Michael Fernandez: We will discuss disease prevention as opposed to therapies or treatments which was the previous discussion topic. We know that many diseases could be prevented through relatively simple behavior and/or dietary changes without considering functional or other new categories of foods. Clare, you mentioned that in your talk.

Clare Hasler: You are right, but the issue of behavior change is not simple. A plethora of low-fat, no-fat products are on the market, yet we have more obesity than ever. And nutritionists have been telling people for years that one of the major things you can do to improve your overall health, and cut cancer significantly, is just to incorporate five to nine servings of fruits and vegetables a day in your diet. But, consumers want to hear a message that is more specific to them and one of the things that I alluded to was individualized nutrition. Rather than just the message of ‘eat a wide variety of foods,’ which makes us all fall asleep although it is important, people need to be aware of their own health profiles. That is where nutritional genomics may play a role, although I have doubts about how much it will impact prevention. With us knowing more about physiologically active components—like lutein and how it selectively accumulates in the macula of the eye—there may come a time when we can make more-specific recommendations for food groups or bioactive compounds for individuals at risk for certain diseases. If eye disease is not an issue, you may be concerned about prostate cancer or breast cancer. We are going to start focusing more, although we don’t want to lose sight of the forest for the trees.
*Fernandez:* Do you think that you run a risk of people hearing the message “if you eat this particular food then you will be okay” and ignoring the bigger picture.

*Hasler:* That does happen. People don't always incorporate the messages that they hear or comprehend the reasons that health claims are worded as they are, such as “may reduce the risk of” in the context of a low-saturated fat, low-cholesterol diet is because we don't want to tell somebody they can eat 25 g. of soy protein and consume a quart of ice cream and reduce their cholesterol levels. That is an important issue.

*Fernandez:* Another of these big themes that has emerged is the idea of blending categories or blurring the lines between food and drug and supplement. We are recognizing that although these areas are the most exciting, they present unique challenges—in the regulatory arena for example. With respect to products that are not foods, but are being made in food crops, edible vaccines for example. How is food safety to be assessed? John?

*John Howard:* Some of these organophosphate pesticides, though toxic, are present in food and we have accepted these risk models. Yet biologic molecules that we see every day are not accepted. In fact we make many of these ourselves. It seems to me that there is a disconnect at the regulatory agencies in terms of how they assess risk for pesticides and what they are looking for in biologics. Not that biologics should be exempt, but similar standards should apply.

*Fernandez:* Are there unique risks with respect to particular products or the technology *per se* that we need to consider?

*Howard:* We need to look at each on a case-by-case basis. Unquestionably, there will be cases that pose unique risks, yet generally we are dealing with proteins and other molecules that we consider to be of much less risk than what is already being regulated. So that is where I see a disconnect. We would like to look at the risk assessment in the same way, and look at the value of these things and at the benefits in the same way.

*Fernandez:* Sam, do you want to touch on that? I think it has a lot to do with what you were talking about.

*Samuel Lehrer:* Well, with assessment of products modified by biotechnology for allergy risk, some feel that it really isn't a level playing field, in terms of the criteria that we are using for GM foods, many other foods would not pass. Allergy risks with GM foods might be much lower as compared to peanuts, soy,
wheat, shrimp, and other foods. Although we should err on the side of caution, we need to keep that in mind.

**Fernandez:** What is needed in the areas that each of you talked about to deliver on the promises of agricultural biotechnology?

**Hasler:** Certainly we have the technology to deliver genetically modified foods with health benefits, which raises the issue of the statement on the label. Such foods would need to be tested in appropriate scientific studies or clinical trials, according to certain criteria set out by the FDA. The health benefit then has to be communicated to consumers effectively, which is an issue that the International Food Information Council is addressing, how information should be disseminated to consumers. One of the hot-button issues regarding communication is at what point in time do we talk to consumers about what is good for them. Where should the line between emerging and consensus be drawn? And there are also free-speech issues. The FDA is being sued because they do not allow information on labels that some consumers feel they should have access to. Having demonstrated that a certain food can provide a health benefit in a controlled setting and getting that information to the consumer is one challenge. Whether consumers are open to the concept is another issue.

