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**Substantial Equivalence: A Valid International
Sanitary and Phytosanitary Risk Assessment
Objective for Genetically Modified Foods**

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NOTES

SUBSTANTIAL EQUIVALENCE: A VALID INTERNATIONAL SANITARY AND PHYTOSANITARY RISK ASSESSMENT OBJECTIVE FOR GENETICALLY MODIFIED FOODS

INTRODUCTION

Controversy over the human health and safety implications arising out of the consumption of genetically modified (GM) foods has led to widespread debate about how these products should be regulated at the international level.¹ Currently, no generally accepted international human health safety standards exist for the assessment of GM foods.² The novelty of these products raises many valid concerns regarding their potential impact on animal and plant life, as well as on the environment.³ This novelty has led many states to fear the unpredictable impact that GM foods may have on human and environ-

¹ See Marsha A. Echols, *Food Safety Regulation in the European Union and the United States: Different Cultures, Different Laws*, 4 COLUM. J. EUR. L. 525 (1998) (examining how European cultural views affect food safety regulations and lead to a preference for traditional foods over those derived from modern technologies); Katharine E. Gourlie, *NAFTA Countries: Convergence and Fracture*, 51 FOOD & DRUG L.J. 423 (1996) (explaining how the chance for expanded global marketing opportunities through international agreements, which exert regulatory compliance pressure on member countries, outweighs the cost of compliance under those agreements); Stevan M. Pepa, *International Trade and Emerging Genetic Regulatory Regimes*, 29 LAW & POL'Y INT'L BUS. 415 (1998) (examining both the difficulties involved in, and the need to develop, appropriate regulations for products derived from genetic engineering); Jennifer L. Gately, Comment, *Novel Foods and Food Ingredients*, 3 COLUM. J. EUR. L. 317 (1997) (examining a 1997 marketing and labeling regulation for genetically modified foods and food components implemented by the European Union). See generally Robin A. Chadwick, Note, *Regulating Genetically Engineered Microorganisms Under the Toxic Substances Control Act*, 24 HOFSTRA L. REV. 223 (1995) (arguing that since there is no evidence of a health or environmental risk posed by genetically engineered organisms, a reasonable basis must exist for their regulation).

² This Note will evaluate human health and safety issues exclusively; it will not deal with the issues surrounding the current debate over labeling provisions for GM foods.

³ Evaluating existing or potential environmental regulations for GM foods or food products is beyond the scope of this Note.

mental health within their respective territories.⁴ As a result, these states may utilize a regulatory regime that is unduly burdensome and restrictive on importers of GM foods without appropriately evaluating the risks posed by these products. Due to the potential benefits that these products hold, and the inevitability of their widespread distribution in foreign trade, international regulations must be developed that account for the risks of these products and also facilitate their safe entry into international commerce. The development and adoption of these standards should be guided by the Agreement on the Application of Sanitary and Phytosanitary Measures (“SPS Agreement”)⁵ of the World Trade Organization (“WTO”).

The SPS Agreement was designed to guide the development and adoption of international trade regulations relating to human, animal, and plant life or health (sanitary and phytosanitary measures, referred to collectively as “SPS measures”) for WTO Member States.⁶ Two objectives of this agreement are to harmonize these types of measures between WTO Member States⁷ and to assure that SPS measures adopted by a Member are “based on scientific principles and . . . not maintained without sufficient scientific evidence.”⁸ By mandating that SPS measures be based on science, the WTO has provided an objective measuring tool to assure that the SPS measures are not applied arbitrarily and will not result in unjustifiable restrictions on trade.⁹ Thus, designing regulations of GM foods pursuant to the SPS Agreement appears to be the most appropriate method of addressing the health and safety concerns surrounding international trade in these products.¹⁰

⁴ The theoretical possibility of adverse and unpredictable effects of GM foods has led to these fears. The vast majority of these fears, however, are not substantiated by scientific analysis.

⁵ Agreement on the Application of Sanitary and Phytosanitary Measures, April 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1A, LEGAL INSTRUMENTS—RESULTS OF THE URUGUAY ROUND [hereinafter SPS Agreement]. The SPS Agreement defines sanitary and phytosanitary measures in Annex A.

⁶ The term “sanitary” refers to measures concerning human and animal health, and the term “phytosanitary” concerns measures affecting plants. Regulations of GM foods, regarding the human, animal and environmental effects of these products, are sanitary and phytosanitary measures for the purpose of this paper. See SPS Agreement, *supra* note 5, Annex A (defining sanitary and phytosanitary measures).

⁷ See *id.* art. 3, para. 1 (explaining that to harmonize members should base their measures on international standards).

⁸ *Id.* art. 2, para. 2.

⁹ See *id.* art. 2 (stating that members should take, only to the extent necessary, measures not inconsistent with the SPS Agreement, provided they do not discriminate against other members or restrict international trade).

¹⁰ Through the SPS Agreement, the WTO defers to three specialized international organizations for the development and maintenance of these standards—the Codex Alimentarius Commission (“Codex”), the International Plant Protection Convention (“IPPC”), and the International Office of Epizootics (“IOE”). See *id.* Annex A, para. 3. See also Terence P. Stewart & David S. Johanson, *The SPS Agreement of the World Trade Organization and International Organizations: The Roles of the Codex Alimentarius Commission, the International Plant Pro-*

In 1990, the Organization for Economic Co-operation and Development ("OECD")¹¹ launched an effort to develop standards for evaluating the safety of GM foods.¹² This effort culminated in the development of the "substantial equivalence" standard.¹³ This is a comparative standard which evaluates several nutritional, toxicological, immunological, and pathogenic criteria of GM foods. These criteria are then compared with the conventional precursor (the non-genetically-modified parental variety of the food), while paying special attention to the genetic modification that has taken place.¹⁴ The "[s]ubstantial equivalence [standard] is established by demonstrating that the characteristics assessed for the genetically modified organ-

tection Convention, and the International Office of Epizootics, 26 SYRACUSE J. INT'L L. & COM. 27, 28 (1998) (focusing on the three organizations listed in Annex A of the SPS Agreement: Codex, the IPPC, and the IOE). All international sanitary and phytosanitary measures designed to meet the obligations of the SPS Agreement are typically developed by one of these agencies. However, there is no requirement that a measure originate with one of these agencies for it to be eligible to become an SPS measure deferred to by the WTO.

Another possible method of developing appropriate safety measures for GM foods would be to re-negotiate the SPS Agreement if the SPS Agreement proves inadequate to balance all interests. Such a re-negotiation could result in an entirely separate regulatory regime for GM products.

¹¹ The OECD is an international organization composed of 29 countries committed to a market economy and pluralistic democracy. As one of its main functions, the OECD provides member countries a forum for developing and perfecting economic and social policy. However, due to the membership limitations explained in the SPS Agreement, the OECD cannot be an organization to which the WTO defers for the development of standards under the SPS Agreement.

¹² See OECD GROUP OF NATIONAL EXPERTS (GNE) ON SAFETY IN BIOTECHNOLOGY, SAFETY EVALUATION OF FOODS DERIVED BY MODERN BIOTECHNOLOGY—CONCEPTS AND PRINCIPLES 7 (1993) (stating the purpose of the GNE). Concurrently, a joint World Health Organization ("WHO") and Food and Agricultural Organization ("FAO") consultation was convened on the same subject. For the report that resulted from this consultation, see JOINT FAO/WHO CONSULTATION ON THE ASSESSMENT OF BIOTECHNOLOGY IN FOOD PRODUCTION AND PROCESSING AS RELATED TO FOOD SAFETY, STRATEGIES FOR ASSESSING THE SAFETY OF FOODS PRODUCED BY BIOTECHNOLOGY (1991) [hereinafter STRATEGIES].

¹³ Through the course of this effort, WHO-organized workshops involving 60 experts from 19 OECD countries developed this standard. See, e.g., *Application of the Principles of Substantial Equivalence to the Safety Evaluation of Foods or Food Components from Plants Derived by Modern Biotechnology*, Food Safety Unit, World Health Organization, U.N. Doc. WHO/FNU/FOS/95.1 (1995) (discussing the application of substantial equivalence); *Health Aspects of Marker Genes in Genetically Modified Plants*, Food Safety Unit, World Health Organization, U.N. Doc. WHO/FNU/FOS/93.6 (1993) (discussing harmonizing approaches to foods produced by biotechnology). The substantial equivalence standard, once developed, was further refined in subsequent workshops. See OECD, AQUATIC BIOTECHNOLOGY AND FOOD SAFETY 7 (1994) (noting that substantial equivalence was the practical method for dealing with food safety); OECD, FOOD SAFETY EVALUATION 98 (1996) (noting that substantial equivalence is not a very useful test). See generally U.N. FOOD & AGRIC. ORG., BIOTECHNOLOGY AND FOOD SAFETY (1996). This standard has not yet been adopted by any of the acceptable and qualified scientific agencies that are deferred to by the WTO for the development of sanitary and phytosanitary measures. See *supra* note 10 (discussing the organizations which maintain standards under the SPS Agreement).

¹⁴ See *Report of the OECD Workshop on the Toxicological and Nutritional Testing of Novel Foods: Meeting of the Ad Hoc Expert Group on Food Safety*, at 10, OECD Report SG/ICGB(98)1 (1998) [hereinafter *Workshop*] (describing the substantial equivalence standard).

ism, or a specified food product derived therefrom, are equivalent to the same characteristics of the conventional comparator.”¹⁵ If the results of the analysis of these criteria of the GM food fall within the natural variation of the corresponding values of the conventional precursor, then the GM food will be deemed “substantially equivalent” to that precursor. Ideally, once the GM food is demonstrated to be substantially equivalent, the GM food may be imported¹⁶ and no further human and animal health and safety inquiry is necessary.¹⁷ This evaluation will be undertaken by each WTO member state for its individualized examination of each GM food sought to be imported.¹⁸

Substantial equivalence is an appropriate SPS measure for the human and animal health and safety assessment of GM foods and it should be deferred to by the WTO as a default standard for the evaluation of these products. By adopting and implementing this standard, WTO member countries would be able to meet the obligations of the SPS Agreement. This standard has numerous advantages over the alternatives, including an objective scientific basis, a definite analysis endpoint, allowance for WTO member sovereignty in carrying out their own risk assessments, and application to whole classes of GM foods.¹⁹

This Note develops the argument for adopting substantial equivalence as an international food quality standard under the SPS Agreement. The Background section discusses the factual and legal background of the controversy surrounding GM foods, the substantial equivalence standard, and the safety assessments performed pursuant to the SPS Agreement. The Analysis section examines how the sub-

¹⁵ *Id.*

¹⁶ *See id.* (stating that if the food meets substantial equivalence standards, no other safety consideration is needed). If the GM food is determined not to be substantially equivalent to the conventional precursor, the human and animal health and safety inquiry may not end. *See* discussion *infra* Part II.A.1.

¹⁷ Note that even if the GM product is proven to be substantially equivalent to its conventional counterpart, the next step in the evaluation of a GM product should be the performance of appropriate environmental risk assessments. Only through these two safety assessments (food quality and environmental risk), may a GM product be evaluated under the SPS Agreement and allowed to be: (1) imported, (2) imported subject to various safety protocols, or (3) banned from importation in a WTO State. *See* SPS Agreement, *supra* note 5, prologue, Annex A.

¹⁸ The SPS Agreement allows an individual WTO member to undertake its own evaluation of products which raise human, animal, and environmental health and safety concerns based upon its own individualized risk management objectives. *See* SPS Agreement, *supra* note 5, arts. 3, 5 (stating that members may set their own standards, be involved in relevant enforcement organizations, perform their own risk assessments, and assess the costs of risks and measures to avoid the risks).

¹⁹ It is important to note that the substantial equivalence approach does not preclude traditional methods of “on-the-shelf” regulation by individual consumers within a member country. This approach merely advocates an efficient and comprehensive method of allowing individuals within a member state to have a choice. This choice must be an informed one. Therefore, GM foods should be labeled as such. However, it is beyond the scope of this Note to examine the GM product labeling debate.

stantial equivalence standard would operate as an SPS measure, and also describes the advantages of this standard and how it would be implemented by WTO members under the SPS Agreement. In order to delineate the strengths and weaknesses of the substantial equivalence standard, the Analysis section compares this standard with an alternative standard through the review of a hypothetical GM food.

I. BACKGROUND

A. *Factual Background*

1. *Genetically Modified Foods*

Genetically modified foods, in general, are foods and food products derived from the genetic modification of, or addition to, a pre-existing conventional food.²⁰ This process is undertaken in order to add desirable traits to, or delete detrimental traits from, the conventional food. Because genes encoding for added traits are selected from pre-existing organisms, they are not novel in and of themselves. However, the product resulting from the introduction of these traits into a conventional food,²¹ with no history of exhibiting these traits, is novel. The following factual inquiry into the nature of these products is required in order to understand the questions and safety issues surrounding them.

Plants and animals have been bred selectively for desired traits for hundreds of years.²² This technique has created genetic combinations that might never have occurred without human intervention.²³ Genetic modification,²⁴ as a subset of selective breeding utilizing re-

²⁰ In this paper, the term "genetically modified foods" (GM foods) refers to both genetically modified foods and food components.

²¹ Genes encoding for specific traits are introduced to the genome of the conventional food. The genome represents "[t]he total genetic constitution of an organism." PETER H. RAVEN & GEORGE B. JOHNSON, *BIOLOGY G-9* (3d ed. 1992). The resulting genetically modified product then develops and reproduces naturally, similar to its conventional parental precursor.

