

APHIS Authority to Regulate Plants Modified Using Synthetic Biology

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Introduction

This paper will look at the regulation of genetically engineered (GE) organisms and products of synthetic biology under Animal and Plant Health Inspection Service (APHIS)¹ regulations in 7 CFR Part 340 (Part 340) and the Plant Protection Act of 2000 (PPA). As discussed below, if all the authorities in the PPA were used, it is likely that most plants modified by synthetic biology techniques would not be covered by this statute. APHIS does not regulate genetically engineered plants under Part 340, unless a plant pest is used as the donor, recipient, vector, or vector agent. That situation is not likely to arise when using synthetic biology or other newer technologies to modify plants.

In 2008, APHIS proposed amending its regulations to include its authorities over noxious weeds, so that a broader range of genetically modified organisms would be covered, but those proposed regulations have never been finalized. However, to use its noxious weed authority, some rational scientific basis to include such products would have to be developed. Even if a theory is developed, there will likely be significant gaps in the regulation of genetically engineered plants. If other agencies and authorities cannot cover those gaps, additional legislation may be needed to ensure review of products of synthetic biology before they are commercialized.

Regardless of pre-market assessment or regulation, APHIS has strong authorities to take remedial action to prevent dissemination of a plant pest or noxious weed whenever there is reason to believe a plant or other organism meets the appropriate definition. This would include unintended and unforeseen consequences of the use of modified plants.

Background and Current Part 340

APHIS issued its initial regulations governing the importation and interstate movement (including release into the environment) of GE organisms in 1986 under the authority of the Federal Plant Pest Act of 1957 (FPPA) and the Plant Quarantine Act of 1912 (PQA). Those acts with others, including the Federal Noxious Weed Act (FNWA), were consolidated into the PPA. APHIS regulations governing the release into the environment of GE organisms in Part 340 because of their association with known plant pests have covered most GE plants to date, but are not likely to cover most products of synthetic biology. In addition, the regulations in Part 340 could be found to exceed APHIS' authority under the PPA and be struck down by courts.

¹ The United States Department of Agriculture (USDA) regulates genetically engineered (GE) plants under the authority of the PPA. The Secretary of Agriculture has delegated the authority and responsibility to administer the PPA to APHIS.

Part 340 defines covered GE organisms as “regulated articles”² and restricts or prohibits the importation, interstate movement and release into the environment of those regulated articles except in accordance with the regulations. Regulation under plant pest authority covered most GE plants because known plant pests, such as *Agrobacterium tumefaciens* and cauliflower mosaic virus, were the vectors of choice for transferring DNA into plants.

A “regulated article” includes any organism altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent is a plant pest³. If a plant pest is not used, the plant is usually not regulated under Part 340.

The definition of a “regulated article” is based on a “reason to believe” standard. The Administrator determined that to be a “regulated article,” the GE organism must have some connection with DNA from a plant pest. The main thrust for part 340 is that there is a risk of transferring plant pest properties by the use of DNA from a known plant pest. The definition also allows the Administrator of APHIS to determine that the new organism is a regulated article if he or she has any other “reason to believe” it is a plant pest. It is not clear whether the Administrator would consider a plant containing synthetically produced DNA that is similar to or identical with DNA from a known plant pest to be a regulated article. Synthetically produced DNA that is identical to DNA from a plant pest would not appear to meet the definition of a regulated article under Part 340 because a plant pest was not involved in the process.

The way that this definition is written and has historically been interpreted by APHIS usually results in the initial regulation under part 340 of any GE plant that contains a portion of a plant pest. This was justified under the “reason to believe” that it could produce a plant pest because of the uncertainty as to what the exchange of DNA might produce. However, it is not clear that the PPA authorizes the use of the “reason to believe” standard in this fashion, as explained in more detail below. If the “reason to believe” standard is successfully challenged, it would be the demise of the regulatory scheme in Part 340 and APHIS would not be able to review products of genetic engineering or synthetic biology prior to their release into the environment or commercialization.

