

NAVIGATING THE REGULATORY LANDSCAPE:

GENETICALLY MODIFIED PLANT CASE STUDY



Context

Ornamental plants have been used for centuries to add aesthetic appeal to outdoor and indoor spaces. They are valued for their flowers, leaves, scents, texture, fruit, stem, and bark — or simply their unique aesthetic forms. Ornamental plants have been bred to accentuate desirable traits and minimize undesirable ones through traditional cross-breeding, grafting, and other techniques.

Description of the new technology

With the advent of synthetic biology, there are new opportunities to modify ornamental plants in ways that were not available through

traditional techniques. Examples include novelty plants that are bioluminescent and glow in the dark and lawn grasses that require less mowing and are deeper green in color.

Bioluminescent plants are being developed by two companies and each effort provides an instructive example of evolving technologies. Scientists at BioGlow LLC (BioGlow)¹ inserted genes from luminous marine bacteria into *Nicotiana glauca* (jasmine tobacco), a common flowering ornamental plant. They have produced a plant that is autoluminescent, meaning it glows in the dark with only standard plant nutrients. BioGlow's plants have been commercialized and the



company opened a web store in September 2014 (<http://bioglow.us/blogs/news>); as of July 2015, the Biobulb™ is listed for sale in the store (<http://bioglow.us/collections/glowing-plants-2>).

Glowing Plant, Inc. (Glowing Plant),² a company funded through a Kickstarter³ campaign, also developed a luminescent plant. Building on technology similar to BioGlow's, Glowing Plant has inserted genetic material into *Arabidopsis thaliana* (thale cress) using a "gene gun." Genes from *Photinus pyralis* (common eastern firefly) and two synthetic variants of genes from *Aequorea victoria* (crystal jelly) are inserted into the plant's genome.

A January 1, 2015, *New York Times* article describes commercial efforts to develop genetically modified grass that requires less mowing, is deeper green in color, and is resistant to damage by the herbicide glyphosate.⁴ According to the article, the manufacturer introduces genetic material from other plants that are not considered plant pests and inserts the genes with a gene gun. Publicly available information⁵ suggests that *Arabidopsis thaliana* is the source of the glyphosate resistance, but does not disclose the source of the donated genetic material for the color, thickness, and height properties.⁶

These are three examples of a burgeoning market in which companies are seeking to use modern synthetic biology and genetic technologies to develop ornamental plants with desirable characteristics. The source of genetic material and the manner by which it is introduced into the host plant control how these organisms are regulated — or not — as discussed below.

Discussion of the legal and procedural issues

The USDA's APHIS jurisdiction to regulate genetically modified plants depends on the use of a plant pest as part of the genetic engineering technique. Until recently, use of a plant pest as part of genetic engineering was a common practice. If, however, the donor organism, recipient organism, vector, or vector agent does not meet the PPA definition of a plant pest, then APHIS' position is that it does not have regulatory authority over the modified plant. As gene guns and other new synthetic biology techniques typically do not rely on plant pests, plants modified through these techniques will not be subject to APHIS' review. If either the gene donor or recipient species is a plant pest, or if a plant pest, such as an agrobacterium, is used to introduce the genetic material into the host, the PPA will apply and APHIS will retain regulatory oversight.

BioGlow submitted to APHIS the information pertinent to support a regulatory review. Following its review, APHIS concluded in a March 21, 2013, letter that it did not have regulatory jurisdiction over the plants, stating:

APHIS has determined the plants, as described in the letter, are not plant pests, no organisms used as sources of the genetic material to create the plants are plant pests, and the method used to genetically engineer the plants did not involve plant pests.⁷

BioGlow's APHIS application protects the details of the genetic modification so, unfortunately, the genetic source of the bioluminescence and the method used to modify the jasmine tobacco cannot be evaluated here.

The Glowing Plant luminescent plant uses no genetic material from a plant pest, does not use a plant pest as a recipient organism, and no plant pest is used to modify the genes of the host plant. Based on these facts, APHIS reached a conclusion similar to BioGlow's in a letter to Glowing Plant dated December 23, 2014:

No plant pests, unclassified organisms, or organisms whose classification is unknown are being used to genetically engineer this plant. In addition, APHIS has no reason to believe that this plant is a plant pest. Therefore APHIS does not consider the [genetically engineered (GE)] plant as described in your October 1, 2014 letter to be regulated under 7 CFR part 340.⁸

Glowing Plant is an open-source technology and the developers encourage others to further modify the genome of the plant. If others modify the genome of the Glowing Plant, re-submitting notice to APHIS is likely prudent, to confirm that the revised genome similarly is unregulated. As APHIS points out in its response letter:

APHIS' response that follows evaluated your request for this plant species only and the transformation, genes and donors used to produce this specific plant line, therefore, this response is not considered relevant to other plant species, transformation, donors, or genetic material.⁹

Glowing Plant was funded through Kickstarter and offered inducements at a variety of funding levels, which raise separate regulatory issues. Pledges at the \$150

level will receive a glowing plant, which as discussed above does not appear to be regulated, at least not by APHIS under the PPA. Pledges of \$250, however, receive a "DIY MAKER KIT," which includes "a full set of instructions and all the ingredients you need to transform your own plant at home, in your lab or at school." Two notable issues are raised by the DIY kit. First, the DIY kits employ agrobacterium to perform the genetic modification on plants. Agrobacterium is regulated as a plant pest. Consequently, while the Glowing Plant modified by a gene gun may not be regulated under the PPA, the agrobacterium DIY kit is likely regulated, either under PPA or TSCA. Second, the supporter who receives the kit appears to be legally responsible for obtaining a permit from APHIS for plants they transform. Given the likely lack of regulatory sophistication of the typical Kickstarter supporter, there is a significant opportunity for someone unknowingly to violate one of the statutes that regulate genetically modified plants.

