

# Genetically modified crops for the bioeconomy: meeting public and regulatory expectations

Saharah Moon Chapotin · Jeffrey D. Wolt

Received: 22 March 2007 / Accepted: 7 July 2007  
© Springer Science+Business Media B.V. 2007

**Abstract** As the United States moves toward a plant-based bioeconomy, a large research and development effort is focused on creating new feedstocks to meet biomass demand for biofuels, bioenergy, and specialized bioproducts, such as industrial compounds and biomaterial precursors. Most bioeconomy projections assume the widespread deployment of novel feedstocks developed through the use of modern molecular breeding techniques, but rarely consider the challenges involved with the use of genetically modified crops, which can include hurdles due to regulatory approvals, market adoption, and public acceptance. In this paper we consider the implications of various transgenic crops and traits under development for the bioeconomy that highlight these challenges. We believe that an awareness of the issues in crop and trait selection will allow developers

to design crops with maximum stakeholder appeal and with the greatest potential for widespread adoption, while avoiding applications unlikely to meet regulatory approval or gain market and public acceptance.

**Keywords** Genetic engineering · Biofuels · Bioproducts · Regulatory policy · Genetically modified organism

## Introduction

The United States is moving toward a plant-based bioeconomy to supplant many of the fossil carbon inputs in the current petroleum-based economy. Plants are envisioned to provide fuels, energy, biobased materials, and industrial chemical precursors in addition to the traditional uses of agricultural products for food, feed, and fiber. Innovations to increase the supply, quality, composition, and processability of both traditional and novel crops will be essential to meet accelerating feedstock demand (Biomass Technical Advisory Committee 2002; Boudet et al. 2003; Editorial 2006; Ragauskas et al. 2006). Modern genetic engineering techniques are increasingly being used to accomplish this goal and are viewed by many as a key enabling technology for both production and processing innovations in the bioeconomy (Biomass Research and Development Board 2001; Biomass Technical Advisory Committee

---

The views presented here are those of the authors and do not necessarily represent the views of the US government.

---

S. M. Chapotin  
US Agency for International Development, Washington,  
DC 20523, USA

J. D. Wolt (✉)  
Biosafety Institute for Genetically Modified Agricultural  
Products, Iowa State University, Ames, IA 50011, USA  
e-mail: jdwolt@iastate.edu

J. D. Wolt  
Department of Agronomy, Iowa State University, Ames,  
IA 50011, USA

2002; Editorial 2006; NRC 1999, 2000b, 2006; Paster et al. 2003). For example, genetically modified (GM) microbes, and enzymes can reduce energy requirements in biomass processing, and GM energy crops can reduce input costs through increased yield and optimized processing characteristics. Microbial GM applications are commonly used in industrial settings and their application to the bioeconomy is proceeding at a rapid pace (Herrera 2004; NRC 2000b; Raab et al. 2005). On the other hand, comparatively few GM crops have attained commercial status despite widespread enthusiasm and recognized potential for using GM technologies in crop improvement (Jaffe 2005, 2006).

Genetically modified feedstock crops figure prominently in bioeconomy projections in the United States (Biomass Research and Development Board 2001; Biomass Technical Advisory Committee 2002; Editorial 2006; NRC 1999, 2000b, 2006; Paster et al. 2003; US DOE 2006). The use of GM technologies is central to the strategy of the US Department of Energy (DOE) to deploy, within 10–15 years, feedstock crops having optimized cell wall characteristics, enhanced yield and stress tolerance (US DOE 2006). The DOE has been encouraged to focus its plant genomics research on bioenergy crops and the metabolic engineering of plant biochemical pathways to produce key processing enzymes (NRC 2006). Similarly, bioengineering of new biomass feedstocks for cellulosic ethanol production has been highlighted by the 25 × '25 Vision, a sustainable energy alliance receiving wide support from legislators, farm groups, and environmental organizations across the US (25 × '25 National Steering Committee 2007).

To date, no GM crops have yet been commercialized specifically for biofuels production, and the many projections for the contribution of GM plants to the bioeconomy rarely consider the issues involved in their deployment. These can range from regulatory constraints to marketplace adoption and public acceptance (Biomass Technical Advisory Committee 2002; Jaffe 2006; Paster et al. 2003). We consider here the opportunities and implications for genetic engineering of plants for the bioeconomy by identifying the nature of issues that will be encountered for particular traits and crops which are commonly cited innovations for biofuels production. Recognizing and addressing these issues will ease the deployment of GM plants for the bioeconomy. The US has led the world in the introduction of new GM crops (James

2006) and we are therefore considering bioeconomy crops within the context of US regulatory frameworks and public and market considerations. However, most of the issues discussed in this paper will be equally applicable to countries such as those in the EU, where public opinion tends to be less favorable of GM crops, or to countries with high potential for biomass production but whose regulatory frameworks are still under development.

### GM crops in relation to feedstock enhancement

Accomplishing the transition to a bioeconomy will necessitate large investments in research, development and infrastructure for developing new feedstocks (Koonin 2006), including advances in the fields of plant breeding, genetics, genomics, and agronomy (Biomass Research and Development Board 2001; NRC 1999; Paster et al. 2003; Perlack et al. 2005; US DOE 2006). Meeting current goals for the bioeconomy will require innovations in feedstock yield improvement, crop adaptation to marginal lands, plant modifications to increase amenability for bio-processing; and modifications to allow multiproduct production from a single crop. We focus on these examples of feedstock enhancement to understand the degree to which GM crops may prove pivotal to the success of the bioeconomy. Innovation in feedstock enhancement, whether with GM crops or through the exploration of existing plant materials, is in flux and has been the subject of recent reviews (Boerjan 2005; Boudet et al. 2003; Parrish and Fike 2005; Ragauskas et al. 2006; Vogel and Jung 2001). A further review of this information lies outside of the scope of this paper; instead we focus on a few relevant and frequently cited examples and ask: to what degree will genetic engineering be an enabler? Are there alternatives? To what extent do public and regulatory expectations influence the adoption of a GM enabler or an alternative for feedstock enhancement?

#### Traits for feedstock enhancement

##### *Feedstock yield improvement*

Initial feedstock advancements will involve common input traits such as yield, pest and disease resistance, and stress tolerance, many of which have been and

are being GM into commercial food crops and therefore are not unique to feedstock crops. Increased crop yield is essential to meeting feedstock demand projections, especially given limitations on available farmland (US DOE 2006). For example, targets include yield increases of 50% for corn (*Zea mays* L.) (Perlack et al. 2005) and yields of 15 metric tons per hectare or greater for switchgrass (Parrish and Fike 2005). Approaches to achieve these yield goals include altering photosynthetic pathways, manipulating source-sink relationships, and modifying plant architecture to increase light reception (Long et al. 2006; Van Camp 2005). In addition, increased carbon allocation to the above ground portions of a plant, diameter expansion over height growth in trees, and reduced resource allocation to flowers and seeds would increase growth rates and biomass yields (Ragauskas et al. 2006). Certain of these goals may be accomplished without the benefit of genetic engineering; however, goals, such as optimizing photosynthetic pathways or manipulating reproductive investments will probably entail genetic engineering for their success.

