

AGRICULTURAL BIOENGINEERING AND FOOD MANUFACTURING: NAVIGATING THE REGULATORY TERRAIN

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Advances in gene editing are disrupting agribusiness, but what are these advances? How are they regulated? And what's to come for? In a regulatory landscape that is often overlapping and frequently subject to change, this article is designed to help navigate the complicated terrain.

The era of precision genome editing is underway, and while it is still in its nascent stages for human therapeutics, it is quickly accelerating in the world of agriculture. The application of gene editing techniques, such as CRISPR/Cas9, to food and agriculture poses a unique challenge to both governmental agencies and the private actors subject to their oversight. Determining where modified plant and animal foods fit within the Coordinated Regulatory Framework established between the EPA, the FDA, and the USDA is an ongoing task.

According to [a 2017 United Nations' Food and Agriculture Organization report](#), the world's population is expected to grow to almost 10 billion by 2050, leading to an increase in agricultural demand by roughly 50 percent compared to 2013 levels. Economic growth, population dynamics, land availability, and volatile weather are all variables in an increasingly-complex and interdependent global agriculture industry. As consumption continues on an upward trajectory in the coming decades, bioengineering has become a major factor in [the growth and sustainability of global food supplies](#). There is ample activity in a number of arenas of bioengineering in agriculture, but CRISPR is leading the way and generating the most headlines. It has been used in a host of applications, such as boosting crop resistance and protecting against

disease in livestock. Some companies are also using other gene editing techniques, such as recombinant DNA (rDNA), zinc finger nucleases (ZFN), and transcription activator-like effector nucleases (TALENs), to enhance yields. The market for genetically engineered products was worth almost \$2 billion in 2014 and is expected to double by 2019. Yet despite continued calls for improved and updated oversight, regulation, and ethical accountability, some have declared it [“open season” in gene editing of plants and animals](#).

Regulatory Overview

Spurred by developments in recombinant DNA in the 1980s, the White House Office of Science and Technology Policy (OSTP) issued the “Coordinated Framework for the Regulation of Biotechnology” (hereinafter “coordinated framework”) on June 26, 1986. The Coordinated Framework was designed to outline [a federal regulatory policy for ensuring the safety of biotechnology products](#). Under the framework, congress charged three federal agencies with spearheading the implementation of an array of laws: the EPA, the usda, and the FDA.

The EPA’s primary mission is to protect human health and the environment. In pursuing that goal, the EPA’s statutory authority in the biotechnology space stems largely from the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the Federal, Food, Drug, and Cosmetics Act (FDCA), and the Toxic Substances Control Act (TSCA). Under FIFRA, the EPA regulates pesticides, under the FDCA, the EPA established the amount of pesticide chemical residues that may be present in food, and under the TSCA, the EPA regulates biotechnology products that are new organisms not specifically excluded by the statute. The EPA regulation of bioengineered products is largely focused on plant products which incorporate pesticide substances and toxic materials. To the extent that newly bioengineered products incorporate such pesticides and toxic materials, the EPA may assess the safety of dietary exposures to residues of these substances in human or animal feed. For instance, [if a genetically engineered \(GE\) CRISPR crop is altered to create its own pesticide, that would trigger EPA oversight](#).

The USDA focuses on agriculture and, for biotechnology purposes, this mostly relates to plant health and safety. The Animal and Plant Health Inspection Service (APHIS), an agency within the USDA, has the general authority to regulate the importation, interstate movement, and environmental release of plants that pose a plant pest risk and animals used in feed that pose a health risk to livestock. A bioengineered organism is deemed a

“regulated article” by APHIS if it is engineered using a donor organism, recipient organism, or a vector or vector agent.

The FDA is largely tasked with keeping genetically engineered foods safe. Human and animal foods (including dietary supplements), cosmetics, human and veterinary drugs, human biological products, and medical devices are just some of the categories of goods that fall under the ambit of the FDA’s regulations. The FDA draws much of its authority from the Federal Food, Drug, and Cosmetic Act (FDCA) to ensure that foods offered to consumers, including those developed using genome editing techniques, are in compliance with legal requirements.

Recent Developments

OSTP updated the 1986 Coordinated Framework in 1992, making relatively minor adjustments that remained mostly unchanged until July 2015. In the intervening years, many large biotechnology breakthroughs occurred that have left the coordinated framework outdated and found the OSTP and the three designated agencies playing catch up.

