Agricultural Biotechnology: Beyond Food and Energy to Health and the Environment

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NABC's seventeenth annual meeting, co-hosted by the Universities of Kentucky and Tennessee, convened at the Renaissance Hotel, Nashville, TN, June 27–29, 2005, a few blocks from the Ryman Auditorium (the original venue of the Grand Ole Opry), Broadway (Music City's famous "heartbeat") and the Country Music Hall of Fame. The modular structure of NABC 17 juxtaposed sessions on plant-made pharmaceuticals, bioremediation and associated issues, product development, and regulatory and risk-management considerations. The 151 attendees included university and industry researchers and administrators, educators, members of federal agencies and non-governmental organizations, and journalists.

In the plenary session, keynote addresses were delivered by Roger Beachy (Donald Danforth Plant Science Center) and Michael Rodemeyer (Pew Initiative on Food and Biotechnology). These were followed by modules composed of formal presentations and brief contributions from panelists:

- Module I–*Plants as New Sources of Medicinals: Production of Protein Pharmaceuticals in Food and Non-Food Plants*
  - Speakers: Maelor Davies (University of Kentucky) and Schuyler Korban (University of Illinois)
  - Panelists: Henry Miller (Hoover Institution) and Mark Nelson (Grocery Manufacturers of America)
- Module II–*Bioremediation, Phytosensing, and Ecorestoration*
  - Speakers: Bruce Ferguson (Edenspace Systems Corporation), Jacqueline Shanks (Iowa State University) and Scott Merkle (University of Georgia)
  - Panelists: Lena Ma (University of Florida), Steve Rock (EPA Cincinnati) and Neal Stewart (University of Tennessee)

- Module III–*Gene-to-Product Development*
  - Speakers: Maud Hinchee (ArborGen), Vincent Chiang (North Carolina State University) and Elizabeth Hood (Arkansas State University)
  - Panelists: Roger Conway (USDA Office of Energy Policy and New Uses), Alex Day (Kentucky Life Sciences Organization) and William Goldner (USDA Small Business Business Innovation Research)
- Module IV–*Regulation, Consumer Acceptance, and Risk Management*
  - Speakers: Cindy Smith (USDA-APHIS Biotechnology Regulatory Services), Thomas Redick (Gallop, Johnson & Neuman LC) and Kim Waddell (American Vineyard Association)
  - Panelists: Thomas Hoban (North Carolina State University), Canice Nolan (European Commission to the United States) and Allan Bennett (University of California at Davis)

Banquet and luncheon presentations were delivered by Wayne Parrott (University of Georgia), Gregory Jaffe (Center for Science in the Public Interest) and Michael Phillips (Biotechnology Industry Organization).

Discussion among the participants occurred within three breakout sessions composed of four smaller groups. A summary of those discussions and emerging recommendations is provided elsewhere..

Plenary Session

Roger Beachy ("Controlling Traits in Transgenic Plants: Tools that Enhance Value and Reduce Environmental Release") discussed the benefits of controlling expression of transgenes in plants, for example to maximize the effect of a gene product in a specific tissue at a specific growth stage as a means of eliminating adventitious presence of the product or nonessential release into the environment. He described the development of systems to control gene expression at will, upon induction by environmental conditions or by chemical (small molecule) application to cause a gene to be turned on—at a high, medium or low level like a rheostat—or shut off. The basic components of a good gene-switching system are a suitable inducer and a receptor-like protein that binds to a ligand that regulates the inducer. A promoter that responds to the inducer increases or decreases expression of the gene of interest. An EcR (ecdysone receptor) approach has been developed, employing receptors found in lepidopterous insects that are activated by specific juvenile hormones. When the EcR protein in the cytoplasm complexes with the ligand, it is transported to the nucleus and binds with the gene of interest inducing expression. In this case, the ligand is the insecticide methoxyfenozide (Mimic®). Arabidopsis plants have been engineered with a gene-switching unit that causes production of transcription factors that bind to chimeric promoters that are expected to activate eight or ten different promoters and, therefore, eight or ten different reporter genes. It may soon be possible to modify metabolism in several biochemical pathways simultaneously. How science

becomes relevant to the public and to commercialization depends upon many factors. Gene switching may assist consumer acceptance.

