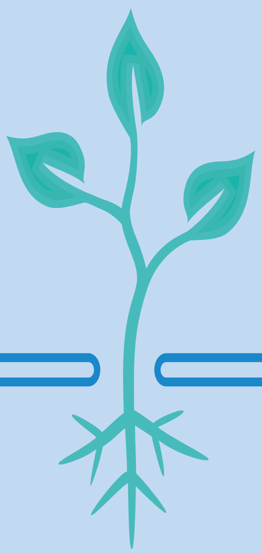
GM Alfalfa

examining the benefits, costs, and potential for genetic cross-contamination

by Madeline Fisher



To say that the USDA's deregulation of "Roundup Ready" alfalfa has brought renewed attention to genetically modified (GM) crops is something of an understatement. Since the agency ruled in January to allow unrestricted planting of alfalfa bioengineered to tolerate the herbicide glyphosate (Roundup), food safety advocates have charged that GM alfalfa will contaminate both conventional and organic alfalfa crops. Others are predicting an end to the nation's organic dairy industry. And there has been particular scorn for the USDA, which critics say turned its back on an opportunity to address the concerns of all farmers and find ways for them to coexist.

What has gone mostly unreported amid the hue and cry, however, is the alfalfa industry's quiet pursuit over the past several years of this very coexistence. Since at least 2007, seed companies have been meeting with "organic growers, growers who want to plant biotech, and everyone in between" to develop practices and programs that will mitigate gene flow between GM and non-GM alfalfa, says CSSA member Mark McCaslin, who is president of the alfalfa seed company Forage Genetics International. The industry also established a third-party monitoring system to keep tabs on any gene flow that does occur. Some will undoubtedly view these measures with skepticism, but they haven't been taken to appease critics. They're meant to protect the alfalfa industry itself, McCaslin says.

Forage Genetics, for example, is probably best known at present for helping Monsanto bring Roundup Ready alfalfa to market. But like many seed companies today, it doesn't just do genetic manipulation, breeding, and trait development, but also seed production, marketing, and sales. "We market transgenic alfalfa, and we market organic alfalfa seed," McCaslin says. "We're probably one of the largest exporters of seed to international markets." Thus, while the company will obviously gain from sales of its new GM varieties, Forage Genetics and others like it will also lose if foreign genes, or "transgenes," spread widely.

"So coexistence is an important part of our business," McCaslin says. "There has been a lot of conversation within the industry to make sure we do this right."

Redesigning Alfalfa with Transgenics

What's at stake isn't just the ability to spray glyphosate on alfalfa, which some opponents call a solution to a nonexistent problem. Alfalfa, like all crops, faces many real problems that transgenic technology—along with conventional breeding and non-GM molecular methods—could help solve. Heat and drought are becoming more common, for example, as global temperatures climb. Alfalfa is also unusually sensitive to acidic soil conditions along with concomitant high aluminum concentrations, both of which are on the rise as well.

But perhaps most pressing is how this "queen of forages" is being replaced in the dairy cow diet by corn silage and other feed sources—a trend that ASA Fellow Neal Martin, director of the U.S. Dairy Forage Research Center (part of the USDA-ARS) in Madison, WI, dearly wants to reverse. Alfalfa not only benefits cow health, asserts Martin, but also the environment when planted in rotation with corn. It's a perennial, so it mitigates soil erosion. It's also a nitrogen-fixing legume that reduces the need for nitrogen fertilizer in corn. Most of all, Martin says, alfalfa's deep roots can scavenge nitrate that will otherwise end up in tile lines—a huge

Left: Shanmugam Rajasekar, Noble Foundation research associate, makes crosses in low-lignin alfalfa as part of the institution's transgenic breeding program. **Below:** Charles Brummer (left), director of the Noble Foundation Forage Improvement Division, discusses the progress of alfalfa research with postdoctoral fellow Xuehui Li.

plus if the federal government begins regulating nitrate discharges from the tile system.

To begin planting alfalfa again, though, farmers will need the right incentives. "So we're trying to redesign alfalfa, so that the reason alfalfa will come back into the diet is economically driven," Martin says. "Economics still drives the truck. Farmers are trying to survive with relatively low milk prices and high feed prices right now."

Despite recent declines in acreage, alfalfa is still America's fourth largest crop, behind corn, soybeans, and wheat. Some 22 to 23 million acres of hay are grown each year in nearly every U.S. state, mainly to feed beef cattle and dairy cows. About 1% of the hay crop is organic.

