USDA Regulation of Organisms Developed Through Modern Breeding Technologies

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The federal government has a coordinated, risk-based system to ensure that new biotechnology products are safe for the environment and for human and animal health. Established as a formal policy in 1986 (US-OSTP, 1986), the coordinated framework for regulation of biotechnology describes the federal system for evaluating products developed using modern biotechnology. The coordinated framework is based upon existing laws designed to protect public health and the environment. The US government has written new regulations, policies, and guidance to apply these laws to biotechnology-derived products.

The US government agencies responsible for oversight of the products of modern agricultural biotechnology are the USDA's Animal and Plant Health Inspection Service (USDA-APHIS), the US Environmental Protection Agency (EPA), and the Department of Health and Human Services' Food and Drug Administration (FDA). Depending on its characteristics, a product may be subject to the jurisdiction of one or more of these agencies. Regulatory officials from the three agencies regularly communicate and exchange information to ensure that any safety or regulatory issues that may arise are appropriately resolved.

Roles of US Regulatory Agencies

APHIS

Within USDA, APHIS is responsible for protecting agriculture from pests and diseases. Under the Plant Protection Act (7 USCC 104, 7701), USDA-APHIS has regulatory oversight over products of modern biotechnology that could pose a risk to plant or animal health. Accordingly, USDA-APHIS regulates organisms and products that are known or suspected to be plant pests or to pose a plant-pest risk, including those that have been altered or produced through genetic engineering. These are called "regulated articles." USDA-APHIS regulates the import, handling, interstate movement, and release into the environment of regulated organisms that are products of biotechnology, including organisms undergoing confined experimental use or field trials. Regulated articles are reviewed with regard to appropriate handling, confinement, and disposal to ensure that, under the proposed conditions of use, they do not present a plant-pest risk.

USDA-APHIS biotech regulations provide a petition process for the determination of nonregulated status. If a petition is granted, that organism will no longer be considered a regulated article and will no longer be subject to oversight by USDA-APHIS biotech regulations. The petitioner must supply information such as the biology of the recipient plant, experimental data and publications, genotypic and phenotypic descriptions of the genetically engineered organism, and field-test reports. The agency evaluates a variety of issues including the potential for plant-pest risk; disease and pest susceptibilities; the expression of gene products, new enzymes, or changes to plant metabolism; weediness and impact on sexually compatible plants; agricultural or cultivation practices; effects on non-target organisms; and the potential for gene transfer to other types of organisms. A notice is filed in the *Federal Register* and public comments are considered on the environmental assessment and determination written for the decision on granting the petition. Copies of the USDA-APHIS documents are available to the public.

APHIS employs the term "biotechnology" to mean the use of recombinant-DNA technology, or genetic engineering (GE) to modify living organisms (7 CFR 340.1). APHIS regulates certain GE organisms that may pose a risk to plant or animal health.

FDA and EPA

FDA has primary responsibility for ensuring the safety of human food and animal feed, as well as proper labeling and safety of all plant-derived foods and feeds. EPA regulates pesticides, including plants with plant-incorporated protectants (pesticides intended to be produced and used in a living plant), to ensure public safety. That agency also regulates pesticide residue on food and animal feed. APHIS, through its Biotechnology Regulatory Services (BRS) program, regulates the introduction of certain GE organisms that may pose a risk to plant health.

APHIS Authority

Federal Statutes

Congress authorizes USDA agencies, including APHIS, to regulate specified areas of

US agriculture under federal statutes. The federal statute from which APHIS derives its authority to write regulations is the Plant Protection Act (7 USC, 7701).

Federal Regulations
APHIS describes in their regulations what (importation, interstate movement and confined release) and how (time frames, permitting processes, penalties) certain GE organisms may be regulated. All formal federal regulations are published in the *Federal Register* and also in the *Code of Federal Regulations* (CFR). Regulations for agriculture and the USDA comprise fifteen volumes and those governing biotechnology as overseen by APHIS are found in Title 7 of the CFR part 340.

Regulatory Trigger Under Current 7 CFR 340.