### *Crop adaptation*

Increased stress tolerance in crop plants allows for marginal lands to be brought into cultivation and extends ranges of plant adaptation for species that are temperature or drought limited (US DOE 2006). Enhancing crop plant tolerance to abiotic stressors such as drought, salt, temperature extremes or heavy metals has proven difficult, due to the multigene nature of these traits and the complex physiological and metabolic pathways involved; but certain approaches using genetic engineering technologies and marker assisted selection have been promising in experimental settings. These include altering levels of metabolites or sugars that confer stress tolerance, modifying stomatal response to water stress, increasing expression of certain proteins such as heat shock proteins and molecular chaperones, or manipulating regulatory pathways (Umezawa et al. 2006; Vinocur and Altman 2005). As the total amount of land under agriculture production expands to meet biomass demand, plant modifications that reduce agricultural inputs will have significant environmental benefits. Drought tolerant plants, for example, can reduce the need for irrigation,

an important consideration given climate change projections for hotter, drier weather in many areas.

The genetic engineering of crop plants for herbicide tolerance and resistance to biotic stressors such as insects and disease is now a commonplace technology for improved production efficiency and chemical use reduction. The benefits and risks surrounding the environmental release of plants with these traits have been considered extensively (Ellstrand 2003b; NRC 2000a, 2002; Peterson et al. 2006; Snow and Palma 1997) and further developments involving these traits should be anticipated in new crop varieties intended for the bioeconomy. For instance, perennial grasses could be transformed for more effective weed and disease control (Wang and Ge 2006) and GM insect resistant trees are under development (Boerjan 2005).

### *Plant modifications to increase amenability for bioprocessing*

Enhanced feedstock utilization depends largely on the improvement of plants for more efficient processing of plant biomass, primarily for cellulosic ethanol production, but also for biodiesel production from oil crops. The resistance of the plant cell wall to breakdown by chemicals and enzymes remains one of the most significant hurdles to producing cellulosic ethanol cheaply (Himmel et al. 2007; US DOE 2006). Advances in processing techniques using various enzymatic and chemical treatments are helping to make cellulosic ethanol economically feasible; but, it is widely recognized that altering the structure of the plant cell wall in feedstock crops could offer enormous advantages in lignocellulosic biomass processing by shortening pre-treatment processing, increasing enzymatic efficiency and offering more processing flexibility (Boudet et al. 2003; Ragauskas et al. 2006; US DOE 2006; Vogel and Jung 2001). Breakthroughs in reducing lignin content in biomass from trees, forage grasses and other biofuel crops will require further knowledge of plant cell wall biochemistry and structure. Improving woody feedstock processability has shown promise, for example, through transgenic modification of the lignin biosynthesis pathway to alter lignin composition and deposition for increased pulping efficiency in trees (US DOE 2006). The composition of oil crops such

as soybean [*Glycine max* (L.) Merr.] and canola [rapeseed (*Brassica napus* L.)] are being modified to enhance suitability for processing into biodiesel, for example by altering fatty acid profiles (Friedt and Lühs 1998; Kinney and Clemente 2005; Paster et al. 2003).

### *Multiproduct production*

The opportunity to generate value-added co-products along with fuels and energy from biomass will help make biorefinery operations viable and improve the economics of biofuel production (NRC 2000b); therefore, it is difficult to consider feedstock production without consideration of co-products that will impact costs of energy production. For instance, the use of crop plants as production platforms for a variety of high-value products, including enzymes, industrial compounds and specialized biomaterial precursors such as biodegradable plastics, spider silks or specialty chemicals may be intimately linked to biofuel production (Conrad 2005; Menassa et al. 2004; NRC 2000b; Paster et al. 2003; Raab et al. 2005; Rishi et al. 2001). The opportunities for biocompound production in plants will be an important factor in the overall cost-benefit analysis for biofuels production since plant-based biocompound production can lower production cost, reduce energy requirements, generate less toxic waste, and can be scaled to meet demand in comparison to competitive process technologies (Horn et al. 2004; NRC 2000b; Twyman et al. 2003).

Genetic engineering of product quality traits or industrial enzymes that directly impact processing efficiency or resolve product-limiting steps in biofuel production is a further important aspect of co-product development. For instance, the development of corn expressing transgenic thermostable alpha-amylase represents a means to more effectively produce reduced sugars during starch liquefaction in the initial stages of ethanol production (Singh et al. 2006). Further innovations for production of industrial enzymes in plants are in the offing (Hood 2002; Horn et al. 2004; Rishi et al. 2001). *In planta* production of cellulase and other enzymes needed to break down plant biomass may allow for efficient cellulosic ethanol production (NRC 2006), especially if the necessary enzymes are produced in those

regions of the cell wall where they can directly act on lignocellulose (Biomass Technical Advisory Committee 2002).

### Feedstock sources

Meeting feedstock demand will entail improved processing of existing biofuel crops and adaptation of new crops. The nature of these crops as they exist today and the successful attainment of national goals for the bioeconomy appears to necessitate some degree of genetic engineering as an enabling technology. A wide range of biomass feedstocks will supply the bioeconomy, but three plants in particular—corn, switchgrass (*Panicum virgatum* L.) and poplar (*Populus* L.)—have been at the center of research efforts to develop dedicated bioeconomy crops. Additional crops such as canola, soybean, sorghum (*Sorghum* L.), and sugarcane (*Saccharum* L.) are in the research pipeline, with GM versions under development.

Corn, a major commodity crop in US, is already grown for ethanol production and for other industrial uses in addition to its use as food and feed. Well over 90% of current fuel ethanol production capacity is based on corn grain as feedstock (Nichols et al. 2006) and the near-term demand for corn as an ethanol feedstock will increase about 50% over present by 2015 as alternative technology for biofuel production develops (World Agricultural Outlook Board 2006). The most important near term innovation for corn will be utilization of stover as a source for cellulosic ethanol production. It is anticipated that with cellulosic ethanol production grain uses of corn will be retained, with stover diverted to fuel production; a scheme which is being closely scrutinized relative to its environmental impacts (Graham et al. 2007).

Corn varieties with improved yields of grain and stover ethanol are already entering the marketplace. Genetic engineering can be expected to play a role, as most of the GM traits important for the bioeconomy are currently under development in corn (Bothast and Schlicher 2005; Reuters 2006; Twyman et al. 2003). Corn generally requires high-energy inputs and significant pesticide and fertilizer applications (Greene 2004; Paster et al. 2003); therefore genetic improvements to corn to reduce its environmental impact, such as pest resistance, lower nutrient requirements or drought tolerance, would be useful.

Ultimately, however, the replacement of corn with perennial crops will provide the most environmental benefits (Perlack et al. 2005) and may result in the greatest biomass yields.

