From: Sandra Cleisz [sanclei@earthlink.net]
Sent: Thursday, April 08, 2004 7:16 PM
To: Chantal Line Carpentier
Subject: Article 13: Transgenic maize

I would like to make a public comment regarding the hoint public advisory committee meeting held in Oaxaca, Mexico on March 12, 2004, and on the Commission for Environmental Cooperation`s study of transgenic maize introduced to Mexico.

I am an environmental planner in Sonoma County, CAlifornia, and happened to be in Oaxaca when the meeting took place. I attended the meeting and found it fascinating and highly informative. I have the following comments to make, and hope that you will consider them in your report to NAFTA.

First, it was clear to me that 99.9% of the public comments made at the meeting were about stopping transgenic corn from entering Mexico, and especially from entering the area deep within Mexico where corn was born and developed over millenia. I believe that the comments made at the meeting reflect the feelings and beliefs of a broad spectrum of people, from farmers and peasants, workers in town, interested people from everywhere, many scientists, activists of many kinds, etc. I also support this belief that under NAFTA, the original resources of the people of an area, and especially corn and food products, should be respected and left alone. Transgenic corn, and mixed (part transgenic or genetically-modified agricultural products, mixed in with non gm products) should not be introduced into Mexico, as such products could endanger the original food, possibly modifying the genetic integrity of corn especially, (an open-pollinated crop) and endangering the food supply for millions of people throughout the world.

Labelling is extremely important, so that people everywhere can understand what product is being sold, and if it contains any GM condition. But labelling is not enough in this case--as the danger of people planting imported GM corn is too high due to the labelling not being understood, or not adequate to explain the dangers to the future of corn production in Mexico. Labelling may be too difficult also due to large shipments being labelled, but after being broken into individual bags, the labelling could disappear. Labelling would have to be more thorough than a scientist or policymaker can even imagine for it to work adequately, and to provide the conscious choice and free will that is so necessary, but inadequate to protect a unique life form.

The other interesting thing that i heard over and over, and completely agree with, is the insistence upon use of the Precautionary Principle: that until 20 to 30 years of research with this corn proves that it is viable over the long term and through disasters, global warming events, etc, AND does not cause any harm of any kind to humans, animals, other plants, and ecosystems in general, that it

should not be brought in/imported or used in Mexico. The research should be funded by and through joint government agencies of the 3 countries (or more if interested), but NOT by those seeking to profit from such products. The research must be independent.

I was especially struck by the lack of studies and relevant research on the natural systems of Mexico, much less about transgenics and corn. None of the scientists had any relevant answers to any of the deep questions being asked and the statements being made, and in fact, most of the scientists there appeared to agree that a lot of research is needed before any definitive statement can be made. The studies that were presented were a very light overview of what has been found so far, and not helpful in discussing the issue comprehensively.

Diversity is critically important to humankind as well as to the entire world we live in of multiple species and beings--plants, animals, soil, bacteria, ecosystems balance, etc. We cannot ignore this issue, and we must not allow corporations who wish to control certain products from forcing decisions on policymakers such as the Commission, and on NAFTA officials, that could affect the future of life on earth. Please take the time needed to consider carefully each decision and recommendation, and recommend the immediate stopping of importation of transgenic products (especially corn-maize) to Mexico.

Thank you very much.
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CFIA Comments on the CEC Article 13 initiative on Maize and Biodiversity: The Effects of Transgenic Maize in Mexico
16 April 2004

CFIA Comments on chapters 1, 2, 4, and 5

Chapter 1: Context and Background on Wild and Cultivated Maize in Mexico

1. This chapter provided extensive background information that is very useful for the topic.

2. However, the detail provided in the section entitled “Presence of Transgenic Maize in Mexico exceeded the scope of this chapter. This topic might better be left to subsequent chapters that go into some detail on the consequences of transgenic maize in Mexico.

Chapter 2: Understanding Benefits and Risks

1. This chapter was a good overview of approaches to benefits and risks, as indicated by the title.

2. The chapter went on to discuss transgenic crops and agricultural biotechnology specifically. Some of this may or may not apply to transgenic maize in Mexico, particularly with respect to unintentional adventitious presence.

3. In Section 2.2, the last paragraph states that “many” products commercialized over the next decade will be pharmaceutical, biologic or industrial compound-producing crops. These crops are mentioned in Section 2.3 also. These references could be misleading, since commercial production of such crops is with very few exceptions still hypothetical, and their importance in the future utterly unknown. Furthermore, in countries with relevant regulatory systems in place, both field trials and commercial production of these crops are under strict control to mitigate against accidental entry into food or feed supply chains.

Chapter Four: Assessment of Effects on Natural Ecosystems

1. In the introduction, the relationship between biodiversity and ecosystem function might be better documented, and its relevance to transgenic maize in Mexico more clearly substantiated. The implication that the introduction of genetically engineered organisms “intersects” with losses of biodiversity and changes in land use should be better defined and supported. (Page 1) It is not clear what if anything would relate genetic engineering in general to changes in biodiversity; in fact, any environmental impacts would be related to the introduced trait and not to genetic engineering itself.

2. It may be helpful to clarify whether risks of unintentional, adventitious introduction of transgenes into landraces or intentional adoption of transgenic varieties are being considered in this paper. The consideration of ecological impacts of changes in farming practices, for example, will depend on which situation is being evaluated. The question raised in the summary on page 14, "Will the introduction of transgenes have a positive or negative effect on natural ecosystems in Mexico?", will be easier to answer if it can clarified whether unintentional or intentional introduction is being discussed.

3. The scientific controversies raised on page 15 regarding the measurement and understanding of biodiversity and its effects on ecosystem function are all good, outstanding questions. The discussion of unresolved issues here is also balanced and logical. However, it is still not clear what might be a scientific basis for expecting genetically-engineered plants to have an effect on biodiversity and other parameters mentioned. It should be emphasized that any environmental impacts of a transgenic crop plant would depend on the trait introduced and would not be related to genetic engineering itself.

Chapter 5: Assessment of Biological Effects in Agriculture in Mexico

1. This chapter provides extensive and very relevant background information on maize agriculture in Mexico and its socio-economic status. It also provides a reasonable discussion of advantages and disadvantages of various transgenic crop traits for Mexican agriculture, from both an environmental safety and a socioeconomic view. Perhaps the title of the chapter could be changed to more accurately fit the apparent objective of the chapter.

2. The discussion on stacking of transgenes in Section 2.8 is somewhat unclear. The reference on page 11 to potential problems of inserting 10 to 20 or more genes in one cassette is not particularly relevant here, given that associated technological problems would need to be overcome by the developer before a commercial product could be launched. The potential risks when "farmers themselves accidently stack transgenes by accumulating multiple ones in their landraces" would depend on the traits involved, but this point is not made clear.

3. Furthermore, The reference to "chromosomal abnormalities" on page 11 of Section 2.8 is not clear. Are the authors suggesting that these abnormalities will arise with stacking? Or that they would be associated with individual transgenes? In either case, scientific substantiation should be provided.

4. In Section 3.3, the first phrase on page 16 stating "The general trend in farming operations is to have the farmer serve as contracted labor…" is unclear. Moreover, how the use of transgenic seeds could advance this trend is unclear.

5. The last paragraph of Section 3.3 also makes reference to selective disadvantages accruing to transgenic plants, particularly those related to the process of regenerating from tissue culture on page 17. As mentioned above for multiple gene cassettes (comment 2), these disadvantages are not particularly relevant here since they are fitness problems that would have to be addressed by the developer in order to produce a viable commercial product.

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CFIA comments on chapters 7 and 8

Chapter 7: Assessment of Human and Animal Health Effects

The following revisions need to be considered:

1. On the website's table of contents, chapter 7 of the report is titled "Assessment of Human and Animal Health Effects". This should be changed to **"Assessment of Human Health Effects"** which would match the actual document's title as there is no discussion of animal health effects in chapter

2. "The transference of a 2S albumen protein from Brazil nut into soybean…that was then withdrawn from human consumption". This allergen was detected at the research stage and was never approved or introduced into the food chain. (page 14)

3. "The Guardian published a note indicating that a new illness (fever, respiratory and skin reactions) is being investigated in Philippines that could be related to Bt maize. Of course, this finding must go through the necessary steps to test." (pages 14, 18) The effects of Bt maize have not been investigated. This article is unsubstantiated.

4. The fifth paragraph on page 14 mentions the appearance of new diseases for which no treatment is available is a concern regarding transgenic foods. The CFIA has not previously heard this raised as a concern. It is difficult to see how this could be related to genetic engineering.

5. Professor Barry Commoner's review for this chapter regarding the importance and frequency of unexpected and unanticipated issues should be removed from the document as it is not substantiated. (page 15)

6. The CFIA does not support the following statement and suggests it be removed: "It is a fact that current technologies modify allergenicity of foods." (page 16, second last paragraph)

7. On pages 19 and 20 there is a discussion on effect of transgenes on landraces. If incorporated, transgenes will not be maintained unless there is a selective pressure. There is also much concern about 3rd generation molecular farming plants; however, these have not been commercialized yet and the discussion seems to assume they have been commercialized.

8. Pages 31 and 32 includes a discussion on unintended effects of recombinant DNA techniques. This discussion fails to consider recombinant DNA in the context of traditional plant breeding and treats it in isolation.

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9. The following statements are not supported by references:

a) "…The growing evidence of genetic instability of purportedly 'successful' transgenic plants" (page 33)
b) "faithful replication of both the transgene and the new host's DNA may be sufficiently disrupted by transgenic process to result in an overwhelming proportion of unpredictable, unintended, unexpected and usually adeverse genetic changes" (page 33)
c) "Accordingly, the only feasible way of protecting Mexican agriculture from this hazard would be to end the commercial production of maize in the United States, Canada and Latin America." (page 37-38)

10. The discussion of different DNA polymerase systems in different species and the effect on mutation frequencies is a theoretical argument that is not supported by the fact that many transgenes have been inserted successfully into plants, which are replicated faithfully. The author makes sweeping conclusions from specific references. Specific evidence is not demonstrated to support this. Cross species transfer of genes occur in nature. (page 33)

11. In the following statement, "…Final marketed product does in some cases such as Bt soybeans exhibit unexpected changes in DNA nucleotide sequence in the region of the transgene," the reference refers to a Roundup ready soybean, not a Bt expressing soybean. Secondly, it is important to differentiate the difference between rearrangement of DNA around an insert which is not a safety concern as opposed to the expression of a protein which may be a safety concern. In the case of the RR soybean there was no corresponding protein changes thus no impact on safety. (page 36)

12. As part of the safety assessment performed, the composition of all modified plant is examined in detail. Thus, this comment "There are.. major uncertainties about the composition of transgenic plants and their potential effect on human and animal health..." on page 36 is not supported by the CFIA.

13. There are grammatical and spelling errors present throughout the document. For instance, "low-fitate", shoul be replaced by "low phytate". (page 13)

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Comments on Chapter 8: A Framework for Judging Potential Benefits and Risks

1. This chapter gives a good, brief review of philosophical approaches to risk management discussed in Chapter Two. It then goes on to overview risk assessment methodologies. These are for the most part sound and balanced discussions.

2. The chapter goes on to discuss the implications for Mexico. Some of the considerations here are a bit vague or not clearly substantiated. For instance, it is stated on page 17 that transgenes could move from varieties grown by commercial farmers into landraces grown by campesino farmers. While this is certainly true, the nature of the potential negative consequences are not clear. Since the campesino farmers do not export their grain, they will not be affected by market concerns around adventitious presence of transgenes. The impacts of adventitious transgenes in landraces on environmental safety would depend on the population genetics (rate of inflow of alleles and selection) and on the trait in question. These points have been omitted from this discussion.

3. Similarly, the potential risks of gene stacking are likely to be related to management issues, such as management of volunteers in the case of stacked herbicide tolerances, or possible incompatible planting strategies to slow development of insect resistance in the case of stacked Bt traits; but not necessarily to the fact that the transgenes “were never tested together” (page 18). This point was not made clear. Furthermore, transgenes that are not intended to enter the human food chain would be a problem on their own, even if not stacked.

4. Also discussed in this section (such as on page 18) were the risks associated with recombination or segregation of multiple transgenes within a single released variety. This is not likely to be an issue since, if there were any anticipated adverse effects of recombination or segregation of multiple transgenes, they would be addressed if not by the developer than by the assessment process prior to approval.

5. On page 19, there is a discussion of the uncertain and unpredictable fate of transgenes in landraces under the control of campesino farmers. It should be noted that this is also true for any genes flowing into landraces, for example from conventional commercial varieties. In addition, the quote repeated from Chapter Ten, page 3, stating that “the introduction of transgenes into an open pollinated crop... will inevitably lead to the widespread distribution of transgenes among these crops...” is a serious exaggeration. The distribution of the transgenes within landraces, once introduced, will depend very much

on the rate of inflow, the fitness of the hybrids and the selection pressures for or against the trait.

6. What is also notably absent from this discussion is the context of the consequences of these transgenes. As mentioned, the presence of the transgene itself does not necessarily imply a socioeconomic or environmental safety risk. The impact, if any, will depend on the trait.

Comments on CEC Draft Report on Maize Biodiversity

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April 9, 2004

Scientists can assess the quality of the scientific review provided by the authors of the chapters of the CEC draft report on transgenic maize. Coming as I do from an economic research institute that has carried out collaborative research with Mexican economists on maize and the environment under NAFTA, I will offer only a brief summary of conclusions I draw from the text of the draft chapters of the report. This is not intended as an exhaustive summary, of course, but rather a logical set of conclusions that follow from the studies. I think the work overwhelmingly points to the need and justification for taking a precautionary approach to this matter, most notably by restricting corn imports from the United States into Mexico in new ways that can prevent future contamination.

The conclusions I draw from the studies are as follows:

1. Contamination has happened, and this has been proven. It is still happening, and under the current set of rules and laws it will undoubtedly continue.

2. Those who have suffered the contamination have never asked to participate in any experimentation with the potential of GM crops, nor are they now expressing any willingness to do so.

3. The field tests that have been done on GM maize tell us little that is relevant to Mexico about its long-term effects:

a. there are no long-term studies;

b. what studies have been done took place in agricultural and ecological systems very different from those in Mexico.

c. the scientific evidence shows that there is still a great deal that is not known about impacts at all levels.

4. It is not too late to take action to protect traditional varieties of Mexican maize. Contamination can be halted, and there is a good chance existing damage can be remediated.

5. Maize diversity is a global common good, of value not only to indigenous Mexican communities but to all of humanity. Therefore, the interest in taking action on this issue is greater than just a local or national interest.

6. While contamination with current varieties of GM maize may present relatively low risks (and there was not consensus on this point), future GM varieties are likely to pose much greater risks.

7. The likely source of most of the contamination was imported corn from the US. Controlling contamination is thus linked to controlling trade.

8. The Mexican government has at its disposal a variety of measures it could take to limit contamination, most notably restricting imports in new ways.

9. Given the unequal distribution of the risks and benefits of GM maize, there are many reasons not to rely on strict risk-benefit analysis; the alternatives presented in the studies are informed consent and precaution.

10. This process has demonstrated that with a high level of information, local communities are not prepared to consent to GM contamination or experimentation. The only appropriate approach is precaution.

11. A precautionary approach necessarily involves both continued restrictions on GM cultivation in Mexico and expanded restrictions on imports from the United States.

Dear Chantal,

I'm a research analyst with Friends of the Earth (FoE), the international environmental organization. FoE U.S. has been actively involved in the issue of transgenic crops for over 5 years. FoE U.S. commissioned the testing which discovered StarLink corn in the food supply. We have released comprehensive, science-based reports on The StarLink Affair, the inadequate regulation and potential allergenicity of pesticidal plants such as transgenic Bt maize, and in 2002 we brought the issue of pharm crops (crops genetically engineered to produce drugs and chemicals) to the attention of the public and the broader scientific community with a major report entitled "Manufacturing Drugs and Chemicals in Crops." See www.foe.org/safefood/ and www.foe.org/biopharm/

As demonstrated by the work cited above, we have significant expertise in the area of Bt crops, particularly in the area of human health, and most transgenic maize incorporates a modified version of one of several bacterial endotoxins derived from the soil bacterium Bacillus thuringiensis.

I have attached two documents as the comments of Friends of the Earth U.S. on the draft of "Maize and Biodiversity: The Effects of Transgenic Maize in Mexico" for the consideration of the advisory group. They relate specifically to Chapter 7 concerning potential human health impacts.

1) A 2-page summary of some of the evidence implicating Bt endotoxins in Bt crops as potential human food allergens;

2) An analysis of grave deficiencies in the U.S. regulatory system and corporate testing practices for genetically engineered crops. While I would like the entire study to be incorporated in my comments, please note that it includes a comprehensive case study of Bt corn and its potential human health impacts that should be of particular relevance to the advisory group.

Both the summary and the study contain detailed references to expert reports, scientific papers and other material relevant to the question of transgenic maize and its human health status that I would like, if possible, to be included in my comments by reference.

Sincerely yours,

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What Do Experts Say About the Potential Human Health Effects of Genetically Engineered Corn?

August 2003

Seven years after U.S. farmers began planting varieties of genetically engineered Bt corn, now grown on over 20 million acres, it still isn't known whether they impact human health. Suggestive evidence of allergenicity has been ignored, the EPA's assessment is deeply flawed, and existing clinical test reagents lay unused. According to independent experts advising the EPA:

> ***"….Bt proteins could act as antigenic and allergenic sources."***[4]

> ***"Only surveillance and clinical assessment of exposed individuals will confirm the allergenicity of Bt products or for any other novel protein introduced into the diet of consumers."***[1]

Unfortunately, the U.S. government has not funded any further research into the allergenicity of Bt crops. Independent scientists, however, report that Bt (Cry) proteins elicit allergy-like immune reactions in farm-workers.[2] Skin prick allergy tests were developed in this study, but the EPA has yet to make use of them to test others. Bt proteins also elicit immune responses in animals, and allergic reactions are one form of immune system response:

> ***"The data obtained in the present study confirm that the Cry1Ac protoxin is a potent immunogen able to induce a specific immune response in the mucosal tissue, which has not been observed in response to most other proteins."***[3]

This same Cry1Ac protein is also as potent as cholera toxin in increasing the immune response to other proteins (e.g. as adjuvants).[4] A version of Cry1Ac is engineered into Bt cotton, and it is very similar in structure to the Cry1Ab toxin found in most Bt corn. Both resemble StarLink corn's Cry9C more than previously believed (see below).

Over 200 people reported allergic reactions to yellow corn products they suspected might be due to StarLink corn, some of them life-threatening. Unfortunately, the Food and Drug Administration (FDA) and Centers for Disease Control (CDC) investigated only a handful of these cases, and their results were inconclusive due to use of an inadequate test. Scientific advisors to the Environmental Protection Agency, who included some of the nation's leading allergists, had this to say about the FDA's allergy test[5]:

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[1] EPA Scientific Advisory Panel, "Bt Plant-Pesticides Risk and Benefits Assessments," March 12, 2001, p. 76. Available at: http://www.epa.gov/scipoly/sap/2000/october/octoberfinal.pdf

[2] Bernstein et al (1999). "Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides," Environmental Health Perspectives 107(7), pp. 575-82.

[3] Vazquez-Padron et al (2000). "Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from Bacillus thuringiensis HD 73 in mice," Brazilian Journal of Medical and Biological Research 33, p. 147.

[4] Vazquez-Padron et al (1999). "Bacillus thuringiensis Cry1Ac protoxin is a potent systemic and mucosal adjuvant," Scandinavian Journal of Immunology 49, p. 583.

[5] "Assessment of Additional Scientific Information Concerning StarLink Corn," EPA's Scientific Advisory Panel, SAP Report No. 2001-09, from meeting held July 17-18, 2001. Available at: http://www.epa.gov/scipoly/sap/2001/july/julyfinal.pdf.

