Genetically Engineered Specialty Crops Need Regulatory Assistance

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Four categories present, or have presented, obstacles or limitations to commercializing genetically modified (GM) specialty crops:

- **The technology itself.** Could we actually identify genes encoding useful traits, clone those genes, transfer them into the cells of specialty crop species *in vitro*, and then regenerate whole plants and have them express those traits at commercially viable levels? We know that that's pretty well overcome. We can transform virtually anything with any piece of DNA, or RNA for that matter.
- **Intellectual property**, including patents on genes and on the fundamental enabling technologies that were held largely by big companies or tied up in litigation. I know many public scientists who have said, "I can't use this technology because it's patented." Some said, "I'm using this technology, although it's patented. So don't tell anybody." We continue to have to respect intellectual property (IP) rights and I certainly encourage everyone to do that. Furthermore, companies that hold the patents are often amenable to negotiation. If you have a good idea—a good product in a specialty crop—and a patent holder isn't actively working in that area, they will probably be reasonably receptive to developing a license or some other freedom to operate. Also, patents for many of these products and enabling technologies are expiring. They may not be first-choice state-of-the-art technologies, but older approaches can be adapted and efficiency improved to get the final product that you're interested in. So, IP is not the obstacle that it used to be.

- **Public acceptance** is not the issue that a lot of people think it is. Several different groups say, "We speak for the public, and we, the public, don't like GM organisms, so don't develop them and don't release them. If you put them out there, we won't buy them, therefore, let's ban them so that people don't have to worry about them." I haven't done a sociological study on this, but, after dealing with the public for 20 years or so, I'd say that about 15 percent of the public definitely will not buy a GM fruit or vegetable in the marketplace. Dennis Gonsalves has suggested it may be 8 percent. Other people will come up with other figures, But it's on that order 8 to 10 to 15 percent—people who say that they really don't like GM organisms (GMOs), and then actually follow through. A lot of people say that they don't like GMOs but buy them anyway, knowing full well what they are. They see what the price is, what the quality is, and that other people are buying them and are not dropping dead in the street. The best way to measure public acceptance is not to listen to activist groups, or any academic for that matter. The best way to measure it is to put the products in the market and let the people show you by whether they buy them. When people are given that actual real-life opportunity, for the most part they buy them. We do have GM papayas, we do have GM sweet corn, and other examples here and there. And there's little problem once people are actually allowed to make the choice on their own directly, to buy the product today or not.
- **The federal regulatory system**, which is what I will discuss mostly.

Specialty Crop Regulatory Assistance Program

The chief obstacle to getting GM fruits and vegetables onto the market, is the regulatory system. Several years ago, a group of us, largely from the federal regulatory agencies said:

> *The genetically modified products on the market now are, in large part, major crops: corn, soybean, cotton, and canola, all from large companies. On the other hand, hundreds of millions of dollars of taxpayers' money have supported the development of genetically modified specialty crops in our public institutions, in USDA, in our universities and other not- for-profit organizations, plus small companies. Where are the results of that effort? Did all of those projects fail? Was it a waste of money?*

A meeting was called in Washington to address whether there was interest in joining forces, either formally or informally, large or small, to promote the use of genetic technologies for improvement of specialty crops. It emerged that there was a great deal of interest. Passionate about the technology, people wanted to develop products that big companies probably wouldn't be interested in: public-good, high-value items, that don't necessarily have sufficient dollar value to generate industry interest in terms of profit but would be good for the environment, for society and for human health. This passionate interest existed mostly in small-company and public-sector scientists.

We discussed ways to facilitate regulatory clearance because of the broadly held view that achieving deregulation was a major stumbling block. The Specialty Crop Regulatory Assistance (SCRA) program was set up in 2004, under the auspices of which we have held several meetings, mostly workshops that have included developers of GM specialty crops and representatives of the regulatory agencies. With seed money from the secretary of agriculture, we hired Kellye Eversole, in DC, who has been involved in this effort ever since. We have moved forward with a number of initiatives. Several workshop-type meetings have:

- Examined the regulatory system, including the hoops a developer has to jump through, and
- Explored costs, obviously a major issue for everyone.