Organisms that were created using recombinant-DNA techniques and are plant pests are regulated under the current version of 7 CFR 340. The definition of a plant pest found in the regulations (7 CFR 340.1) is:

> *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.*

Organisms such as plants that are not normally considered to be plant pests also fall under the regulation if they were engineered with DNA from a donor organism, recipient organism, vector, or vector agent that is listed as a plant pest in 7 CFR 340.2, such as *Agrobacterium tumefaciens*. If a GE organism meets the definition of a regulated article, APHIS authorization is required for its importation, interstate movement, or confined release into the environment.

Petition Process for a determination of Nonregulated Status

Engineered organisms that meet the definition of a regulated article represent a potential plant-pest risk until the agency determines that it does not pose a plant-pest risk. The petitioner is required to provide information under § 340.6(c)(4) related to plant-pest risk that the agency may use to determine whether the regulated article is unlikely to present a greater plant-pest risk than the unmodified organism. A GE organism is no longer subject to the regulatory requirements of 7 CFR part 340 or the plant-pest provisions of the Plant Protection Act when APHIS determines that it is unlikely to post a plant-pest risk.

Am I Regulated?

The current regulations under 7 CFR 340 do not apply to all GE organisms or even all GE plants. For example, plants transformed by particle bombardment with DNA that is not derived from a plant pest do not trigger the regulations under 7 CFR 340. APHIS may be consulted as to whether a specific organism falls under the regulation through a process named *Am I regulated?* APHIS' response specifically addresses whether or not the

GE organism is regulated under 7CFR 340; however, APHIS does consider if other US agencies or other APHIS regulations are triggered and indicates such in the response as appropriate. The APHIS website lists the types of information that should be included in a letter of inquiry at the following link: *Am I Regulated*[1]?

Previous letters and responses are posted at the following link:
Regulated Letters of Inquiry[2].

APHIS has made several decisions on whether GE plants are regulated under 7 CFR 340. Cases where APHIS concluded that the engineered plants were not regulated under CFR 340 include:

- Null segregants from genetically engineered plants (6/6/2012; 10/27/12)
- Deletion of the IPK1 gene in maize using zinc finger nuclease (5/26/12)
- Targeted gene deletions using I-CreI meganuclease (1/6/12)
- Centromere-mediated chromosome elimination (10/27/11)

On two occasions, APHIS responded to letters of inquiry that DNA insertion or editing would be handled on a case by case basis:

- For zinc-finger nuclease (3/8/12)
- For I-CreI meganuclease (5/16/11).

Efforts to Revise 7 CFR 340

Beginning in 2004, APHIS began a process to thoroughly revise the regulations under 7 CFR 340. Stakeholder scoping meetings were held in February and March of that year. In August 2007, a draft EIS was published and a public comment period was held (USDA-APHIS, 2007). About 23,000 comments were received on the draft EIS (USDA-APHIS, 2008). The proposed rule was published four years later, on October 9, 2008. Two meetings to discuss proposed regulations were held, in November 2008 and April 2009.

APHIS has two options to close out the proposed rule. It can withdraw it or it can finalize it in whole or in part. Because APHIS is still in active rulemaking, APHIS is not

[1]http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/biotechnology/sa_regulations/!ut/p/a1/rZLLcoIwFIafpksmEYSEpYjKRWqntlXYMCFySYsEIXaqT99Au7Ez3maa3Zl85_L_54AIrE-FUkU-WE8F4RcoujozYWzjqwIKqO5tNLOg-TudPyPdUqOoSCE-ApTmRwNs0wHOk-R46zcfIg-dCdLjzfspcatAdgBSIQ0UrUogAhqQvWxpRXIq1EXLKkIc3hAbYk5vsmzjdt32UMC5SWlS85PnPf5Pm-7lfuu0K1pRtQJgmEOl-GoiumgTfKkGpEwYjoCtpQqGEzo6au_gqAZ94I3mvAKeDrt-WPZyNniOay4xGr0LUtx0ZmIL0yruX3Bl5ZQQ9cknixSaehBy-4MGUoV6GwFCSzvXIt3g2_sfbeLRvJ8uoP5EmD9P_cjK6tNMA5yOTARhcKqJlP1H6jevm6xdmBM-Xh2ji_ZdoXbbzOWZ0U!/?1dmy&urile=wcm%3apath%3a%2Faphis_content_library%2Fsa_our_focus%2Fsa_biotechnology%2Fsa_regulations%2Fct_am_i_reg