> ***"The test, as conducted, does not eliminate StarLink Cry9C protein as a potential cause of allergic symptoms."*** (p. 29)

In fact, the advisors cautioned that ***any*** level of StarLink in food might be harmful:

> ***"... the Panel concluded that based on reasonable scientific certainty, there is no identifiable maximum level of Cry9C protein that can be suggested that would not provoke an allergic response and thus would not be harmful to the public."*** *(p. 35)*

One advisor was concerned enough to urge that all corn products be labeled:

> ***"One Panel member considered labeling products as "may contain" StarLink corn since consumers would then be alerted to the possible presence of Cry9C. Without labeling, there would be no basis for consumers to recognize that a given corn product is different from that produced from non-Cry9C containing corn."*** *(p. 39)*

Even though StarLink continues to linger in the food supply over two years after cultivation of the corn was banned in the fall of 2000[6], the EPA never conducted or funded the additional research recommended by its expert advisors, including: 1) Gather more biochemical data on StarLink's Cry9C protein; 2) Develop a reliable assay to detect Cry9C in processed foods; 3) Alert the medical/allergy community to the possibility of allergenic corn; 4) Test sensitive populations, such as food-allergic children, for allergic reactions; 5) Develop skin prick tests and antibody detection assays; 6) Conduct additional testing on those with severe reactions. As a result, those who reported allergic reactions to StarLink still do not know for sure if StarLink was in fact the cause.[7]

Friends of the Earth has found additional evidence suggestive of the allergenicity of Bt corn's Cry1Ab in little-known studies by an FDA researcher and other scientists:

1) **Structural similarity to a known allergen:** A 1998 study by an FDA scientist warns that "the similarity between Cry1A(b) [in Bt corn] and vitellogenin [egg yolk allergen] might be sufficient to warrant additional evaluation."[8]
2) **Resistance to digestion:** Studies by an independent scientist show that Cry1Ab is 60 times more resistant to digestion than indicated in Monsanto's digestive stability test.[9]
3) **Resistance to heat:** Cry1Ab is comparable in heat stability to StarLink's Cry9C.[9]

Despite this evidence of allergenicity, in 2001 the EPA re-registered all Bt corn varieties for an additional seven years.[10] Is Bt corn at least partly responsible for the increase in food allergies observed in recent years? We will have no way of knowing until the U.S. government starts getting serious about regulating genetically engineered crops.

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[6] "Japan finds StarLink in US corn cargo -U.S. exporters say," by Randy Fabi, Reuters, Dec. 27, 2002.
[7] For a full, scientifically-based critique of the StarLink investigation, see: "The StarLink Affair," by Bill Freese for Friends of the Earth, submitted to the EPA's Scientific Advisory Panel, July 2001, at www.foe.org/safefood/starlink.pdf.
[8] Gendel, S. (1998). "The use of amino acid sequence alignments to assess potential allergenicity of proteins used in genetically modified foods," Advances in Food and Nutrition Research 42, pp. 45-62.
[9] Noteborn, H. (1998). "Assessment of the Stability to Digestion and Bioavailability of the LYS Mutant Cry9C Protein from Bacillus thuringiensis serovar tolworthi," submitted to the EPA, EPA MRID No. 447343-05. (Cry1Ab was tested along with Cry9C)
[10] See "A Critique of the EPA's Decision to Re-Register Bt Crops and an Examination of the Potential Allergenicity of Bt Proteins," by Bill Freese for Friends of the Earth, submitted to the EPA Dec. 9, 2001. www.foe.org/safefood/comments.pdf.

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July 2003
(updated 10-31-03)

Genetically Engineered Crop Health Impacts Evaluation

A Critique of U.S. Regulation of Genetically Engineered Crops and Corporate Testing Practices, with a Case Study of Bt Corn

Prepared by Bill Freese, Research Analyst
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Introduction

It seems a simple question: "Are genetically engineered foods harmful to human health?" The purveyors of sound-bite science have an equally simple and satisfying string of answers: "No, not at all. Genetic engineering is precise. These foods are thoroughly tested. The regulatory agencies vouch for their safety."

But take a closer look and these simple answers fall apart.

In fact, genetic engineering is a haphazard process, more of an art than a science because it lacks repeatability, and results in many more abortions than successes. With rare exceptions, the transgenic proteins actually produced in these foods have not been tested at all, providing no answer regarding their health impacts, if any. And contrary to popular opinion, the Food and Drug Administration (FDA) has ***not*** approved ***any*** GE food as safe.

In the following GAPS analysis, we delve deeply into some of the most important concerns about GMOs rather than cite every single study suggesting potential health impacts. Another feature that sets this review apart is reference to material that is largely or completely unknown to the scientific community (e.g. unpublished studies submitted to the EPA by Monsanto, FDA consultation documents). This GAPS analysis is broken down into three parts:

1) Gaps in the U.S. GE foods "regulatory" system;
2) Glaring inadequacies of the testing regimens ***as practiced;*** and
3) Case study of Bt corn

Gaps in the U.S. GE Foods "Regulatory" System

Regulation or Rubber Stamp?

Genetically engineered (GE) food "regulation" in the U.S. is based on the dogma of substantial equivalence – the extremely strong presumption that neither the genetic transformation process nor the foreign gene construct or protein will impair the wholesomeness of the transgenic crop[1]. Think about this for a moment. The regulatory system is founded on the notion that GE foods are unchanged, hence safe, and so do not require testing or regulation[2]. All the weaknesses of the system flow from this paradoxical assumption.

This explains why:

1) The FDA has a ***voluntary*** "consultation process" rather than a ***mandatory*** review; that is, a company wishing to introduce a novel GE crop is NOT required to consult with the FDA at all, but is merely encouraged to do so[3];
2) FDA never examines the original studies conducted by companies, but rather only the company's summary assessment of its own research[4];
3) Companies can and do deny FDA requests for additional data, and FDA misses obvious errors in company-provided data summaries that a thorough review would have uncovered[5]; and finally,
4) At the end of a voluntary consultation, the FDA merely issues a note conveying *the company's* conclusion that its GE crop is "substantially equivalent" to conventional varieties; that is, the FDA does NOT approve any GE crop as safe, but rather lets the GE crop developer decide this question.[6] This is perhaps due to liability concerns on the part of the government.

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[1] The FDA steps in only when there is glaring reason to think substantial equivalence does not apply – i.e. the transgenic protein comes from a known allergenic source, something which all companies avoid anyway, especially since it was demonstrated in 1996 that a soybean spliced with a Brazil nut gene elicited skin prick reactions in Brazil-nut allergic people, as well as IgE binding of their sera.

[2] In fact, GE foods "regulation" was introduced as a "de-regulatory" initiative by the Bush Senior administration. See "Biotechnology Food: From the Lab to a Debacle," New York Times, Jan 25, 2001 for a revealing look at how the U.S. "regulatory" system for GE foods was developed, as told by industry and government officials.

[3] A good example of the political rather than scientific nature of GE foods regulation is the FDA's recent decision to shelve long-standing plans to make consultations mandatory. The Bush Administration wanted to avoid any hint that U.S. regulation of GE foods is deficient while the WTO challenge of European Union GE foods regulation is underway.

[4] "Holes in the Biotech Safety Net: FDA Policy Does Not Assure the Safety of Genetically Engineered Foods," by Doug Gurian-Sherman, Center for Science in the Public Interest, January 2003.

[5] Ibid, pp. 4-7. See also the Bt Corn Case Study below.

[6] The letter sent by the FDA to Monsanto upon completion of the consultation process for Monsanto's Bt corn (events MON809 and MON810) is typical. It reads in part: "Based on the safety and nutritional assessment you have conducted, it is our understanding that *Monsanto has concluded* that corn products derived from this new variety are not materially different in composition, safety, and other relevant parameters from corn currently on the market, and that the genetically modified corn does not raise issues that would require premarket review or approval by FDA. … as you are aware, it is *Monsanto's responsibility* to ensure that foods marketed by the firm are safe, wholesome and in compliance with all applicable legal and regulatory requirements" (my emphasis). See Letter for BNF No. 34, dated Sept. 25, 1996, at: http://www.cfsan.fda.gov/~lrd/biocon.html.

In Europe, on the other hand, "substantial equivalence" is hypothetically assumed only as a ***starting point*** for investigation[7]. A particular GE crop may very well not be substantially different than its conventional counterpart, say European scientists, but first we must subject them to an in-depth examination to confirm or deny this hypothesis.

Another reason for the lack of meaningful regulation in the U.S. is the enormous influence the biotechnology industry, particularly the Monsanto Corporation, has had in writing the rules. According to an important *New York Times* article on this subject (see footnote 2):

> *"What Monsanto wished for from Washington, Monsanto and, by extension, the biotechnology industry got. If the company's strategy demanded regulations, rules favored by the industry were adopted. And when the company abruptly decided that it needed to throw off the regulations and speed its foods to market, the White House quickly ushered through an unusually generous policy of self-policing.*
>
> *Even longtime Washington hands said that the control this nascent industry exerted over its own regulatory destiny through the Environmental Protection Agency, the Agriculture Department and ultimately the Food and Drug Administration was astonishing.*
>
> *"In this area, the U.S. government agencies have done exactly what big agribusiness has asked them to do and told them to do," said Dr. Henry Miller, a senior research fellow at the Hoover Institution, who was responsible for biotechnology issues at the Food and Drug Administration from 1979 to 1994."*

This testimony – from government and biotech industry sources – makes other claims regarding the undue influence of the biotech industry on GE food issues more credible. For instance, there is evidence to suggest that Monsanto initiated the chain of events leading to the dismissal and discrediting of Dr. Arpad Pustzai, whose animal research suggested that potatoes engineered to produce lectins (which are similar in nature to the Bt toxins in GE pesticidal crops) could be responsible for causing gastric lesions.[8]

Obstacles to independent evaluation of GE crops:

Despite numerous calls by scientists for more independent research into the potential health and environmental impacts of GE foods, the U.S. government allocates shamefully little money to this end. The U.S. Department of Agriculture, for instance, spends just $3.6 million out of a $193 million research budget to support studies that examine potential environmental impacts. Even when independent researchers are

[7] Kuiper et al (2001). "Assessment of the food safety issues related to genetically modified foods," The Plant Journal 27(6), p. 504.

[8] "The Sinister Sacking of the World's Leading GM Expert – and the Trail that Leads to Tony Blair and the White House," by Andrew Rowell, The Daily Mail (UK), July 7, 2003

funded, a finding of potential harm requiring follow-up can effectively disqualify those scientists from additional funding. For instance, one scientist found suggestive evidence that the insecticidal proteins found in Bt spray and Bt crops could be allergenic in a study approvingly cited and reviewed by expert advisers to the Environmental Protection Agency (EPA). He has been unable to obtain funding for further research in this area. Another scientist has done EPA-sponsored research on unintended effects in Bt corn, as well as the environmental impacts of Bt insecticidal proteins. He, too, has had difficulty obtaining funds to continue these lines of research (source: personal communications).

Other scientists have been unable to obtain the GE crop for independent animal feeding studies. One example is a Japanese scientist who was denied access to modest amounts of DuPont's high-oleic soybeans by both DuPont and the Japanese government when that crop was being reviewed by Japanese regulatory authorities (source: personal communication). A scientist studying the potential for a GE crop to spread beneficial traits to sexually compatible weeds (creating so-called "superweeds") was denied access to the transgene by the GE crop developer.[9]

Still other researchers have obtained permission to study GE crops only after agreeing to onerous restrictions. For instance, one common condition forced on scientists is a pledge not to sequence the transgenic protein (source: personnel communication). Ironically, full sequencing of the transgenic protein *as generated by the plant from the inserted transgene* has long been recommended by numerous expert bodies as a basic prerequisite for a sound evaluation[10], but this information has never been supplied by companies in any of the many cases we have seen.[11].

In fact, even prestigious government review bodies have been denied access to basic information required for sound reviews of these crops owing to excessive claims of "confidential business information."[12]

As a result, there is hardly ever any independent research available to confirm or dispute the GE crop developer's claims of safety. And as we shall see, even when such research is available, U.S. regulators tend to ignore it, preferring to base their evaluations solely on company-provided information.

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[9] Dalton, R. (2002). "Superweed study falters as seed firms deny access to transgene," *Nature* 419(6908), p. 655.
[10] For instance, see: "Mammalian Toxicity Assessment Guidelines for Protein Plant Pesticides," EPA's Scientific Advisory Panel, SAP Report No. 2000-03B, Sept. 28, 2000, pp. 10, 14. http://www.epa.gov/scipoly/sap/2000/june/finbtmamtox.pdf.
[11] Companies sequence only the 5-25 amino acids at the N-terminal of the transgenic protein. See, for example, EPA's review of Mycogen/Pioneer's Bt (Cry1F) corn. Less than 1% of the Cry1F protein – only 5 of the 605 amino acids – were sequenced. "Biopesticides Registration Action Document – *Bacillus thuringiensis* Cry1F Corn," US EPA, August 2001. http://www.epa.gov/pesticides/biopesticides/ingredients/tech_docs/brad_006481.pdf.
[12] See, for example: "Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation," Committee on Environmental Impacts Associated with Commercialization of Transgenic Plants of the National Research Council, National Academy of Sciences (2002), pp. 11, 177. http://books.nap.edu/catalog/10258.html.

Flaws in reviews of GE crops that appear to demonstrate safety:

One source of confusion on the potential health impacts of genetically engineered foods is the tendency of many expert scientific bodies to issue reports that are inherently contradictory. (Examples include committees of the National Academy of Sciences and the U.K. Royal Society). That is, they often call for more stringent testing regimens ***and*** state (or imply) that currently marketed GE crops are safe – which of course begs the question of how inadequately tested crops can be judged safe. The purveyors of sound-bite science have made a cottage industry of publicizing the latter claims while ignoring the serious criticisms of current testing regimens made by the very same bodies.

Often, the contradiction is only apparent. The expert body will say that there is no evidence that GE foods on the market are unsafe. Yet "lack of evidence" often reflects the lack of adequate studies – absence of evidence rather than evidence of absence.

A related error is to make an unjustifiable distinction between currently marketed GE crops, which are said to be safe because they have "simple" and well-understood modifications, and future applications, which because of their greater complexity will require more robust testing regimens[13]. While stacked crops, for instance, may in some cases pose greater risks than those with single-transgene traits, there is no scientific basis for distinguishing the two categories with respect to stringency of testing required. This is especially true in the arena of unintended effects, which can be triggered by the genetic transformation process *per se* (or by widely used viral promoter sequences) rather than the particular transgene(s) introduced.

A third common thread in the numerous expert reviews is their reliance on the opinions of national regulatory agencies, particularly the FDA, which as noted above are themselves based on "data summaries" from the financially interested biotech companies rather than the company's full, original studies. Even if members of such expert bodies want to examine the original studies, they often either cannot gain access to this sensitive material (considered proprietary, see footnote 12) or simply do not have time to examine those studies that may be available, relying instead on selective summaries of these studies by the regulatory agencies (e.g. Scientific Advisory Panels to the EPA, source: personal communication).

A fourth consideration is conflict of interest. The expert bodies are often comprised mainly of plant science specialists who themselves receive research funding from biotechnology companies, or whose institutions receive such funding.

[13] For one example, see: G. J. Persley, "New Genetics, Food and Agriculture: Scientific Discoveries - Societal Dilemmas," for The International Council of Science, June 2003.

To take just one example, in a 2002 report on the potential health impacts of genetically engineered crops[14], the pro-biotech U.K Royal Society called on the U.K. Food Standards Agency to "consider whether post-marketing surveillance should be part of the overall safety strategy for allergies, especially of high-risk groups such as infants and individuals in 'atopic' families." The Royal Society also concedes that ***the current criteria for human health assessments of GE crops are neither explicit nor objective.*** In other words, testing regimens for GE crops are subjective, undefined and fail to account for potential risks to infants (here, GM soy-based formulas come to mind) and other groups prone to allergies. Given these grave failings, the report's familiar statement that "There is at present no evidence that GE foods cause allergic reactions" must be regarded as irresponsible, because it clearly conveys (and is intended to convey) the misleading impression that these crops have been exhaustively tested and demonstrated safe. But one simply cannot demonstrate, based on reasonable scientific certainty, that a GE crop is safe with the use of subjective, undefined testing regimens that don't even consider the most vulnerable sectors of the population. A second example is detailed in the following section.

[14] "Genetically modified plants for food use and human health – an update," The Royal Society, February 2002. Available at http://www.royalsoc.ac.uk/templates/search/websearch.cfm?mainpage=/policy/cur_gm.htm.

Inadequacies of the testing regimens *as practiced*

Four especially troubling issues are detailed below. The list is not exhaustive. Please note that the treatment below, unlike most critiques of this sort, deals with specific examples of commercialized or field-tested GE crops. Sources include difficult-to-obtain, unpublished corporate studies and other documents, such as Scientific Advisory Panel reports to the EPA, that are mostly unknown to the scientific community.

Surrogate proteins:

Biotech companies almost never test the transgenic protein actually produced in their engineered crops. Instead, for testing purposes they make use of a bacterial-generated ***surrogate*** protein that may differ in important respects from the plant-produced one. The same genetic construct used to transform the plant is spliced into ***bacteria*** (usually *E. coli*), and these bacteria are grown out. The surrogate transgenic protein is then extracted from the bacteria, and sometimes processed (e.g. cleaved with trypsin to generate its "tryptic core"). This bacterial-derived surrogate protein (or its derivative) is then employed for all subsequent testing: short-term animal feeding studies, allergenicity assessments, etc.

Several scientists to whom we described this practice expressed amazement. They take it for granted that plant and bacteria will generate different transgenic proteins from the same gene, even if transformed with the very same genetic construct. Testing a surrogate, they say, is no substitute for testing the real thing. This is because:

1) The foreign DNA actually integrated into the plant genome will differ from that taken up as a plasmid by bacteria due to the peculiarities of each transformation "event" (as the name implies, each "event" is unique and non-repeatable); for instance, it is not uncommon to find that only fragments of the intended gene have been incorporated into the plant's genome; disruption of native DNA often occurs adjacent to the site(s) of insertion.

2) Even if precisely the same foreign DNA is incorporated into bacteria and plants, the two organisms – which are kingdoms apart in biological terms – generate and process proteins differently. For instance, most bacteria do not add sugar molecules to proteins, while plants do, in a process known as glycosylation. Plant glycosylation patterns present the risk of immune responses, including allergic reactions.

As a result, animal feeding studies and allergenicity assessments that make use of bacterial surrogate proteins or their derivatives may not reflect the toxicity or

allergenicity of the plant-produced transgenic protein to which people are actually exposed.

Biotech companies use surrogate proteins for testing purposes because they find it inconvenient to extract sufficient quantities of transgenic proteins from their plants. Yet several expert bodies on both sides of the Atlantic have criticized this practice. To take just one example, according to a National Academy of Sciences committee that conducted an exhaustive review of Bt crops: "Tests should preferably be conducted with the protein as produced in the plant." If surrogates are nonetheless used:

> *"The EPA should provide clear, scientifically justifiable criteria for establishing biochemical and functional equivalency when registrants request permission to test non plant-expressed proteins in lieu of plant-expressed proteins."*[15]

Three years later, the EPA has still failed to do this, even though its scientific advisers have proposed such "test substance equivalence" criteria.[16] In fact, the toxicity and allergenicity assessments of Bt crops currently on the market employed surrogate proteins that did ***not*** meet these criteria[17]. The same is true of most or all non-Bt engineered crops as well.

This is not an academic point. The StarLink Scientific Advisory Panel – comprising some of the nation's leading allergists – strongly criticized the FDA for using such a bacterial surrogate Cry9C (rather than StarLink Cry9C) in its allergy assay: "The use of non-equivalent, bacteria-derived coating antigen raises the possibility that IgE directed against plant derived Cry9C may not be detected" (which would mean false negatives). For this and other reasons: "The test, as conducted, does not eliminate StarLink Cry9C as a potential cause of allergic symptoms."[18]

In fact, the advisors cautioned that ***any*** level of StarLink in food might be harmful:

> *"... the Panel concluded that based on reasonable scientific certainty, there is no identifiable maximum level of Cry9C protein that can be suggested that would not provoke an allergic response and thus would not be harmful to the public." (p. 35)*

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[15] "Genetically Modified Pest-Protected Plants: Science and Regulation," Committee on Genetically Modified Pest-Protected Plants, National Research Council, National Academy of Sciences, 2000, p. 65, see: http://books.nap.edu/catalog/9795.html. For similar recommendations, and examples of immunologic differences between nearly identical proteins, see: "The StarLink Affair," Friends of the Earth, July 2001, sections 9.2 to 9.4, at www.foe.org/safefood/starlink.pdf.

[16] "Mammalian Toxicity Assessment Guidelines for Protein Plant Pesticides," EPA's Scientific Advisory Panel, SAP Report No. 2000-03B, Sept. 28, 2000, p. 14. http://www.epa.gov/scipoly/sap/2000/june/finbtmamtox.pdf.

[17] Freese, B. (2001), "A Critique of the EPA's Decision to Reregister Bt Crops and an Examination of the Potential Allergenicity of Bt Proteins," adapted from comments of Friends of the Earth to the EPA, Dec. 9, 2001. Available at: www.foe.org/safefood/comments.pdf.

[18] "Assessment of Additional Scientific Information Concerning StarLink Corn," EPA's Scientific Advisory Panel, SAP Report No. 2001-09, pp. 29-30. http://www.epa.gov/oscpmont/sap/2001/july/julyfinal.pdf.

Given the use of bacterially produced surrogate proteins as the norm, one cannot avoid the conclusion that the plant produced transgenic proteins we actually eat in our food are virtually untested.

