNA, which directly participate in diverse functions such as the production of proteins and the regulation of gene expression. Genetic engineering often uses so-called recombinant DNA ("rDNA") technology to transfer a gene with a desirable trait from one organism into the genome of a different (and often distantly related) organism. Scientists often refer to the gene or genetic material that has been transferred from one organism to another as a "transgene." Thus, for example, "Bt corn" is corn that is genetically engineered to contain a gene from a bacterium, known as *B. thuringiensis* ("Bt"), which produces proteins that are toxic to certain insects. Similarly, "Roundup Ready" crops have been genetically engineered so that they contain genes from a certain strain of bacteria that confer tolerance to glyphosate-based herbicides such as Roundup.

14. The first step of the genetic engineering process is to identify and isolate the gene that encodes for the trait of interest – say, tolerance to a particular herbicide. The gene is then "cloned" or propagated in a genetically engineered bacterium as part of a DNA molecule known as a plasmid.

15. Before it can be used to produce a genetically engineered plant, the gene of interest must be joined up with genetic control elements that will allow it to be switched on in its

[1] Michael Antoniou, Claire Robinson, John Fagan, *GMO Myths and Truths: An Evidence-Based Examination of the Claims Made for the Safety and Efficacy of Genetically Modified Crops*, Earth Open Source (2012 and 2014).

new plant host, so that it will efficiently produce the protein that it encodes. Other elements – notably the "promoter" and "termination" sequences – are spliced into or around the gene of interest for various purposes.

16. Genetic engineers use enzymes to cut the DNA carrying the cloned gene into specific sequences and to splice the various pieces of DNA into the plasmid that will then carry the gene of interest. The result of many cutting and splicing steps is the complete genetically engineered construct, called the "gene cassette." The first-generation Roundup Ready gene cassette, for example, combines gene sequences from four diverse organisms: two species of soil bacteria, a flowering plant, and a plant virus. These gene sequences all ultimately end up in the genetically engineered crop. This diverse array of genetic elements, linked together and inserted into a crop plant of yet another species, would not occur in nature.

17. To introduce the genetically engineered gene cassette into the genome of the recipient plant, millions of cells from the recipient plant species are subjected to the gene insertion, or "transformation" process. This is done by growing cells from the recipient plant in dishes 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 genetically engineered gene cassettes being inserted into the DNA of some of the plant cells present in the tissue culture.

18. The process of inserting the gene cassette is generally 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 genetically engineered DNA into the plant cells, a process called particle bombardment or "biolistics." In a few instances, DNA released from the nanoparticles end up in the nucleus of the plant cells and, in an even smaller number of cases, the DNA from the

particles gets incorporated into the DNA of the plant cell. This is a random process that genetic engineers have no ability to control.

19. A second mechanism of gene insertion is by infection of the cultured plant cells with the soil bacterium known as *A. tumefaciens*. This is done by first linking the genetically engineered 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 genetically engineered gene cassette-Ti plasmid DNA complex. A small fraction of the plant cells exposed to the *A. tumefaciens* are successfully infected and incorporate the genetically engineered gene cassette into their own DNA. As with the "gene gun" method, the *A. tumefaciens* insertion process is random. Thus, the genetic engineer has no way of controlling where in the plant cell genome the genetically engineered gene cassette will be inserted.

20. Only a small percentage of genetically engineered gene cassette insertion events result in expression of the genetically engineered genes in the plant cells. The few plant cells that have successfully incorporated the GE gene cassette and survived the chemical treatment are then treated with plant hormones. The hormones stimulate the genetically modified plant cells to proliferate and differentiate into small genetically engineered plants that can be transferred to soil and grown to maturity.

21. Finally, the genetically engineered plants are tested to identify one or more that express the genetically engineered genes at the desired levels and locations within the plant. Out of many hundreds or thousands of genetically engineered plants produced, only a few may fit this requirement. Each of these genetically engineered plants carries the same genetically engineered gene cassette, but the cassette will be inserted at a different location in the genome of

the plant, severely impacting the efficiency of its function. As a result, the genetically engineered gene will express at different levels in different GE plants (meaning that the gene will cause the production of different levels of protein), and even in different parts of the same genetically engineered plant.

22. Genetically engineered organisms can be produced with other techniques too. For example, the definition of genetic engineering set forth in European Law includes "cell fusion (including protoplast fusion)."[2] Genetic engineers are also using new "genome editing" techniques such as nucleases, or "genome scissors," to cut DNA and insert the new DNA into a pre-determined site in the host organism's DNA. These techniques include TALENs (transcription activator-like effector nucleases), ZFNs (zinc finger nucleases), and CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats). In my view, the products of these "genome editing" techniques also fall under the definition of GMOs set forth in European Parliament Directive 2001/18/EC, since they are organisms in which "the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination."[3]

23. As discussed further below, the steps by which GE crops are created illustrate that genetic engineering is not merely an extension of natural breeding. Rather, it results in the creation of particular combinations of genes that would not otherwise occur in nature.

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[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.

[3] 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.

GE Food Differs from Food Produced by Traditional Breeding

24. Genetic engineering is technically and conceptually different from traditional breeding. For example, European law defines a genetically modified organism ("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.[4] The Cartagena Protocol on Biosafety,[5] an international agreement signed by 166 governments worldwide that seeks to protect biological diversity from the risks posed by GE technology, and the United Nations food safety body, Codex Alimentarius,[6] agree that genetic engineering differs from traditional breeding and that safety assessments should be required before GE organisms are used in food or released into the environment.[7] For that reason, more than 60 countries have laws requiring the labeling of GE food. Those countries include all European Union member states, as well as Japan, Australia, China, Russia, and Brazil.

25. Genetic engineering is inherently riskier than traditional breeding. It is true that, as Alan McHughen states in his declaration, "[a]ll plant breeding methods may cause unintended consequences." McHughen Decl. ¶ 101. But food crop plants derived from traditional breeding, which draw on gene pools for food crops often established over millennia, have a history of safe use. Genetic engineering of food, in contrast, does not have a history of safe use. And genetic

[4] 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.

[5] Secretariat of the Convention on Biological Diversity. Cartagena Protocol on Biosafety to the Convention on Biological Diversity (2000). Available at http://bch.cbd.int/protocol/text/.

[6] Codex Alimentarius, *Foods Derived from Modern Biotechnology* (2nd Ed. 2009). Rome, Italy: World Health Organization/Food and Agriculture Organization of the United Nations. Available at: ftp://ftp.fao.org/codex/Publications/Booklets/Biotech/Biotech_2009e.pdf.

[7] Codex Alimentarius, *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants: CAC/GL 45-2003* (2003).

engineering is inherently more likely than traditional breeding to cause unintended consequences. Such unintended effects can include altered composition of the plant and the production of new toxins and allergens. All these effects have been found to occur, as revealed in peer-reviewed studies that I discuss below.

26. In traditional breeding, moreover, the gene of interest is attached to many other genes, which can accompany the gene of interest in the cross-breeding process and end up in the progeny plant or organism. That is not a sign of the imprecision of traditional breeding (as McHughen suggests in ¶ 18 of his declaration), but rather of its complexity: Multiple genes work together in a precisely regulated way to express desirable complex traits such as disease resistance and high yield. This complexity cannot be replicated by the currently available GE techniques or by any GE techniques in the pipeline. That is because GE techniques can introduce or alter only one or a few genes at a time. The effects of those genes on other, related genes, are not controllable or predictable.

27. A report from the National Research Council ("NRC") of the U.S. National Academies of Science and Engineering, moreover, concluded that genetic engineering poses a higher risk of introducing unintended changes into food than any other crop breeding method other than mutation breeding (which the committee believed may pose an even higher risk of producing such changes than genetic engineering). See Figure ES-1 ("Relative likelihood of unintended genetic effects associated with veracious methods of plant genetic modification").[8] I agree with that conclusion. The NRC report also states that genetic engineering "has increased the number and type of substances that can be intentionally introduced into the food supply, as

[8] National Research Council, *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects* (2004), at p. 4. Available at http://www.nap.edu/openbook.php?isbn=0309092094.

well as the magnitude of these changes. While these intended changes can be readily evaluated for their safety in food, unintentionally introduced changes in the composition of foods may be more difficult to identify and assess."[9] Thus, while McHughen states in his declaration (at ¶ 70) that the NRC report concluded that GE and non-GE breeding methods are "equally safe," no such conclusion appears in the report – which as noted, actually states that GE techniques are more likely to produce unintentional compositional changes.

28. Molecular analytical methods have shown that GE crops can have an unexpectedly different composition than their non-GE counterparts. That is true even when the two crops are grown under the same conditions, at the same time, and in the same location (suggesting that the changes are not due to different environmental factors but to the genetic engineering process). For example:

- Genetically engineered soy had 12–14% lower amounts of isoflavones (compounds that play a role in sex hormone metabolism) than non-GE soy.[10]
- A study conducted by the Monsanto Corporation showed that GE soy had 27% higher levels of a major allergen (trypsin-inhibitor) than the non-GE parent variety.[11]

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[9] National Research Council, *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects* (2004), at p. ix. Available at: http://www.nap.edu/openbook.php?isbn=0309092094.

