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# Genetically Modified Plants Used for Food, Risk Assessment and Uncertainty Principles: Does the Transition from Ignorance to Indeterminacy Trigger the Need for Post-Market Surveillance?

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# ARTICLE

## GENETICALLY MODIFIED PLANTS USED FOR FOOD, RISK ASSESSMENT AND UNCERTAINTY PRINCIPLES: DOES THE TRANSITION FROM IGNORANCE TO INDETERMINACY TRIGGER THE NEED FOR POST- MARKET SURVEILLANCE?

KATHARINE A. VAN TASSEL\*

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## I. INTRODUCTION

Most consumers in the United States are unaware of their high daily and long-term exposure levels to novel and untested genetically modified substances. This exposure occurs through a heavy consumption of genetically modified plant food (“GM food”).<sup>1</sup> Consumers are not aware that they are eating large amounts of GM plant food as GM ingredients are not listed on food labels. Labeling of GM ingredients on food packaging is not required by the Food & Drug Administration (“FDA”) because genetically modified plant food is presumed by FDA regulations to be bioequivalent to traditional plant food. This means that GM plant food is regulated by the FDA in the same way as traditional plant food. Thus, manufacturers of GM plant food are not required to test their products for safety for human consumption, are not required to obtain premarket approval from the FDA and are not required to list GM ingredients on product labels.

The FDA’s regulatory presumption of bioequivalence is based on the now dated Central Dogma of molecular biology. The Central Dogma views genes as discrete packets of information arranged like beads strung on a thread of DNA<sup>2</sup> and states that “each gene in living organisms, from humans to bacteria, carries the information needed to construct one protein.”<sup>3</sup> According to the Central Dogma, a gene is a static stretch of genetic code that acts like a blueprint, or a complete set of instructions, on how to build a protein.<sup>4</sup> Based

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<sup>1</sup> See *infra* notes 14-26 and accompanying text. “GM food” has also been referred to in the literature as genetically modified food, biotech food, transgenic food and, pejoratively, as Frankenfood. For the purposes of this Article, all of these terms will be used synonymously. Though the majority of the same issues exist, this Article discusses the FDA’s regulation of GM plant food and does not discuss the FDA’s regulations of GM animals coming soon to a plate near you.

<sup>2</sup> Mark B. Gerstein et al., *What Is a Gene Post ENCODE? History and Updated Definition*, 17 GENOME RESEARCH 669, 679 (2007).

<sup>3</sup> Denise Caruso, *A Challenge to Gene Theory, a Tougher Look at Biotech*, N.Y. TIMES, July 1, 2007, at 3, available at <http://select.nytimes.com/mem/tnt.html?tntget=2007/07/01/business/yourmoney/01frame.html>; Gerstein et al., *supra* note 2, at 670-71.

<sup>4</sup> Gerstein et al., *supra* note 2, at 670-71.

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on this model, scientists have presumed that a gene from any organism can be precisely excised and neatly, predictably and safely moved into another organism.<sup>5</sup>

Directly contrary to the Central Dogma, in the past year numerous scientific discoveries involving the network effects of junk DNA, hybrid mRNA, SNPs and epigenetics have created a new model of a Networked Gene. Instead of viewing DNA as just a string of biological code, scientists have a new understanding that DNA is a highly complex operating system where a gene which expresses itself one way in a donor organism may not express itself the same way when dropped into an entirely different organism with its own complex operating system. In other words, scientists now know that genes operate in a highly contextual way, engaging in intricate biochemical cross-talk. Consequently, changing the context in which a gene operates can change the way the gene works. And changing how even one gene works can have a 'butterfly effect' on the entire organism. Critically, epigenetics and epigenetic inheritance explain that these unintended consequences can be passed on to future generations and may not manifest themselves until triggered by external environmental factors.

In the context of GM foods, a genetic modification changes the biochemical cross-talk between genes, creating genetic material that has never existed before in nature. This novel genetic material can create unintended health risks, as seen with the case of the GM peas that contained a novel and unexpected allergenic protein and primed test mice to react to other allergens.<sup>6</sup> The bottom line is that the scientific acceptance of the existence of the networked gene establishes that the FDA's presumption that GM plant food is bioequivalent to traditional plant food is no longer scientifically supportable and that a new system for GM plant food regulation is required.

This Article discusses the public health, regulatory, legal and ethical issues raised by the new understanding of the networked gene and is arranged as follows. Part I is this Introduction. Part II outlines the prevalence of GM products in the U.S. food supply and explains why the U.S. consumer has come to have both very high daily and long-term exposure levels to novel and untested GM substances. Part III describes the explosion in new studies that reveal that, directly contrary to the dated Central Dogma model, genes operate in a highly contextual fashion. This Article explains how changing the context in which a gene operates can change the way the gene works and why these unintended consequences can have current and intergenerational health effects. Part IV describes the scientific and regulatory assumptions made by the FDA in formulating its current policy regarding GM ingredient safety and labeling and unravels the regulatory provisions that reflect these policy choices. This section spells out why the new Networked Gene model both challenges the health risk assumptions made by the FDA in formulating its regulatory

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<sup>5</sup> *Id.*

<sup>6</sup> *See infra* notes 72-77 and accompanying text.

structure and throws a deep shadow of doubt over the ability of the FDA's current regulations to protect public health. Part V points out that the lack of transparency in the FDA's regulatory framework bars a consumer's ability to choose to avoid the unknown additional health risks associated with heavy exposure to GM substances, while the insensitivity of the tort system to injuries from innovative technologies means that an injury from a GM food product will be borne by the consumer and not the manufacturers who are reaping the profit from product sales. Part VI proposes an alternative method of regulating GM plant foods that protects public health while encouraging technical innovation.

## II. GM FOOD: EXPOSURE, BENEFITS AND RISKS

For hundreds of years, traditional breeding techniques have been used to add resistance to disease, enhance nutritional value and increase production yields of plants used for food.<sup>7</sup> However, traditional techniques are limited to transferring genetic material between the same species, or a closely related species or genera: for example, between a wild variety of a plant and its modern crop variety.<sup>8</sup> With the development of recombinant genetic technologies, genetic information can be transferred between different genera such as a fish and a tomato<sup>9</sup> or, through a process called gene stacking, between a round worm, a chicken and a pig.<sup>10</sup> Thus, a desirable trait from any source can be added to a plant used for food. Examples of traits that have been genetically engineered into host organisms are the ability to stay fresh longer,<sup>11</sup> to have added nutritional value<sup>12</sup> and to resist pests.<sup>13</sup>

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<sup>7</sup> See Kenneth J. Frey, *An Overview of Crop Improvement: Chairman's Introduction*, in *GENETIC ENGINEERING OF PLANTS: AN AGRICULTURAL PERSPECTIVE 3* (Tsune Kosuge et al. eds., 1983); Michael A. Whittaker, Comment, *Reevaluating the Food and Drug Administration's Stand on Labeling Genetically Engineered Foods*, 35 *SAN DIEGO L. REV.* 1215, 1216 (1998).

<sup>8</sup> Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22,984, 22,986 (May 29, 1992) [hereinafter *Foods Derived from New Plant Varieties*].

<sup>9</sup> The Pew Initiative on Food and Biotechnology, *How Consumers Process Information at the Heart of the Debate Over the Labeling of Genetically Modified Foods*, June 27, 2002, <http://pewagbiotech.org/newsroom/releases/062702.php3> (discussing Calgene's slow rotting Flavor Savr tomato, the first GM product intended for human consumption).

<sup>10</sup> This creates a GM pig which is rich in the omega-3 fatty acids a consumer would normally find in fish. L. Lai et al., *Generation of Cloned Transgenic Pigs Rich In Omega-3 Fatty Acids*, 24 *NATURE BIOTECHNOLOGY* 435-36 (2006).

<sup>11</sup> The Pew Initiative on Food and Biotechnology, *supra* note 9.

<sup>12</sup> COMMITTEE ON GENETICALLY MODIFIED PEST PROTECTED PLANTS, BOARD ON AGRICULTURE AND NATURAL RESOURCES, NATIONAL RESEARCH COUNCIL, *GENETICALLY MODIFIED PEST-PROTECTED PLANTS* (2003), <http://www.nap.edu/openbook/0309069300/html/R1.html> [hereinafter *PEST PROTECTED PLANTS 2003*].

<sup>13</sup> John Charles Kunich, *Mother Frankenstein, Doctor Nature, and the Environmental*

The amount of GM plant food produced and consumed in the United States is growing annually.<sup>14</sup> In spite of this trend, most consumers remain unaware that any part, much less a large part, of their diet is bioengineered.<sup>15</sup> This lack of awareness is the result of the FDA's position that biotech ingredients in food need not be disclosed to consumers.<sup>16</sup>

A. *Exposure Levels*

Consumers' ignorance of their daily exposure to GM food through consumption is startling as approximately seventy percent of the packaged food in supermarkets contains GM substances.<sup>17</sup> An examination of food ingredients, coupled with an understanding of how many of these ingredients are manufactured from GM food, explains this high percentage. Just look at corn. Eighty percent of the corn grown in the United States is GM corn.<sup>18</sup> And, of the 45,000 items in the average grocery store, more than one fourth contain corn.<sup>19</sup> After water, high-fructose corn syrup is the main ingredient in most sodas and fruit drinks.<sup>20</sup>

Read the ingredients on the label of any processed food and, provided you know the chemical names it travels under, corn is what you will find. For modified and unmodified starch, for glucose syrup and maltodextrin, for crystalline fructose and ascorbic acid, for lecithin and dextrose, lactic acid and lysine, for maltose and HFCS, for MSG and polyols, for the caramel color and xanthan gum: read corn. Corn is in the coffee whitener and Cheez Whiz, the frozen yogurt and TV dinner, the canned fruit and ketchup and candies, the soups and shakes and cake mixes, the frosting and gravy and frozen waffles, the syrups and the hot sauces, the

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*Law of Genetic Engineering*, 74 S. CAL. L. REV. 807, 808 (2001).

<sup>14</sup> Biotech crops increased "in 2007 by 5.5 percent over 2006, for a total of 142.5 million acres." BUSINESS WIRE, *Agricultural Biotechnology Continues to Increase Crop Yield and Farmer Income Worldwide While Supporting the Environment*, Feb. 13, 2008, [http://findarticles.com/p/articles/mi\\_m0EIN/is\\_2008\\_Feb\\_13/ai\\_n24260354](http://findarticles.com/p/articles/mi_m0EIN/is_2008_Feb_13/ai_n24260354). See also International Service for the Acquisition of Agri-Biotech Applications, *ISAA Brief 37-2007: Executive Summary, Global Status of Commercialized Biotech/GM Crops: 2007*, available at <http://www.isaaa.org/resources/publications/briefs/37/executivesummary/default.html>.