Unintended effects:

Artificial introduction of foreign genetic constructs into plants creates numerous opportunities for potentially hazardous unintended effects, which include over-production of native allergens or toxins, nutritional deficits, creation of novel fusion proteins (i.e. proteins from inadvertent combination of plant and foreign DNA in the transformation process) with unknown properties, and horizontal transfer of transgenic DNA (including antibiotic resistance markers) to bacteria residing in the human gut. As the regulatory system was being designed in the early 1990s, FDA scientists called for GE crop-specific regulations to test for such "pleiotropic" effects. But they were overruled by administrative superiors, who insisted on a "deregulatory" system that permitted biotech companies to bring their novel GE crops to market as cheaply as possible, meaning no mandatory testing or even review.[19]

Unintended effects are common. Some – especially blatant effects – are caught and weeded out during the development process. Subtle effects may remain undetected for years after commercialization. David Schubert, professor of cell biology at the Salk Institute, reports that engineering a human gene into human cells has been shown to significantly increase or decrease the expression levels of fully 5% of the genes in the cell (as measured by mRNA levels.)[20] The same is likely true of engineered plants, though no regulatory agency requires or applies techniques to detect such changes.

Some phenomena likely to cause unintended effects, such as horizontal gene transfer, were once dismissed as all but impossible. However, recent evidence from what has been called the first human GE food feeding trial demonstrates that the herbicide resistance gene in glyphosate-resistant soybeans is indeed transferred to, ***and expressed in***, human gut bacteria.[21] There is no reason to think that antibiotic resistance marker genes used in GE crops may not also transfer to gut bacteria, and from there through conjugation to other, perhaps pathogenic, bacteria. This finding has strengthened long-standing concerns on the part of the British Medical Association and many others that GE crops might promote the spread of antibiotic-resistant, pathogenic bacteria and so impair the efficacy of these drugs.

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[19] See www.bio-integrity.org/list.html for internal memos from FDA scientists concerning the inadequacy of the regulatory framework proposed and adopted in 1992. See also "Biotechnology Food: From the Lab to a Debacle," by Kurt Eichenwald, Gina Kolata and Melody Petersen, New York Times, 1/25/01 for a revealing look at how biotech firms influenced development of the U.S. regulatory framework.

[20] For one of many references, see: "A different perspective on GM food," by David Schubert, professor of cell biology at the Salk Institute, Nature Biotechnology, Vol. 20, October 2002.

[21] Netherwood T, Martin-Orue SM, O'Donnell AG, Gockling S, Gilbert HJ and Mathers JC. Transgenes in genetically modified Soya survive passage through the small bowel but are completely degraded in the colon. Study conducted for the UK Food Standards Agency, July 2002.

In 2002, the National Academy of Sciences convened a panel to consider unintended, health-related effects of plant genetic engineering, and the means to detect them. (The very fact that this panel was convened validates the decade-old concerns of FDA working scientists.) European scientists advocate non-targeted techniques for measuring the levels of hundreds of proteins, metabolites, and/or messenger RNAs to increase the chances of detecting unintended effects,[22] as does Dr. Schubert (footnote 20). Monsanto, for some reason, opposes this approach,[23] which means that U.S. regulators will most likely not even recommend its use. In the U.S., regulators generally see nothing but summary data from companies on gross compositional analyses (i.e. fat, protein and starch levels) together with targeted screening of a handful of compounds (e.g. amino acids). However, there are no data requirements; companies submit summaries of whatever research they choose to conduct.

Visual inspection, or the "gross abnormality" test:

The case of barnase:

Barnase is an enzyme that degrades single-stranded RNA molecules. A bacterial form of barnase is a known toxin, causing kidney damage when perfused into rats.[24] A bacteria-derived version of barnase is spliced into corn and other crops to induce male sterility, which it does by rendering the anthers incapable of producing viable pollen grains. For example, the barnase gene has been engineered into Aventis' MS6 line of male-sterile corn,[25] which was deregulated by USDA for commercial cultivation in 1999. It is linked to a promoter fragment from an "anther-specific" gene, which is designed to limit expression of the toxin to anther tissue. However, it is well-known that so-called tissue-specific promoters drive production of low levels of transgenic protein in non-target tissues. Thus, more careful scientists refer to them as "tissue-preferred" promoters rather than "tissue-specific," admitting that "some expression may occur in other parts of the plant."[26]

Because of its toxicity to the rat kidney, barnase could present food or feed safety concerns if expressed in corn kernels or fodder. How did Aventis test for possible expression of barnase in its MS6 corn? According to the FDA, Aventis: 1) Assumed that any level of barnase expression in tissues other than the anther would result in "abnormal plant growth"; 2) Not observing abnormal plant growth, Aventis concluded

[22] Kuiper et al (2001), op. cit.
[23] Roy Fuchs of Monsanto, Power Point presentation to the NAS committee cited above.
[24] Ilinskaya and Vamvakas (1997). "Nephrotic effect of bacterial ribonucleases in the isolated and perfused rat kidney," Toxicology 120, pp. 55-63.
[25] FDA's Consultation Note on Aventis' Male-Sterile Corn, *MS6* Line, April 4, 2000. See Memo for BNF No. 66 at http://www.cfsan.fda.gov/~lrd/biocon.html. (Note: FDA issues an extremely brief document – a "note to the file" – for genetically engineered crops that are the subject of "voluntary consultations" between the FDA and the developer. The note to the file [normally about 4 pages of 1 ½-space text] merely conveys some basic facts about the crop and the developer's assurances that it is substantially equivalent to the conventional crop.)
[26] For example, see: "Commercial production of aprotinin in plants," U.S. Patent 5,824,870 awarded to Baszczynski et al.

that barnase was not present anywhere else in the corn plant. There is no analysis of the assumption that any level of barnase will entail abnormal plant growth. Nor is there any discussion of the potential human toxicity of bacteria-derived barnase in corn kernels, despite its troubling mechanism of action (nucleic acid-degrading) and nephrotic effects in rats.

In any case, visual inspection is obviously not the best method for detecting a toxin in a food crop. Aventis should have performed ELISAs or similar protein detection assays to detect any barnase present in kernels and other non-anther tissues.

Interestingly, a 2002 patent on male sterile plants granted to the very same company (Aventis) frankly admits that "expression of the sterility DNA (e.g. barnase DNA) in tissues other than the stamen cells, e.g., in cells during tissue culture or in somatic cells of the plants or seeds" can occur. ***In fact, one of the chief aims of the patent is "to counteract the undesired effects of possible low level expression of the male-sterility gene (e.g. comprising the barnase DNA)"***[27] through co-engineering barstar, a barnase inhibitor, into the plant.

What are these "undesired effects"? We are not told, but Aventis was surely aware of them in 1999, when the USDA cleared MS6 male-sterile corn for commercial cultivation. Despite its recognition that even low levels of barnase can have "undesired effects," Aventis brought MS6 corn to market without even testing corn kernels or other tissues for the presence of barnase. USDA deregulated MS6 for commercial cultivation in 1999, and FDA issued its consultation memo in 2000, without such data.

One final note. Aventis ***did*** perform an ELISA to detect the phosphinothricin acetyltransferase enzyme (PAT) that is co-engineered into the MS6 line along with barnase. PAT lends resistance to the herbicide glufosinate, has been widely used in genetic engineering, and is generally considered safe. Why did Aventis take the trouble to assay for the likely innocuous PAT and neglect to do the same for a known toxin? One possible explanation is that the company realized that barnase would be found in corn kernels, and that this would raise food safety concerns that it preferred not to deal with. Does Aventis male-sterile corn pose a health risk to consumers? We don't know, and neither do the FDA or Aventis. "Don't look, don't find" is a common strategy in both industry and regulatory circles.

The case of viral-vectored trichosanthin:

In 1991, 1996 and perhaps subsequent years, the USDA approved open-air field trials of tobacco engineered to produce an extremely toxic compound – trichosanthin – derived from the roots of a Chinese plant. Trichosanthin belongs to the class of ribosomal inhibitor proteins (RIPs), which operate by inactivating a cell's protein-making

[27] Michiels et al. "Method to obtain male sterile plants," U.S. Patent 6,344,602 awarded to Aventis CropScience, February 5, 2002.

machinery (i.e. ribosomes). It is similar to two other members of this group – ricin and abrin – that are among the most toxic substances known to man. It is an extremely potent RIP, able to inhibit protein synthesis by 50% in an assay involving young rabbit blood cells at a concentration of just 0.1 ng/ml.[28] Trichosanthin has a long history of use in China to induce abortions. Effects associated with the intravenous use of trichosanthin include toxicity to embryos and fetuses,[29] renal toxicity,[30] neurological disorders,[31] fever, headache, arthralgia and skin rashes.[32]

The tobacco plants were infected with a tobacco mosaic virus (TMV) that had been transformed with the trichosanthin gene. TMV is known to infect tomatoes, peppers, eggplant, potatoes and other tobacco relatives in the Solanaceous family. Thus, these trials obviously raised food safety concerns.

In its environmental assessment of the 1991 trial[33], the USDA made three key assumptions on the basis of little or no evidence:

1) Low level: The level of trichosanthin in the infected tobacco "should be below any significant level of biological activity;"

2) No contamination: Tobacco plants would die if high levels of trichosanthin were generated, thus limiting spread of the trichosanthin-bearing virus to conventional tobacco and related food crops;

3) No human health impact: Trichosanthin would have no human health impacts upon oral ingestion, based in part on assumptions 1 (low expression level) and 2 (low potential for contamination of food crops) above. Dermal and inhalant exposure were not even considered.

[28] Kumagai et al (1993). "Rapid, high-level expression of biologically active α-trichosanthin in transfected plants by an RNA viral carrier," Proc. Natl. Acad. Sci., Vol. 90, p. 430.
[29] Chan et al (1993). ""Developmental toxicity and teratogenicity of trichosanthin, a ribosome-inactivating protein, in mice," Teratog Carcinog Mutagen 1993, 13(2), pp. 47-57.
[30] Ko & Tam (1994). "Renal reabsorption of trichosanthin and the effect on GFR," Renal Failure 16(3), pp. 359-66.
[31] Kahn et al (1990). "The safety and pharmacokinetics of GLQ223 in subjects with AIDS and AIDS-related complex: a phase I study," AIDS 4(12), pp. 1289-91.
[32] Dharmananda, Subhuti, Ph.D., Director, Institute for Traditional Medicine, Portland, Oregon. "Trichosanthines." See www.itmonline.org/arts/tricho.htm.
[33] "Environmental Assessment and Finding of No Significant Impact" for Permit No. 91-007-08 granted to Biosource Genetics for a field trial conducted in North Carolina in 1991. See: http://www.isb.vt.edu/biomon/relea/9100708r.eaa. No EAs are available for the 1996 or any subsequent trials. See Appendix 4 of "Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment," by Bill Freese for Friends of the Earth (2002) for a detailed examination of viral-vectored trichosanthin. Available at: www.foe.org/biopharm/.

These three assumptions all proved to be wrong:

1) High level: An experiment conducted around the same time with this same system demonstrated that TMV-vectored trichosanthin was generated at a level of 2% of total soluble protein in tobacco, at that time ***"the highest accumulation of a foreign protein ever reported in any genetically engineered plant;"*** [34]

2) Potential for contamination: Despite this high level of expression, there was no indication that the tobacco plants were killed, contrary to the USDA's assumption: "The viral symptoms consisted of plant stunting with mild chlorosis and distortion of systemic leaves…"[35]

3) Possible health impacts upon ingestion: In 2001, Health Canada (Canada's FDA) issued a warning against ***ingestion*** of a Chinese medication containing "trichosanthin alkaloid, which is known to cause mutations in human cells and malformations in embryos, suppress the immune system, and produce severe allergic reactions. The safe and effective dose of this herb is not known."[36]

In both cases – barnase and trichosanthin – biotech companies and federal regulators failed to assess transgenic crops for their potential to expose consumers to known toxins because they relied strictly on visual inspection and irresponsible assumptions.

Failure to establish/follow test protocols:

There are very few established protocols for assessing the potential human health impacts of GE crops. Instead, one finds loose guidelines that in most cases only recommend certain tests or procedures without specifying how they are to be conducted. Allergenicity test guidelines are an important case in point. Since 1996, various groups have devised so-called "decision trees" that lay out a series of tests (e.g. structural similarity to known allergens, digestive and heat stability, sera screening, etc.) to assess the potential allergenicity of transgenic crop proteins.[37]

Until a 2001 report by an FAO-WHO expert consultation[38], however, none of these decision-trees specified test conditions. As a result, biotech companies have been free to devise procedures of their own choosing – procedures that have invariably yielded negative results. Still worse, regulators have failed to collect ***any*** studies on some of

[34] Kumagai et al, op. cit., p. 429, my emphasis.
[35] Ibid, p. 429.
[36] "Health Canada Warns Consumers About Chinese Medications," Health Canada press release, Feb. 28, 2001. See www.acupuncture.com/herbology/chest-relief2.htm.
[37] For instance, see: Metcalfe et al (1996). "Assessment of the Allergenic Potential of Foods Derived from Genetically Engineered Crop Plants," Critical Reviews in Food Science and Nutrition 36(S), pp. S165-186.
[38] "Evaluation of Allergenicity of Genetically Modified Foods," Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, Jan. 22-25-2001. www.fao.org/es/esn/food/pdf/allergygm.pdf.

these important parameters in the case of most Bt crops. In one particularly egregious case, the EPA even ignored a 1998 study by an FDA scientist indicating the potential allergenicity of the transgenic protein in most Bt corn, and instead requested that the financially interested developer (Monsanto) submit its own analysis, without specifying test conditions, by March 15, 2003.[39] (See case study below.)

The broader scientific community, including even some scientists who have reviewed GE crops for allergenicity, are largely unaware of these facts. Perhaps due to the repeated assurances of the public spokespeople for federal regulatory agencies about the supposed viability of the regulatory process, they incorrectly assume that currently marketed GE crops have passed stringent reviews for allergenicity.

As we shall see, if evaluated according to the detailed 2001 FAO-WHO allergenicity test protocol cited above, most currently registered Bt corn would not pass muster.

[39] "Biopesticides Registration Action Document: Bt Plant-Incorporated Protectants – Overview," Environmental Protection Agency, October 15, 2001. http://www.epa.gov/pesticides/biopesticides/pips/bt_brad2/1-overview.pdf

Case Study – Bt Corn

Our concerns about Bt corn derive from four sources:

1) Suggestive evidence of allergenicity from human and animal studies as well as allergen-like properties of the Bt insecticidal protein Cry1Ab;
2) Unintended consequences of the genetic engineering process;
3) Regulatory failure; and
4) Differences between insecticidal proteins in Bt sprays and Bt crops.

Bt sprays versus Bt crops:

Bacillus thuringiensis (Bt) is a soil microbe that produces a variety of insecticidal crystalline proteins. Preparations of Bt spores are widely used in spray form by organic and conventional farmers to control certain pests. Most Bt corn varieties are engineered to generate modified versions of Cry1Ab, one of the major insecticidal proteins found in Bt sprays. There has been next to no independent testing of Bt corn and other Bt crops for potential human health impacts. However, even the very few studies conducted on the related Bt sprays raise concerns about the potential allergenicity of Bt corn. We will first briefly examine the evidence from Bt spray studies. At the end of this case study, we will examine similarities and differences between the insecticidal proteins in Bt sprays versus Bt crops to gain a better idea of how these data apply.

Suggestive evidence of allergenicity from:

Human studies

Allergic symptoms including allergic rhinitis, angioedema, dermatitis, pruritus, swelling, erythema with conjunctival injection, exacerbations of asthma, angioedema and rash have been reported in farm-workers and others exposed to Bt spraying operations.[40]

Bernstein et al (1999) demonstrated that purified Cry protein extracts of Bt microbial pesticides containing Cry1Ab and Cry1Ac elicited positive skin tests and IgE antibody responses in two farm-workers exposed to them by the inhalant, dermal and possibly oral routes. Positive skin tests and the presence of IgE antibodies in serum are considered indicators of allergenicity. Though Bernstein did not observe allergic reactions in these workers, he notes that they were tested after only 1 to 4 months of exposure, and that "clinical symptoms would not be anticipated unless there was repeated long-term exposure…" In addition, he notes that the "healthy worker effect" might have skewed his results – that is, susceptible farm-workers might have associated their allergic symptoms with Bt, sought other employment to avoid exposure, and hence not have been included in his study (see study cited in footnote 40).

[40] See references 6-8 in Bernstein et al (1999), "Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides," Environmental Health Perspectives, 107(7): pp. 575-582.

Animal studies

Additional evidence is provided by Vazquez and colleagues in a series of studies demonstrating that Cry1Ac protoxin[41] and toxin are potent immunogens that elicit both mucosal and systemic immune responses,[42] and that Cry1Ac protoxin is a systemic and mucosal adjuvant similar in potency to cholera toxin.[43] They also found that Cry1Ac binds to surface proteins in the mouse small intestine.[44] It should be noted that Cry1Ac is very similar in structure to the Cry1Ab insecticidal protein in most varieties of Bt corn.

In an assessment of Bt crops[45], expert advisors to the Environmental Protection Agency (EPA) who reviewed the Bernstein study and one of Vazquez et al's four studies concluded that:

> *"These two studies suggest that Bt proteins could act as antigenic and allergenic sources." (p. 76)*

Different approaches – including post-market surveillance – are called for to further characterize the allergenic risk of Bt proteins:

> *"With respect to allergenicity, the Panel concluded there is a continuing need to explore further approaches whereby the potency of allergic reactions of [sic] the isolated Cry-pesticidal protein and the transgenic plant can be more comprehensively assessed." (p. 75)*
>
> *"Only surveillance and clinical assessment of exposed individuals will confirm the allergenicity of Bt products or for any other novel protein introduced into the diet of consumers." (p. 76).*

Finally, the EPA's experts note that testing for potential reactions to Cry proteins in Bt spray and Bt crops could be undertaken now:

> *"The importance of this [Bernstein's] report is that reagents are available that could be used for reliable skin testing and serological evaluation of Bt protein exposed individuals." (p. 76)*

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[41] Protoxin = inactive precursor protein that yields the insecticidally active toxin upon cleavage.

[42] Vazquez et al (1999a). "Intragastric and intraperitoneal administration of Cry1Ac protoxin from Bacillus thuringiensis induces systemic and mucosal antibody responses in mice," Life Sciences, Vol. 64, No. 21, pp. 1897-1912; Vazquez et al (2000a). "Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from Bacillus thuringiensis HD 73 in mice," Brazilian Journal of Medical and Biological Research 33: pp. 147-155.

[43] Vazquez et al (1999b). "Bacillus thuringiensis Cry1Ac protoxin is a potent systemic and mucosal adjuvant," Scandinavian Journal of Immunology 49, pp. 578-584.

[44] Vazquez et al (2000b). "Cry1Ac protoxin from Bacillus thuringiensis sp. kurstaki HD73 binds to surface proteins in the mouse small intestine," Biochemical and Biophysical Research Communications 271, pp. 54-58.

[45] SAP Bt Plant-Pesticides (2000). "Bt Plant-Pesticides Risk and Benefit Assessments," FIFRA Scientific Advisory Panel Report No. 2000-07, March 12, 2001. http://www.epa.gov/scipoly/sap/2000/october/octoberfinal.pdf.

Unfortunately, in 2001 the EPA re-registered Bt corn for 7 years without making use of these reagents. The Agency also ignored other evidence of the potential allergenicity of Cry proteins in Bt crops.

Similarities to known allergens:
The versions of Cry1Ab protein found in hybrids derived from the two major Bt corn events (Monsanto's MON810 and Syngenta's Bt11) exhibit at least three properties considered characteristic of food allergen proteins by leading experts: structural similarity to known allergens, digestive stability and heat stability.

Structural similarity: All allergenicity testing protocols require that the structure of the novel, transgenic protein be compared to those of known allergens. Matching sequences of 6 to 8 amino acids (depending on the protocol) raise a red flag necessitating further testing. Food and Drug Administration scientist Steven Gendel demonstrated amino acid homology between several Cry proteins and known food allergens. Gendel found that Cry3A (Bt potatoes) and β-lactoglobulin, a milk allergen, shared sequences 7-10 amino acids in length. He also identified sequences of 9-12 amino acids shared by Cry1Ab (Bt corn) and vitellogenin, an egg yolk allergen. Gendel concluded that:

> *"…the similarity between Cry1A(b) and vitellogenin (Fig. 4) might be sufficient to warrant additional evaluation."*[46] *(p. 60)*

The EPA failed to collect any amino acid homology studies from Monsanto prior to the product's original registration in 1996, or even upon its re-registration in 2001.