Genetic Mixing in Alfalfa

Alfalfa's importance as a livestock feed is what has the organic beef and dairy industries upset over the approval of GM varieties, but most agronomists agree there is little chance of genetic mixing between GM and non-GM hay. For one, hay is grown for forage rather than seed (like corn and soybeans), and farmers typically harvest it when the first flower buds appear or shortly afterward, says Purdue University crop physiologist Jeff Volenec, an ASA and CSSA Fellow and CSSA president-elect. If alfalfa is allowed to flower, forage quality drops precipitously, Volenec adds. "So you rarely find an alfalfa field with very many blooms in it."

Alfalfa is also bee- rather than wind-pollinated, putting up a second barrier. Say, for instance, that a few plants along a field edge aren't cut before they flower or some feral alfalfa blooms in a ditch. Pollination is limited because most hay-growing regions of the country lack the right bees to carry the pollen between plants, says University of Wisconsin–Madison agronomist and ASA and CSSA Fellow Dan Undersander. Moreover, even if two hay patches were blooming concurrently, bees were around, and pollinated flowers were allowed to form seed, those seeds would have only a tiny chance of germinating, Undersander adds. That's because alfalfa is "autotoxic": Mature plants produce soil chemicals that keep new seedlings from establishing.

In short, McCaslin says, alfalfa's biology combined with its cutting management makes genetic cross-contamination between hay fields unlikely. "A whole series of things would all have to happen in sequence," he says. "You break any one of them, and you eliminate the opportunity for gene flow."

Alfalfa is not only grown for cattle feed, however. On roughly 100,000 acres in 13 western states, it's also grown for seed, using three species of cultivated bees as pollinators. The United States is in fact the largest alfalfa seed producer in the world, with about 20% of the crop destined for overseas markets. Those markets and the fact that seed is allowed to ripen make gene flow between GM and non-GM plants a genuine concern in these areas, which is why the industry has focused on them in pursuing coexistence.

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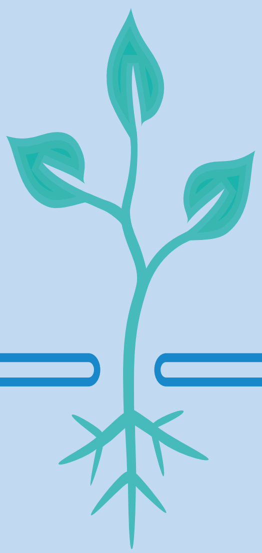


Based on crude estimates of how far the three bee species travel, the industry for years has imposed isolation distances of 165 ft between one seed field and another seed field, hay field, or feral alfalfa patch, to ensure the genetic purity of different seed stocks. But when Roundup Ready alfalfa became available in the early 2000s, scientists saw a chance to collect much better data on pollinator-mediated gene flow, McCaslin says.

In roughly 10 studies with the three bees, researchers planted plots of Roundup Ready alfalfa with "trap" plots of conventional alfalfa set at various distances around them. After pollination and seed ripening, seed from the trap plots was harvested, grown in a greenhouse, and the emerging seedlings were sprayed with Roundup to see how many had acquired the glyphosate-tolerance trait. The assay's simplicity permitted scientists to screen hundreds of thousands of seeds, McCaslin says, and thereby measure very low levels of gene flow.

The findings then became the basis for the best practices and stewardship programs that the National Alfalfa and Forage Alliance (NAFA)—alfalfa's version of the National Corn Growers Association—adopted to curb transgene flow. In California, for example, the isolation distance for certified, genetically pure seed remains 165 ft, while for Roundup Ready alfalfa pollinated by honeybees, it's three miles. In other words, McCaslin says, "You can't plant a Roundup Ready seed field in California unless you have three miles of isolation from the nearest conventional seed field. That's extraordinary compared with the certified seed isolation requirements."

Whether the best practices are actually being followed is monitored by another group, the American Organization of Seed Certification Agencies (AOSCA), which oversees the seed certifying, or crop improvement, agencies of each state. Farmers who want to plant a seed field of Roundup Ready alfalfa must first visit their local seed certification office, McCaslin explains, which checks whether they meet the NAFA isolation requirement for their area. If a farmer does meet the requirement, AOSCA records the field's map coordinates and later conducts a field visit to verify the location.

AOSCA doesn't just enforce the requirements, though; it also monitors whether they're having the intended effect. Each year, seed companies and genetic suppliers must submit data on the accidental, or "adventitious," presence of transgenes in non-GM seed, which AOSCA compiles in a national database. NAFA's isolation requirements are designed to keep that presence below 0.05%—a goal that so far is being met, McCaslin says. However, the industry will continue monitoring the effectiveness of the best practices closely and will revise them if they stop working.

Worth the Costs?