<sup>15</sup> Katharine A. Van Tassel, *The Introduction of Biotech Foods to the Tort System: Creating a New Duty to Identify*, 72 U. CIN. L. REV. 1645 (2004); The Pew Initiative on Food and Biotechnology, *supra* note 9.

<sup>16</sup> See *infra* notes 122-25.

<sup>17</sup> The Pew Initiative on Food and Biotechnology, *supra* note 9.

<sup>18</sup> NATIONAL AGRICULTURAL STATISTICS SERVICE, AGRICULTURAL STATISTICS BOARD, U.S. DEPARTMENT OF AGRICULTURE, ACREAGE 32 (June 30, 2008), available at <http://www.nass.usda.gov>. In 2008, ninety-two percent of soybeans grown in the U.S. are genetically modified. *Id.*

<sup>19</sup> MICHAEL POLLAN, *THE OMNIVORE'S DILEMMA* 19 (Penguin Books 2006).

<sup>20</sup> *Id.* at 18.

mayonnaise and mustard, the hotdogs and bologna, the margarine and shortening, the salad dressing and the relishes and even the vitamins.<sup>21</sup>

This explains how it happens that many people eat GM food several times a day and just don't know it. And yes, the old adage that 'you are what you eat' is true. "Every day, our bodies take in new atoms from the foods we eat, the liquids we drink and the air we breathe."<sup>22</sup> Ninety-eight percent of our atoms are replaced every year.<sup>23</sup> "Atoms make-up molecules, which make up cells, which make up tissues, which make up organs."<sup>24</sup> So, as the Mayans might say,<sup>25</sup> U.S. consumers are "corn walking."<sup>26</sup> Or, more accurately, GM corn walking.

### B. Benefits

The benefits of each new GM food are varied in their type and ultimate advantages. The benefits of some GM products are modest. For example, the first GM food to be introduced onto the market was a tomato that was genetically modified to add a gene from a cold tolerant fish, a flounder.<sup>27</sup> This modification merely added to the convenience of shipping, storage, and handling by allowing the tomato to thaw without turning into mush.<sup>28</sup>

On the other hand, many GM foods may have an important role in the world's struggle to create a global food supply. The year 2008 brought a new global awareness of food shortages. In the next fifty years, the planet's population will increase from six billion to nine billion.<sup>29</sup> Couple this with dire warnings of water and food shortages from global warming and the picture looks grim. Scores of GM plants and animals are being genetically engineered to meet these new population and environmental demands. A wide variety of

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<sup>21</sup> *Id.* at 18-19.

<sup>22</sup> David Kestenbaum, *Atomic Tune-Up: How the Body Rejuvenates Itself*, NATIONAL PUBLIC RADIO, July 19, 2007, <http://www.npr.org/templates/story/story.php?storyId=11893583>.

<sup>23</sup> *Id.*

<sup>24</sup> Shannon Fowler, *Why New Atoms Aren't a Fountain of Youth*, NATIONAL PUBLIC RADIO, July 14, 2007, <http://www.npr.org/templates/story/story.php?storyId=11893583>.

<sup>25</sup> "Decedents of the Maya living in Mexico still sometimes refer to themselves as 'the corn people.' The phrase is not intended as a metaphor. Rather, it's meant to acknowledge their abiding dependence on this miraculous grass [*Zea Mays*, known as corn], the staple of their diet for almost 9,000 years." POLLAN, *supra* note 19, at 19.

<sup>26</sup> *Id.*

<sup>27</sup> The Pew Initiative on Food and Biotechnology, *supra* note 9.

<sup>28</sup> *Id.*

<sup>29</sup> *Talk of the Nation: Sustainable Agriculture* (National Public Radio broadcast Aug. 9, 2002). Over the next forty years, the amount of food required to meet the nutritional needs of the world population is quantitatively equal to the amount of food produced throughout the entire history of mankind. *Id.*

plants and animals are being modified to provide greater nutritional value,<sup>30</sup> enhance crop production<sup>31</sup> and provide pest resistance.<sup>32</sup> A good example of a plant that has been specifically modified to deal with population growth and environmental concerns is a GM tomato plant that has been genetically modified to add a gene from a mustard plant.<sup>33</sup> This new, modified version will grow in salty soil and desalinate the soil while it grows.<sup>34</sup> Twenty-five million acres of farmland in the world become too salty to support crops every year.<sup>35</sup> It is hoped that this novel GM tomato will counter the shrinking amount of agriculturally viable land.<sup>36</sup>

### C. Risks

The two major types of risks most often discussed in the literature are physical harm to humans and environmental harm. As more fully discussed herein, the risk of physical harm from the ingestion of GM food is related to the real possibility, as discussed *infra* with the case of the GM peas, that genetic modification will produce novel allergens and toxins with the potential to produce serious injury or death.<sup>37</sup>

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<sup>30</sup> Golden rice has been called the “poster child” for the potential of GM food. Golden rice is engineered to contain beta-carotene, which the human body turns into vitamin A. Vitamin A deficiencies cause blindness and death in hundreds of thousands of children every year in Asia and Africa. *Biotech Crop Roundup*, NATIONAL PUBLIC RADIO, Nov. 2001, <http://www.npr.org/programs/morning/features/2001/nov/biotech/011115.crops.html>.

Another example is the sweet potato, which contains very little protein, but is a staple food in Asia and Africa. Researchers inserted a gene that boosts protein production; the result was a sweet potato with five times the amount of protein of the original potato. *Id.*

<sup>31</sup> Salmon and other fish have been genetically modified to grow faster, while consuming less food. The closest to market is the Atlantic salmon with an added gene from another fish, the ocean pout. The ocean pout gene helps the salmon produce more growth hormone that speeds the salmon’s growth to consumable size. *All Things Considered Profile: California Assembly Considers Tough New Restrictions on Genetically Altered Salmon and Other Meat* (National Public Radio broadcast Mar. 11, 2002).

<sup>32</sup> An example is BT corn which has been bioengineered to contain natural insecticides that decrease the need for pesticides. The assertion is that this could benefit the environment, the farmers who handle pesticides and consumers who ingest food coated with pesticide residues. Plants that have been engineered with an increased resistance to herbicides also arguably increase crop yields. Rick Weiss, *EPA Restricts Gene-Altered Corn in Response to Concerns*, WASH. POST, Jan. 16, 2000, at A2. Also under development is a potato that resists viruses and fungi of the type that caused the Great Potato Famine in Ireland. *Biotech Crop Roundup*, *supra* note 30.

<sup>33</sup> *Talk of the Nation: Genetically Modified Salt Tolerant Tomato* (National Public Radio broadcast Aug. 3, 2001) (citing statistics from the Department of Agriculture).

<sup>34</sup> *Id.*

<sup>35</sup> *Id.*

<sup>36</sup> *Id.*

<sup>37</sup> See *infra* notes 72-77 and accompanying text.



The risks to the ecosystem appear to focus on three major areas. First, there is the risk that the insect population will adapt to the plants engineered to create their own insecticides (the first documented case came in 2008).<sup>38</sup> This adaptation could increase pest tolerance to the natural insecticides used by organic farms.<sup>39</sup> Second, there is the risk that GM plants with herbicide resistance may allow farmers to use more than normal amounts of herbicides to control weeds as there will be no damage to the GM plant. This could ultimately increase the amount of toxic chemicals introduced into the environment.<sup>40</sup> Finally, there is a risk that containment efforts will continue to be ineffective as the number of incidents where GM crops have contaminated non-GM crops are increasing every year.<sup>41</sup> In addition, there have been multiple incidents where GM plants and animals not approved for human consumption have inadvertently slipped into the human food supply.<sup>42</sup>

The FDA gave the green light to the use of GM plants for food based on a public health risk assessment using a risk-benefit analysis that concluded that the benefits of feeding future generations outweighed any potential human health risks. Built into this calculus were the presumptions of safety engendered by the Central Dogma model of the gene. As this was a decision over the safety of GM plants for human consumption, the environmental risks associated with GM plants were not initially part of the equation.

As discussed *infra* in Sections III and VI, the new model of the Networked Gene significantly changes this analysis. A risk-benefit analysis performed today that factors in different levels of uncertainty as reflected in trade-off analysis, suggests that the benefits of GM food only outweigh human health risks if risk mitigation strategies, such as premarket testing, GM ingredient

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<sup>38</sup> *First Documented Case of Pest Resistance to Biotech Cotton*, SCIENCE DAILY, Feb. 8, 2008, <http://www.sciencedaily.com/releases/2008/02/080207140803.htm>. The bollworm is the first pest insect to develop resistance to Bt cotton. Bt cotton is bioengineered with a gene from a bacterium to create its own pesticide. "Generating one of the largest selections for insect resistance known," over 400 million acres of Bt cotton and corn have been grown world-wide since 1996. *Id.*

<sup>39</sup> Kunich, *supra* note 13, at 820.

<sup>40</sup> Whittaker, *supra* note 7, at 1220.

<sup>41</sup> In 2007 alone, there have been 39 new occurrences of crop contamination in 23 different countries. GREENPEACE, GM CONTAMINATION REGISTER REPORT 2007 (2008), [http://www.gmcontaminationregister.org/index.php?content=nw\\_detail1](http://www.gmcontaminationregister.org/index.php?content=nw_detail1).

<sup>42</sup> "Over the past 10 years, the annual Register Report has recorded 216 incidents where biotech plants and animals not approved for human consumption have inadvertently slipped into the human food supply." *Id.*; Shelley Smithson, *Eat, Drink and Be Wary*, GRIST: ENVIRONMENTAL NEWS AND COMMENTARY, Jul. 30, 2003, <http://www.grist.org/news/maindish/2003/07/30/and/index.html>. One highly publicized occurrence occurred at the University of Illinois where pigs were genetically modified with cow genes to increase milk production and a synthetic gene was inserted to ease milk digestion for the piglets so they could grow faster. 386 piglets were accidentally sold and ended up on consumer tables as pork chops, sausage and bacon. *Id.*

labeling and post-market surveillance, are employed. Unfortunately, modern day risk assessment used to evaluate public health regulations has been functionally co-opted and has become a two-step process. The first step is the risk-benefit step discussed above. The second step entails the performance of a cost-benefit analysis that is both inappropriate and destructive in the context of evaluating the impact of new technologies on public health.