Michael Rodemeyer ("Can You Get There From Here? Speed Bumps in the Road To Health And Environmental Biotech Applications") questioned whether plant biotechnology can be harnessed to provide benefits outside of the area of food and feed. Can the kind of global deadlock that has emerged from the introduction of genetically modified (GM) crops and food be avoided? Is the opposition to the use of plant biotechnology limited to its use in food? Can the potential health and environmental benefits of the next generation of plant biotechnology change the contours of the global debate? What obstacles await the commercialization of health and environmental applications of plant biotechnology? Experience and common sense suggest that every application is likely to have its own opportunities and challenges; Rodemeyer suggested that across-the-board predictions are likely to be misleading. Although the hurdles to commercialization of health and environmental plant-biotechnology applications are significant, he sees reason for cautious optimism. The regulatory system is slowly responding to the need to evolve for new and different types of biotechnology products. Management and stewardship requirements are becoming clearer. And experience suggests that the market welcomes safe, innovative products that provide perceived benefits to buyers and to the public. The challenge to developers is to ensure that the potential benefits of this technology are clearly explained to the public while the government continues to ensure safety. If developers can do that, then there is indeed a way to get there from here.

Plants as New Sources of Medicinals: Production of Protein Pharmaceuticals in Food and Non-Food Plants

The concept of "molecular farming" was born in the early 1980s when it became possible to envisage crops as sources of proteins that originally derived from microbial or animal sources. Maelor Davies ("Plant-Made Pharmaceuticals: An Overview and Update") described the advantages of plant-made pharmaceuticals: overall economy of production, lack of need for major capital investment (*e.g.* in fermentation bioreactors), ease and economy of scale-up, lack of risk of contamination with human pathogens, *etc*. However, significant markets for plant-made proteins failed to develop; by the mid-1990s plant molecular farming was essentially stalled. Concerns about contamination of existing crops—and food or feed products—with compounds from the corresponding transgenic crop would be moot if pharmaceuticals, for example, were synthesized with "vehicle" plants that had hitherto not been developed for food or feed. Tobacco and related *Nicotiana* species offer excellent potential for development of a new, dedicated system for crop synthesis of pharmaceuticals and other useful products.

Schuyler Korban ("Opportunities and Challenges for Plant-Based Vaccines") described the move, in recent years, towards developing subunit vaccines whereby linear immunogenic epitopes of a pathogen elicit production of antibodies. These alleviate concerns over risk of reversion of attenuated strains to aggressive forms of the pathogen. And a novel approach for developing subunit vaccines has emerged as a result of genetic engineering technology: use of plants as vehicles for developing new products. As the technology to

produce vaccines in plants goes through the regulatory pathway and demonstrates its economic feasibility, it may also overcome public-perception concerns that have dogged agricultural biotechnology in the past decade. The likelihood that plant-based vaccines can be administered via oral or intranasal routes—rather than via the hypodermic needle—will add to their desirability as well as their economic benefits. All this will have a major impact on public health, particularly in developing countries. However, much work remains to be done, including the establishment of standardized safety-assessment models. Risk assessment must be science-based for the results to be believable and trustworthy. Increased funding of research in this field will accelerate the advances made thus far, and bring this technology closer to commercialization and worldwide use.

Henry Miller, who spent several years with FDA, made the case against regulation of transgenic organisms based on the process used to produce them rather than on the host and the added trait. He criticized both highly activist and more moderate public-interest organizations, and emphasized that the regulatory system and associated costs have debilitated public-sector agricultural biotechnology.

Mark Nelson expressed concern over the possibility of adulteration of food if PMPs are produced in crops such as corn, soy and canola. The Grocery Manufacturers of America has asked for a safety evaluation of the implications if PMP-producing food crops are commingled in the food supply; reasonable standards are needed.