²² Artificial selection is accomplished by selecting parents with the desired phenotype and breeding those parents with the goal of perpetuating or amplifying the desired trait in the offspring. In-depth analysis of selective breeding is beyond the scope of this Note. For general discussion of this topic, see ROBERT F. WEAVER & PHILIP W. HEDRICK, *GENETICS* 583-88 (2d ed. 1992).

²³ See Leighton Jones, *Science, Medicine, and the Future: Genetically Modified Foods*, 318 *BRIT. MED. J.* 581, 581 (1999).

Just about everything we eat is derived from livestock, crops, and micro-organisms bred specifically to provide food. Humans have also redistributed genes geographically: the soybean is native to Asia but is now grown throughout the Americas, and the potato, native to the American continent, is grown throughout the temperate world. DNA has never been "static," neither naturally nor at the hand of people.

Id.

²⁴ The Food and Drug Administration defines "genetic modification" as the

combinant DNA technology,²⁵ takes this process one step further. This process allows one to transfer specific genes between species while encoding for the outward expression of desired traits or phenotypes. Depending upon the desired outcome, this “between species” transfer of genetic material will convey, amplify, or decrease the expression of the desired trait within the donee species.²⁶ Genetic modification may also reduce or eliminate expression of a naturally occurring gene.²⁷

These techniques are used primarily in agricultural settings for the modification, protection, and enhancement of crops. Examples of the results of this technology include tomatoes that have been developed with the characteristics of delayed ripening and increased shelf

alteration of the genotype of a plant using any technique, new or traditional. “Modification” is used in a broad context to mean the alteration in the composition of food that results from adding, deleting, or changing hereditary traits, irrespective of the method. Modifications may be minor, such as a single mutation that affects one gene, or major alterations of genetic material that affect many genes.

Statement of Policy: Foods Derived From New Plant Varieties, 57 Fed. Reg. 22,984 n.3 (Food and Drug Admin. 1992) [hereinafter Statement of Policy]. See also OECD, *Biotechnology & Food Safety, Frequently Asked Questions* (visited Nov. 20, 1999) <<http://www.oecd.org/subject/biotech/faq.htm>> (discussing genetic engineering).

²⁵ For an excellent overview of recombinant DNA technology, see *Biotechnology and the American Agricultural Industry*, 265 J. AM. MED. ASS’N 1429 (1991):

The manipulation of DNA by recombinant techniques underlies the molecular advances in both medical and agricultural biotechnology. Recombinant DNA is a term that describes the joining or recombining of two or more pieces of DNA, one of which might be the gene fragment of interest and the other a “vector” DNA. DNA derived from bacterium, virus, or plant or animal cell can be recombined with the DNA from a bacteriophage, retrovirus, yeast, or plasmid vector. The “recombinant vector DNA” is then inserted, by chemical or physical means, into a mammalian, plant, or bacterial cell. The gene of interest may then integrate randomly within the host cell DNA or remain as episomal DNA capable of replicating independent of the host. On rare occasions, the gene may combine with and replace or inactivate the resident gene Both integration and independent replication represent stable mechanisms to express a gene of interest in a foreign cell.

Id. at 1430 (emphasis and footnotes omitted).

²⁶ See Statement of Policy, *supra* note 24, at 22,985-86 (noting that DNA manipulations make modifications possible that could not be achieved with traditional breeding methods); *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1429 (noting the ability to enhanced desired traits); Jones, *supra* note 23, at 581 (noting the ability to “switch[] off” particular genes).

²⁷ For an explanation of this approach, the “anti-sense” approach to genetic modification, see *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1429 (discussing the ability to “rapidly improve” desired characteristics); Jones, *supra* note 23, at 583 (discussing the procedure of decreasing the expression of selected genes).

life,²⁸ and commercial crops that have been developed with the desirable traits of pesticide²⁹ and/or viral resistance.³⁰

Genetic modification has significant commercial usefulness and potential. Currently, genetic modification of crops is used to increase production, to resist disease and herbicides, to produce natural pesticides, to enable crops to tolerate long-term storage and resist adverse environmental conditions, and to improve nutritional value and digestibility.³¹ Additional potential commercial uses include the removal of undesirable traits in foods (natural toxicants, antinutrients, and allergens)³² and providing "renewable sources of valuable materials such as vaccines, drugs, [and] bioplastics."³³ The intra-species transfer of genes through this process is significant in that it allows genetic combinations that may not have occurred randomly through nature.³⁴ However, these beneficial applications are not without potential adverse consequences to human, animal,³⁵ and environmental health.³⁶

²⁸ See *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1431 (footnotes omitted) ("Tomatoes have been transfected with 'antisense' gene responsible for polygalacturonase, which solubilizes pectin. Since pectin degradation increases fruit ripening and decreases fruit shelf life, preventing the translation of the message . . . for polygalacturonase [will delay these events].").

²⁹ See *id.* at 1430-31. This source describes the process for producing this resistance in the following manner:

One mechanism for inducing pesticide resistance in plants is to transfer the gene for the delta endotoxin originating from select *Bacillus thuringiensis* subspecies (the Bt protein). When ingested by an insect, the recombinant endotoxin is converted to an active poison that disrupts ion transport of cell membranes in the gut of pests.

Id. (emphasis and footnotes omitted).

³⁰ A gene has been introduced into these plants "that encodes the coat protein of the viral pathogen into the genome of the plant. The expression of the coat protein retards subsequent viral infection and/or replication and spread." *Id.* at 1431.

³¹ See *id.* at 1432 (noting uses for disease resistance, herbicide resistance, and increased tolerance for long-term storage); Jones, *supra* note 23, at 582 (noting uses for resisting herbicides and insects). This listing is not meant to be comprehensive, but it is merely an example of the wide range of current and potential uses of these products.

³² See Jones, *supra* note 23, at 583 (stating that it is possible to manipulate genes for natural toxicants, antinutrients, and allergens).

³³ *Id.*

³⁴ See, e.g., *supra* notes 28-30 (discussing suppression of undesirable traits or enhanced resistances).

³⁵ See *infra* Part I.A.2. (discussing such consequences as allergenicity, gene transfer, pathogenicity, and toxicity).

³⁶ See *infra* note 40 (giving examples of such effects).

2. Potential Public Health Consequences of GM Foods or Food Products³⁷

Genetic modification has the potential to alter the resulting food product in a way that may affect food safety.³⁸ Different safety issues are involved depending on whether the food is derived from microorganisms, plants, or animals.³⁹ The following discussion refers only to direct effects of the GM food on human/animal health and/or life. Discussion of the indirect effects of these products on human or animal health or life by means of their effects on the environment is beyond the scope of this Note.⁴⁰

³⁷ In-depth examination of this issue is beyond the scope of this Note. For an excellent summary, see Jones, *supra* note 23, at 583-84. See also Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Safety Assessment* (visited Nov. 11, 1999) <<http://www.fao.org/esn/biotech/safety.htm>> (discussing the possible adverse effects on food safety posed by genetically altered food and microorganisms, and establishing standards for the evaluation of such products).

³⁸ The Food and Agriculture Organization ("FAO") of the U.N. has delineated various food safety considerations that should take place whether the resultant food product is produced by conventional breeding or by recombinant DNA technology. These include:

- the direct consequences (e.g. nutritional, toxic or allergenic effects) of the presence in foods of new gene products encoded by genes introduced during genetic modification;
- the direct consequences of altered levels of existing gene products encoded by genes introduced or modified during genetic modification;
- the indirect consequences of the effects of any new gene product(s), or of altered levels of existing gene product(s), on the metabolism of the food source organism leading to the presence of new components or altered levels of existing components;
- the consequences of mutations caused by the process of genetic modification of the food source organism, such as the interruption of coding or control sequences or the activation of latent genes, leading to the presence of new components or altered levels of existing components;
- the consequences of gene transfer to gastrointestinal microflora from ingested genetically modified organisms and/or foods or food components derived from them; and
- the potential for adverse health effects associated with genetically modified food microorganisms.

Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Food Safety Considerations*, Sept. 30, 1996 (visited Nov. 11, 1999) <<http://www.fao.org/esn/biotech/safety.htm>>.

³⁹ The main considerations for each one of these categories are: pathogenicity and toxicity for micro-organisms; toxicity and allergenicity for plants; and allergenicity and pathogenicity for animals. The considerations are discussed *infra*.

⁴⁰ The following are examples of the potential adverse indirect effects of introducing GM crops into the environment:

- [E]ffects on population dynamics in the receiving environment through effects on non-target species which may occur directly or indirectly, for example the reduction of an important food or habitat resource which other organisms may depend on for survival;
- [E]ffects on biogeochemistry, for example changes in nitrogen and carbon recycling through GM crops affecting organisms which are important in soil decomposition processes;

a. Allergenicity

The Food and Agricultural Organization (“FAO”)⁴¹ has defined “allergy” as “a hypersensitive state acquired through exposure to a particular allergen, [or] re-exposure bringing to light an altered capacity to react by an immune response.”⁴² In some cases, this reaction can lead to anaphylactic shock and death.⁴³ Allergens are typically proteins and are found in many food products.⁴⁴ Because DNA encodes for specific proteins, the introduction of foreign DNA into another organism may allow transference of food allergenicity. This possibility is increased dramatically when the donor organism contains known allergens.⁴⁵ These types of GM products warrant extra testing to determine if allergens have been transferred.⁴⁶ Even if the donor organism does not have any history of allergenicity or does not contain any known allergens, the inquiry is not over. Further analysis may be required in order to determine lack of allergenicity through the evaluation of the GM food, while paying particular attention to several common characteristics of known allergens. Criteria that may be evaluated in this analysis include: (1) molecular weight (most allergens have a specific molecular weight range); (2) amino acid se-

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- [T]he dispersal of the GM crop in the environment through possible increased persistence, invasiveness and competitiveness with native plan [sic] species, which could change the population dynamics of the release site and the surrounding environment. For example, if native plant species suffer severe competition with an invasive plant and decline, there would also be reductions in the animal species which directly and indirectly depend on them for survival.
 - [T]ransfer of the inserted genetic material to other crops or native plants, through pollination by wind or insects, could cause adverse effects. For example the inheritance of pest resistance genes in closely related native plant species may confer a significant selective advantage over other native species, because feeding by herbivores such as insects, slugs or birds is an important factor in controlling population growth in plants. These hybrid native plants could become more competitive and potentially invasive . . .

Advisory Committee on Releases to the Environment, Department of the Environment, Transport and the Regions, *The Commercial Use of Genetically Modified Crops in the United Kingdom: The Potential Wider Impact on Farmland Wildlife* (visited Nov. 12, 1999) <<http://www.environment.detr.gov.uk/acre/wildlife/02.htm>> (emphasis omitted).

⁴¹ The Food and Agricultural Organization is an autonomous agency within the United Nations charged with the mandate of raising levels of nutrition, standards of living, and improving agricultural productivity.

⁴² *Safety Assessment of New Foods: Results of an OECD Survey of Serum Banks For Allergenicity Testing, and Use of Databases*, at 11, OECD Report SG/ICGB(97)1 (1997) (visited Oct. 22, 2000) <<http://www.oecd.org/ehs/ehsmono/surveydrEN.pdf>> [hereinafter *Safety Assessment*].

⁴³ See *id.*

⁴⁴ Most of these products are fairly well-known, such as fish, peanuts, soybeans, milk, eggs, shellfish, wheat, and tree nuts.

⁴⁵ See *Safety Assessment*, *supra* note 42, at 15 (“Methods exist to predict the potential allergenicity of proteins in food but they are of limited value and they are not infallible.”).

⁴⁶ See *Workshop*, *supra* note 14, § 5.1 (“Sera from individuals documented to be sensitive to that specific food source should be used in validated *in vitro* assays to establish that the transferred gene does not encode an allergen.”).

quence homology to known allergens (comparison should be made against a molecular weight database in order to screen for immunologically significant sequence similarities to known allergens); (3) heat and processing stability (if the product being evaluated is typically cooked prior to consumption, then there is a decreased risk); and (4) the effect of pH and/or gastric juices (allergens are typically resistant to these).⁴⁷ In addition, various *in vitro*⁴⁸ and human *in vivo*⁴⁹ allergenicity testing methodologies may provide reliable information about the existence of known allergens in GM foods or food products.⁵⁰

b. Gene Transfer

The genetic modification of a conventional food through the incorporation of foreign genes typically requires the introduction of more genes than specifically encode for the desired trait within the conventional precursor. These “additional” genes may be non-physiologically active genes (inadvertently or unavoidably included), or “functional” genes specifically coupled with the genes which are effecting the desired genetic modification (purposely included). Genes encoding for antibiotic resistance, referred to as “marker genes,” are frequently used in the “functional” capacity.⁵¹ These antibiotic resistance genes are incorporated into the package of material introduced into the parental precursor for a very specific reason. The incorporation of these genes allows researchers to identify GM material in subsequent generations of the product—“[a]ll cells containing the [antibiotic resistance gene] will be resistant to the [corresponding] antibiotic and, unlike cells that do not have the gene of interest, will be selected for on a medium containing the antibiotic.”⁵² This process

⁴⁷ See Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Special Issues*, Sept. 30, 1996 (visited Nov. 11, 1999) <<http://www.fao.org/es/esn/biotech/six.htm>> (proposing that the source, molecular weight, amino acid sequence, processing stability, resistance to acidity, and prevalence in edible materials of a genetically modified protein when predicting allergenicity). See also *Safety Assessment*, *supra* note 42, at 11 (suggesting that molecular weight, resistance to processing and digestion, prevalence in food products, and amino acid sequences similar to known allergens should be factored into predictions of allergenicity).

⁴⁸ An artificial environment outside of the body of a living organism.