Switchgrass, a perennial, high-yielding native prairiegrass (Schmer et al. 2006; Vogel and Jung 2001), is often considered to be the ideal biomass crop due to the environmental and agronomic advantages it offers (McLaughlin et al. 1999). Switchgrass is relatively unimproved, and there is considerable potential for increasing biomass yield and enhancing composition for more efficient conversion into biofuel and bioproducts (Parrish and Fike 2005). In order to meet the demands for the bioeconomy, further domestication and optimization of switchgrass for intensive agriculture might be anticipated. For instance, large gains in yield could entail germplasm improvements coupled with increased inputs of chemicals and fertilizers. Recent studies indicate that using highly diverse mixtures of perennial grassland species may be a better strategy for biomass production than monoculture planting. Such a strategy may provide optimal energy production along with the environmental benefit of minimizing agricultural inputs (Tilman et al. 2006). The direction taken for switchgrass utilization is presently unclear, but genetic engineering is clearly a means to improve switchgrass and other grasses for biomass production (NRC 1999; Vogel and Jung 2001). Forage and turf grasses are being engineered for more efficient cultivation (Wang and Ge 2006) and progress in this direction would be anticipated to impact development of switchgrass as a source of biomass for energy production.

A number of studies have projected increased usage of forest products, woody residues, and woody energy crops for electricity, fuel and biomaterial production (Mead 2005; Perlack et al. 2005; Strauss and Bradshaw 2001). Shifting to highly productive tree plantations would reduce the pressure on natural forests but will necessitate extensive breeding advances in plantation tree species such as poplar. Until now this has been difficult because the long generation time in trees makes conventional breeding a very slow process (Boerjan 2005). Genetic engineering techniques have the potential to greatly shorten the breeding timeline for trees and allow for more targeted breeding. As with switchgrass, altered lignin content and increased yield have been the most

sought after traits. Additional efforts are aimed at reducing reproductive investment, modifying stature and belowground resource allocation, introducing sterility, and enhancing disease and pest resistance (Boerjan 2005).

Biodiesel produced from oil crops is another petroleum fuel substitute; in the US it is primarily made from soybean oil and in the EU from rapeseed oil (NRC 1999). Biodiesel production and use are currently dependent on substantial economic incentives; therefore increasing crop yield and oil content are two essential breeding goals along with oil modification. Plant oils have long been used in the oleochemical industry in the production of various products such as biolubricants and waxes, and as with other biofuel production platforms, lipid based coproducts will help to make biodiesel production more profitable (Tyson 2005).

### **Policy implications of deploying GM crops for the bioeconomy**

We have described here trait and crop innovations that are commonly considered for meeting projections for biofuel production. These examples point to the complexity of effective choices for application of genetic engineering to the appropriate combination of crops and traits. Development of coherent policy toward the adoption of GM plants, and therefore anticipation of their impact on the bioeconomy, is further complicated by persistent issues of technology acceptance due variously to concerns over health and environmental safety and socioeconomic considerations (Biomass Technical Advisory Committee 2002; Bradford et al. 2005). Some early projections for the potential for biotechnology to improve traditional food crops through application of genetic engineering have not materialized (Jaffe 2005, 2006). There is widespread recognition that factors such as increasingly complex and lengthy regulatory procedures and concerns over consumer and market acceptance of GM products have contributed to the disparity between anticipated and available products (Bradford et al. 2005; Fedoroff and Brown 2004; Jaffe 2006; Trewavas and Leaver 2001).

Genetically modified plants developed specifically for the bioeconomy may receive scrutiny from environmental organizations, consumer advocacy

groups and the scientific community because of expectations for the bioeconomy to be an environmentally sustainable alternative to the petroleum economy (e.g., Marris 2006; Ulgiati 2001). Biofuels and bioproducts are perceived as 'green technologies,' intended to replace products and manufacturing practices considered environmentally harmful; as such they may be held to an unusually high-environmental standard (Landis and Theis 2006). For example, the use of cellulosic ethanol as a transportation fuel is expected to reduce net CO<sub>2</sub> emissions relative to fossil fuel usage (Farrell et al. 2006), but projections of increased ethanol production are also generating considerable discussion on the environmental impacts of the intensified agriculture necessary to supply biomass demand (Greene 2004; Landis and Theis 2005). Public interest groups have asked whether the breeding of improved biomass feedstock requires genetic engineering and have proposed that the transition to a bioeconomy be accomplished entirely using conventionally bred feedstocks (Greene 2004).

Certain applications of genetic engineering in crops would deliver environmental benefits, yet GM technologies are perceived by some to be ecologically unsound (Wolfenbarger and Phifer 2000), even though many of the criticisms leveled at GM crops apply equally to conventional crops. The bioeconomy is currently gaining wide and unprecedented support from a broad coalition of government, industry, agriculture and environment stakeholders (25 × '25 National Steering Committee 2007; Herrera 2006). Continued widespread support hinges to some extent on the notion of green technology, as new bioeconomy crops may be evaluated more stringently than traditional food and feed crops (Editorial 2006; Landis and Theis 2006). Addressing real or perceived issues regarding the environmental impact of genetic engineering could, therefore, slow the adoption of GM bioeconomy crops. The additional time and cost required for crop developers to address environmental issues should be taken into consideration when projecting biomass production goals and timelines.

Public opinion of genetic engineering has been a significant factor affecting the deployment of new GM crops (Fedoroff and Brown 2004). Several highly publicized incidents have been used by interest groups to foster public distrust of agricultural biotechnology (e.g., Greenpeace 2006; Mellon and

Rissler 2004), leading to calls for bans and stricter regulations on GM crops. These include the Star-Link™ corn case, where a GM corn variety approved for animal feed but not human consumption was detected in US corn supply and led to recalls of corn-based food products (Fedoroff and Brown 2004; Miller 2001). In another instance, inadequate field test confinement procedures resulted in commingling between GM corn plants producing a pharmaceutical compound and food crops (Fox 2003). More recently, the detection of unapproved GM rice (*Oryza sativa* L.) varieties in commercial rice supplies led to blocked imports around the world and a class action lawsuit filed by rice growers (Lee 2006). The impact of public perception extends to environmental considerations as well; preliminary studies suggesting that *Bt* corn (containing a gene from the bacterium *Bacillus thuringiensis*) was toxic to monarch butterflies (*Danaus plexipus* L.) drew intense public interest (Pew Initiative on Food and Biotechnology 2002). Further studies found only minimal risk, but the notion that GM crops harm monarch butterflies has persisted (Fedoroff and Brown 2004).

Developers of new GM crops will have to consider market and trade influences in addition to public perception and regulatory constraints (Kalaitzandonakes and Bijman 2003). Despite a track record of safety and widespread adoption of the first generation GM crops by farmers in US and abroad, persistent consumer wariness has led food retailers and manufacturers to preemptively reject some new GM crops even though they have regulatory approvals for commercialization. In the US, for example, transgenic varieties of beet (*Beta vulgaris* L.), potato (*Solanum tuberosum* L.), wheat (*Triticum aestivum* L.) and rice have received deregulated status but are not commercially available, due to industry concerns over consumer acceptance (Castle et al. 2006; Paster et al. 2003; USDA 2006).