In the end, McCaslin believes these self-imposed restrictions and monitoring programs helped convince the USDA to deregulate Roundup Ready alfalfa without adding restrictions of its own. Still, while the approval effort was successful, the work, expense, and uncertainty involved aren't lost on plant breeders like ASA and CSSA member Charlie Brummer, who directs the forage improvement division at the Samuel Roberts Noble Foundation, a nonprofit research institute in Ardmore, OK. That is, although Brummer considers transgenes a valuable breeding tool, he tends to think twice about using them.

Photo of leafcutting bee by Peggy Greb (USDA-ARS). Photo of flowering alfalfa by Danielle Mongrain.

For example, his group's work to improve tall fescue, white clover, and other minor forages is all done through conventional breeding, aided by molecular marker-assisted breeding when appropriate. The reason, he explains, is that unlike alfalfa, these forages have small markets, making it tough for seed companies to justify moving transgenic varieties through the regulatory process. The cost of doing so would likely never be recouped.

Similarly, because the goal always is to get new varieties into farmers' hands, Noble researchers minimize the use of transgenes in crops where they anticipate large regulatory hurdles, Brummer says. One exception is switchgrass, which Noble is funded to study through a number of outside grants. Earlier this year, a research team led by Noble professor Zeng-yu Wang reported in the *Proceedings of the National Academy of Sciences* on a transgenic switchgrass that produces less lignin and could therefore be a better feedstock for cellulosic ethanol production. But switchgrass is also a wind-pollinated, native prairie species, suggesting the likelihood of unwanted gene flow could be high and, thus, the chances of deregulation low, Brummer says.

"I think a lot of programs are probably in the same boat," he says. "You can see potential with various transgenes, but you don't see the potential for getting them deregulated."

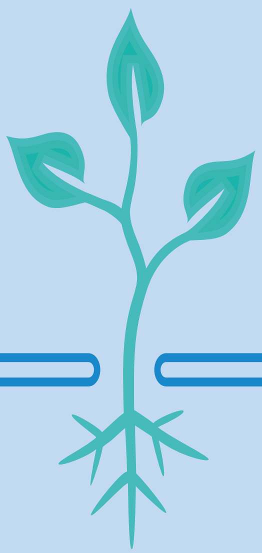
Part of the issue, he thinks, is the black-and-white dichotomy that exists right now between conventionally bred crops, on the one hand, and GM varieties, on the other—a split he finds artificial. For one, adding a transgene doesn't instantly create a commercial cultivar. Any new trait or variation for a trait—whether it comes from a novel source of germplasm or a foreign gene—must be fed into a conventional breeding program to be selected upon and crossed. "That's essentially what plant breeders always do," he says.

Secondly, although the gene for Roundup resistance confers a brand new trait on alfalfa, many other transgenes simply broaden a plant's own natural genetic variation. And that, Brummer thinks, is their greatest value.

"At least for me, I'm much more interested in transgenes as a way to expand the variation I can select on in my breeding program," he says. "I'm not just interested in a new herbicide tolerance trait."

Low-Lignin Alfalfa

As an example, he points to a new set of transgenic alfalfa varieties that Forage Genetics is currently testing and taking through the regulatory process, with help from the Dairy Forage Research Center and UW-Madison's Undersander. Developed by Rick Dixon at Noble, the plants produce abnormally low levels of lignin, which coats cellulose and other cell wall polysaccharides in plant tissues, making them difficult for cattle to digest. Feeding trials with the varieties show they can increase the amount of carbohydrate that animals digest by 10%, while simultaneously reduc-



Long Path to Deregulation for Transgenic Crops

When the USDA deregulated Roundup Ready alfalfa earlier this year, it wasn't actually for the first time: The genetically modified crop first received regulatory approval back in 2005. Court challenges in 2006 and 2007 then halted the crop's planting until the USDA could complete an assessment of its environmental impacts—an effort that took nearly four years. By the time the agency ruled in January to allow unrestricted planting of Roundup Ready alfalfa once again, nearly 14 years had passed since Forage Genetics International and Monsanto first began working to bring it to market.

Even without lawsuits and court cases, however, the path to deregulation is long for any crop containing transgenic—or what the industry calls "biotech"—traits. At Pioneer Hi-Bred, a DuPont business, for example, 7 to 10 years typically elapse from the time that a promising transgene is first put into a crop to when Pioneer receives the last regulatory approval needed to launch the new product, says Jerry Flint, the company's senior director of registration and regulatory affairs.

Along the way, a series of complicated and evolving requirements must be met—both within the United States and globally—that can stymie even the smartest Ph.D. "The regulatory system is a necessary component of what we do," Flint says. "But it's not always easy for people to understand."