² Regulated article is defined in 340.1 as “Any organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belong to any genera or taxa designated in Sec. 340.2 and meeting the definition of plant pest, or is an organism whose classification is unknown, or any product which contains such an organism, or any other organism or product altered or produced through genetic engineering which the Administrator, determines is a plant pest or has reason to believe is a plant pest. Excluded are recipient microorganisms which are not plant pests and which have resulted from the addition of genetic material from a donor organism where the material is well characterized and contains only non-coding regulatory regions.” (7 CFR 340.1)

³ “The term “plant pest” is defined in the PPA as “any living stage of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product:

- (A) A protozoan.
- (B) A nonhuman animal.
- (C) A parasitic plant.
- (D) A bacterium.
- (E) A fungus.
- (F) A virus or viroid.
- (G) An infectious agent or other pathogen.
- (H) Any article similar to or allied with any of the articles specified in the preceding subparagraphs.” (7 USC 7702(14))

The statutory authority in the PPA may have been stretched beyond its original intent to try to cover new scientific developments in the field of GE organisms. The problems associated with regulation of GE organisms under Part 340 are also present for products of synthetic biology, and some additional problems are introduced with this newer technology. In order to provide a better understanding of the potential problems with using the PPA to regulate products of synthetic biology, we need to examine the statutory basis for the definition of a “regulated article” in Part 340.

Sections 7711(a) and 7712(a) of the PPA are the two main authorities for Part 340 regulating the interstate movement of plant pests and noxious weeds. Section 7711(a)⁴ prohibits movements of plant pests unless they are accompanied by a permit and moved in accordance with regulations the Secretary may issue. Section 7711 of the PPA was historically used to promulgate requirements for interstate movements of known plant pests.

Section 7712(a)⁵ authorizes the regulation of movements into the U.S. and interstate of plants, plant products, articles and means of conveyance “if the Secretary determines it is necessary to prevent the introduction or dissemination of a plant pest or noxious weed.” Section 7712 was historically used to regulate plants, plant products, articles and means of conveyance that could carry known plant pests and noxious weeds, such as nursery stock, packing materials, means of conveyances etc. However, neither section specifically authorizes the use of the “reason to believe” standard contained in the definition of “regulated article”.

Section 7714(a)⁶ is the only section of the PPA that specifically authorizes action by the Secretary when there is only a “reason to believe” something is a plant pest or noxious weed. It authorizes APHIS to take very broad remedial measures, including to hold, treat, quarantine and destroy, if necessary, any plant, plant product, article or means of conveyance that the Secretary has “reason to believe” is or may be infested or infected with a plant pest or noxious weed. This section has been historically used to eliminate or destroy new plant pests and noxious weeds when they are found at ports of entry and in orchards or contaminating or hitch hiking on other

⁴ Section 7711(a) of the PPA (7 USC 7711(a)) provides, in pertinent part, that “[N]o person shall import, enter, export, or move in interstate commerce any plant pest, unless the importation, entry, exportation, or movement is authorized under general or specific permit and in accordance with such regulations as the Secretary may issue to prevent the introduction of plant pests into the United States or the dissemination of plant pests within the United States.”

⁵ Section 7712(a) of the PPA (7 USC 7712(a)) provides that “[t]he Secretary may prohibit or restrict the importation, entry, exportation, or movement in interstate commerce of any plant, plant product, biological control organism, noxious weed, articles, or means of conveyance, if the Secretary determines that the prohibition or restriction is necessary to prevent the introduction into the United States or the dissemination of a plant pest or noxious weed within the United States.”

⁶ Section 7414(a) of the PPA (7 USC 7714(a)) provides “[i]f the Secretary considers it necessary in order to prevent the dissemination of a plant pest or noxious weed that is new to or not known to be widely prevalent or distributed within and throughout the United States, the Secretary may hold, seize, quarantine, treat, apply other remedial measures to, destroy, or otherwise dispose of any plant, plant pest, noxious weed, biological control organism, plant product, article or means of conveyance that is moving into or through the United States or interstate, or has moved into or through the United States or interstate and the Secretary has reason to believe is a plant pest or noxious weed or is infested with a plant pest or noxious weed at the time of the movement or is otherwise in violation of this title.”

articles, such as nursery stock, packing materials and means of conveyance before they can spread. The "reason to believe" standard was used in this section in case there was any doubt about whether the organism of concern was actually a plant pest or noxious weed. Congress wanted the Secretary to be able to take appropriate action to eliminate the threat to American agriculture as soon as possible rather than waiting for a definitive identification, which sometimes is a lengthy process. The phrase "reason to believe" is specifically mentioned only in section 7414 regarding remedial measures.

