Navigating Existing US regulations on Forest Biotechnology Research

May 2011 by Mr. Tom Redick

In agriculture, biotech crops were rapidly adopted in the US and to a lesser extent worldwide (over 800 million hectares in just over a decade[1]). This brought substantial environmental or human health benefits and improved various agricultural systems while increasing yield in some instances[2;3;4]. Biotech trees released into forests have the potential to promote ecosystem sustainability, and bring life cycle benefits for greenhouse gas mitigation[5]. This can occur via traits that speed growth or increase nut yields, reduce runoff in forest management, reduce pest damage, and improve stress tolerances so trees can be grown with less water, fertilizer, or crop protection inputs. To reap the benefits of biotech trees in U.S. forests, innovators in tree breeding must first navigate the research and development pathway. This includes regulatory and marketplace approval, including stakeholders who value the forest for aesthetic, recreational and ecological interests. A recent survey of forest scientists about how regulations affect the development of transgenic forest biotechnology in the USA cited research in "containment options" as the number one research priority[6]. However, the development and field verification of containment technology performance is itself made extremely difficult by today's process-based regulations, including by a ban on field trials with GURTs (genetic use restriction technologies) that has been recommended by parties to the Cartagena Protocol on Biosafety[7].

While the US has only one federal law specific to GE crops (the 2000 Plant Protection Act) this law was tinkered with the 1986 "Coordinated Framework"[8] and again in the 2008 Farm Bill, arguably expanding USDA's authority to regulate biotech crops. This existing regulatory authority to regulate biotech organisms is distributed through three agencies:

1. The United States Department of Agriculture, Animal and Plant Health Inspection Service (APHIS), for all crops under their authority to regulate introductions of agricultural pests and noxious weeds;
2. The Environmental Protection Agency (EPA) for plant-incorporated protectants (PIPs), including fungicides, against various plant pests; and
3. The Food and Drug Administration (FDA). These cover virtually all recombinant DNA plant breeding, while comparable traits (e.g., herbicide-resistance, pest tolerance) obtained through conventional breeding continues to be unregulated.

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[1] International Service for the Acquisition of Agri-biotech Applications. 2007. Global Status of Commercialized Biotech/GM crops. ISAAA. 16 July 2010; www.isaaa.org/Resources/Publications/ briefs/37/executivesummary/default.html

[2] Brookes G, Barfoot P. 2005. GM crops: The global economic and envi- ronmental impact: The first nine years 1996–2004. AgBioForum 8: 187–196.

[3] Fernandez-Cornejo J, Caswell M. 2006. The First Decade of Genetically Engineered Crops in the United States. US Department of Agriculture Economic Information Bulletin 11. (25 June 2010; www.ers.usda.gov/ publications/eib11/eib11.pdf)

[4] Kleter GA, Bhula R, Bodnaruk K. 2007. Altered pesticide use on transgenic crops and the associated general impact from an environmental per- spective. Pest Management Science 63: 1107–1115.

[5] Sheehan JJ. 2009. Biofuels and the conundrum of sustainability. Current Opinion in Biotechnology 20: Table 1: 318–324.

[6] Strauss SH, Schmitt M, Sedjo R. 2009. Forest scientist views of obstacles to research and commercial development of transgenic forest biotechnology. Journal of Forestry 107: 350–357.

[7] Strauss SH, et al. 2009. Strangled at birth? Forest biotech and the Conven- tion on Biological Diversity. Nature Biotechnology 27: Box 1: 519–527.

[8] Office of Science and Technology Policy. 1986. Coordinated framework for regulation of biotechnology. Federal Register 51: 23302–23309.

In 2009, the USDA Forest Service, in cooperation with a power company (Duke Energy) and a foundation (the U.S. Endowment for Forestry and Communities), formed the Forest Health Initiative (FHI). See www.foresthealthinitiative.org (last visited Mar. 23, 2010). FHI is a "collaborative effort to advance the country's understanding and role of biotechnology to address some of today's most pressing forest health challenges." FHI plans to build on the extensive research already accomplished on the American chestnut by the American Chestnut Foundation and others as a model system for how biotechnology can potentially protect trees. This approach is being accomplished in conjunction with coordinated efforts directed to social/environmental issues and regulatory requirements.