*D. Cost-Benefit Analysis of GM Ingredient Labeling*

Public opinion polls consistently reveal that the vast majority of U.S. citizens support GM food ingredient labeling.<sup>43</sup> In spite of this, it is not surprising that there has been no proposal by the FDA to establish labeling regulations to reflect this opinion. Pursuant to a series of legislative and executive orders with their genesis in 1994 in the then Speaker of the House Newt Gingrich's "Contract with America,"<sup>44</sup> all new federal regulative proposals must include a cost-benefit analysis<sup>45</sup> justifying the cost of regulation.<sup>46</sup> This cost-benefit hurdle has been detrimental to public health and safety as it is common for the development of new technologies to far outpace the development of the science necessary to test for the health risks associated with these technologies.<sup>47</sup> As health risks take time to quantify, there is no measurable benefit for the implementation of risk mitigation strategies available to out-balance the associated costs. Thus, the result of a cost-benefit analysis is a foregone conclusion when many new technologies first enter the market. This has been the case with GM food.

Until recently, a risk assessment using cost-benefit analysis has counseled against the need for GM food ingredient labeling. The risks to public health appeared to be based on little more than speculation, limiting the benefit of GM ingredient labeling to the protection of consumer choice. Therefore, even though the costs of requiring the industry to make labeling changes would be

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<sup>43</sup> The Coordinating Council, Compilation and Analysis of Opinion Pools on Genetically Engineered Foods, [http://www.tccouncil.org/surveys\\_cfs.htm](http://www.tccouncil.org/surveys_cfs.htm) (last visited Mar. 18, 2009).

<sup>44</sup> Nicholas A. Ashford, *The Legacy of the Precautionary Principle in U.S. Law: The Rise of Cost-Benefit Analysis and Risk Assessment as Undermining Factors in Health, Safety and Environmental Protection*, in IMPLEMENTATION THE PRECAUTIONARY PRINCIPLE: APPROACHES FROM THE NORDIC COUNTRIES, THE EU AND THE UNITED STATES 356-61 (Nicolas de Sadeleer ed., 2006).

<sup>45</sup> "In theory, cost-benefit analysis of a policy option enumerates all possible consequences, both positive and negative; estimates the probability of each; estimates the benefit or loss to society should each occur, expressed in monetary concerns; computes the expected social benefit or loss from each consequence by multiplying the amount of the associated benefit or loss by its probability of occurrence; and computes the net expected social benefit or loss associated with the government policy by summing over the various possible consequences. The reference point for these calculations is the state of the economy in the absence of the government policy, termed the 'baseline.'" *Id.* at 366.

<sup>46</sup> *Id.*

<sup>47</sup> *Id.* at 352-53.

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relatively small, the costs of new GM ingredient regulation were greater than the public health benefits to be gained.

The year 2007 brought a dramatic change to this picture in the form of the new scientific understanding of the Networked Gene. The discovery of the Networked Gene, and all that it implies, coupled with the case of the GM peas that created novel and unexpected allergenic properties, means that the FDA is now faced with more than just speculation over the possible health risks associated with GM plants used for food. As discussed in the next section, while still not quantified, the level and extent of the risk of unintended health consequences from heavy GM substance exposure is now quantifiable. When regulating new technologies, such as GM food, if the FDA continues to rely on rigid cost-benefit analysis when a risk is not yet quantified, but is quantifiable through scientific testing, the FDA will be continuously operating behind the curve, reacting to public health crises rather than preventing them. Instead, this Article argues that cost-benefit analysis should be abandoned, as discussed *infra*,<sup>48</sup> and trade-off analysis should be applied when engaging in a risk assessment to evaluate new technology regulations designed to protect public health.

### III. RISK ANALYSIS AND THE SPACE BETWEEN: MOVING FROM IGNORANCE TO INDETERMINACY

The FDA's presumption that GM plant foods are bioequivalent to traditional food is a consequence of the remarkable growth in the development of new technologies which far outpaces the science necessary to identify the human health risks associated therewith. This scientific lag time creates a period when there is an information void with regard to risks to human health. As this information void is slowly filled through scientific experimentation, the level of uncertainty over health risks commonly progresses from ignorance (where scientists *don't know* what they don't know) to indeterminacy (where scientists *know* what they don't know but can plan the scientific experiments necessary to find out) to, finally, a tipping point in the state of knowledge when classic probability analysis can be applied to predict, or quantify, risk levels to human health. This Article refers to this lag time when the state of knowledge over health risks has moved out of ignorance and into indeterminacy as 'the space between' or 'the health risk information void.' This Article points out that government regulators are operating in 'the space between' when it comes to genetically modified plants marketed for human consumption

When the FDA first made its choice over how to regulate GM foods, much less was known regarding gene function. Scientists simply 'did not know what they did not know' about the risks to public health of GM food. Thus, with regard to uncertainty, scientific decisions and FDA regulatory choices based on those scientific decisions were made in an environment of ignorance. Acting in ignorance, scientists at the FDA chose to regulate based on what we now know

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<sup>48</sup> See *infra* notes 166-68 and accompanying text.

to be a false assumption of bioequivalence based on the Central Dogma. In the past five years, numerous ground breaking scientific discoveries have shifted the general nature of uncertainty over the public health risks of GM food from ignorance to indeterminacy. In other words, from *not knowing* what we don't know, to *knowing* what we don't know.

Scientists now understand that GM plants create biological components that have never before existed in nature. In order to move from indeterminacy to classical risk analysis, scientists must determine whether these novel components are biologically active, and, if so, whether they are harmful to public health. Then, using classic uncertainty principles, scientists must quantify the probability and degree of the harm. Thus, scientists are aware of the risks they must rule out through the systematic study of each transplanted gene as it functions in the new organism and as that new organism responds to environmental triggers. A good example of this process is that which was used to discover the health risks associated with GM peas discussed *infra*.

#### A. *The Role of Genes*

To appreciate the magnitude of the role that genes play in how well, or how poorly, an organism functions, one just needs to understand that a gene provides the coding for the sequence of amino acids that make up proteins. The term "protein" originated with the Greek word  $\pi\rho\omega\Gamma\alpha$  ("prota"), meaning "of primary importance."<sup>49</sup> Proteins are integral parts of organisms and play a role in every process within cells.<sup>50</sup> A defect in the way a gene expresses a protein can have dire consequences. For instance, enzymes are a type of protein that catalyze biochemical reactions and are essential to metabolism.<sup>51</sup> Damage to just one enzyme can lead to life-threatening or disfiguring problems. Illustrations of life threatening conditions include Tay-Sachs disease, which is caused by impairment of the gene for the enzyme hexosaminidase which leads to the abnormal buildup of a chemical which destroys the brain;<sup>52</sup> sickle cell anemia, which results from a defect on the coding of hemoglobin;<sup>53</sup> and, muscular dystrophy, the consequence of a defective gene that results in the absence of dystrophin, a protein necessary to the maintenance of muscle.<sup>54</sup> An

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<sup>49</sup> MERRIAM WEBSTER'S COLLEGIATE DICTIONARY 936 (10th ed. 1993).

<sup>50</sup> See ANTHEA MATON ET AL., HUMAN BIOLOGY AND HEALTH (Annotated Teacher's ed., Prentice Hall 1993).

<sup>51</sup> See A. Bairoch, *The ENZYME Database in 2000* (2000), <http://www.expasy.org/NAR/enz00.pdf>.

<sup>52</sup> National Institute of Neurological Disorders and Stroke, *NINDS Tay-Sachs Disease Information Page*, <http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm> (last visited Mar. 17, 2009).

<sup>53</sup> Sickle Cell Association of America, *What Is Sickle Cell Disease?*, [http://www.sicklecelldisease.org/about\\_scd/index.phtml](http://www.sicklecelldisease.org/about_scd/index.phtml) (last visited Mar. 26, 2009).

<sup>54</sup> National Institute of Neurological Disorders and Stroke, *NINDS Muscular Dystrophy Information*, <http://www.ninds.nih.gov/disorders/md/md.htm> (last visited Mar. 17, 2009).

example of a condition that can change appearance is albinism, which can be caused by a missing tyrosine gene necessary for the production of melanin.<sup>55</sup> Of the 60,000 genes that make-up the human genome, there are 5,000 that, if defective or missing, can cause a wide variety of genetic diseases.<sup>56</sup>

*B. The ENCODE Discoveries*

In June of 2007, the ENCyclopedia Of DNA Elements consortium (ENCODE), organized by the National Human Genome Research Institute, published its major scientific findings on the networking effects of Junk DNA.<sup>57</sup> The ENCODE consortium involved the collaboration of hundreds of scientists located in eleven different countries who spent four years building a parts list of all of the biologically functional elements in one percent of the human genome.<sup>58</sup>

The ENCODE scientists have reshaped our understanding of how the human genome functions by challenging our traditional view of genes as discrete packets of information arranged like beads strung on a thread of DNA.<sup>59</sup> This model of the gene is based on the Central Dogma of molecular biology which states that “each gene in living organisms, from human to bacteria, carries the information needed to construct one protein.”<sup>60</sup> The Central Dogma views DNA as a static stretch of genetic code where each gene is clearly delimited by a promoter where the gene starts, the codons that are the blueprint for the protein and the stop codon that signals the end of the gene.<sup>61</sup> According to this model, a gene provides the complete set of instructions on how to build a particular protein, just like a small blueprint. Therefore, a gene from any organism can be precisely excised and neatly and predictably moved into another organism.<sup>62</sup> For example, under this model, tomatoes can safely gain fungal resistance, and no other new properties, by adding a gene that produces a protein called chitinase. A chitinase breaks down chitin which forms the cell walls of a fungus cell.<sup>63</sup>

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<sup>55</sup> National Organization for Albinism and Hypopigmentation, *What is Albinism?*(2005), <http://www.albinism.org/publications/whatis.pdf>.

<sup>56</sup> Marshal Brain, *How Cells Work*, <http://science.howstuffworks.com/cell12.htm> (last visited Mar. 26, 2009).

<sup>57</sup> Rick Weiss, *Intricate Toiling Found in Nooks of DNA Once Believed to Stand Idle*, WASH. POST, June 14, 2007, at A01; Gerstein et al., *supra* note 2, at 669; Caruso, *supra* note 3.

<sup>58</sup> Caruso, *supra* note 3; Weiss, *supra* note 57; Gerstein, *supra* note 2.

<sup>59</sup> Gerstein et al., *supra* note 2, at 679.

<sup>60</sup> Caruso, *supra* note 3. *See also* Gerstein et al., *supra* note 2, at 670-71.

<sup>61</sup> Gerstein et al., *supra* note 2, at 670-71.

<sup>62</sup> *Id.*

<sup>63</sup> Matteo Lorito et al., *Genes Form Mycoparasitic Fungi as a Source for Improving Plant Resistance to Fungal Pathogens*, 95 PROC. NATL. ACAD. SCI. USA 7860-65 (1998).