⁴⁹ Within a living organism.

⁵⁰ See *Safety Assessment*, *supra* note 42, at 12-13 (outlining a number of *in vivo* and *in vitro* tests for determining allergenicity). *In vitro* tests include: radioallergosorbent (“RAST”), RAST inhibition, crossed immunoelectrophoresis (“CIE”), crossed radioimmunolectrophoresis (“CRIE”), and sodium dodecyl sulphate-polyacrylamide gel electrophoresis (“SDS-PAGE”); *in vivo* tests include the double-blind placebo-controlled food challenge (“DBPCFC”) and the skin-prick test. See *id.* (explaining the procedures and purposes of each of these tests).

⁵¹ See *id.* “Marker genes” are important for research purposes because they allow investigators to monitor whether the foreign DNA introduced into plants has successfully integrated into the host plant DNA. This is accomplished by the subsequent treatment of the plant with the appropriate antibiotic; if the incorporation has been successful all plant cells containing the antibiotic resistance gene will survive the antibiotic treatment.

⁵² Jones, *supra* note 23, at 583.

allows selection for genetically transformed cells and the subsequent development of a "pure" GM food containing only the native and specifically introduced desired genes. Although utilizing these marker genes aids the development of GM products, their residual existence in foods that reach the consumer raises numerous health concerns.⁵³

One of the major fears surrounding the consumption of GM foods is the potential transference of genetic material, including marker genes, to a consumer of the GM food. Though this is an extremely unlikely event,⁵⁴ there is a *theoretical possibility* that an introduced gene may be transferred from a GM food to a consumer of that food.⁵⁵ The significance of this event is that the transference of, for instance, an antibiotic resistance gene to a person presents the

⁵³ Some of these fears are related to the potential, though unlikely, gene transference and expression of the marker genes within the genome of the consumer. This potentiality is discussed *infra*.

⁵⁴ The research for this project did not uncover any scientifically demonstrated evidence of this event occurring.

There are several steps that would have to occur for gene transfer to take place:

- the plant DNA would have to be released from the plant tissue or cells and survive in the presence of the hostile environment of the GI tract, including exposure to gastric acid and nucleases;
- the recipient microorganisms would have to be competent for transformation;
- the recipient microorganisms would have to bind the DNA to be transferred;
- the DNA would have to penetrate the cell wall and translocate across the cell membrane;
- the DNA would have to survive the restriction/modification system developed by the microorganism to degrade foreign DNA; and
- the DNA would have to be integrated into the host genome or plasmid, which requires at least 20 base pairs in a complete homologous DNA sequence for significant recombination at both ends of the foreign DNA.

See Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Special Issues*, *supra* note 47.

⁵⁵ "GM food" is used here for simplicity's sake. In actuality, gene transfer would be limited to the transfer of a gene from a genetically modified organism to microorganisms existing in the gastrointestinal tract of the consumer. Gene transfer involves "the transfer of an introduced gene from material derived from a genetically modified organism [(GMO)] to microorganisms in the gastrointestinal (GI) tract, in such a way that the gene can be successfully incorporated and expressed." *Id.*

However: "Evidence to date suggests that the resistance markers are *not* transposable between ingested plant material and potentially pathogenic microorganisms, although further evaluation is indicated." *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1430.

Gene transfer between microorganisms is a more likely and well understood method of transfer of genetic information. See Statement of Policy, *supra* note 24, at 10-11. Though this method has never been documented within the GI tract, the possibility cannot be ruled out. The transferred genetic material must, to produce any significant health consequences, convey some sort of selective advantage to the recipient microorganism over the other indigenous microorganisms so that the lineage of that or those specific microorganism(s) may flourish. (For example: phage resistance, virulence, adherence, substrate utilization, or production of bacterial antibiotics.) With a selective advantage, the transferred genetic material has a dramatically increased chance of being replicated within the host organism/micro-organism. This replication could manifest itself as various disease states within the host organism. See *id.*

chance of that person developing microbial antibiotic resistance to the specific antibiotic resistance marker used in the GM food.⁵⁶ Potential antibiotic resistance is significant because some of the most-used marker genes are also frequently used as therapeutic antibiotics.⁵⁷ Thus, use of these markers may reduce the overall efficacy of these very effective antibiotics. Though the chance of transfer is quite small, it was real enough to prompt the FAO and World Health Organization (“WHO”) to form an expert consultation with the purpose of evaluating “conditions or circumstances in which antibiotic marker gene(s) should not be used in [GM] plants intended for commercial use and . . . to define those conditions/circumstances.”⁵⁸

c. Pathogenicity of Microorganisms

Genetically modified microorganisms may be utilized in processing foods or contained within the final food product. The transfer of these GM microorganisms through food to the consumer poses a significant health risk if these microorganisms are potentially pathogenic.⁵⁹ A pathogen is an agent, such as bacteria, capable of causing disease. Because a “very large proportion of a pathogen’s genetic material is devoted to generating its pathogenicity,”⁶⁰ it is possible that the genetic modification of the pathogen will cause increased virulence, whether the modification was intentional or not.⁶¹ Disease

⁵⁶ If an antibiotic resistance gene marker were to be transferred and expressed in the GI tract, it might then result in antibiotic resistance to that specific marker. The antibiotic resistance genes most frequently used as markers induce resistance to kanamycin, chloramphenicol, gentamycin, and trimethoprim, all widely used therapeutic antibiotics in humans. See *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1430.

⁵⁷ See Statement of Policy, *supra* note 24, at 22,987-88 (discussing the use of the common therapeutic antibiotic kanamycin as a selector for genetically modified foods); Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Special Issues*, *supra* note 47 (discussing the use of therapeutic antibiotics in the selection of genetically modified cells and the possibility that antibiotic resistance selector genes from such foods could be transferred to microorganisms in the gastrointestinal tract). In addition to the possibility of the transference of microbial antibiotic resistance there is a possibility of therapeutic antibiotic degradation in the digestive tract. This would happen through the existence of residual antibiotic resistance proteins in the digestive tract, directly breaking down the antibiotics. See *id.*

⁵⁸ Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Special Issues*, *supra* note 47. See also Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Conclusions and Recommendation* (visited Nov. 11, 1999) <<http://www.fao.org/es/esn/biotech/conclude.htm>> (describing the reasons the FAO and WHO conducted the expert consultation).

⁵⁹ Pathogenic microorganisms have the ability to cause disease. See Chadwick, *supra* note 1, at 224 n.3. For purposes of this Note, this discussion is limited to the effect of pathogenic microorganisms on humans and does not explore the issues surrounding potential pathogenic effects on plants and other animals. These potential effects may have significant detrimental environmental consequences.

⁶⁰ *Id.*

⁶¹ This possibility is speculative because there has not been sufficient experimentation with genetically modified microorganisms on this subject. See *id.* at 228 (stating that although no known environmental or health problems have resulted from genetically engineered microorganisms, our lack of experience in the field requires caution). Virulence is defined as “the rela-

risks may be realized only if GM foods containing viable pathogens are passed on to the consumer.⁶² If these foods are subsequently consumed without preparation, or if preparation of the food, such as heating, does not destroy the pathogen, the consumer is at considerable risk.⁶³ Microorganisms that pose the most obvious risks are those with a history of causing disease in humans. Until more is known about genetic exchange between microorganisms,⁶⁴ known pathogens should not be genetically modified with the purpose of developing, or becoming part of, foods or food components.⁶⁵

d. Toxicity

Humans consume many species of plants that contain varying amounts of toxins in such a small concentration (or of a type) that they are harmless.⁶⁶ Many of these toxins are processed out during the development of the plant or are effectively neutralized through preparation for consumption.⁶⁷ Genetic modification may activate or stimulate toxin production,⁶⁸ thus unpredictably increasing toxin levels in plants.⁶⁹

Although it may at first appear counterintuitive, inducing an increased level in toxicity through genetic modification may be a planned event without adverse human health consequences. This may be the case if the toxin is neutralized during preparation for consump-

tive ability of an individual strain to cause disease under defined conditions, for example, in different types of organisms." *Id.* at 224 n.3. Chadwick notes that "minor genetic changes may not destroy this pathogenicity. In fact, when the recipient of genetic material is a pathogen, that genetically engineered pathogen may acquire *increased* virulence, and thus be able to infect new types of organisms." *Id.* (emphasis added).

⁶² "Viability" means capable of living or developing under favorable conditions to the pathogen. Pathogens may be single-celled organisms. *See id.*

⁶³ Because this discussion is examining *potential* risk, this risk will be assumed to exist even if (1) the pathogen has no history of developing disease in humans, and (2) the pathogen, prior to genetic modification, has been proven not to develop disease in humans.

⁶⁴ Appropriate studies would focus on the effects of genetic modification on virulence and pathogenicity (whether the pathogenicity is enhanced or induced).

⁶⁵ "Known pathogens" refers to microorganisms which are pathogenic to organisms other than humans (e.g., plants and animals) as well as to humans.

For an excellent analysis of risk regulations of genetically engineered microorganisms in the U.S. and the numerous issues surrounding this complicated area, see generally Chadwick, *supra* note 1.

⁶⁶ Statement of Policy, *supra* note 24, at 22,987. This discussion of toxins does not include allergenic factors discussed *supra*.

⁶⁷ *See id.* at 22,987 (evaluating a few types of foods such as legumes, cereals and cruciferae, which contain endogenous toxins).

⁶⁸ *See id.* ("[S]ilent pathways may be activated by mutations, chromosomal rearrangements, or new regulatory regions introduced during breeding, and toxicants hitherto not associated with a plant species may thereby be produced.")

⁶⁹ Experience indicates, however, that the chance of the development of unknown or unexpected toxins in plants that have a long history of safe use is very low. *See id.* (addressing the possibility that dormant metabolic pathways in plants may be activated by genetic modification, leading to increased toxicity, but then dismissing the possibility as remote).

tion or if it has no adverse physiological effects in humans. As an example, toxin production may be induced in a GM organism to create an indigenous pesticide in a plant.⁷⁰ The toxin produced in this way may not be toxic to the consumer.⁷¹ The main concern here is the possible exposure of humans to an increased toxicological risk. Though still in development, a test which may accurately predict the effect of toxins on specific populations exists.⁷² This test should be utilized when a GM food presents a risk of increased toxicity over its conventional counterpart.

e. Unexpected Effects of Genetic Modification

Genetic modification may have other unexpected deleterious effects in the GM food in addition to (or completely separate from) toxic, pathogenic, allergenic, and immunological effects.⁷³ These changes may be the only effects of the modification, or they may result in addition to the desired changes. Nevertheless, the reasoning behind initiating genetic modification of the particular host species is to effect a specific change; without that specific change, the experiment will fail.⁷⁴ If the change comes in addition to unexpected effects, methods of diagnosing the existence and magnitude of these

⁷⁰ See *Biotechnology and the American Agricultural Industry*, *supra* note 25, at 1430-31. This process is described in the following manner:

One mechanism for inducing pesticide resistance in plants is to transfer the gene for the delta endotoxin originating from select *Bacillus thuringiensis* subspecies (the Bt protein). When ingested by an insect, the recombinant endotoxin is converted to an active poison that disrupts ion transport of cell membranes in the gut of pests One public health concern is whether the concentration of the Bt protein in the transgenic plant exceeds the concentration of the exogenously applied toxin following plant processing. Whereas the toxin contained within the pesticide spray may degrade or wash away, minimizing human exposure, the protein produced by the plant may be constitutively present in high concentrations.

. . . .
 . . . [H]erbicides destroy weeds by inactivating an essential metabolic enzyme that is present in the targeted weeds as well as the crop plant. To avoid destruction, the genetically modified crop plants have been engineered to produce an enzyme less sensitive to the herbicide, produce greater quantities of endogenous enzyme, or produce an enzyme that inactivates the herbicide [C]ritics contend that the use of herbicide-resistant plants will result in greater application of herbicides

Id. (emphasis omitted) (footnotes omitted).

⁷¹ The Bt endotoxin "produces no apparent toxic effects in mammals, fish, birds, [and] most plants In fact, the Bt endotoxin has been used in a pesticide spray for the last 30 years." *Id.* at 1431.

⁷² See *Workshop*, *supra* note 14, at 15.

⁷³ *Id.* at 8 ("Virtually all breeding techniques have potential to create unexpected effects.")

⁷⁴ The experiment will be a failure unless the intended genetic modification produces other intended desirable effects. These effects must also be reproducible and apparent to researchers.

types of effects must be developed.⁷⁵ This diagnosis may appropriately come at the time when researchers are seeking to establish the substantial equivalence of the GM food to its conventional counterpart.⁷⁶ If the resultant product contains traits that are detrimental to human health, then it follows that substantial equivalence may not be demonstrated.⁷⁷

B. Legal Background

1. The SPS Agreement

The WTO is the only agency that oversees the rules of international trade.⁷⁸ In this capacity the WTO is responsible for ensuring that trade flows smoothly between member countries by developing and maintaining international trade standards and resolving disputes. The WTO is comprised of numerous countries with differing priorities and values. This regime must be on the lookout for members imposing trade restrictions on imported products, labeled as health and environmental safety measures, but which are in fact protectionist measures aimed at foreign producers. When a member faces a possible violation of the SPS Agreement in this manner, the ultimate responsibility rests on this member to challenge the sanitary and phytosanitary measures of the other member.⁷⁹ Measures in violation of the SPS Agreement may impose undue costs on foreign producers without a legitimate safety objective. In order to maintain free flowing trade between members, the WTO must identify and eliminate arbitrary and disguised restrictions on trade. It is understood that safety is of prime importance and that different cultural safety ideals of WTO members must be respected. The SPS Agreement is an attempt by the WTO to address these concerns while providing an objective method for evaluating the safety measures of members.