If crops developed for the bioeconomy incorporate environmentally sustainable traits that offset the impact of their production, this could ease acceptance of GM plants and ensure continued stakeholder commitment. Improving nutrient use efficiency in crops is a promising approach; for instance, research on altering nitrogen uptake, transport and metabolism is underway in a number of crop species (Good et al. 2004). Attempts to engineer the perennial habit into annual crops may also provide significant

environmental benefits, such as reduced soil erosion, increased soil carbon content and better wildlife habitat (Grigal and Berguson 1998; Kort et al. 1998; US DOE 2006). Reducing inputs would provide economic as well as environmental benefits, as chemical fertilizers and pesticides, fuel, and irrigation are substantial expenses in agricultural production systems. Product developers, however, cannot assume that these benefits will be readily apparent or broadly acceptable to all parties. For instance, currently pest and disease resistant GM crops reduce the need for agrichemical applications and GM herbicide tolerant crops reduce soil erosion through better weed management practices, yet their adoption is not uniformly viewed as a net benefit to the environment (NRC 2002; Wolfenbarger and Phifer 2000).

Regardless of whether GM technologies are employed or not, the advent of the bioeconomy will likely have adverse environmental impacts. Increased biomass production may entail intensified agricultural practices and conversion of other land uses to farmland (McLaughlin and Walsh 1998; Perlack et al. 2005; US DOE 2006). Maximizing crop yield may entail the use of additional agricultural inputs. And harvesting corn stover and other biomass materials has implications for nutrient and carbon cycling in soils (Grigal and Berguson 1998; Perlack et al. 2005; US DOE 2006). Some projections for biomass production include using land from the Conservation Reserve Program for the cultivation of perennial grasses (Perlack et al. 2005; US DOE 2006). Wise policy formulation will allow for those GM innovations that mitigate rather than exacerbate these impacts.

#### Challenges of deploying GM traits and crops for the bioeconomy

The successful deployment of new GM crop varieties for the bioeconomy, as with any new GM crop, will depend on evolving federal regulations, complex intellectual property issues, public perception of the safety or desirability of novel traits, and market forces (Paster et al. 2003). Many GM crop concepts for biofuels production will readily receive regulatory approval and market acceptance; whereas, other applications may prove challenging to deploy and

will require special consideration by regulators and crop developers.

#### Enhanced yield and stress tolerance, modified lignin composition

Genetic modifications for increased yield or enhanced stress tolerance may be more acceptable to critics of genetic engineering than those that introduce toxins or radically alter crop composition. Regardless, they will be scrutinized because of the potential for increased fitness and consequent concerns over invasiveness and gene flow (Pedersen et al. 2005; Stewart et al. 2003; Strauss 2003). The relationship between yield and fitness is quite complex, yet there is no a priori reason to expect that increasing biomass yield in a controlled agronomic setting should make a plant more competitive outside of the agronomic setting.

Similarly, plants with modified cell wall composition will probably not pose significant risks for environmental release. Reduced lignin content is likely to negatively impact plant fitness, but this may not be true for all species or modifications (Pedersen et al. 2005). Lignin content and composition pathways are complex, and unexpected effects have accompanied their modification, such as increased growth rates in transgenic aspen (*Populoides tremuloides* Michx) (Hu et al. 1999) and compensating linkages between lignin and cellulose pathways in tobacco (*Nicotiana tabacum* L.) and *Arabidopsis thaliana* (L.) Heynh (Boudet et al. 2003). Many of these modifications will be in long-lived plants, such as trees, or in dedicated energy crops intended for widespread cultivation. Therefore, any such proposed modifications will need to be evaluated for their potential to increase whole plant fitness. The anticipated modifications to oil crops to increase suitability for processing into biodiesel are not likely to pose an environmental risk, however changes to oil quality and composition would warrant evaluation from a food safety and nutritional perspective.

The widespread adoption of abiotic stress-tolerant biomass crops may also have indirect effects on biodiversity and land use, when their introduction enables the cultivation of formerly fallow and unused land. Such indirect ecological consequences fall outside of normal biosafety considerations by

regulators, yet these concerns will have to be addressed in the public arena.

### *Food crops for biomass and multiproduct production*

Most of the GM crops developed to date have been common food crops. These crops are easier to transform; are well understood in terms of their food safety, production and processability; and, thus, have higher economic returns and more rapid development times than do novel varieties of trees, minor crops or previously uncultivated plants. Most bioeconomy projections assume the eventual adoption of perennial crops such as grasses and trees for biomass production, due to the environmental benefits and yield advantages they confer (US DOE 2006). Additionally, when novel traits are unsuitable for human or animal consumption, the use of non-food crops could avoid many potential biosafety issues. Developing alternative crops and traits for biofuels and bioproducts may require greater research effort and take more time than developing new varieties of conventional crops. Assuring future acceptance of these applications, however, may be worth the cost and effort, particularly if such considerations are addressed before new varieties are conceived rather than during field testing and regulatory approval. Despite the attractiveness of non-food crop utilization, it is important to recognize that for the near-term food crops will be used to meet the biomass needs of the emerging bioeconomy; therefore, means must be sought to accommodate their use.

For those biofuel crops that represent modifications of food or feed crops, commingling, and gene flow between GM and conventional crops will emerge as a major concern as plants are transformed to express novel compounds. This concern has been advanced as a rationale for avoiding food crops for biofuel production (Stewart 2007). Grain production, distribution, and processing facilities in US are so highly integrated that such commingling is unavoidable from a practical standpoint, especially given the likelihood of human error (Editorial 2004; Ellstrand 2003a; NRC 2004). In fact, this has already occurred in many instances (Fedoroff and Brown 2004; Fox 2003; Herrera 2005; Miller 2001). Selecting the appropriate host plant for industrial crops will be especially important to receiving regulatory and

public approval, as different systems will differently expose humans, animals, and non-target organisms to novel substances. Species not used for food or feed and not typically entering food or processing streams should, therefore, have greater acceptability.

Regulatory approvals for plants engineered to produce compounds that already occur in food plants will be more straightforward than for plants engineered with genetic material from non-food plants, animals or bacteria. Developers of specialized bioproducts using GM food crops as production platforms will continue to rely on the biotechnology consultation process with the Food and Drug Administration (FDA) in order to avoid adulteration concerns arising from accidental commingling in the general food supply. Additionally, developers have the option of completing an early food safety evaluation with the FDA prior to entering those stages product development when commingling or gene flow with the general food supply could occur. Crops modified to produce non-food products have to date met resistance from food manufacturers and other industry associations even when the trait was non-hazardous. Prudent selection of species-trait combinations will therefore also be beneficial to ensuring consumer support for GM products.

Whether the consideration is for biofuel production alone or in conjunction with value-added co-products, it is clearly important to carefully match GM product concepts with the most appropriate plant production platform. This is well-understood from experiences with biopharma crops where there is an extensive literature addressing biosafety (Christensen et al. 2004; Ellstrand 2003a; Ma et al. 2005; Peterson and Arntzen 2004; Pew Initiative on Food and Biotechnology 2003). Biosafety issues for these crops are intermixed with public and regulatory concerns, especially when the production platform is a GM food or feed crop. The regulatory and market uncertainties surrounding pharmaceutical crops have important implications for GM applications developed for the bioeconomy, since industrial intermediates, enzymes, and other biomaterials engineered into plants will face similar scrutiny to the extent that they have food or environmental safety ramifications.