The Central Dogma model created what many call the “industrial gene.”<sup>64</sup> “The industrial gene is one that can be defined, owned, tracked, proven acceptably safe, proven to have uniform effect, sold and recalled.”<sup>65</sup> For example, the U.S. Patent and Trademark Office defines a gene as an ordered sequence of DNA “that encodes a specific functional product.”<sup>66</sup>

Directly contrary to the Central Dogma’s view of the gene, the ENCODE project reveals that many genes actually *overlap* one another and share stretches of molecular code.<sup>67</sup> This study also overturns the long-held assumption that *vast* stretches of DNA that flank genes are just biologically inactive junk.<sup>68</sup> Instead, sections of previously characterized junk DNA modulate a labyrinthine of silencing, switching and splicing operations (described below) necessary to sort out the complex messages sent by the overlapping genes.<sup>69</sup> Adding another dimension to this complicated system, the ENCODE project demonstrated that “genes and the DNA sequences that regulate their activity are often far apart along the six-foot long strands of DNA.”<sup>70</sup>

This network effect, or biochemical cross-talk, can have a significant effect on protein expression, as was the case with the GM peas discussed in the next section. These effects are currently undetectable by the FDA as the products of gene expression are not tested as produced by the novel organism.<sup>71</sup> For example, under the FDA testing scheme, the fact that these GM peas had novel and unexpected allergenic properties would not have been discovered until after the GM peas had been introduced into the market and caused allergic reactions.

### 1. Genetically Modified Peas

An example of the impact that the network effect can have on protein expression came in 2002 when scientists at Australia’s national research organization, The Commonwealth Science and Industrial Research Organization (“CSIRO”), decided to end their 10 year-long project to bring GM peas to market.<sup>72</sup> Green beans contain a natural protein that inhibits weevils from digesting starch which causes the weevils to starve to death.<sup>73</sup>

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<sup>64</sup> Caruso, *supra* note 3 (quoting Jack Heinemann, Professor of Molecular Biology and Director of Integrated Research in Biosafety at the University of Canterbury, New Zealand).

<sup>65</sup> *Id.*

<sup>66</sup> Gerstein et al., *supra* note 2, at 673-79.

<sup>67</sup> *Id.*

<sup>68</sup> *Id.*

<sup>69</sup> *Id.*

<sup>70</sup> Weiss, *supra* note 57; Gerstein et al., *supra* note 2, at 673-79.

<sup>71</sup> See *infra* notes 126-32 and accompanying text.

<sup>72</sup> Press Release, CSIRO GM Pea Study Backs Case-By-Case Risk Assessment (Nov. 17, 2005), <http://www.csiro.au/news/GMPeaStudy.html>.

<sup>73</sup> GMO Compass, *GM Peas Cause Immune Response – A Gap in the Approval*

This protein has no history of allergenicity.<sup>74</sup> In the CSIRO project, peas were genetically modified to contain this protein to provide the peas with the same protection against weevils that is found in green beans.<sup>75</sup> Right before the GM peas were scheduled for market release, one of the scientists decided to perform animal testing on the protein as expressed by the GM peas. Surprisingly, not only was the protein discovered to be allergenic, it also primed the test mice to react to other allergens.<sup>76</sup> The researchers discovered subtle differences in the way that sugars were added to the protein that were thought to be due to post-translational modification.<sup>77</sup>

This post-translational modification can't be explained by the Central Dogma model; however, there are several possible explanations under the Networked Gene model. The first possibility is that the differences in the protein was caused by hybrid mRNA.

## 2. mRNA Hybrids

In addition to the discoveries regarding junk DNA, the ENCODE Project made several other significant discoveries, one of which involves mRNA. To create a protein, a cell must first transcribe a gene in DNA into messenger RNA (mRNA).<sup>78</sup> The mRNA then drifts over to a ribosome which uses the mRNA as the instructions for assembling the amino acids into a chain that forms the protein.<sup>79</sup> Another basic precept of the Central Dogma is that one gene makes one copy of mRNA which makes one protein.<sup>80</sup> The ENCODE project has demonstrated that DNA produces over twice the amount of mRNA than the Central Dogma predicts it should.<sup>81</sup> In addition to the mRNA produced by the genes, mRNA transcripts are being produced that include both genes and their adjacent sections of junk DNA.<sup>82</sup> Approximately eighty percent of mRNA produced by DNA is this "extra" mRNA.<sup>83</sup> None of this extra

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*Process?*, Jan. 3, 2006, [http://www.gmo-compass.org/eng/news/stories/175.gm\\_peas\\_australia\\_cause\\_immune\\_response.html](http://www.gmo-compass.org/eng/news/stories/175.gm_peas_australia_cause_immune_response.html).

<sup>74</sup> Vanessa E. Prescott et al., *Transgenic Expression of Bean  $\alpha$ -Amylase Inhibitor in Peas Results in Altered Structure and Immunogenicity*, 53 J. AGRIC. FOOD CHEM. 9023, 9023-30 (2005).

<sup>75</sup> Prescott et al., *supra* note 74 at 9023; *GMO Compass*, *supra* note 73.

<sup>76</sup> Prescott et al., *supra* note 74 at 9028.

<sup>77</sup> *Id.* at 9024.

<sup>78</sup> Brain, *supra* note 56.

<sup>79</sup> *Id.*

<sup>80</sup> Gerstein et al., *supra* note 2, at 670-71.

<sup>81</sup> Andy Coghlan, *'Junk' DNA Makes Compulsive Reading*, 2608 NEW SCIENTIST 20 (2007), available at <http://www.newscientist.com/article/mg19426086.000-junk-dna-makes-compulsive-reading.html>; Gerstein et al., *supra* note 2, at 673-79.

<sup>82</sup> Coghlan, *supra* note 81 at 20; Gerstein et al., *supra* note 2, at 673-79.

<sup>83</sup> Coghlan, *supra* note 81 at 20; Gerstein et al., *supra* note 2, at 673-79.

mRNA is being used to create proteins.<sup>84</sup> Some ENCODE scientists theorize that this extra mRNA may “fine-tune” or “modulate the activity of the genes themselves.”<sup>85</sup>

In the context of genetic modification, when a gene from one species is transplanted into the DNA of another species, mRNA is being created that is a hybrid of the transplanted gene and the host junk DNA. This is the creation of hybrid mRNA that has never existed before in nature. Whether this newly introduced genetic material is biologically active and whether this activity will alter the way in which critical proteins are produced (possibly the situation with the GM peas) and the amount of that production, have yet to be examined.

### C. *The Splicing Role of SNPs in Junk DNA*

Another mechanism that could have produced the allergenic properties of GM peas is the splicing role of SNPs discovered by the Genome Regulators in Disease (GRID) Project published in January of 2008.<sup>86</sup> This study revealed that very small variations in junk DNA, called SNPs (single nucleotide polymorphisms), control the natural processing of messenger RNA via a process called splicing.<sup>87</sup> The SNP's that are unique to an individual lead to changes in the splicing process that could be responsible for dramatic differences in the way that genes produce proteins.<sup>88</sup> These differences are responsible for the vast variety of phenotypic differences (physical and physiological attributes) in individuals.<sup>89</sup>

“‘Regular’ splicing is the process by which long strings of nucleotides in a gene’s pre-messenger RNA (pre-mRNA) are discarded, and the remaining strings of nucleotides are spliced together into one continuous strand of messenger RNA (mRNA) that produces one unique protein.”<sup>90</sup> However, regular splicing fails to explain how only 25,000 genes can produce all of the 100,000 proteins in the human cell.<sup>91</sup> A new study published in December of 2008 reveals that the additional 75,000 proteins are produced by a process referred to as “alternative splicing,” defined as “a process that selectively

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<sup>84</sup> Coghlan, *supra* note 81 at 20.

<sup>85</sup> *Id.*

<sup>86</sup> *Tiny Genetic Differences Have Huge Consequences*, SCIENCEAILY, Jan. 20, 2008, <http://www.sciencedaily.com/releases/2006/01/080118165005.htm>. The study, part of the Genome Regulators in Disease (GRID) Project, relied on the data put together by the immense HapMap (Haplotype Map) Project, “a global comparative map of the human genome . . .” *Id.*

<sup>87</sup> *Id.*

<sup>88</sup> *Id.*

<sup>89</sup> *Id.*

<sup>90</sup> *Genetic Diseases More Complicated: Mechanisms Underlying Alternative Splicing of Premessenger RNA into Messenger RNA Discovered*, SCIENCEAILY, Dec. 26, 2008, <http://www.sciencedaily.com/releases/2008/12/081224215710.htm>.

<sup>91</sup> *Id.*



activates alternative splicing sites along the pre-messenger RNA strand to assemble different subsets of RNA nucleotides into a variety of mRNAs. Each mRNA then produces a single protein.”<sup>92</sup> The authors of this cutting edge study point out that the majority of genes utilize alternative splicing.<sup>93</sup>

More than one-half of all genetic diseases are caused by mistakes made in the alternative splicing process caused by mutations in DNA sequences.<sup>94</sup> These mistakes can cause mRNA to include sequences that should have been deleted. Importantly, “small changes in a nucleotide sequence near a splice point can lead to large changes in the splice site choice and proteins produced.”<sup>95</sup> Metaphorically, consider pre-mRNA as a long sentence. The “nucleotides and splice sites are the words of the sentence. Adding or deleting one word . . . can radically change the meaning of the sentence.”<sup>96</sup> Taking this metaphor one step further, when scientists are genetically modifying a plant, they are making major edits to these sentences. These edits can make changes in the splicing processes, producing altered proteins that could have a ‘butterfly effect’ on the entire organism. This type of alteration may have been the cause of the newly allergenic properties of the GM peas.

#### 1. Quality Control Enzymes

Continuing to work with this metaphor, while not likely to be the cause of the newly allergenic properties of the GM peas, it is important to mention the role of quality control enzymes in cleaning up defective ‘GM edits’ to the pre-mRNA ‘sentence.’ The amino acid sequence of a protein controls how that protein folds, and how that protein folds controls how it functions.<sup>97</sup> A change in the amino acid sequence of a protein can change how that protein folds.<sup>98</sup> Another new study has identified an enzyme that acts as a quality control mechanism.<sup>99</sup> If a protein is not manufactured correctly so that it fails to fold perfectly, this enzyme will destroy the protein.<sup>100</sup> Thus, the enzyme acts like a quality control inspector and recognizes when a protein has ‘manufacturing defects.’ The enzyme degrades the protein before it can be distributed.

Scientists hypothesize that proteins which are only slightly defective, but which could still complete their functions, may be destroyed by “over zealous” quality control enzymes causing genetic diseases.<sup>101</sup> This may be the cause of

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<sup>92</sup> *Id.*

<sup>93</sup> *Id.*

<sup>94</sup> *Id.*

<sup>95</sup> *Id.*

<sup>96</sup> *Id.*

<sup>97</sup> *Cell's ‘Quality Control’ Mechanism Discovered*, SCIENCE DAILY, July 30, 2008, <http://www.sciencedaily.com/releases/2008/07/080729133525.htm>.