A first step will be to safely and effectively develop an American chestnut that resists chestnut blight and root rot. Researchers have biotech versions of the American chestnut in sapling form, too young to determine their viability against the fungus. This could restore the original American chestnut – fast growing to 100 feet tall – back to its former glory in the forests of the Eastern U.S.

The Food and Drug Administration (FDA) would expect, under its "voluntary consultation" process, to hear about plans to develop a GE American Chestnut to introduce to North American forests[9] and which produces nuts that are used for food by humans, as well as wildlife (the latter is only an FDA concern insofar as they conduct cursory assessments of environmental impacts). This tree can also be an energy crop due to its very fast growth on poor soils and its calorie-rich wood, and parallel to the biotech breeding effort, traditional breeding methods are producing 15/16 Chinese-American hybrid chestnuts. Before tree breeders succeed in restoring the American Chestnut to all or part of its natural range, they must develop and test a number of varieties to find those that are adequately resistant to the invasive exotic chestnut blight fungus that devastated this tree in the first half of the 20th Century. Chestnuts might encounter other serious pest threats like the *Phytophthora* blight that is attacking oaks in the US. Full and timely restoration is likely to require a combination of conventional hybridization/backcross and biotech tree breeding methods.

The EPA regulates plants with genes that provide protection against any form of pest, but only if breeding employs GE methods (as this is considered most likely to lead to new types of toxicological exposures)[10]. If a fungicidal trait were bred into a Chestnut tree using biotech methods, this would be a regulated PIP. There are new methods of genetic manipulation ("Cisgenics") that move DNA around within closely related plant species, and which might not trigger the same regulatory response (but there is no guarantee that the regulatory review might expand to address this, as Canada's regulatory oversight expanded to cover non-GMO herbicide-resistance and other traits produced using mutagenesis forms of plant breeding).

APHIS has generally been reviewing and approving biotech crops under its "plant pest" authority as "regulated articles" that require field trials, with EPA approval required for PIPs. For field trials over 10 acres, EPA needs an "Experimental Use Permit". Evaluations of a crop with a new GE trait would normally proceed thorough four general stages:

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[9] Merkle SA, et al. 2007. Restoration of threatened species: A noble cause for transgenic trees. Tree Genetics and Genomes 3: 111–118.

[10] Environmental Protection Agency. 2001. Regulations under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-incorporated Protectants (Formerly Plant-Pesticides). Federal Register 66: 37771–37817.

1. Lab/greenhouse studies to observe, under controlled conditions, the existence of a desirable trait imparted by a gene in a model species and a model crop variety;
2. Limited field trials in one or a few model varieties and environments to see if the trait persists in the field to a useful degree, or has adverse consequences for other traits. Most genes that pass stage 1 fail at this second stage.
3. Testing of several different forms of the gene that might have different promoters to vary expression pattern and level, and includes a large number of different insertion events to identify those with favorable expression patterns. This stage also normally includes an initial analysis of agronomic properties, though in a limited sample of commercial varieties and environments. During this process, there are usually hundreds to thousands of other genotypes under evaluation at the same locations for general plant breeding goals that must be kept free of any possible comingling. Thus, the tracking of all of the inserts, and accounting for the containment of each, presents a logistical problem, even without flowering.
4. Movement of the gene into a variety of different commercial genotypes and testing in a wide variety of environments for the new trait and agronomic properties. These tests are essentially normal breeding trials, except for the required regulatory approvals, monitoring, use of buffer zones, and other steps required to assure segregation from actual commercial varieties and products. As evidenced by the many cases of adventitious presence of unapproved GE varieties that have entered the food supply at a low level, this is perhaps the most risky step in crop development when using transgenes. For example, a chestnut grove growing food chestnuts for export to overseas buyer would have to avoid pollen flow from a flowering biotech American chestnut.