[10] Lappé, M., B. Bailey, C. Childress, and K.D.R. Setchell. 1999. Alterations in clinically important phytoestrogens in genetically modified herbicide-tolerant soybean. *J. Med. Food.* 1:241–245.

[11] Padgette, S.R., N.B. Taylor, D.L. Nida, et al. 1996. The composition of glyphosate-tolerant soybean seeds is equivalent to that of conventional soybeans. *J. Nutr.* 126(3):702-716 (Supplementary information from Puerto Rico trials, excluded from the main publication but deposited with the American Society for Information Science, National Auxiliary Publication Service (NAPS) and in the archives of the Journal of Nutrition). Although the authors of the study claimed that the GE soybean was nevertheless "equivalent" to the non-GE soybean, they reached that conclusion by comparing 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 GE plant to be compared with the non-GE isogenic (with the same genetic background) variety, grown at the same time in the same conditions.

- 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-GE canola.[12]

- Experimental genetically engineered rice varieties had major unintended nutritional disturbances compared with non-GE counterparts, when grown side-by-side in the same conditions. The structure and texture of GE rice grain was affected and its nutritional content and value were dramatically altered. The authors of the study said that their findings provided "alarming information with regard to the nutritional value of transgenic rice" and showed that the GE rice was not substantially equivalent to non-GE rice.[13]

- Commercialized MON810 GE corn had a markedly different profile in the types of proteins it contained compared with the non-GE counterpart when grown under the same conditions.[14] These unexpected compositional differences also showed that the MON810 maize was not substantially equivalent to the non-GE isogenic comparator, even though worldwide regulatory approvals of this maize had assumed that it was.[15]

- Bt corn of the variety MON810 Ajeeb YG showed significant differences from its isogenic non-GE counterpart, with some values being outside the range recorded in the scientific literature. Some fatty acids and amino acids present in the non-GE corn were absent in the Bt corn. The researchers concluded that the genetic modification process had caused alterations in the maize that could result in toxicity to humans and animals.[16]

29. These studies show that GE plants are not necessarily substantially equivalent to, or the same as, non-GE varieties. That applies to varieties of genetically engineered crops that

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[12] Shewmaker, C., J.A. Sheehy, M. Daley, S. Colburn, and D.Y. Ke. 1999. Seed-specific overexpression of phytoene synthase: Increase in carotenoids and other metabolic effects. *Plant J.* 20:401-412.

[13] Jiao, Z., X.X. Si, G.K. Li, Z.M. Zhang, and X.P. Xu. 2010. Unintended compositional changes in transgenic rice seeds (Oryza sativa L.) studied by spectral and chromatographic analysis coupled with chemometrics methods. *J. Agric. Food Chem*. 58:1746-54.

[14] Zolla, L., S. Rinalducci, P. Antonioli, and P.G. Righetti. 2008. 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.

[15] European Food Safety Authority (EFSA) GMO Panel. 2004. 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*. 2004:1-25.

[16] Abdo, E.M., O.M. Barbary, O.E. Shaltout. 2013. Chemical analysis of Bt corn "Mon-810: Ajeeb-YG®" and its counterpart non-Bt corn "Ajeeb." *IOSR J. Appl. Chem*. 4(1):55–60.

are already commercialized, and which were claimed to be compositionally substantially equivalent at the time of commercial approval. These studies also show that the differences between GE and non-GE plants are not limited to the obvious difference that GE plants contain the transgene artificially transferred through the genetic engineering process. Rather, these studies make clear that the GE process can cause biochemical changes in the plant *in addition* to the insertion of the transgene. These changes may result in altered nutritional value or the presence of novel toxins or allergens in the GE food. And they certainly show that GE foods are not "identical" to non-GE foods.

30. Nor is it necessarily true that ingredients *derived* from GE plants are identical to ingredients derived from non-GE plants. In his declaration, McHughen states (at ¶ 50) that "[t]he sucrose produced by GE sugarbeets is chemically identical to the sucrose produced by non-GE sugarbeets and, for that matter, to sucrose from sugarcane." He further states that "There is no DNA or protein present in sucrose, whether derived from GE or non-GE plants. Thus, there is no means to independently or reliably distinguish the product of the GE sugarbeet plant from the others, even using the most powerful and sensitive laboratory tests." While that may be true with respect to the sugarbeets McHughen discusses in his declaration (though that can be proven only by showing metabolite profiling data), the GE process could result in novel toxins being introduced into the food that are not proteins or DNA – and would therefore escape McHughen's analysis, which looks only to proteins and DNA. For example, in 1989 the food L-tryptophan, produced with genetic engineering in bacteria, was found to be toxic, killing 37 people and disabling 1500 others in the United States.[17] There was debate over whether the

[17] Mayeno, A.N. and G.J. Gleich. 1994. Eosinophilia-myalgia syndrome and tryptophan production: A cautionary tale. *Trends Biotechnol.* 12:346-52; House Committee on Government Operations: Human Resources and Intergovernmental Relations Subcommittee. *FDA's*

toxin was the result of the genetic engineering process or inadequate purification practices. But the authors of a 1990 study sponsored by the Centers for Disease Control and Prevention stated that blaming the purification process does not explain how the novel toxin got into the L-tryptophan in the first place. The CDC concluded that the new genetically engineered bacterial strain introduced by the manufacturer before the outbreak "may have produced larger quantities" of the toxin than earlier strains.[18] Because the L-tryptophan was greater than 99.6% pure, devoid of genetically engineered DNA (it was just derived from a bacterium with genetically engineered DNA), and the suspected novel toxin was present at less than 0.1% of the final marketed product, it would be considered "substantially equivalent" to the same supplement derived from the non-GE organism – even though it may well have produced a greater risk of toxicity. Thus without metabolite profiling, it cannot be assumed that sucrose from GE sugarbeet is chemically identical to sucrose from non-GE sugarbeet.

31. In his declaration, McHughen states that there is no natural barrier to genes from one species entering the genome of another species. McHughen Decl. ¶ 19. But genetic engineering is an artificial laboratory-based technique specifically designed to enable the transfer of genes between very distantly related organisms – for example, it allows engineers to put a gene from a bacteria or fish into a tomato genome. It even enables the introduction of synthetic

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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; Slutsker, L., F.C. Hoesly, L. Miller, L.P. Williams, J.C. Watson, and D.W. Fleming. 1990. Eosinophilia-myalgia syndrome associated with exposure to tryptophan from a single manufacturer. *JAMA*. 264:213-7.

[18] Belongia, E.A., C.W. Hedberg, G.J. Gleich., et al. 1990. An investigation of the cause of the eosinophilia-myalgia syndrome associated with tryptophan use. *N. Engl. J. Med.* 323:357-65.

DNA – i.e., DNA that is engineered in a laboratory – into the genome of living organisms. Those techniques are used precisely because those results *cannot* be accomplished by traditional breeding techniques.

32. It is true that so-called horizontal gene transfer (*i.e.*, transfer of genes between organisms through means other than traditional reproduction) can occur in nature. But such gene transfer is accompanied by genetic selection by food crop breeders and natural conditions over millennia. During that time, any toxic or unhealthy plants would likely be identified and selected out of the breeding process. That differs markedly from genetic engineering, in which radical changes to the genome are made in a short period of time. Thus, with GE crops and foods, we do not have the benefit of hundreds or thousands of years of experience to tell us which plants are safe to eat and which are not. As Nassim Nicholas Taleb and his co-authors have explained, "systemic modifications require a very long history in order for the evidence of lack of harm to carry any weight".[19] We do not have that long history with respect to any GE foods. We therefore lack the confidence that GE foods are as safe as novel foods produced with traditional methods.

33. In his declaration, McHughen discusses a tomato that contains genes from another species. McHughen Decl. ¶ 20. That example does not support the contention that GE foods are no different from natural foods. The tomato variety cited, *Solanum lycopersicon,* is related to *L. peruvianum*, from which the genes in question originated; the latter is known as a "wild tomato," and both come from the same family, the *Solanaceae* (or nightshades). As noted, however, genetic engineering allows engineers to modify a plant's genome by inserting genes from

[19] Taleb, N.N., R. Read, R. Douady, J. Norman, and Y. Bar-Yam. 2014. The precautionary principle (with application to the genetic modification of organisms). *Extreme Risk Initiat. NYU Sch. Eng. Work. Pap. Ser*. 12. Available at: http://arxiv.org/abs/1410.5787.

distantly related and unrelated organisms. In nature, horizontal gene transfer, or the exchange of genetic material through a mechanism other than sexual reproduction, occurs often between different species of bacteria. But horizontal gene transfer in higher organisms occurs only rarely and in special circumstances, such as in infections with viruses. An example is the type of viral infection that results in the development of endogenous retroviruses – viruses that write themselves into the host's DNA. Such endogenous retroviruses are estimated to make up as much as 8% of the human genome.[20] But the fact that 'natural' horizontal gene transfer has taken place does not mean that the process is safe or desirable – or that it is prudent to replicate it on a large scale by genetically engineering food crops.