<sup>98</sup> *Id.*

<sup>99</sup> *Id.*

<sup>100</sup> *Id.*

<sup>101</sup> *Id.*

cystic fibrosis which is caused by a defect in the protein CFTR.<sup>102</sup> This quality control mechanism “sometimes works a little too well . . . it insists on BMW quality when a Honda will do . . . It is the degradation of the protein, not the mutation itself, which causes cystic fibrosis.”<sup>103</sup>

Applying this hypothesis to GM food, if a gene that is transferred from one organism into another produces a protein in just a slightly different way as a result of the networking effect, quality control enzymes could destroy the protein, causing disease or otherwise negatively impacting the organism.

#### D. Epigenetics: Switching and Silencing Functions

Add to this picture the discoveries of the rapidly developing field of study called epigenetics. Epigenetics concentrates on the multiple influences on DNA and the proteins that encase it that determine whether genes are turned on or off during development, disease processes and exposure to different environments.<sup>104</sup> Epigenetics has established that there is information “above and beyond” the gene that plays a major role in gene expression that can influence an organism’s phenotype and which can be inherited by an organism’s progeny.<sup>105</sup> Epigenetic mechanisms don’t alter DNA sequences, but affects the DNA by preventing its expression through various processes including DNA methylation,<sup>106</sup> DNA packaging,<sup>107</sup> protein

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<sup>102</sup> *Id.*

<sup>103</sup> *Id.*

<sup>104</sup> *Epigenetic Research Uncovers New Targets for Modification Enzymes*, SCIENCE DAILY, Apr. 28, 2008, <http://www.sciencedaily.com/releases/2008/04/080427194710.htm>.

<sup>105</sup> *Does Environment Influence Genes? Researcher Gives Hard Thoughts on Soft Inheritance*, SCIENCE DAILY, Aug. 8, 2006, <http://www.sciencedaily.com/releases/2006/08/060807154715.htm> [hereinafter *Does Environment Influence Genes?*]; Jablonka et al, *Transgenerational Epigenetic Inheritance: Prevalence, Mechanisms, And Implications For The Study Of Heritability And Evolution*, 84 THE QUARTERLY REV. BIOLOGY (2009) (listing over 100 well-documented cases of epigenetic inheritance between organisms, including the exposure of a pregnant rat to chemicals that alters reproductive hormones that led to generations of sick offspring).

<sup>106</sup> DNA methylation is a “chemical modification of cytosine, one of the four chemical subunits of DNA. Without proper DNA methylation, higher organisms from plants to humans have a host of developmental problems, from dwarfing in plants to certain death in mice.” *Id.*

<sup>107</sup> DNA packaging refers to the fact that “DNA is wrapped around proteins [histones] similar to the way that thread is wrapped around a spool. Loosely wrapped DNA is more readily accessible and therefore more easily expressed than tightly wrapped DNA, allowing another mechanism for gene expression.” *Does Environment Influence Genes?*, *supra* note 105. This DNA packaging “hides the DNA sequence from the cellular machinery that reads its genetic information, so the DNA sequence is ‘silenced.’ The genes it contains are effectively turned off. . . This inherited [packaging] of DNA, which causes genes to be expressed in distinctive ways, is one of the series of phenomena that scientists call

methyltransferases,<sup>108</sup> and the location of the DNA within the nucleus.<sup>109</sup> These mechanisms turn genes on and off during the course of an organism's life in response to environmental factors. For example, this accounts for vernalization, the well-known process of exposing certain plants to low temperatures to trigger flowering.<sup>110</sup> Epigenetic inheritance between organisms means that a GM food might produce generations of offspring before an environmental trigger or disease activates a DNA sequence to produce a toxic or allergenic protein. Thus, a GM plant that may be safe to consume when first produced, could cause unintended health consequences when one of its progeny is consumed at some future point in production.

*E. The New Understanding of the Networked Gene*

Instead of viewing DNA as just a string of biological code, scientists now understand that DNA is a highly complex operating system that processes a great deal more information than previously assumed. An apt analogy is a phone line that carries multiple voices simultaneously and what was previously thought to be meaningless junk DNA sorts out the interwoven messages.<sup>111</sup> In 2008, a new definition of the gene has been proposed: "A gene is a union of genomic sequences encoding a coherent set of potentially overlapping functional products."<sup>112</sup>

These studies all add up to a rapidly emerging picture of an exceptionally dynamic system where a gene which expresses itself one way in a donee organism to produce a particular protein, in a particular amount, in response to a particular stimulus, may not express itself the same way when dropped into an entirely different organism with its own complex operating system, as was the case with the GM peas. This new operating system may cause the transferred gene to change the phenotype of the donee organism in a way that is undetectable by the FDA as the products of gene expression by the donee gene are not tested as expressed in the donee organism.

#### IV. THE CHALLENGE

The FDA's choice of method to regulate GM plant food is predicated on the

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epigenetic. The same sequence of nucleotides in two people can produce different patterns of gene expression if the way the DNA is [packaged] happens to be different." *Mechanism of Epigenic Inheritance Clarified*, SCIENCE DAILY, Apr. 24, 2008, <http://www.sciencedaily.com/releases/2008/04/080422151826.htm>.

<sup>108</sup> "Protein methyltransferases[ ] add methyl groups to lysine amino acids within the histones [the proteins that wrap around DNA] and change their influence on gene expression." *Epigenetic Research Uncovers New Targets for Modification Enzymes*, *supra* note 104.

<sup>109</sup> *Does Environment Influence Genes?*, *supra* note 105.

<sup>110</sup> *Mechanism of Epigenic Inheritance Clarified*, *supra* note 107.

<sup>111</sup> Weiss, *supra* note 57.

<sup>112</sup> Gerstein et al., *supra* note 2, at 673-79.

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dated Central Dogma model of the gene. This Central Dogma model allows for a presumption that a gene will express itself in the donee food product in the same way that it expresses itself in the donor product. According to the FDA's view, if a gene produces a protein that has been traditionally safe for human consumption in the donor product, then the protein that the gene produces in the donee product will be equally safe in the donee product. The new understanding of how genes work revealed by the ENCODE Project and the GRID Project challenges this basic presumption and, in so doing, challenges the FDA's GM plant food regulatory scheme.

A. *GM Food Regulations*

Most common foods predate the establishment of national food safety laws and are presumed to be safe for human consumption under the FDCA based on extensive use and experience.<sup>113</sup> Government regulation to protect public health involves achieving the proper balance between the protection of individual choice in matters involving self-regarding behavior, like food choices, with the need to protect vulnerable consumers from harm from third parties. When it comes to traditional food, consumers can protect themselves against common risks associated with different foods, such as allergens and toxins, by a body of common knowledge and customs that have been passed down from generation to generation. Thus, the FDCA does not require any premarket testing of these traditional foods as the risks and benefits are well-known.<sup>114</sup>

In spite of the fact that consumers have no equivalent experience, and thereby, no body of common understanding of the risks associated with GM food, the FDA regulates GM plant foods just like traditional plant foods and does not require any premarket testing. The FDA reasons that food has been

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<sup>113</sup> 21 U.S.C. § 321(s) (1994).

<sup>114</sup> If the food product is deemed adulterated, the FDA will use its seizure and injunctive powers to remove the product from the market. In these court actions, the FDA has the burden of proving that the product is adulterated. 21 U.S.C. § 342(a)(1) (1994); Richard A. Merrill, *Regulating Carcinogens in Food: A Legislator's Guide to the Food Safety Provisions of the Federal Food, Drug, and Cosmetic Act*, 77 MICH. L. REV. 171, 186-90 (1978). For a naturally occurring substance found in the food product, the food product is rendered adulterated if the substance is ordinarily injurious to health. 21 U.S.C. § 342(a)(1)(1994). However, if the substance in the food product is "added," the food product is adulterated if the substance "may render" the food injurious to health. *Id.* Of course, this "may render" injurious category is significantly narrowed by provisions that allow for certain amounts of contaminants such as pesticides and mercury. These "added" ingredients avoid being labeled as adulterants as long as they fall within government approved tolerance levels. Regardless, as the FDA carries the burden of proof, it must first conduct scientific studies of the food product in order to gather the data necessary to proving its case. Merrill, *supra*, at 186-90. This may take years. The practical result is that an unsafe food may remain on the market for a long period of time before the FDA can take action. *Id.*

genetically manipulated through traditional breeding techniques for over a century. Therefore, because both traditional and biotech foods have been genetically manipulated, they both can be regulated the same way.<sup>115</sup>

Another way to view the added genetic material is as a food additive. According to FDA regulations, if substances added to food are “food additives,” premarket testing for safety is required.<sup>116</sup> The exception to this rule is when a food additive is generally regarded as safe or “GRAS.”<sup>117</sup> If a substance added to food is considered to be GRAS, it will not require pre-market approval.<sup>118</sup> A substance is considered to be GRAS if there is a general consensus among informed experts that a substance is safe for human consumption.<sup>119</sup> Examples are salt and sugar.

The FDA has declined to regulate GM ingredients as food additives, taking the position that, even if the added gene(s) initially fall into the food additive category, they fall within the GRAS exception based on the Central Dogma model of the gene. As discussed above, the Central Dogma model creates the presumption that a gene will express itself in the donee food product in the same way that it expresses itself in the donor product.<sup>120</sup> According to the FDA’s view, if a gene produces a protein that has been traditionally safe for human consumption in the donor product, then it will be equally safe in the donee product.<sup>121</sup> For this reason, GM food does not require pre-market

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<sup>115</sup> “FDA considers the existing statutory authority under sections 402(a)(1) and 409 of the act, and the practical regulatory regime that flows from it, to be fully adequate to ensure the safety of new food ingredients and foods derived from new varieties of plants, regardless of the process by which such foods and ingredients are produced.” *Foods Derived from New Plant Varieties*, *supra* note 8, at 22,989.

<sup>116</sup> A “food additive” is “any substance whose intended use results in it becoming a component of food or affecting the characteristics of food, unless the substance is generally regarded as safe (GRAS).” 21 U.S.C. § 321(s) (1994). In response to the public’s concern over the steadily increasing amounts of chemicals added to food as food processing technology developed, Congress enacted the Food Additives Amendment of 1958. Pub. L. No. 85-929, 72 Stat. 1784 (1958) (codified in scattered sections of 21 U.S.C.). The Food Additives Amendment established a pre-market approval requirement for “food additives.” This placed the burden on the food processor to establish, through scientific methodology, that the additive was safe for its intended use before placing the food additive on the market. *Id.* This is referred to as the pre-market approval process.