Effective confinement of propagules therefore generally means the complete prevention of flowering, via GURTs or manual bagging over all flowers on every experimental plant. Manual bagging is extremely difficult and costly for large-scale plant breeding in any crop, and may be too risky given the legal consequences of comingling discussed above, especially for public sector breeders or small companies[11]. Due to most trees' large size, it is virtually impossible to remove or bag all flowers on large trees such as poplars once they are beyond the small scale field trial stage and into larger scale field evaluation and variety development (stages 3 and 4 above).

Potential Impact of Emerging US regulations on Biotechnology Research

As noted above, USDA is considering a number of changes in its regulations about transgenic plants, publishing a draft environmental impact statement in 2007 (APHIS 2007a, APHIS 2007c), and draft rules for GE crops in 2008 (APHIS 2008c).

In the 2007 and 2008 GE regulatory proposals, APHIS has suggested a preferred alternative to regulate all GE organisms as noxious weeds, ensuring that all GE crops are subject to regulation. At present, APHIS only has authority to regulate GE crops with sequences derived from plant pests, or that are truly plant pests (e.g., a parasitic GE plant). In practice, however, all commercialized GE crops appear to have gone through USDA for approval. Although APHIS seems unlikely to treat every GE plant as equivalent to a noxious weed, it remains unclear what a change in

[11] Vinluan F. 2009. Genetically modified rice leads to ruling against Bayer CropScience. Triangle Business Journal. 7 December. (16 July 2010; http://greenbio.checkbiotech.org/news/genetically_modified_rice_leads_ruling_against_bayer_cropscience)

regulatory coverage may mean for researchers, developers, markets, and public perception.

The 2000 Plant Protection Act (PPA) expanded APHIS authority over "noxious weeds" but APHIS has not yet determined what "other effects" it might assert responsibility to manage. Secretary Vilsack has promised to finalize regulations and issue them for public comment soon, since USDA did not meet the 18 month deadline set by Congress. Coexistence issues are at the top of USDA's agenda, given litigation stopping approval of two Roundup Ready® crops – sugar beets and alfalfa (Monsanto's Roundup Ready "RR" Alfalfa reached the US Supreme Court). This litigation could force USDA to consider, for any biotech chestnut tree, various indirect commingling "injury" or economic damage to alternative agriculture (organic or non-GMO) chestnut. This economic risk should not make a "noxious weed" of a biotech plant that has US Approval, but APHIS may soon have new regulatory authority to look beyond plant pest risks and agronomic impacts to "other effects" under the PPA. USDA is considering a number of changes in its regulations about transgenic plants, publishing a draft environmental impact statement in 2007[12;13] and draft rules for GE crops in 2008[14].

USDA's controversial decision to grant nationwide approval for RR Alfalfa in February 2011 was due to its perceived "limited authority" legally restricting its review to "plant pest" risks. Other pending litigation by CFS against GE eucalyptus trees challenges USDA to use the 2008 Farm Bill (which still has not been fully implemented by USDA) to expand its regulatory oversight to include "other effects" of "noxious weeds" to put herbicide-resistant crops into tighter containment. This litigation is pressuring the USDA to issue new rules under the 2008 Farm Bill, which could expand its authority over "noxious weeds" to make approvals more cumbersome for many biotech crops.

USDA Secretary Vilsack spoke in early April to the Organic Trade Association policy conference, noting that the now-overdue Plant Protection Act regulations (which Congress wanted by 2010) would address hot-button issues as noxious weeds and economic harm from biotech crops commingling with organic or non-GMO crops. He assured the producers that USDA is in the process of finalizing the needed regulations in order to "properly evaluate biotech crops" and their potential impacts. USDA will not dictate "co-existence" rules but instead to get the "good, hard-working, fundamentally sound folks" on both sides of the biotech issue to agree on reasonable solutions among themselves. Moreover, he still supports a compensation fund for organic and NonGMO contamination claims as a possible option. The bottom line – plant pest-based regulatory limits are soon to be a thing of the past. This will mean more extensive review of economic impacts and perhaps some USDA victories on NEPA claims in the courts, with even more need for the third party review that USDA is seeking to test out.