There is no scientific consensus on GMO safety

34. In his declaration, McHughen claims that there is a "clear consensus" on GMO safety. McHughen Decl. ¶¶ 71, 72. In my view, that is false. There was no consensus at the time GMOs were first released onto world markets, and none has emerged since.

35. To begin with, numerous scientific, health-related, and legislative bodies from around the world (including the United States) have variously stated that GE foods have not been proven safe, that mandatory safety assessments should be carried out on GE foods, or that they support GE labeling. Representative examples include:

- **American Public Health Organization**: "Recognizing that the report of the Scientific Advisory Panel to the US Environmental Protection Agency on genetically engineered crops expressed concerns related to human exposure to and consumption of these plant proteins [from GE plants]," the American Public Health Association "Resolves that APHA declare its support that any food product containing genetically modified organisms be so labeled."[21]

[20] Hughes, J.F. and J.M. Coffin. 2001. Evidence for genomic rearrangements mediated by human endogenous retroviruses during primate evolution. *Nat. Genet.* 29:487-9

[21] American Public Health Association. 2001. Support of the labeling of genetically modified foods: Policy Number 200111. Available at: http://www.apha.org/policies-and-

- **British Medical Association**: "Many unanswered questions remain, particularly with regard to the potential long-term impact of GM foods on human health and on the environment. There is a lack of evidence-based research with regard to medium and long-term effects on health and the environment. . . . Labelling of GM-containing foods should be continued [in Britain] in order to facilitate further health research and allow the public to choose whether they consume GM food or not."[22]

- **California Medical Association**: "Whereas, [a]gricultural genetic engineering can introduce new proteins into food crops not just from known sources of common allergens (e.g., peanuts or shellfish), but from plants of all kinds, animals, bacteria and viruses, whose allergenicity is largely unknown," it is "Resolved, that the CMA support accurate labeling requirements for foods, including genetically modified foods, by appropriate regulatory agencies."[23]

- **American Cancer Society**: "At this time, there is no evidence that genetically modified foods that are currently on the market or the substances found in them are harmful to human health or that they would either increase or decrease cancer risk because of the added genes. However, the absence of evidence of harmful effects is not equivalent to evidence of safety, and since their introduction into the food supply is relatively recent, long-term health effects are unknown."[24]

- **European Network of Scientists for Social and Environmental Responsibility ("ENSSER")**: "As scientists, physicians, academics, and experts from disciplines relevant to the scientific, legal, social and safety assessment aspects of genetically modified organisms (GMOs), we strongly reject claims by GM seed developers

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advocacy/public-health-policy-statements/policy-database/2014/07/28/13/18/support-of-the-labeling-of-genetically-modified-foods.

[22] British Medical Association Board of Science and Education. *Genetically Modified Food and Health: A Second Interim Statement*. London, UK: British Medical Association Board of Science and Education; 2004. Available at: http://www.argenbio.org/adc/uploads/pdf/bma.pdf.

[23] Russell, C. 2002. *Labeling of Genetically Modified Foods: Resolution 107-02 (Adopted 2-24-02)*. California Medical Association House of Delegates 2002. Available at: http://labelgmoscv.wordpress.com/2012/01/31/california-medical-associations-current-policy-statement-supporting-the-labeling-of-gmos.

[24] Kushi, L.H., C. Doyle, M. McCullough, et al. 2012. American Cancer Society guidelines on nutrition and physical activity for cancer prevention. *CA: Cancer J. Clin.* 62(1):30-67.

and some scientists, commentators, and journalists that there is a 'scientific consensus' on GMO safety and that the debate on this topic is 'over.'"[25]

- **American College of Physicians**: "WHEREAS, lack of labeling denies health professionals the ability to trace potential toxic or allergic reactions to, and other adverse health effects from, genetically engineered food," it is "RESOLVED that the Board of Regents supports legislation and/or federal regulatory action which requires all foods containing genetically engineered ingredients to be clearly labeled."[26]

- **American Nurses Association**: "[T]he American Nurses Association supports the public's right to know through support of appropriate food labeling, including country-of-origin and genetic modification."[27]

- **International Assessment of Agricultural Knowledge Science and Technology for Development**: "The safety of GMO foods and feed is controversial due to limited available data, particularly for long-term nutritional consumption and chronic exposure. Food safety is a major issue in the GMO debate. Potential concerns include alteration in nutritional quality of foods, toxicity, antibiotic resistance, and allergenicity from consuming GM foods. . . . Significant effects have been found on a number of measured parameters and a call has been made for more research to establish their safety." [28]

- **Public Health Association of Australia** (1,900 individual members and representing 40 professional groups): "The precautionary principle should be

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[25] European Network of Scientists for Social and Environmental Responsibility (ENSSER). 2013. *Statement: No Scientific Consensus on GMO Safety* (internal citations omitted). Available at: http://www.ensser.org/increasing-public-information/no-scientific-consensus-on-gmo-safety/.

[26] American College of Physicians. 2004. Resolution 14-S11: Supporting Federal Legislation and/or Regulations that Require Clearly Labeling Food with Genetically Engineered Ingredients, at 108-09 (internal citations omitted). Available at http://www.acponline.org/acp_news/misc/apr11/page%2053.pdf.

[27] American Nurses Association. 2008 House of Delegates: Resolution: Healthy Food in Health Care. Available at http://www.nursingworld.org/MemberCenterCategories/ANAGovernance/HODArchives/2008HOD/ActionsAdopted/HealthyFoodinHealthCare.aspx.

[28] McIntyre, B.D., H.R. Herren, J. Wakhungu, and R.T. Watson. 2009. *Agriculture at a Crossroads: International Assessment of Agricultural Knowledge, Science and Technology for Development Global Report*, at 199-200. Available at: http://www.unep.org/dewa/agassessment/reports/IAASTD/EN/Agriculture%20at%20a%20Crossroads_Global%20Report%20%28English%29.pdf. This report was co-sponsored by the World Health Organization, the World Bank, the Food and Agriculture Organization, the United Nations Environment Programme, the United Nations Development Programme, the Global Environment Facility, and the United Nations Educational and Scientific and Cultural Organization.

applied in developing GM food as it is not certain whether there are serious risks to the environment or to human health involved in producing or consuming GM foods or their products. . . . GM foods should not be assessed as safe to eat unless they have undergone long-term animal safety assessments utilizing endpoints relevant to human health and conducted by independent researchers. . . . There are no surveillance systems set-up to determine the effects of GM foods on health, and no-one is paid to look in existing surveillance systems for problems. . . . The labelling system should be improved to the standards desired by consumers, so that consumers can easily identify foods containing ingredients originating from GM animals and plants, and from animals fed GM feed."[29]

- **Royal Society of Canada:** "In general, the Panel found 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. In particular, the Panel was unaware of any validated study protocols currently available to assess the safety of GM foods in their entirety (as opposed to food constituents) in a biologically and statistically meaningful manner. The Panel therefore concurs with the US National Research Council (NRC, 2000) in recommending the immediate initiation of research into the development of practical and scientifically robust approaches for the safety assessment of such foods."[30]

- **European Parliament and Council**: "In order to protect human and animal health, food and feed consisting of, containing or produced from genetically modified organisms (hereinafter referred to as genetically modified food and feed) should undergo a safety assessment through a Community procedure before being placed on the market within the Community."[31] "In order to ensure that the presence of GMOs in products containing, or consisting of, genetically modified organisms is appropriately identified, the words 'This product contains genetically modified organisms' should appear clearly either on a label or in an accompanying document."[32]

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[29] Public Health Association of Australia. 2007. *Genetically Modified Foods*. Available at: http://www.phaa.net.au/documents/policy/GMFood.pdf.

[30] Royal Society of Canada. 2001. *Elements of Precaution: Recommendations for the Regulation of Food Biotechnology in Canada. An Expert Panel Report on the Future of Food Biotechnology*, at 48. Available at: https://rsc-src.ca/sites/default/files/pdf/GMreportEN.pdf. Report prepared at the request of Health Canada, Canadian Food Inspection Agency, and Environment Canada.

[31] European Parliament and Council. 2003. 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*. 268:1-23.

[32] European Parliament and Council. 2001. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment

36. In his declaration, McHughen includes a list of scientific groups that, he says, have stated that GE foods are safe. McHughen Decl. ¶ 71. But the fact that some scientific societies take that position is not evidence that there is a scientific "consensus" that GE foods are safe. To the contrary, as noted above, many other scientific groups have taken the position that the safety of GE foods is still an open question. By definition, then, there is no "clear consensus" on the issue; rather, there is a good-faith scientific disagreement on the issue.