The SPS Agreement⁸⁰ was designed to “harmonize[] sanitary and phytosanitary measures between [WTO] members.”⁸¹ Through this

⁷⁵ See *Workshop*, *supra* note 14, at 8 (“Plant breeders using well established practices have successfully identified and eliminated plants that exhibit unexpected, adverse traits prior to commercial use.”).

⁷⁶ See discussion *infra* Part I.C.1 (discussing application of substantial equivalence standard).

⁷⁷ See discussion *infra* Part I.C.1 (discussing how a GM food can fail under the substantial equivalence standard).

⁷⁸ For general information about the WTO, see WTO, *What is the WTO?* (visited Sept. 21, 2000) <http://www.wto.org/english/thewto_e/whatis_e/whatis_e.htm>.

⁷⁹ See SPS Agreement, *supra* note 5, art. 5, para. 8 (stating situations when complaints about members may be made).

⁸⁰ For a more detailed analysis of the SPS Agreement, see generally John J. Barcelo III, *Product Standards to Protect the Local Environment—The GATT and the Uruguay Round Sanitary and Phytosanitary Agreement*, 27 CORNELL INT’L L.J. 755 (1994).

⁸¹ SPS Agreement, *supra* note 5, prologue.

harmonization objective, the WTO sought to establish similar SPS measures for all members in order to provide predictable regulations of designated products. This goal was to be achieved by developing a “multilateral framework of rules and disciplines to guide the development, adoption and enforcement of sanitary and phytosanitary measures in order to minimize their negative effects on trade.”⁸² This design was established in order to prevent member countries from adopting animal or plant health standards that were disguised or unjustified restrictions on international trade.⁸³ These types of restrictions were typically based on cultural values or political ideals, and thus, were not predictable to exporting members. The WTO sought to gain the value of a predictable trade regime, as well as allow members to protect themselves, through the use of science as an objective measurement of sanitary and phytosanitary measures.⁸⁴ Science is used as the measurement of the validity of a member’s safety measures because it provides reproducible objective measurements and results.⁸⁵

a. *WTO Interpretation of the SPS Agreement*

Due to the tremendous scope of the SPS Agreement, much of the language used in the Agreement is broad, slightly ambiguous, and open to various interpretations. In order to predict how a proposed SPS measure will be evaluated under the SPS Agreement, one must rely on the interpretation of the Agreement by the WTO dispute settlement system, which is charged with the responsibility of interpreting international agreements in force under the WTO.⁸⁶ This is an essential part of the dispute settlement system developed to arbitrate disputes arising under treaties governed by the WTO. To date there have been three disputes involving the SPS Agreement.⁸⁷

⁸² *Id.*

⁸³ An inherent conflict exists between the SPS Agreement objectives of harmonizing SPS measures between members and allowing members to base their individual SPS measures on their individual risk management objectives. The economic interests underlying the SPS Agreement will lead to an inevitable, though not necessarily appropriate, compromise between these two factors. Evaluating the scope of this conflict may become necessary if the many issues surrounding GM foods cannot be adequately addressed by the current version of the SPS Agreement. *See supra* note 10 (discussing the re-negotiation of the SPS Agreement).

⁸⁴ *See* SPS Agreement, *supra* note 5, prologue (requiring sanitary and phytosanitary measures maintained by members to have a scientific justification).

⁸⁵ Science is viewed by the SPS Agreement as a method of cutting through political ideals with objective measurements and values. However, there always exists a level of uncertainty in scientific values, and certain scientific results do not necessarily correspond to detrimental human, animal and environmental health effects.

⁸⁶ *See generally* WTO, *Understanding on Rules and Procedures Governing the Settling of Disputes* (visited Oct. 23, 2000) <www.wto.org/wto/english/docs_e/legal_e/final_e.htm> [hereinafter *WTO, Rules*] (listing rules and procedures on dispute settlement).

⁸⁷ *See Report of the Panel on Japan—Measures Affecting Agricultural Products*, WTO Doc. WT/DS76/R (October 27, 1998) (complaint by United States); *Report of the Appellate*

The SPS Agreement applies exclusively to sanitary and phytosanitary measures.⁸⁸ In order to determine if the international regulation of GM foods is governed by the SPS Agreement, two questions must be answered. First, is the regulation meant “to protect animal or plant life or health”?⁸⁹ Second, does the measure protect against “food-borne” risks or against pest or disease related risks?⁹⁰ If both of these questions are answered in the affirmative, and the regulation affects international trade, then it is covered by the SPS Agreement.

Once it is determined that the regulation is governed by the SPS Agreement, one must evaluate the scientific risk assessments in place under the regulation. Examination of a safety regulation under the SPS Agreement requires evaluation of the sufficiency of scientific evidence supporting the regulation.⁹¹ The sufficiency requirement consists of fulfilling two criteria: (1) adequate scientific evidence supporting the regulation affecting the product, and (2) “a rational or objective relationship between the SPS measure and the scientific evidence.”⁹² These criteria form the basis of the justification for the SPS measure in question.⁹³ Due to the wide range of possible sanitary and phytosanitary measures, the sufficiency requirement must be evaluated on a case-by-case basis.⁹⁴ In order to enact an SPS measure, member states must either perform independent scientific testing required by the measure or rely on the sufficiency of testing per-

Body on Japan—Measures Affecting Agricultural Products, WTO Doc. WT/DS76/AB/R (Feb. 22, 1999) [hereinafter *Japan Appellate Body Report*]; *Report of the Panel on Australia—Measures Affecting the Importation of Salmon*, WTO Doc. WT/DS18/R (June 12, 1998) (complaint by Canada); *Report of the Appellate Body on Australia—Measures Affecting the Importation of Salmon*, WTO Doc. WT/DS18/AB/R (Oct. 20, 1998); *Report of the Panels on European Communities—Measures Affecting Meat and Meat Products (Hormones)*, WTO Doc. WT/DS26/R/USA (Aug. 18, 1997) (complaint by the United States); *Report of the Appellate Body on European Communities—Measures Affecting Meat and Meat Products (Hormones)*, WTO Doc. WT/DS26/AB/R (Jan. 16, 1998) [hereinafter *European Appellate Body Report*].

⁸⁸ This description of the interpretation of the SPS Agreement by the WTO Appellate Body is meant only as an overview. For a detailed analysis of this topic, see generally Joost Pauwelyn, *The WTO Agreement on Sanitary and Phytosanitary (SPS) Measures as Applied in the First Three SPS Disputes: EC-Hormones, Australia-Salmon and Japan-Varietals*, 2 J. INT'L ECON. L. 641 (1999).

⁸⁹ SPS Agreement, *supra* note 5, Annex A, para. 1. See Pauwelyn, *supra* note 88, at 643 (explaining that this requirement is often a subjective determination).

⁹⁰ See Pauwelyn, *supra* note 88, at 643 (explaining that this portion of the inquiry is more of an objective evaluation).

⁹¹ See SPS Agreement, *supra* note 5, art. 2, para. 2 (“[A]ny sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based upon scientific principles and is not maintained without sufficient scientific evidence . . .”).

⁹² Pauwelyn, *supra* note 88, at 645 (“‘Sufficiency’ requires the existence of a sufficient or adequate relationship between . . . the SPS measure and the scientific evidence . . . [and] sufficient scientific evidence requires that there be a rational or objective relationship between the SPS measure and the scientific evidence.”).

⁹³ See *Japan Appellate Body Report*, *supra* note 87, para. 82

⁹⁴ See *id.*

formed by another member pursuant to the same measure.⁹⁵ Regardless of where the scientific testing is performed, it may always be challenged by another WTO member state.

A member challenging an SPS measure of another member must initially file a complaint specifying the measure or products in controversy and the claim being made.⁹⁶ A WTO dispute settlement committee is then established for the purpose of addressing these claims.⁹⁷ The findings of the committee are limited to the criteria set forth in the complaint, although it need not address them all.⁹⁸ The party "asserting a fact (e.g., the existence of a relevant international standard), claim (e.g., a claim that an SPS measure is not maintained with sufficient scientific evidence), or defense bears the burden to prove it."⁹⁹ The committee is limited to an objective assessment of the facts presented—it cannot initiate its own risk assessment, develop its own facts, and then tell the member the measure it *should* have adopted.¹⁰⁰

b. International Regulatory Organizations

The SPS Agreement lists three international organizations as having the responsibility for developing and maintaining international sanitary and phytosanitary standards based on their respective areas of expertise.¹⁰¹ For this analysis, the only two agencies of relevance are Codex and the IPPC.¹⁰² Codex, in particular, is responsible for establishing standards relating to human health and would appear to be the proper organization for developing human and animal health standards relating to genetically modified foods. In June 1999, however, the leaders of the leading industrial countries invited the OECD to review food safety aspects of GM foods.¹⁰³ Though the OECD has

⁹⁵ The SPS Agreement allows member countries to rely on studies performed by other member countries that have enacted the identical international standard. See SPS Agreement, *supra* note 5, art. 4, para. 1.

⁹⁶ See WTO, *Rules*, *supra* note 86, art. 3, para. 8. See also Pauwelyn, *supra* note 88, at 659-60 (explaining which party bears the burden of proof).

⁹⁷ See WTO, *Rules*, *supra* note 86, art. 2, para. 1 (creating rules and procedures on dispute settlement).

⁹⁸ See Pauwelyn, *supra* note 88, at 659.

⁹⁹ *European Appellate Body Report*, *supra* note 87, para. 104. This proof must come by establishing a *prima facie* case, which is defined as "one which, in the absence of effective refutation by the defending party, requires a panel, as a matter of law, to rule in favor of the complaining party presenting the *prima facie* case." *Id.*

¹⁰⁰ See Pauwelyn, *supra* note 88, at 659.

¹⁰¹ These agencies are Codex, the IPPC, and the IOE. See *supra* note 10. See also SPS Agreement, *supra* note 5, art. 3, para. 3 (stating criteria for adopting the sanitary or phytosanitary measures).

¹⁰² See *supra* note 10. Codex is relevant for human health issues surrounding genetically modified foods; the IPPC is relevant for environmental concerns of these products.

¹⁰³ See OECD, *Food Safety and Biotechnology: Next Steps on the Recent G8 Request to OECD*, (visited Nov. 5, 1999) <<http://www.oecd.org/media/reference/index1999a.htm>>. Both

considerable experience in the field of biotechnology, and has the advantage of combining both scientific standard and international policy development capabilities, it is still primarily a political organization. The political nature of this organization indicates that it is virtually impossible for this agency to develop purely scientific standards that are not influenced by political motivations. And, more importantly, though the OECD has recently added new members, it is not open for membership to all WTO members—a prerequisite for a standard setting organization under the SPS Agreement.¹⁰⁴ Thus, the findings of the OECD Group on the Harmonization of Regulatory Oversight in Biotechnology will not be adopted as international standards for GM foods until they are first adopted or recognized by Codex and subsequently deferred to by the WTO.¹⁰⁵

2. Risk Assessments

The SPS Agreement requires all sanitary and phytosanitary measures adopted by WTO members to be based on a risk assessment¹⁰⁶ of the effects of the product being regulated on the life or health of humans, animals, or plants.¹⁰⁷ These risk assessments must

Codex and the OECD are ancillary organizations under the WHO. The OECD has been asked to investigate food safety rather than Codex or other international organizations because the OECD has been building expertise on biotechnology for more than a decade and has excellent capabilities for dealing with all aspects of the issue using a science-based, rules-based approach. As an example can be cited the work of the Group of National Experts on Safety in Biotechnology which developed science based safety assessment principles that underlie many international agreements and the OECD's pioneering work on the concept of 'substantial equivalence' which is now accepted world-wide by food safety assessment experts.

OECD, *Biotechnology & Food Safety, Frequently Asked Questions*, *supra* note 24.

¹⁰⁴ See *supra* note 11 (discussing the makeup and function of the OECD).

¹⁰⁵ See *id.* (discussing the relationship between the OECD and the WTO).

¹⁰⁶ Annex A of the SPS Agreement defines "risk assessment," as it pertains to food, as "the evaluation of the potential for adverse effects on human or animal health arising from the presence of additives, contaminants, toxins or disease-causing organisms in food, beverages or feedstuffs." SPS Agreement, *supra* note 5, Annex A, para. 4.