The threat posed by NEPA litigation and nationwide injunctions stopping sale (which occurred to Roundup Ready ("RR") Alfalfa in 2007) is among the biggest potential barriers to entry for the pipeline of biotech American chestnuts and other biotech trees. In response to this threat, the biotech tree industry has begun to discuss with

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[12] APHIS 2007. Programmatic Environmental Impact Statement. USDA APHIS. (25 June 2010; www.aphis.usda.gov/publications/biotechnol- ogy/content/printable_version/fs_programmatic_eis.pdf)

[13] AHPIS 2007. Introduction of organisms and products altered or produce through genetic engineering. Federal Register 72: 39021–39025.

[14] APHIS 2008. Proposed rules for the importation, interstate movement, and release into the environment of certain genetically engineered organisms. Federal Register 73: 60008–60048.

USDA the concept of using industry-funded third party consultants to conduct the USDA-required environmental assessments or more detailed "environmental impact statements" ("EIS"). USDA does not have the resources to conduct these EA's and court-ordered EIS reviews (as occurred with RR Alfalfa and RR Beets under court orders now on appeal, one to the Supreme Court). With third-party review, USDA may open its bottleneck in regulatory approval while simultaneously addressing the threat of NEPA injunctions. In another effort to stem the tide of NEPA litigation that is extending US biotech approvals into multi-year messes, the APHIS biotech unit has asked for volunteers for a NEPA pilot project that will attempt to improve EIS handling, increasing improve the quality, timeliness, and cost effectiveness of NEPA environmental impact reviews. See, Solicitation of Letters of Interest To Participate in National Environmental Policy Act Pilot Project**,** 76 Federal Register 19309-19310, April 7, 2011 at www.edocket.access.gpo.gov/2011/2011-8329.htm. APHIS has asked for volunteers for a NEPA pilot project involving non-USDA consultants to conduct regulatory environmental reviews, including any court-ordered Environmental Impact Statement ("EIS") that will lead to faster approvals. While larger companies can afford to pay this for faster approval, smaller companies consider it a cost that they can ill afford. As a result, this pilot may not lead to changes in USDA policy.

In the case of nationwide approval for planting biotech trees, the USDA may need policy support from the regulatory framework that already exists to conduct third party review, mainly occurring to date under the USDA Forest Service, which has been subject to EIS requirements under NEPA for decades on a localized project basis. The industry approach is likely to seek a "pilot" or trial period to determine the viability of this process – biotech trees could be in such a pilot. This proposed approach invites comparison to the Food and Drug Administration's use of third-party reviewers for medical devices, which succeeded and broke a logjam in approvals in the 1990's (with some notable rollbacks that merit study to avoid similar problems with a biotech tree pilot program).

Potential Impact of Existing and Near-Term Case Law on Biotechnology Research

There are two types of cases pending that will determine how biotech seed companies need to manage the risks of causing economic loss to non-biotech growers. The first is a series of federal lawsuits, starting with *Geertson v. USDA,* under the National Environmental Policy Act (NEPA), with anti-biotech activists and organic growers suing to challenge USDA policy of conducting relatively quick environmental assessments (with a finding of no significant impact) rather than the multi-year environmental impact statements that California federal courts have ordered. The second involves the common law liability of biotech seed companies, in a jury trial underway in St. Louis federal court (*In re LL601 Rice Contamination),* for experimental rice that commingled, prior to US approval, with the foundation seed used in rice production throughout the US, causing loss of the European Union market for export-oriented growers. The LLRice 601 case is costly civil liability arising from unauthorized releases from biotech rice field trials that led to comingling of research genes with the commercial seed supply, and this billion-dollar liability is likely to cause reexamination of the the risks of many cooperative breeding programs between biotechnology companies and research universities.

A. Under Geertson, Federal Law Mandates Segregation of Biotech Crops

In the first case addressing agricultural biotechnology's environmental impacts, the Supreme Court in *Geertson v. USDA*[15] ruled 7-1 on June 22, 2010 to reverse a three-year-old injunction against planting Monsanto's Roundup Ready™ alfalfa ("RR Alfalfa "). This ban was granted in 2007 on a preliminary injunction motion by California District Court Judge Charles Breyer (the brother of the environmental regulation scholar, Justice Breyer, who recused himself) effectively halting further planting of Monsanto's Roundup Ready™ alfalfa.