<sup>117</sup> 21 U.S.C. § 321(s) (1994).

<sup>118</sup> A substance added to food is not a food additive and, therefore, does not require pre-market approval if it is “GRAS.” A substance that is “GRAS” is defined as a substance that is “generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use.” *Id.*

<sup>119</sup> *Id.*

<sup>120</sup> *See supra* notes 59-66.

<sup>121</sup> “With respect to transferred genetic material (nucleic acids), generally FDA does not

testing.

### 1. Listing GM Ingredients on Food Labels

The FDA also does not require that GM food manufacturers list GM ingredients on food product labels. The FDCA requires that a traditional food product be described by its common name.<sup>122</sup> As a GM plant food is considered to be no different than its traditional host product, the FDA requires that the name of the traditional host product be used. According to the FDA, labeling is only required if “a new plant variety differs from its traditional counterpart such that the common or usual name no longer applies to the new food, or if a safety or usage issue exists to which consumers must be alerted.”<sup>123</sup>

Moreover, omitting a GM ingredient on a food label is not considered by the FDA to be false or misleading. A label will be considered false or misleading by the FDA only if “it fails to reveal all facts that are material . . . with respect to consequences which may result from the use of the article.”<sup>124</sup> The FDA

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anticipate that transferred genetic material would itself be subject to food additive regulation. Nucleic acids are present in the cells of every living organism, including every plant and animal used for food by humans or animals, and do not raise a safety concern as a component of food. In regulatory terms, such material is presumed to be GRAS.” Foods Derived from New Plant Varieties, *supra* note 8, at 22,990.

<sup>122</sup> “Section 403(i) of the act and regulations promulgated thereunder require that a food product be described by its common or usual name or, in the absence thereof, an appropriately descriptive term (21 C.F.R. § 101.3). Section 403(i) of the act also requires that, in the case of foods fabricated from two or more ingredients, a food product bear on the label the common or usual name of each ingredient.” Food Labeling; Food Derived from New Plant Varieties, 58 Fed. Reg. 25,837, 25,838 (Apr. 28, 1993).

<sup>123</sup> Food Derived from New Plant Varieties, *supra* note 8, at 22,991. “FDA stated that developers should initially assume that a protein derived from a food that commonly causes allergic reactions is an allergen and that labeling would be required to alert sensitive individuals, unless scientific evidence demonstrated that the introduced protein was not an allergen. FDA cited several examples of foods that commonly cause allergic reactions: milk, eggs, fish, crustacea, molluscs, tree nuts, wheat, and legumes (particularly peanuts and soybeans) (57 FR 22984 at 22987 and 22991). Although not expressly addressed in the 1992 policy, FDA did not anticipate that labeling would be necessary in cases where the protein was not present in the finished food (e.g., refined vegetable oil).” DISCUSSION PAPER: EVALUATION OF ALLERGENICITY OF PROTEINS INTRODUCED INTO BIOENGINEERED FOODS 2 (2002), *available at* [http://www.fda.gov/OHRMS/DOCKETS/ac/02/briefing/3886b1\\_Discussion%20Paper%20Allergenicity.pdf](http://www.fda.gov/OHRMS/DOCKETS/ac/02/briefing/3886b1_Discussion%20Paper%20Allergenicity.pdf).

<sup>124</sup> *See* Food Labeling; Food Derived from New Plant Varieties, *supra* note 122, at 25,838. “[A] food is misbranded if its labeling is false or misleading. Under section 201(n) of the act (21 U.S.C. § 321(n), labeling is misleading if it fails to reveal all facts that are ‘material in light of . . . representations or material with respect to consequences which may result from the use of the article to which the labeling . . . relates under the conditions of use prescribed in the labeling . . . or such conditions of use as are customary or usual.’” *Id.* at

states that the method by which the food is produced, here genetic modification, is not material.<sup>125</sup>

## 2. Informal Encouragement of Premarket Testing of GM Food

Based on its position that GM ingredients fall into either the traditional food category or the GRAS exception to the food additive category, the FDA has no power to require premarket testing of GM plant food and GM plant food producers do not have to have FDA approval prior to placing a GM product on the market.

While acknowledging this limitation, the FDA has encouraged producers to consult voluntarily with the FDA prior to commercializing a GM food.<sup>126</sup> However, none of the information that the FDA asks a producer to provide voluntarily includes any data collected from the actual testing of the new protein as it is expressed in the GM food.<sup>127</sup> In addition, no information from *in vivo* or *in vitro* testing is requested,<sup>128</sup> such as the serum testing and the type of animal studies highly recommended by experts from the World Health Organization or the type of testing that revealed the novel and unexpected allergenic properties of the GM peas.<sup>129</sup>

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25,839. For example, the FDA states that “a tomato does not become ‘fish-like’ following the addition of a copy of a fish gene” which was added to prolong freshness. *Id.* As long as the tomato looks and tastes like a tomato, the only information that will be provided to the consumer is that which is traditionally provided with tomatoes. *Id.*

<sup>125</sup> Genetically Engineered Foods Fears & Facts: An Interview with FDA’s Jim Maryanski, FDA CONSUMER, Jan.-Feb. 1993, at 11-13, <http://www.fda.gov/bbs/topics/CONSUMER/CON00191.html>. “The law says labeling for foods must disclose information that’s material, as well as avoid false or misleading statements. It’s our view that the method by which a plant is developed by a plant breeder is not material information in the sense of the law . . . If genetic engineering or any other technique changes the composition of a tomato in a way that it’s really not the same tomato anymore, then it would have to be called something different.” *Id.*

<sup>126</sup> Premarket Notice Concerning Bioengineered Foods, 66 Fed. Reg. 4706 (Jan. 18, 2001), *available at* <http://www.cfsan.fda.gov/~lrd/fr010118.html>.

<sup>127</sup> Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced By New Plant Varieties Intended for Food Use, 71 Fed. Reg. 35,688-35,689 (June 21, 2006), *available at* <http://www.cfsan.fda.gov/~dms/bioprgu2.html#format>. There are seven categories of requested information: 1. The name, identity, and function of any new protein produced in the new plant variety; 2. Data and information as to whether the new protein has been safely consumed in foods; 3. A list of the identity (ies) and source(s) of the introduced genetic material; 4. A description of the purpose or intended technical effect of the new protein; 5. An assessment of the amino acid similarity between the new protein and known allergens and toxins; 6. The overall stability of the protein, and the resistance of the protein to enzymatic degradation using appropriate *in vitro* assays; and, 7. Any other pertinent information. *Id.*

<sup>128</sup> *Id.*

<sup>129</sup> DISCUSSION PAPER, *supra* note 123, at 7. *See also* CODEX ALIMENTARIUS, DRAFT

The FDA only asks for information about the protein's allergenicity when consumed in the host product and the similarity between the protein's amino acid sequences and those of known allergens.<sup>130</sup> If there is no history of allergenicity when the protein was consumed in the host product, and the new protein's amino acid sequence does not match those of known allergens, it is presumed to have no allergenicity in the donee product and no further information is required.<sup>131</sup> Like food additives, once a new protein has been 'approved,' it goes on a central registry and can be used in any donee plant without further consultation with the FDA.<sup>132</sup>

*B. The Networked Gene Model and Its Impact on FDA Regulation*

The new Networked Gene Model teaches that DNA is not just a static string of code but a complex processing system whose parts interact with each other - silencing, switching and splicing to create a complex informational network. Putting this new understanding of the highly contextual nature of genes together with epigenetic studies which demonstrate the myriad ways that the environment can activate or silence certain genes (allowing for billions of possible outcomes), it is easy to see how the new model of gene function challenges the simplistic assumption engendered by the Central Dogma which underlies the FDA's regulatory scheme.

In fact, the hybrid mRNA discovery and the case of the GM peas do more than just challenge the presumption of bioequivalence; they provides direct evidence that the transferred genes and the products of their expression are not

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GUIDELINE FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF FOODS DERIVED FROM RECOMBINANT-DNA PLANTS (2003), *available at* <http://www.codexalimentarius.net/biotech/en/DNAPlant.htm>; FAO/WHO, SAFETY ASPECTS OF GENETICALLY MODIFIED FOODS OF PLANT ORIGIN 10 (2000), *available at* <http://www.who.int/fsf/GMfood/FAO-HOConsultationreport2000.pdf>; FAO/WHO, EVALUATION OF ALLERGENICITY OF GENETICALLY MODIFIED FOODS 14 (2001), *available at* <http://www.who.int/fsf/GMfood/ConsultationJan2001/report20.pdf>.

<sup>130</sup> Three of the other factors deal with descriptive information regarding the name, source and intended use of the new proteins in the GM food. The last factor deals with the digestibility of the protein; however, allergens can be digestible and studies have shown that the results of industrial testing vary depending on the techniques used and that many of the tests do not accurately simulate the digestive process as the strength of the pepsin is too high. Gregory S. Ladics et al., *Workshop Overview: Approaches to the Assessment of the Allergenic Potential of Food From Genetically Modified Crops*, 73 TOXICOLOGICAL SCIENCES 8, 9 (2003) (this article summarizes a workshop that was presented at the 41st Annual Meeting of the Society of Toxicology held in 2002), *available at* <http://toxsci.oxfordjournals.org/cgi/reprint/73/1/8.pdf>. In addition, the protein that is tested in most cases is created by a "surrogate," a bacterium such as e-coli that is able to produce the proteins easily in amounts necessary to do this testing. Guidance For Industry, *supra* note 127, at 35,688-35,689.

<sup>131</sup> *Id.*

<sup>132</sup> *Id.*



bioequivalent to their counter parts in the original organism. The ENCODE project demonstrated that eighty percent of the products of expression of a transferred gene are new. These mRNA hybrids, the product of the coupling of junk DNA from the donee, and the transferred gene from the donor, have never before existed in nature. Thus, the FDA can no longer claim that the donor product and the donee product are bioequivalent. Because they are not bioequivalent, the FDA will be hard pressed to continue in its position that common experience with the donor product can be used as proxy, or indirect, evidence that the donee product is equally safe.

If the presumptions based on the industrial gene model are no longer scientifically justifiable, should scientists conclude that transferred genes and the products of their expression are GRAS? If they are not GRAS, they must be considered to be food additives, undergo premarket testing and be listed as one of the ingredients on food labels.