[2]http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/biotechnology/sa_regulations/ct_am_i_reg/!ut/p/a1/tVLLVoMwFPyWLlxykgbawBJKWx7FeqxaYMMJEUqUVyH1WL_egC5k0dfC7G4yk3tn7oAQ-CAsyQfbEc6qkuRdHU4jZ22hsQGRvVzODWjfL1YP2HUQRBMBCAaAjTYXgJeFp66w7-Dp4yFexBaG9WDuuYW5kaI7BFoQgpCWveQYCUmesjWhV8qTkUc7ihjTHO9iSqDo0UVrR-Q9tXMat4QrOyyqvdz3uT7A55P7RAUB6RImLdZfd7TdkrCFIliRVMqaQpqiYpJIVSDGVFo-imBcIJThMbTXzXwxNHhrW4MAe7kOv5sqVsKXomOioqgbRqWiTVPGDe9xO_dvLCPHnBO4tk-mnYYecGbIQKjAJ38QgM2Na3Gu8I297fehLrLUpeeTA_8fwiTaoMabeSJWNeGZxMq0Av6QAfy_jL-p4LlT5yJj0_mh9PaXFVm11fTT6BmBMwKo!/?1dmy&urile=wcm%3apath%3a%2Faphis_content_library%2Fsa_our_focus%2Fsa_biotechnology%2Fsa_regulations%2Fct_reg_loi

at liberty to discuss the ensuing agency deliberations that have occurred since April 2009. APHIS may discuss the fundamental revisions that were proposed in the rule in 2008.

Noxious-Weed Authority

When 7 CFR 340 was codified in 1987, it derived its authority from the Federal Plant Pest Act of 1957 (PL 85-36) and the Plant Quarantine Act of 1912 (7 USC 151), which provide APHIS authority to regulate plant pests. In 2000, the Federal Plant Pest Act and Plant Quarantine Act were subsumed into the Plant Protection Act (7 USC 7701). In addition, the PPA incorporates authority that previously was under the Noxious Weed Act of 1974 (PL 93-629), which gave APHIS additional authority to regulate noxious weeds. One of the most fundamental changes APHIS proposed for the new 7 CFR 340 was to include a provision for noxious-weed authority. As defined under the current regulations and the PPA, most plants are not plant pests, with the exception of a few parasitic species, such as striga, witchweed, and dodder. Hence the noxious-weed authority may be more appropriate for regulation of genetically engineered plants that may pose a weed risk.

Risk-Based Regulation/Regulatory Trigger.

As noted in the proposed rule (USDA-APHIS 2008 p. 60011):

> *[T]echnological advances have led to the possibility of developing GE organisms that do not fit within the plant pest definition, but may cause plant pest or weed damage covered by the definition of noxious weed in the PPA.*

One objective of the proposed rule was to make the regulatory trigger consistent with current science and to provide regulatory oversight commensurate with the risk due to the organism. Under such a change, APHIS could conclude that organisms that were not previously regulated under the old 7 CFR 340 regulation might fall under the oversight of the new regulation.

Reduced Regulatory Burden

Just as there is the possibility that organisms that do not fall under the current regulations at 7 CFR 340 may cause plant-pest or weed damage covered by the definition of noxious weed in the PPA, there are many examples of organisms that do not cause such harm, but, nevertheless, are regulated under 7 CFR 340. The proposed rule sought to reduce regulatory burden by applying regulatory oversight commensurate with risk. For example, to quote the proposed rule (USDA-APHIS 2008 at p. 60012);

> *APHIS would subject a GE organism to regulatory oversight based upon known plant pest and noxious weed risks of the parent organisms, or based upon the traits of the GE organism, or based upon the possibility of unknown risks as a plant pest or noxious weed when insufficient information is available.*

Principles for the Oversight of Emerging Technologies

Although APHIS is not in a position, as mentioned above, to discuss agency deliberations on the proposed rule until closeout, there is a relevant document that describes overarching principles for the regulation and oversight of the products of emerging technologies.