First, the good news for the biotech seed industry: USDA is freed from the nationwide injunction. Second, the Supreme Court found USDA's granting nationwide approval to RR Alfalfa may have been overly broad, given impacts to organic and "non-GMO" crops. While RR Alfalfa is unchained, USDA has to find a way to change the nationwide launch of biotech crops that it approves (wherever there is a legally recognized risk of an economic impact to organic, non-GMO or export-oriented crops.) A Monsanto representative hailed the decision as "exceptionally good news" that would allow farmers to plant the crop in the coming season, which would presumably include late-season planting in 2010. The Center for Food Safety, which is filing NEPA cases (including the pending RR Beets and Eucalyptus cases noted below) warn that the ruling still makes it illegal for farmers to use the seed until the USDA EIS is out. USDA just closed comment on the EIS which will be out in early 2011.

Second, Justice Samuel Alito wrote that while the court went too far in issuing a nationwide ban on the seeds, the court correctly ruled in sending the deregulation of the crop back to the Agriculture Department to conduct an environmental impact study. While "contamination" of other crops must be avoided, the choice of remedy was too drastic given USDA's proposed judgment.

The future of USDA containment of contamination may lie in its proposed "partial deregulation" that would have kept RR Alfalfa contained using the following mandates:

1. Isolation distances between RRA and other alfalfa to avoid gene flow;
2. Harvesting conditions;
3. Steam-cleaned planting and harvesting equipment after RRA and before further use with other alfalfa;
4. Identification and handling (i.e., traceability) for RRA seed;
5. RRA grower contracts requiring compliance with all other limitations set out in the proposed judgment.

A partial release pending EIS review would have prevented the injury to organic and non-GMO farmers, and the Supreme Court found that this fact was conceded by plaintiffs; hence the District Court should have remanded the matter "to the [USDA] so that it could determine whether to pursue a partial deregulation during the pendency of the EIS process." *Geertson* at 4. If USDA had been allowed to establish a regional approach, it could have found the middle path and removed the threat of harm that the plaintiff-respondents feared. (If USDA's approach failed to address the risk, it can expect another lawsuit challenging that partial deregulation decision).

[15] http://en.wikipedia.org/wiki/Monsanto_Co._v._Geertson_Seed_Farms

The Supreme Court sent a message to both USDA and biotech seed companies, however, when it rejected Monsanto and other petitioners argument[16] that protection against the risk of commercial harm was not "an interest that NEPA was enacted to address." The Supreme Court held that the uncontested fact that there was a "risk that the RRA gene conferring glyphosate resistance will infect conventional and organic alfalfa" was a "significant" impact worth protecting from harm. Moreover, Monsanto's hope to plant RR alfalfa in Fall 2010 might run afoul of the order that no RR alfalfa "can be grown or sold until such time as a new deregulation decision is in place."*Geertson* at 22.

In sum, this historic Supreme Court ruling shunned the blunt-object nationwide approaches that both the District Court and USDA took to complex agricultural management and coexistence questions. USDA will have to manage the interrelated economic and environmental impacts of biotech crops better; the federal courts may be called upon to determine if a partial deregulation is adequate.

Geertson will influence two NEPA cases pending against "GMOs". First, in a hearing to be held in August 2010, USDA and Monsanto will seek to prevent another nationwide injunction (against RR Beets, after a summary judgment requiring an EIS). The judge denied a previous preliminary injunction motion due to excessive delay in bringing the motion, since over 90% of US acres are planted in RR Beets. Briefing filed on July 9 by plaintiffs suggested that they would like to see a partial deregulation from USDA that protected the interests they represent – but they reserve the legal right to challenge such decisions.

The second NEPA case was filed promptly on July 1, 2010 in Florida U.S. District Court (by the same activist groups who delayed with RR beets) suing USDA for its approval of Arborgen's biotech eucalyptus in *Center for Biological Diversity v. U.S. Department of Agriculture*, U.S. District Court, Southern District of Florida (West Palm Beach)[17].

