Q&A

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Tom Tomich (University of California-Davis): Martina, you talked about the huge regulatory hurdles. Carl talked earlier about the notion of risk and benefit, and so my question has two parts. Who credibly do those risk/benefit balancing studies and how are they communicated to the public?

Martina Newell-McGloughlin: The regulations in this country are at least somewhat rational. The three main agencies that cover biotechnology are the ones you might expect. The USDA, where most of the deregulation process is gone through, was one of the first to determine that, in fact, they didn't have to introduce any new regulations—that those on the books were sufficient—but, that they would need to develop guidelines that allowed people to go through this process of determining if something had, or could reach, deregulation status, that is generally regarded as safe. The other agencies then are the EPA, looking at the environmental impact, and the FDA, where there is actually a voluntary consultation. You would be pretty stupid not to consult with them, so every company does.

Tomich: But my question wasn't who regulates. In order to look at the risk/benefit you would actually have to look at the agricultural, environmental and health—

Newell-McGloughlin: All they are looking at is the risk. There is no focus—and, in fact, that is one of the points I made here—there is no focus at all, anywhere, on the benefits.

Tomich: So in academia? Why doesn't somebody do it?

Newell-McGloughlin: It's not part of the process. We do it. Absolutely the benefit component is done. Nobody would be doing any of the work that I told you about because most of that is still sitting in the lab. It's all aspirational. One would hope that this will get through the deregulation process. But in some areas—Europe—it appears to be going backwards. There is such a focus on the precautionary principle that, in fact, it would probably be illegal, if you are going to interpret it to its fullest extent; it would be illegal to do anything for the first time. How ridiculous is that? So you are actually forced to depend on older, less-safe technologies. I'll give you an example from a personal heritage perspective. Growing up, we used to use a particular fungicide called bluestone, copper sulfate, to control late blight in potato. Now BASF has developed a potato with resistance to *Phytophthora infestans* by taking two genes from another potato, a solanaceous species in Mexico, and introducing them and getting complete resistance, and stable resistance—which is often hard with our genes—against late-blight disease. I thought they would be going with open arms in Ireland to get them. Instead they pulled out the plug, because they were told by certain groups that these were toxic. They failed under the precautionary principle. The alternative is using copper sulfate, which has organic approval because it is considered "natural." This is a complete false dichotomy, as Carl said earlier, this notion of natural and non-natural. The focus should be on good and efficacious versus non-good, or less good. With the precautionary principle, people are stuck, depending on older, less-safe, less-efficacious and—for sure—less sustainable production systems. So, when you are in that sort of situation and there is no focus on efficacy and benefits, it is really difficult to get past it.

Barbara Schneeman (US Food and Drug Administration): I just wanted to comment on the risk-benefit paradigm because—at least coming from the FDA perspective—to be on the market, foods have to be safe. They don't have to prove a benefit to be on the market and on the food side of FDA you actually, in fact, separate the risk-benefit construct, because, to be on the market, you have to be safe. You don't have to prove a benefit. It's really in drugs that you get into a risk-benefit balance. Now I think, Martina, you are trying to also address environmental benefits, but, at the end of the day, you still have to consider, "Is the food safe?"

Newell-McGloughlin: Yes. That's what I said, it's all risk in that respect. Now, of course, we could run ourselves into a real problem here if we are suggesting proving efficacy. Now you are up against drugs. You are now looking at $1 billion to $2 billion dollars to take it to market, if we are going to be looking at a pharmaceutical effect from a bioactive component. It's a very finely balanced line we need to walk here, because we don't want to have approval purely based on demonstrating efficacy.

Michael Jacobson (Center for Science in the Public Interest): Martina, on your last slide you listed a bunch of challenges. I would think a key challenge is finding something that consumers find useful, and I haven't seen anything that is anywhere near the pipeline. Monsanto has come to me and said, "Do you have ideas of something that might be use-

ful?" Until you get something obviously useful, like taste, consumers will say, "Why should we eat the genetically modified wheat or canola oil or whatever?" Do you have ideas?