Industrial crops require stringent confinement measures during testing and development stages, are subject to lengthy regulatory review (USDA-APHIS 2006; USFDA and USDA-APHIS 2002), and have not

yet advanced beyond the field test stage. When intended for widespread unconfined release, GM crop varieties receive deregulated status prior to commercialization. Certain industrial crops might not be appropriate candidates for deregulation under existing regulation, therefore the US Department of Agriculture, Animal and Plant Health Inspection Service (USDA-APHIS) is exploring options to confer partial deregulation while still requiring appropriate biosafety measures such as confinement practices. The on-going process of regulatory revision by USDA-APHIS will take time and interim guidelines on how and whether crops intended for the bioeconomy should be commercialized will be needed.

### *Transgene confinement*

The aforementioned issues regarding public and regulatory concerns with respect to gene flow necessitate considerations of transgene confinement and product channeling as a consequential aspect of regulatory safety determinations for some bioeconomy crops. The appropriate use of genetic confinement strategies could significantly alleviate some concerns over gene flow. And in certain applications they may be considered essential, especially if the traits are unfamiliar and physical confinement measures for large scale plantings of industrial biomass crops are impractical. Control over trait expression through confinement and channeling also addresses public and market concerns regarding product adulteration and crop segregation for different export markets. Seed companies would undeniably gain from genetic confinement strategies through stricter intellectual property rights enforcement, as will organic farmers and others who may wish to grow conventional crops and need strong assurances that their crops would not become adulterated. Genetic confinement could also be of value to producers of GM crops with high-value traits as a way of maintaining trait quality and ensuring identity preservation.

Various methods for achieving reproductive confinement have been considered, including those that alter the development of reproductive structures or that prevent the transmission of transgenes through seeds or pollen (Daniell 2002; Lee and Natesan 2006; NRC 2004; Stewart et al. 2003). Other confinement approaches use inducible promoters to control the

expression of the gene or trait of interest (Daniell 2002; NRC 2004). For example, plants could be engineered to produce cellulases only when triggered by specific conditions prior to processing into ethanol (Farmacule 2006). In situations where gene flow from transgenic crops to conventional crops or wild relatives is considered undesirable, even when no ecological impacts are expected, the use of molecular switches could contribute to increased public and commercial acceptance of GM crops. The efficacy of molecular switches for biosafety measures has yet to be demonstrated and absolute control may be difficult to achieve (Daniell 2002). Regulatory agencies may therefore not treat such plants differently than plants where the trait is continuously expressed, and confinement measures reflecting the possibility of switch failure could still be required. Reproductive confinement technologies will need to be proven under field conditions, and even experimental trials of such technologies can be anticipated to be problematic with respect to avoiding unintended gene flow.

### *Acceptance and environmental impact of certain GM bioeconomy crops*

The relative environmental impact of the various crops used as bioeconomy production platforms will influence their adoption, given expectations for the bioeconomy to be an environmentally sustainable alternative to the current petroleum-based economy. Bioeconomy crops will have varied potential for impact depending on the nature of innovation involved. For instance, genetic modification to alter lignocellulose on one hand could reduce fitness of the GM crop and reduce concerns regarding gene flow to wild plants or feral escapes. On the other hand, the altered nature of the crop might increase its susceptibility to pests and disease thereby increasing the chemical inputs necessary for plant protection. Altered plant morphology to favor higher biomass production could involve similar tradeoffs to realize the yield potential of the plant modification.

We have already described corn, perennial grasses, and trees as lead platforms for feedstock production. Each has particular attributes which impact the public and regulatory acceptability when GM for biofuels production.

In the near term, corn is indisputably the leading platform for feedstock production in US; although in

other regions of the world sugarcane may represent a more immediately attractive alternative. GM corn has been widely accepted by US farmers and consumers. Over 60% of the corn grown in US has been GM with traits for herbicide tolerance or insect resistance (Lawrence 2007). Therefore, the introduction of new GM corn varieties may be fairly straightforward as long as they also receive approval for food and feed use. For many of the traits useful in biomass production, the corn grain will be considered substantially equivalent to conventional corn, so that commingling with corn intended for human and animal consumption would not be a problem. Resistance to the expanding hectareage of corn for the bioeconomy is more likely to be based on environmental impacts, such as high fertilizer use and soil erosion; however these issues are common to both GM and conventionally bred corn varieties.

Switchgrass currently enjoys a reputation as an environmentally friendly biomass alternative to crops such as corn (McLaughlin and Walsh 1998; Wang and Ge 2006). Unless GM switchgrass varieties are rendered sterile, however, there will almost certainly be gene flow to wild switchgrass as well as the possibility for the establishment of self-sustaining populations of engineered switchgrass. A concern over transgenic and other introduced plants is that when wild populations are small, gene flow from related cultivated species can lead to extinction or loss of genetic diversity, especially when the novel traits confer a selective advantage (Ellstrand et al. 2002). Most of the native prairie in US has been converted to agricultural and other uses and only persists in small scattered reserves (Vogel and Jung 2001); therefore populations of wild switchgrass and related species may be at risk for extinction or loss of genetic diversity if surrounded by reproductively viable GM switchgrass. This concern will hold for the introduction of any improved cultivar, but will garner greater regulatory and public scrutiny if genetic engineering is involved. Engineering sterility or inhibiting flowering in grasses is an option to reduce gene flow; however this has implications for the efficiency of seed production (Wang and Ge 2006).

Prospects for the deregulation and commercialization of GM grasses should be considered in the context of the first GM grass to be submitted to the USDA for deregulation, an herbicide tolerant variety of creeping bentgrass (*Agrostis stolonifera* L.)

(Pollack 2004). Cross pollination between GM bentgrass in seed production areas and non-GM bentgrass and related species has been shown to occur at large distances from experimental test plots (Watrud et al. 2004). This has led to concerns that GM bentgrass populations could become established in natural areas or through cross pollination with related species, and that because of the herbicide tolerance trait, fewer options would be available for control of such populations. A USDA-APHIS decision on deregulation of the GM bentgrass is pending the outcome of an environmental impact statement, but there has been resistance to its commercial release and several lawsuits were initiated in an attempt to forestall further field testing and commercialization (Pulaski 2004). Critics may be more forgiving of GM switchgrass, a fossil fuel alternative with obvious consumer and environmental benefits, than they have been of the GM bentgrass, a plant intended for use on golf courses. Yet gene flow issues and other concerns could still lead very enthusiastic proponents of biofuels to resist the deployment of GM switchgrass, and reproductive sterility may be necessary before it can be commercialized on a large scale.

Trees are long-lived organisms having large quantities of wind-dispersed pollen and seeds; therefore, large scale environmental release of GM trees is controversial (Mayer 2001) given the high potential for gene transfer and the uncertainty over how traits such as rapid growth may impact fitness or invasiveness. Reproductive sterility may be a required biosafety component of any commercial deployment of GM trees (Strauss and Bradshaw 2001), whether for the bioeconomy or for more traditional uses such as paper and timber production. Additionally, if varieties are engineered to resist pests, the potential for widespread impact on insect communities will be an issue (Campbell and Asante-Owusu 2001), despite the fact that pesticide applications would be reduced. Similarly, herbicide tolerant tree plantations have additional implications for biodiversity (Johnson and Kirby 2001).