Both judges should follow the Geertson lead and the case to USDA for partial deregulation pending completion of the EIS. With more limited launches and legal challenges to EIS findings ahead, however, innovation in biotech crops may suffer over the coming decade. For biotech trees, the increased level of regulatory oversight – now confirmed by the US Supreme Court – will provide innovators with a clearer path to market. If USDA takes its new mandate seriously, its partial deregulations will include plans for peaceful coexistence without litigation over economic impacts. This could lead to a friendlier legal environment for biotech trees.

B. Bayer Mass Tort Trials Add up to Billions in Liability Risk

In the second landmark case, *In re LL601 Rice Contamination*, Bayer Crop Sciences is defending nuisance and negligence claims for an illegal release of experimental herbicide-resistant Liberty Link® rice that commingled in export-bound rice in 2006-2007, causing rice prices to drop. The jury trials of test plaintiffs (from a growing pool of 6,000) started in December 2009, continuing through this year. Plaintiffs prevailed in four trials, with juries finding Bayer Cropsciences negligent in allowing its Louisiana-based field trials of herbicide-resistant Liberty Link rice to be too close to the foundation seed used in US rice production. While the planting distances that

[16] *Bennett v. Spear*, 520 U. S. 154, 162–163 (1997)
[17] http://www.biologicaldiversity.org/news/center/articles/2010/businessweek-07-01-2010.html

the Louisiana State researcher used were adequate, commingling occurred during post-harvest handling, according to plaintiffs' experts on identity preservation.

Bayer has lost a series of trials, and the statute of limitations of five years has not yet run, so more cases may be filed. Bayer is facing compensatory damage awards estimated at over $4 billion, if 6,000 farmers recover similar amounts (verdicts are averaging over $550,000 in compensatory damages). Most notably, an Arkansas jury awarded Arkansas farmers $48 million in punitive damages on April 14, 2010 in the fourth trial. Bayer may feel compelled to appeal this case to higher courts – potentially making legal precedent that will influence future cases.

Like the Supreme Court, these jurors are seeing economic damage to other crops as a problem that biotech seed companies should have paid more attention to in years past. The future of biotech crops and the companies that sell them will depend upon continuous improvement in stewardship strategies that protect export, non-GMO and organic interests from undue economic impact.

C. Will State Common Law Nuisance Evolve in Response to Geertson?

US courts have yet to rule that the sale of USDA-approved biotech crops that lack approval in major markets overseas is common law nuisance or negligence, where there is a prevailing standard of care that requires biotech seed companies to avoid export impact. For example, the American Soybean Association has long required, as a matter of "due care" in stewardship, that biotech seed companies obtain export approvals in all major overseas markets before commercial launch. Any biotech soybean lacking this approval has to be produced in closed-loop identity preservation (similar to the USDA proposed "partial deregulation").

Moreover The Supreme Court's finding of "contamination" under NEPA could influence common law rulings. For example, this finding could also influence some courts to require that biotech crops be "fenced-in" in regions that depend on exports or non-GMO/organic markets, as has occurred with livestock in the East. See, A. Bryan Endres, **Coexistence Strategies, the Common Law of Biotechnology and Economic Liability Risks**, 13 Drake J. Agric. L. 115-148 (Spring 2008).

The preemptive or presumptive power of US approval under new partial deregulation decisions remains to be determined. Will evidence of compliance with federally-mandated identity preservation provide a defense for biotech seed companies? For example, if USDA implements a partial deregulation approach for a controversial new biotech corn from Syngenta that contains amylase, this Environmental Assessment Finding of No Significant Impact (EA-FONSI) might survive legal challenges. (See, Environmental Assessment for Syngenta Event 3272, available at www.aphis.usda.gov/brs/aphisdocs/05_28001p_ea.pdf *).* This may also be sufficiently protective of economic impacts to avoid common law nuisance liability.

D. Conclusion

Going forward, both USDA and biotech seed companies will need to monitor and prevent economic impacts, even after regulatory approval. USDA assessments of environmental impacts must include relevant economic interests, and maintain peaceful coexistence between and among biotech, non-GMO and organics. In avoiding new commingling episodes, they will prevent nuisance liability for the seed companies selling those biotech crops. As biotech trees, including the American chestnut, enter the marketplace and environment in the coming decade, their economic impacts will be assessed and they will find their proper place.