

## Reasons for Labeling of Genetically Engineered Foods

March 19, 2012

**TO:** AMA Council on Science and Public Health

**FROM:** Michael Hansen, Ph.D., Senior Scientist, Consumer Reports

**RE:** Resolutions 508 (Illinois) and 509 (Indiana) Supporting Federal Legislation and/or Regulations that Require Clearly Labeling Food with Genetically Engineered Ingredients

**SUMMARY:** Based on the scientific uncertainty surrounding both the molecular characterization of genetically engineered (GE) crops as well as the detection of potential allergenicity, there is more than enough uncertainty to decide to require labeling of foods produced via GE as a risk management measure as a way to identify unintended health effects that may occur post approval. If foods are not labeled as to GE status, it would be very difficult to even identify an unexpected health effect resulting from a GE food.

Dear Council Members:

I am writing to submit scientific evidence which strongly supports the intent of *Resolutions 508 and 509 Supporting Federal Legislation and/or Regulations that Require Clearly Labeling Food with Genetically Engineered Ingredients*. Consumer Union<sup>1</sup> supports mandatory labeling for foods produced with genetically engineered (GE) ingredients for a number of reasons.

- 1. There has been global agreement that genetically engineered foods are different than conventionally bred foods and that all genetically engineered foods should be required to go through a safety assessment prior to approval.** Codex Alimentarius is the food safety standards organization of the United Nations, and is jointly run by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO). From 2000 – 2008, there were two rounds of the Codex Alimentarius *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology. This Task Force developed a number of documents, including a Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (CAC/GL 45, 2003)<sup>2</sup>; there are separate Guidelines for GE animals and GE microorganisms, as well. The World Trade Organization (WTO) considers that, in terms of food safety, the standards or guidelines of Codex Alimentarius are deemed the global science-based standard and, thus, immune to trade challenges, i.e. they are not considered to be a “non-tariff trade barrier.”

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<sup>1</sup> Consumers Union is the public policy and advocacy division of Consumer Reports. Consumers Union works for telecommunications reform, health reform, food and product safety, financial reform, and other consumer issues. Consumer Reports is the world's largest independent product-testing organization. Using its more than 50 labs, auto test center, and survey research center, the nonprofit rates thousands of products and services annually. Founded in 1936, Consumer Reports has over 8 million subscribers to its magazine, website, and other publications, and a few noncommercial grants. Roughly 8 million people subscribe to Consumer Reports or Consumer Reports online.

<sup>2</sup> At: [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

The reason for two rounds of the Codex Alimentarius *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology came as a result of a global agreement that genetic engineering is a process that is sufficiently different from conventional breeding that foods developed via genetic engineering should go through a safety assessment before such foods are allowed on the market. For information on the ways genetic engineering differs from conventional breeding, see Hansen, 2000.<sup>3</sup>

Last year, after more than 15 years of debate, the Codex Committee on Food Labeling agreed to forward a document on labeling of GE foods to the Codex Alimentarius Commission for approval. Last July, at the conclusion of the meeting of the Codex Alimentarius Commission, the World Health Organization News put out a letter to journalists, noting that the "Codex Alimentarius Commission has stated that governments are free to decide on whether and how to label foods derived from modern biotechnology, including foods containing genetically-modified organisms. The labeling should be done in conformity with the text approved by the Codex Commission, to avoid a potential trade barrier. The decision, which will help inform consumers' choices regarding genetically-modified foodstuffs, was taken at the 34<sup>th</sup> Session of the Commission, held in Geneva from 4-9 July 2011. More than 600 delegates from 145 of the 184 member countries, UN, inter-governmental and non-governmental organizations attended."<sup>4</sup>

Unlike all other developed countries, the US Food and Drug Administration (FDA) does not require safety testing for GE plants. The FDA's original policy on GE (or GM, for genetically modified) plants was introduced at a press conference at an industry gathering on May 28, 1992 by then Vice-President Dan Quayle as a de-regulatory initiative. The policy was based on the notion "that the new techniques [e.g. genetic engineering] are extensions at the molecular level of traditional methods and will be used to achieve the same goals as pursued with traditional plant breeding,"<sup>5</sup> and therefore should be regulated in the same way. In other words, no requirement for human safety testing; instead there are "voluntary safety consultations."

The lack of adequate safety testing can be seen in the letter FDA sends to the company after completion of a "safety consultation." For example, the letter sent to Monsanto on September 25, 1996 about one of their first Bt-corn varieties, MON810, states, "Based on the safety and nutritional assessment you have conducted, **it is our understanding that Monsanto has concluded that corn grain and forage derived from the new variety are not materially different in composition, safety, or other relevant parameters from corn grain and forage currently on the market, and that they do not raise issues that would require premarket review or approval by FDA**" bold added.<sup>6</sup> Note that FDA does not state its own opinion about

<sup>3</sup> Hansen, M. 2000. Genetic engineering is not an extension of conventional plant breeding: How genetic engineering differs from conventional breeding, hybridization, wide crosses and horizontal gene transfer. 13 pp. At: <http://www.consumersunion.org/food/widecpi200.htm>

<sup>4</sup> Email from [WorldHealthOrganizationNews@who.int](mailto:WorldHealthOrganizationNews@who.int) to journalists dated July 9, 2011.