Digestive stability: Many food allergens are stable to digestion. It is thought that the longer a protein survives in the gut, the more likely it is to induce the cascade of immune system events leading to allergic sensitization and reaction in susceptible individuals. Most food proteins – both native and transgenic – break down rapidly in the gut due to the action of protein-degrading enzymes and acid. Novel proteins (or rather, their bacterial surrogates) are normally tested *in vitro* in acidic solutions containing pepsin. The rate of breakdown is significantly influenced by the amount of pepsin relative to test protein in, and the acidity of, the "simulated gastric fluid."

Two digestive stability studies[47] on Cry1Ab by Bt protein expert Dr. Hubert Noteborn established that:

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[46] Gendel, S. (1998). "The use of amino acid sequence alignments to assess potential allergenicity of proteins used in genetically modified foods," Advances in Food and Nutrition Research 42, pp. 45-62.
[47] Noteborn, H. (1998). "Assessment of the Stability to Digestion and Bioavailability of the LYS Mutant Cry9C Protein from Bacillus thuringiensis serovar tolworthi," submitted to the EPA by AgrEvo, EPA MRID No. 447343-05 (Cry1Ab was also tested for purposes of comparison); Noteborn et al (1995). "Safety assessment of the *Bacillus thuringiensis* insecticidal crystal protein CRYIA(b) expressed in transgenic tomatoes," in Engel, et al (eds.), American Chemical Society Symposium Series 605, Washington, DC, pp. 134-47.

1) After 30-180 minutes in simulated gastric fluid (SGF), 9-21% of Cry1Ab remains undigested;
2) After two hours in SGF, Cry1Ab degrades only to fragments of substantial size at the low end of the range considered typical of food allergens (15 kilodaltons);
3) Cry1Ab is substantially more resistant to digestion than 4 other transgenic proteins tested (including one other Cry protein, Cry3A); of the six proteins tested, only StarLink corn's Cry9C exhibited greater digestive stability.

Aventis CropScience also found that Cry9C and Cry1Ab possessed similar digestive stability:

> *"The Cry1Ab protein was digested at a similar, if slightly faster, rate than the E. coli-derived Cry9C protein in simulated gastric fluid."*[48] *(p. 17)*

In contrast, Monsanto's digestive stability test on Cry1Ab employed highly acidic conditions (pH 1.2) and a huge excess of pepsin relative to test protein – conditions that favor the most rapid possible digestion[49]. Thus, it's no surprise that Monsanto's results (over 90% degradation in just 2 minutes) vary by a factor of 60 from those of Hubert Noteborn (cited above). Dr. Noteborn found that 10% of Cry1Ab survived for 1-2 hours, not 2 minutes. Under the authoritative allergenicity testing protocol recommended by international experts at FAO/WHO and accepted widely by national regulators outside the U.S., Cry1Ab would show itself to be still more stable than in Noteborn's test.

Heat stability: Dr. Noteborn also found that Cry1Ab possessed "relatively significant thermostability … comparable to that of the Lys mutant Cry9C protein" found in StarLink corn.[50] The EPA failed to collect any heat stability studies from Monsanto.

The similarities discussed above are summarized in Appendix 1. The EPA's lack of response to these studies is discussed below (Regulatory Failure).

Unintended consequences of the genetic engineering process:

Fragmented and uncharacterized fusion protein in MON810

Many Bt corn hybrids planted on millions of acres in the U.S. are derived from Monsanto's MON810 "event," which contains the Cry1Ab insecticidal toxin discussed above. However, Monsanto's unpublished molecular characterization study on

[48] Byard, J. (2000). "Cry9C protein: The digestibility of the Cry9C protein by simulated gastric and intestinal fluids," submitted to the EPA by Aventis CropScience. EPA MRID No. 451144-01.
[49] Ream, J.E. (1994). "Assessment of the *In vitro* Digestive Fate of *Bacillus thuringiensis* subsp. *kurstaki* HD-1 Protein," unpublished study submitted to the EPA by Monsanto, EPA MRID No. 434392-01.
[50] Noteborn (1998), op. cit., p. 22.

MON810[51] reveals that the genetic construct broke apart during the transformation process, resulting in several unintended consequences whose implications have not been adequately assessed (or acknowledged) even now, 7 years after market introduction:

1) Only a gene fragment (about 70%) of the intended full-length cry1Ab protoxin gene was incorporated into MON810;

2) As a result, the NOS termination sequence was not incorporated; instead, the cry1Ab gene fragment fused with adjoining corn DNA;

3) Monsanto scientists were unable to detect the putative 92 kD fusion protein presumably generated by the fused cry1Ab gene fragment and corn DNA; tests on the corn apparently revealed only the 63 kD "tryptic core" protein that Monsanto presumes to be a breakdown product of the fusion protein.

None of Monsanto's safety testing was conducted on the putative 92 kD fusion protein produced by MON810 (which was undetectable). Thus, its properties remain unknown. Even worse, the bacterial surrogate protein (see Surrogate Protein above) used by Monsanto for testing purposes was not even the same size as that produced by MON810. Monsanto generated a full-length 131 kD version of Cry1Ab in *E. coli*, extracted it, then treated it with trypsin to generate the 63 kD active fragment. Results of testing with this bacterial surrogate "tryptic core protein" may not reflect the toxic and allergenic profile of the putative corn-produced fusion protein[52].

The EPA glossed over the potential implications of this failed transformation process in its review of MON810 corn. Because it relied on confusing and/or incomplete summary information provided by Monsanto, ***the FDA was apparently not even aware that MON810 contained a gene fragment and produced a fusion protein.***[53] Appendix 2 details the fundamental errors in the FDA's consultation document on MON810. The regulatory failures with respect to MON810 are addressed more fully below.

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[51] Levine et al (1995). "Molecular Characterization of Insect Protected Corn Line MON 810," unpublished study submitted to the EPA by Monsanto, EPA MRID No. 436655-01C.

[52] Lee et al (1995). "Assessment of the Equivalence of the *Bacillus thuringiensis* subspecies *kurstaki* HD-1 Protein Produced in *Escherichia coli* and European Corn Borer Resistant Corn," unpublished study submitted to the EPA by Monsanto, EPA MRID No. 435332-04; Lee and Bailey (1995). "Assessment of the Equivalence of *B.t.k.* HD-1 Protein Produced in Several Insect Protected Corn Lines and *Escherichia* coli," unpublished study submitted to the EPA by Monsanto, EPA MRID No. 436655-03. Contrary to their titles, these studies did ***not*** demonstrate equivalence between bacterial surrogate and corn-produced Cry1Ab according to criteria recommended by the EPA's advisers (see reference in "Surrogate Proteins" section above). See also: Freese, B. (2001). "A Critique of the EPA's Decision to Reregister Bt Crops and an Examination of the Potential Allergenicity of Bt Proteins," adapted from comments of Friends of the Earth to the EPA, Dec. 9, 2001. Available at: www.foe.org/safefood/comments.pdf.

[53] The author has pointed out these serious errors at an FDA scientific forum and personally to James Maryanski, head of biotech at FDA. To my knowledge, neither Mr. Maryanski nor anyone else at FDA has followed up on this matter.

Increased lignin - failure to detect/follow up on a striking unintended effect
Bt corn hybrids derived from Monsanto's MON810 and Syngenta's Bt11 events exhibit increased levels of lignin in stem tissue[54]. This finding accords with anecdotal reports from farmers that Bt corn is stiffer and less desirable to farm animals as fodder (lignin is the woody component of plants and is non-digestible).

Lignin is the product of three aromatic compounds – coniferyl alcohol, p-coumaryl alcohol and sinapyl alcohol – all of which are derived from phenylalanine, an essential aromatic amino acid. Phenylalanine, in turn, is a product of the shikimic acid pathway, which is reportedly responsible for generating compounds comprising 35% and more of the dry mass of higher plants[55]. The discovery of increased lignin levels in Bt corn raises the question of whether other intermediates and products associated with the lignin and shikimic acid biosynthetic pathways have been affected by the transformation process. Aromatic biomolecules are extremely important in both plants and mammals as building blocks for hormones and other bioactive substances. The limited testing for a handful of compounds undertaken by Monsanto and Syngenta might easily have missed unintended increases or decreases in the levels of these other bioactive substances.

Finally, the finding that two completely different transformation events (MON810 and Bt11) are associated with increased lignin levels raises an interesting question. Normally, one would expect that each non-repeatable, unique transformation "event" would yield unique unintended effects related to the site of insertion (i.e. interruption, up- or down-regulation of a native gene(s)), scrambling of plant DNA adjacent to the site of insertion, number of (fragmented) copies of the gene that were introduced, or other factors unique to the event. Finding the very same unintended effect from two different transformation events suggests that the genetic transformation process *per se* (here, particle bombardment) might be responsible for an increase in lignin levels, and perhaps other, yet undetected, effects. Why was the increased lignin content of Bt corn brought to light only 5 years after market introduction? Why hasn't targeted testing been conducted for other bioactive substances associated with the lignin and shikimic acid pathways? Why haven't non-targeted techniques such as metabolic profiling been applied? Why are we asking these questions only now rather than 7 years ago? All these unanswered questions represent gaps in the human health assessment of Bt corn.

[54] Saxena and Stotzky (2001). "Bt Corn Has a Higher Lignin Content than Non-Bt Corn," American Journal of Botany 88(9), pp. 1704-1706.
[55] Alibhai and Stallings (2001). "Closing down on glyphosate inhibition – with a new structure for drug discovery," Proceedings of the National Academy of Sciences, Vol. 98, No. 6, pp. 2944-46.

Similarities and differences between Bt crops and sprays:

The EPA's chief justification for approval of Bt crops in the absence of crucial data is that Bt sprays have a history of safe use, and so Bt crops are presumed to be safe as well. This presumption is not justified for several reasons. First of all, it is reasonably clear that Bt sprays do cause allergic symptoms, as detailed at the start of the case study above. Expert advisers to the EPA have advised the Agency that more studies are needed to determine the allergenic risk posed by Cry proteins in general – whether from Bt sprays or crops. Secondly, there is likely much greater exposure to Cry proteins in Bt crops than in sprays. Cry proteins in Bt sprays break down quickly upon exposure to sunlight, while this is obviously not the case with Bt crops, which produce the toxin internally in most or all plant tissues, including grain. Thirdly, Bt sprays are composed of bacterial spores comprised chiefly of Cry protoxins – the inactive precursors of the insecticidal Cry toxins. These protoxins become active toxins upon cleavage under alkaline conditions obtaining in the guts of certain insects. Bt crops, on the other hand, are generally engineered to produce the Bt toxin, which is active without processing. There is also evidence indicating that Cry toxins are more immunoreactive than Cry protoxins.[56]

Even if one ignores the evidence that Cry proteins from Bt sprays are likely allergenic, it is completely unacceptable to conclude that Bt crops are safe due to the absence of testing of the plant-derived proteins.

Breakdown in the regulatory system:

The question of whether Bt corn hybrids are harmful to consumers is still open. Testing along the lines indicated above is urgently needed to answer it. However, even if proper testing were to prove them to be safe, this case study dramatically illustrates the fundamental flaws in our "de-regulatory" system for genetically engineered crops. Consider the following:

1) The EPA approved Monsanto's Bt corn, MON810, with virtually no consideration of the potential implications of the failed transformation event leading to generation of a putative (because undetectable) 92 kD fusion protein;

2) The EPA approved MON810 on the basis of studies that employed a derivative of a surrogate bacterial protein rather than the plant-produced fusion protein; studies purporting to demonstrate the equivalence of the surrogate and fusion proteins for testing purposes did not meet standards recommended by experts;

3) The EPA registered and re-registered (in 2001) MON810 without making any effort to follow up on suggestive evidence of allergenicity. In particular, the EPA ignored an important study by an FDA scientist showing structural similarity to a known

[56] See Freese, B (2001), op. cit., Section 8.

food allergen, did not require submission of a heat stability study, and accepted a rigged digestive stability study.

4) The FDA's consultation document on MON810 contains fundamental errors regarding the basic molecular features of the transgenic protein, despite the fact that the pertinent study was available at its sister agency, the EPA. Once these errors were pointed out, the FDA apparently made no effort to follow-up;

5) There has likewise been no effort to investigate the potential health implications of a marked unintended effect of the engineering process – namely, increased lignin levels in Bt corn stalks, suggesting that the levels of lignin or related compounds could be altered in other corn tissues.

The case of MON810 is not exceptional. It illustrates not just that the U.S. regulatory system has holes that need fixing. Rather, it shows that the system is not about food safety at all, but rather was designed to speed transgenic crops to market as quickly as possible on the strong ***a priori*** presumption of no human health impacts. That there is any shell of a regulatory system in place at all in the U.S. has more to do with the perceived need by industry and government to reassure a rightly concerned public that these foods have received the government's stamp of approval.[57]

[57] See "Biotechnology Food: From the Lab to a Debacle," NYT, cited in footnote 2.

Appendix 1: Allergenicity Assessment of Bt Crops

In October of 2001, the EPA re-registered the entire class of Bt crops: 3 varieties of corn and one of cotton (potatoes were originally given an unlimited registration). The Agency was supposed to undertake a thorough-going reassessment, taking account of the most current scientific information and the recommendations of its scientific advisors, prior to making a decision. As detailed below, the EPA not only failed to do this, but did not even collect the most basic information needed to conduct an allergenicity assessment of the Cry1Ab, Cry1Ac/Ab, Cry1F and Cry3A crop varieties.

The following table outlines key deficiencies in the EPA's assessment. The three parameters are those chosen by the EPA (EPA BRAD Human Health Assessment). The notes following the table provide references for those wishing to explore this matter further. The table is excerpted from a study by Friends of the Earth, available at: www.foe.org/safefood/comments.pdf.

Summary of Available Data for Human Health Assessment

Company Crop Bt protein	**Digestive Stability**	**Heat Stability**	**Amino Acid Sequence Homology**
Monsanto Yieldgard Corn Cry1Ab	**RED FLAG** Digestive stability similar to (though lesser than) that of StarLink Cry9C (1)	**RED FLAG** Heat stability comparable to that of StarLink Cry9C (2)	**RED FLAG** Matches found with vitellogenin, an egg yolk allergen, over 9-12 amino acid-length subsequences (3)
Syngenta Bt 11 Corn Cry1Ab	**RED FLAG** Digestive stability similar to (though lesser than) that of StarLink Cry9C (1)	**RED FLAG** Heat stability comparable to that of StarLink Cry9C (2)	**RED FLAG** Matches found with vitellogenin, an egg yolk allergen, over 9-12 amino acid-length subsequences (3)
Monsanto BollGard Cotton Cry1Ab/Ac	**INADEQUATE** Flawed study shows degradation in 2-7 minutes (4)	**INADEQUATE** Only shown to be "inactive" in processing study (5)	**RED FLAG** Cry1Ab/Ac has the same vitellogenin-matching subsequences as Cry1Ab in the pertinent region (3, 6)
Mycogen & Pioneer Herculex Corn Cry1F	**INADEQUATE** Test conditions not specified by EPA (7)	**INADEQUATE** Only shown to be "inactive" in bioassay after 30 min. at 75° & 90°C (5)	**OK** Though more stringent test would be desirable (8)
Monsanto NewLeaf Potato Cry3A	**INADEQUATE** Test conditions not specified by EPA (7)	**NONE** (9)	**RED FLAG** Amino acid sequences found in which 7-10 matched β-lacto-globulin, a milk allergen (10)

Notes to Human Health Assessment Table

(1) "The Cry1Ab protein was digested at a similar, if slightly faster, rate than the E. coli-derived Cry9C protein in simulated gastric fluid." (Aventis CropScience 2000, "Cry9C Protein: The Digestibility of the Cry9C Protein by Simulated Gastric and Intestinal Fluids," study submitted to the EPA by Aventis CropScience, p. 17). In another study, Noteborn (1998) found that it took two hours to achieve > 90% degradation of Cry1Ab(5) in SGF (165 µg/ml SGF, pH = 2.0) Noteborn (1998), p. 21, Annex 1 – Table 1, p. 31. See note (2) for full Noteborn citation.

(2) "Studying the Cry1Ab5 protein a relatively significant thermostability was observed which was comparable to that of the Lys mutant Cry9C protein." Noteborn (1998). "Assessment of the Stability to Digestion and Bioavailability of the LYS Mutant Cry9C Protein from Bacillus thuringiensis serovar tolworthi," study submitted to the EPA by AgrEvo, p. 22)

(3) "…the initial alignment between Cry1A(b) and vitellogenin located subsequences in which 9 to 11 amino acids were identical (82% similarity). Realignment indicated that these regions contained stretches of 11 biochemically similar and 12 evolutionarily similar amino acids (100% similarity over 11 or 12 amino acids." "For example, the similarity between Cry1A(b) and vitellogenin might be sufficient to warrant additional evaluation." Gendel, Steven M. "The use of amino acid sequence alignments to assess potential allergenicity of proteins used in genetically modified foods," Adv. in Food and Nutrition Research , Vol. 42, 1998, pp. 58-60. The EPA apparently did not consider this study in its reassessment of Cry1Ab corn. The Agency states merely that companies did not submit structural comparisons: "Amino acid homology comparisons for Cry1Ab, Cry1Ac and Cry3A against the database of known allergenic and toxic proteins were not submitted." (EPA BRAD 2001, p. IIB2)

(4) Monsanto conducted this study under conditions that proved extremely favorable to rapid digestion of the Cry1Ab/Ac hybrid protein: pH = 1.2, 2 µg test protein / ml SGF. Experts now recommend testing with much higher concentrations of test protein at a milder (at least pH = 2.0).

(5) "Inactive" here means "unable to kill insects" in bioassays, which provide little or no information about degradation of the protein into amino acids and small peptides, which is what should have been measured (e.g. by HPLC or SDS-PAGE)

(6) "Cry1A(c) has the same sequence as Cry1A(b) in the region involved, and therefore produced the same alignments, but this was not considered an independent alignment because the proteins are closely related." Gendel, Steve, p. 59. (See note (3) for citation)

(7) EPA fails to cite the pH value of SGF. If test conducted at pH = 1.2, it should be repeated at pH = 2.0. See note (4).

(8) Many experts recommend a more stringent test than one based on 8 contiguous amino acids.

(9) "No heat stability studies were available for Cry3A." EPA BRAD 2001, p. IIB2.

(10) "First, the initial alignment between Cry3A and β-lactoglobulin located subsequences in which 7 of 10 amino acids matched exactly. Realignment with both the evolutionary and biochemical matrices indicated that the intercalary amino acids were similar, meaning that the alignment was 100% similar over 10 amino acids." Gendel, Steve, pp. 58-59. See note (3) for citation. The EPA apparently did not consider this study in its reassessment of Bt crops, stating merely that "additional amino acid sequence homology" data are needed to "complete product database" for Cry3A NewLeaf potatoes. EPA BRAD 2001, Table B1, p. IIB3.

Appendix 2

A Sampling of Errors in the FDA's "Note to the File" for Monsanto's Bt Corn Event MON810

	FDA's "Note to the File"[58]	**Monsanto's Study**[59]
Nature of the inserted genetic material: **FDA: Complete copy of gene** **In fact: Partial gene**	"MON810 contains 1 ***complete copy*** of the *cryIA(b)* gene and its associated regulatory sequences." (p. 2)	"During the process of particle acceleration, ***the plasmid DNA can become broken resulting in the integration of partial genes*** into the genomic DNA. Southern blots and genomic clone sequence results described below established that the first 2448 bp of the 3468 bp *cryIA(b)* integrated into the corn line to produce MON810. In order to assess the protein products produced from the ***partial cryIA(b)*** gene…" (p. 14)
NOS 3' termination sequence: **FDA: NOS present** **In fact: NOS absent**	"***The NOS 3" nontranslated sequence served to terminate transcription*** of *cryIA(b)* [sic] gene, and to direct mRNA polyadenylation." (p. 2)	"…the *cryIA(b)* gene terminated its integration into the genomic DNA at position 2448 bp nucleotides of the *cryIA(b)* gene event. … The 2454 bp ***open reading frame*** codes for a protein containing amino acids 1-816 of the *B.t.k.* HD-1 protein[60] ***plus two additional amino acids [from corn] followed by a stop codon***." (p. 19; see also Figure 1)
Nature of the Bt protein: **FDA: nature-identical** **In fact: odd-length fragment**	"Monsanto states that the cryIA(b) protein present in MON809 and MON810is ***identical to that present in nature and commercial microbial preparations*** approved by the Environmental Protection Agency (EPA)." (p. 3)	"***The full length 131 kD B.t.k. HD-1 protein was not observed in line MON810***, as expected, since the full length gene was not incorporated into the corn genome. … ***The predicted molecular weight of the B.t.k. HD-1 protein from the partial cryIA(b) gene is 92 kD but is not detected***, probably due to low expression or rapid degradation to the trypsin-resistant product during the extraction procedure." (p. 15)

[58] FDA's Consultation Note for Monsanto's MON809 and MON810 Bt corn lines, September 18, 1996. See Memo for BNF No. 34 at http://www.cfsan.fda.gov/~lrd/biocon.html.