Bioremediation, Phytosensing, and Ecorestoration

Bruce Ferguson ("Systems Agriculture: Towards a Sustainable Agricultural and Environmental Policy") described Edenspace's projects in phytotechnology: using ferns to remove arsenic from soils; engineering plant biosensors—"phytosensors"—to detect and monitor environmental parameters such as heavy metals; engineering plants to produce higher yields of ethanol per acre; and forming a new agricultural cooperative to provide additional income to producers who work on environmental projects. These and similar projects have afforded a broad range of experiences, including site characterization and environmental remediation, plant genetic engineering and APHIS field permitting, market research, and marketing and sales. From this experience Ferguson offered the following observations and recommendations:

- Change agricultural policy from insulation to innovation.
  - When subsidies cease, farmers may be left without a means of competing with lower-cost food imports. To address this problem, rapid innovation and product development should be encouraged allowing farmers to compete by offering higher-margin value-added products.
- Promote "systems agriculture."
  - Systems agriculture is the engineering of plant traits and agricultural protocols on an integrated basis with other production technologies so as to minimize total costs of end-user products and services. The approach requires that new agricultural products and techniques be developed by considering

multiple areas of upstream and downstream production expertise together—on an integrated basis—that are now considered separately.

- Create more-receptive public opinion.
  - Traditional breeding methods are too imprecise and too slow to achieve the rapid product development needed to support a competitive US agricultural sector. A key element is to develop public demand for new transgenic plant products that directly promote human health, provide low-cost energy, *etc.*, rather than simply (though importantly) reduce producer costs with no significant benefit perceived by consumers.
- Increase government R&D funding.
  - Transgenic plant development is under-funded by the private sector, largely because of the divisiveness of the transgenic crop wars of the last 10 years. To address this market imbalance, the plant biotechnology budget should be at least quadrupled in size. Half of the increase should be apportioned to the USDA and half to other government agencies—EPA, NIH, HUD, DOT, *etc.*—to fund crop-plant research related to their missions.

Explosive chemicals that contaminate groundwater and soil—at ammunition-production and military-training sites—are toxic to many microorganisms, mammals and plants. However, some plant species have the ability to remove and transform them into less harmful compounds. Jacqueline Shanks ["Plant Transformation Pathways of Energetic Materials (RDX, TNT, DNTs)"] described genetic and biochemical studies of pathways that transform explosives and development of transgenic plants for phytoremediation purposes. An important consideration is that explosive compounds assimilated by plants can be released from the tissues by action of water, *e.g.* rain and runoff, and thus may be returned to the environment as hazardous contaminants; research is required on post-harvest fate. Less information is available on phytoremediation of dinitrotoluenes, compared to trinitrotoluene (TNT) and hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX).

Forest trees, with their extensive root systems and ability to rapidly accumulate biomass, would be attractive tools for remediation of soil and water contaminated with heavy metals—mercury, arsenic, *etc.*—if they could be modified to handle high levels. Scott Merkle ("Engineering Forest Trees with Heavy Metal Resistance Genes for Phytoremediation") discussed the engineering of fast-growing trees with modified bacterial genes that allow them to detoxify or sequester some heavy metals, with the objective of using them for phytoremediation. Insertion of these genes required optimization of *in vitro* culture systems followed by adaptation of *Agrobacterium*- and microprojectile-mediated gene-transfer methods for each species. Yellow poplar (*Liriodendron tulipifera*) expressing a modified bacterial mercuric-ion reductase (*merA*) showed enhanced resistance to mercuric ion *in vitro*. Eastern cottonwood (*Populus deltoides*) engineered with the same gene demonstrated the ability to tolerate ionic mercury up to 400 ppm in soil; these trees are being field-tested at a mercury-contaminated site. While eastern cottonwood engineered with the organomercurial lyase (*merB*) gene

showed only slightly enhanced tolerance of organomercury, trees engineered with both *merA* and *merB* were able to convert phenylmercury acetate to elemental mercury. Preliminary work with eastern cottonwood expressing a γ-glutamyl synthetase (γECS) gene indicated that it had slightly enhanced tolerance to arsenate *in vitro*. Continuing work involving the combination of γECS with other genes for mercury or arsenic resistance may enhance the phytoremediation ability of transgenic trees.