<sup>5</sup> Pg. 22991 in FDA. Statement of Policy: Foods Derived From New Plant Varieties, May 29, 1992, Federal Register vol. 57, No. 104. At: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/Biotechnology/ucm096095.htm>

<sup>6</sup> At: <http://www.fda.gov/Food/Biotechnology/Submissions/ucm161107.htm>

the safety of this crop; it only states what the company believes. The letters for all 84 “safety consultations” done since the Flavr Savr tomato contain basically the same language. This clearly shows that the FDA does not conduct safety assessments.

Other scientists have noted the lack of proper safety testing. For example, Dr. Belinda Martineau, the scientist who conducted the safety studies on the first GE plant, the Flavr Savr tomato (engineered for long shelf life) at Calgene, points out in her book **First Fruit: the Creation of the Flavr Savr Tomato and the Birth of Biotech Foods**: “Rather than personal opinion, the scientific community should give the public facts, hard facts; the results of studies that indicate these foods are safe to eat and that growing them on a large scale will not cause environmental damage. Scientists and regulators throughout the ag biotech industry agree that more public education about genetic engineering research is necessary, but, thus far, few have provided much information beyond how the technology works and the wondrous things that might be done with it. . . . *And simply proclaiming that ‘these foods are safe and there is no scientific evidence to the contrary’ is not the same as saying ‘extensive tests have been conducted and here are the results.’ In fact, without further elaboration, ‘no scientific evidence to the contrary’ could be construed as ‘no scientific evidence, period.’*”<sup>7</sup> italics added.

Since the 1992 Statement of Policy on genetically engineered food, FDA has admitted that its original policy was based on a false notion. In 2001, the FDA proposed requiring companies to notify the government at least 120 days before commercializing a transgenic plant variety. As part of that proposed rule, the FDA admits that insertional mutagenesis is a problem and suggests requiring data on each separate transformation event: “[B]ecause some rDNA-induced unintended changes are specific to a transformational event (e.g. those resulting from insertional mutagenesis), FDA believes that it needs to be provided with information about foods from all separate transformational events, even when the agency has been provided with information about foods from rDNA-modified plants with the same intended trait and has had no questions about such foods. *In contrast, the agency does not believe that it needs to receive information about foods from plants derived through narrow crosses [e.g. traditional breeding]*” italics added (FR 66(12), pg. 4711).<sup>8</sup> In other words, FDA has admitted that there is a difference between GE and traditional breeding. In spite of this, FDA is still following the 1992 policy rather than the 2001 policy.

Global agreement has been reached on what constitutes proper safety assessment of foods derived from GE plants, yet such suggested studies have not been carried out on GE Bt corn (or any other GE crop approved in the US). In 2003, the Codex Alimentarius *Ad Hoc* Task Force on Foods Derived from Biotechnology reached agreement on a “Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants.”<sup>9</sup> This Guideline was formally adopted by the full Codex Alimentarius Commission in 2003, and was updated in 2008. This is important because in the case of trade disputes, the World Trade Organization considers

<sup>7</sup> Pp. 232-233 in Martineau, B. 2001. *First Fruit*. McGraw-Hill.

<sup>8</sup> Pg. 4711 in FDA. Premarket Notice Concerning Bioengineered Foods. Federal Register January 18, 2001. Federal Register Vol. 51(12): pp. 4706 – 4738. At:

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/Biotechnology/ucm096149.htm>

<sup>9</sup> See Codex Alimentarius Guideline 45. At: [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

that, in terms of food safety, the standards or guidelines of Codex Alimentarius are deemed the global science-based standard and, thus, immune to trade challenges, i.e. they are not considered to be a “non-tariff trade barrier.” At present, none of the GE plants on sale in the US can meet this standard.

Since the US does not require safety assessments of GE plants, while the Codex Alimentarius Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants states that such a food safety assessment should be done, this means the US cannot meet the global standards for safety assessment of GE foods. Consequently, countries that require food safety assessments for GE foods could block shipments of such GE foods from the US without fear of losing a WTO challenge.

We believe that the US should require safety assessments on foods derived from GE organisms, and that those safety assessments should be consistent with the guidelines developed by the Codex Alimentarius *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology so that US food products are not potentially subject to a WTO challenge from another country.