### 1. Pre-Market Testing

The new networked model of gene function, epigenetic studies, and the case of the GM peas suggest that premarket testing should both be mandatory and be conducted on the actual products of expression of the new gene. All presumptions based on the old Central Dogma model should be thrown out. This means that actual *in vitro* and *in vivo* studies should be carried out that include serum and animal testing. An example of an appropriate decision tree that is that of the WHO/FAO.<sup>133</sup>

Adding to this testing protocol, epigenetic studies suggest that the GM organism should be tested under all of the environmental conditions to which it will be exposed as the products of the transferred gene's expression could differ depending on the environmental exposure.<sup>134</sup>

### 3. Ingredient Labeling and the Discovery of New Allergens

However, it is important to note that even ramping up testing to an appropriate level will not detect many of the potential allergens as the tests for allergenicity provide vague results, at best. The existing testing protocols for allergenicity, including those recommended by the WHO, can only provide a *probability* of allergenicity that ranges from high to low.<sup>135</sup> There are no existing tests that give an absolute 'yes' or 'no' answer.<sup>136</sup> There is also a

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<sup>133</sup> DISCUSSION PAPER, *supra* note 123, at 7. See also CODEX ALIMENTARIUS, *supra* note 129; FAO/WHO, SAFETY ASPECTS OF GENETICALLY MODIFIED FOODS OF PLANT ORIGIN, *supra* note 129; FAO/WHO, EVALUATION OF ALLERGENICITY OF GENETICALLY MODIFIED FOODS, *supra* note 129.

<sup>134</sup> See *supra* notes 104-110 and accompanying text.

<sup>135</sup> FAO/WHO, SAFETY ASPECTS OF GENETICALLY MODIFIED FOODS OF PLANT ORIGIN, *supra* note 129; FAO/WHO, EVALUATION OF ALLERGENICITY OF GENETICALLY MODIFIED FOODS, *supra* note 129.

<sup>136</sup> "[T]oday, our scientific understanding of food allergy is incomplete, making it

significant chance of both false negative and false positives occurring. This is because the science of allergenicity is in its infancy.<sup>137</sup> Scientists know very little about what causes allergic reactions<sup>138</sup> and new allergens are regularly being discovered.<sup>139</sup>

As the science necessary to accurately evaluate the risks associated with GM food simply does not exist, the only way that allergens created by GM food will be discovered is after a new food is introduced into the food system, exposed to the genetic diversity of the population and triggers a reaction.<sup>140</sup> A

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difficult for food regulatory agencies to evaluate the potential allergenicity of novel foods . . . [and] current federal efforts are insufficient to provide the timely and comprehensive information needed by food safety regulators . . . . This deficit has left food safety regulators without some of the critical tools they need to fully assess the potential allergenicity of novel food products, particularly those developed through biotechnology.” Luca Bucchini & Lynn R. Goldman, *A Snapshot of Federal Research on Food Allergy: Implications for Genetically Modified Food*, Pew Initiative on Food and Biotechnology (2002), <http://pewagbiotech.org/research/allergy.pdf>.

<sup>137</sup> “To properly regulate novel food products and protect public health, scientists, health professionals, and regulators must be able to predict whether new proteins introduced to food have the potential to cause allergic reactions in susceptible individuals. To make such predictions we need to understand what characteristics make a protein allergenic, how people become sensitized to food allergies, how allergic reactions are triggered, and whether safe levels of a potential allergen can be established. Furthermore, we need a comprehensive picture of the prevalence and incidence of food allergy in the U.S. population and how it is changing over time . . . . Although scientists and health professionals have been working on answers to these questions for some time, our understanding of food allergy is still far from complete.” *Id.* at 9. See also Report of the Expert Panel on Food Allergy Research, National Institute of Allergy Research and Infectious Disease, National Institutes of Health, 6 (June 30 and July 1, 2003), available at <http://www.niaid.nih.gov/dait/pdf/11-20-03FAreport1.pdf> (“The Expert Panel on Food Allergy concluded that food allergy research is poised to make significant advances in the prevention and treatment of food allergies and anaphylaxis. New initiatives will eliminate *critical gaps* in understanding GI physiology and immunology and the mechanism of oral tolerance; the pathophysiology of food allergy and anaphylaxis and the molecular characteristics of food allergens.”) (emphasis added) [hereinafter Expert Panel].

<sup>138</sup> “In spite of the extensive efforts to characterize the mechanisms of allergy at both cellular and molecular levels, we still have only a limited understanding of the characteristics that allow a protein to produce a specific IgE response, and that render an individual susceptible to allergenicity.” Ladics, *supra* note 130, at 9.

<sup>139</sup> FAO/WHO, SAFETY ASPECTS OF GENETICALLY MODIFIED FOODS OF PLANT ORIGIN, *supra* note 129; FAO/WHO, EVALUATION OF ALLERGENICITY OF GENETICALLY MODIFIED FOODS, *supra* note 129.

<sup>140</sup> “The more difficult issue is posed by the introduction of novel proteins that have not been previously in the food supply. Without prior exposure data, the ability to predict the potential of the protein to cause an allergic reaction is very limited. This problem became readily apparent in the recent recall of food products that had been inadvertently contaminated with StarLink, a genetically modified corn variety that had not been approved for human food by the Environmental Protection Agency (EPA) because it could not be

comparable example is the introduction of novel substances into the population by the drug industry. The drug industry uses distribution to large populations to flush out adverse reactions to novel substances.<sup>141</sup> The clinical trials mandated by the FDA to establish premarket safety are fairly small and can have relatively low statistical power.<sup>142</sup> Even after this testing, serious adverse effects were not detected for approximately one-half of the drugs on the market until after the drugs received regulatory approval and were made available to the general population.

With novel substances distributed for use as drugs, there is a regulatory recognition that premarket testing will not detect many adverse reactions. For this reason, a rudimentary post-market surveillance system is in place. After the spate of highly-publicized drug withdrawals,<sup>143</sup> including Vioxx, this tracking system is being updated and fortified. Comparably, both premarket safety testing and a post-market surveillance system should be created for the introduction of other novel, man-made substances, such as GM food, into the food supply.

### C. Allergic Reactions

Under the current U.S. food safety system, public health officials have no way of knowing whether GM foods are triggering allergic reactions. Most consumers are unaware of the extent of their exposure to GM food,<sup>144</sup> in spite of the fact that the United States and global production of GM food is growing yearly.<sup>145</sup> While more and more countries are entering the market, the United States continues to be the largest producer of GM foods by a wide margin, placing U.S. consumers on the frontline of exposure to these new, untested ingredients.<sup>146</sup>

Currently, it is highly unlikely that many of the health risks from this exposure can be identified and eliminated. If a consumer eats a GM food in the U.S. and has an allergic reaction for the first time, the consumer will assume the reaction is to the host food and avoid it in the future.<sup>147</sup> For example, if a

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shown that the novel protein in StarLink was not an allergen.” Bucchini & Goldman, *supra* note 136, at 5.

<sup>141</sup> Shelby D. Reed et al., *Use of Larger Versus Smaller Drug-Safety Databases Before Regulatory Approval: The Trade-Offs*, 27 HEALTH AFFAIRS 360-70 (2008).

<sup>142</sup> *Id.* at 360.

<sup>143</sup> H.A. Waxman, *The Lessons of Vioxx – Drug Safety and Sales*, 352 NEW ENG. J. MED. 2576-78 (2005); Rena Steinzor & Margaret Clune, *The Hidden Lesson of the Vioxx Fiasco: Reviving a Hollow FDA*, THE CENTER FOR PROGRESSIVE REFORM (2005) 15-17.

<sup>144</sup> The Pew Initiative on Food and Biotechnology, *supra* note 9.

<sup>145</sup> International Service for the Acquisition of Agr-Biotech Applications, *supra* note 14; Business Wire, *supra* note 14.

<sup>146</sup> International Service for the Acquisition of Agr-Biotech Applications, *supra* note 14; Business Wire, *supra* note 14.

<sup>147</sup> Van Tassel, *supra* note 15, at 1162-63.

consumer eats GM peas and has an allergic reaction, the consumer will assume that she is allergic to peas and will simply avoid eating peas generally in the future. A mild reaction will not warrant a trip to the doctor.<sup>148</sup> So the incident will never be reported to a doctor.<sup>149</sup> If the reaction is moderate to severe,<sup>150</sup> the consumer will be likely to seek medical treatment.<sup>151</sup> However, as the consumer is unaware that she ate a GM food, the adverse reaction will be incorrectly reported as a reaction to the host product (in this example, peas generally), not to a GM food.<sup>152</sup>

This problem is compounded by the fact that data on food allergies is only being collected in small, isolated studies conducted by interested researchers.<sup>153</sup> The Centers for Disease Control and Prevention (“CDC”) does not collect this data and there is no national reporting system in place. While the incidence of food allergies reported to small, independent researchers has risen significantly over the past ten years,<sup>154</sup> there is no way of eliminating GM

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<sup>148</sup> *Id.* at 1163.

<sup>149</sup> *Id.*

<sup>150</sup> See David Kitts et al., *Adverse Reactions to Food Constituents: Allergy, Intolerance, and Auto Immunity*, 75 CAN. J. PHYSIOLOGY & PHARMACOLOGY 241 (1997). Food hypersensitivity is an abnormal reaction resulting from a heightened immunologic response to glycoprotein components in foods. Food allergies involve an IgE response. The classic “immediate” hypersensitivity reactions are hives, asthma, gastrointestinal problems, and anaphylaxis within a few minutes of exposure. Oral allergy syndrome is an immediate reaction largely confined to the mouth. Atopic dermatitis is an eczema-like reaction. Other types of reactions include allergic eosinophilic esophagitis, gastritis, and gastroenterocolitis. There are non-IgE reactions seen exclusively in infants and children, such as dietary protein enterocolitis, proctitis, enteropathy, and celiac disease. These are seen in 1%-2% of children. See *Medication Protects Patients with Peanut Allergies*, National Jewish Medical Research Center, Mar. 10, 2003, <http://www.njc.org/news/peanut.html>; *Anaphalaxis*, National Jewish Medical Research Center, <http://www.njc.org/medfacts/anaphalaxis.html>.

<sup>151</sup> National Jewish Medical Research Center, *supra* note 151.

<sup>152</sup> *Id.*

<sup>153</sup> Bucchini & Goldman, *supra* note 136, at 10 (pointing out that researchers and policy makers lack data on the prevalence, incidence, or trends of food allergy. Tracking data on allergies as a whole indicates an increased incidence of these diseases. However, without appropriate epidemiological data, no conclusions regarding causation can be drawn). The data that supports the conclusion that the total number of food allergies, and their severity, is believed to be increasing is an extrapolation from small, isolated studies. Hugh A. Sampson et al., *Fatal and Near-Fatal Anaphylactic Reactions to Food in Children and Adolescents*, 327 NEW ENG. J. MED. 380, 384 (1992) (“It is our belief and that of other investigators studying food allergy that the frequency of fatal and near fatal food-induced [allergic] reactions has risen over the past several years.”).