In the United States, Flint explains, three agencies take part in regulating ag biotech: the USDA, USFDA, and, less frequently, the USEPA. The USFDA examines the safety of biotech traits in food for people and livestock, while the USEPA gets involved when the trait functions as a pesticide, as in Bt corn. The most common participant is the USDA, which evaluates how ag biotech traits will be introduced into the field and used by farmers. Regardless of the agency, though, companies must conduct studies, compile data, and submit a dossier of evidence demonstrating that the new trait is safe for humans and the environment.

This typically takes two to three years at Pioneer, Flint says, but it's only the beginning. After submitting registration packets to U.S. agencies, Pioneer begins the process in other countries—where things can get really complicated. Different countries vary widely in how long they take to review submissions, for example, or even how soon they begin the process. China, for instance, won't look at a submission until the United States has issued its final regulatory approval, Flint says.

Another issue is the evolving nature of global regulatory processes. The requirements of the European Union, in particular, tend to be something of a moving target, Flint says. "So this is a challenge for us, and something we watch as a company."

Litigation, changes in presidential administrations, and increased workloads at agencies, especially the USDA, have also slowed the U.S. regulatory process significantly since the mid- to late-1990s, Flint adds. Still, he looks forward to the future with hope.

"I'm an eternal optimist—I'll just say that up front," he laughs. "But I do think governments and regulatory agencies around the globe realize that we need to streamline these processes and speed things up. Here in the U.S., the USDA has already been talking about this. And I know other countries are doing the same."

ing manure production. In this way, they resemble "brown mid-rib" corn, a variety that produces less lignin because of a natural genetic mutation.

However, such a large lignin reduction in alfalfa would probably never have been possible through conventional breeding, Brummer says: There just isn't enough natural variation in the trait to work with. So, instead, Dixon inserted reversed copies of select lignin biosynthesis genes into the alfalfa genome, whose expression interferes with normal lignin production.

"In one fell swoop, they drop lignin a lot," Brummer says. "And then once a gene is in the plant, there's no reason why you couldn't select for even lower levels through conventional breeding."

Reduced lignin is an important trait that alfalfa growers already manage for, Martin adds. The longer alfalfa matures

in the field, the more lignin it produces, the less digestible it becomes, and the less energy cows can derive from it. So, for years, dairy farmers have controlled forage quality and "put more milk in the tank," Martin says, by cutting alfalfa early and often. In southern Wisconsin, for example, alfalfa is cut up to five times a summer, whereas three or four cuttings used to be the norm.

But all that harvesting comes at a cost: Farmers get higher quality forage, but lower yields. In field trials with the reduced-lignin varieties, on the other hand, Undersander and others showed that plants can be harvested up to 10 days later than standard lines, while still maintaining the same quality. "A farmer in the Madison [Wisconsin] area, for example, could go from four cuttings to three cuttings, get 20% more yield, and the same quality of forage but with less work," Undersander says.

In addition, alfalfa stems from the reduced-lignin lines contain higher amounts of sugars—amounts that suggest they could yield 50% more ethanol than conventional varieties. "So, we're pushing pretty hard for alfalfa to be put on the plate as a cellulosic ethanol source," Martin says.

Reduced-lignin alfalfa could hit the market by 2016 or 2017, and there are several other transgenic varieties lining up behind it. "Alfalfa has about as interesting a pipeline of traits as any other crop I'm aware of," McCaslin says. They include lines bioengineered to make alfalfa protein more digestible, and ones containing an enzyme from red clover, which prevents the breakdown of protein that normally occurs when alfalfa is ensiled.

Company Partnerships Necessary

Meanwhile, the public outcry over Roundup Ready alfalfa continues, with some food safety and organic advocates vowing to sue over the USDA's decision. While alfalfa is the target, however, Brummer thinks the uproar isn't truly about alfalfa at all. What people most object to, he suspects, is the rise of corporate influence in agriculture, with all its perceived negative consequences—in particular, more and more GMOs.

Brummer understands the concerns to some extent. But as a plant breeder at a not-for-profit research institute, he also knows this: The only way that Noble's new varieties will ever become available to farmers is through partnerships with companies like Forage Genetics.

"That's part of the deal: As a non-profit, we have to work with for-profit companies to get varieties out there," he says. "At the end of the day, if you don't have somebody who's in business and is willing to push [new cultivars] through the marketing channels, you can forget about farmers getting to grow them—at least in forages."

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Photo of chopped alfalfa courtesy of the U.S. Dairy Forage Research Center.