The "reason to believe" standard could have been included in sections 7411 and 7412, but it was not. In a court challenge, this could be interpreted as meaning that it was not intended to be used for the purpose of permits and interstate movements. Part 340 was also the first time the "reason to believe" language was used in the definition of a "regulated article."⁷ It can also be argued that the "reason to believe" standard in the definition of "regulated article" goes further than the "reason to believe" in section 7414. The "reason to believe" standard in section 7414 comes into play when there is reason to believe something *is* a plant pest. In the definition of "regulated article" it comes into play when there is "reason to believe" it may *produce* a plant pest. Believing something may produce a plant pest is one step further removed from believing something is a plant pest. This is a subtle, but possibly very important, distinction. The "reason to believe" standard in Part 340 has never been challenged in court and it is not clear it could be successfully defended if contested.

Additional issues may arise if and when APHIS seeks to regulate products of synthetic biology. Current products of synthetic biology use DNA sequences only from known organisms, but it is foreseeable that at some time in the future sequences from unknown or unclassified organisms could be incorporated into products of synthetic biology. This could bring into play the "unknown organism and organisms whose classification is unknown" provision in the definition of "regulated article." There are a number of potential problems with this part of the definition.

First, the proposed regulations published in the Federal Register in 1986 that became part 340 did not contain the "unknown organism" provision. The general public never had a chance to comment on it. It was added in the final rule, apparently based on a legal memorandum that was dated the day before the proposed rule was published. The final rule does not contain a good explanation of exactly what the agency was trying to accomplish with this provision and why it was added without the opportunity for public comment.⁸ Furthermore, the reasoning in the legal memorandum itself is problematic.⁹

⁷ See domestic quarantines in 7 CFR Part 301

⁸ There is some ambiguity about how to properly read this clause. Is it independent or does it modify something else? The question has been asked whether it could apply to a DNA sequence that does not copy a sequence found in nature, even though a sequence is not an organism. It is not known how APHIS might interpret this provision until such a situation arises. Additional issues may arise as synthetic biology progresses.

⁹ The memorandum responded to the request from the Acting Assistant Secretary for Marketing and Inspection Services for an "opinion as to the Department's authority to regulate genetically engineered plants, pursuant to the FPPA, when the plant pest status of such plants is unknown." (See the Department's legal position concerning this issue attached as Appendix G at pp114-117 of "Issues in the Federal Regulation of Biotechnology: From Research to Release", a report prepared by the Subcommittee on Investigations and Oversight of the Committee on Science and Technology of the House of Representatives, 99th Cong., 2nd Session, December 1986). (Continued)

There is no indication in the record why the proposed rule was published for comment the day after the legal opinion was issued without any reference to the possibility of including “unknown organisms and organisms whose classification is unknown” in the definition of “regulated article.” If APHIS wished to make significant changes in the rule, especially other than in response to comments received, it could have re-proposed the regulation with the new material to give the general public an opportunity to comment on it. Some would consider the insertion of this language in this manner to be a violation of the Administrative Procedure Act that could be successfully challenged.

Even though the definition of “regulated article” in part 340 includes “unknown organisms and organisms whose classification is unknown,” APHIS has not used this provision, and has not taken a position whether they would try to use it to regulate products of synthetic biology, including, for example, an organism with chloroplasts modified using a gene gun that had been inserted into a feedstock, such as sugar cane or sugar beets.

Several issues may arise if APHIS tries to regulate products of synthetic biology using the “unknown organisms” provision. The first question is that of authority for APHIS to regulate in this fashion. If the DNA sequences incorporated into an organism are unknown to APHIS, then how can they say the organism is a plant pest or even may be a plant pest, unless the process

The opinion stated that “[a]fter review of the FPPA and its legislative history, we have concluded that the language of the Act and its legislative history allow the regulation of genetically engineered plants pursuant to the Act, when the plant pest status is unknown. ...The Department’s construction is sufficiently rational to preclude a court from substituting its judgment for that of the Department.” (citing *Younes v. Community Nutrition Institute*, Sup Ct. June 17, 1986)

The rationale in the opinion states that “it is necessary to regulate unclassified organisms in order to prevent the introduction or dissemination of plant pests. Many types of organisms, particularly microorganisms, were unknown until recent years, including groups of fungi, bacteria, viruses, and viroids. In every group, a significant number of plant pests is now found.” The opinion went on to state that “the novelty of GE plants and the lack of experience with them make it more difficult to predict their impact on agriculture and the environment.”