37. Indeed, as noted above, in 2013 the European Network of Scientists for Social and Environmental Responsibility ("ENSSER") published a statement that there is "No consensus on GMO safety."[33] In his declaration, McHughen attempts to dismiss that statement on the ground that ENSSER is "not a professional society," but is instead composed of an "eclectic group of people with varying credentials, few of which are directly related to genetics, agriculture or biosafety." McHughen Decl. ¶ 72. But the ENSSER statement was signed by 300 well-credentialed scientists, physicians, and experts in the legal and biosafety ramifications of genetically engineered organisms. These signatories include the former head of the GMO biosafety program at the U.S. EPA, the former assessor of health and environmental risks from GMOs at the EPA, a former winner of the World Food Prize, and the developer of the world's first commercialized whole GE food (a tomato). I am also a member of ENSSER and one of the signatories.

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of genetically modified organisms and repealing Council Directive 90/220/EEC. *Off. J. Eur. Communities* 2001:1-38.

[33] European Network of Scientists for Social and Environmental Responsibility (ENSSER). 2013. Statement: No Scientific Consensus on GMO Safety. Available at: http://www.ensser.org/increasing-public-information/no-scientific-consensus-on-gmo-safety/.

38. Not all of the statements cited by McHughen even support his assertion that there is a "clear consensus" regarding GE foods. For example, McHughen cites (at ¶ 71) a statement by the World Health Organization that "No effects on human health have been shown as a result of the consumption of GM foods by the general population in the countries where they have been approved." But the declaration omits the preceding text, which states that "Different GM organisms include different genes inserted in different ways. This means that individual GM foods and their safety should be assessed on a case-by-case basis and that it is not possible to make general statements on the safety of all GM foods."[34] The WHO statement also recommends "adequate post market monitoring" be carried out to ensure the safety of GM foods – which does not happen anywhere in the world – and states that, "[o]n issues such as labelling and traceability of GM foods as a way to address consumer preferences, there is no worldwide consensus to date."[35]

Numerous Studies Show That GE Foods Can Be Toxic

39. Given the legal, ethical, and logistic barriers to experiments on humans, scientific organizations and scientists have to base their opinions on GMO safety largely on data from animal feeding studies. Such studies are the best way, consistent with ethical norms, to identify potential health consequences of GE foods. Ideally, such studies should be long-term (a minimum of 2 years) and carried out in rats or mice, which are a widely accepted model for human toxicity. Long-term studies on commercialized GMO products, however, are few. Rather, most studies conducted by the industry in support of regulatory authorisation in Europe

[34] World Health Organization (WHO). 2002. 20 questions on genetically modified foods. Available at: http://www.who.int/foodsafety/publications/biotech/20questions/en/index.html.

[35] *Id.*

last for a maximum of 90 days, a medium-term (subchronic) period that, by definition, is not able to detect long-term chronic effects, such as cancer, severe organ damage, or premature death.

40. Even short- and medium-term experiments, however, have revealed unexpected toxic and allergenic effects in GE-fed animals, when compared to animals fed a non-GE diet. Examples include:

- **Altered blood biochemistry, multiple organ damage, and potential effects on male fertility**: Rats fed a variant of genetically engineered Bt (insect-resistant) corn for 45 and 91 days showed differences in organ and body weights and in blood biochemistry compared with rats fed the non-GE parent variety grown in the same conditions. The authors of the study noted that the changes could indicate "potential adverse health/toxic effects," which needed further investigation.[36] An investigation by the same group of researchers found toxic effects in multiple organs in the rats fed Bt corn 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.[37]

- **Intestinal abnormalities**: Mice fed a diet of genetically engineered Bt potatoes or non-GE potatoes spiked with natural Bt toxin protein over two weeks showed abnormalities in the cells and structures of the small intestine, compared with a control group of mice fed non-GE potatoes only. The abnormalities were more marked in the Bt toxin-fed group.[38] This study showed that the genetically engineered Bt potatoes caused mild damage to the intestines. It also showed that the Bt toxin protein is not harmlessly broken down in digestion, as some claim, but rather survives in a functionally active form in the small intestine and can cause damage to that organ.

- **Excessive growth in the lining of the gut**: Rats fed GE potatoes for only ten days showed excessive growth of the lining of the gut similar to a pre-cancerous

[36] Gab-Alla, A.A., Z.S. El-Shamei, A.A. Shatta, E.A. Moussa, and A.M. Rayan. 2012. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 8(9):1117–1123.

[37] El-Shamei, Z.S., A.A. Gab-Alla, A.A. Shatta, E.A. Moussa, and A.M. Rayan. 2012. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 8(10):684–696.

[38] Fares, N.H. and A.K. El-Sayed. 1998. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. *Nat. Toxins* 6(6):219-33.

condition, as well as toxic effects in multiple organ systems.[39]

- **Immune disturbances**: Young and old mice fed genetically engineered Bt corn 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 corn feeding was also found, an effect associated with allergic and inflammatory responses.[40] A study in rats fed genetically engineered Bt rice for 28 or 90 days found a Bt-specific immune response in the non-GE-fed control group as well as the GE-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 GE-fed group. They recommended that for future tests involving Bt crops, GM-fed and control groups should be kept separate. This study indicates that animals can be sensitive to small amounts of GE proteins, so even low levels of contamination of conventional crops with GMOs could be harmful to health.

- **Liver and kidney toxicity**: A review of 19 studies (including industry's own studies submitted to regulators in support of applications to commercialize GE crops) on mammals fed with commercialized GE soy and corn 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.[41] In a separate study, the same research group, led by Prof Gilles-Eric Séralini at the University of Caen, France, re-analyzed Monsanto's own 90-day rat feeding trial data, submitted to obtain approval in Europe for three commercialized GE corn varieties, two expressing Bt toxin insecticides and one engineered to tolerate application of Roundup herbicide. Séralini's team concluded that all three GE corn 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.[42] These data suggest that GE corn varieties are not substantially equivalent to non-GE corn and may be toxic.

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[39] Ewen, S.W. and A. Pusztai. 1999. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. *Lancet* 354:1353-4; Pusztai, A. and S. Bardocz. 2006. GMO in animal nutrition: Potential benefits and risks. In: Mosenthin, R., J. Zentek, and T. Zebrowska, eds. *Biology of Nutrition in Growing Animals*. Vol 4. 513–540. Available at: http://www.sciencedirect.com/science/article/pii/S1877182309701043.

[40] Finamore, A., M. Roselli, S. Britti, et al. 2008. Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. *J. Agric. Food Chem.* 56:11533–39.

[41] Séralini, G.E., R. Mesnage, E. Clair, S. Gress, J.S. de Vendômois, and D. Cellier. Genetically modified crops safety assessments: Present limits and possible improvements. *Environ. Sci. Eur.* 2011;23.

[42] De Vendomois, J.S., F. Roullier, D. Cellier, and G.E. Séralini. A comparison of the effects of three GM corn varieties on mammalian health. *Int. J. Biol. Sci.* 2009;5:706–26.

- **Unexpected allergenicity:** Mice fed GE peas engineered with an insecticidal protein (alpha-amylase inhibitor) from beans showed a strong, sustained immune reaction against the GE protein, similar to an allergic reaction.[43] The protein in its natural form in the beans produced no such immune response in the mice. The mice fed on GE peas also developed an immune reaction to chicken egg white protein. The findings showed that the GE insecticidal protein acted as a sensitizer, making the mice susceptible to developing immune reactions and allergies to normally non-allergenic foods – a phenomenon called immunological cross-priming.[44]

- **Disturbed liver, pancreas and testes function**: A series of longer-term studies by Professor Manuela Malatesta and colleagues showed toxic effects from feeding GE soy to mice. In a two-generational experiment, mice fed GE 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.[45]

- **Liver aging:** Another study by Professor Malatesta showed that mice fed GE soy over a longer-term (24-month) period exhibited changes in the expression of proteins relating to hepatocyte (liver cell) metabolism, stress response, and calcium signaling, indicating more acute signs of aging in the liver, compared with the control group fed non-GE soy.[46] It should be noted that this study, and the other Malatesta studies discussed above, did not use the non-GE isogenic

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[43] Prescott, V.E., P.M. Campbell, A. Moore, 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.

[44] One of the researchers on this study later co-authored a second study, which he later claimed resolved the health concerns raised by the first study. See Lee, R.Y., D. Reiner, G. Dekan, A.E. Moore, T.J.V. Higgins, and M.M. Epstein. 2013. Genetically modified α-amylase inhibitor peas are not specifically allergenic in mice. *PloS ONE* 8(1): e52972. But this claim is unfounded, as the two studies used markedly different methodologies to elicit and evaluate immune reactions. The second study therefore does not in any way contradict or disprove the allergenic potential of the protein in the GE peas found in the first study, which more accurately reflects the way a human consumer would be exposed to a GE food.

[45] Malatesta, M., M. Biggiogera, E. Manuali, M.B.L. Rocchi, B. Baldelli, and G. Gazzanelli. Fine structural analyses of pancreatic acinar cell nuclei from mice fed on genetically modified soybean. Eur. J. Histochem. 2003;47:385–388.; Malatesta, M., C. Caporaloni, S. Gavaudan, et al. Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. Cell Struct. Funct. 2002;27:173–80.; Vecchio, L., B. Cisterna, M. Malatesta, T.E. Martin, and M. Biggiogera. Ultrastructural analysis of testes from mice fed on genetically modified soybean. Eur. J. Histochem. 2004;48:448-54.