[59] Levine et al (1995). "Molecular Characterization of Insect-Protected Corn Line MON810," unpublished study submitted to the EPA by Monsanto, completed on May 30, 1995. EPA MRID No. 436655-01C.

[60] *B.t.k. = Bacillus thuringiensis*, subspecies *kurstaki*. HD-1 identifies the strain of *B.t.k.* from which the inserted gene was derived.

From: doreen.stabinsky@dialb.greenpeace.org
[mailto:doreen.stabinsky@dialb.greenpeace.org]
Sent: Thursday, March 25, 2004 7:39 PM
To: Chantal Line Carpentier
Cc: gustavo Alanis Ortega
Subject: timeline for advisory group recommendations

Dear Chantal Line:

It has recently come to our attention that the Advisory Group on Maize and Biodiversity will finalize its recommendations to the CEC Council by 31 March.

As we expressed at the CEC meeting in Oaxaca, if the public comment period lasts until 12 April but the Advisory Group finalizes its recommendations prior to reading these comments, one can only conclude that the exercise of writing those comments is a waste of time.

Could you please inform us of the exact timeline under which the Advisory Group is operating, as well as the procedures that have been developed for their consideration of all the public comments to be submitted?

Thank you for your attention to this matter.

Regards,

Doreen Stabinsky
Greenpeace

Gustavo Alanis
Centro Mexicano de Derecho Ambiental

Comments to the NAFTA Commission for Environmental Cooperation Article 13 report
Maize and Biodiversity: The effects of transgenic maize in Mexic0

Submitted by Greenpeace, 12 April 2004

In chapter 2 of the report, the author suggests that chapter 8 will deal with the precautionary principle. However, nowhere in the chapter is the principle explained. In fact, there is only a single reference listed the precautionary principle – the EC Communication on the precautionary principle. The principle is not addressed in the text at all, except to say that it is being debated. There is some attention given to "scientific uncertainty," but precaution is not the same as uncertainty.

The precautionary principle is a central piece of the Cartagena Protocol on Biosafety, the international legal instrument dealing with trade in engineered organisms. As such, it should be more seriously reflected in the CEC report. This submission is meant to compensate for the sparse coverage of the principle. We hope the authors of the report find our analysis useful as the make their final revisions.

In this document we also provide an analysis of the scientific critiques of ecological risk assessment, both in general and as a methodology for judging risks of GMOs, and we provide a more thorough analysis of scientific uncertainty in this area.

Finally, we discuss specific risks of GMOs and the special case of maize in Mexico, as they relate to the precautionary principle.

The precautionary principle, risks of GMOs, and the specific case of maize in Mexico

1. The Precautionary Principle

introduction

What is this principle that is so politically charged, to the point that the authors of chapter 8 would rather not even mention the words "precautionary principle"? Some simple definitions that have been put forward include "Do no harm" and "Better safe than sorry." A more technical explanation of the Principle is that in the face of serious or irreversible threats to the environment, and in situations of scientific uncertainty, we should take action to minimize or prevent those threats.

Why is the principle so politically charged? One reason is that it allows a serious regulatory challenge to particular industries, such as the genetic engineering industry, where scientific understanding of long-term threats of introducing genetically engineered organisms into the environment is minimal. In defense of their domestic GE industry, countries such as the United States and its allies such as Canada are actively working to impede the use of the principle in environmental decision-making throughout the world. However, the principle is widely accepted, to the point that numerous international

lawyers consider it has already crystallized into a norm of international law. (see for example, McIntyre and Mosedale 1997; Saladin 2000; Sands 2002)

a brief history of The Principle

The history of the precautionary principle varies depending on the teller. Many persons write that the precautionary principle has its roots in German environmental policy. *Vorsorgeprinzip*, the principle of precautionary action, is one of five principles defined in the early eighties as the basis for German environmental policy. (Boehmer-Christiansen 1994) Germany took the lead in introducing the principle of precaution in the international arena in North Sea Ministerial Conferences held throughout the eighties. It became a legally binding principle in international marine law when it was incorporated specifically into the 1992 Convention for the Protection of the Marine Environment of the North-East Atlantic (OSPAR)[1]:

> The Contracting Parties shall apply the precautionary principle, by virtue of which ***preventive measures <u>are</u> to be taken when there are reasonable grounds for concern that substances*** or energy introduced, directly or indirectly, into the marine environment ***may bring about hazards to human health, harm living resources and marine ecosystems***, damage amenities or interfere with other legitimate uses of the sea, ***even when there is no conclusive evidence of a causal relationship between the inputs and the effects***. (emphasis added)

Numerous other treaties and non-binding declarations since then have incorporated a version of the precautionary principle. (These are too numerous to mention here in an exhaustive way. See McIntyre and Mosedale 1997; Saladin 2000; Sands 2002 for further discussion.) The most famous articulation of the principle in international law, at least prior to the conclusion of the Cartagena Protocol negotiations, is Principle 15 of the Rio Declaration on Environment and Development (1992). It reads:

> In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.

basic elements of the precautionary principle

The precautionary principle, in essence, is about decision-making in the face of uncertainty. As numerous writers have articulated, "precaution is a means to explicitly recognize fundamental, empirical short-comings in science." Sandin (1999) notes that the principle contains four essential points: if there is a 1) threat, 2) even in the face of scientific uncertainty, then 3) some kind of action 4) is mandatory. This is how we might view the formulation of the principle in the OSPAR Convention. Another way the principle is often phrased is: if there is a 1) threat, then 2) actions taken by governments 3) should not be postponed 4) even in the face of scientific uncertainty about the extent of

[1] Convention for the Protection of the Marine Environment of the North-East Atlantic, art. 2(2)(a), September 22, 1992, reprinted in 32 I.L.M. 1069 (1993) (entered into force March 25, 1998)

the potential adverse effects. This latter formulation is similar to the principle as found in Articles 10.6 and 11.8 of the Cartagena Protocol. Article 11.8 (dealing with imports of commodities such as maize) reads as follows (basic elements are highlighted):

> ***Lack of scientific certainty*** due to insufficient relevant scientific information and knowledge ***regarding the extent of the potential adverse effects*** of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, ***shall not prevent that Party from taking a decision***, as appropriate, with regard to the import of that living modified organism intended for direct use as food or feed, or for processing, ***in order to avoid or minimize such potential adverse effects***.

For many authors, the precautionary principle exists on several levels. It is, as noted above, a framework for decision-making, for advocating or permitting action in the face of scientific uncertainty if faced with serious or irreversible threats to the environment or human health. It is also seen as:

> a paradigm to resolve some of the tensions inherent in translation of scientific knowledge into policy,… a means explicitly to recognize fundamental, empirical shortcomings in the science applied to decision-making process, … an overarching principle to guide decision making in the absence of analytical or predictive certainty. (Santillo *et al.* 1998)

precaution and risk assessment

Why would governments be interested in invoking the precautionary principle when making decisions about genetically engineered organisms? We are led to believe in chapter 8 that ecological risk assessment is an adequate method for determining the risks of GMOs. Further, decision-makers are assumed to have all the information needed from the risk assessment process in order to weigh benefits and costs and to manage whatever risks might be posed. However, methods currently used to assess risks of GMOs may in fact not be able to provide decision-makers with an adequate amount of information on the impacts of GMOs at this point in time. Certainly this is the conclusion of chapter 4 regarding the impacts of transgenes on Mexico's natural ecosystems.

Risk assessment as a discipline has its roots in the structural and product engineering fields, whereby technocrats sought to determine probabilities of structural collapse or product failure. Risk assessment has since been adapted for a number of purposes, including the impacts of chemicals on human health, and most recently ecological impacts of chemicals and other potential environmental stressors.

There is an ongoing debate in the risk assessment field over whether or not ecological risk assessment is able to provide adequate answers on the magnitude and consequences of risks being studied. (See for example Power and Adams 1997; Adams and Power 1997) Numerous papers over the past decade have been written on the limitations of ecological risk assessment, the majority of which deal with risk assessment of chemicals

in the environment. Santillo and Johnston (1999), for example, take issue with the fact that in the practice of risk assessment, effects are considered predictable, quantifiable and manageable:

> Risk assessments start from the premise that the *likelihood of adverse effects* in the field *can be quantitatively and reliably forecast and* that, subsequently, potential stressors may be *effectively managed* at levels of risk deemed acceptable. (emphasis added)

In the following sections, we provide more detail on critiques of risk assessment found in the scientific literature.

limits of ecological risk assessment

As mentioned above, the criticisms of ecological risk assessment are found predominantly in the literature on the environmental impacts of chemicals in the environment. Much of this literature actually comes from the field of marine pollution (remember the first instances of the precautionary principle in international law concern the prevention of chemical pollution in marine environments). In this large literature, one can find discussion of a number of methodological limitations of ecological risk assessment relevant to our discussion of genetically engineered organisms. The methodological limitations then limit and color the information available for decision-making. The following is not meant to be an exhaustive list:

- In ecological risk assessment, as in chemical risk assessment, the endpoints that can be studied are limited to quantifiable, major effects, such as lethality or cancer, and to effects that can be detected within the experimental time frame of the assessment. Effects that are difficult to measure are often ignored in chemical risk assessment:
    - altered behaviour,
    - reduced learning ability,
    - immune system impacts,
    - reduced fertility,
    - altered development time,
    - species shifts.

  These types of sublethal effects may be very significant at the ecosystem level, and often develop over much longer time frames than a risk assessment can measure. (Suter 1994; Johnston *et al*. 1998) There are, of course, similar kinds of difficult to measure impacts of GMOs that could have ecological significance. (see chapter 4) We could certainly say the same for impacts on landrace and wild relative genetic diversity.

- The measurable time frame of a risk assessment is necessarily short-term, but impacts show up over much longer time scales. For example, scientists have looked through records of plant introduction and weed development and note that this process occurs on time scales of 30-150 years. (Johnston *et al*. 1998 ; ESA 2004)

- Test organisms are limited to those that are easily culturable or measurable; quite often these organisms are of limited ecological significance. Not all organisms can be cultured in the laboratory, nor can endangered species easily be tested for obvious reasons. This means that for chemical impacts on a soil ecosystem, effects on a small number of soil-dwelling organisms – earthworms and collembola – might be measured. These organisms are expected to serve as proxies for the entire ecosystem, as other organisms cannot be tested. Of greater ecological relevance would be an examination of impacts on soil microbial and fungal populations, because of the essential roles they play in the soil processes of nutrient cycling, decomposition, and making nutrients bioavailable for other organisms. (However, even if we could measure the changes in soil microbial diversity, our understanding of soil ecosystems is minimal – we know a minute fraction of the microorganisms that live in any particular soil – and current techniques are inadequate to provide meaningful data for assessing the significance of such population changes.) (Berg and Scheringer 1994; Cairns and Pratt 1989; Holdway 1997; Power and McCarty 1997)

- It is impossible to extrapolate to an entire ecosystem from effects shown through tests on single organisms. As a simple example, food web effects that might result from a reduction in the population of soil predators such as carabids cannot be predicted, nor longer term, downstream consequences of alterations in the food web. (Holdway 1997; Power and McCarty 1997)

- Uncertainty and ignorance are the dominant conditions in dynamic ecological systems.

general epistemological problems of ecological risk assessment

- **The complexity of ecosystems can't be taken into account.** There are parameters of ecosystems that are fundamentally unknowable because of webs of interdependency, multiple causalities, and feedback loops. (Berg and Scheringer 1994; Calow 1994; Calow and Forbes 1997)

- **What you can measure is not necessarily what's relevant**. The organizational levels of relevance – population, community, and ecosystem – are least understood. With risk assessment techniques, scientists can measure changes at the organismal and sub-organismal levels – but we want to be able to predict and prevent changes at the higher organizational levels. In many instances we may not be able to determine *a priori* what end points are even relevant for assessing impacts on these higher levels of organization, nor will the endpoints necessarily be conveniently measurable parameters. (Johnston *et al.* 1998; Power and McCarty 1997; Santillo *et al.* 1998; Santillo *et al*. 2000)

- **Lack of statistical power.** Type II errors – not detecting an effect when there actually is one – in ecological assessments can be common. Take, for example, the laboratory experimental evidence that showed a 30% reduction in fecundity

for lacewings feeding on Bt-crop-fed prey. Field experiments would not be able to provide enough statistical power to detect such a reduction. Statistical power for manageable field studies would limit you to seeing deviations of 200-300%. Sub-lethal effects with potential long-term consequences would routinely go undetected; lack of evidence of impact cannot be considered evidence of safety. From Underwood (1992): "Type-II errors are a serious problem for environmental management – and much more so than Type I errors. … not detecting impacts (Type II) is not precautionary." (Andow 2003; Holdway 1997; Marvier 2001, 2002; Peterman and M'Gonigle 1997; Underwood 1992)

- **Assumes that you can quantify risks**, now or sometime in the future. This is problematic with chemicals, where you can apply a measurable amount of a chemical to an organism to find a dose-response relationship (only with particular endpoints like cancer; exposure assessments are difficult). There is, of course, the added problem with GMOs in that you cannot establish any sort of dose-response relationship. It is impossible to derive quantitative relationships for many parameters of ecological importance. It is also impossible to quantify risks for those hazards that are completely unpredictable, or that derive in a complex, non-linear way. (Santillo *et al.* 1998)

    - A corollary to the assumption that risk can be objectively quantified is that non-quantitative, subjective factors only enter into the discussion at the risk management phase. This is clearly incorrect – for example, the choice of endpoints is not an objective, technical decision. Someone, based on subjective parameters, decides that cancer is an appropriate endpoint to test for and that developmental abnormalities are not.

- **Reduces risk to two dimensions – hazard and exposure.** Risk is, in fact, multidimensional. Sterling and his colleagues have explored this in some depth in their study for the European Science and Technology Observatory (1999). Appraisal of technological risk should be able to examine risk across multiple dimensions, moreover, the evaluation of diverse aspects of risk should not be relegated to the management phase of the process. Multiple dimensions of risk according to ESTO include: severity, immediacy, gravity, reversibility, spatial distribution, balance of benefits and burdens, fairness, public or worker exposure, intergenerational equity, voluntariness, controllability, familiarity, trust. These multiple dimensions are incommensurable – "they cannot be readily or unambiguously be reduced to a single measure of performance," a single articulation of "hazard." (ESTO 1999)

  Most importantly, "the relative priority attached to the different dimensions of risk is intrinsically a matter of subjective value judgment. These properties of multidimensionality and incommensurability are crucial and intractable features of technological risk." (ESTO 1999)

further thoughts on "uncertainty"

As should be clear from both the above discussion as well as the various chapters of the CEC report, "uncertainty" is the norm in evaluations of risks of GMOs. We can add to our understanding of this topic with a more nuanced look at types of uncertainty identified in the literature on risk. A very common approach to risk (Wynne 1992) identifies useful a taxonomy of uncertainty: risk, uncertainty, ignorance and indeterminacy (we do not address indeterminacy here).

> ***Risk*** is the condition under which it is possible both to define a comprehensive set of all possible outcomes and to resolve a discrete set of probabilities across this array of outcomes. This is the domain under which the various probabilistic techniques of risk assessment are applicable.
>
> ***Uncertainty*** is the condition under which there is confidence in the completeness of the defined set of outcomes, but no valid theoretical or empirical basis for assigning probabilities to these outcomes.
>
> In a situation of ***ignorance***, there not only exists no basis for the assigning of probabilities, but the definition of a complete set of outcomes is also problematic, that is, an acknowledgement of the possibility of surprises. (after ESTO 1999)

From ESTO (1999): "the unprecedented nature of genetic modification technology [is] such as to render ignorance and uncertainty (in their formal senses) the dominant condition in the management of … risk … The curious thing is that these are routinely treated in the regulatory appraisal of technology by using the probabilistic techniques of risk assessment."

If not risk assessment, then what?

This discussion is not meant to advocate tossing the baby out with the bath water. Ecological risk assessment, for better or worse, is an important tool in our toolbox to evaluate impacts of GMOs and to inform regulatory decision-making. But risk assessment is only a tool, and the decision-making process is ultimately a political process. As numerous authors have mentioned, the more transparent scientists are about the limits of their knowledge, the better informed decision-makers, including the general public, can be. And if indeed they are faced with the prospect of severe and irreversible consequences, decision-makers may well decide to take precautionary action, even in the face of significant uncertainty.

If not risk assessment, then what? How do you make your technological appraisal robust and useful, if you can't rely completely on methods of risk assessment? According to the European Science and Technology Observatory (1999): more humility, more scientific disciplines involved, more types of information and knowledge, more constituencies, and use of other systematic approaches to analysis, for example, multicriteria analysis and consensus conferences. As well, they include as essential to the evaluation process the

placing of the proof of burden on the advocate, and an openness to alternatives, a consideration of multiple options, rather than a single option in isolation. (see also Kriebel *et al.* 2001)

Given that at the end of an ecological risk assessment we are inevitably left with a great deal of uncertainty, decision-makers (or risk managers) are left somewhat in the dark. A risk assessment will hardly ever provide a decision-maker with unambiguous information for how to proceed. At that point, politics must prevail. The decision to undertake a particular risk, or to undertake unknown or unknowable risks, is always political – informed by science, but nothing more. For science can never determine how much risk is acceptable to any particular set of people, and the unknowability of ecological impacts means science provides much less technical information than a decision-maker would desire or require.

In the face of substantial uncertainty, decision-makers may look to specific characteristics of a particular technology that may cause them more caution. In the case of chemicals, decision makers around the world have identified several characteristics of concern: irreversibility, persistence, bioaccumulation, ubiquity. Persistent organic pollutants, that is, organochlorines and other chemicals that are long-lived, accumulate in body tissues, and have properties that allow them to be transported around the globe and to the far reaches of the Arctic and Antarctic have attracted the most attention; recently negotiations concluded on the Stockholm Convention on Persistent Organic Pollutants (POPs), where twelve such chemicals were targeted by the international community for eventual phase-out, and where an entire class of chemicals (POPs) singled out for concern. Under OSPAR, hazardous substances are defined as those that are toxic, persistent and liable to bioaccumulate. Governments have agreed to continually reduce discharges of hazardous substances to the North Sea, with the goal of eliminating discharges within one generation.

Persistence, environmental accumulation, potential for serious harm, and irreversibility – these are characteristics that the international community has singled out for concern – all characteristics that GMOs share with POPs.

implementing the Precautionary Principle: the Cartagena Protocol, the EC white paper, and the WTO

In its most simple form, the precautionary principle states what should be done in the situation of scientific uncertainty. Recognizing a lack of information is key, and so is taking precautionary action in the face of uncertainty, particularly when risks are long-term, serious, or irreversible. This of course entails a political decision that society values the preservation of the environment.

The principle in its purest form – consider Article 15 of the Rio Declaration – leaves out much of what has been frequently ascribed to the principle. For example, many writers also consider an alternatives assessment as part of the precautionary principle. An alternatives assessment may be key to decision-making that affords the greatest amount of environmental protection, and we certainly would not argue against its necessity, but

this is not part of any currently existing legal formulations of the principle. Another ascribed component of the principle is the reversal of burden of proof – that is, under the precautionary principle it is up to the proponent of the technology to provide *prima facie* evidence of safety. Again, no international legal formulation of the precautionary principle contains this requirement. However, in the implementation of the protocol within national decision-making apparatuses, this could certainly be incorporated as a regulatory requirement. It does not mean, though, that this is an essential element of the Principle.

To conclude this section, we look at three different international legal regimes that have something to say about when precautionary action might be taken: the European Union, the Cartagena Protocol, and the World Trade Organization.

operationalizing precaution: The European Commission's communication on the precautionary principle

In 2000, the European Commission published a white paper on the precautionary principle, laying out guidance to member states, and to the rest of the world, on how to operationalize the principle within the EU. (Commission of the European Communities 2000) We do not analyze the white paper at all here, but merely provide some statements from that communication relevant to our discussion:

> A decision to take measures without waiting until all the necessary scientific knowledge is available is clearly a precaution-based approach.
>
> An analysis of the precautionary principle reveals two quite distinct aspects: (1) **the political decision to act or not to act as such**, which is linked to the **factors triggering** recourse to the precautionary principle; (ii) in the affirmative, **how to act, i.e.,** the **measures** resulting from application of the precautionary principle. (emphasis in the original)
>
> The implementation of an approach based on the precautionary principle should start with a scientific evaluation, as complete as possible, and where possible identifying at each stage the degree of scientific uncertainty.
>
> Judging what is an "acceptable" level of risk for society is an eminently political responsibility. Decision-makers faced with an unacceptable risk, scientific uncertainty and public concerns have a duty to find answers.
>
> Whether or not to invoke the Precautionary Principle is a decision exercised where scientific information is insufficient, inconclusive, or uncertain and where there are indications that the possible effects on the environment, or human, animal or plant health may be potentially dangerous and inconsistent with the chosen level of protection.