The opinion went on to state that “[i]f congress explicitly left a gap for the agency to fill, there is express delegation of authority to the agency to elucidate a specific provision of the statute by regulation.”

According to the 1986 proposed rule published in the FR the next day, “[t]he FPPA was intended as gap filling legislation for the purpose of protecting American agriculture against invasion by foreign plant pests and disease, which are “new to or not theretofore known to be widely prevalent or distributed within or throughout the United States. The FPPA was enacted because of deficiencies in such acts as the Insect Pest Act (repealed), the Plant Quarantine Act (7 U.S.C. 151 et seq.) the Mexican Border Act (7 U.S.C. 149) and the Mollusk Act (repealed).” (51 FR 23353). This contemporaneous description of the gap filling properties of the FPPA in the proposed rule does not appear to leave an explicit gap for the agency to fill with regard to GE plants. In fact, it was not an issue being considered by Congress at that time. Therefore, I don’t see how the regulation of unknown organisms was a gap that Congress explicitly left for the agency to fill? This is a very bald assertion that has not been tested in court.

In addition, I have been told that it is very unlikely that there are “types of organisms” that are still unknown. It would also appear that with APHIS’ experience with GE plants in the intervening years and with the tremendous scientific advances that have been made in this field since 1986, that the “novelty” argument is not as strong as it once was.

used to create it is known to produce plant pests or there is “reason to believe” it may produce a plant pest?¹⁰ APHIS denies that it is regulating the process and there would appear to be nothing that would indicate the organism is or may be a plant pest.

It appears to defy logic to argue that an unknown or unclassified organism that has no ties to a known plant pest and shows no plant pest properties or “reason to believe” it may be a plant pest should be regulated as if it were a plant pest until the negative can be proven. Including “unknown organisms” in the definition of “regulated article” shifts the burden of proof from the Secretary to show why an organism is a plant pest and should be regulated to the person moving the organism to show why it isn’t a plant pest. A very clever shift, if it can be successfully defended.¹¹

Regulating under current Part 340 without using the “unknown organism” provision may be as far as APHIS can go under its plant pest authority for GE plants or products of synthetic biology. It would be in accord with APHIS’ original proposed rule in 1986 and its description of the authority it was proposing to use to promulgate Part 340.

APHIS could continue to fully regulate under part 340, including “unknown organisms” until it is challenged. If USDA were challenged and lost, however, it would create a void until new legislation could be enacted or regulations promulgated. This could take years and leave large numbers of products of synthetic biology unregulated or in regulatory limbo in the interim.

Recent APHIS interpretations regarding regulated articles

APHIS’ authority over modified plants has already been eroded by newer technologies. APHIS recently agreed that Scott’s herbicide tolerant Kentucky bluegrass was not a “regulated article” under part 340.¹² It was genetically engineered without plant pest components and the new DNA was inserted by means of a gene gun. APHIS stated in a letter dated July 1, 2011 that it “does not meet the definition of a ‘regulated article’ and is not subject to the regulations in 7 CFR part 340. Kentucky bluegrass itself is not a plant pest, no organisms used as sources of the genetic

¹⁰ Some believe that since synthetic DNA sequences are created de novo, there may be more certainty regarding the properties that are being inserted and expressed than when DNA is removed from another organism and transferred. It has been argued that new technologies for plant genetic engineering “enable more precise and subtler modification of plant genomes (Weinthal et al. 2010) than the comparably crude methods that were used to create the current stock of GM crops (Fig 1A). These methods allow scientists to insert foreign DNA into the plant genome at precise location, remove unwanted DNA sequences or introduce subtle modifications, such as single base substitutes that alter the activities of individual genes.” (EMBO Reports, Vol. 12, No. 9, 2011)