Cost of Gaining Regulatory Approval

Discussions at this conference have questioned the actual cost of gaining regulatory approval; is it $50 million to $100 million as some companies have indicated? We have learned that it isn't necessarily that expensive. You have to calculate the cost above and beyond the routine R&D involved in producing a new crop variety, which comes down to an interesting accounting exercise. When I developed a transgenic flax many years ago, I worked at a major plant-breeding institution. We had huge farms and research plots, and several teams evaluated the project, supervising seeding, harvesting, quality analyses, chemical analyses, amino acid analyses, and performing efficacy and yield trials. All of these functions were part of a large infrastructure within which my lines were tested. Tens of thousands of lines of various species underwent tests, all within the same infrastructure. It was virtually impossible to determine my segment of the overall bill. Furthermore, if this were not a GM product, but a conventionally bred variety of the same crop type, how much would that have cost? And then, how much in addition has to be spent to generate the additional data required by regulatory agencies for appraisal of a GM trait? When you do those calculations, the marginal cost comes down to the order of a few tens of thousands of dollars.

When Dennis Gonsalves[1] and I compared notes—his papaya and my flax went through the regulatory system at approximately the same time—we came up with similar figures. Of course, nowadays, it is likely that neither Dennis's papaya nor my flax would get through the regulatory system; it is that much more onerous than it was in the mid-1990s. But, don't believe those $50 million price tags that are thrown out. It can be done a lot less expensively, and one of the things that we've learned during our various workshops is the need to talk to the regulators themselves, which is the best way to find out what's actually needed. There are ways to satisfy the requirements without necessarily doing what you think you might have to do in terms of additional experimentation or field trials or feeding tests on humans for ten years, *etc*. You may be surprised to learn that you can achieve deregulation without investing a lot of time and/or spending a lot of money.

[1]Pages 37–46.

Modeling on IR-4

We wanted to set up a structure similar to that of the IR-4 program or the FDA's orphan drug program, recognizing that many specialty crops are of insufficient value in terms of market size to justify full-blown costs of deregulation. We thought that it would be useful to propose an institution, modeled particularly after IR-4, within which the SCRA program would sponsor a given GM specialty crop event or variety, and actually carry it through the regulatory system to obtain approvals. Although IR-4 works through EPA, the program is based in USDA. And in our situation with SCRA, it could involve our taking this product to all three of the regulatory agencies and navigating the system, so that the developer— a university-based person or from a small company—wouldn't bear the total cost. It would be largely subsidized. We're not looking for shortcuts here in terms of exemptions from requirements, but rather rationalizing and organizing the dossier so that it meets the requirements, and we have assurance of safety of the product, but without "bells and whistles" that may be attached to some of the other dossiers that our regulators see.

We decided to focus on the US regulatory system. Many US products are sent overseas; we have trading partners in various countries and regions. There was no point in getting approval in the United States for a product that served a large export market. Also, we are more familiar with the US regulations and majority of our members are in this country. There is good coordination between the Canadian and US regulatory systems. Although differences exist in legislation and the regulations themselves, the same data package can be used, to a great extent, in both Canada and the United States. That certainly was true with my flax. We decided that Europe was schizophrenic and paranoid when it came to GMOs. They ignore their own laws, so there was no point in going through the European Food Safety Authority (EFSA) system and getting an approval only to have some member countries initiate a ban anyway.