¹⁰⁷ See *id.* art. 5, para. 1 ("Members shall ensure that their sanitary or phytosanitary measures are based on an assessment . . . of the risks to human, animal or plant life or health . . ."). Professor Pauwelyn provides an excellent analysis of risk assessment as it pertains to the SPS Agreement in his article:

For [food-borne and disease or pest risks], the following principles were developed through case law:

- there is no requirement to make a "quantitative" evaluation[;] a risk assessment can either be quantitative *or* qualitative;
- a proper risk assessment does not need to establish a "minimum magnitude of risk." A WTO Member may determine that its acceptable level of risk is "zero risk;"
- the risk evaluated in a risk assessment must, nevertheless, be an "ascertainable risk." Theoretical uncertainty is not the kind of risk to be assessed. The existence of unknown and uncertain elements does not justify a departure from the risk assessment requirement;

evaluate scientific, economic, environmental, and ecological evidence.¹⁰⁸ Together these data should form the scientific basis of the subsequently adopted sanitary or phytosanitary measure, and as such, are not measures in and of themselves. Because the SPS Agreement requires a scientifically based measure, yet forbids undue restriction on trade, non-scientific evidence must also be evaluated in developing an SPS measure.¹⁰⁹ The sufficiency of this evidence will be evaluated by the WTO dispute settlement system in the event of a controversy over the measure.¹¹⁰ In this circumstance, the adopting state bears the burden of proving that it complied with the adopted measures, and that those measures comply with the SPS Agreement.¹¹¹

Because they involve scientifically based justification for policy measures, SPS Agreement risk assessments are plagued with uncertainty.¹¹² This uncertainty may yield varying, and often conflicting, conclusions, all of which are reasonable based on available scientific evidence.¹¹³ The process of accounting for this uncertainty and choosing the most appropriate conclusion is guided by the “science policy” of the state implementing the measure(s).¹¹⁴ Science policies “reflect the broader goals of risk regulation, such as protecting human health.”¹¹⁵ Because these policies often result in the compromises that are typical of a politicized judgment, it is important to make the scientific basis of the policy as transparent as possible to aid inquiry

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- a risk assessment needs to be specific enough. For example, a separate risk assessment must be conducted for each substance, [sic] a generic risk assessment for a class of substances is not enough. Also, the studies part of a risk assessment need to be specific enough in that they address the particular kind of risk at stake;
 - the WTO Member imposing an SPS measure does not necessarily have to conduct the required risk assessment itself. It can use assessments carried out by other Members or international organizations.

Pauwelyn, *supra* note 88, at 646 (footnotes omitted).

¹⁰⁸ See SPS Agreement, *supra* note 5, art. 5, para. 2 (“In the assessment of risks, Members shall take into account available scientific evidence; relevant processes and production methods; relevant inspection; sampling and testing methods; prevalence of specific diseases or pests; existence of pest- or disease-free areas; relevant ecological and environmental conditions; and quarantine or other treatment.”).

¹⁰⁹ See *id.* art. 5, para. 3.

¹¹⁰ See discussion *supra* Part I.B.1.a. (describing the WTO dispute settlement system).

¹¹¹ See SPS Agreement, *supra* note 5, art. 5, para. 8 (stating circumstances where a Member has to provide the reasons for its sanitary or phytosanitary measures).

¹¹² See Vern R. Walker, *Keeping the WTO from Becoming the “World Trans-science Organization”*: *Scientific Uncertainty, Science Policy, and Fact-finding in the Growth Hormones Dispute*, 31 CORNELL INT’L L.J. 251, 258 (1998) (“Scientific uncertainty is due to a lack of knowledge, and therefore reflects the potential for error inherent in scientific information.”).

¹¹³ See *id.* at 258-59 (discussing the nature of risk assessments).

¹¹⁴ See *id.* at 259 n.42 (“‘Science policies’ are determinations about how risk assessors should proceed when they encounter uncertainties involving multiple plausible accounts.”).

¹¹⁵ *Id.* at 261 (“Explicit science policies or inference guidelines allow risk assessments to remain ‘objective’ by maintaining consistency and transparency in the face of scientific uncertainty, even though some risk management goals are used to provide guidance to risk assessors about how to proceed.”).

into the adequacy of the evidence. This transparency is especially important because WTO members implement their own science policies reflecting their individual risk regulation goals.

Ultimately, all WTO states must adopt their own measures for the safety assessment of GM foods if they wish to regulate the development and importation of these products. As part of this process, these states will compile scientific data about the products to be regulated and then develop measures to achieve their safety objectives based upon their individual science policies. These measures involve compromise because they must balance important objectives of human, animal and environmental health and safety with the free flow of trade and international commerce.¹¹⁶ The SPS Agreement requires these measures to be based on international standards where they exist.¹¹⁷ Members are allowed to adjust the protection level to that which is equal to or above the international level as long as there is a scientific justification for this decision.¹¹⁸ The level of protection adopted by the member, however, must take into account a major objective of the SPS agreement—"minimizing negative trade effects."¹¹⁹

C. Potential SPS Measures for the Evaluation of GM Foods

1. Substantial Equivalence

Substantial equivalence is a comparative standard that evaluates several nutritional, toxicological, immunological, and pathogenic criteria of the GM food and compares the criteria with the conventional precursor (the non-genetically-modified parental variety of that food), while paying special attention to the genetic modification that has taken place.¹²⁰ This standard "embodies the concept that if a new food or food component is found to be substantially equivalent to an existing food or food component, it can be treated in the same manner

¹¹⁶ The SPS Agreement requires that these measures only be enforced "to the extent necessary to protect human, animal or plant life or health." SPS Agreement, *supra* note 5, art. 2, para. 2.

¹¹⁷ These international standards must be "deemed necessary to protect human, animal or plant life or health," [and that they are] based on scientific principles and . . . not maintained without sufficient scientific evidence." *Id.* art. 3, para. 2.

¹¹⁸ See *id.* art. 3, para. 3 (explaining that members may introduce sanitary or phytosanitary measures resulting in a higher level of protection than international standards).

¹¹⁹ *Id.* art. 5, para. 4 ("Members should, when determining the appropriate level of sanitary or phytosanitary protection, take into account the objective of minimizing negative trade effects.").

¹²⁰ See *Workshop*, *supra* note 14, at 10 (reporting on workshop designed to help those concerned with safety assessments of foods derived from genetically modified plants).

Substantial equivalence forms the basis of the current regulations of GM foods and GM organisms in both the United States and Canada. See generally Lars Noah & Richard A. Merrill, *Starting from Scratch?: Reinventing the Food Additive Approval Process*, 78 B.U. L. Rev. 329 (1998).

[as its previously existing counterpart] with respect to safety.”¹²¹ Although this standard provides a guiding principle by which regulators can orchestrate safety assessments of GM foods, “[it] is not a safety assessment in itself.”¹²² Substantial equivalence takes a number of factors into account in determining that the GM product is basically interchangeable with its conventional parental precursor in the market where the evaluation is taking place.¹²³ Knowledge regarding the composition and characteristics of the parent product/organism as well as the new product or organism should be considered in this comparison.¹²⁴ Determination of substantial equivalence should also include factors such as: (1) any processing that the food may undergo,¹²⁵ (2) the intended use of the food or food product,¹²⁶ and (3) its intended exposure.¹²⁷ Concluding that the GM food is substantially equivalent to its conventional precursor requires the evaluation of these factors compared to its conventional counterpart. If the GM

¹²¹ Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Safety Assessment*, *supra* note 37. This method has been described in the following manner: “Establishment of substantial equivalence is not a safety assessment in itself, but a dynamic, analytical exercise in the assessment of the safety of a new food relative to an existing food.” *Id.*

¹²² *Id.* (discussing a safety assessment and the concept of substantial equivalence).

¹²³ One source sums up the substantial equivalence approach in the following way:

[D]emonstration of substantial equivalence takes into consideration a number of factors, such as:

—knowledge of the composition and characteristics of the traditional or parental product or organism;

—knowledge of the characteristics of the new component(s) or trait(s) derived, as appropriate, from information concerning:

- i. the component(s) or trait(s) as expressed in the precursor(s) or parental organism(s);
- ii. transformation techniques (as related to understanding the characteristics of the product) including the vector(s) and any marker genes used;
- iii. possible secondary effects of the modification; and the characterization of the component(s) or trait(s) as expressed in the new organism;

—knowledge of the new product/organism with the new component(s) or trait(s), including the characteristics and composition [i.e. the amount of the component(s) or the range(s) of expression(s) of the new trait(s)] as compared with the conventional counterpart(s) (i.e. the existing food or food component).

AgBioS, Inc., *Substantial Equivalence and its Application in GM Food Safety Assessment*, (visited Dec. 12, 2000) <<http://www.plant.uoguelph.ca/plant/safefood/riskcomm2/plant-ag/se-response.htm>>.

¹²⁴ Information about the new product or organism may be obtained from “traits as expressed in the precursor or parental organisms; transformation techniques (as related to understanding the characteristics of the product) including the vectors and any marker genes used; possible secondary effects of the modification; and the characterization of the component traits as expressed in the new organism.” *Id.*

¹²⁵ If the existing food is consumed only after preparation, the comparison must take this into account: “[T]he safety question relates to whether the normal use of these plants as food involves cooking sufficient for its inactivation.” See OECD GROUP OF NATIONAL EXPERTS (GNE) ON SAFETY IN BIOTECHNOLOGY, *supra* note 12, at 12.

¹²⁶ This component may include assessment of the level of the food or food component in the diet, and will vary between populations and geographic regions. See *id.*

¹²⁷ Intended exposure “includes . . . the pattern of dietary consumption, and the characteristics of the consuming population.” *Id.*

food yields results which lie within the natural variation range of the conventional precursor, then the GM food should be deemed to be substantially equivalent to that precursor for that member state. There are three endpoints to this comparative analysis: (1) the GM food is determined to be substantially equivalent to its parent/precursor; (2) the GM food, if not determined to be substantially equivalent, may be determined to be substantially equivalent aside from particular differences; or (3) substantial equivalence may not be ascertainable either because the differences are not well defined or because no conventional counterpart exists.¹²⁸ If the comparison results in either of these last two endpoints then further analysis will be required. This analysis will appropriately evaluate the differences between the GM food and the parent/precursor on a case-by-case basis.

2. *An Alternative to Substantial Equivalence—the “In-Depth Assessment” Approach*

It has recently been argued that the substantial equivalence standard is not adequately defined and that it is applied in ways that are “useful to industry but unacceptable to the consumer.”¹²⁹ Critics contend that the substantial equivalence standard “should be replaced with a practical approach that would actively investigate the safety and toxicity of GM foods rather than merely taking them for granted, and which could give due consideration to public-health principles as well as to industrial interests.”¹³⁰ The approach advocated by these parties is to bypass substantial equivalence as an inadequate safety assessment and replace it with various immunological, toxicological and biological tests.¹³¹ Advocates of this approach urge that this is the only way that consumers can be adequately protected against the potential adverse effects of novel GM foods and the industry that is trying to force them on the consumer. This Note will refer to this approach as “in-depth assessment.”¹³²

In the absence of the default standard of substantial equivalence, the process of evaluation of GM foods would vary depending on the GM food involved.¹³³ Each evaluation would entail extensive scien-

¹²⁸ See Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Safety Assessment*, *supra* note 37 (discussing occasions where substantial equivalence may not be ascertainable).

¹²⁹ Erik Millstone et al., *Beyond ‘Substantial Equivalence,’* 401 NATURE 525, 525 (1999) (arguing for a more structured and thorough examination of GM foods and food products).

¹³⁰ *Id.* at 526.

¹³¹ *See id.* at 525.

¹³² The label chosen here for this methodology is merely for ease of use and reference. Though this approach involves comparative analysis to a certain degree, it is primarily an in-depth case-by-case examination of individual GM foods.

¹³³ Although Millstone et al. criticize the substantial equivalence standard, they have not provided alternative methods of evaluating GM foods beyond the mere suggestion that extensive scientific tests must take place, as well as a reference to a 1998 Dutch government team

tific exploration into potential adverse public health consequences of releasing each GM food for public consumption.¹³⁴ The goal in this evaluation would be to develop a purely scientific basis, supported by substantial evidence, for the regulation of GM foods.¹³⁵ Although this approach has protection of public health as the main objective, policy decisions would be necessary in order to set threshold standards for every GM food.¹³⁶ As compared with substantial equivalence, which is a comparative standard with a definite endpoint in its analysis,¹³⁷ “in-depth assessment” would require the development and determination of new threshold values for each product,¹³⁸ as well as new legislation corresponding to the potentially ill-conceived threshold values.¹³⁹ This process potentially runs contrary to one of the main objectives of the SPS Agreement—“to further the use of harmonized sanitary and phytosanitary measures between members, on the basis of international standards, guidelines and recommendations.”¹⁴⁰ With its individualized approach, in-depth assessment appears to discourage the development of harmonized international standards. Implementation costs of in-depth assessment would be high due to the complexities involved in carrying out this evaluation. WTO member countries that are financially or technologically unable to perform this analysis on their own could be forced to adopt what might be viewed as an analogue to the substantial equivalence standard by relying on the scientific evaluations of other members.¹⁴¹ This reliance may not matter because one goal of in-depth assessment is to develop safer standards for GM foods.¹⁴² However, this reliance on threshold values determined by other members may be detrimental because they

evaluation of GM foods. The Dutch team recommendations are for “a finer-grained screen to test for differences in some of the relevant biological variables, such as DNA analysis, protein fingerprinting, secondary-metabolite profiling and *in vitro* toxicity testing.” *Id.* at 526.

¹³⁴ Evaluative criteria would examine those public health issues explained in discussion *supra* Part I.A.2.

¹³⁵ See SPS Agreement, *supra* note 5, art. 2, para. 2.

¹³⁶ See discussion *supra* Part I.B.2.

¹³⁷ The endpoint being the determination that the GM food is substantially equivalent to its conventional precursor.

¹³⁸ The nature of in-depth assessment precludes the luxury of defaulting to pre-existing standards for the conventional counterparts to GM foods. If such a default were allowed, the in-depth assessment would become substantial equivalence. See Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Safety Assessment*, *supra* note 37.

¹³⁹ Threshold values, if they are possible to attain without a comparative analysis between the GM food and its conventional precursor, may be ill-conceived for two reasons: (1) because the *de novo* analysis of each GM food may result in threshold values exceeding those which are acceptable to the member for the conventional counterpart of the GM food, and (2) because if no conventional counterpart exists which has been available for widespread human consumption, determination of threshold values will be a truly arbitrary process.

¹⁴⁰ SPS Agreement, *supra* note 5, prologue.

¹⁴¹ The SPS Agreement permits a member to adopt standards developed by another member under certain conditions. See *id.* art. 4, para. 1.