**Lehrer:** In terms of delivering on the promise of biotechnology—I believe that it can be done. It is a matter of resources and will. But will consumers be receptive to the products?

**Fernandez:** Following up on that—one branch of the decision tree you showed had properties like digestibility that are common to known allergens, and if you got a “yes” there the box led you to the regulatory agency. In the case of StarLink™, the developer was in a similar situation and went to the agency with information. One interpretation is that the EPA did not have the regulatory tools or enough knowledge to determine whether that information was sufficient. Do we need more work in that area to be able to deliver on that promise.

**Lehrer:** You’ve raised a number of issues. Let’s talk about the decision tree first. It had some problems, such as how to define the digestibility of proteins. Do you look at mixed proteins? Do you look at purified proteins? There has been a lot of discussion and it will be improved and defined. With regard to StarLink™—I should mention as a disclaimer that I have consulted for Aventis—there were several issues. The whole thing was a fiasco in my opinion. But with regard to the decision tree, StarLink™ was never approved for human consumption, so the failure wasn’t in terms of assessing it for the potential allergenicity. Actually, the protein was never shown to be allergenic. The
problem was in the split decision: approving it for animal consumption only. A lot of people said years ago that adequate segregation was impossible because of the way agricultural products are grown and stored in the United States. In that context, the folks who were supposed to be minding the shop weren’t doing so, and it contaminated the human food supply. It had nothing to do with the decision process. It was the split-decision approval for animal feed; from what I understand, that will never happen again.

Fernandez: John, that brings me to you. Although there is an obvious difference with a commodity crop like StarLink™ you were talking about split approval in a sense for food and non-food uses. Is that going to be an issue? It becomes a matter of perception: “if it’s in my corn is it in my cornflakes?”

Howard: I agree with what was just said. We have all been sensitized by StarLink™: the consumers, the regulatory agencies and the lawyers. In hindsight it can be viewed as useful. Something that turned out to be a non-problem sensitized us, made us all a lot more aware of what we need to do. These crops could, in fact, have been segregated, but it simply wasn’t done. When we are making pharmaceuticals or vaccines, we are always under regulations, we’re always growing under permits. We have training manuals and standard operating procedures. But what is very standard for making pharmaceuticals is not standard for agriculture. It is standard for food products such as yeast that are used to make pharmaceuticals. We should view it as analogous to making a pharmaceutical product, as has been done for decades, rather than as an agricultural product. I don’t think we are risk-free, but I think our sensitivities are heightened.

Fernandez: I’m going to invite the audience to ask questions.

Barbara Schneeman (University of California, Davis, CA): My comment has to do with our traditional way of looking at risk analysis, which was developed for the food-additive system and actually works quite well. FDA has recognized that as we move into an era looking at whole foods or looking at macro-replacers in foods such that new factors need to be considered: GI tolerance, drug/nutrient interactions, allergenicity. Some have argued that perhaps the only way to deal with this adequately is to think about post-market surveillance or post-launch surveillance rather than putting our hopes completely on the pre-market approval process. I would like the panelists to comment on what role post-market surveillance might play; does it have any value, is it something we should be talking about?

Lehrer: There are varying opinions on this. I believe that it depends on the product. For example, if it is one that we have hard and fast information about
a product and there was little doubt about the decision, I don't know that it is necessary to have post-market surveillance. On the other hand there may be some, novel proteins for example, with which we won't have that kind of information. We will get better information on them, but we still won't have the final test that we can take the serum from an allergic individual and test it. They are working on a lot of interesting animal models now, which may help, but in that kind of situation there, I can see a need for some type of system to assess whether or not there is a problem. I gave a lecture recently at the American Academy of Allergy, to allergists and the other healthcare professionals in allergy, and I really was amazed because I think they really hadn't thought about it that much and they are the ones who should be the first line of defense, so to speak, at least in regard to allergy. Other health issues are another matter. But I think that these individuals should be educated more about what the issues are and should be aware of it. It is certainly more problematic to identify someone who may have an allergic reaction to a novel food because of the way our system is, nevertheless I think one can get information and they should be alert to that. I think some kind of assessment system would be useful.