Where action is deemed necessary, measures based on the precautionary principle should be, *inter alia*:

- Proportional
- Non-discriminatory
- Consistent with similar measures already taken
- Based on an examination of the potential benefits and costs
- Subject to review
- Capable of assigning responsibility for producing the scientific evidence

The dimension of the precautionary principle goes beyond the problems associated with a short or medium-term approach to risks. It also concerns the longer run and the well-being of future generations.

risk assessment and precaution in the Cartagena Protocol on Biosafety

One of the obligations imposed on Parties by the Cartagena Protocol is the obligation to carry out a risk assessment prior to taking a decision. This obligation is found in Article 10, paragraph 1: Decisions taken by the Party of import shall be in accordance with Article 15 (the article dealing with risk assessment). This is in keeping with obligations under at least one other treaty, the Agreement on the Application of Sanitary and Phytosanitary Measures (the SPS Agreement) – a side-agreement of the World Trade Organization.

But as we have described in a previous section, the results of an ecological risk assessment for a particular GMO (living modified organism – LMO – in Protocol language) may be extremely inconclusive. What then is a government to do? It clearly depends on the tolerance of a particular government to the potential risks posed by the GMO. As noted above, the Protocol provides guidance on the application of the precautionary principle in this situation.[2]

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[2] **The Precautionary Principle and the Cartagena Protocol**

It is instructive to look at the wording of the precautionary principle in the Cartagena Protocol. Relevant text is found in four places throughout the protocol:

> Reaffirming the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development. (preamble)
>
> In accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements. (Article 1)
>
> Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate,

Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of the living modified organism in question as referred to in paragraph 3 above, in order to avoid or minimize such potential adverse effects. (Article 10, paragraph 6)

In lay terms, the Protocol legitimizes actions to avoid or minimize such potential adverse effects, including a ban on the importation of certain GMOs.

the World Trade Organization and zero risk

In some situations of potential damage to the environment or human health, societies will decide to accept zero risk. Nothing in international law prevents a country from establishing a zero risk standard, as long as certain procedural requirements are carried out, such as undertaking a risk assessment and notification of trading partners in the case of a ban on imports of the risky product. The articulation of the right of states to set zero risk standards is found in recent jurisprudence of the Appellate Body of the dispute settlement framework of the World Trade Organization (WTO).

In *EC – Asbestos* (WTO 2001), the Appellate Body clearly stated that States have the right to determine the level of risk they consider appropriate. The issue at hand was whether France could ban the use of asbestos, which included banning imports of asbestos from Canada, based on health considerations. Canada challenged this action of the French government by filing a complaint at the WTO. In upholding the right of France to set a standard of ***zero risk*** for potential health effects related to the use of asbestos, here is what the Appellate Body had to say:

> (W)e note that it is undisputed that WTO members have the right to determine the level of protection of health that they consider appropriate in a given situation (para 168).

The original dispute settlement panel and the Appellate Body came to two other conclusions relevant to our discussion of precaution and uncertainty. First, the panel found that an absolute level of certainty cannot be required for a Member to take action

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with regard to the import of the living modified organism in question as referred to in paragraph 3 above, in order to avoid or minimize such potential adverse effects. (Article 10, paragraph 6)

Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of the living modified organism intended for direct use as food or feed, or for processing, in order to avoid or minimize such potential adverse effects. (Article 11, paragraph 8)

under the GATT exceptions Article XX, second, the Appellate Body concluded that governments do not need to base decisions on majority scientific opinion. Here are the relevant paragraphs from their decisions:

> To make the adoption of health measures concerning a definite risk depend on establishing with certainty a risk … would have the effect of preventing any possibility of legislating in the field of public health. (WTO 2000, para 8.221)

> In addition, in the context of the *SPS Agreement*, we have said previously, in *European Communities – Hormones*, that "responsible and representative governments may act in good faith on the basis of what, at a given time, may be a divergent opinion coming from qualified and respected sources." In justifying a measure under Article XX(b) of the GATT 1994, a Member may also rely, in good faith, on scientific sources which, at that time, may represent a divergent, but qualified and respected opinion. A member is not obliged, in setting health policy, automatically to follow what, at a given time, may constitute a majority scientific opinion. (WTO 2001, para 178)

Article XX is the exceptions article of the GATT and includes provisions for exceptions for measures taken to protect human, animal or plant life or health, and exhaustible natural resources; based on these decisions, we can expect measures taken to protect maize diversity will be accorded the same deference, as decisions by sovereign states on levels of protection they consider appropriate. In fact, a zero risk standard for Mexican maize contamination, and measures such as bans on the import of transgenic maize to accomplish that standard, would likely be judged WTO-legal.

2. Risks of GMOs

We can make the critique of risk assessment real and the discussion of precaution concrete by considering the ecological risks of GMOs. While the CEC report is intended to examine all potential impacts of GM maize – impacts on genetic diversity, on agriculture, human health, and natural ecosystems – we will concern ourselves here with impacts on natural ecosystems. Natural ecosystems are at the same time very complex and yet a simple topic compared to the complexities involved in peasant agricultural systems. We use them as an example, noting that this is just one of the dimensions of uncertainty surrounding the introduction of transgenes into Mexican maize.

If you investigate what we know about potential impacts of transgenes on natural ecosystems, you read a litany of statements about what we really don't know. As noted by the Ecological Society of America (2004), many of the ecological questions they raise have yet to be examined empirically. There is no need to re-state all these here, but for sake of example, let us take the case of impacts on non-target organisms as elaborated by

the authors of chapter 4. The potential impacts are extensive, and little to no research has yet been carried out to assess impacts that introduced transgenes might have on on non-target organisms in Mexican ecosystems.

Some of the general and specific impacts on non-target organisms discussed in chapter 4 include (these are all direct quotes from the chapter):

General impacts

- At an individual level, impacts of significance could include lethal and sublethal effects (e.g., effects on development time, reproductive characteristics, morphological characteristics)
- Impact on populations will depend on the consequence of effects on individuals and the variation of those effects. Sublethal effects on individuals may have impacts on the population growth rate, leading to small or inviable population sizes and to local extinction. Loss of genetic variation increases population or species risk of extinction.
- The presence or absence of populations or species within a community or ecosystem may have significant impacts on biodiversity, if the species provides a critical role in ecosystem dynamics. … (T)he removal or addition of a species or population may affect the function of an ecosystem, including nutrient dynamics and energy flow. Lastly, if a susceptible species is rare or has small populations, any mortality or sublethal impacts on its populations may exacerbate and existing high risk of extinction.

Specific impacts from a Bt gene

- Lethal and sublethal effects to non-pest species in these orders (Lepidoptera and Coleoptera) could produce changes in biodiversity within these orders, depending on the susceptibility of other species within these orders to Bt toxin and their exposure to the toxin. Indirect effects on community and ecosystem diversity could occur if other more distantly related species or taxon groups were connected witht these species through ecological relationships. For example, the abundance and diversity of the Lepidoptera could affect plant populations and species that depend upon butterflies and moths for pollination or could affect populations and species of predators that prey upon butterflies and moths. Predatory species could be impacted in two ways by impacts on Lepidopteran species. Alterations in abundance or availability of prey could alter abundance or diversity of predators, or Bt toxin in prey species could affect individuals, populations and species of predators susceptible to Bt toxin.
- Non-target effects could have implications for nutrient cycling and decomposition as well as plant pollination and abundance and diversity of prey and predator species depending upon Coleopterans.

The question then that must be asked is “so what?” Are any of these impacts likely to have serious or long-term irreversible consequences for maize producers in Oaxaca, for natural ecosystems, for species of special concern, and so on? We do not know.

What then do we know about engineered organisms? They are alive. They produce seeds. Farmers share those seeds. They can germinate on their own and live as weeds around agricultural fields. All this is to say that if there were a transgene that was a problem, there exist numerous mechanisms whereby that gene could persist in the environment, both in natural and farmer-managed ecosystems.

When ought we exercise concern? According to its recent position paper on genetically engineered organisms, the Ecological Society of America counsels:

> Long-term ecological impacts of new types of GEOs[3] may be difficult to predict or study prior to commercialization, and we strongly recommend a cautious approach to releasing such GEOs into the environment. Engineered organisms that may pose some risk to the environment include cases where:
>
> - there is little prior experience with the trait and host combination;
> - the GEO may proliferate and persist without human intervention;
> - genetic exchange is possible between a transformed organism and non-domesticated organisms; or
> - the trait confers an advantage to the GEO over native species in a given environment.

Clearly, maize with herbicide-tolerant and pesticidal transgenes, found in Mexico, fit most of these categories. Maize that contains pharmaceutical transgenes would also clearly fit these criteria. Additionally, the ESA recommends that "large-scale or commercial release of GEOs be prevented ***if scientific knowledge about possible risks is inadequate*** or if existing knowledge suggests the potential for serious unwanted environmental (or human health) effects." (ESA 2004) (emphasis added)

Significantly, the ESA makes comments similar to our regarding the limits of traditional risk assessment techniques to predict what the consequences of GMOs might be for natural ecosystems. For example, in the discussion on non-target effects, and risks assessment carried out to date on these effects, they conclude:

> Single-species studies of non-target effects represent a narrow approach to assessing the positive and negative ecological impacts of non-target effects. Understanding the ecological consequences of non-target effects also depends on accurately identifying what physical and biological processes a transgenic organism may alter, and understanding what impacts these alterations have on ecosystems. Much of the focus of non-target studies has relied on measuring changes in survival and reproduction of a limited number of focal species in laboratory and small-scale field studies, without addressing the potential for community and

[3] The Ecological Society of America uses the term genetically engineered organisms (GEOs) rather than genetically modified organisms (GMOs). The Cartagena Protocol on Biosafety uses the term living modified organisms (LMOs).

> ecosystem level effects after large-scale introductions. Negative non-target effects on one species or a group of species may cause a cascade of ecological changes that result in the disruption of biotic communities or in the loss of species diversity or genetic diversity within species …, or they may have no repercussions, especially in communities with high redundancy of ecological function.

Later in the document, the authors note that:

> Risk assessment that is carried out prior to commercialization has several inherent weaknesses. In general, small-scale, pre-commercial field experiments are not sufficiently sensitive enough to detect small or moderate effects of a GEO. Small-scale field studies will readily detect order-of-magnitude differences in an ecological effect, but less dramatic effects will be difficult to document due to variability among replicates. Adding more replicates can address this problem, but pre-commercial field studies are not likely to include the large amount of replication needed to identify small but important effects.
>
> Small-scale studies … may be insufficient and misleading, depending on the questions being asked and the statistical power of the data analysis.

A final conclusion from the ESA document: "***The scientific rationale for a precautionary approach to regulation should not be ignored amidst this controversy.*** (on precaution)… ***Simply put, precautionary actions have been justified even in the absence of clear scientific evidence that a hazard is likely to occur… these actions involve "scientific evidentiary standards that err on the side of preventing serious and irreversible health and environmental effects."*** (NRC 2002)**"**

3. Maize, GMOs and precaution

Maize in Mexico is an exceptional case to consider as we evaluate the potential impacts of GMOs. Mexico is the center of origin and diversity of maize; maize is one of the world's most important food crops. It would be difficult to overestimate the value to humankind of the crop and the genetic diversity of Mexico's maize landraces.

Maize also plays a central role in the culture of people's throughout Mexico. As proclaimed in the manifesto delivered to the CEC on behalf of many organizations and communities in Oaxaca: "We are people of maize. The grain is our brother, foundation of our culture, reality of our present. It is in the center of our daily life. … We eat it, but it is not only food. It is a cause for celebration, for exchange, for coexistence, for mutual help. It is our life. Maize is in the center of our culture, in that which has a sacred character. We don't want it to be otherwise."

Maize plays an important economic role in agricultural production, and indeed the life, of the peasant farmer. The farmer is dependent on production whether or not the crop is sold to the market. In fact, the subsistence farmer is perhaps even more dependent on the crop than those farmers with more links to the marketplace. He or she is likely producing on marginal lands, characterized by uneven terrain, high slopes, irregular rainfall, and/or low soil fertility. Poor farmers are more vulnerable to the vagaries of the weather and the market. Crop failures and negative impacts on agro-ecosystems will have more serious effects on those already living on the margins of existence. This point is also made in chapter 2 of the CEC report:

> Farmers who depend solely on their primary production for subsistence face much more immediate food security risks. Smallholder farmers in Mexico are dependent on their own production for food on the table and crop failures are a significant risk. … Long-term stability concerns the ability of the farming operation to continue over a period of years. Here, damage to agro-ecosystem function in the form of fertility losses can have economic as well as environmental consequences.

Mexico is one of the mega-diverse countries of the world, with an astounding diversity of plants, insects, other animals, ecosystems, fungi and bacteria. Ecological impacts on an ecosystem scale in Mexico may have consequences more far-reaching than those that might occur in the industrial corn-belt of the United States.

It is within this scenario that we must consider the possible impacts of GMOs, in particular, transgenic maize. Clearly there is much of value to protect, there is much of value to lose. And we know that with the open genetic system of *campesino* farmers in Mexico, there is little damage that we could prevent once transgenes are introduced into Mexican maize agriculture. Consider the scenario put forward by the authors of chapter 8; imagine that one or more of the transgenes mentioned codes for a drug or an industrial chemical:

> First, an uncontrolled diffusion of transgenes to non-transgenic populations may take place. Second, if varieties with different transgenes become available and are planted, it is possible that, due to gene flow and recombination, maize populations may end up harboring multiple transgenes. These combinations may include transgenes that were never tested together and could even include transgenes that should not enter the human food chain. Third, if transgenic varieties that have been designed and produced with several transgenes, which may or may not be linked, enter the system, the same process of recombination and migration may cause the multiple transgenes to diffuse… Fourth, the introgressed transgene(s) will be introduced into different genetic backgrounds – those of local maize populations – and since the expression of a gene depends on the genetic background in which it exists, the expression (or lack) of the transgene may be very different from the expression in the original phenotype.

Given all that we do not know about the potential impacts of transgenes in Mexican maize – impacts on culture, on genetic diversity, on natural ecosystems, on agricultural production in marginal environments, why would we take the step to introduce engineered maize into Mexico? Given that only a few small steps along this path will likely lead us down a road of no-return, why take the risk?

Bt cotton and precaution in the United States

The US Environmental Protection Agency (EPA) has had to address the question of gene flow into wild and feral species of cotton. Without admitting to it, they have implemented the Precautionary Principle – they have taken action to prevent gene flow even in the absence of scientific information that there is some harm that will result. In fact, one might conclude from their actions that they view gene flow to wild and feral species of *Gossypium* (cotton) as something to avoid – a pollutant, if you will. In their determination, the risks posed by gene flow to these cotton relatives are unacceptable.

In order to prevent hybridization of Bt cotton with Hawaiian cotton and feral populations of cotton in the Florida keys and on the Virgin Islands and Puerto Rico, the US EPA has instituted restrictions on the planting of Bt cotton in those areas. There is **no** planting of Bt cotton allowed in south Florida nor in the Virgin Islands. Only experimental uses (no commercial planting) of Bt cotton are allowed in Hawaii and Puerto Rico, with significant containment requirements. (USEPA 2001)

If such measures are taken to prevent gene flow to feral cotton in south Florida, surely the maize center of diversity is worth at least as much precautionary action.

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Comments to the NAFTA Commission for Environmental Cooperation Article 13 report

Maize and Biodiversity: The effects of transgenic maize in Mexico Comments on chapters 2 and 8

Submitted by Greenpeace, 12 April 2004

We provide here comments on chapter 8 of the CEC draft report on transgenic maize. We also address briefly chapter 2.

In a separate document we provide detailed comments on three topics that are not adequately addressed in this chapter: the precautionary principle, specific risks of GMOs relevant to risk assessment, and the specific case of GMOs and maize.

Comments on chapter 8

a. The chapter would benefit from a careful review and standardization of terminology. There is a huge amount of conflation to terms in the chapter that must be clarified in order for any of the discussion to make sense. For example, the word assessment is used in various ways – to describe the process of determining risks, but also in a more general way meaning judging risks and benefits. The first paragraph of the abstract also reflects this terminological chaos.

Risk optimization and prior informed consent are characterized at various times as philosophies, principles, orientations, methods or approaches to assessing risk. They are probably none of these. Rather risk optimization, prior informed consent, and the precautionary principle may be considered ***frameworks*** for decision-making. The author of chapter 2 calls them "strategies in risk management" or "philosophical approaches" to risk management. The decision frameworks differ in terms of a number of variables: who makes decisions and whose opinion matters, different mechanisms for involvement of affected parties; what kind of information is relevant to the decision process; what kinds of information is balanced during decision-making (cost-benefit, ability to opt out of risk). ***These frameworks/strategies all rely on techniques of risk assessment to provide information for that decision-making; precautionary approaches to decision-making are also dependent on risk assessment for information.***

Whether or not a society is "democratic" is by and large irrelevant to the discussion in section 8.2, and the section should be given a more appropriate title.

b. The tone of the chapter is at times very condescending – expert opinion is clearly the most important information for the decision-making process in the eyes of the authors. There is no reflection of some of the most basic conclusions of chapter 2 in the chapter.

For example in chapter 2, the author notes that whether a transgene "in the wrong place" is already a harmful event or whether it needs to have demonstrable adverse impact before it can be considered harmful, "***is not the sort of question that the biological sciences are equipped to answer***." The authors of chapter 8 then indicate on page 21 that indeed, biological scientists are equipped to answer that question and assert dismissively that "***this view of hazards*** (transgenes as contaminants) ***has been rejected by a number of scientific committees convened to review the risks of transgenic crops***."

The authors go on to state that farmers can have their own opinions, but only if "based on accurate information and sound reasoning." (p. 22) It appears that farmers can't think for themselves, but that peasant view of contamination "may be more related to the perceptions from other groups in society and to whether a stigma is associated with transgenes." (p. 22) Such condescending perspectives are hardly likely to engender trust in the scientific community.

Chapter 2 goes on to explain what some consequences for this type of behavior might be. On page 14, Thompson states:

> It is also worth noting that when people feel that their values and concerns have been subverted in a systematic way, there is the potential for fairly widespread damage to public confidence in public and private institutions… When scientific studies are used to legitimate such actions, the upshot may be a decline in public support for science-based activities , or for the use of science to inform public decision-making.

The chapter 8 authors have apparently not even read some of their own words. On page 5 of chapter 8, the authors state that "it is thus almost always critical for people with a rich and locally informed understanding of the values, institutions and practices at risk in a given setting to be intimately involved in the process of ***identifying and conceptualizing risk***." That is, people – not just scientists – should be involved in identifying what exactly a hazard may be in any particular situation. In the case of maize contamination, a transgene in the wrong place may indeed be what people determine as the hazard itself. This is certainly the message that came from the Oaxacan community members during the public forum. That ***community members have an essential role to play in identifying and conceptualizing what is at risk*** is an important message from chapter 2.

Chapter 2 ends with a final comment on this point.

> Failure to note a category of risk that is extremely important to one group of affected parties can either bias the results unfairly, or can undermine the credibility and legitimacy of the entire effort to base decisions on a scientific assessment of risks. Such sources of significant … bias may arise when technical experts more accustomed to analyzing risk as a form of decision support are enlisted to prepare documents that have a more ambiguous and less easily controlled function. …

> This report itself … may reflect existing practices utilized in risk analyses designed for much narrower advisory purposes more than it reflects a complete or balanced compendium of the benefits and risks relevant to open-ended political decision making and debate.

The authors should really re-read chapter 2 and revise the chapter accordingly.

c. Sections 8.3 through 8.6 have some technical problems, some of which result from the improper use of terminology. The paragraph in the abstract that describes these sections is the most problematic:

> Methodologies based on risk optimization have traditionally been used to assess transgenic technologies around the world. Elements of the informed consent approach have also been employed. The precautionary principle has gained prominence, particularly with the ratification of the Cartagena Protocol on Biosafety by many countries, including Mexico. Risk optimization methodologies rely to a great extent on the scientific method and on scientific evidence, but also involve assumptions, value judgments, and uncertainty.

There are two serious inaccuracies in this paragraph:

- Methods to assess transgenic technologies are not based on risk optimization. As noted above and in chapter 2, risk optimization is a management framework. So neither have "elements of informed consent" also been employed in risk assessment. The description of risk assessment in section 8.3 is more or less accurate and appropriately doesn't mention anything about risk optimization or informed consent.
- All management methods rely on the scientific method and on scientific evidence. The precautionary principle and informed consent also rely on the scientific method and on scientific evidence. It doesn't make any sense to single out risk optimization methods of decision making as relying on science.