¹⁴² Developing safer standards and/or developing initial standards for novel foods is the main objective of in-depth assessment.

would be applied to two or more separate and distinct populations with different nutritional requirements and underlying physiologies.¹⁴³

II. ANALYSIS

A. Regulation Under the SPS Agreement

Establishment and/or adoption of an SPS measure by a WTO member state is an important process subject to extensive examination by other members. One of the primary driving forces behind the development of the SPS Agreement was to prevent disguised and/or arbitrary restrictions on trade by member countries. In evaluating an SPS measure it is important to understand that the actual evaluations that take place under a member's risk management objectives should be transparent enough, and provide enough objective criteria, to allow impartial examination of the methods used. This will aid investigation of the measure should a controversy arise. Additionally, this transparency will provide better protection against WTO members establishing SPS measures which are in fact disguised and unsubstantiated restrictions on trade.

1. Substantial Equivalence

Initially it must be determined that the substantial equivalence concept is of the type contemplated in the SPS Agreement. This analysis must take into account how WTO dispute settlement panels and the WTO Appellate Body have interpreted the SPS Agreement.¹⁴⁴ Since the substantial equivalence concept is indeed a measure directed at the protection of human health, it would protect against food borne risks and, if implemented, would directly affect international trade. This concept also fulfills the "scientific basis" requirement of the SPS Agreement because it is based on science and cannot be proven without sufficient scientific evidence.¹⁴⁵

Substantial equivalence contemplates that the GM food being evaluated is considered equivalent to its conventionally produced counterpart.¹⁴⁶ This equivalence is evaluated with respect to the uses of the conventional counterpart in specific regions. For example, po-

¹⁴³ This is a problem whenever international health standards are sought to be harmonized. Although populations vary between members and within member states, the clearest dividing line, prior to "on-the-shelf" regulation by the individual consumer, is at the member state level.

¹⁴⁴ See generally Pauwelyn, *supra* note 88 (examining the SPS Agreement in light of the first three disputes under it).

¹⁴⁵ The Appellate Body Report in the Japan-Varietals dispute required a certain sufficiency of scientific evidence. See *Japan Appellate Body Report*, *supra* note 87, paras. 72-85 (discussing the SPS Agreement in terms of assessing measures affecting agricultural products of Japan).

¹⁴⁶ A conventional counterpart here refers to conventional foods or food components already available in the food supply.

tatoes are consumed in the U.S. and elsewhere only after being cooked. Without this essential step, under certain conditions the potato may be toxic. A GM potato, and all other products that require preparation prior to consumption, must be evaluated with respect to this step. Because substantial equivalence seeks to ensure the continuance of existing quality standards with respect to conventional products, it is implicit that the GM product is at least as healthy as the preexisting product with respect to those standards.

Many conventional foods present various risks to human health.¹⁴⁷ As a safety assessment of GM foods, substantial equivalence would account for these potential risks.¹⁴⁸ Establishing that a GM food is substantially equivalent to its conventional counterpart is based upon a range of assorted variables occurring naturally.¹⁴⁹ In order to establish that the GM food is substantially equivalent to its conventional counterpart, the experimental values of these variables for the GM food must be within the range that occurs naturally for the conventional counterpart. These variables must include the molecular characterization and phenotypic characteristics of the GM organism and/or food and the key nutrients and toxicants of the conventional counterpart.¹⁵⁰ A broader examination of the characteristics of the GM food or food component may be warranted in situations where there is an indication that unintended effects of genetic modification may exist. However, in general, these extra inquiries will not be necessary.¹⁵¹ Further safety assessments should only take place if the examined variables fall outside the naturally occurring range or if unexpected effects of genetic modification arise.¹⁵² These further safety assessments will likely focus on the issues of allergenicity and gene transfer—areas where theoretical uncertainties are certain to exist.

¹⁴⁷ These risks may be dose-related, due to existing allergens, toxicity, or pathogenicity. See discussion *supra* Part I.A.2. (discussing allergenicity, pathogenicity, and toxicity).

¹⁴⁸ See discussion *supra* Part I.C.1. (describing the substantial equivalence standard).

¹⁴⁹ This range of variables corresponds to that which occurs naturally in the conventional counterpart. Databases containing the naturally occurring range of these variables in plants, animals, and microorganisms should be made accessible for substantial equivalence determinations.

¹⁵⁰ See Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Conclusions and Recommendations*, *supra* note 58 (finding that substantial equivalence is established by demonstrating that the characteristics assessed for the genetically modified organism are within the natural variation for such characteristics).

¹⁵¹ See *id.* (concluding that analysis of a broader spectrum of components is generally unnecessary except where there is an indication of the possibility of an unintended effect of genetic modification).

¹⁵² See *id.* (“The [WHO/FAO] Consultation established a sequential approach focusing on the new gene product(s) and the(ir) structure, function, specificity and history of use. If these indicate a potential safety concern, additional *in vitro* and/or *in vivo* studies may be appropriate.”).

Potential allergenicity of foods, whether GM foods or their naturally occurring counterparts, is a significant concern.¹⁵³ Allergic reactions in individuals to ingested food may range from mild to life threatening. Though the affected population tends to be small, it still remains a significant portion. Consequently, several important steps must be undertaken to ensure a comprehensive reliable method of determining allergenicity of GM foods. In 1996, a Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety examined this issue and provided recommendations. This consultation made four recommendations with respect to allergenicity that should be included in the establishment of substantial equivalence:

[(1)] The transfer of genes from commonly allergenic foods should be discouraged unless it can be documented that the gene transferred does not code for an allergen. [(2)] Foods found to contain an allergen transferred from the organism which provided the DNA should not be considered for marketing approval unless such products can be clearly identified in the marketplace and this identity will not be lost through distribution and processing . . . [(3)] Involved organizations should consider the appropriateness of, and/or actions to take, in respect to foods containing new protein(s) that are determined to have the characteristics of an allergen, even though no patient population is known to exist which has an allergy to this gene product. [(4)] The identification of food allergens and the characteristics of these allergens that define their immunogenicity should be encouraged.¹⁵⁴

One method for evaluating the potential allergenic effects of a GM food is through the use of serum banks. These banks contain samples of human sera that have been documented to exhibit adverse reactions to a range of known allergens. Through exposure of selected sera samples to the GM food being evaluated, it is possible to determine whether that food will have allergenic effects in the population at large. In 1995, the OECD conducted a survey of serum banks in OECD member countries for allergenicity testing and use of databases of known allergens. The survey concluded, among other things, that national databases of monoclonal antibodies and human sera used in determining allergenicity should be established, made easily accessible, and that the information should be available at a

¹⁵³ See discussion *supra* Part I.A.2.a. (discussing allegenicity).

¹⁵⁴ Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Conclusions and Recommendations*, *supra* note 58.

centralized location.¹⁵⁵ Access to this information by those undertaking the testing of GM foods for known allergens would prove very advantageous. However, a coordinated system between the groups that have the information and groups that need the information must be established. Since databases of such information may be costly to build, maintain, and coordinate, a cost-sharing methodology will probably be necessary. A recommendation that this type of database should be developed and maintained by the WTO, and perhaps delegated to Codex, may not be novel but may become necessary under the SPS Agreement.¹⁵⁶

Gene transfer conferring immunity to certain antibodies presents a fairly small health risk in that the chances of this event occurring are very slight.¹⁵⁷ However, even the slight potentiality of this event occurring has tremendous detrimental human health consequences and thus warrants attention in the design of policy dealing with GM foods.¹⁵⁸ In 1990, a Joint FAO/WHO consultation took a cautionary tone in their recommendation that use of viable cells and genetic material from microbes that encode for antibiotic resistance should be prohibited.¹⁵⁹ Though this recommendation may be overly precautionary, it holds the potential to lay to rest one of the major areas of confusion and concern to the consuming public.

In order to illustrate the strengths and weaknesses of the substantial equivalence standard as an SPS measure this Note will follow the progression of a hypothetical GM food from the offering up of the product by an agricultural biotechnology firm for approval, through to the actual establishment of substantial equivalence. The hypothetical

¹⁵⁵ See *Safety Assessment*, *supra* note 42, at 15 ("A central index or database of existing facilities could however be useful and could provide a single entry point for numerous databases.").

¹⁵⁶ The 1996 FAO/WHO Joint Commission on Biotechnology and Food Safety has made a similar recommendation in its urging for the development of information databases in general in order to aid in substantial equivalence determinations:

The Consultation stressed the need for the development, maintenance and accessibility of databases regarding food plants, food microorganisms and food animals for the purpose of the establishment of substantial equivalence. Of particular interest are databases on: the nutrient, toxicant and allergen content of foods; the amino acid sequence of protein toxins and allergens found in food.

Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Conclusions and Recommendations*, *supra* note 58.

¹⁵⁷ See discussion *supra* Part I.A.2.b. (discussing gene transfer).

¹⁵⁸ See *id.* (discussing potentially harmful consequences of such a gene transfer).

¹⁵⁹ See STRATEGIES, *supra* note 12, § 6.3.1 ("Food ingredients obtained from microbes that encode such antibiotic-resistance marker genes should be demonstrated to be free of viable cells and genetic material that could encode resistance to antibodies."). The 1996 Joint Consultation added to this recommendation "that certain antibiotic resistant marker genes should be precluded from commercial food crops." Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety, *Conclusions and Recommendations*, *supra* note 58.

product that will be used here will be Bt- based oranges (“*Bugz Surpriz Orange*”).¹⁶⁰

The question to be analyzed is whether *Bugz Surpriz Oranges* are as safe as conventional oranges. Along with a compositional analysis of the GM oranges, the source, identity, function, and stability of genetic material introduced into the oranges should be analyzed. Additionally, the safety of the kanamycin resistance gene used in the product should be evaluated.

The nutritional profile of the *Bugz Surpriz Orange* must be compared with the conventional orange to ensure that the GM orange does not exhibit unexpected changes in composition. Oranges and orange products provide an important source of vitamins C and, to a lesser extent, A. Thus, it is important that the *Bugz Surpriz Orange* is not deficient in these vitamins as compared with regular oranges. In order to evaluate this, both types of the orange should be examined for vitamin content under storage conditions that are similar to those which conventional oranges are typically subjected.¹⁶¹ The results of this comparative analysis must indicate that there is not a significant difference in nutritional profile between the *Bugz Surpriz Orange* and the parental variety.¹⁶² If the GM orange yields values that are significantly different from the parental variety then it will fail the substantial equivalence test. If the analysis of several representative GM fruits yields numbers which lie within the natural variation range of the conventional oranges, however, then the next step is toxicity analysis.

The introduction of the Bt- gene into the parental line of oranges creates a real concern about the resulting toxicological aspects of the GM orange.¹⁶³ Though the Bt- gene encodes for the expression of Bt-endotoxin, which has been used for years as a pesticide without toxic effects in humans and animals,¹⁶⁴ there are a couple of other concerns due to the actual process of genetic modification. First, one must be sure that the Bt- protein does not exist in a concentration exceeding that which currently is applied to conventional crops. The Bt- protein

¹⁶⁰ Bt- based transgenic crops incorporate insect resistance within the developed products. Bt- proteins are toxic to many insects and have the beneficial effect of allowing fewer insecticides to be used. See *supra* note 70 (discussing Bt- proteins).

¹⁶¹ The phrase “examined for vitamin content” used here refers to the examination of the GM food for total protein, fat, ash, fiber, and macro- and micro-nutrients similar to current methods for evaluating conventional foods.

¹⁶² A significant difference in nutritional profile between the two varieties of oranges is determined through analysis of several representative fruits of the parental line in order to obtain the vitamin concentration range that exists in nature for the parental variety; this is its natural vitamin concentration variation. The *Bugz Surpriz Orange* must not yield numbers that lie outside of this natural variation range.

¹⁶³ For an excellent, in-depth analysis of the various toxicological concerns surrounding genetic modification of foods, see generally *Workshop, supra* note 14.

¹⁶⁴ See *Biotechnology and the American Agricultural Industry, supra* note 25, at 1431.

exists within the fruit after genetic modification, whereas the conventional use of this protein is an external application that degrades or washes off. Thus, there is a fear that the Bt- protein will exist in the fruit at a higher concentration after genetic modification. This fear is allayed due to the fact that Bt- gene expression is generally limited to a single developmental stage in the plant's life cycle.¹⁶⁵

Second, the genetic modification must be monitored to determine whether it induces any chemical structure changes in the Bt-protein that may have detrimental health consequences.¹⁶⁶ This may be accomplished through the use of data compiled with respect to the use of the Bt- gene in the genetic modification of corn.¹⁶⁷ If there exists information indicating a change in the chemical structure of the Bt- protein in corn, where it has been used for some time, then the Bt-oranges may require continued monitoring. Otherwise, periodical monitoring for this chemical change will be unnecessary due to convenience and cost concerns.

In addition to introduction of the Bt- gene, the *Bugz Surpriz* Oranges are developed using the marker gene encoding for antibiotic resistance to kanamycin and neomycin—APH(3')II.¹⁶⁸ The enzyme produced as a result of the introduction of this gene has been demonstrated to break down rapidly when exposed to stomach acid and digestive enzymes.¹⁶⁹ This enzyme poses little danger to the consumer from a toxicological and allergenic standpoint, even absent digestive degradation. Extensive examination of this gene product indicates that it, and similar phosphorylating enzymes, have no significant homology to known allergens and toxins.¹⁷⁰ In other words, the introduction of this antibiotic resistance gene does not create a risk of allergic and/or toxic reactions in consumers of the GM orange.