¹¹ It should be remembered that the authority for Part 340 has not been reviewed in a court of law. It is not clear where the line may be drawn if and when there is such a legal challenge. The stakes are potentially very high if APHIS should lose such a challenge. Most court cases to date have been for violations of procedural statutes, such as NEPA or ESA. See for example, *Center for Food Safety v. Johanns*, 451 F.Supp.2d 1165 (USDC, Hawaii, 2006)); *International Center for Technology Assessment v. Johanns*, 473 F.Supp.2d 9 (USDC, DC 2007); *Gertson See Farms v. Johanns*, 541 F.3d 938 (Ninth Cir. 2008); *Center for Food Safety v. Vilsack*, Nos. 10-17719 and 10-17722 (Ninth Cir. 2011)

¹² 76 FR 39812, July 7, 2011

material used to create the GE Kentucky bluegrass are plant pests, and the method used to genetically engineer the GE Kentucky bluegrass did not involve plant pests.”¹³

APHIS took a similar position in a letter dated May 26, 2010 after evaluation of maize plants created using zinc finger nuclease technology to delete IPK1 or similar genes to reduce phytate production, without the use of a plant pest. APHIS concluded there was no basis to believe that the resulting organism is a plant pest or is likely to pose a plant pest risk and, therefore, it is not considered a regulated article under part 340. Therefore, it was never subject to regulation or oversight under part 340.

Based on these decisions, it would appear that as long as known organisms are used and no plant pests are involved, APHIS will not regulate GE products under part 340, including products of synthetic biology.

Now that it has been shown that it can be done, other plant developers may be tempted to test USDA’s authority over their products, according to an article in *Nature Biotechnology*.¹⁴ However, plants escaping APHIS oversight would not escape all government regulation.¹⁵ Food crops would still be subject to FDA oversight and products intended for export would be subject to the approval process in recipient countries. In addition, as a practical matter, “the USDA’s imprimatur remains valuable to some companies as a stamp of approval to offset public fears fomented about biotech crops.”¹⁶ However, this scenario would leave major gaps with regard to oversight of environmental risks involving products of synthetic engineering.

In another case, APHIS recently decided to de-regulate Alpha-Amylase corn. The reasoning used to de-regulate Alpha-Amylase corn, discussed below, would also seem to support not regulating many products of synthetic biology in the first place. It also undermines any action APHIS might try to take against a product of synthetic biology that a person chose not to subject to review under Part 340.

In its NEPA decision and FONSI for Alpha-Amylase maize, APHIS stated that “in order to be a plant pest the GE organism in question must be one of the organisms listed in the plant pest definition in the PPA or an article similar to or allied with one of the listed organisms. Event 3272 corn is not an organism listed in the definition of plant pest and therefore is not itself a plant pest. Event 3272 corn does not harbor any living stage of any of the organisms (article) that are defined as potential plant pests, nor does Event 3272 corn act as an article and increase susceptibility to plant disease or insect pests and harbor plant pests. Collectively, these scientific

¹³ APHIS did go on to state that “[b]ecause no plant pests, unclassified organism, or organisms whose classification is unknown were used to genetically engineer this variety of GE Kentucky bluegrass, APHIS has no reason to believe it is a plant pest and therefore does not consider the (Kentucky bluegrass)... to be regulated under 7 CFR part 340 and is not subject to the plant pest provisions of the PPA.”

¹⁴ *Nature*, Volume 29, No. 9 September 2011 at 772

¹⁵ For an extensive listing of the agencies and statutes that are or can be used to regulate the products of biotechnology, see the Office of Science and Technology Policy (OSTP) joint assessment with the Council on Environmental Quality (CEQ) titled CEQ and OSTP Assessment: Case Studies of Environmental Regulations for Biotechnology (pages 4-5, 2001) (66 FR 7905, January 26, 2001)

¹⁶ *Nature*, Volume 29, No. 9 September 2011 at 772

facts led APHIS to the conclusion that Event 3272 corn does not meet the definition of a plant pest and its unrestricted movement and use will not result in the introduction or dissemination of plant pests.”¹⁷

Given the reasoning enunciated by APHIS in its original rule and regarding herbicide resistant Kentucky bluegrass, zinc finger nuclease technology, and Alpha-Amylase corn, among others, it appears that APHIS may be taking a position that is consistent with not regulating most products of synthetic biology, unless a plant pest is actually used as a donor, recipient, vector or vector agent. It should also be noted that nearly all GE organisms reviewed under part 340 have been found not to be a plant pest. Every time APHIS reviews a plant under Part 340 and finds that it is not a plant pest, it chips away at the “reason to believe” standard in the original theory of regulation. At some point, it may be found that there is not a sufficient scientific basis to support this theory.