Lena Ma noted that phytoremediation of organic contaminants, energetic materials and metals is mostly in the demonstration stage; there are no full-scale applications to date. Problems and needs are the slowness of the process—5 to 10 years—and what to do with the resultant biomass.

Neal Stewart pointed out applications of phytosensors: as indicators of phytoremediation progress, coupled with GPS to guide management of crops, to monitor agro-security, and to detect explosives (*e.g.* buried landmines). He also suggested that we need to rebuild regulations based on our current knowledge-base.

Steve Rock called attention to the Interstate Technology Regulations Council, a group of about forty state regulatory bodies that banded together to share regulation information and eliminate repetition and duplication. He observed also that many researchers in transgenics in Europe have redirected their efforts to phytoremediation.

Gene-to-Product Development

Maud Hinchee ("The Application of Biotechnology to Sustainable Forestry") stated that forest genetics, because of long generation times, is only now reaching the stage at which genetically superior trees are being planted. Improved tree genetics is occurring through mass controlled pollination: controlled crosses to create varieties that capture superior parental qualities. Biotechnology is being applied to this new germplasm base. ArborGen's mission is to develop and commercialize technologies, products and services that will ensure sustainability of the world's forests. The first-tier products are focused on *Eucalyptus*, *Populus* and *Pinus*. The largest market for *Eucalyptus* is Brazil's pulp and paper industry, and ArborGen is examining the potential to modify lignin for improved efficiency of pulp production and to accelerate growth rate. Accelerated growth in plantations, without compromising wood quality, is an objective also for *Populus* and *Pinus*; asexual propagation technologies are being employed. ArborGen is developing transformation methods applicable to elite varieties of *Eucalyptus* spp. and hybrids, loblolly pine (*Pinus taeda*), Monterey pine (*Pinus radiata*), grown in Australasia, and eastern cottonwood. Pine is transformed using a somatic embryogenesis-based protocol, with *Agrobacterium*-mediated transformation. Eucalyptus transformation is based on micro-propagated elite material; a shoot organogenic process is used after inoculation with *Agrobacterium*. ArborGen has the capacity to generate thousands of transgenic events per year for field screening and selection for each of the species of interest.

Vincent Chiang ("Understanding Gene Functions and their Control for Lignin Formation in Wood") summarized his research on genetic engineering of lignin biosynthesis for the purposes of improving wood-pulping and bleaching efficiencies. His objectives include the production of transgenic trees of low lignin content. Using aspen (*Populus*

tremuloides) as a model species, he and colleagues have characterized the biochemical functions of various genes and kinetic properties of products involved in the monolignol biosynthetic pathway. There is strong evidence that a principle phenolic flux leads to the formation of monolignols. Biochemical evidence has further demonstrated that, in this principle flux, 4-coumarate:CoA ligase (4CL) could be the enzyme limiting total lignin accumulation, whereas coniferaldehyde 5-hydroxylase (CAld5H) might control the lignin syringyl:guaiacyl (S/G) ratio. These propositions are fully supported by the *in vivo* functions of these enzymes. Transgenic trees with inhibited 4CL enzyme activity exhibit 5% to 45% reduction in lignin content. The chemical structure of the resulting lignin is essentially unchanged. More importantly, lignin reduction is compensated for by a concomitant increase in cellulose content. When antisense *4CL* and sense *CAld5H* genes were simultaneously transferred into aspen via *Agrobacterium*, transgenic trees expressing each one and both of the transgenes were produced. Lignin reductions up to 55% were achieved in antisense *4CL* plants and up to three-fold increases in S/G were observed in sense *CAld5H* plants. These effects were independent but additive, and plants expressing both transgenes had less lignin and higher S/G ratio. These transgenics are potentially valuable for pulp production. But, more importantly, these benchmark transgenics are rich sources of information for functional genomics and metabolic engineering, allowing the generation of the ultimate raw materials for wood-pulp production.