<sup>154</sup> Expert Panel, *supra* note 137, at 1 (“Published reports document the increasing prevalence of food allergy and food-induced anaphylaxis; reasons for these increases are poorly understood.”); Susan Dominus, *The Allergy Prison*, N.Y. TIMES, June 10, 2001, at 62-63 (reporting that the incidence of all allergic diseases appears to be on the increase in industrialized societies). See also A. Wesley Burks & J. Steven Stanley, *Food Allergy*, 10

food as a cause.

#### V. DISTRIBUTIONAL JUSTICE AND ACCOUNTABILITY

Because GM ingredients are not listed on food labels, a consumer cannot choose to avoid products that contain GM ingredients. And yet, if there is an injury, who will bear the cost of the loss? In the realm of scientific uncertainty, two types of error can be made. A 'type I' error occurs when "society regulates an activity that appears to be hazardous, but turns out to be harmless (a 'false positive' in the parlance of experimental findings) and resources are needlessly expended."<sup>155</sup> A 'type II' error occurs "when society fails to regulate an activity because the evidence is not initially thought to be strong enough, but that finally turns out to be harmful (a 'false negative')."<sup>156</sup> In the case of GM food, the cost of a type I error will be borne by the companies who produce the GM food. That cost is passed on to all of the consumers who purchase the products.

However, the cost of a type II error will be born only by those consumers who suffer an allergic or toxic injury from the consumption of GM food. Few are aware that, if a consumer is injured by exposure to GM ingredients, she is unlikely to recover under the tort system. There are three basic reasons for this outcome. First, the consumer is unlikely to be aware that the exposure to the GM ingredient caused the injury as she will not be aware that she consumed a GM ingredient.<sup>157</sup> Second, even if the consumer was aware that a GM ingredient caused her injury, with regard to a negligence claim, she must prove fault by showing that the manufacturer could have foreseen the risk of harm.<sup>158</sup> Unfortunately, under the current FDA regulatory system, the rate of the development, marketing and distribution of GM products has far outpaced the science needed to demonstrate its associated risks. This research lag acts to insulate a manufacturer from liability based on a lack of foreseeability.<sup>159</sup> Finally, with regard to both negligence and strict liability claims, the consumer's case will be dismissed unless she can prove that she is a member of a substantial class of people who are at risk for the same reaction under what is commonly referred to as the "idiosyncratic plaintiff defense."<sup>160</sup> This *de minimus* harm liability threshold can range from tens of thousands to millions of people.<sup>161</sup> Of course, as GM food is unlabeled, injured consumers are

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CURRENT OPINION IN PEDIATRICS 588-93 (1998); S. Allan Bock, *Prospective Appraisal of Complaints of Adverse Reactions to Foods in Children During the First 3 Years of Life*, 79 PEDIATRICS 683-88 (1987).

<sup>155</sup> Ashford, *supra* note 44, at 369.

<sup>156</sup> *Id.*

<sup>157</sup> Van Tassel, *supra* note 15, at 1679.

<sup>158</sup> *Id.* at 1683-84.

<sup>159</sup> *Id.* at 1686.

<sup>160</sup> *Id.* at 1680-81.

<sup>161</sup> *Id.* at 1681.

unlikely to recognize what actually caused their injuries. Therefore, collecting the data necessary to make the “member of a substantial class” showing creates an almost impassable barrier to recovery.<sup>162</sup> Even if the products were labeled, it could be years before enough people were injured to reach the large threshold numbers.<sup>163</sup>

Thus, the cost of the losses arising from any injuries will be born by innocent consumers, not the food producers who are reaping the profit from product sales. This leads to a morally incorrect result under principles of distributive justice that counsel that one ought to act in such a manner that no one person or group bears a disproportionate share of benefits or burdens.<sup>164</sup>

#### VI. POST-MARKET SURVEILLANCE

Under the current food safety system, there is no mechanism in place for public health officials to monitor whether the heavy exposure of U.S. consumers to new GM foods is causing allergic or toxic reactions. The new understanding that genetic modification of food creates new, biologically active ingredients, the experience with GM peas and the lack of definitive testing for allergenicity of new proteins all counsel for the establishment of a post-market surveillance system for monitoring for any unintended effects of GM food.

The most practical course of action is for the FDA to acknowledge that the products of the expression of genes transferred from one organism to another are not GRAS and, therefore, must be categorized as food additives. In light of the scientific discoveries discussed herein, this conclusion seems almost inescapable. Recognizing GM ingredients in food as food additives means that premarket testing and ingredient labeling will be required, removing the major obstacle to gathering data on allergenicity and toxicity.

But requiring premarket testing is only half the battle. It is likely that many allergens won't be detected until the novel genetically modified substance is distributed to the general population and exposed to the enormously diverse U.S. gene pool. Thus, a post-market surveillance system must be created. Monitoring this data will provide an early warning system to alert public health officials if there are toxic or allergic reactions to a particular GM food, allowing the product to be recalled quickly and preventing needless injuries to consumers.

As the type of uncertainty over public health risks of GM food is indeterminacy, the FDA should avoid the application of formulaic cost-benefit analysis when performing a risk assessment to decide whether regulations

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<sup>162</sup> *Id.* at 1682.

<sup>163</sup> *Id.*

<sup>164</sup> For a further discussion of the ethical issues involved in the regulation and ingredient labeling of genetically modified animals coming soon to a plate near you, see Katharine A. Van Tassel, *Genetically Modified Animals Coming Soon To A Plate Near You: Ethics, Ingredient Labeling and the New Networked Gene* (work in progress).

creating a post-market surveillance system is warranted. Among other criticisms,<sup>165</sup> cost-benefit analysis reflects an ‘if you can’t quantify it, it does not exist’ framework and produces a single number that fails to disclose who benefits and who pays.<sup>166</sup> The FDA should unlink cost-benefit analysis from risk assessment to avoid being in the position of reacting to public health crises rather than preventing them. Instead, regulators should apply trade-off analysis. Applying trade-off analysis allows for the consideration of new kinds of uncertainties and attendant risk mitigation strategies. Trade-off analysis also factors into the calculus the societal distribution of possible costs and benefits of policies and technologies. Elements of trade-off analysis include:

- the seriousness and irreversibility of the harm addressed;
- the social distribution of possible costs and benefits of policies and technologies;
- the technological options for preventing, arresting, reversing or mitigating possible harm – and the opportunity costs of selecting a given policy option;
- society’s inclinations regarding erring on the side of caution and erring on the side of laxity;
- the nature of uncertainty encountered: classical uncertainty, indeterminance or ignorance?<sup>167</sup>

Application of the above factors to GM food reveals the following: the harm is suffering an allergic or toxic reaction causing physical injury or death; the cost of the loss associated with any harm will be born by innocent consumers while manufacturers reap the profits; the cost of labeling is small and the cost of setting up a web-based reporting system modeled on systems already in place at the FDA is even smaller; consumer surveys indicate that consumers have a significant preference for labeling and notice; and, finally, scientists are no longer operating in ignorance as the state of the science has moved into

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<sup>165</sup> Cost-benefit analysis attempts to describe the consequences of a candidate regulation in monetary terms. “This poses two problems. One is the difficulty, even arbitrariness, of placing a monetary value on human life, health and safety and a healthy environment. Another is by translating all of these consequences into equivalent monetary units, discounting each to current value (since a US\$/Euro invested now is expected to earn interest over time) and aggregating them into a single US\$/Euro value intended to express the net social effect of the government policy, the effects on the economy from investing now in future health, safety and environmental benefits are weighted far more heavily than those benefits that occur in the future, including those to future generations.” Ashford, *supra* note 44, at 367.

<sup>166</sup> *Id.* at 371.

<sup>167</sup> *Id.* For an alternative model presented in the context of the protection of biodiversity hotspots that calls for decision-making that acknowledges, and deals with, different levels of uncertainty, see John Charles Kunich, *The Uncertainty of Life and Death: The Precautionary Principle, Gödel, and the Hotspots Wager*, 17 MICH. STATE J. INT’L L. 1, 30-39 (2008).

indeterminance and the possibility of serious health risks are no longer based on mere speculation. Therefore, as the risk of harm is life threatening and irreversible, the state of the science is indeterminance not ignorance, the cost of the risk mitigation strategy of labeling and post-market surveillance is small, and the public will is to err on the side of caution, trade-off analysis appears to suggest the use of the risk mitigation strategy of labeling.

The application of trade-off analysis results in a recognition that GM ingredient labeling coupled with a post-market tracking will fill in the critical gaps in our public health system and will supply the accountability that is necessary to maintaining a safe food supply as each new GM product is introduced into the food system. This labeling and tracking will also provide the missing link that will allow consumers to recover for personal injury and reflects the inclinations of an overwhelming majority of U.S. citizens in keeping with our democratic society. GM ingredient labeling and post-market tracking easily fits in with the post-market surveillance system contemplated by many of the food safety bills now being proposed in Congress.

## VII. CONCLUSION

The new understanding of the networked gene has shifted the general nature of uncertainty over the public health risks of GM food from ignorance to indeterminacy. In other words, from not knowing what we don't know, to knowing what we don't know. When the FDA first made its choice over how to regulate GM plant foods much less was known regarding gene function. Scientists simply 'did not know what they did not know' about the risks to public health of GM food. Thus, with regard to uncertainty, the scientific decisions and FDA regulatory choices based on those scientific decisions, were made in an environment of ignorance. Acting in ignorance, scientists at the FDA chose to regulate based on a false assumption of bioequivalence.

Now, scientists have a much better grasp of what they don't know and are operating in the realm of indeterminacy with regard to the health risks associated with GM food. They are aware that the assumption of bioequivalence is no longer scientifically supportable. Now, scientists must determine whether the network effects of gene transfers create unintended harmful effects. Thus, scientists are aware of the risks that they must rule out through the systematic study of each transplanted gene as it functions in the new organism and as that new organism responds to environmental triggers.

A large proportion of the U.S. consumers' diet is GM food, reflecting a heavy exposure to novel substances. Now that the nature of the uncertainty the FDA is dealing with is indeterminacy, not ignorance, GM ingredient labeling and post-market surveillance should be required in order to provide for both the transparency and accountability necessary to protect public health. It will be a simple matter to either acknowledge that GM ingredients are food additives requiring labeling under current regulations or to add a provision for identifying GM ingredients on food labels into one of the numerous food safety proposals currently pending before Congress. In addition, post-market



tracking of GM foods can piggy-back onto the post-market tracking system being created for food generally by each of these bills. These measures will provide the safety net necessary to protect public health and allow for compensation of personal injury victims, while, at the same time, allowing GM food technologies to continue to advance to meet pressing world demands for innovative methods of food production.