2. **Significant scientific uncertainty exists in the risk analysis of foods derived from GE and this is recognized in the Codex.** In fact, the Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants has a whole section on unintended effects which clearly states that they can have an unintended effect on human health: “*Unintended effects due to genetic modification may be subdivided into two groups: those that are “predictable” and those that are “unexpected” . . . A variety of data and information are necessary to assess unintended effects because no individual test can detect all possible unintended effects or identify, with certainty, those relevant to human health.*”<sup>10</sup> italics added (paras 16 and 17, CAG/GL 45-2003). Furthermore, this section recognizes that the unintended effects could also be caused by changes in genes that are expressed at the molecular level and how the gene products are processed: “Molecular biological and biochemical techniques (that) can also be used to analyze potential changes at the level of gene transcription and message translation that could lead to unintended effects” (para 16, CAG/GL 45-2003).
3. **Labeling of GE food can serve as a risk management measure to deal with scientific uncertainty.** This would be consistent with the recommendations developed by the Codex Alimentarius Ad Hoc Intergovernmental Task Force on Foods Derived from Modern Biotechnology and adopted by the Codex Alimentarius Commission in 2003. The *Principles for the Risk Analysis of Foods Derived from Modern Biotechnology* (CAC/GL 44—2003) clearly state that labeling can be used as a risk management option to deal with scientific uncertainties associated with the risk assessment of GE foods: “18. Risk managers should take into account the uncertainties in the risk assessment and implement appropriate measures to manage these uncertainties. 19. Risk management

<sup>10</sup> pars 18, 19 in CAC/GL 44—2003. At: [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

measures may include, as appropriate, food labeling, conditions for market approval and post-market monitoring.”<sup>11</sup>

If there are unexpected adverse health effects that happen as a result of GE, then labeling could serve as a risk management mechanism that would allow us to track such health problems if they arose. If a food with GE ingredients is not labeled as such, and that food causes an adverse health effect, such as an allergic reaction, there would be virtually no way to determine that the GE process was linked to the adverse health effect. For example, suppose a company decides to insert a synthetic gene, which codes for a modified protein, into tomatoes. Suppose that the novel protein causes a strong but delayed (say by 24 hours) allergic reaction (e.g. serious rash, upset stomach, or anaphylactic shock) in some relatively small subset of the population. To start with, doctors would have an extremely difficult time identifying the source of the problem. If the offending tomato variety is not very prevalent (i.e. does not have a large market share), then the regular allergy test, making a list of all foods eaten in the last 24 hours, might not uncover the tomato as the source of the problem (the person would have to obtain and eat the offending tomato variety a second time and get the same reaction). It might well take large numbers of people being adversely affected and having the offending tomato variety be a large share of the market before there would be any hope of figuring out what was causing the problem.

Even if the food *has* undergone rigorous premarket safety testing, scientific uncertainties remain associated with the risk analysis. In addition, when a large population (in the millions or tens of millions) is exposed to a GE food, rare unexpected health problems can appear. Take the case of Vioxx, a drug that was found to be safe in premarket testing but had to be removed from the market after adverse health effects were seen when the drug was used by large numbers of people. Because these drugs are labeled, doctors are able to associate the unexpected health problem with the specific drugs. With GE foods, labeling would serve a similar purpose.

In addition to FDA not requiring any premarket safety testing, there is virtually no independent safety testing of these crops in the US due to intellectual property rights. When farmers buy GE seed in the US, they invariably must sign a product stewardship agreement which forbids them from giving such seeds to researchers.<sup>12</sup> In addition, researchers must get permission from the biotech companies before they can do research, which means there is a paucity of independent research. Scientists have even been threatened with legal action if they revealed information obtained via freedom-of-information.<sup>13</sup> In early 2009 26 public sector scientists in the US took the unprecedented step of writing to the US Environmental Protection Agency (EPA) protesting that “as a result of restricted access, no truly independent research can be legally conducted on many critical questions regarding the technology.”<sup>14</sup> As a result, the editors of *Scientific American* published a perspective stating that “we also believe food safety and environmental protection depend on making plant products available to regular scientific scrutiny. Agricultural technology companies should therefore immediately remove the restriction

<sup>11</sup> At: [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

<sup>12</sup> Waltz, E. 2009. Under wraps. *Nature Biotechnology*, 27(10): 880-882. At: [http://www.emilywaltz.com/Biotech\\_crop\\_research\\_restrictions\\_Oct\\_2009.pdf](http://www.emilywaltz.com/Biotech_crop_research_restrictions_Oct_2009.pdf)

<sup>13</sup> IBID

<sup>14</sup> <http://www.scientificamerican.com/article.cfm?id=do-seed-companies-control-gm-crop-research>

on research from their end-user agreements.” We concur and believe that only truly independent safety tests will give us an answer about the safety of GE foods. In the meantime, it’s crucial that GE foods be labeled as a risk management measure to deal with scientific uncertainty.