Elizabeth Hood ("Commercialization of a Protein Product from Transgenic Maize") described the steps involved in commercializing bovine trypsin as a product synthesized in transgenic maize, including proof of concept, product development (market development, patent protection, final formulation, safety assessment, *etc.*) and public acceptance and sales. Lack of public acceptance is the major barrier to producing pharmaceutical or industrial products in plants. Response to this public distrust has driven current regulations to be quite restrictive. The scientific community and the regulatory agencies are striving to gather substantive safety data to support regulations that are based on scientific principles and will protect the public as well as allow this new industry to develop. The critical asset for general acceptance is whether the consumer sees benefits and whether these perceived benefits outweigh costs and risks. When products with obvious benefits are available to the consumer, public acceptance, science-based regulations and sales will fall into place.

William Goldner described a new initiative to assist in the navigation of regulatory requirements for specialty or minor crops: the Specialty Crops Regulatory Initiative. It should assist public-sector and small private companies in meeting regulatory requirements.

Alex Day described obstacles in bringing products to market. He mentioned the challenge of bridging scientists and business people for effective communications, and noted the lack of money for seed-stage investments.

Roger Conway listed programs that assist commercialization of industrial biotechnology products. These include the Federal Biobased Products Preferred Procurement Program, which provides government markets especially for early-stage products, and the USDA CCC Bioenergy Program, which has catalyzed investment in the biodiesel industry. Other opportunities/needs exist in capital investment and education.

Regulation, Consumer Acceptance, and Risk Management

The United States Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) has regulated transgenic organisms since 1987, and in 2002 established Biotechnology Regulatory Services (BRS) to place a renewed emphasis and priority on biotechnology. APHIS has authorized more than 10,000 permits and notifications for the introduction of GM organisms and deregulated over sixty products for use, establishing itself as an international leader in the safe regulation of transgenic products. Cindy Smith ("Regulating Pharmaceutical Plants: Meeting the Challenge") described the significant reorganization that has occurred at BRS since its inception, making it better prepared to anticipate and respond to challenges resulting from the evolving nature of biotechnology. The newly reorganized BRS goes beyond a staff of scientists to evaluate permit applications and petitions for deregulation. It includes a Compliance and Inspection Branch, a Communications and Capacity Building Branch, a Regulatory Analysis Branch, an Office of Science, and a forecasting function that help BRS address these challenges and keep pace with the advancing science. In addition, BRS has developed five priority areas of emphasis that set program direction and provide the foundation for decision-making. The following priority areas are key to BRS's ability to meet the challenges of regulating biotechnology in general, and, specifically, plants engineered to produce pharmaceuticals:

- maintaining rigorous regulation that thoroughly and appropriately evaluates and ensures safety and is supported by strong compliance and enforcement;
- ensuring that BRS's regulatory process and decision-making are transparent to stakeholders and the public;
- maintaining a science-based system that ensures that the best science is used to support regulatory decision-making and to assure safety;
- maintaining communication, coordination, and collaboration with the full range of stakeholders; and
- establishing international leadership to ensure that international biotechnology standards are science-based, international regulatory capacity building is supported, and international implications of domestic policy and regulatory decisions are considered.

As the science progresses, BRS will continue to evaluate the implications of new technologies, enhance its processes and procedures, and develop appropriate regulations to meet the challenges posed by this new science while continuing to safeguard American agriculture, the nation's food supply, and the environment.