[46] Malatesta, M., F. Boraldi, G. Annovi, 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.

> (parental) variety as the comparator, but rather used a "wild type" non-GE soy. That means that the study does not prove that the genetic modification was the cause of the toxic effects. As noted by the researchers, the cause could have been the herbicide used with the GE soy. Nonetheless, these studies do show that the GE soy was more toxic than the non-GE "wild type" soy. Further studies would be needed to clarify the exact cause.

41. There are three possible sources of adverse health effects from GM foods suggested by the studies outlined above: (1) The GE gene product – for example, the Bt toxin produced by genetically engineered insecticidal crops – may itself be toxic or allergenic; (2) The GE 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 plant composition, resulting in new toxins or allergens and/or altered nutritional value; and (3) 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 genetically engineered Roundup Ready crops.

42. Few animal-feeding studies with GMOs are designed in such a way as to distinguish among these three different sources of adverse health effects. One of the few studies that was designed to do so was a long-term rat feeding study on NK603 GE corn and the Roundup herbicide it is engineered to tolerate.[47] The study found that both extremely small amounts of Roundup (well below regulatory limits) and the GE corn (both sprayed with Roundup and left unsprayed) caused toxic effects in the rats. Effects included severe liver and kidney damage, disturbance to pituitary gland function, and hormonal disruption.

[47] Séralini, G-E., E. Clair, R. Mesnage, et al. Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environ. Sci. Eur.* 2014;26(1):14. doi:10.1186/s12302-014-0014-5.

43. McHughen claims that, "while there are a small handful of published reports that appear to disagree with the scientific and medical consensus (based on hundreds of safety studies), all of these 'negative' reports have been retracted, debunked, or unable to withstand replication (that is, repeated by others with similar results)." McHughen Decl. ¶ 100. That is false. The only way to "debunk" empirical findings of harm is to replicate and extend the study, possibly improving the design in the process, and get a different result. But no one has attempted to replicate a single study that has found toxic effects from a GE food. Thus, the findings of toxic effects from GMOs reported in these studies have not been refuted.

44. I am only aware of one animal-feeding study with GE crops that was retracted – the rat feeding study by Séralini and colleagues showing that GE corn NK603 and extremely small amounts of the Roundup herbicide it is grown with caused liver, kidney, and pituitary gland toxicity, as well as hormonal disruption. The study was retracted by the editor-in-chief of the journal Food and Chemical Toxicology more than a year after it was first published. In my view, the study was retracted for unscientific reasons – reasons that have been condemned by many scientists.[48] And the paper was subsequently republished by another peer-reviewed journal, Environmental Sciences Europe.[49]

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[48] 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. Accessed February 21, 2014; EndScienceCensorship.org. 2014. 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; 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; Roberfroid, M. Letter to the editor. *Food Chem. Toxicol.* 2014;65:390.

[49] Séralini, G-E., E. Clair, R. Mesnage, et al. 2014. Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environ. Sci. Eur.* 2014;26(1):14. The paper was peer reviewed again for this second publication, though the editor-

45. Critics of the Séralini study, moreover, treated it as a failed carcinogenicity (cancer) study, not as what it really was: a (long-term) *toxicity* study that unexpectedly observed a trend of increased tumors and mortality. These observations require follow-up in a full-scale carcinogenicity study, which typically uses 50 animals per sex per group, as compared with the 10 per sex per group used by Séralini's group. However, 10 animals per sex per group is the same number recommended to be analyzed for blood and urine chemistry in the Organisation for Economic Cooperation and Development's ("OECD's") test guidelines for chronic toxicity studies.[50] These guidelines are used by industry for the testing of chemicals in support of regulatory authorizations. While the OECD recommends that 20 animals per sex per group are included in the experiment, it only requires 50% of the animals – 10 per sex per group – to be analyzed with regard to these key parameters.[51] Similarly, the Monsanto 90-day feeding study with the same GE corn, NK603, also analyzed only 10 out of 20 animals for blood and urine chemistry.[52] I conclude that the chronic toxicity findings of the study, including the liver, kidney and pituitary gland toxicity and hormone disruptions as revealed by histological (macroscopic and microscopic organ analysis) and blood and urine chemistry measurements, are statistically reliable and should be taken seriously by regulators.

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in-chief of the journal stated that he did not commission a "scientific peer review," "because this had already been conducted by Food and Chemical Toxicology, and had concluded there had been no fraud nor misrepresentation." The role of the three reviewers hired by ESEU was to check that there had been no change in the scientific content of the paper. Casassus, B. June 26, 2014. Paper claiming GM link with tumours republished. *Nature*, available at http://www.nature.com/news/paper-claiming-gm-link-with-tumours-republished-1.15463.

[50] Organisation for Economic Cooperation and Development (OECD). *OECD Guideline No. 452 for the Testing of Chemicals: Chronic Toxicity Studies: Adopted 7 September 2009*.; 2009.

[51] *Id.*

[52] Hammond, B., R. Dudek, J. Lemen, and M. Nemeth. 2004. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. *Food Chem. Toxicol.* 42:1003-14.

46. Significantly, Séralini designed his two-year rat feeding study as a direct follow-up to Monsanto's short 90-day rat feeding trial on the same GE NK603 corn, which the company had conducted to support its application for regulatory authorization. The Monsanto study itself reported differences in the GE-fed rats, but the Monsanto authors dismissed those findings as not related to the GE corn diet and as not "biologically meaningful."[53] Séralini's team obtained Monsanto's raw data and re-analyzed it. They found signs of liver and kidney toxicity in the GE-fed rats, publishing their findings in a peer-reviewed journal in 2009.[54] Séralini then carried out his 2-year study[55] on NK603 corn and Roundup to see whether these initial findings of potential toxicity really were of no biological significance, as Monsanto 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 (2 years to Monsanto's 90 days) and far more detailed in scope; included three rather than two doses (as Monsanto had used) of the GE corn feed; measured a larger number of bodily functions; and was designed to separate out the effects of the GE corn 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. Séralini's team found that the initial findings of toxicity seen in Monsanto's 90-day experiment did indeed escalate into serious disease – organ damage and hormonal disturbances – over a long-term period of 2 years. Of course, the question whether GE foods present health risks does not stand or fall on the validity of the Séralini study. As noted above, many other

[53] Hammond, B., R. Dudek, J. Lemen, and M. Nemeth. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. *Food Chem. Toxicol.* 2004;42:1003-14.

[54] De Vendomois, J.S., F. Roullier, D. Cellier, and G.E. Séralini. A comparison of the effects of three GM corn varieties on mammalian health. *Int. J. Biol. Sci.* 2009;5:706–26.

[55] Séralini, G-E., E. Clair, R. Mesnage, et al. Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environ. Sci. Eur.* 2014;26(1):14.

studies suggest that GE foods present health risks. But in my view, the Séralini study, too, suggests that GE foods may present health risks.

47. Many of the studies I discuss above were considered by the Vermont Legislature when it enacted Act 120. I believe that those studies, and others, suggest that GE foods may present a risk to human health and safety.

Many Analyses Purporting To Demonstrate
The Safety Of GE Foods Are Flawed

48. The studies discussed above show that GE foods can be harmful to human health. Just as importantly, however, many of the studies relied on by opponents of GE labeling are flawed, and therefore do not prove that GE foods are perfectly safe.

49. For example, in support of his contention that there is a scientific consensus on the safety of GE foods, Alan McHughen states in his declaration that "the European Union, which is well known to be skeptical of biotechnology, spent over €270,000,000 (approximately $360 million) on 130 separate safety studies conducted by over 400 public research teams in the EU between 1985 and 2010. In that quarter century of *actively* evaluating health and safety problems, not one of those studies documented any evidence suggesting that genetically engineered crops were any more risky than conventionally bred crops." McHughen Decl. ¶ 96. But the European Union ("EU") report to which McHughen refers 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 rather to focus on "the development of safety assessment approaches."[56]

[56] European Commission Directorate-General for Research and Innovation, Biotechnologies, Agriculture, Food. *A Decade of EU-Funded GMO Research (2001–2010)*. Brussels, Belgium; 2010.

50. In researching our book *GMO Myths and Truths*, I and my coauthors searched the EU report for animal feeding studies that could provide hard data on GMO safety. That was a difficult task, because the EU report is not written as a scientific document, and the authors often fail to reference specific studies to back up their claims. In the report, we found only five published and referenced animal feeding studies with GMOs.[57] None of the studies tested a commercialized GE food; none tested the GE food for long-term effects beyond the medium-term period of 90 days; and all found differences in the GE-fed animals, which in some cases were statistically significant. For example, one study found a markedly higher water intake by the GE-fed group, as well as differences in blood biochemistry, immune response, gut bacteria, and organ weights. While the authors claimed that none of these differences were "adverse,"[58] there is no way of telling in such a short study. In short, none of the five studies concluded on the safety of the GE food tested, let alone on the safety of GE foods in general. The EU research project therefore provides no evidence to support claims of safety for any single GE food or of GE crops in general.