8.3 the risk assessment approach: overview of distinct methodologies for RA and approaches/models for RM.

The title here is not correct. This is not actually an overview of distinct methodologies for risk assessment, nor does it discuss approaches/models for risk management. It lays out in a general way the common steps used in traditional risk assessment approaches. It addresses some critiques and shortcomings of risk assessment but not in any sort of systematic way and with little to no reference to existing literature. The risk management section provides little information. We provide some further discussion of risk assessment in a separate document on the precautionary principle.

Value judgements in the discussion, such as "whether this popular conception should be adopted by policy-makers is, however, not all certain" (p. 8) are inappropriate.

Some discussion of why other dimensions of risk (p. 9) are not taken into consideration during the risk assessment phase would be appropriate.

8.4 assumptions behind methodologies for risk assessment and approaches/models for risk management

This is a completely inaccurate title. These are some assumptions made by some scientists and some regulators in some agencies in some countries. They are not assumptions behind risk assessment methodologies, nor are they assumptions underpinning models of risk management. They are not general assumptions at all, but specific assumptions by a specific set of individuals, about how they think about transgenes "out of place."

In particular, the treatment of assumption 1 disregards a whole realm of the scientific literature, as well as some of the chapters in this report. It ignores the conclusions of the Ecological Society of America (ESA) in its recent position paper on genetically engineered organisms. (Ecological Society of America 2004) To be at all accurate, this assumption must be highly qualified in its presentation. Moreover, use of a single citation (Crawley 2001) to conclude that "current evidence supports the familiarity model" is a rather bold overstatement of what those data actually show.

assumption 2 – This assumption is qualified in the recent ESA position paper. "We reaffirm that risk evaluations of GEOs should focus on the phenotype or product rather the (sic) process of genetic engineering…, but we also recognize that some GEOs possess novel characteristics that require greater scrutiny than organisms produced by traditional techniques of plant and animal breeding." (Ecological Society of America 2004)

assumption 3 – It's not clear why there is so much text devoted to this assumption. It is almost a truism that there is no way to demonstrate absolute safety. All technologies may carry some risk; it is a political decision for a society to determine whether it wants to accept that risk, in part or at all.

8.5 uncertainty and irreversibility in decision-making

Scientific uncertainty should be dealt with first in the section on risk assessment. There are many ways that traditional techniques of risk assessment can generate uncertainty and these should be included in any discussion of risk assessment. The types of uncertainty described here are some types of uncertainty that are described in the literature, but this is certainly not an exhaustive list and does not reflect an academically rigorous approach (nor does this section include a single citation).

It is not clear from the chapter exactly how uncertainties are integrated into decision-making. Uncertainties that result from the risk assessment process are certainly important to the decision-making process, regardless of the framework chosen for making decisions, and this point should be clarified.

At least two claims in the section are incorrect:

- "Lack of evidence of adverse effects at the organismal and population levels in small-scale trials is a good indicator that no adverse effects are likely to occur at the community and ecosystem levels."
- "Experimental data from field trials of transgenic organisms have increased the level of confidence in the technology."

Neither of these claims are supported by either the discussion in chapter 4 of this report, nor by the Ecological Society of America (2004).

Straw men and hyperbole (current evidence does not point to potential global calamities – p. 14) are inappropriate to this discussion.

Regarding social uncertainty – if this topic is to be addressed, there should be some academic foundation to the discussion and some reference to published literature. As it is written now, it seems to be used as a mechanism to cast as inferior those parts of society that don't really know what the risks of GMOs are and therefore irrationally judge GMOs as risky.

Irreversibility is never discussed in this section, so should be eliminated from the title.

8.6 the special case of Mexico and implications for risk assessment and management

At least one more sub-section should be added here. There is little assessment of the potential risks of transgene contamination outside of the agricultural context, in particular touching on issues raised in chapter 4 and chapter 7, in light of the specific conclusions found at the bottom of p. 18. This is a huge lacuna in the chapter. The specific case of introgression of pharmaceutical transgenes in a center of diversity needs to be addressed.

8.6.6 assessing benefits

Two comments regarding baselines. First, the discussion of the first baseline on p. 24 is completely inappropriate with respect to Bt genes in Oaxaca. There is no target insect and hence no current pesticide use to control the target insect. How any of this information could be useful in an evaluation of the broad range of impacts of a contaminating transgene in Oaxaca is not explained.

In addition, the human health and natural ecosystem baselines need to be included in section 8.6.6 on page 24.

Finally, it seems that the authors are treating irreversibility as a problem in itself, and cavalierly dismissing the issue with the statement that "humans constantly make decisions that lead to … irreversible consequences." Actually, what is relevant to this discussion is what it is actually that is irreversible, that is, the severity of the threat, the value of the resource that is damaged, and so on. Planting a garden in your backyard is irreversible, as is paving your driveway. These are not the kinds of effects we are worried about here. Irreversible contamination of maize landraces with a pharmaceutical transgene is. We don't imagine the authors mean to so cavalierly dismiss this potential

threat; the chapter should discuss the problem of a pharmaceutical transgene as a contaminant of landraces and the center of diversity in the context of its discussion of irreversibility.

8.6.7 balancing benefits and risks.
None of the risk management strategies introduced in chapter 2 have been discussed; we had thought this was to be one of the central pieces of the chapter. It is merely asserted, without discussion, that a precautionary approach should be considered together with a risk optimization approach. Then the precautionary approach is dismissed in the next sentence. We attempt to add significantly to this analysis with our accompanying contribution on the precautionary principle.

8.9 Conclusions

We do not agree that available methodologies for risk assessment are adequate for the case of transgenic maize in Mexico. We elaborate on this point in our document on the precautionary principle.

Comments on chapter 2

Two additional references should be included in the discussion. Charles Benbrook reviewed US pesticide use data from 1996-2004 and found results different from those cited in the CAST report. Also, in February, the Ecological Society of America published a new position paper on genetically engineered organisms and the environment that has some bearing on the issues considered in this report. Both citations are below.

One final comment, on page 11 the author felt the need to qualify risks with potential benefits. If this is done in the section on environmental risks, then a similar qualification on risks could be added to the benefits section. Either the sections should be balanced, with a paragraph in each (e.g., for completeness, it is important to reiterate that there is also the potential for offsetting environmental risks that correlate with each of these categories of environmental benefit) or each of the sections should be left solely to reflect what is in the title.

Benbrook, C. 2003. Impacts of genetically engineered crops on pesticide use in the United States: The first eight years. BioTech InfoNet, Technical Paper Number 6. Sandpoint, Idaho: Benbrook Consulting Services. www.biotech-info.net/highlights.html#technical_papers

Ecological Society of America. 2004. Genetically engineered organisms and the environment: Current status and recommendations. Ecological Society of America position paper on genetically engineered organisms. 26 February.

Comments to the NAFTA Commission for Environmental Cooperation Article 13 report

Maize and Biodiversity: The effects of transgenic maize in Mexico Comments on chapter 10

Submitted by Greenpeace, 12 April 2004

We would like to make three brief points regarding this chapter.

1. First, we underline the citation in chapter 10 of the Cartagena Protocol, Article 11.8, where the precautionary principle is articulated in the text of the agreement. This article in fact deals with imports of commodities. The provision in question clearly says that (excerpting): "lack of scientific certainty… shall not prevent that Party from taking a decision… with regard to the import of that LMO… in order to avoid… potential adverse effects."

This is a clear reference to the possibility of a country banning the import of an LMO – even in the situation of scientific uncertainty – that is, taking trade-related measures in a precautionary way to avoid potential impacts.

2. Second, we note that even the Mexican government has recently announced a ban on cultivation of certain types of maize (producing drugs and industrial chemicals) in Mexico – not just areas free of such transgenics. We call attention to the curious fact that the government has gone further than the chapter authors in what they suggest as necessary measures to take to prevent contamination of Mexican maize.

We quote here the English translation of the Mexican government announcement (Statement by México on transgenetic maize with properties that limit its consumption as food):

> Being a center of origin and diversification of maize, México
> - Paying due attention to the reproductive biology of maize as an open-pollenization (mainly subject to wind) crop;
> - Considering the dynamic character of the traditional farming systems regarding seed exchange and gene flow between local varieties and varieties originated in several geographical regions;
> - Reaffirming the importance of conservation and sustainable use of that resource and biodiversity, and
> - Understanding the strategic nature of the crop as food for the Mexican people;
>
> Manifests
>
> That has decided not to allow the release to the environment of genetically modified maize that has been modified in such way as to be no longer suitable as food. That is, México prohibits both experimentation and

> release to the environment of maize that has been modified to obtain pharmaceutical products, vaccines, industrial oils, plastics, or any modification that limits or affects its properties as food.

3. Given precedent in international and national law, it is difficult to understand how it a chapter that is supposed to be a comprehensive look at management options should leave out the potential for a ban or moratorium as possible options.

However, the chapter authors are well-known promoters of biotechnology. One of the authors is a well-known critic of México's moratorium on field trials of transgenic maize. One of the authors is a well-known advocate of US agricultural biotechnology, including transgenic maize, and was flown in to be a speaker at the official US government press conference announcing its WTO complaint against the EU.

Certainly all the chapter authors write from particular political positions. However, the lack of even a mention of bans or moratoria as management options at the very least displays a significant lack of academic rigor. The very grave problem here is that the CEC has a general obligation to member governments, petitioners, and civil society at large to present the entire range of management options in an unbiased way. The significant bias presented by the chapter authors does nothing to enhance the credibility of the CEC, the report, or the process and, in fact, does a great deal instead to damage their credibility.

The chapter authors have not taken a comprehensive look at all potential measures to manage risks; their ideological affiliations have clearly stood in the way of their ability to present an appropriate final chapter. The chapter does not belong in this report. The CEC should commission another chapter to take its place or risk challenging the legitimacy of the entire report and process.

From: dinah [dinah@ualberta.ca]
Sent: Tuesday, March 30, 2004 6:43 PM
To: Chantal Line Carpentier
Subject: Comment

Dear Chantal Line:

I believe the CEC is right to have considered the undertaking of a work like the one developed by Larson and Chauvet. I think that this type of study should be extended to have feedback with producers, since the report has two approaches: a scientific one and another with input from the indigenous world, and both interact. Freedom to perform traditional practices is part of the indigenous cosmovision. Any change affecting the landrace varieties will affect their identity and ancestral practices, without losing sight of the economic variable that GMOs require the payment of royalties, which would endanger their families' finances.

Yours truly,

Dinah Rodriguez Chaurnet

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Yours truly,

Dinah Rodriguez Chaurnet

From: ryan hill [ryan.hill@biodiv.org]
Sent: Wednesday, April 07, 2004 3:22 PM
To: Chantal Line Carpentier
Subject: Follow-up to CEC mexico maize workshop

Hi Chantal,

This is Ryan Hill from the CBD Secretariat. I hope you have recovered from the considerable efforts organizing the Oaxaca workshop. I found the workshop to be very worthwhile from the perspective of the CBD. Since the workshop, we have reviewed the chapters of the draft report and we do not have any official comments.

However, in my personal capacity as a scientific officer dealing with risk assessment issues under the Biosafety Protocol, I am interested in following up on the three chapters (2, 8, 10) that address issues related to risk assessment and risk management. In particular, in an effort to spread the word about the Protocol, I thought it might be worthwhile to provide some commentary for information purposes to the authors and advisory group members who were involved with chapters 2, 8, and 10. Many of the authors are very familiar with the Protocol, but for those who are not this may be useful.

If possible, therefore, I would appreciate if you could circulate this email with the comments below to those individuals (note of course that these comments are not to be made public).

Thanks and regards,

Ryan Hill
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Maize Adivsory Group's Response to Public Comments

The Advisory Group would like to thank all who took the time to read and offer comments on the terms of reference and the report outline for this important project. We have reviewed the comments received on the TOR and outline for the Article 13 report on transgenic maize in Mexico and have included those we felt were relevant. Others will not be included for diverse reasons that we feel are important to make public. Clearly many comments were contradictory to one another and we use the principles of inclusiveness and usefulness of the end results to decide which comments to include. Changes resulting from the comments can be found in the revised terms of reference and outline.

We have confirmed with the Secretariat that:

1. The Article 13 review must be independent of the governments and involve all stakeholders.

2. The Article 13 review is not related to Articles 14 and 15 and does not follow or require any submission process. Though the Secretariat accepted the request to look at the issue following a petition by ENGOs and community groups, it will follow the lead of the group of experts brought in to determine the terms of reference and the outline.

3. The terms of reference should be those decided by the working group (in consultation) and not dictated by governments or petitioners.

4. Human and animal health fall within the mandate of the CEC as is clear from the Children's Health and the Environment program and from the definitions of environment below. “Environment” is understood to include non-specific effects on human’s:

    - Physical surrounding and conditions, especially as affecting people's lives
    - Conditions or circumstances of living
    - External conditions affecting the growth of plants and animals.

Comments received that were not incorporated into the final terms of reference or outline are generally of six categories:

1. They assume something about the Article 13 process that we believe does not apply.
2. They are policy recommendations that may result from the Article 13 report but cannot be assumed *a priori*.
3. They represent further details, flag issues to be careful about, and ways that certain topics might be addressed. These comments will be compiled by chapter and provided to the consultants who will write the chapters.
4. They limit *a priori* the scope of the report, which may limit its usefulness and credibility. The Advisory Group feels strongly that the scope should remain large

at the beginning and be narrowed down as the process proceeds, if certain issues appear less relevant.

5. They limit the scope of the report to past events while this is a dynamic issue with other potential benefits and costs that are relevant to preventing environmental damage before it occurs or to ensure that benefits can be reaped.
6. They limit the scope of the report to issues not addressed elsewhere. Though the Advisory Group knows certain issues are being addressed in CODEX and other international fora, it does not believe it would necessarily address all of the relevant issues and may not be specific enough to North America. References will be made in the report to international-level discussions.

In conclusion, the Advisory Group feels it is important to review all the implications for North America of the release of transgenic maize in Mexico.

Consejo Nacional Agropecuario
Comisión de Biotecnología Agroalimentaria

In response to the call for opinions on the draft document *Maize and Biodiversity: The Effects of Transgenic Maize in Mexico,* the Agroalimentary Biotechnology Commission (*Comisión de Biotecnología Agroalimentaria*) of the National Farm Council (*Consejo Nacional Agropecuario*—CNA), after carefully reading the documents published on the web page and attended the symposium held in Oaxaca last month, offers the following comments that, in addition to commenting on some of the core topics, seeks to reduce the level of disinformation generated by the release of unfounded arguments on the phenomenon at hand.

First, we believe that it is essential for the CEC Advisory Committee to maintain its original commitment to make objective, honest, balanced and scientifically supported recommendations, since we have been greatly concerned to see ideological judgments prevail at the symposium, to the point that attendees were no longer paying attention to the speakers' topics and the discussion period was used for reading previously prepared documents, with no correlation to the problem analyzed at the time.

Furthermore, it is important that these recommendations give priority to address the need clearly expressed during the symposium, to establish a mechanism that provides reliable information on what genetically improved maize is and what it really represents for the inhabitants of regions where landrace materials are grown. The priorities in the release of information should consider the concerns expressed by the attendees with regard to the safety of biotechnology product consumption. In this sense, it is essential to recognize that the genetically modified maize currently on the market has passed the evaluation by regulatory bodies, which have determined the innocuity thereof with exhaustive, detailed scientific studies evidenced by multiple reports. Mexico's case is clear, considering the list of authorizations granted by the Secretariat of Health (*Secretaría de Salud*) pursuant to the General Health Law (*Ley General de Salud*) with reference to biotechnology products. Who benefits from hiding this fact? What do the country and the populace of Oaxaca gain with false and misleading information with respect to the health risks of products approved for consumption, the innocuity of which has been proven? The CEC Advisory Group members' lack of attention to this concern during the meeting has only contributed to reinforcing the fears expressed, far from helping to provide scientific and official information.

Also at the symposium Dr. Amanda Gálvez Mariscal, coordinator of the CIBIOGEM Advisory Board, presented the results of studies on the presence of elements of genetically improved materials in landrace maize collected in the states of Puebla and Oaxaca, requested by the Mexican government. These results clearly show the notable decrease of positive tests throughout the different crop cycles, from which it may be inferred that such characteristics are not fixed in such populations. This confirms the opinion of renowned scientists in Mexico and other countries that the simple presence of material from genetically improved maize **does not represent a threat to landrace maize breeds** (this was highlighted by Dr. Berthaud at the symposium). In fact, it is widely known that landrace maize exchanges genes with different materials, including maize improved by conventional techniques. The grower himself selects the desirable attributes for his subsequent crops, with respect to tastes, consumer preferences and performance, dynamically maintaining their distinctive characteristics.

The symposium demonstrated the maize's relevance in Mexico, and the need to assess each and every technological option so that production ensures the required supply. This evaluation should consider the benefits and costs of each alternative as a whole, contemplating all links on the value chain. It appears to us to be irresponsible to have proposals geared at prohibiting the import of genetically improved maize, in favor of flour, with the argument that flour cannot be planted, and thereby inhibits gene flow. This measure would worsen the broken agroindustrial chains in the country, with devastating effects to employment and harmful socioeconomic effects, particularly for the development of the nation's farm sector. It would also increase the importation of processed end products, losing the opportunity to generate added value in Mexico.

There should be attention to the fact that in commercial maize production, biotechnology offers important economic and environmental benefits that should be evaluated under the current regulatory framework to ensure food safety, which was cited frequently at the symposium. It is unfortunate that the chapters of the draft document that were allotted for analyzing the framework of benefits and risks make such a detailed analysis of the risks and so poor an analysis of the benefits, which have been found in opinions similar to ours. In this sense, it is necessary to approach biotechnology as a dynamic set of techniques offering solutions to problems such as drought, the adaptation of high-yield materials to local conditions, contributions to solving pest and weed problems, the improved contribution of nutrients by landrace maize, etc.

Furthermore, we stress that the benefits of products of agricultural biotechnology are for small-scale farmers and commercial growers alike, especially because the technology is incorporated into the seed. Consider that the products currently available on the market, in addition to the direct benefits of greater production, should consider the benefits resulting from the decreased application of pesticides and a smaller environmental impact for farming.

We are certain that the exercise of this assessment would be more useful and enriching if it were undertaken with greater scientific objectivity. This would prevent ideological biases from leading to wrong decisions that could marginalize entire regions of the country from the benefits of technological progress. We wonder whether the decision makers and their advisors are entitled to disqualify these technologies *a priori* without performing a scientific analysis that is solidly supported by data from Mexican field evaluations. This would prevent small and large growers from using advanced technologies without consultation, dooming them to missing out on innovation.

Comments on the report:

Maize biodiversity: The effects of Transgenic Maize in Mexico

Francisca Acevedo, Erika Aguirre, Alejandra Barrios, Elleli Huerta[3], Alma Delia, Sol Ortiz, Laura Saad.

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GENERAL COMMENTS.

Given the scope of the recommendations that may arise from the report, and considering that the repercussions of certain measures may be felt far beyond the environmental sector, as well as the intersectoral nature of the phenomenon under analysis, and in order that all recommendations may be implemented efficiently, they should be submitted not only to the environment ministers but also to the Secretaries of Agriculture, Health, Economy, Education, Social Development and Finance [in Mexico], and to their US and Canadian counterparts.

It is highly important that all chapters be available in the three languages. Given that the persons who first filed the suit are mostly indigenous organizations, all chapters should be available in Spanish in order for them to have access to the report.

It should be ensured that the summaries presented for each chapter be consistent with the respective chapter's text. In some cases the summary does not correspond to the chapter text; this is understandable as in most cases the summaries were submitted before the full text was prepared. However, their congruence must now be sought, either by correcting the summary or by adding the chapter's complementary information.

As a result of this lack of consistency between the summary and content of the chapters, it also appears that some authors refer to the contents of other chapters that again do not correspond to the [present] text.

Most of the chapters lack bibliographical references, both for specific data without providing citations, and also for quotations in the text for which no reference is cited at the end of the chapter. This lack detracts from the formality of the chapter text and limits its use and service, and therefore it is very important to correct it.

During the Oaxaca conference, there was a perception that Chapter 10 dealt with a summary or conclusion for the other chapters. It should be made clear that this is one more chapter on a particular topic, and as such does not deal with the conclusions for the rest of the report.

We suggest that the cultural aspects relating to maize be covered in more detail, as none of the chapters deals properly with the religious, symbolic or culinary aspects of maize. Consideration of these and other cultural aspects may allow for an improved perception of maize by small growers and Mexican consumers.

The order of chapters makes overall comprehension difficult. The order proposed by Larson and Chauvet (Chapter 9) is more logical and facilitates chapter comprehension. Thus, it would be appropriate to change the order in the final draft.