At the SCRA, we have our own expertise, provided by plant breeders, molecular geneticists, people who are experienced in the regulatory system, and political people who know how the machinery works in Washington. We also have several consultants to help individual entities. At our last workshop 18 months ago, we had a session at which we provided access to consultants experienced in dealing with our regulatory system and our regulators. We also brought in regulators, *i.e.* not policy people necessarily—they were there as well—but agency people who actually work hands-on with dossiers, whose job it is to come in every morning and see a stack of papers saying, "Here's yet another *Bt* corn for you to evaluate." We conducted this workshop under Chatham House Rules—*i.e.* confidential with no attribution—which lends itself to people saying things that they wouldn't say in a public setting or in a conventional workshop. They didn't want to be in a situation where they could be quoted later: "You told us at that workshop that we could provide this data set instead of that data set," when in actuality they said, "Well, we're thinking about maybe this or maybe that, or here's a tentative idea. What do you think?' We wanted fresh ideas without necessarily holding the speakers to those ideas.

It was a great success. Comments received afterwards were enlightening. A number of people said that it was the best workshop they had ever attended, having learned more than at any other workshop or conferences, and that the information was really useful, due to communication between the developers and the consultants, and between the developers and the regulators, the people who actually do hands-on work with the dossiers. A similar workshop is planned.

Attempts continue to secure long-term funding to maintain SCRA functions, including meetings and direct and indirect assistance to GM specialty-crop developers. Of course, in the past five years, no one has obtained the funding they wanted. We don't have an IR-4-like office yet, but we will continue to give varying levels of handholding advice and encouragement to people who request it.

Languishing GM Specialty Crops

We know of many GM specialty crops that have not been deregulated. We commissioned Kent Bradford and a student at UC Davis to compile a list of GM crops that were developed at land-grant universities, other universities and smaller companies. He compiled a fairly substantial list of different crops with a number of different traits that had gone through various stages of development and field evaluation and pre-commercialization trials, but then stalled because the developers were unable, for one reason or another, to continue. In some cases, the developers were misinformed and didn't approach the regulatory agencies to gain approval for commercialization. Therefore, we know that these things exist; it's not a technical problem and there may be a few IP problems, but it's largely a regulatory issue. Whether misunderstood or not, gaining deregulation is still the major stumbling block.

We wanted to contact some of these people, draw them out, and try to help them, encourage them, tell them whom they needed to talk to at the federal agencies to help them when compiling their dossiers, to tell them that they are not alone, first of all, and that successful examples are available. Ralph Scorza finally made it through with his virus-resistant plum, as the third public-sector GM specialty crop to be approved. The other two were back in the 1990s and others are currently in the pipeline, including Neal Carter's non-browning Arctic apple[2].

Clearly, achieving deregulation of GM specialty crops is doable. It can be frustrating, but we can provide help—admittedly in a limited capacity because we don't have a lot of funds. Hopefully, that will change in the future as the economy turns around, and we form an establishment where we can actually take particular products that need some additional trials or tests, and either commission those trials on behalf of a developer who doesn't have the in-house capability of doing them, or pair them up with people who do have the expertise, to generate essential data.

We want to encourage the commercialization of these products, because only then can we provide consumers with real choice: "Here. If you like it, buy it. And if you don't, don't."

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[2]Pages 87–94.

Encouraging Acceptance of GM

Overcoming citrus greening is going to be interesting. I am betting that a transgenic, or at least a molecular genetic technology, is going to be part of the answer, if not the whole answer. And the disease is not confined to Florida. It's appearing in Texas and California. Similarly interesting will be tackling Pierce's disease of grapevines in California, which will also probably involve a molecular genetic technology. There's a whole range of traits that we really need to address, for which genetic technologies are the best tools in the toolbox to address them. They are not the only tools, but we have to be able to use those tools, which means that we have to overcome what appears to be public resistance. And we have to overcome misperceptions about the onerousness of our regulatory system.

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Having developed internationally approved commercial crop varieties using both conventional breeding and genetic engineering techniques, Dr. McHughen has firsthand experience with the relevant issues from both sides of the regulatory process. As an educator and consumer advocate, he helps non-scientists understand the environmental and health impacts of both modern and traditional methods of food production. His book, *Pandora's Picnic Basket; The Potential and Hazards of Genetically Modified Foods*, explodes the myths and explores the genuine risks of GM technology.