¹⁶⁵ This stage occurs prior to maturation and harvesting of the crop, and the Bt- protein subsequently degrades within the crop prior to harvest and consumption. *See id.*

¹⁶⁶ Extensive toxicological studies were performed on Bt- endotoxin, prior to its approval as an insecticide, which determined that it was safe for human consumption. However, these tests did not (and could not) evaluate the toxicity of Bt- endotoxin if its chemical structure were altered during genetic modification. *See* John Beringer, *Keeping Watch Over Genetically Modified Crops and Foods*, 353 THE LANCET 605, 606 (1999) (“[I]n some GM plants the sequences of toxin gene might be a modification of those of the natural toxin. Risk assessments must take such change into account . . .”).

¹⁶⁷ *See id.* (discussing data that shows the use of the Bt- gene to be safe where used to confer resistance to insects in maize).

¹⁶⁸ The need for the utilization of these types of markers is explained in the background section. *See* discussion *supra* Part I.A.2.b. (discussing gene transfer).

¹⁶⁹ *See* Secondary Direct Food Additives Permitted in Foods for Human Consumption; Food Additives Permitted in Feed and Drinking Water of Animals; Aminoglycoside 3'-Phosphotransferase II, 59 Fed. Reg. 26,700, 26,702 (1994) (“APH(3')II is rapidly activated by stomach acid.”).

¹⁷⁰ Phosphorylating enzymes such as APH(3')II are heat labile and have no significant homology to known allergens and toxins, and APH(3')II in particular does not have any inherent characteristics that distinguish it from other phosphorylating enzymes. *See id.*

Introduction of a gene encoding for antibiotic resistance is significant because it gives rise to the possibility of reducing the efficacy of therapeutic antibiotics.¹⁷¹ The potency of these antibiotics could be decreased by either their inactivation upon direct exposure to the APH(3')II enzyme or by the development of microbial antibiotic resistance.¹⁷² As previously mentioned, the enzyme produced as a result of the introduction of APH(3')II degrades rapidly during digestion, so a significant amount of inactivation of orally administered antibiotic is unlikely.¹⁷³ More significantly, the use of the antibiotic resistance gene gives rise to the fear that it may be transferred to a pathogenic microbe in the intestinal tract or in the soil.¹⁷⁴ The mechanisms by which this transference could take place, from a plant chromosome to an animal microbe, are not known. Moreover, recent studies indicate that this possibility is excessively small.¹⁷⁵ Thus, a small amount of risk and uncertainty exists in the utilization of an antibiotic resistance marker in our GM oranges, which may be acceptable for safety assessment purposes under the SPS Agreement.¹⁷⁶

The SPS Agreement allows members to develop their own risk management policies, which include deciding on their own level of acceptable risk.¹⁷⁷ According to the SPS Agreement, members must base their sanitary and phytosanitary measures on transparent scientific justification. Thus, if a member has a valid reason for imposing very strict, difficult to achieve safety standards on a product, it may do so only as long as it can provide scientific evidence to support the regulations. Certain risk management objectives maintained by the member will guide the level of risk acceptable to that member.¹⁷⁸

¹⁷¹ See J. H. Maryanski, *FDA's Policy for Foods Developed by Biotechnology* (visited Dec. 12, 2000) <<http://www.cfsan.fda.gov/~lrd/biopolicy.html>>.

¹⁷² See discussion *supra* Part I.A.2.b.

¹⁷³ The biotechnology firm of Calgene, Inc. ("Calgene") of Davis, California, conducted a recent examination of the effects of APH(3')II introduction in GM tomatoes. It concluded that, even in a "worst-case assessment," that "only a small fraction of the antibiotic would be inactivated." Maryanski, *supra* note 171. See generally Keith Redenbaugh et al., *Regulatory Issues for Commercialization of Tomatoes with an Antisense Polygalacturonase Gene*, 29P IN VITRO CELL. DEV. BIOL. 17, 24 (1993) (concluding that "the issue of comprised efficacy of antibiotic therapy resulting from consumption of the genetically engineered tomato is not of significant concern").

¹⁷⁴ See discussion *supra* Part I.A.2.c. (discussing the pathogenicity of microorganisms).

¹⁷⁵ See *supra* note 54 and accompanying text (noting the series of events required for gene transfer to occur).

¹⁷⁶ The FDA evaluated the testing done on the Flavr Savr Tomato developed by Calgene, which incorporated APH(3')II, and concluded that the risk involved in the use of this marker is not substantial enough to preclude generally recognized as safe ("GRAS") determination. This product was subsequently approved for marketing by the FDA. See Maryanski, *supra* note 171.

¹⁷⁷ See discussion *supra* Part I.B.2. (discussing risk management objectives).

¹⁷⁸ See *id.*

This level must be a “scientifically identified risk,” not one based on an unascertainable theoretical risk.¹⁷⁹

Based upon the genetic modifications and a safety and nutritional assessment of the *Bugz Supriz* Orange, the determination is made as to which criteria should be evaluated in determining the substantial equivalence of this product to its parental counterpart.¹⁸⁰ If experimental values of the GM orange fall within the natural variation of the parental variety, the first step in determining substantial equivalence has been achieved. In addition, a safety assessment with respect to the changed genetic composition of the GM orange must be conducted. If this safety assessment yields values that fall within the acceptable level of risk of a WTO member,¹⁸¹ then the GM orange will be deemed substantially equivalent to its parental precursor, and thus safe for importation into that member state. Under the SPS Agreement, this determination of substantial equivalence applies only to the member making the determination, based upon its individualized risk management objectives.¹⁸² This determination does not apply to the entire population of the specific GM food with respect to every member. Each member has the obligation and opportunity to make this determination on its own.

2. In-Depth Assessment

In-depth assessment of GM foods, like substantial equivalence, requires a case-by-case examination of GM foods. These two policies differ markedly, however, in their actual implementation. Where substantial equivalence evaluates characteristics of the GM food that are obvious from the type of modification,¹⁸³ in-depth assessment evaluates all health-related criteria of the GM food, regardless of the type of modification. The in-depth assessment approach has been advocated as an alternative to substantial equivalence for various reasons.¹⁸⁴ Advocates of this approach claim that substantial equivalence has not been adequately defined and that the process used to achieve this designation for genetically modified foods has not been confined into a useable format.¹⁸⁵ Advocates of the in-depth assess-

¹⁷⁹ See *European Appellate Body Report*, *supra* note 87, para. 186 (“[I]f a risk is not ascertainable, how does a Member ever know or demonstrate that it exists?”).

¹⁸⁰ See discussion *supra* Part II.A.2.

¹⁸¹ See discussion *supra* Part I.B. (discussing the allowance for different risk assessments for individual WTO Members).

¹⁸² See *id.*

¹⁸³ See discussion *supra* Part I.C.1. (discussing the substantial equivalence standard).

¹⁸⁴ See Erik Millstone et al., *supra* note 129, at 523-26 (arguing that the substantial equivalence standard favors industry at the expense of the consumer). See also M. S. Swaminathan, *What Should We Do With Genetically Modified Foods in the Twenty-First Century?*, WORLD AND I, Dec. 1, 1999, at 150 (urging strict regulation of genetically modified foods because the benefits and risks of these foods are not fully understood).

¹⁸⁵ It is obvious based upon the previous discussion that this is not necessarily true.

ment approach prefer the decreased risk resulting from the extensive safety assessments involved in this approach.

Suppose that an in-depth assessment were to be conducted on the same hypothetical product, *Bugz Supriz Oranges*, as in the hypothetical application of the substantial equivalence standard above. In-depth assessment makes use of immunological, toxicological and biological tests to evaluate the oranges. Starting with a nutritional assessment, threshold values that the GM food must achieve to be deemed safe for normal consumption are set. Rather than perform a full nutritional analysis with respect to the prospective use of the products in varying markets, it may be preferable to perform a comparative analysis with the parental precursor, similar to the analysis under substantial equivalence.¹⁸⁶ Based upon the approach taken, there will be a range of threshold variables that the *Bugz Surpriz Orange* must meet. The comparative route will prove to be much quicker and less expensive than this threshold development approach.¹⁸⁷ If the nutritional analysis yields acceptable results, the in-depth assessment next moves to evaluate the safety concerns raised by the genetic modification.¹⁸⁸

In-depth assessment must account for the potential activation or stimulation of toxin production in the GM food. Because oranges do not have a toxin production history, the analysis will focus on both the potential induction of unexpected toxin production and the effects of the introduction and resulting concentration of the Bt- endotoxin. Evaluating unexpected toxin production will be a very difficult and time-consuming process, involving extensive *in vitro* and *in vivo* analyses. Similarly, evaluating the unexpected toxic effects of genetic modification involving Bt- endotoxin may be prohibitively difficult and time-consuming.¹⁸⁹ These processes also lack a reasonable analysis endpoint because they involve purely theoretical possibilities and thus a great deal of uncertainty.¹⁹⁰

The same concerns regarding the use of an antibiotic resistance marker gene arise here as they did with substantial equivalence ap-

¹⁸⁶ Without a comparative analysis for nutrition, it would be very time-consuming and prohibitively expensive (for some WTO Member nations) to perform the testing required to develop threshold values based upon the parental precursor product. Many variables would have to be evaluated, such as average and expected consumption (adjusted for varying populations), uses, methods of preparation of the product, and existence and concentration of anti-nutrients (toxins) within the product.

¹⁸⁷ See *supra* note 162.

¹⁸⁸ These concerns are: toxicological, pathogenic, gene transfer, and allergenicity. See *supra* Part I.A.2.

¹⁸⁹ The evaluation of the toxicological effects of genetic modification involving Bt- endotoxin might prove to be easier than evaluating unexpected toxicological effects in general because of existing research on the topic.

¹⁹⁰ "Reasonable" here refers to scientifically based SPS Agreement safety assessments and their respective endpoint valuations.

proach. There are two easy answers to the questions raised regarding utilization of antibiotic resistance markers: (1) Follow the advice of the FAO/WHO to avoid using these markers in the development of GM foods; or (2) accept the unlikely possibilities of therapeutic antibiotic degradation or immunity development as allowable risks.

Although the development of *Bugz Supriz* Oranges does not involve the use of substances with a history of allergenicity, this category must be extensively analyzed under the in-depth assessment approach. Assessing potential allergenicity in this case would involve various *in vitro* and *in vivo* tests.¹⁹¹ This testing would be expensive, time-consuming and may not even yield acceptable results.¹⁹²

3. Substantial Equivalence Versus In-Depth Assessment

The goals of both the substantial equivalence standard and the in-depth assessment standard are to ensure the safety of GM products distributed for public consumption. In-depth assessment seeks to achieve this goal through the use of extreme caution and extensive testing. Substantial equivalence provides a comparative analysis with the availability of further testing if certain risk factors are present.

When both of these approaches are analyzed under the SPS Agreement, various problems arise under the in-depth assessment approach.¹⁹³ Through an in-depth assessment and use of an extensive array of scientific testing, the question is the sufficiency of the evidence obtained: Is there an objective relationship between the scientific evidence and the SPS measure? The SPS Agreement requires this type of relationship, which will be determined on a case-by-case basis by the WTO dispute settlement system.¹⁹⁴ Additionally, this same methodology hinders the member's ability to set threshold values and develop corresponding policy for individual GM products.¹⁹⁵ Based upon their individual risk management objectives, WTO members would have to develop and set new threshold values¹⁹⁶ and draft legislation (SPS measures) corresponding to these values for every GM product that seeks approval for international trade. This process could delay distribution of the GM product for an unreasonable

¹⁹¹ See *supra* note 50 (discussing testing for allergenicity).

¹⁹² It is impossible to determine potential allergenicity with one hundred percent certainty until the product is released for public consumption.

¹⁹³ See discussion *supra* Part II.A. (comparing the substantial equivalence standard to the in-depth assessment standard).

¹⁹⁴ See *supra* text accompanying notes 93-94 (discussing the basis for the criteria used to establish substantial equivalence).

¹⁹⁵ See discussion *infra* Part II.B. The phrase "threshold values" refers to a point in the scientific analysis of a GM food where the potential risk posed by the product, based upon experimental values, exceeds the risk that the WTO member state is willing to accept as per its individual risk management objectives.

¹⁹⁶ These threshold values could only be set if there is a scientific basis for the determination, based upon risk to human and animal health and life. See *supra* note 92.

amount of time while policy is being developed.¹⁹⁷ For example, the toxicological, immunological, allergenic, and pathogenic effects of the GM food on the relevant population would have to be tested.¹⁹⁸ These types of population studies would either extrapolate upon an evaluation of a representative selection of the population,¹⁹⁹ or, in the case of assessing allergenicity, reference testing may be performed utilizing a pre-existing serum database representative of the members' population, if such a database exists.²⁰⁰ After this testing is performed and scientific evidence obtained, the SPS measure must be developed and objectively related to the evidence. This will prove exceedingly difficult if testing yields inconclusive results.

Areas where extensive testing yields inconclusive results are a major concern with the in-depth assessment approach. How much testing will be required before a state must either accept or deny the GM product? How does one recognize a disguised restriction on trade, which is prohibited under the SPS Agreement?²⁰¹ Through the in-depth assessment approach, members seeking to prevent the importation of a specific GM product could tie the product up for an unreasonable amount of time in testing prior to coming to a decision regarding its importation status.²⁰²

¹⁹⁷ "Tying up" the product here means preventing the product from being available to consumers while the member state performs the testing required pursuant to its risk management objectives and develops appropriate policy to regulate the importation of the product.

¹⁹⁸ See discussion *supra* Part I.A.2.

¹⁹⁹ The extrapolation would relate to the toxicological, immunological, allergenic, and pathogenic effects of the GM food on the tested population.