## Conclusion

There are a wide range of methods to introduce novel germplasm into crops and breed new varieties, including conventional cross breeding, wide crosses

with distant relatives, mutagenesis, marker assisted selection, embryo rescue, and genetic engineering. Alternatives to GM will continue to be used, where appropriate and effective, to develop crops for the bioeconomy. The choice as to whether or not to use GM technologies for any breeding program will depend on factors such as the type of crop, the nature of the trait, and continuing technology advances.

It is becoming clear, however, that GM technologies, when harnessed responsibly, have the potential to accelerate the breeding of crops to meet projected biomass demand. Certain bioeconomy objectives would be impossible without the advantages that precision plant engineering can offer. It is important to recognize that achieving a bioeconomy will be both a technological and a political endeavor requiring multiple innovative strategies. We have sought here to identify some crop- and trait-specific concerns that may arise as new crop varieties are developed for the bioeconomy. By identifying problems and highlighting avenues likely to succeed, effort can be directed toward productive avenues of research and toward the development of new crop varieties that will appeal to growers, regulators and consumers and be embraced by industry and the environmental community.

Many of the issues addressed in this paper are also under consideration by federal regulators and will be faced in any national jurisdiction where there is an emerging focus on the bioeconomy. Regulatory assessments and determinations with respect to the risk involved in the introduction of new GM plant and animal varieties are appropriately based on scientific evidence for the likelihood to cause harm. As we point out, however, crop developers must recognize factors of consumer acceptance and public opinion in determining what direction this technology should grow. For example, two different applications of genetic engineering could present the same level of risk, but one might be more acceptable to consumers based on the biological origin of the inserted genetic material (Nielsen 2003). Although the regulatory mandate does not—and should not—allow regulatory agencies to distinguish between these two applications, crop developers could choose to self-regulate at this level by evaluating new crop-trait combinations not only for their safety, but also for their economic costs and the potential to impede future applications of biotechnology.

Crop developers need to be aware that certain particularly novel applications of biotechnology may carry a stigma of risk that must be openly addressed as products are deployed (Gregory et al. 2001). Special interests and public advocacy groups have shown themselves to be very successful at directing suspicion toward GM products. Simply the perception of unsafe practices may be sufficient to derail the deployment of novel crops, even those that could have considerable societal and environmental benefit. Significant public funds are supporting bioeconomy research and development through federal and state initiatives which emphasize sustainable solutions for supplying energy and materials (Advanced Energy Initiative 2006; Ames 2002; Biomass Technical Advisory Committee 2002; Schwarzenegger 2006; State of Illinois 2006; Sun Grant Initiative 2007; US Congress 2000, 2005). Realizing the opportunity for this investment to find sustainable alternatives to fossil fuel consumption, promote new environmentally friendly industries, and bring economic revitalization to rural areas requires that new applications and products find widespread acceptance by regulators, consumers and industry groups. With this understanding, scientists and developers will be better able to wisely position use of GM crops to benefit the bioeconomy.

## References

- 25 × '25 National Steering Committee (2007) 25 × '25 Action plan: charting America's energy future. Energy Future Coalition, Washington, DC
- Advanced Energy Initiative (2006) [Online]. Available at <http://www.whitehouse.gov/news/releases/2006/01/20060131-6.html> (posted 31 January 2006; verified 7 January 2007). Office of the Press Secretary, The White House, Washington, DC
- Ames J (2002) New federal incentives promote biopower and biobased products. *BioCycle* 43:52–55
- Biomass Research, Development Board (2001) *Fostering the bioeconomic revolution in biobased products and energy: an environmental approach*. USDA & Department of Energy, Washington, DC
- Biomass Technical Advisory Committee (2002) *Roadmap for Biomass Technologies in the United States*. Biomass Research and Development Technical Advisory Committee, Washington, DC
- Boerjan W (2005) Biotechnology and the domestication of forest trees. *Curr Opin Biotechnol* 16:159–166
- Bothast RJ, Schlicher MA (2005) Biotechnological processes for conversion of corn into ethanol. *Appl Microbiol Biotechnol* 67:19–25

- Boudet AM, Kajita S, Grima-Pettenati J, Goffner D (2003) Lignins and lignocellulosics: a better control of synthesis for new and improved uses. *Trends Plant Sci* 8:576–581
- Bradford KJ, Van Deynze A, Gutterson N, Parrott W, Strauss SH (2005) Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology and genomics. *Nat Biotechnol* 23:439–444
- Campbell FT, Asante-Owusu R (2001) GE trees: proceed only with caution. In: Strauss SH, Bradshaw HDT (eds) First international symposium on ecological and societal aspects of transgenic plantations. College of Forestry, Oregon State University, OR
- Castle LA, Wu G, McElroy D (2006) Agricultural input traits: past, present and future. *Curr Opin Biotechnol* 17:105–112
- Christensen MJ, Misra MK, Rai S, Shyy Y-Y, Wolt JD (2004) Confined production processes for non-food corn. Biosafety Institute for Genetically Modified Agricultural Products, Ames, IA
- Conrad U (2005) Polymers from plants to develop biodegradable plastics. *Trends Plant Sci* 10:511–512
- Daniell H (2002) Molecular strategies for gene containment in transgenic crops. *Nat Biotech* 20:581–586
- Editorial (2004) Drugs in crops—the unpalatable truth. *Nat Biotechnol* 22:133
- Editorial (2006) Bioethanol needs biotech now. *Nat Biotechnol* 24:725–725
- Ellstrand NC (2003a) Going to “Great Lengths” to prevent the escape of genes that produce specialty chemicals. *Plant Physiol* 132:1770–1774
- Ellstrand NC (2003b) Current knowledge of gene flow in plants: implications for transgene flow. *Philos Trans R Soc Lond Ser B Biol Sci* 358:1163–1170
- Ellstrand NC, Prentice HC, Hancock J (2002) Gene flow and introgression from domesticated plants into their wild relatives. In: Syvanen M, Kado CI (eds) Horizontal gene transfer, 2nd edn. Academic Press, San Diego, CA, pp 217–236
- Farmacule (2006) Genetic technology to produce cheaper ethanol from sugarcane [Online]. Available at <http://farmacule.com/news/news/7/> (verified 7 January 2007). Farmacule Bioindustries, Brisbane, Australia
- Farrell AE, Plevin RJ, Turner BT, Jones AD, O’Hare M, Kammen DM (2006) Ethanol can contribute to energy and environmental goals. *Science* 311:506–508
- Fedoroff N, Brown NM (2004) Mendel in the kitchen: a scientist’s view of genetically modified foods. Joseph Henry Press, Washington, DC
- Fox JL (2003) Puzzling industry response to ProdiGene fiasco. *Nat Biotechnol* 21:3–4
- Friedt W, Lühs W (1998) Recent developments and perspectives of industrial rapeseed breeding. *Fett/Lipid* 100:219–226
- Good AG, Shrawat AK, Muench DG (2004) Can less yield more? Is reducing nutrient input into the environment compatible with maintaining crop production? *Trends Plant Sci* 9:597–605
- Graham RL, Nelson R, Sheehan J, Perlack RD, Wright LL (2007) Current and potential US corn stover supplies. *Agron J* 99:1–11
- Greene N (2004) Growing energy: how biofuels can help end America’s oil dependence. National Resources Defense Council, Washington, DC
- Greenpeace (2006) Say no to genetic engineering [Online]. Available at <http://www.greenpeace.org/international/campaigns/genetic-engineering>. Greenpeace International, Amsterdam, The Netherlands
- Gregory R, Flynn J, Slovic P (2001) Technological stigma. In: Flynn J et al (eds) Risk, media and stigma. Earthscan, London, pp 3–8
- Grigal DF, Berguson WE (1998) Soil carbon changes associated with short-rotation systems. *Biomass Bioenergy* 14:371–377
- Herrera S (2004) Industrial biotechnology—a chance at redemption. *Nat Biotechnol* 22:671–675
- Herrera S (2005) Syngenta’s gaff embarrasses industry and White House. *Nat Biotechnol* 23:514–514
- Herrera S (2006) Bonkers about biofuels. *Nat Biotechnol* 24:755–760
- Himmel M, Ding S-Y, Johnson DK, Adney WS, Nimlos MR, Brady JW, Foust TD (2007) Biomass recalcitrance: engineering plants and enzymes for biofuels production. *Science* 315:804–807
- Hood EE (2002) From green plants to industrial enzymes. *Enzyme Microb Technol* 30:279–283
- Horn ME, Woodard SL, Howard JA (2004) Plant molecular farming: systems and products. *Plant Cell Rep* 22:711–720
- Hu W-J, Harding SA, Lung J, Popko JL, Ralph J, Stokke DD, Tsai C-J, Chiang VL (1999) Repression of lignin biosynthesis promotes cellulose accumulation and growth in transgenic trees. *Nat Biotechnol* 17:808–812
- Jaffe G (2005) Withering on the vine: will agricultural biotech’s promises bear fruit? Center for Science in the Public Interest, Washington, DC
- Jaffe G (2006) Regulatory slowdown on GM crop decisions. *Nat Biotechnol* 24:748–749
- James C (2006) Global Status of Biotech/GM Crops: 2006. ISAAA Brief No. 35, ISAAA: Ithaca, NY
- Johnson B, Kirby K (2001) Potential impacts of genetically modified trees on biodiversity of forestry plantations: a global perspective. In: Strauss SH, Bradshaw HDT (eds) First international symposium on ecological and societal aspects of transgenic plantations. College of Forestry, Oregon State University, OR
- Kalaizandonakes N, Bijman J (2003) Who is driving biotechnology acceptance? *Nat Biotechnol* 21:366–369
- Kinney AJ, Clemente TE (2005) Modifying soybean oil for enhanced performance in biodiesel blends. *Fuel Process Technol* 86:1137–1147
- Koonin SE (2006) Getting serious about biofuels. *Science* 311:435
- Kort J, Collins M, Ditsch D (1998) A review of soil erosion potential associated with biomass crops. *Biomass Bioenergy* 14:351–359
- Landis AE, Theis TL (2005) Workshop on the economic and environmental impacts of biobased production. *Int J Lifecycle Assess* 10:226–227
- Landis AE, Theis TL (2006) Response to ‘Comments on workshop report on the economic and environmental