Pledges at the \$500 level receive a message (up to 140 characters of the donor's choice) encoded in a string of single-stranded, synthetic DNA using Craig Venter's ASCII-to-DNA translation table. Even though the amounts of DNA produced in this way were exceedingly small, just a few micrograms, their manufacture is regulated by TSCA and the company was required to notify EPA prior to manufacturing the DNA strands. Glowing Plant opted to file a low-volume exemption for each of the message strings ordered by its eligible donors.

The legal and policy takeaway

Whether these plants pose any risks to human health or the environment is unclear. Gaps in federal oversight of such products, however, allow their market entry absent an assessment of potential risk other than simply the presence of plant pests or plant pest genes. Whether these plants may out-compete other plants in the ecosystem into which they are introduced, have an adverse effect on an animal that may consume them, or generate allergens, are among the issues that have not been comprehensively examined under current legal authorities. It is not clear that modern synthetic biology techniques raise greater risk issues than traditional cross breeding, grafting, or irradiation techniques that have been used for decades — or even centuries. These techniques have, in many cases, escaped regulatory scrutiny, but also have not introduced substantial identified risks. It would appear, however, that modern synthetic biology allows a greater range of genetic combinations at a faster pace than previous techniques, thereby meriting a conversation about whether pre-market review is warranted.

To respond to this increased pace and ability to modify plants, APHIS has been attempting to update the regulations governing genetically modified organisms under its purview. APHIS proposed a rule in 2008 and received 88,000 comments.¹⁰ After suggesting it would proceed with a final rulemaking, APHIS formally abandoned that effort on March 4, 2015.¹¹ The Service announced it would restart discussions on modernizing genetically modified organism regulations, starting with “an open and robust policy dialogue to drive the development of a forward-looking rule that will provide a foundation for our future regulatory activities.”¹² In its communication withdrawing the rule, APHIS stated “current regulations have been effective in ensuring the safe introduction of GE organisms,” adding that “revising our biotechnology regulations will better position us to address new challenges, as well as meet current needs in evaluating and addressing the plant pest or noxious weed risks associated with the importation, interstate movement, and field release of certain GE organisms.” This text has since been removed from APHIS’s website.

Endnotes

- 1 BioGlow, available at <http://www.bioglowtech.com/>.
- 2 Glowing Plant, available at <http://www.glowingplant.com/>.
- 3 Kickstarter, Glowing Plants: Natural Lighting with no Electricity, available at <https://www.kickstarter.com/projects/antonyevans/glowing-plants-natural-lighting-with-no-electricit>.
- 4 Andrew Pollack, By “Editing” Plant Genes, Companies Avoid Regulation, N.Y. Times, Jan. 1, 2015, accessed at http://www.nytimes.com/2015/01/02/business/energy-environment/a-gray-area-in-regulation-of-genetically-modified-crops.html?_r=0.
- 5 Letter from Richard Shank, Ph.D., Senior Vice President Regulatory and Government Affairs, The Scotts Miracle-Gro Company, to Tom Vilsack, Secretary, U.S. Department of Agriculture (USDA), September 13, 2010, available at http://www.aphis.usda.gov/brs/aphisdocs/scotts_kbg.pdf (response to Dr. Richard Shank, The Scotts Miracle-Gro Company, from Michael C. Gregoire, Deputy Administrator, USDA APHIS, July 1, 2011, available at http://www.aphis.usda.gov/brs/aphisdocs/scotts_kbg_resp.pdf).
- 6 Letter from Richard Shank, Ph.D., Senior Vice President Regulatory and Governmental Affairs, The Scotts Miracle-Gro Company, to Michael C. Gregoire, Deputy Administrator, Biotechnology Regulatory Services, April 5, 2013, available at http://www.aphis.usda.gov/biotechnology/downloads/reg_loi/scotts_tall_fescue_air_cbidel_20130903.pdf.
- 7 Letter from Michael C. Gregoire, USDA APHIS, to Dr. Alexander Krichevsky, BioGlow LLC, March 21, 2013, available at http://www.aphis.usda.gov/biotechnology/downloads/reg_loi/aphis_response_bioglow_032113.pdf.
- 8 Letter from Michael Firko, Ph.D., Deputy Administrator, Biotechnology Regulatory Services, to Mr. Antony Evans, Glowing Plant, Inc., December 23, 2014, available at <https://www.dropbox.com/s/h8aujio5whb1nfw/Aphis%20am%20%20regulated%20response.rotated.pdf?dl=0>, linked from <http://blog.glowingplant.com/>.
- 9 Id.
- 10 APHIS, Biotechnology Regulatory Services, Factsheet (Feb. 2015), available at http://www.aphis.usda.gov/publications/biotechnology/2015/faq_withdrawal.pdf.
- 11 Importation, Interstate Movement, and Release Into the Environment of Certain Genetically Engineered Organisms, 80 Fed. Reg. 11598 (Mar. 4, 2015), available at http://www.aphis.usda.gov/brs/fedregister/brs_20150304.pdf.
- 12 Id.



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