[57] Poulsen, M., M. Schrøder, A. Wilcks, 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; Knudsen, I. and M. Poulsen. 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; Schrøder, M., M. Poulsen, A. Wilcks, 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; Poulsen, M., S. Kroghsbo, M. Schroder, 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; Kroghsbo, S., C. Madsen, M. Poulsen, et al. Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. *Toxicology* 2008;245:24-34.

[58] Poulsen, M., S. Kroghsbo, M. Schroder, 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.

51. To the contrary, the studies cited in the EU report provide evidence that: (1) Over a decade after GE foods were released into the food and feed supplies, regulators still have not agreed on methods of assessing them for safety; (2) The GE foods tested were markedly different in composition from their non-GE counterparts – probably due to the mutagenic or epigenetic (i.e., producing changes in gene function) effects of the GE process; and (3) The GE foods tested caused unexpected, potentially adverse effects in GE-fed animals that should be investigated further in long-term tests.

52. McHughen also claims that the Bt insecticidal proteins in genetically engineered Bt crops are "harmless to humans and other animals" and harm only certain insects. McHughen Decl. ¶ 35. McHughen bases his argument on the fact that farmers have used natural non-GE Bt toxin, which is derived from a soil bacterium, as an insecticide spray since the 1940s. That argument is misleading.

53. To begin with, the Bt toxin expressed by genetically engineered Bt plants is different from natural Bt, both in terms of its structure and its mode of action. Structurally, there is at least a 40% difference between the toxin in Bt176 corn (formerly commercialized in the EU, now withdrawn) and natural Bt toxin.[59] And the EPA stated that the commercialized Monsanto GE corn MON810 produced a "truncated" version of the protein – a much shorter form of the protein that is different from the natural form.[60] Such changes in a protein can mean that it has very different environmental and health effects, including being a novel toxin or allergen. The genetically engineered Bt toxin loses the selectivity that characterizes natural Bt. And the

[59] Séralini, G-E., R. Mesnage, E. Clair, S. Gress, J.S. de Vendômois, and D. Cellier. Genetically modified crops safety assessments: Present limits and possible improvements. *Environ. Sci. Eur.* 2011;23. doi:10.1186/2190-4715-23-10.

[60] Freese, W., and D. Schubert. 2004. Safety testing and regulation of genetically engineered foods. *Biotechnol. Genet. Eng. Rev.* 21: 299-324.

genetically engineered Bt toxin can harm non-target insects, including butterflies and other non-target insects,[61] beneficial pest predators,[62] bees,[63] aquatic organisms,[64] and beneficial soil organisms.[65]

54. Genetically engineered Bt toxin, moreover, may indeed have negative health impacts on people or animals that eat a crop containing it. Even extremely small changes in a protein can completely change its properties. For example, soybeans can be genetically engineered to tolerate an herbicide that would normally kill them by changing a gene that gives

[61] Losey, J.E., L.S. Rayor, and M.E. Carter. Transgenic pollen harms monarch larvae. *Nature* 1999;399:214; Jesse, L.C.H. and J.J. Obrycki. Field deposition of Bt transgenic corn pollen: Lethal effects on the monarch butterfly. *J. Oecologia* 2000;125:241–248; Lang, A. and E. Vojtech. 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.

[62] Hilbeck, A., M. Baumgartner, P.M. Fried, and F. Bigler. Effects of transgenic Bt corn-fed prey on immature development of Chrysoperla carnea (Neuroptera: Chrysopidae). *Environ. Entomol.* 1998;27(2):480–487; Hilbeck, A., M. Meier, and M. Trtikova. Underlying reasons of the controversy over adverse effects of Bt toxins on lady beetle and lacewing larvae. *Environ. Sci. Eur.* 2012;24(9); Hilbeck, A., J.M. McMillan, M. Meier, A. Humbel, J. Schlaepfer-Miller, and M. Trtikova. A controversy re-visited: Is the coccinellid Adalia bipunctata adversely affected by Bt toxins? *Environ. Sci. Eur.* 2012;24(10); Hilbeck, A., W.J. Moar, M. Pusztai-Carey, A. Filippini, and F. Bigler. Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator Chrysoperla carnea. *Entomol. Exp. Appl.* 1999;91:305–316; Marvier, M., C. McCreedy, J. Regetz, and P. Kareiva. A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. *Science* 2007;316:1475-7; Lövei, G.L. and S. Arpaia. The impact of transgenic plants on natural enemies: A critical review of laboratory studies. *Entomol. Exp. Appl.* 2005;114:1–14.

[63] Ramirez-Romero, R., N. Desneux, A. Decourtye, A. Chaffiol, and M.H. Pham-Delègue. Does Cry1Ab protein affect learning performances of the honey bee Apis mellifera L. (Hymenoptera, Apidae)? *Ecotoxicol. Environ. Saf.* 2008;70:327–333.

[64] Rosi-Marshall, E.J., J.L. Tank, T.V. Royer, et al. Toxins in transgenic crop byproducts may affect headwater stream ecosystems. *Proc. Natl. Acad. Sci. USA* 2007;104:16204-8; Bøhn, T., T. Traavik, R. Primicerio. Demographic responses of Daphnia magna fed transgenic Bt-maize. *Ecotoxicology* 2010;19:419-30.

[65] Castaldini, M., A. Turrini, C. Sbrana, 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.

rise to a protein differing from the natural protein by just two amino acids.[66] As researchers at the Centre for Integrated Research in Biosafety in New Zealand pointed out,[67] a change even of a single amino acid can radically change the properties of proteins, which in turn can result in changed behavior of a plant.[68]

55. Indeed, as noted above, feeding studies in mammals have been performed with GE Bt crops and have found adverse effects, including (1) Toxic effects or signs of potential toxicity in the small intestine, liver, kidney, spleen, pancreas;[69] (2) Disturbances in the functioning of the digestive system;[70] (3) Increased or decreased weight gain compared with

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[66] 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.

[67] Kurenbach, B., D.S. Coray, J.A. Heinemann, R,J, Catchpole, and L.A. Turner. *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.

[68] Doyle, M.R. and R.M. Amasino. 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; Hanzawa, Y., T. Money, and D. Bradley. 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.

[69] Séralini, G-E., D. Cellier, and J. Spiroux de Vendomois. 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; J.S. de Vendomois, F. Roullier, D. Cellier, and G-E. Séralini. A comparison of the effects of three GM corn varieties on mammalian health. *Int. J. Biol. Sci.* 2009;5:706–26; Trabalza-Marinucci, M., G. Brandi, C. Rondini, 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; El-Shamei, Z.S., A.A. Gab-Alla, A.A. Shatta, E.A. Moussa, and A.M. Rayan. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 2012;8(10):684–696; Fares, N.H. and A.K. El-Sayed. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. *Nat. Toxins* 1998;6(6):219-33.

[70] El-Shamei, Z.S., A.A. Gab-Alla, A.A. Shatta, E.A. Moussa, and A.M. Rayan. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 2012;8(10):684–696; Trabalza-Marinucci, M., G. Brandi, C. Rondini, et al. A

controls;[71] (4) Male reproductive organ damage;[72] (5) Blood biochemistry disturbances;[73] and (6) Immune system disturbances.[74]

56. In addition, studies in mice have shown that genetically engineered and natural Bt toxin produces a potent immune response when delivered into the stomach (a method considered similar to human dietary exposure) or injected into the abdomen.[75] The Bt toxin protein was found to bind to the surface of the small intestine of the mice, an effect that could lead to changes in the physiological status of the intestine.[76] The Bt toxin protein also enhanced the immune

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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.

[71] Séralini, G.E., D. Cellier, and J. Spiroux de Vendomois. 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; Gab-Alla, A.A., Z.S. El-Shamei, A.A. Shatta, E.A. Moussa, and A.M. Rayan. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 2012;8(9):1117–112.

[72] El-Shamei, Z.S., A.A. Gab-Alla, A.A. Shatta, E.A. Moussa, and A.M. Rayan. Histopathological changes in some organs of male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 2012;8(10):684–696.

[73] Gab-Alla, A.A., Z.S. El-Shamei, A.A. Shatta, E.A. Moussa, and A.M. Rayan. Morphological and biochemical changes in male rats fed on genetically modified corn (Ajeeb YG). *J. Am. Sci.* 2012;8(9):1117–1123.

[74] Finamore, A., M. Roselli, S. Britti, 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.

[75] Vázquez-Padrón, R.I., L. Moreno-Fierros, L. Neri-Bazan, G.A. de la Riva, and R. Lopez-Revilla. Intragastric and intraperitoneal administration of Cry1Ac protoxin from Bacillus thuringiensis induces systemic and mucosal antibody responses in mice. *Life Sci.* 1999;64:1897-912; Vázquez-Padrón, R.I., L. Moreno-Fierros, L. Neri-Bazan, A.F. Martinez-Gil, G.A. de-la-Riva, and R. Lopez-Revilla. 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.

