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ARTICLE

Gene-Edited Crops Growing Ripe for Renewed Regulatory Focus at USDA

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Article in Brief

Genetically engineered crops, what many call "GMO," have garnered a large amount of popular press coverage in recent years. Misconceptions abound. But many in the public don't realize that there is a complex network of federal regulations – from the U.S. Food and Drug Administration (FDA), the U.S. Environmental Protection Agency (EPA), and the U.S. Department of Agriculture (USDA) – that is intended to protect the public, and that developers of gene-edited crops must navigate before they can sell their products.

Recently, the Trump Administration's USDA abandoned an Obama-era proposal to update the agency's regulations, and has returned to the drawing board. USDA now says it intends to engage more productively with industry to create updated USDA requirements that would better reflect the real issues posed by gene-edited crops.

This article provides a synopsis of how USDA regulates gene-edited crops today, recent technological developments, and a recommended approach for any potential updates to USDA requirements.

Days before the Trump Administration took office, the USDA released a proposed rule [1] to update its aging biotechnology regulations. Ten months later, the new Administration withdrew it. Last month, Agriculture Secretary Perdue issued a new policy statement. But further guidance is needed, ultimately, along with flexible, science based updates to USDA's biotechnology regulations.

Practice Areas

Environment & Product Regulation
Food & Drug

Introduction

At the start of 2018, the USDA released a report on Agriculture and Rural Prosperity.[2] The report flagged innovation in agricultural biotechnology as a driver of the "fourth industrial revolution." In 2016, for example, genetically engineered crops accounted for over 170 million acres of farmland across the U.S. This dramatic market penetration was propelled by advancements in genome editing and genomic selection. Those advances have produced favorable crop traits ranging from enhanced nutritional value to drought and disease resistance.

Regulation in this arena occurs pursuant to the Plant Protection Act of 2000 (PPA).[3] Industry generally applauded the Obama Administration's last-minute effort to amend the existing rules, but at the same time, many stakeholders objected to the specific approach proffered. They saw a number of proposed revisions as unnecessarily expanding USDA's review process in ways that could hamstring developers.

When the Trump Administration's USDA subsequently withdrew the proposed rule, it promised to re-engage stakeholders in the future revisions. As explained below, on March 28, 2018, a statement from the Secretary of Agriculture signaled the Agency's current thinking as it pertains to plant breeding innovation and USDA regulatory oversight. Now is the time for further action. The federal regulatory framework[4] – and USDA requirements in particular – should be updated to be more flexible and reflect a well-reasoned, science-based approach. Gene-edited crops, in particular, have emerged as an area ripe for focus in future USDA rulemaking.

Current USDA Regulation

The PPA requires USDA's Animal and Plant Health Inspection Service (APHIS) to review genetically engineered crops and organisms to determine whether they pose plant pest risks to domestic agriculture.[5] If APHIS concludes that they do, the Agency requires a permit or notification to facilitate the article's importation, interstate movement or environmental release.

A plant pest is defined at 9 C.F.R § 340.1 as:

- "Any living stage (including active and dormant forms) of insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof; viruses; or any organisms similar to or allied with any of the foregoing; or any infectious agents or substances, which can directly or indirectly injure or cause disease or damage in or to any plants or parts thereof, or any processed, manufactured, or other products of plants."

The importation, interstate movement, or environmental release of any organism, GE or not, that poses a plant pest risk, including plants, insects, or microbes, must be authorized by USDA. Under current requirements, this can be done using either permitting or notification procedures. When a developer can demonstrate that a GE organism poses no more of a plant pest risk than an equivalent non-GE organism, the developer may petition USDA to grant that GE organism a non-regulated status. If USDA approves the petition, then the GE organism may be imported, domestically distributed, or otherwise released into the environment without any further

USDA regulatory oversight.[6]

Gene-Edited Crops

Until recently, plant biotechnology has always involved the intentional insertion of very specific genetic material to introduce new traits or characteristics into a plant. For example, under the PPA, inserting a gene into a plant using the bacterial vector *Agrobacterium*, which USDA classifies as a "plant pest," would render the plant a regulated article. But biolistic transformations can produce an event without use of a plant pest vector, in which case APHIS's ability to assert jurisdiction is limited.[7] Recently, trending gene-editing techniques like CRISPR (the clustered regulatory interspersed short palindromic repeats) have been employed to achieve desired agronomical traits, without use of a plant pest vector and without adding new genetic material, but the regulatory status of the resulting seed is uncertain.

For example, in April 2016, USDA opined that a CRISPR-edited waxy corn (enhanced to contain an altered starch profile) fell outside its regulatory purview because the technique simply deleted a particular gene.[8] In this context, the use of CRISPR involves the temporary introduction of sequences for expression of the Cas9 protein (effector protein) as well as (typically) sequences that show the Cas9 protein where to "cut." The introduced sequences are then removed or simply lost due to lack of selection. This leaves no extraneous DNA behind. In the case of the CRISPR-edited waxy corn, the genetic "scissors" used to accomplish the deletion did not contain any plant pest sequences, and were not introduced into the parent plant with a plant pest vector.