4. **We believe that consumers have a right to know what is in the food they eat.** A number of polls from 1995 to 2011 have found that between 70% and 95% of people polled supported mandatory labeling.<sup>15</sup> “Information of material importance” to consumers is far broader than just “changes in the organoleptic, nutritional or functional properties” of a food. The fact that more than 850,000 people have sent comments to the FDA in support of a citizen’s petition asking FDA to require labeling of GE foods, shows that consumers overwhelmingly want food from GE sources to be labeled as such.<sup>16</sup> In addition, on March 12, 2012, US Senator Barbara Boxer and Congressman Peter DeFazio joined with 53 other Senate and House lawmakers in sending a letter urging the FDA to require the labeling of GE foods.<sup>17</sup>

FDA has tried to argue that they don’t have the authority to label GE foods unless there is a “material change” in the food, which FDA defines as “change in the organoleptic, nutritional or functional properties” of the food that is not obvious to the consumer at the point of purchase. We strongly disagree with FDA and feel that they are trying to ignore their own history. In the past FDA has required labeling under the “material fact” analysis that did not entail a change in nutritional value, organoleptic properties, or functional characteristics of a food. FDA’s authority to require labeling of all foods derives, in part from section 201(n) and 403(a)(1) of the Federal Food Drug and Cosmetic Act. A label is considered “misleading” if it “fails to reveal facts that are **material** in light of representations made. . .” **bold added.** FDA articulated this position in the 1986 final rule that required labeling of irradiated foods, even though the FDA had ruled that irradiated foods were safe. FDA stated in this final rule on food irradiation that the large number of respondents who asked for labeling of retail products was one factor indicative of the materiality of food irradiation: “*Whether information is material under section 201(n) of the act depends not on the abstract worth of the information but on whether consumers view such information as important and whether the omission of label information may mislead a consumer. The large number of consumer comments requesting retail labeling attest to the significance placed on such labeling by consumers*”<sup>18</sup> **emphasis added.** **Thus, materiality clearly does not always include “some change in nutritional value, organoleptic properties, or functional characteristics” of the food.**

Material facts other than material changes have long been required for other reasons that are important to consumers. Labeling the source of protein hydrolysates was required because of the concern of vegetarians and observant Jews and Muslims. As the FDA stated, “the food source of a protein hydrolysate is information of material importance for a person who desires to avoid certain foods for religious or cultural reasons.”<sup>19</sup> Thus, “information of material

<sup>15</sup> <http://gefoodlabels.org/gmo-labeling/polls-on-gmo-labeling/>

<sup>16</sup> <http://gefoodlabels.org/>

<sup>17</sup> IBID

<sup>18</sup> Pg. 13380. FDA. Final Rule on Food Irradiation. Federal Register April 18, 1986, Federal Register, Vol. 51, pg. 13376

<sup>19</sup> 56 FR 28592 [1991]

importance” to a consumer is not simply restricted to “information about the characteristics of a food.”

In 2007, FDA proposed a revision to their labeling requirements for irradiated foods, such that labeling would only be required on those irradiated foods in which the irradiation has lead to a “material change”—defined as a “change in the organoleptic, nutritional or functional properties”—in the food that is not obvious to the consumer at the point of purchase. Thus, not all irradiated food would be required to be labeled. This proposed revision to the irradiation labeling standard went nowhere. However, this attempted weakening of the food irradiation labeling standard clearly demonstrates that FDA is now trying to narrow the concept of “materiality,” so as to avoid the labeling of GE foods.

A number of recent scientific studies have pointed out unexpected effects in genetically engineered crops and have shown that they can lead to potential adverse health effects:

- **GE plant materials are finding their way into the human body.** A study done by Canadian scientists and published last year was very disturbing. The study involved 30 pregnant and 39 non-pregnant women in Quebec, Canada.<sup>20</sup> Blood was taken from women and from fetal cord blood and tested for 3 pesticides associated with GM: glyphosate, glufosinate, and Cry1Ab. The surprising finding was that Cry1Ab was detected in 93% and 80% of maternal and fetal blood samples, respectively and in 69% of tested blood samples from nonpregnant women. The scientists noted that “trace amounts of the Cry1Ab toxin were detected in the gastrointestinal contents of livestock fed on GM corn, raising concerns about this toxin in insect-resistant GM crops; [suggesting] (1) that these toxins may not be effectively eliminated in humans and (2) there may be a high risk of exposure through consumption of contaminated meat.”<sup>21</sup> They concluded, “To our knowledge, this is the first study to highlight the presence of pesticides-associated genetically modified foods in maternal, fetal and nonpregnant women’s blood. 3-MPPA and Cry1Ab toxins are clearly detectable and appear to cross the placenta to the fetus. Given the potential toxicity of these environmental pollutants and the fragility of the fetus, more studies are needed, particularly those using the placental transfer approach.”<sup>22</sup>
- **A major food safety concern for GE plants is allergenicity.** In 2001, the report of a Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation on Allergenicity of Foods Derived from Biotechnology, held at WHO headquarters in Rome, laid out a detailed protocol (a decision tree) for evaluating the allergenicity of GE foods.<sup>23</sup> None of the GE

<sup>20</sup> Aris, A and S Leblanc. 2011. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology*, 31(4): 528-533.