- impacts of biobased production.' *Int J Lifecycle Assess* 11:213–214
- Lawrence S (2007) Agbiotech booms in emerging nations. *Nat Biotechnol* 25:271
- Lee C (2006) Genetically engineered rice wins USDA approval. *The Washington Post*, Washington, DC, p 3
- Lee D, Natesan E (2006) Evaluating genetic containment strategies for transgenic plants. *Trends Biotechnol* 24:109–114
- Long SP, Zhu X-G, Naidu SL, Ort DR (2006) Can improvement in photosynthesis increase crop yields? *Plant Cell Environ* 29:315–330
- Ma JKC, Chikwarmba R, Sparrow P, Fischer R, Mahoney R, Twyman RM (2005) Plant-derived pharmaceuticals—the road forward. *Trends Plant Sci* 10:580–585
- Marris E (2006) Drink the best and drive the rest. *Nature* 444:670–672
- Mayer S (2001) International regulation and public acceptance of GM trees: demanding a new approach to risk evaluation. In: Strauss SH, Bradshaw HDT (eds) *First international symposium on ecological and societal aspects of transgenic plantations*. College of Forestry, Oregon State University, OR
- McLaughlin S, Bouton J, Bransby D, Conger B, Ocumpaugh WR, Parrish DJ, Taliaferro C, Vogel KP, Wullschlegler S (1999) Developing switchgrass as a bioenergy crop. In: Janick J (ed) *Perspectives on new crops and new uses*. ASHS Press, Alexandria, VA, pp 282–298
- McLaughlin SB, Walsh ME (1998) Evaluating environmental consequences of producing herbaceous crops for bioenergy. *Biomass Bioenergy* 14:317–324
- Mead DJ (2005) Forests for energy and the role of planted trees. *Crit Rev Plant Sci* 24:407–421
- Mellon M, Rissler J (2004) Gone to seed: transgenic contaminants in the traditional seed supply. *Union of Concerned Scientists*, Cambridge, MA
- Menassa R, Zhu H, Karatzas CN, Lazaris A, Richman A, Brandle J (2004) Spider dragline silk proteins in transgenic tobacco leaves: accumulation and field production. *Plant Biotechnol J* 2:431–438
- Miller HI (2001) The Bush administration deals a blow to biotechnology—and itself. *Nat Biotechnol* 19:807–808
- Nichols NN, Dien BS, Bothast RJ, Cotta MA (2006) The corn ethanol industry. In: Minteer S (ed) *Alcoholic fuels*. CRS Press, Boca Raton, FL, pp 59–78
- Nielsen KM (2003) Transgenic organisms—time for conceptual diversification? *Nat Biotechnol* 21:227–228
- NRC (1999) *Review of the research strategy for biomass-derived transportation fuels*. National Academies Press, Washington, DC, USA
- NRC (2000a) *Genetically modified pest-protected plants: science and regulation*. National Academies Press, Washington, DC, USA
- NRC (2000b) *Biobased industrial products: research and commercialization priorities*. National Academies Press, Washington, DC, USA
- NRC (2002) *Environmental effects of transgenic plants: the scope and adequacy of regulation*. National Academies Press, Washington, DC
- NRC (2004) *Biological confinement of genetically engineered organisms*. National Academies Press, Washington, DC, USA
- NRC (2006) *Review of the department of energy's genomics: GTL program*. National Academies Press, Washington, DC, USA
- Parrish DJ, Fike JH (2005) The biology and agronomy of switchgrass for biofuels. *Crit Rev Plant Sci* 24:423–459
- Paster M, Pellegrino J, Carole TM (2003) *Industrial bioproducts: today and tomorrow*. Energetics Inc., Columbia, MD
- Pedersen JF, Vogel KP, Funnell DL (2005) Impact of reduced lignin on plant fitness. *Crop Sci* 45:812–819
- Perlack RD, Wright LL, Turhollow AF, Graham RL, Stokes BJ, Erblich DC (2005) Biomass as feedstock for a bioenergy and bioproducts industry: the technical feasibility of a billion-ton annual supply. *Oak Ridge National Laboratory*, Oak Ridge, TN
- Peterson RKD, Arntzen CJ (2004) On risk and plant-based biopharmaceuticals. *Trends Biotechnol* 22:64–66
- Peterson RKD, Meyer SJ, Wolf AT, Wolt JD, Davis PM (2006) Genetically engineered plants, endangered species and risk: a temporal and spatial exposure assessment for Karner blue butterfly larvae and Bt maize pollen. *Risk Anal* 26:845–858
- Pew Initiative on Food and Biotechnology (2002) Three years later: lessons learned from the monarch butterfly controversy [Online]. Available at <http://pewagbiotech.org/resources/issuebriefs/monarch.pdf> (posted 30 May 2002; verified 7 January 2007), Washington, DC, USA
- Pew Initiative on Food and Biotechnology (2003) *Pharming the field: a look at the benefits and risks of bioengineering plants to produce pharmaceuticals*, Washington, DC
- Pollack A (2004) Genes from engineered grass spread for miles, study finds. *The New York Times*, New York, p 1
- Pulaski A (2004) Lawsuit tries to block grass tested in Oregon. *The Oregonian*, Portland, OR, p 1
- Raab RM, Tyo K, Stephanopoulos G (2005) Metabolic engineering. *Adv Biochem Eng/Biotechnol* 100:1–17
- Ragauskas AJ, Williams CK, Davison BH, Britovsek G, Cairney J, Eckert CA, Frederick WJJ, Hallett JP, Leak DJ, Liotta CL, Mielenz JR, Murphy R, Templar R, Tschaplinski T (2006) The path forward for biofuels and biomaterials. *Science* 311:484–489
- Reuters (2006) Biotech seen doubling US corn yields by 2030, December 12. *Reuters News Service*, Chicago
- Rishi AS, Nelson ND, Goyal A (2001) Molecular farming in plants: a current perspective. *J Plant Biochem Biotechnol* 10:1–12
- Schmer MR, Vogel KP, Mitchell RB, Moser LE, Eskridge KM, Perrin RK (2006) Establishment stand thresholds for switchgrass grown as a bioenergy crop. *Crop Sci* 46:157–161
- Schwarzenegger A (2006) Executive Order S-06-06 by the Governor of the State of California [Online]. Available at <http://gov.ca.gov/index.php?/executive-order/183/> (posted 25 April 2006; verified 7 January 2007). State of California, Sacramento, CA
- Singh V, Batie CJ, Aux GW, Rausch KD, Miller C (2006) Dry-grind processing of corn with endogenous liquification enzymes. *Cereal Chem* 83:317–320