[76] Vázquez-Padrón, R.I., J. Gonzales-Cabrera, C. Garcia-Tovar, 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.

response of the mice to other substances in a process called immunological cross-priming.[77] I therefore conclude that GE Bt crops, including those already commercialized, cannot be assumed to be safe for humans and animals to eat.

57. In his declaration, Alan McHughen also cites (at ¶ 99) a recent review by Nicolia and colleagues "surveying over 1700 independent peer-reviewed scientific studies reporting on various safety aspects of genetically engineered products," and stating that "none of them revealed any indication that GE posed greater risks than "traditional" methods." [78] The Nicolia review, however, provides little evidence for the safety of commercialized GMOs that are in the food supply. It suffers from important omissions, fails to show GMOs are safe, and actually provides evidence of risk for some GMOs.

58. For example, only a relatively small proportion of the studies reviewed by Nicolia look at the long-term impacts of GE foods on animal health or the effects of GE crop cultivation on soil microbial life, non-target insects, and other wildlife. The bulk of the studies cited in the Nicolia review are irrelevant or tangential to investigation of the safety of GE foods and crops. For example, the review cites animal production studies, often performed by GE companies on their own product.[79] Those studies often do not examine in detail the health impacts of GE feed, but rather look at aspects of animal production of interest to the food and agriculture industry,

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[77] Vázquez-Padron, R.I., L. Moreno-Fierros, L. Neri-Bazan, G.A. de La Riva, and R. Lopez-Revilla. Bacillus thuringiensis Cry1Ac protoxin is a potent systemic and mucosal adjuvant. *Scand. J. Immunol.* 1999;49:578-84.

[78] Nicolia, A., A. Manzo, F. Veronesi, and D. Rosellini. An overview of the last 10 years of genetically engineered crop safety research. *Crit. Rev. Biotechnol*. 2013:1-12.

[79] Taylor, M., G. Hartnell, D. Lucas, S. Davis, and M. Nemeth. 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; Bakke-McKellep, A.M., M. Sanden, A. Danieli, 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.

such as weight gain and milk production. And they typically follow the animals for only a small fraction of their natural lifespans, meaning that long-term health effects cannot be detected.

59. Nicolia and colleagues also omit from their discussion important studies that find risks and toxic effects from GMOs. In some cases, the omissions are due to the authors' arbitrary 10-year cut-off date; by including only the last 10 years of scientific research, the authors excluded early studies that found toxic effects in animals fed GM crops, including some studies I discuss above.[80] And the authors failed to explain why they omitted other, more recent studies, many of which I also discuss above, that show potential health effects of GE foods. Nicolia and colleagues also ignore important findings of adverse environmental and agronomic impacts from GMOs. A more detailed critique of Nicolia and colleagues' review is available in my book *GMO Myths and Truths* (at section 2.3).

60. Nor is it sufficient to state, as McHughen does in his declaration (at ¶ 90), that "GE food crops are subject to more safety testing than any other food in the market." That statement is misleading. It is true that non-GE foods are not required to be safety tested, and that any safety testing required for GE foods is therefore more than that required for non-GE foods. But the U.S. regulatory system does not require *any* animal feeding trials to be carried out with GE foods. Instead, GE foods are "deregulated," since the FDA assumes that GE foods are generally recognized as safe ("GRAS") and therefore do not require testing or special regulatory

[80] Ewen, S.W. and A. Pusztai. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. *Lancet* 1999;354:1353-4; Fares, N.H. and A.K. El-Sayed. Fine structural changes in the ileum of mice fed on delta-endotoxin-treated potatoes and transgenic potatoes. *Nat. Toxins* 1998;6(6):219-33.

oversight.[81] For the reasons stated in this Declaration, I do not believe that GE foods meet the strict GRAS criteria.

61. Producers can submit safety studies to the FDA. As McHughen acknowledges in his declaration (at ¶ 90), that testing is conducted and/or sponsored by the GE food's developer. And the animal feeding studies routinely performed by industry to support regulatory authorization of their products generally last for a maximum of 90 days. As noted above, 90 days in a rat is too short a period to reveal long-term effects, as it is equivalent to only approximately 7-8 years of the average human lifespan. These industry studies can suffer from other weaknesses, too, such as using animals that are irrelevant to assessing human health risks (for example, chickens).

62. The industry studies also often fail to conduct the correct comparison to determine whether GE foods present a safety risk. A well-controlled study would look at the effects on animals fed a GE plant as compared to animals fed what is referred to as an "isogenic" plant (i.e., the non-genetically engineered parent of the GE plant that has the same genetic background as the GE plant, with the exception of the genetic modification) and would restrict the comparison to these two diets, with the GE and non-GE plants grown at the same time in the same conditions, to minimize changes in plant composition caused by different environmental conditions. That would mean that any changes that are seen in the GE-fed animals were an effect of the genetic modification, and not due to irrelevant factors such as environmental conditions or different genetic background of the plant. Most industry studies, however, fail to restrict the comparison to the isogenic plants. Instead they add a range of "reference" control diets containing different

[81] Statement of Policy: Foods Derived From New Plant Varieties, 57 Fed. Reg. 22,984 (May 29, 1992).

varieties of the crop, grown in different conditions and at different times.[82] This practice introduces many uncontrolled variables into the experiment and has the effect of masking the effects of the genetic modification on the feed crop. Thus the researchers are likely to find "no effect" when in fact there may be an effect that is missed because of the poor study design.

63. McHughen states in his declaration (at ¶ 90) that "[m]uch of the data provided" for regulatory approval "come from testing conducted by the developer, but many of the studies are also conducted by university research scientists or third-party contractors." But even tests conducted by university scientists or third-party contractors are sponsored by the GE industry. And the GE developer may therefore decide which data are sent to regulators and which data, if any, are submitted for publication in peer-reviewed journals. That does not qualify as an independent analysis.

64. Many of these studies demonstrating the limitations of current testing of GE foods were also considered by the Vermont Legislature when it enacted Act 120. For the reasons stated above, I agree with the Vermont Legislature that existing studies are inadequate to establish the long-term safety of GE foods.

GE Crops Have Led To Increased Herbicide Use,
With Potential Health And Environmental Effects

65. The development of genetically engineered herbicide-tolerant crops has led to an increase in herbicide use in the United States. For example, GE 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, compared with the amount that would have been used if the same acres had been planted to non-GE crops. And the increased use of herbicides is not sustainable. For

[82] See, e.g., Hammond, B., R. Dudek, J. Lemen, and M. Nemeth. 2004. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. *Food Chem. Toxicol*. 42:1003-14.

example, while in 1996 GE herbicide-tolerant soy needed 0.30 pounds per acre less herbicide than non-GE soy, in 2011 the cultivation of GE herbicide-tolerant soy needed 0.73 pounds per acre more herbicide than non-GE soy.[83]

66. Human and animal consumers of GE crops eat residues of the herbicides with which GE plants are grown. And GE plants often contain higher amounts of herbicide residues than non-GE plants. A recent study illustrates this point. Researchers analyzed the composition of genetically engineered glyphosate-tolerant soybeans, conventionally grown non-GE soybeans, and organic soybeans. They found that the GE soybeans contained high residues of glyphosate and its toxic metabolite AMPA, but industrially grown non-GE soybeans and organic soybeans contained neither chemical.[84] Monsanto itself had previously called these levels of glyphosate – which have become the industry norm – "extreme."[85] The mean level of glyphosate in the GE soybeans was 3.3 mg/kg. That is a 19,500-fold higher concentration than the level found to have estrogen-mimicking effects and cause proliferation of human breast cancer cells in test tube experiments.[86] These results need to be confirmed in experiments with living animals. Thus far,

[83] Benbrook, C.M. 2012. Impacts of genetically engineered crops on pesticide use in the U.S. – The first sixteen years. *Environ. Sci. Eur.* 24:24.

[84] Bøhn, T., M. Cuhra, T. Traavik, M. Sanden, J. Fagan, and R. Primicerio. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. *Food Chem.* 2013;153(2014):207–215.

[85] Bøhn, T. and M. Cuhra. 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/.

[86] Thongprakaisang, S., A. Thiantanawat, N. Rangkadilok, T. Suriyo, and J. Satayavivad. Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food Chem. Toxicol.* 2013;59:129-36.

only experiments with higher concentrations of glyphosate have been carried out in animals, even though in endocrine-disruptive effects, lower doses can be more toxic.[87]

67. One reason for the massive increase in herbicide use is that, before the advent of genetically engineered herbicide-tolerant crops, farmers had to use herbicides sparingly in order to avoid damaging the crop. But GE herbicide-tolerant crops remove that restriction. Thus, large amounts of herbicide can be sprayed without killing the resistant crop. At the same time, farmers have reduced the application rate of herbicides other than glyphosate applied to non-GE crops.[88]

68. Another reason for the increase in herbicide use is the evolution of herbicide resistance in weeds that has resulted from the increased use of herbicides on genetically engineered crops. The area of US cropland infested with more than 20 different species of glyphosate-resistant weeds expanded to 61.2 million acres in 2012, according to a survey conducted by Stratus Agri-Marketing. Nearly half of all U.S. 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.[89]

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[87] Vandenberg, L.N., T. Colborn, T.B. Hayes, 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.