²⁰⁰ See discussion *supra* Part I.A.2.a. (discussing allergenicity). Both the substantial equivalence and in-depth assessment approaches would benefit from the "development, maintenance and accessibility of databases regarding food plants, food microorganisms and food animals." Joint FAO/WHO Expert Consultation on Biotechnology and Foods Safety, *Conclusions and Recommendations*, *supra* note 58. Because substantial equivalence is a comparative approach, these types of databases would greatly enhance the determination of substantial equivalence of GM foods to their conventional counterparts. Databases of interest are "the nutrient, toxicant and allergen content of foods [and] the amino acid sequence of protein toxins and allergens found in food." *Id.*

²⁰¹ Typically, disguised restrictions are challenged by members, and the WTO dispute settlement committee will assess the policies of the challenged state. Because the SPS Agreement requires a scientific basis for regulations, most members' SPS measures are transparent. See SPS Agreement, *supra* note 5, art. 2, para. 3 ("Sanitary and phytosanitary measures shall not be applied in a manner which would constitute a disguised restriction on international trade.").

²⁰² The SPS Agreement addresses these time concerns in Article 5, paragraph 7:

In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information Members shall seek to obtain the additional information necessary for a more objective assessment of risk and review the sanitary or phytosanitary measure accordingly within a *reasonable* amount of time.

SPS Agreement, *supra* note 5, art. 5, para. 7 (emphasis added).

The SPS Agreement does not elaborate upon the meaning of "reasonable," so one must look to the WTO dispute settlement system for guidance. On this issue, the WTO Appellate Body determined that a "'reasonable period of time' has to be established on a case-by-case basis and depends on the specific circumstances of each case, including the difficulty of obtain-

The in-depth approach is also flawed in that it does not provide an analysis endpoint. Where the substantial equivalence inquiry ends with the determination that the GM food is substantially equivalent to its conventional counterpart, in-depth assessment will continue to require testing into theoretical possibilities because it does not start with the goal of threshold value determination.²⁰³ Genetic modification under the substantial equivalence standard has the goal of producing a product very similar to the preexisting product. Thus, early in product development it may become obvious that the modification has yielded a product which is quite different from that which was initially planned. Absent other circumstances, the development of that product would have to go back to the drawing board.²⁰⁴ In contrast, product development under the in-depth assessment approach may yield a significantly different GM product from its conventional counterpart, but the safety assessment may take place regardless of the previous ends to be achieved. In this case there would be no pre-existing nutritional, toxicological and allergenic values,²⁰⁵ thus a considerable amount of time and resources would be spent on a product that is either unsafe or has no existing market.²⁰⁶ These potential consequences of the in-depth approach are contrary to the objectives of the SPS Agreement.²⁰⁷

In addition to the unreasonable delay and the potential for arbitrary restrictions by members, the in-depth assessment approach would be expensive. The scientific testing and development of policy required by this approach may not be feasible for many WTO member states. As a potential remedy, members could require biotechnology firms offering the product to perform the required testing pursu-

ing the additional information necessary for the review *and* the characteristics of the provisional SPS measure.” *Japan Appellate Body Report*, *supra* note 87, para. 93.

²⁰³ The SPS Agreement requires that there be an “ascertainable risk” evaluated in the risk assessment. Inquiry into a theoretical possibility is not the appropriate inquiry. *See* SPS Agreement, *supra* note 5, art. 5.

²⁰⁴ The difference between the GM food and its conventional counterpart may lie in the various criteria evaluated under the substantial equivalence standard. Most notably, there may be a significant disparity in nutritional content, toxicity and allergenicity, which evaluation under the substantial equivalence inquiry would note immediately.

²⁰⁵ Note that if reference were to be made to pre-existing values, the in-depth assessment approach would become quite similar to the substantial equivalence standard.

²⁰⁶ Genetic research holds many potential benefits and it should be encouraged in order to develop new and useful products. If this research results in the development of unintended products, it is not necessarily a failure. These novel products may be evaluated on other bases than those examined here, or perhaps through the in-depth assessment approach. However, as a default approach, the in-depth approach is too burdensome to carry out the obligations under the SPS Agreement.

²⁰⁷ *See* discussion *supra* Part I.B.1. (noting that the in-depth assessment approach would conflict with SPS Agreement goals of prohibiting disguised trade restrictions and undue costs on foreign producers).

ant to their individualized risk management objectives.²⁰⁸ However, depending on the potential market within such states and the difficulties inherent in dealings between private firms and skeptical governments, most biotechnology firms will probably be hesitant to undertake such testing. Thus, the costs will fall back onto the states, and some will be forced to rely on other members' tests. Thus, such states would not have the opportunity to set their own standards according to their respective risk management objectives.²⁰⁹

B. Objective Regulation Through Science and Policy

The SPS Agreement requires sanitary and phytosanitary measures to be based on and supported by science.²¹⁰ Intended as an objective method of cutting through disguised restrictions on trade, this requirement is not as cut-and-dried as it may at first appear. Values obtained through scientific methods represent a range of certainties, and experiments rarely yield answers with one hundred percent certainty. Therefore, decisions and policies made by trade organizations based on science involve, at a minimum, a fair amount of compromise and negotiation as to what scientific values are acceptable given the goals to be achieved. This is the major problem of mixing scientific evidence with policy considerations.²¹¹

The SPS Agreement provides an appropriate and well established method of dealing with controversies surrounding food safety by allowing scientific conclusions to guide political judgment. A frustrating aspect of developing trade standards is deciding whether SPS measures should delineate specific threshold values or should merely provide a paradigm under which a range of acceptable scientific values should be determined. From a practical viewpoint, the goal of this type of analysis should be to develop methodologies that are accessible and useable to all member countries.²¹²

The problem of coordinating the efforts of scientific and policy making agencies is thus inescapable. Scientific agencies, in general, are not capable of weighing the many variables required for the development of policies affecting members of international political

²⁰⁸ The United States currently utilizes this approach through their GRAS standard. See *supra* note 176 (noting that the FDA evaluated the testing of the "Flavr Savr" tomato developed by the biotech firm Calgene).

²⁰⁹ See discussion *supra* Part I.B.2. (noting that the SPS Agreement requires states to develop their own risk assessment policies, based on scientific evidence, weighing environmental and health concerns against foreign trade).

²¹⁰ See SPS Agreement, *supra* note 5.

²¹¹ Though this Note is not directed at the topic of resolving the complex matter of science/policy, an examination of this issue is required in order to understand whether these decisions are properly made and by whom, especially with respect to the fact that this Note is seeking to develop trade standards applicable to all WTO member countries.

²¹² The "transparency" of the risk regulation is very important in this analysis. See discussion *supra* Part I.B.2.

organizations. Similarly, politicized organizations responsible for the development of international policy do not have the capability to make scientific judgments. The WTO, as a political organization, has recognized its natural limitations in making scientific judgments by deferring to scientific agencies for these judgments.²¹³ With respect to the development of policy regarding GM foods, however, a great deal of uncertainty exists due to the novel nature of the scientific procedures used, and, as a result, science/policy determinations are quite difficult. In balancing the competing aspects of the advantages of GM foods with the uncertainties surrounding them, compromises must be struck while maintaining the highest level of safety practical and acceptable for a member.

Substantial equivalence provides a principle under which scientific testing can occur during the evaluation of the safety of GM foods. This principle combines both the scientific and policy aspects of an SPS measure because it provides an endpoint for the scientific analysis of GM foods. It allows examination of the troubling aspects of GM foods while promoting the current methods of regulating their conventional counterparts. Prior to reaching the conclusion of substantial equivalence for a given food, scientists must be certain that the GM food presents no more risks to the population in question than its conventional counterpart. Thus, if a GM food is deemed substantially equivalent to its conventional counterpart with respect to a given member, then that food will be deemed safe enough for importation and/or production by that member.

C. Substantial Equivalence and the WTO

The implementation of the substantial equivalence standard as an SPS Measure would not mark the end of the debate surrounding GM foods within WTO countries. Because the SPS Agreement allows varying levels of protective measures between members (as long as there is a scientific justification for the higher level),²¹⁴ not all members will adopt substantial equivalence as their safety objective for evaluating GM foods. If Codex adopts the substantial equivalence standard, conflicts will arise between the members that use this standard and those using another standard or methodology for evaluating GM foods.²¹⁵

²¹³ See *supra* note 10 (noting that the WTO defers to three specialized international organizations for the development and maintenance of scientific standards).

²¹⁴ See SPS Agreement, *supra* note 5, art. 3, para. 3 (noting provisions allowing members to develop higher standards than those internationally recognized, as long as they are based on scientific evidence).

²¹⁵ These conflicts would be addressed through the WTO dispute settlement system in a manner similar to previous disputes arising under the SPS Agreement. For a concise analysis of these disputes, see generally Pauwelyn, *supra* note 88.

A conflict may arise under the substantial equivalence standard if one member challenges another member's determination that a specific GM food is not substantially equivalent to the conventional precursor.²¹⁶ This determination would allow the member making this determination (the blocking member) to ban the importation of the product or to limit its importation subject to various restrictions. The exporting member would then file a complaint with the WTO, and a dispute settlement committee would be formed.²¹⁷ Of the several inquiries that the dispute settlement committee would undertake under the SPS Agreement, the sufficiency of scientific evidence supporting the blocking member's regulation would be the most extensive.²¹⁸ Members are allowed to adjust regulations according to their acceptable level of risk. This level, however, must represent a "scientifically identified risk."²¹⁹ If the regulation is found to rest on a theoretical possibility, then it will not pass muster when examined by the committee.²²⁰ The committee inquiry may result in one of a few findings.²²¹ First, the committee may find that the blocking member was justified in its determination that the GM food is not substantially equivalent to its conventional precursor. The blocking member would then be allowed to block the importation of the product. Second, the committee may find that the blocking member has failed to present sufficient scientific evidence for its determination, in which case it will not be found to have been justified in blocking the GM

²¹⁶ It would clearly be impossible to illustrate all potential conflicts that may arise under this regulatory regime. This dispute is based on the circumstance that the importing member has already determined that the GM food is substantially equivalent to the conventional precursor.

²¹⁷ For example, the complaining member might claim that the blocking member's determination was in error and that based upon the risk assessments performed by the exporting member, the GM food should have been determined to be substantially equivalent.

²¹⁸ After the complaint is filed, in the circumstance presented, the exporting member would then have to provide scientific evidence for its determination that the GM food is "substantially equivalent" to the Committee. If after the review of this evidence, the Committee decides that the exporting member has presented a *prima facie* case, the blocking member must present evidence in rebuttal. This rebuttal evidence might consist of that member's risk management objectives, the risk assessments performed, and its own scientific findings. See generally WTO, *Rules*, *supra* note 86.

²¹⁹ See *supra* text accompanying note 181.

²²⁰ As per the SPS Agreement, theoretical possibilities are not ascertainable risks, and thus not valid justifications for burdensome trade restrictions imposed on a specific product by the Member fearing those possibilities. See SPS Agreement, *supra* note 5, art. 2, para. 2 ("Sanitary and phytosanitary measures shall not be applied in a manner which would constitute a disguised restriction on international trade."), *id.* art. 5, para. 2 ("In the assessment of risks, Members shall take into account available scientific evidence . . .").

²²¹ The findings listed here are based on the hypothetical circumstance that the blocking member has adopted the substantial equivalence standard for all evaluations of GM foods. These findings do not contemplate circumstances where the blocking member has adopted substantial equivalence as only a provisional SPS measure, where it has adopted another SPS measure for the evaluation of GM foods, or where the blocking member has presented an undue delay in their substantial equivalence determination, whether they use substantial equivalence or another methodology.

product.²²² Third, the committee may find that the blocking member has not rebutted the objective evidence presented by the exporting member; as a result, the committee would find that the blocking member was not justified its conclusion.²²³ These findings could then be appealed to the Appellate Body of the WTO.²²⁴

CONCLUSION

Though a given GM food may taste better, last longer, or be more abundant than its conventional counterparts, the uncertainties surrounding its underlying composition and the means used to produce it are the major roadblocks to general public acceptance of these products. This issue strikes deeply into various cultural beliefs and, as a result, it is not likely to be resolved any time soon. As newer products come along, another set of questions, new and old, will accompany them. The potential benefits of GM foods require that these products be regulated fairly, but the unanswered questions and the inevitability of their international expansion require a tight leash on the approval process.

Substantial equivalence presents a thorough and economical means of monitoring the expansion of GM foods in international markets. Although this standard provides a safety objective under which the testing of GM foods may be organized, it does not provide a specific limitation on the types of testing that will be required for this class of products. This standard has an objective scientific basis and a definite analysis endpoint. It allows WTO members autonomy in carrying out their own risk assessments and would apply to whole classes of GM foods. This flexibility combined with strictness fits appropriately into the regulations set forth under the SPS Agreement and could be adopted, in any one of countless forms, by a WTO member state. Thus, this standard should be deferred to by the WTO as a default standard for the evaluation of GM foods.

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²²² This conclusion is based on the circumstance where the importing and blocking members have different risk management objectives.

²²³ If there is sufficient scientific evidence that the GM food is substantially equivalent, and the two members have very similar risk management objectives which achieve the same level of sanitary and phytosanitary protection, then the blocking member may be required to adopt the determination of the importing member. See SPS Agreement, *supra* note 5, art. 4, para. 1.

²²⁴ See *Working Procedures for Appellate Review*, WTO Report WT/AB/WP/3 at Part II[20] (Feb. 28, 1997) (citing WTO rules to appeal committee decisions). A further analysis of this topic is beyond the scope of this Note.

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