Thomas Redick ("Liability Prevention and Biotechnology: A Brief History of Successful Industrial Stewardship") summed up the regulatory and liability hurdles that stand in the way of launching a new transgenic product. He briefly reviewed successes and failures and existing risk-management methods to help overcome legal barriers to entry. Despite past successes, and the knowledge gained from failures and near misses, the road to future commercial success in agricultural biotechnology remains fraught with difficulties. The European Union and its like-minded trading partners will continue to hold their zero-

adventitious-presence standards over the heads of grain exporters and will increasingly drive innovation in agricultural biotechnology into contained, closed-loop production systems. Like a game of three-dimensional chess, transgenic crops will face three levels of regulatory oversight, starting with federal approvals, but with more requirements emerging at the state level (even in counties or cities) and overseas. For many transgenic crops, international approvals may be required prior to market launch within the United States (for soybean, rice, wheat and other primarily export-bound crops). As a result, US agricultural biotechnology operations will need to maintain perfect divisions between its "green," "white" and "red" sectors—food and feed, plant-pharmaceutical, and industrial applications.

In 2000, the federal government completed an interagency review of its regulatory oversight of biotechnology products that revealed that ensuring confinement could become a regulatory requirement for approval of some transgenic organisms. In 2001, the USDA asked the National Academies to review and evaluate biological methods and report on their application in confining transgenic crop plants, shellfish, trees, grasses, fish, microbes, insects and other organisms. Kim Waddell ("Biological Confinement of Genetically Engineered Organisms: Opportunities for Reducing Environmental Risks?") summarized that report (*Biological Confinement of Genetically Engineered Organisms*) with particular emphasis on: definition of bioconfinement, when and why to consider bioconfinement, bioconfinement of plants, bioconfinement of animals, bioconfinement of microorganisms, and biological and operational considerations for bioconfinement. Recommendations in the report include:

- Evaluation of the need for bioconfinement should be considered for each transgenic organism separately.
- Early evaluation of the need for bioconfinement in the development of a transgenic organism or its products is recommended.
- Bioconfinement techniques should be assessed with reference to the temporal and spatial scales of field release.
- An adequate level of bioconfinement should be defined early in the development of a transgenic organism, after considering worst-case scenarios and the probability of their occurrence.
- An "integrated confinement system" approach (defined in the report) should be used in deployment of the transgenic organism.

Current lack of quality data and science is the single most significant factor limiting ability to assess effective bioconfinement methods. Methods need to be tested in a variety of appropriate environments and in representative genotypes of the transgenic organism under consideration. In order to implement effective bioconfinement of GM organisms, the report recommended support for additional scientific research that:

- characterizes the potential ecological risks and consequences of a failure of bioconfinement,
- develops reliable, safe, and environmentally sound bioconfinement methods, especially for transgenic organisms used in pharmaceutical production,

- designs methods for accurate assessment of the efficacy of bioconfinement,
- integrates the economic, legal, ethical, and social factors that might influence the application and regulation of specific methods, and
- models the dispersal biology of organisms targeted for genetic engineering and release, where sufficient information does not exist.

Thomas Hoban was highly critical of industry, government and universities regarding agricultural biotechnology and its products, especially those from cloned animals and PMPs from food crops.

Canice Nolan identified the major problem in European acceptance of GM foods as the consumer not the regulators; food processors aren't going to source when risk is commonly associated with GM. There is consensus in Europe that the regulatory system works well and should remain in place.

Allan Bennett described the Public Intellectual Property Resource for Agriculture (PIPRA), a public-sector consortium that hopes to provide bundles of proprietary technologies—enabling and trait—to allow the benefits of biotechnology to accrue to a broader base of crops and consumers, *e.g.* specialty crops and developing-country farmers. He noted that 25% of crop-biotech patents belong to the public sector.