[88] Benbrook, C.M. 2012. Impacts of genetically engineered crops on pesticide use in the U.S. – The first sixteen years. *Environ. Sci. Eur.* 24:24.

[89] Fraser, K. *Glyphosate Resistant Weeds – Intensifying*. Guelph, Ontario, Canada: Stratus Ag Research; 2013. Available at: http://stratusresearch.com/blog/glyphosate-resistant-weeds-intensifying; Glyphosate-resistant weed problem extends to more species, more farms. Farm Industry News; 2013. Available at: http://farmindustrynews.com/ag-technology-solution-center/glyphosate-resistant-weed-problem-extends-more-species-more-farms.

69. 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.[90] Farmers are therefore 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.[91]

70. The industry's solution to the glyphosate-tolerant superweeds crisis has been first, to market pre-mixed herbicide products to farmers; and second, to develop stacked-trait GE 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.[92]

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[90] Nandula, V.K., K.N. Reddy, S.O. Duke, and D.H. Poston. 2005. Glyphosate-resistant weeds: Current status and future outlook. *Outlooks Pest Manag.* 16:183–187; Syngenta module helps manage glyphosate-resistant weeds. Delta Farm Press; 2008. Available at: http://deltafarmpress.com/syngenta-module-helps-manage-glyphosate-resistant-weeds.

[91] Mortensen, D.A., J.F. Egan, B.D. Maxwell, M.R. Ryan, and R.G. Smith. 2012. Navigating a critical juncture for sustainable weed management. *BioScience* 62(1):75-84; Robinson R. Resistant ryegrass populations rise in Mississippi. Delta Farm Press; 2008. Available at: http://deltafarmpress.com/resistant-ryegrass-populations-rise-mississippi; Johnson, B. and V. Davis. 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; Nice, G., B. Johnson, and T. Bauman. 2008. A little burndown madness. *Pest & Crop*. Available at: http://extension.entm.purdue.edu/pestcrop/2008/issue1/index.html.; Nice, G. and B. Johnson. 2006. Fall applied programs labeled in Indiana. *Pest Crop* 2006;(23). Available at: http://extension.entm.purdue.edu/pestcrop/2006/issue23/table1.html; Randerson, J. Genetically-modified superweeds "not uncommon." *New Sci.* 2002. Available at: http://www.newscientist.com/article/dn1882-geneticallymodified-superweeds-not-uncommon.html; Kilman, S. Superweed outbreak triggers arms race. *Wall Street Journal*, June 4, 2010. Available at: http://biolargo.blogspot.com/2010/06/round-up-weed-killer-and-acquired.html; Brasher P., Monsanto paying farmers to increase herbicide use. *Des Moines Register*, October 19, 2010. Available at: http://bit.ly/az3fSo.

[92] Kilman, S. Superweed outbreak triggers arms race. *Wall Street Journal*, June 4, 2010. Available at: http://biolargo.blogspot.com/2010/06/round-up-weed-killer-and-acquired.html.

71. In 2014, the USDA deregulated Dow Chemical's multi-herbicide-tolerant genetically engineered soybean and maize, engineered to tolerate being sprayed with 2,4-D, glyphosate, and other herbicides.[93] Shortly afterward, the EPA registered Enlist Duo, a combined 2,4-D and glyphosate herbicide that will be sprayed on the growing crop.[94] Weed scientists have warned that these 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.[149] 2,4-D has been linked to serious health hazards, including cancer, neuroendocrine disruption, and reproductive effects.[95]

72. With the advent of glyphosate-resistant weeds and the new multi-herbicide-tolerant GE crops, McHughen's point (at ¶ 40) that GE herbicide-tolerant crops "could be safely sprayed with RoundUp™ herbicide to give the farmer control over a broad range of weed species without the need to use multiple herbicidal chemicals" is out of date and inaccurate.

73. Thus, the claim that GE crops are equivalent to non-GE crops is particularly flawed in light of the herbicide residues found in herbicide-tolerant GE crops. These doses of residues have never been tested for safety for regulatory purposes. And the complete herbicide formulations as sold and used by farmers have never been tested for long-term safety; only the isolated presumed "active" ingredient in each herbicide (e.g. glyphosate in the case of Roundup) has been tested for long-term safety in rodents. There is evidence that the mixtures of chemicals

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[93] U.S. Department of Agriculture (USDA)-APHIS. *Record of Decision: Dow AgroSciences Petitions (09-233-01p, 09-349-01p, and 11-234-01p) for Determination of Nonregulated Status for 2,4-D-Resistant Corn and Soybean Varieties*. Washington, D.C.: U.S. Department of Agriculture; 2014. Available at: http://www.aphis.usda.gov/brs/aphisdocs/24d_rod.pdf.

[94] Environmental Protection Agency, Registration of Enlist Duo. 2014. Available at: http://www2.epa.gov/ingredients-used-pesticide-products/registration-enlist-duo.

[95] Solomon, G.M. *2,4-D Health Summary*. Natural Resources Defense Council; 2012. Available at: http://www.panna.org/sites/default/files/2-4-D-Health-Summary_NRDC-4-12.pdf

that make up herbicide formulations are more toxic than the isolated "active" ingredient[96] and that this is a general principle of pesticide toxicity.[97]

74. In addition, the potential health effects of ingesting residues of mixtures of different herbicides, as applied to multi-herbicide-resistant crops, have not been assessed by regulators. For the reasons stated above, it is not possible to conclusively state that the levels of herbicide residues found in GE crops are safe.

75. In addition to having potential implications for consumer health, GE herbicide-tolerant crops have significant implications for biodiversity.

76. For example, the increased use of glyphosate herbicide due to the spread of GM glyphosate-tolerant crops has been found to severely impact monarch butterflies. 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. That sharp population drop has been attributed to the spread of glyphosate-tolerant GE crops and the resulting over-use of glyphosate herbicides. Specifically, the glyphosate spraying killed the milkweed that was the prime food source for monarchs.[98]

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[96] Mesnage, R., N. Defarge, J.S. de Vendomois, and G-E. Séralini. Major pesticides are more toxic to human cells than their declared active principles. *BioMed. Res. Int.* 2014;2014; Lin N. and V.F. Garry. 2000. 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.* 60:423-39; Lee, H-L., C-D. Kan, C-L. Tsai, M-J. Liou, and H-R. Guo. 2009. Comparative effects of the formulation of glyphosate-surfactant herbicides on hemodynamics in swine. *Clin. Toxicol. Phila. Pa*. 47(7):651-658.

[97] Mesnage, R, N. Defarge, J.S. de Vendomois, and G.E. Séralini. Major pesticides are more toxic to human cells than their declared active principles. *BioMed Res. Int.* 2014;2014.

[98] Conniff, R. 2013. Tracking the causes of sharp decline of the monarch butterfly. *Yale Environment 360*. Available at: http://e360.yale.edu/feature/tracking_the_causes_of_sharp__decline_of_the_monarch_butterfly/2634/.

77. That view has been confirmed by a peer-reviewed study that found a 58% decline in milkweeds 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 GE glyphosate-tolerant maize and soybeans and consequent increased use of glyphosate herbicide to control weeds, including milkweed. The authors conclude that a loss of agricultural milkweeds is a major contributor to the decline in the monarch population.[99]

78. Considering the effects of GE herbicide-tolerant crops on biodiversity more broadly, in the late 1990s and early 2000s the U.K. government's Farm Scale Evaluations ("FSEs") looked at the effects on farmland wildlife of the cultivation of four GE herbicide-tolerant crops, compared with non-GE crops grown under intensive chemically based management. The overall outcome of the FSEs was that the management of all but one of the GE herbicide-tolerant crops tested was more damaging to farmland wildlife than the management of non-GE crops grown under a conventional chemically intensive system.[100] GE corn was found better for wildlife. However, the non-GE comparator corn was grown with the highly toxic herbicide atrazine, which was banned in Europe before the results of the FSEs were published.

79. The Vermont Legislature considered several studies relating to the potential environmental effects of GE foods, including the study on monarch populations that I discuss above. I agree with the Legislature's conclusion that GE foods present potential environmental risks.

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[99] Pleasants, J.M. and K.S. Oberhauser. 2013. Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population. *Insect Conserv. Divers.* 6:135–144.

[100] 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.

Conclusion

80. In conclusion, it is my opinion that there is no scientific consensus that GE foods are perfectly safe. On the contrary, numerous studies suggest that GE foods present significant risks to human health and the environment.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge, information, and belief.

Dated: November 13, 2014

Michael Antoniou