Newell-McGloughlin: The short-chain fructans is a particular example there, where they actually taste sweet. Cynthia Kenyon, looking at genes that increase longevity, found most of them are actually sensate. Our primitive ancestors, the worms, *et cetera*, when sensing the environment, are actually responding to sugars. She has completely cut sugar from her diet and she looks good. The idea with the short-chain fructans is that you can, potentially, eliminate, high fructose corn syrup, sucrose and fructose from your diet.

Jacobson: How many years away do you think those are from market?

Newell-McGloughlin: That's the problem. It's sitting in Dr. Coop's lab because he knows that to get it through EU approval would be an enormous hurdle; the activation energy is so high, especially in Europe. Rather interestingly, on the animal side—since I talked about using plants as factories—the very first approval of using a genetically engineered animal to produce pharmaceuticals in its milk was given in Europe. There was a whole different view here, because, in fact, it was a pharmaceutical, an anti-thrombin agent at that point in time. It was a full year afterwards that the US approved it because, rather interestingly enough, the US was focusing on the health of the animal as well—this sounds counterintuitive—whereas Europe was looking at the safety and efficacy of the anti-thrombin drug itself, ATryn. But that's just an aside. The issue is the cost, the time, the enormous effort to get it through.

Michael Kahn (Washington State University): I've come to the conclusion that many people oppose GMOs less from the risk of the GMO itself than from the companies that are trying to put them out. We are in a situation now, which is ironic, where the Monsantos have figured that they can make enough money by pushing these things through the regulatory process, that they are willing to go ahead and do it, whereas, as you have indicated, small companies, and particularly producers of minor crop fruits and vegetables that we have been talking about as being nutritious here, are not going to be able to afford it. The whole market of those crops, in many cases, is less than what people are estimating for the certification. And so, instead of blocking monopolistic properties of Monsantos, the current regulatory situation is actually promoting them.

Newell-McGloughlin: For sure you could debate that and I absolutely agree, small commodities have a much harder row to hoe. The potato is a perfect example. Again it was produced by a big company, but, in fact, I heard from one individual who blithely told me, "We are not allowing that BASF product in here." No focus on the notion that you are going to reduce the actual amount of chemical used to control it. The big focus was that it was intellectual property owned by BASF. But the reason PIPRA exists actually is to focus on small commodity groups, which is a huge issue, of course, in California. We produce about 250 commodities. So it is much, much more difficult for us to go through

the process of deregulation because of the cost of the biosafety hurdle. But Monsanto will tell you they find it a total pain too. They were talking specifically about new abiotic-stress-resistant strains that they are bringing in, using transcription factor modifications. But they are back to square one with the USDA and EPA. Of course, needless to say, they have deeper pockets than we do in academia, so it's definitely an easier process for them than it is for us. And there have been very few products, in fact probably the only really strong product that has come out of academia is the ringspot-resistant papaya, from Dennis Gonsalves in Hawaii, and most of that work was done when he was at Cornell. There is no natural resistance against this virus, so it doesn't matter how good your marker-assisted selection process is. If the genes aren't in there you can't breed them in, no matter how much you try. So he took a copy of the coat protein from the virus, stuck it in there and it worked through the process that got the Nobel Prize, but not for him, called RNA interference, which confers protection against ring spot. In addition, it helps organic farmers, who grow rings of biotech crop around their non-engineered varieties to reduce the viral reservoir. However, back to your point, that was one of the few products that has gone through the process from an academic situation. All of the others have come from companies.

Alan McHughen (University of California-Riverside): Thank you Martina—enlightening and entertaining as usual. Just a quick comment on where are the products of benefit to consumers. If you ask consumers whether they would support a product, a food, a crop that could be developed with fewer pesticides, they would say, "Yeah, that is a good product. I'll support that and I'll even pay extra for it." So that is a benefit to consumers. They might not be aware of it directly. And, secondly, several recent economic studies, including one from our own National Research Council of the National Academies, have resulted in publication of economic analyses of the benefits of biotechnology to US agriculture, and determined there is a huge economic return that is not being captured exclusively by companies or even by farmers, but by society at large. And that means in practical terms you are paying less for your food because of agricultural biotechnology. That's something that consumers can relate to, but they are generally not aware of it.

McGloughlin: They're not aware of it. It's opaque to them.