Myron Just (Minnesota Agri-Growth Council, St. Paul, MN): The discussion this morning reminds me that Hippocrates, the father of medicine, made the famous comment that “food is medicine and medicine is food.” Is medicine coming full circle and are we now recognizing that he was on to something 2,400 years ago that we should have been thinking about? Also, some years ago I traveled extensively in China and was struck by how traditional medicine and modern medicine overlap there and respective practitioners work side by side. I'll be grateful for comments from the panel.

Hasler: You are right and I usually include that statement from Hippocrates in my presentations. I think we have come full circle. Many indigenous populations still use foods and plants for medical intervention. Forty percent or more of our synthetic drugs still come from plants. The 1800s saw the development of synthetic drugs and the ability to patent those technologies, which really stimulated the drug industry. But, the current focus is switching more to prevention—in which foods can really play a role. I’m not sure how much foods will be used as therapy. Drugs traditionally are used as therapy and I think that will continue. But a preventative approach needs to be taken in many diseases that result from lifestyle choices and environmental factors and foods can be very successful in that regard, recognizing that alternative or complementary therapeutic approaches are not snake oil. A couple of years ago a whole issue of the Journal of the American Medical Association was devoted to the issue of alternative medicine, which would have been unheard of 10 years ago. I agree. We are coming full circle in this regard.
Phyllis Johnson (USDA, Beltsville, MD): My question has to do with the relationships between those who are producing these unique pharmaceuticals and the processor and those who will sell the vaccine. In our conventional marketing system, if you get your high-grade malting barley mixed up with feed barley there may be a loss of profit, but it is not going to hurt anybody. I guess that is the kind of system that failed with StarLink™. It seems to me, if I were a farmer, I wouldn't want to start growing corn that was going to produce some pharmaceutical unless I already had a contract to sell it, and maybe knew that the processing plant was down the road. Are you vertically integrated? Do you have these kinds of relationships with producers, or how is this working?

Howard: I'd say some of it is out there, but there are some major differences. First of all the grower never buys the seed. He is only licensed. The grain must be grown under specific conditions. The grower is guaranteed the price. It is completely vertically integrated in that sense. In fact, it is what we call a closed-loop system. The transport is arranged, the storage, the harvesting, the dedicated equipment, all that is covered in this case by us or by another company. So the grower has an important role, but it is a very different role from that with normal commodity crops. So, in that sense, they are very separate. You have to ask yourself why would they want to do this in the first place, since it becomes a great pain to them. But the other part of it is that we pay them extra to do it. So they are being paid for these extra steps—there are economic incentives. There are also contracts such that if they don't do it they are legally liable. So it is a very, very different system from what you were talking about with barley segregation.

David Poland [International Maize and Wheat Improvement Center (CIMMYT), Mexico]: I work in communications so I have been in the middle of this transgene Mexican land-race issue. I'm a proponent of the technology, but it scares me—if I had to be a communications person responding to questions about pharmaceuticals in maize, I wonder how would I do it, given the questions we are already getting from Europe and other places. There is a tendency to say “well it's just a perception problem,” but it's a big perception problem. So my question is: given the costs that are going to be involved with convincing the public that this is acceptable, has any cost analysis been done on using a non-food crop for these same purposes?

Howard: Actually, some people are developing non-food crops, but we seek the benefits of using a food crop. Many companies are using corn for product safety. We could use a non-food crop, but the product would be less safe. Would you want to produce an edible vaccine in tobacco leaves? Although, potentially, non-food crops could be used, we would lose the knowledge base that Mich Hein mentioned, and we would lose product safety. Those are the choices.