<sup>21</sup> Pg. 533 in Aris, A and S Leblanc. 2011. Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology*, 31(4): 528-533.

<sup>22</sup> IBID

<sup>23</sup> FAO/WHO. 2001. Evaluation of Allergenicity of Genetically Modified Foods. Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, January 22-25, 2001. Rome, Italy. At: <http://ftp.fao.org/es/esn/food/allergygm.pdf>

crops, including GE corn, on the market in the U.S. have been assessed using such a protocol.

- **Various types of scientific evidence suggest that Bt corn may contain a transgenic allergen.** Bt corn contains various modified endotoxins from the soil bacterium *Bacillus thuringiensis* (Bt). These  $\delta$ -endotoxins are called Cry proteins, in particular Cry1Ab or Cry1Ac. A study of farmworkers who worked in onion fields where foliar Bt sprays were used found that 2 of them contained antibodies to the  $\delta$ -endotoxins, Cry1Ab and/or Cry1Ac, consistent with an allergy.<sup>24</sup> A survey of Bt cotton farmers in India done by local doctors found that numerous Bt cotton farmers, as well as workers in a ginning factory, had symptoms consistent with an allergic reaction to Bt cotton within a year of the introduction of Bt cotton in the region.<sup>25</sup>
- **One of the endotoxins found in GE corn, Cry1Ac, has been found to have sequence similarity to a known human allergen.** One of the first steps in assessing the allergic potential of a protein (most allergens are proteins) is to determine if it has similarity in amino acid sequence to a known allergen. A paper published in 1998 by the head of FDA's own biotechnology studies branch, Dr. Steven Gendel, found significant amino acid sequence similarity between Cry1Ab and Cry1Ac (found in Bt maize and Bt cotton) and vitellogenin, the main precursor to egg yolk protein and a known allergen, as well as between Cry3A (Bt potatoes) and  $\beta$ -lactoglobulin, a major milk allergen.<sup>26</sup>
- **Scientific studies also show Cry1Ac has a strong effect on the immune system as well as being a potent adjuvant.** A series of five studies carried out by a team of scientists from two Mexican universities and from Cuba have suggested that the Cry1Ac protein has immunogenic and allergenic properties. A mouse study demonstrated that the Cry1Ac was a potent systemic and mucosal adjuvant: "We conclude that Cry1Ac is a mucosal and systemic adjuvant as potent as CT [cholera toxin] which enhances mostly serum and intestinal IgG antibody responses".<sup>27</sup> Another mouse study which further characterized the mucosal and systemic immune response induced in mice "confirm[ed] that the Cry1Ac protoxin is a potent immunogen able to induce a specific immune response in the mucosal tissue, which has not been observed in response to most other proteins"

<sup>24</sup> Bernstein, I.L., Bernstein, J.A., Miller, M., Tierzieva, S., Bernstein, D.I., Lummus, Z., Selgrade, M.K., Doerfler, D.L. and V.L. Seligy. 1999. Immune responses in farm workers after exposure to *Bacillus thuringiensis* pesticides. *Environmental Health Perspectives*, 107(7): 575-582. At:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1566654/pdf/envhper00512-0103.pdf>

<sup>25</sup> Gupta, A. et al. 2006. Impact of Bt cotton on farmers' health (in Barwani and Dhar District of Madhya Pradesh). At: <http://www.lobbywatch.org/archive2.asp?arcid=6265> and <http://www.lobbywatch.org/archive2.asp?arcid=6266>

<sup>26</sup> Gendel, S.M. 1998. The use of amino acid sequence alignments to assess potential allergenicity of proteins used in genetically modified foods. *Advances in Food and Nutrition Research*, 42: 44-61.

<sup>27</sup> Vazquez-Padron, R.I., Moreno-Fierros, L., Neri-Bazan, L., de la Riva, G.A. and R. Lopez-Revilla. 1999. *Bacillus thuringiensis* Cry1Ac protoxin is a potent systemic and mucosal adjuvant. *Scandinavian Journal of Immunology* 49: 578-584.



italics added.<sup>28</sup> Another study concluded, “We think that previous to commercialization of food elaborated with self-insecticide transgenic plants it is necessary to perform toxicological tests to demonstrate the safety of Cry1A proteins for the mucosal tissue and for the immunological system of animals.”<sup>29</sup> Such tests have never been carried out on GE Bt-corn.