Due to the substantial advancements in the gene editing field, the Obama administration’s Executive Office of the President (EOP) issued [a memorandum](#) on July 2, 2015 to the three government agencies to update the Coordinated Framework. Their task was to clarify current roles and responsibilities, with the stated goal of preventing unnecessary barriers to future innovation. In response to EOP’s request, the National Academies of Science produced an “Update to the Coordinated Framework,” released in January 2017. While the Update is comprehensive in its discussion of the statutory basis for regulating biotechnology, it does little to modernize the framework or discuss [how to regulate emerging technologies](#), such as CRISPR.

In the absence of needed adjustments to the Coordinated Framework, the FDA, the USDA, and the EPA have each taken a different tack on how to proceed in response to the gaps in regulation. In January 2017, the FDA published [draft guidance on regulating intentionally altered genomic DNA in animals](#), as well as guidance on gene-edited foods and mosquitoes. [The FDA regulates bioengineered animals as “new animal drugs”](#) since the modifications are intended for use in diagnosis, cure, mitigation, or treatment of animal diseases and/or affect the structure or function of the animals. The draft guidance indicated that the safety and efficacy of genetically edited animals would need to be demonstrated in a new animal drug application

(NADA) submission. The guidance raised some eyebrows in the bioengineering field because it discussed making the trigger for regulation whether the GE animal was **intended to be made**, rather than [the specific attributes of the GE animal or its manufacturing process](#). The period for comment on the draft guidance ended, however, and the results of the final guidance did not issue. As of April 2018, according to an FDA spokesperson, [the agency is considering new public comments on whether gene-edited plants and foods pose added risks](#), but they have not provided any timeline for new policies.

On July 29, 2016, Congress amended the Agricultural Marketing Act of 1947 to establish a [National Bioengineered Food Disclosure Standard](#). The amendment gave the USDA's Agricultural Marketing Service (AMS) two years to establish the standard and procedures for its implementation. In response, AMS recently issued a proposed rule which was open to public comment until July 3, 2018. The proposed rule includes:

- ▶ Suggested uses of the term "bioengineering" (BE) or "BE foods," instead of GMO
- ▶ Request for comments on two alternate definitions of BE food, the first requiring that any food derived from BE material is subject to disclosure requirements, and the second narrowing the meaning to only those foods containing "genetic material"
- ▶ Lists of bioengineered commodities (both highly adopted and non-highly adopted);
- ▶ Different options as to the parameters of a BE disclosure statement, including a one-sentence label, a standardized icon, a QR code or digital marker, and separate options for small food manufacturers;
- ▶ Three suggested thresholds for bioengineered food content that could necessitate disclosure;
- ▶ Record keeping procedures;
- ▶ A discussion of AMS's enforcement power; and
- ▶ Compliance deadlines, currently set at January 1, 2020 for large companies and a year later for small companies (those with less than \$10 million in annual receipts).

Since this proposed rule is not yet finalized, the list above is still subject to change.

In tandem with the proposed rule, the USDA has been steadily approving more CRISPR edited crops. In April 2016, the USDA announced that it would forego regulation of a CRISPR edited mushroom altered to resist browning. Not long after, it made a similar announcement regarding

[CRISPR edited corn created by DuPont](#). In September 2017, the USDA greenlit an oilseed crop altered with CRISPR to produce enhanced omega-3 oil. The unifying logic in the recent string of approvals is that, [although these crops are certainly gene-edited, they are not genetically "modified,"](#) since they do not include foreign DNA.

In a formal statement in March 2018, Secretary of Agriculture, Sonny Perdue, [confirmed and clarified the USDA's trend of allowing plant gene editing](#), saying the 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 implies that as long as a genetic alteration could have been bred in a plant – for example, a deletion, a base pair swap, or insertion – [the plant will not be regulated, including CRISPR edited crops](#). His statement has led to speculation that a number of recently approved crops could reach supermarket shelves much quicker than originally anticipated

The Path Ahead

With aforementioned guidances in the works, but not yet finalized, and proposed rule changes frequently withdrawn, the regulatory landscape for genetically engineered foods and animals is recalibrating. The multi-pronged approach to regulation of bioengineered products established by the EPA, the USDA, and the FDA's coordinated regulatory framework is still evolving and in flux. Efforts to develop and commercialize bioengineered foods will require careful scrutiny and attention to the changing regulations surrounding these products. As circumstances fluctuate and technologies evolve, it is necessary to have counsel dedicated to monitoring regulatory changes and approval standards. After all, "open season" in agricultural bioengineering can shift quickly.

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