These principles are described in a memo by the White House Office of Science and Technology Policy (US-OSTP, 2011) that APHIS has been adhering to in its deliberations on the new 7 CFR 340. These principles are listed below:

- *[T]o ensure the fulfillment of legitimate objectives such as of the protection of safety, health, and the environment while avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, and creating trade barriers. … When no significant oversight issue based on a sufficiently distinguishing attribute of the technology or the relevant application can be identified, agencies should consider the option not to regulate.*
- *Scientific Integrity—Federal regulation and oversight of emerging technologies should be based on the best available scientific evidence. Adequate information should be sought and developed, and new knowledge should be taken into account when it becomes available. To the extent feasible, purely scientific judgments should be separated from judgments of policy. … Decisions should be based on the best reasonably obtainable scientific, technical, economic, and other information, within the boundaries of the authorities and mandates of each agency.*
- *Public Participation—To the extent feasible and subject to valid constraints (involving, for example, national security and confidential business information), relevant information should be developed with ample opportunities for stakeholder involvement and public participation. Public participation is important for promoting accountability, for improving decisions, for increasing trust, and for ensuring that officials have access to widely dispersed information.*
- *Communication—The Federal Government should actively communicate information to the public regarding the potential benefits and risks associated with new technologies.*
- *Benefits and Costs—Federal regulation and oversight of emerging technologies should be based on an awareness of the potential benefits and the potential costs of such regulation and oversight, including recognition of the role of limited information and risk in decision making. … The benefits of regulation should justify the costs (to the extent permitted by law and recognizing the relevance of uncertainty and the limits of quantification and monetary equivalents).*
- *Flexibility—To the extent practicable, Federal regulation and oversight should provide sufficient flexibility to accommodate new evidence and learning and to take into account the evolving nature of information related to emerging technologies and their applications.*
- *Risk Assessment and Risk Management—Risk assessment should be distinguished from risk management. The Federal Government should strive to reach an appropriate level of consistency in risk assessment and risk management across various agencies and offices and across various technologies. Federally mandated risk management actions should be appropriate to, and commensurate with, the degree of risk identified in an assessment.*

- *Coordination—Federal agencies should seek to coordinate with one another, with state authorities, and with stakeholders to address the breadth of issues, including health and safety, economic, environmental, and ethical issues (where applicable) associated with the commercialization of an emerging technology, in an effort to craft a coherent approach. There should be a clear recognition of the statutory limitations of each Federal and state agency and an effort to defer to appropriate entities when attempting to address the breadth of issues.*

In Conclusion

At the present time, APHIS considers products of emerging technologies under the current 7 CFR 340. Organisms engineered without plant-pest sequences may not fall under the 7 CFR 340 regulations. The *Am I Regulated?* process is specifically used to ascertain whether the agency concludes that the organism is regulated under 7 CFR 340 or whether other APHIS regulations are triggered. APHIS is still in active rule making having proposed changes to 7 CFR 340 such as including a noxious-weed provision, changing the regulatory trigger, implementing oversight commensurate with risk, and reducing regulatory burden. A revised 7 CFR 340 may fundamentally change the oversight of the products created with emerging technologies compared to the current regulations.

References

USDA-APHIS (2007) Draft Environmental Impact Statement-Introduction of Genetically Engineered Organisms. Regulations.gov Docket 2006-0112.

USDA-APHIS (2008) 7 CFR 340. Proposed Rule. Importation, Interstate Movement, and Release into the Environment of Certain Genetically Engineered Organisms. FR 73 60008.

US-OSTP (1986) The Coordinated Framework for Regulation of Biotechnology. FR_51: 23302.

US-OSTP (2011) Memorandum for the Heads of Executive Departments and Agencies: Principles for Regulation and Oversight of Emerging Technologies. http://www.whitehouse.gov/sites/default/files/microsites/ostp/etipc-memo-3-11-2011.pdf.

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