- Corn allergen gene turned on as result of genetic engineering.** A carefully designed study involved growing Monsanto’s Bt corn varieties, MON 810, in a growth chamber along with its near isoline (corn variety engineered to produce MON 810). Since MON 810 and its near isoline are grown in the same environment, the only difference in the plants will be due to the effect of genetic engineering. This was a proteomic study, which is a study of the expressed proteins, not just of the protein(s) expressed as a result of genetic engineering. Proteomic studies are a good way to detect unintended effects associated with genetic engineering, particularly the disruptive effects due to the random insertion of a transgene. The study found that 43 proteins in the MON 810 plants were significantly disrupted, compared to the non-GE near isoline. As the study notes, “a newly expressed spot (SSP 6711) corresponding to a 50 kDa gamma zein, a well-known corn allergenic protein, has been detected. Moreover, as a major concern, a number of seed storage proteins (such as globulins and vicilin-like embryo storage proteins) exhibited truncated forms having molecular masses significantly lower than the native ones.”<sup>30</sup> The safety implications of the truncated seed storage proteins are unknown, as no feeding study was done. So, this study demonstrates that the process of genetic engineering turned on a known corn allergen gene that is normally turned off as well as caused changes to the main proteins found in the seed.
- Bt corn may cause adverse effects on gut and peripheral immune response.** A carefully designed study (MON 810 and near isoline grown simultaneously in neighboring fields in Landriano, Italy, to control for environmental effects) done by Italian scientists involved feeding a diet containing MON 810 or its near isoline to mice in vulnerable conditions, e.g. weaning and old mice, and looking at a variety of measures of the gut and peripheral immune response. The main finding was that “compared to the control maize, MON810 maize induced alterations in the percentage of T and B cells and of CD4+, CD8+,  $\gamma\delta$ T, and  $\alpha\beta$ T subpopulations of weaning and old mice fed for 30 or 90 days, respectively, at the gut and peripheral sites. An increase of serum IL-6, IL-13, IL-12p70, and MIP-1 $\beta$

<sup>28</sup> Pg. 147 in Vazquez-Padron, R.I., Moreno-Fierros, L., Neri-Bazan, L., Martinez-Gil, A.F., de-la-Riva, G.A., and R. Lopez-Revilla. 2000a. Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from *Bacillus thuringiensis* HD 73 in mice. *Brazilian Journal of Medical and Biological Research* 33: 147-155.

<sup>29</sup> Pg. 58 in Vazquez-Padron, R.I., Moreno-Fierros, L., Neri-Bazan, L., Martinez-Gil, A.F., de-la-Riva, G.A., and R. Lopez-Revilla. 2000a. Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from *Bacillus thuringiensis* HD 73 in mice. *Brazilian Journal of Medical and Biological Research* 33: 147-155.

<sup>30</sup> Pg. 1855 in Zolla, L., Rinalducci, S., Antonioli, P 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. *Journal of Proteome Research*, 7: 1850-1861. At: [http://stopogm.net/webfm\\_send/288](http://stopogm.net/webfm_send/288)

after MON810 feeding was also found. **These results suggest the importance of the gut and peripheral immune response to GM crop ingestion as well as the age of the consumer in the GMO safety evaluation” bold added.**<sup>31</sup>

- **A meta-analysis of feeding studies involving GE crops suggests health problems and that longer term studies are needed.** A carefully designed meta-analysis was done of 19 published studies involving mammals fed GE corn or soy.<sup>32</sup> The meta-analysis also included the raw data from a number of 90-day-long feeding studies that were obtained as a result of court action or official requests. The data included biochemical blood and urine parameters of mammals eating GE crops with numerous organ weights and histopathology findings. The meta-analysis of all the *in vivo* studies found that the majority of statistically significant results came from parameters involving the liver or kidney. The authors conclude that longer-duration tests are needed, noting that “90-day-long tests are insufficient to evaluate chronic toxicity, and the signs highlighted in the kidneys and livers could be the onset of chronic diseases. However, no minimal length for the tests is yet obligatory for any of the GMOs cultivated on a large scale, and this is socially unacceptable in terms of consumer health protection. We are suggesting that the studies should be improved and prolonged, as well as being made compulsory, and that the sexual hormones should be assessed too, and moreover, reproductive and multigenerational studies ought to be conducted too.”<sup>33</sup>
- **A 2005 animal study on transgenic peas found that the genetic engineering process unexpectedly turned a protein that is relatively “safe” into one that causes adverse health effects and increased the potential for adverse effects in other proteins.**<sup>34</sup> A group of Australian scientists looked at the transfer of a gene from beans into peas. The gene codes for a protein, a-amylase inhibitor (aAI), that confers resistance to certain weevil pests. The aAI in raw beans inhibits the action of amylase, an enzyme that degrades starch. So aAI in raw beans can cause gastrointestinal problems in humans. When beans are cooked, the aAI is easily digested and causes no problems. However, when the gene for aAI was inserted into peas, the resultant protein had the same amino acid sequence as the bean aAI, yet the structure of the protein had been subtly altered (through a process called post-translational processing), causing an immunological reaction in mice fed the transgenic peas, but not in mice fed normal beans. The

<sup>31</sup> Pg. 11533 in Finamore, A., Roselli, M., Britti, S., Monastera, G., Ambra, R., Turrini, A. and E. Mengheri. 2008. Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. *Journal of Agriculture and Food Chemistry*, 56: 11533-11539. At:

[http://www.gioannimonastera.info/documenti\\_pdf/Monastera\\_J\\_Agr\\_Food\\_Chem\\_2.pdf](http://www.gioannimonastera.info/documenti_pdf/Monastera_J_Agr_Food_Chem_2.pdf)

<sup>32</sup> Séralini, G-E, Mesnage, R., Clair, E., Gress, S., de Vendômois, JS and D. Cellier. Genetically modified crops safety assessments: present limits and possible improvements. *Environmental Sciences Europe*, 23: 10. At: <http://www.enveurope.com/content/pdf/2190-4715-23-10.pdf>

<sup>33</sup> Pg. 1 in IBID

<sup>34</sup> Prescott, VE, Campbell, PM, Moore, A, Mattes, J, Rothenberg, ME, Foster, PS, Higgins, TJV and SP Hogan. 2005. Transgenic expression of bean  $\alpha$ -amylase inhibitor in peas results in altered structure and immunogenicity. *Journal of Agricultural and Food Chemistry*, 53: 9023-9030.

adverse/immunological reaction to the transgenic pea aAI was not mitigated by boiling the peas. The mice fed transgenic peas, in addition to developing an immunological reaction to the pea aAI, also developed an immunological reaction to a number of proteins normally found in peas; mice fed these same proteins from non-engineered peas developed a far smaller immunological response, thus demonstrating that the transgenic pea aAI acts as an adjuvant to increase the immunogenicity of native pea proteins.

This new study involving aAI is extremely important. This study found that moving the same gene between two relatively closely related plants (common beans and peas) can result in a protein that, although it contains the exact same amino acid sequence, is relatively safe in the donor plant (common beans), but is potentially harmful in the recipient plant (peas) and can increase the potential hazardousness of other proteins found in peas. These are all clearly unintended and unexpected effects that clearly result in an adverse health effect.

- **New data confirm unintended and unexpected effect from genetic engineering.** Other studies in the last 5 years have found all sorts of unexpected changes/effects in GE crops. A detailed molecular characterization of various GE crops (three different Bt maizes, an herbicide-tolerant maize, RoundUp Ready soybean, and a male-sterile canola) currently on the market, done in Belgium, has shown that of the transgenic lines looked at, all but one were found to have differences in the molecular characterization in products on the market compared to the original structure reported by the company.<sup>35</sup> Except for the canola, all these reports found that the structure (e.g. molecular characterization) of transgenic inserts as reported by the companies in their initial submission were different than the structure found in subsequent studies. The differences in structure involved rearranged inserts, partial copies of genes inserted, multiple copies of transgenes inserted, scrambling of DNA near the border of the transgenic inserts, etc., suggesting that the transgenic lines are unstable and/or more likely to result in unintended effects. In fact, in virtually all the cases, the SBB/IPH recommends that further analysis “should be done to determine the presence of chimaeric open reading frames in the border integration sequences”, e.g. an analysis should be done to see if there are any unexpected proteins being produced.
- **A paper reviewing the food safety issues associated with genetically engineered crops listed a range of documented unintended effects and concluded that** “The development and validation of new profiling methods such

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<sup>35</sup> Dr. Moens, with the Service of Biosafety and Biotechnology (SBB) of the Scientific Institute of Public Health (IPH), a government agency reported on the molecular characterization of the genetic map for six transgenic crops: 3 different Bt maizes—Bt 176, Syngenta ([www.biosafety.be/TP/MGC\\_reports/Report\\_Bt176.pdf](http://www.biosafety.be/TP/MGC_reports/Report_Bt176.pdf)); MON 810, Monsanto ([www.biosafety.be/TP/MGC\\_reports/Report\\_MON810.pdf](http://www.biosafety.be/TP/MGC_reports/Report_MON810.pdf)); Bt11, NorthrupKing ([www.biosafety.be/TP/MGC\\_reports/Report\\_Bt11.pdf](http://www.biosafety.be/TP/MGC_reports/Report_Bt11.pdf))—a herbicide tolerant maize (LibertyLink maize, Bayer)([www.biosafety.be/TP/MGC\\_reports/Report\\_T25.pdf](http://www.biosafety.be/TP/MGC_reports/Report_T25.pdf)), glyphosate tolerant soybeans (RoundUp Ready soybeans, Monsanto) ([www.biosafety.be/TP/MGC\\_reports/Report\\_MON810.pdf](http://www.biosafety.be/TP/MGC_reports/Report_MON810.pdf)), and a canola engineered for male sterility (Ms8 x Rf3, Bayer Cropscience)

as DNA microarray technology, proteomics, and metabolomics for the identification and characterization of unintended effects, which may occur as a result of the genetic modification, is recommended.”<sup>36</sup>