- Snow AA, Palma PM (1997) Commercialization of transgenic plants: potential ecological risks. *BioScience* 47:86–96
- State of Illinois (2006) Gov. Blagojevich unveils ambitious energy independence plan to reduce Illinois' reliance on foreign oil [Online]. Available at <http://www100.state.il.us/PressReleases/PressReleasesListShow.cfm?RecNum=5200> (posted 22 August 2006; verified 7 January 2007). Office of the Governor
- Stewart CN (2007) Biofuels and biocontainment. *Nat Biotechnol* 25:283–284
- Stewart CN, Halfhill MD, Warwick SI (2003) Transgene introgression from genetically modified crops to their wild relatives *Nat Rev Genet* 4:806–817
- Strauss SH (2003) Genomics, genetic engineering, and domestication of crops. *Science* 300:61–62
- Strauss SH, Bradshaw HDT (2001) Forest biotechnology perspective. In: Strauss SH, Bradshaw HDT (eds) First international symposium on ecological and societal aspects of transgenic plantations. College of Forestry, Oregon State University, OR, pp 223–224
- Sun Grant Initiative (2007) Initiative Description [Online]. Available at <http://www.sungrant.org/description.cfm> (verified March 11, 2007)
- Tilman D, Hill J, Lehman C (2006) Carbon-negative biofuels from low-input high-diversity grassland biomass. *Science* 314:1598–1600
- Trewavas AJ, Leaver CJ (2001) Is opposition to GM crops science or politics? An investigation into the arguments that GM crops pose a particular threat to the environment. *EMBO reports* 2:455–459
- Twyman RM, Stoger E, Schillberg S, Christou P, Fischer R (2003) Molecular farming in plants: host systems and expression technology. *Trends Biotechnol* 21:570–578
- Tyson KS (2005) DOE analysis of fuels and coproducts from lipids. *Fuel Process Technol* 86:1127–1136
- US Congress (2000) Biomass Research and Development Act. Bill No. 106–224. 106th Session
- US Congress (2005) Energy Policy Act. Bill No. 109–58. 109th Session
- US DOE (2006) Breaking the biological barriers to cellulosic ethanol: a joint research agenda. DOE/SC-0095, Office of Science and Office of Energy Efficiency and Renewable Energy, US Department of Energy, Washington, DC
- Ulgiati S (2001) A comprehensive energy and economic assessment of biofuels: when “green” is not enough. *Crit Rev Plant Sci* 20:71–106
- Umezawa T, Fujita M, Fujita Y, Yamaguchi-Shinozaki K, Shinozaki K (2006) Engineering drought tolerance in plants: discovering and tailoring genes to unlock the future. *Current Opin Biotechnol* 17:113–122
- USDA (2006) Fact sheet: genetically engineered rice. Release No. 0306.06. US Department of Agriculture, Washington, DC
- USDA-APHIS (2006) Draft guidance for APHIS permits for field testing or movement of organisms with pharmaceutical or industrial intent. Biotechnology Regulatory Services, USDA-APHIS, Washington, DC
- USFDA, USDA-APHIS (2002) Guidance for industry: drugs, biologics, and medical devices derived from bioengineered plants for use in humans and animals. US Food and Drug Agency and US Department of Agriculture, Washington, DC
- US DOE (2006) Breaking the biological barriers to cellulosic ethanol: a joint research agenda. DOE/SC-0095, Office of Science and Office of Energy Efficiency and Renewable Energy, U.S. Department of Energy, Washington, DC
- Van Camp W (2005) Yield enhancement genes: seeds for growth. *Curr Opin Biotechnol* 16:147–153
- Vinocur B, Altman A (2005) Recent advances in engineering plant tolerance to abiotic stress: achievements and limitations. *Curr Opin Biotechnol* 16:123–132
- Vogel KP, Jung H-JG (2001) Genetic modification of herbaceous plants for feed and fuel. *Crit Rev Plant Sci* 20:15–50
- Wang Z-Y, Ge Y (2006) Recent advances in genetic transformation of forage and turf grasses. *In Vitro Cell Dev Biol Plant* 42:1–18
- Watrud LS, Lee EH, Fairbrother A, Burdick C, Reichman JR, Bollman M, Storm M, King G, Van de Water PK (2004) Evidence for landscape-level, pollen-mediated gene flow from genetically modified creeping bentgrass with *CP4 EPSPS* as a marker. *Proc Natl Acad Sci USA* 101:14533–14538
- Wolfenbarger LL, Phifer PR (2000) The ecological risks and benefits of genetically engineered plants. *Science* 290:2088–2093
- World Agricultural Outlook Board (2006) USDA Agricultural Baseline Projections to 2015. USDA OCE-2006-1 [Online]. Available at <http://www.ers.usda.gov/Publications/OCE061> (posted 10 February 2006; verified 7 January 2007). Economic Research Service, USDA, Washington, DC