Banquet and Luncheon Presentations

Wayne Parrot ("The Nature of Change: Towards Sensible Regulation of Transgenic Crops Based on Lessons from Plant Breeding, Biotechnology and Genomics") reminded the audience that the literature contains many suggestions that plant genomes are highly variable. One early indication was the discovery that maize inbreds differ in the number of rDNA copies, ranging from a low of 5,000 in "W23" to 23,000 copies in "Illinois Reverse High Protein." Total DNA content varies also within crop varieties—up to 12% for soybean, 25% for red pepper and 42% for maize. Until the advent of genetic engineering technology, it is true that scientists had not crossed the species barrier in terms of gene transfer between kingdoms. On the other hand, it must be acknowledged that DNA from unrelated species is transferred and incorporated into plant genomes. Plantain bananas contain the entire genome of the banana streak virus, rice contains DNA from the rice tungro bacilliform virus, and tomato has DNA from the tobacco vein-clearing virus. The integration of viral sequences may be widespread in the plant kingdom, having occurred for a long period of time. Genes from the bacterium, *Agrobacterium rhizogenes*, have been found incorporated into the genome of some tobacco species while DNA from unrelated higher plants has been found to be transferred between their mitochondria, and, from there, to their nuclei. Although not a common phenomenon, horizontal gene transfer does take place, at least on an evolutionary time scale, and does not appear to pose any hazards to recipient plants. This and other information lead Parrot to conclude that plant genomes are variable and dynamic, constantly changing in response to breeding efforts and even to environmental conditions. Therefore, it is a mistake to treat transgenes and their associated DNA changes as inherently dangerous. Ultimately, it is the trait imparted by the transgene that matters, and, as such, it is the trait that should

be the focus of regulatory efforts, should these be warranted. In Parrot's opinion, risk to health and the environment posed by most traits is sufficiently low as to preclude the need for regulatory oversight.

Gregory Jaffe ("Creating the Proper Environment for Acceptance of Agricultural Biotechnology") stated that the past 10 years have been extremely successful for the biotechnology industry. Several blockbuster products were marketed in the 1990s, including soybeans, corn, cotton, and canola that are herbicide-tolerant and corn and cotton that produce their own insecticide to control specific pests. These varieties have been widely adopted by farmers in the United States and, to varying extents, in seventeen other countries: over eight million farmers grew 200 million acres of GM crops in 2004. These herbicide-tolerant and insect-resistant crops—biotechnology's "first generation"—have provided benefits to farmers and the environment by increasing yields and reducing the use of insecticides. Despite this success, the introduction of new GM products has slowed considerably. In February, 2005, CSPI released a study—*Withering on the Vine: Will Agricultural Biotech's Promises Bear Fruit?*—showing that from 1995 through 1999, forty-seven crops (an average of nine per year) completed the FDA regulatory process, whereas from 2000 through 2004 only fifteen crops (an average of three per year) completed the process. Although the pipeline has slowed, international controversy over GM crops has continued. Whereas most governments and many distinguished scientists have found that these crops are safe, some people continue to be concerned over perceived risks to human and/or environmental health. The controversy over genetic engineering will only increase with the next generation of products. Biotechnology-industry and university researchers are inserting a wide range of engineered traits into many different organisms. While research on drought or salt tolerance may reduce the controversy over genetic engineering if it benefits small-scale farmers in developing countries, engineering plants to make pharmaceuticals or industrial products is particularly worrisome when food crops are employed; no one would want to eat corn flakes containing a vaccine, for example. With the current state of affairs and controversial new applications on the horizon, international debate over the pros and cons of agricultural biotechnology is likely to increase.

Michael Phillips ("The Importance of Stewardship in Agricultural Biotechnology") described a training program being developed by the Biotechnology Industry Organization (BIO), laying out principles for confining plants making pharmaceuticals and those making industrial products. Workshops dealing with compliance aspects affecting GM corn, cotton and soybean will be offered in conjunction with professional society meetings and conferences such as those organized by NABC. Not only is industry participation expected, the courses will be offered also to universities and federal research agencies to help ensure that all abide by the federal requirements and understand the legal implications involved in conducting field trials with GM crops. Furthermore, BIO is planning to provide accreditation as part of the incentive to participate. It is hoped that continuing education credits (CECs) will be offered. For biotechnology to continue to evolve, commitment to good stewardship on the part of the industrial sector will be essential, together with embracement of federal regulatory policies.