- **An Annex to the Codex Plant Guideline on the assessment of possible allergenicity states that no definitive test exists to accurately predict allergenicity of a given protein:** “At present, there is no definitive test that can be relied upon to predict allergic response in humans to a newly expressed protein.”<sup>37</sup> So there is scientific uncertainty around assessment of potential allergenicity of foods derived from GE/GM. Furthermore, a study done by Dutch scientists, using a modified, and more conservative, methodology for screening transgenic proteins for potential allergenicity (e.g. the analysis of sequence homology to known food and environmental allergens) as laid out in the Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology (January, 2001), found that a number of transgenic proteins have significant sequence homology to known allergens and recommended further study for a number of these proteins: “Many transgenic proteins have identical stretches of six or seven amino acids in common with allergenic proteins. Most identical stretches are likely to be false positives. As shown in this study, identical stretches can be further screened for relevance by comparison with linear IgE-binding epitopes described in the literature. In the absence of literature values on epitopes, antigenicity prediction by computer aids to select potential antibody binding sites that will need verification of IgE binding by sera tests. **Finally, the positive outcomes of this approach warrant** [papaya ringspot virus coat protein, acetolactate synthase GH50, and glyphosate oxidoreductase] **further clinical testing for potential allergenicity**”<sup>38</sup> - bold added. Another study done by Dr. Steven Gendel of the US Food and Drug Administration found that there was significant sequence similarity between a gene in Bt maize and Bt cotton (e.g. Cry1Ab or Cry1Ac) and an egg yolk allergen and recommended further study: “the similarity between Cry1A(b) and vitellogenin might be sufficient to warrant additional evaluation.”<sup>39</sup>

While science demonstrates the need to track potential health impacts of genetically engineered food, there is also broad support for labeling genetically engineered food as indicated by the following endorsements by the public health, nursing, medical and healthcare communities:

- In 2001, the American Public Health Association passed a resolution entitled Support of the Labeling of Genetically Modified Foods which “Resolves that APHA declare its

<sup>36</sup> Pg. 503 in Kuiper, HA, Kleter, GA, Notebom, HPJM and EJ Kok. 2001. Assessment of food safety issues related to genetically modified foods. *The Plant Journal*, 27(6): 503-528.

<sup>37</sup> para 2, Annex, CAG/GL 45-2003. At: : [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

<sup>38</sup> Pg. 1 in: Kleter, GA and ACM Peijnenburg. 2002. Screening of transgenic proteins expressed in transgenic food crops for the presence of short amino acid sequences identical to potential, IgE – binding linear epitopes of allergens. *BMC Structural Biology*, 2:8. Accessed at <http://www.biomedcentral.com/1472-6807/2/8>

<sup>39</sup> Pg. 44 in Gendel, S.M. 1998. The use of amino acid sequence alignments to assess potential allergenicity of proteins used in genetically modified foods. *Advances in Food and Nutrition Research*, 42: 44-61.

support that any food product containing genetically modified organisms be so labeled.”<sup>40</sup>

- In 2008, the American Nurses Association adopted a resolution on Healthy Food in Health Care, which specifically, “Supports the public’s right to know through support of appropriate food labeling including country-of-origin and genetic modification...”<sup>41</sup>
- In 2011, the Illinois Public Health Association adopted a resolution supporting “legislation and/or regulations that require clearly labeling food with genetically engineered ingredients.”<sup>42</sup>
- Catholic Healthcare West (a network of 41 hospitals and 10,000 physicians) avoids genetically engineered food and advocates for public policies that include the labeling of genetically engineered food.<sup>43</sup>

Furthermore, twenty state legislatures have introduced bills to require mandatory labeling of GE foods. (IL, AK, CA, NC, IA, MD, NY, OR, RI, WV, VT, TN, HI, CT, MA, MO, NJ, WA, MI, NH).

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<sup>40</sup> American Public Health Association Policy Statement Database. “Support of the Labeling of Genetically Modified Foods.” Available from: <http://www.apha.org/advocacy/policy/policysearch/default.htm?id=250>

<sup>41</sup> House of Delegates Resolution: “Healthy food in health care.” Silver Spring, MD: American Nurses Association. 2008. Available from:

<http://www.nursingworld.org/MemberCenterCategories/ANAGovernance/HODArchives/2008HOD/ActionsAdopted/HealthyFoodinHealthCare.aspx>

<sup>42</sup> At: [http://www.ipha.com/Public/ContentArticle.aspx?type=Policy\\_Resolution](http://www.ipha.com/Public/ContentArticle.aspx?type=Policy_Resolution)

<sup>43</sup> Catholic Healthcare West. “Catholic Healthcare West Presses Suppliers to Prohibit Animal Cloning and Genetically Engineered Foods.” Available from:

[http://www.chwhealth.org/stellent/groups/public/@xinternet\\_con\\_sys/documents/webcontent/194274.pdf](http://www.chwhealth.org/stellent/groups/public/@xinternet_con_sys/documents/webcontent/194274.pdf)