SPECIFIC COMMENTS

CHAPTER 1

All information in the first part of this chapter, from the origin of maize to the section on erosion of the germplasm of maize and its wild relatives, is clear and well-founded. However, this contrasts with the text and contents, starting with the section on the presence of transgenic maize in Mexico through the end of the document, which is confusing and lacking foundation.

Following are some relevant comments, mostly on the second part of the document. In the second paragraph of [the text on] page one it is important to clarify that Mexico's imports of transgenic maize are for food or feed and processing, and furthermore the *de facto* moratorium imposed applied only to the environmental release of genetically

modified (GM) maize for experimental purposes, as the environmental release for commercial purposes has yet to be regulated.

In the list of factors causing genetic erosion, not all numerals correspond to different causal factors but rather to different examples of the same factor, namely the substitution of landrace maize varieties with crops that may provide an economic advantage.

Starting at the heading on page 18 ["Presence of transgenic maize in Mexico"], where the report seeks to narrate a series of events about the presence of transgenic maize in Mexico, many references are incorrectly cited and do not appear at the end of the chapter.

It is not clear whether the first paragraph following the heading on page 18 refers to the entry of transgenic maize into Mexico from the transboundary movement of commodities or its intentional release into the environment.

The text states that the importation of transgenic maize was not regulated, and that presently it remains unregulated [page 19, second paragraph]. This assertion is incorrect, as from the September 2003 entry into force of the Cartegena Protocol—of which Mexico forms part—the transboundary movement of living modified organism commodities are regulated, precisely under the Protocol.

The types of seeds produced by biotechnology companies mention "resistance" to herbicides in addition to resistance to insects [page 19, fourth paragraph]. We suggest that this be changed to the appropriate, commonly used term of "tolerance" to herbicides.

On several occasions the text uses the term "deregulated," but as there is no legal concept in Mexico associated with "deregulation" of crops it is important to clarify to what such term refers—whether GM maize does not require notices, permits or authorizations for planting, movement, storage, use and consumption, or for only some of these activities.

We suggest that the authors take into account [in their revision] the new policies of DICONSA, which is the government agency responsible for bringing low-cost food to Mexico's poor regions. Due to the problems in Oaxaca, this state-run agency apparently has restricted the acquisition of maize, for storage and subsequent distribution, only to domestic production, and no longer buys imported maize.

Last, we consider that the inclusion of "alternatives" requiring the government's yes/no response [beginning on page 21] is an oversimplification of the complex phenomenon we face, and adds no relevant information worthy of serious treatment.

CHAPTER 2

This chapter considers theoretical elements of risk analysis, and represents an appropriate introduction to Chapter 8. However, some paragraphs should be modified or deleted because they represent value judgments mixed into paragraphs that describe "true" facts or events but that do not necessary apply in the case of Mexico. Furthermore, we believe that this chapter involves a subjective analysis of the potential consequences of the presence of transgenics in Mexico, which is not the purpose of this document.

The Latin name of the bacteria used to introduce nucleotide sequences should be corrected to *Agrobacterium tumefasiens*. Section *2.3* is repeated twice in the chapter numbering, on two different topics.

The fact should be considered that to a great extent the application of farm technology, which has worked in developed countries for high-input growers, will not necessarily work in developing countries for subsistence agriculture, which mostly takes place in highly diverse environments with marginal physical or socioeconomic conditions. For example, the International Center for Agricultural Research in the Dry Areas (ICARDA[1]) questions conventional improvement and for years has been implementing a new policy of improvement, called participation and decentralization. This system involves grower participation and the use of hybrid-breed and local varieties. These kinds of experiences in Mexico are mentioned in Chapter 9 of the report.

Section 2.6 [beginning on page 12], under the topic "Socioeconomic risks," states that food production by small subsistence farmers has a considerable risk component. This is followed by a series of reasons why crop damage may have both economic and environmental consequences, and ends by emphasizing that such problems are faced by independent growers whether or not they have GM crops. However, the section does not clarify that this type of risk is also faced by high-

[1] ICARDA. *Farmer participation and use of local knowledge in breeding barley for specific adaptation*. Final Report. GTZ Project No 95.7860.0-001.13. February 2001.

input farmers in the United States and Canada, perhaps even to a greater extent that low-input farmers because low-input growers often diversity their crops.

It is also important to distinguish the types of economic risks faced by large businesses that make informed decisions whether or not to invest in a given technology, from the economic risks of small farmers facing a type of technology they opted not to use and for which information is lacking.

Lastly, we believe that the comparison of risks and benefits is inappropriate. Risks are identified and levels of exposure and damage are estimated, where quantification and analysis are not monetary. To a large extent it is preventive, as risk management and mitigation strategies are based on the risk analysis. In contrast, an analysis of the benefits also implies a cost analysis, and this type of cost-benefit analysis is monetary.

We believe it is important to put the benefits of biotechnological farming in context, recognizing that no one technology solves all problems (see <http://www.cimmyt.org/whatiscimmyt/Transgenic/Iwanaga_051202.htm>). It should also be recognized that the use of different agricultural alternatives should be decided as a function of the types of problems and characteristics of the application of the systems themselves.

With respect to pesticide reduction being one of the positive impacts of GM crops that offer resistance to certain pests, we believe that this assertion is premature because in many cases the elimination of a pest will open an ecological niche for another. Such a later pest will limit the aforementioned benefit and would be a common occurrence in megadiverse environments—and pests—such as in the case of Mexico.

CHAPTER 3: Assessment of Effects on Genetic Diversity

This chapter deals primarily with the effects of gene flows on the genetic diversity of maize. It mentions different studies that could be undertaken, and provides the following recommendations, the comments on which follow.

Although the chapter states or can be understood as saying that the matter of maize is complicated and the studies that have been done in other countries, such as the United States, are insufficient or cannot be extrapolated for countries such as Mexico it does not state specifically in the case of maize that studies are required before transgenic maize is intentionally released in Mexico. In this regard, one recommendation could be to permit experimentation with transgenic maize, to try to obtain answers to Mexico's specific problems. In this respect, we would add the following to the final recommendations:

- As the diversity and taxa of teosinte are unknown, it would be advisable to estimate such diversity and the gene flow rates.

- The presence of F1 hybrids among maize and teosinte is recognized, but studies are needed on what happens with the subsequent generations of hybrids, in particular to determine whether there is any introgression. Detailed, specific studies are required to know if any introgression exists.

- It is necessary to perform studies on the stability of the transgene when inserted into new genetic contexts, and how it would affect individuals.

Page 14, paragraph 2 discusses the effects on genetic diversity from the introduction of a transgene for individuals with high levels of heterozygosis and effective recombination. It says that the genome region linked with the transgene may be very small, and therefore the region that may be affected by selection and present a decrease in diversity as a result of selection may be very small, when compared to maize's overall genome. However, if these individuals show better adequateness and there is sufficient migration of the transgene, there could be a displacement of individuals not having this modification, along with the rest of the genetic diversity they contain.

CHAPTER 4

This chapter is well-developed with current information properly focused on the topic being analyzed. It could be improved by presenting the specific data from studies performed in other countries, principally Canada and the United States, on the effects of transgenic crops on natural ecosystems, focusing on aspects of population ecology. In this regard, we believe it is important to include studies performed in Mexico, in an analysis of this kind of information.

CHAPTER 5

This chapter is an essential part of the report. It gives true importance to the reasons why there are problems from the loss of maize biodiversity in Mexico, and suggests that the intelligent use of technology might even solve part of the essential problems under which Mexico is losing diversity in its landrace breeds.

The authors further recommend, correctly, that if GMOs represented a real threat, the solution would be to strengthen germplasm banks and maintain and develop appropriate genetic improvement programs.

They should clarify the legal liabilities in the case where transgenics appear in landrace maize.

The chapter is clear and provides well-founded information with respect to the fact that if there were a national will, Mexico could be maize self-sufficient.

CHAPTER 6

There are three groups of growers considered in the chapter's context: noncommercial, semi-commercial and commercial producers. However, Mexico has documented more than 100 ways to produce maize, and therefore it seems to us that this view reduces the forms of production to a minimum. While the chapter perhaps does not deal exclusively with a single topic, we suggest it be broadened, as it is covered only very briefly on page 4. This is an important component to consider for the analysis of the social and cultural effects of the production of transgenic maize.

It would be appropriate to differentiate, from the figure of total tons imported, how many are yellow maize and how many are white maize, as well as in the reference made to the distribution of Mexican production for the different maize uses ([last paragraph,] page 7).

The authors' mention of how maize is regarded as a commodity in the United States is very important with respect to Mexico, emphasizing the fact that US production for human consumption is minimal. This should be considered not only in this chapter, but rather be taken into account in the recommendations.

We suggest that the topic of subsidies be covered in greater detail and with more emphasis on the difference between US and Mexican subsidies, also recognizing the fact that US subsidies are for producers while Mexican subsidies are for production (Section I.B.2.a).

We suggest that the cultural aspects be covered in more detail. In fact, as we mentioned in the general comments, none of the chapters deals specifically with the religious or culinary aspects of maize. In this case, Section I.C.1. refers to cultural aspects, but very briefly and without any reference to the different uses of maize associated with the different varieties. However, on page 23, paragraph 7 of Section I.C.3., "Use of new technology," very superficially mentions that *"improved maize [varieties] is [sic: are] limited because they are developed for tortillas but not for other uses, such as pozole (hominy soup). Traditional varieties are kept for these uses…."* It is **VERY** important to recognize the cultural aspects associated with maize; if a specific chapter on them has not been considered, this could be one of the more appropriate chapters to do so.

The second paragraph of section I.C.6 [found on page 27], states that *"gene insertion has not produced plants that are substantively different from plants produced by conventional breeding methods…"* We believe it is dangerous to use this type of assertion without having a serious reference, because it may give the wrong impression that a transgenic is the same as a plant produced by conventional handling. Furthermore, this assertion brings us to discuss the term "substantial equivalence," which has been used on products and byproducts (food) produced from GMOs. But in biological terms, and in reference to a whole living organism, it is not appropriate to use the term "substantial equivalence." A Bt maize plant expresses a bacteria protein and this differentiates it from a maize plant improved by traditional methods. Phenotypically the plants may seem the same, but this is not enough to call them "substantially equivalent." Lastly, generalizations should not be made, as the biotechnological application is far from reaching its limits.

It is important to consider the fact that, given the diversity of producers, ecosystems and farm practices in Mexico, it is necessary to undertake multidisciplinary studies by region to assess the socioeconomic impacts of the introduction of transgenic maize, considering the CEC recommendations to the three governments.

CHAPTER 7

There should be emphasis on the need to perform studies on the innocuity and allergenicity of GM-maize based foods in the context of the actual Mexican diet. The needed subdivisions, *i.e.*, rural and urban diets, also should be considered, given that maize portions—in proportion to total food and level of processing—is not the same in both sectors. The precautionary principle should be applied even where there are no scientific reports in the United States or Canada on the toxicity and/or allergenicity derived from maize consumption. In this sense, the chapter succeeds at differentiating the consumption patterns of the Mexican diet.

The statement made by Héctor Bourges, that maize and Mexican gastronomy are regarded as patrimony of humanity and as such should be respected, conserved and promoted by the Mexican government, should be emphasized.

We highlight the need for a chapter that truly deals with the religious and cultural components in the discussion of transgenic maize in Mexico. After the public declarations made in Oaxaca during the symposium and other statements, it is imperative to consult with a specialist on the topic (such as historians, anthropologists, philosophers, etc.). The ethical, moral and religious discussion should not be a loose end, and as mentioned, it will help our trade partners to understand the negative response and uncertainty of some sectors of Mexican society.

Although Dr. Lehrer says that the Cry9c protein is not allergenic based on the available scientific information, there are studies (Gálvez, Quirasco, Plascencia and Fagan, 2004) indicating that the protein Cry9c may be detected by antibodies even after having been subjected to the process of milling, cooking and frying. Thus, there should be more care in analyzing the food risk, not taking for granted that there is no allergenic risk associated with GMOs. This point is fully based on the precautionary principle.

CHAPTER 8

Following are some of the points in this chapter that we believe should be pointed out and taken into account for the recommendations:

It is necessary for all interested parties (farmers, peasants, businesses) to be involved from the start of the decision-making

process, so as to facilitate the communication of the different aspects of the different aspects or dimensions of risk that that they may or may not assume, with the necessary awareness.

Peasant practices deviate considerably from the goals of commercial agriculture. Transgenics that peasants would be willing to test would be those that offer them a clear benefit.

It is important to keep in mind that the relationship between a transgene and the characteristic it is to express has much less control and more uncertainty in the conditions under which peasants manage maize. When a transgene is under such handling, and under greater stress or with a greater environmental variability, natural selection plays a major role as well. This emphasizes the need for detailed studies on the possible effects of introgression of transgenes into landrace maize populations under traditional management in Mexico.

It is important to take the cultural meaning of maize into account. Maize has a meaning for peasants beyond being a product produced for profit, and this meaning adds another dimension to the perception of risk of introgression of transgenes into local maize populations. While this is mentioned in the chapter, it should be stressed in the final recommendations.

CHAPTER 9

It is important that this chapter in particular be available in Spanish, and that it include the word-for-word comments of the attendees at the organized workshops.

Since it has been said that maize has a strong religious component, a specific report should be included on this topic, stressing its importance (*e.g.*, referring to the case of New Zealand). This would help to clarify the answers to many questions raised by the public with respect to transgenic maize in Mexico.

This chapter makes clear that a comprehensive response is expected of the Mexican government, not only from the Environment Secretary, but a clear policy involving the Secretariats of Agriculture, Health and Environment, of course the Education Secretariat and even what used to be the National Indigenous Institute (*Instituto Nacional Indigenista*). The community response and questions may set the basis for a more comprehensive Mexican government policy.

The recommendations should stress the real need for communication, inclusion and respect for the communities involved in the planting, conservation and use of native maize. This implies a greater commitment from the responsible government agencies.

CHAPTER 10

A small introduction is needed on the chapter's objectives, the aspects to be covered, etc. As all chapters have an introduction, this changes the approach of the chapters in the report.

This chapter appears to be a text written some time ago and which has not been updated. For example, it has data such as the reference to the National Agricultural Biosafety Committee (*Comité Nacional de Bioseguridad Agrícola*—CNAB)—now the the Specialized Agricultural Subcommittee (*Subcomité Especializado de Agricultura*)—which has not existed for several years. Another example is the reference to the General Bureau of Plant Health (*Dirección General de Sanidad Vegetal*), which is no longer so named. It is also necessary to update the number of existing ratification instruments for the Cartagena Protocol (90, as of 6 April).

In the last paragraph of the first section, when it states that there are national programs applying GM technology to solve specific programs in Mexican and Brazilian communities, it should give some examples, especially for Mexico.

In several instances this chapter makes assertions that are not founded or documented and therefore may appear biased, such as the statement that "*Most of the current GM maize applications available to growers in US would be welcomed by framers in Mexico*" (page 3, Section III, first paragraph).

When it states that there are two positions on whether the gene flow to wild varieties is a low-risk topic versus other authors who argue that it is necessary to take more notice, it would be advisable to state the arguments (or least expand on this point) supporting each position [Section III, third paragraph].

The fourth paragraph of Section III (page 3) oversimplifies population genetics and the behavior of genes within populations. It is not so

simple; in fact, there are several studies and references in this regard (Norman Ellstrand has written many), and therefore we suggest it not be taken so lightly.

Throughout the chapter, talk of gene flows refers to the possibility that this exists between GM crops, landrace varieties and wild relatives, although it does not consider that non-GM maize crops that are not landraces", such as improved hybrids, which could in fact arise.

Section III states that the introduction of transgenes in an open pollination system, in particular those subject to farm practices promoting extensive seed exchange, inevitably will lead to the dispersion of transgenes among crops, with the future impossibility of returning to their original state (page 4). However, other sections later mention the possibility of returning to their original state (page 5 and [Section VIII, sixth paragraph] on page 16), which is contradictory.

In Section IV, the author mentions that to prepare the management strategies, the possible risks should be defined and it should be begin with a series of questions to answer. Four questions are raised on page 5, although they are not readdressed. We believe it is very important to develop these questions in the chapter, as it appears that the chapter is more focused on a review of policy tools more than on a series of guidelines for the development risk management strategies.

Section V asserts that the transgenes found in Oaxaca are not the product of gene flows but rather from the use of seeds that "*somehow*" came to rural communities. We find this to be unobjective, since while seeds could be brought into the country by Mexican migrants, it is a fact—and a possibility that has not been disproved—that the introduction could have occurred by reason of the planting of US maize imported to Mexico, not identified as transgenic.

With respect to the mention of the "substantial increase" in price due to maize segregation, we believe that unless there are figures from an *ex professo* study on imports to Mexico, such increase should not be qualified. In fact, an international discussion recognized by the International Grain Trade Coalition itself finds that no one is sure how much such a price increase would be, since it has been qualified but not quantified. Thus, it has been proposed that it is necessary to perform studies to estimate such costs.

As regards PIC under the Cartagena Protocol, there should be a distinction that not all transboundary movements of LMOs are under

this procedure, whereas the second paragraph of page 7 seems to state that they are. While later statements say something about commodities, the difference between LMOs for which PIC is or is not applied is not very clear for people not involved in the Cartagena Protocol.

The fifth paragraph on page 7 states that *"Under the Protocol, a 2-year process was established through which further documentation requirements will be considered."* However, to be specific, it should mention that this is two years after the entry into force of the Cartagena Protocol, which represents a very clear date, namely September 11, 2005.

We believe the chapter devotes too much space to the section on development and national implementation of biosafety systems (page 8), when other matters such as the questions mentioned on page 5 are not covered at all.

In the section *"The national biosafety system in Mexico"*, there seems to be a contradiction between paragraphs 2 and 3 on page 13. First it states that the standard NOM-056-FITO-1995 establishes the requirements for field testing, and then it mentions which products are approved for commercial planting. This should be clarified.

The last paragraph [of Section VI] makes reference to the Biosafety Law (*Ley de Bioseguridad*), specifically the identification of "restricted zones" for the release of GMOs, and mentions the centers of origin and protected areas. However, the correct reference is to "centers of origin and genetic diversity" and "protected nature areas."

CONCLUSION

A system of participatory improvement for maize in Mexico would be consistent with the open and dynamic system of small peasant farmers described by Bellon & Berthaud (2004, as referenced in Chapter 8) and Louette & Smale (2000, as referenced in Chapter 8).

The Secretariat of Agriculture, Stockbreeding, Rural Development, Fisheries and Food (*Secretaría de Agricultura, Ganadería, Desarrollo Rural, Pesca y Alimentación*—SAGARPA), through the National Institute of Forestry, Agricultural and Livestock Research (*Instituto Nacional de Investigaciones Forestales, Agricolas y Pecuarias*—INIFAP), should

have a policy promoting agriculture with a participatory improvement to sustainably achieve increased yields. In addition, it would be the best time to justify a higher budget with lines of research into maize improvement, extensionism—which has been lacking for some time—and justifying a policy aimed at maize self-sufficiency and the consequent reduction of transgenic maize imports.

From: Gustavo Alanis Ortega [galanis@cemda.org.mx]
Sent: Monday, March 29, 2004 1:31 PM
To: Chantal Line Carpentier
Cc: doreen.stabinsky@dialb.greenpeace.org; hguerrero@ccemtl.com
Subject: Re: timeline for advisory group recommendations

Thanks Chantal Line for your response. I would like to reiterarte to you by writing some of my comments from Oaxaca in order for them to be taken into consideration in the final report and actions to be undertaken in the near future.

1) That the request for the Article 13 on Maize be published along with the report. This is important in order for the general public to know how this started and also for the public to know which were the precise requests from the NGO´s and the Communities in Oaxaca to the CEC.

2) That the recommendations that will come out from the report by directed to the Mexican Government (as they did in the Presa de Silva article 13 report) and not to the Council. It is clear that given the situation in Oaxaca, is Mexico who will have to do some things in order to deal with this matters. A lot of things may be recommended, but they will not be able to be fully implemented if we do not engage the CEC in the process. What I want to say with this, is that there has to be a follow up by the CEC after the report is published, which will help us as a country to comply and implement the recommendations. From the workshop in Oaxaca, it is clear that there is a lot be done with respect difussion, materials, mannuals, etc.

3) Even though the 10 years report of the NAAEC-CEC may be the issue of the June Ministerial meeting, I think that the Minsiters will need some time to talk about the Maize report, so it would be great to ask the organizers of the meeting to allocate some time for it.

4) Finally, I beleive that the Secretariat of the CEC cannot loose the opportunity of publishing the report for the June Ministerial meeting.

It is a great opportunity to do so and to move forward with this very important issue for some sectors in México.

I thank you for taken this comments into consideration.

Gustavo Alanis-Ortega