USDA also has consistently found that GE crops derived from the use of plant pest sequences employed to induce genetic deletions fall outside USDA's jurisdiction, if the developer can demonstrate that no genetic material, including plant pest sequences, were inserted into the final GE plant genome.[9]

In short, under current Agency policy, to the extent that a genetic editing technique can be shown to not introduce plant pest sequences in the final plant genome and USDA agrees, then the GE plant is not subject to USDA oversight.

USDA March 28, 2018 Statement on Plant Breeding Innovation

On March 28, 2018, USDA released a statement from U.S. Secretary of Agriculture Sonny Perdue clarifying departmental oversight of plant breeding innovation. It explained that USDA does not regulate or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques, as long as they are not plant pests or developed using plant pests. This would exclude from PPA regulation crops produced through genome editing techniques that are indistinguishable from those developed through traditional breeding methods.

Unfortunately, however, this recent clarification, while helpful, simply restates what savvy industry stakeholders already understood to be the case. That is, under current USDA policy and regulation, USDA presumes regulatory oversight of all new GE crops on the basis that all such crops pose plant pest risks until proven otherwise, i.e., a "regulate first, analyze later" approach. It is time to reconsider that strategy.

Considerations for Future Rulemaking

The January 2017 proposed rule would have moved away from the "regulate first, analyze later" system towards an approach under which new GE plant varieties would be subject to a plant pest *and* noxious weed assessment prior to imposing permit and control requirements. That proposed approach, however, would have been logistically untenable. It would have imposed on companies unnecessary delays while an already-inundated APHIS completed its risk assessment, and precluded developers from moving forward with their product development plans. Moving away from the "regulate first, analyze later" paradigm is key to reducing regulatory burden on industry. The trick will be to devise an updated regulatory framework that both achieves the PPA's statutory plant protection goal and reduces regulatory burden.

To be sure, the protection of American agriculture is paramount. But gene-editing technologies that can be readily demonstrated to not pose plant pest risks – including, for example, CRISPR, RNAi (RNA interference), TALENs (transcription activator-like effector nucleases) and ZFN (zinc finger nucleases) – warrant a streamlined regulatory approach. Such an approach could both achieve the Agency's statutorily mandated plant protection goal and facilitate innovation in agricultural biotechnology.

Now that the USDA has refocused on this issue, industry has a prime opportunity to work with the current Administration to develop appropriate revised policies. New rules should be adopted that are commensurate with the limited risks posed by gene-edited crops, thus positioning the United States to lead globally on innovation in agricultural biotechnology.

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[1] *See* USDA, Proposed Rule, Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms, 82 Fed. Reg. 7008 (Jan. 19, 2017), available at: https://www.regulations.gov/docket?D=APHIS-2015-0057.

[2] *See* USDA Press Release, "Secretary Perdue Presents Agriculture and Rural Prosperity Task Force Report to President Trump," available at: https://www.usda.gov/media/press-releases/2018/01/08/secretary-perdue-presents-agriculture-and-rural-prosperity-task

[3] The PPA is codified at 7 U.S.C. 7701 et seq._

[4] The federal government regulates GE plants and organisms under a regulatory framework called the "Coordinated Framework for the Regulation of Biotechnology" (Coordinated Framework). The three key agencies comprising the Coordinated Framework are the U.S. Food and Drug Administration (FDA), the U.S. Environmental Protection Agency (EPA), and the USDA. The FDA ensures the safety and proper labeling of GMO-derived foods and feed pursuant to the Federal Food, Drug, and Cosmetic Act (FD&C Act), and the EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as well as certain biological control organisms under the Toxic Control Substances Act (TSCA).

[5] APHIS regulations at 7 CFR part 340 specifically govern the importation, interstate movement, or environmental release of certain genetically engineered (GE) organisms that are referred to as "regulated articles" in USDA parlance. The key APHIS agency charged with regulatory oversight is "Biotechnology Regulatory Services." See 7 CFR Part 340, "Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which are Plant Pests or Which There is Reason to Believe are Plant Pests."

[6] For additional information on USDA's Permits, Notifications, and Petitions, see USDA's APHIS Online Guidance here: https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions

[7] *See*, for example, a May 18, 2015 letter from USDA confirming that Benson Hill Biosystems' biolistically derived BHB Hi-Yield Maize is not a "regulated article," https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-013-01air_resp.pdf.

[8] Letter from USDA/APHIS to DuPont Pioneer, Confirmation of Regulatory Status of Waxy Corn Developed by CRISPR-Cas Technology (Apr. 18, 2016), available at: https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-352-01_air_response_signed.pdf.

[9] *See*, e.g., Letter from USDA/APHIS to Pennsylvania State University, Request for Confirmation that Transgene-Free, CRISPR-Edited Mushroom is not a Regulated Article (Apr. 13, 2016), available at: https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-321-01_air_response_signed.pdf.