APHIS proposal to include noxious weed authority

APHIS could potentially use its noxious weed authority to regulate additional GE plants and products of synthetic biology. The definition of a noxious weed is broader than the definition of a plant pest in many respects.¹⁸ It specifically includes direct and indirect injury or damage to “the natural resources of the United States, the public health, or the environment.” These are very broad concepts.

APHIS proposed to use the noxious weed authority in the PPA to expand and update the regulation of GE organisms under part 340 in 2008.¹⁹ It was stated that “technological advances have led to the possibility of developing GE organisms that do not fit within the plant pest definition, but may cause environmental or other types of physical harm or damage covered by the definition of noxious weed in the PPA. Therefore, we consider that it is appropriate to align the regulations with both the plant pest and noxious weed authorities of the PPA.”²⁰

APHIS proposed to delete the list of genera and taxa in 340.2 because, under this new scheme, it was “not needed.” Instead, they proposed to consider whether a donor or recipient species is likely to be a plant pest or noxious weed based on “the most up-to-date pest information maintained by PPQ.”²¹

¹⁷ APHIS went on to “emphasize that the scope of our regulations and the definition of a regulated article in 7 CFR part 340, did not change with the publication of the notice to reopen the public comment period on this docket. Rather, APHIS was clarifying the scope of these regulations. All GE organisms that are regulated articles (including GE plants like Event 3272 corn) must conform to the requirements stated in 7 CFR part 340.” (Page 30)

¹⁸ A noxious weed is defined as “any plant or plant product that can directly or indirectly injure or cause damage to crops (including nursery stock or plant products), livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment.” It should be noted that most plant pests are not plants, but are other types of organisms that harm plants. All noxious weeds are plants or plant products. (73 FR 60011)

¹⁹ See 73 FR 60008 to 60048, Oct. 9, 2008

²⁰ Id. at 60011

²¹ Id. at 60015

The proposed regulations were described as including GE organisms where “[t]he risk that the GE plant poses as a plant pest or noxious weed is unknown”²² and when “there is not enough information about the GE organism’s potential plant pest or noxious weed risks to make a decision regarding those risks.”²³ These proposals appear to be broader than the “reason to believe” standard and the “unknown organism” provision currently in the definition of “regulated article.”

However, APHIS has not taken any further action regarding this proposed rule or any other action to include noxious weed authority in Part 340. It is not clear what it may do or when it may do anything further regarding its noxious weed authority and to what extent such action would affect the regulation of products of synthetic biology.

If all the authorities of the PPA were brought to bear, it is still not clear how many plants modified with synthetic biology techniques would be covered. It might not be many. The PPA has expansive authority to deal with known plant pests and noxious weeds and to take remedial measures when there is a “reason to believe” they are a plant pest or noxious weed. The basic concept of current Part 340 appears to stretch APHIS authority and may go farther than it can regulate under its plant pest authority. Even if APHIS did the same for noxious weeds, it is not clear how many additional products of synthetic biology may be covered.²⁴ There would still need to be a rational scientific basis as to why it is, or there is “reason to believe” it is, or even may be a noxious weed in order to regulate in a manner as currently done for plant pests.

For the reasons previously discussed, I believe there would be potential problems if APHIS did try to finalize the proposed regulations to cover all GE organisms whose plant pest or noxious weed risks were unknown. If additional regulation of the products of synthetic biology is desirable, an agency other than APHIS may have to step in or additional legislative authority may be necessary.²⁵

It should also be noted that just because a product may meet the definition of a noxious weed does not mean that the Secretary is required to take action under the PPA. For example, APHIS received a petition to add genetically engineered Glyphosate tolerant Kentucky bluegrass to the Federal Noxious Weed list. In a response dated June 30, 2011, after conducting a weed risk assessment, APHIS concluded that both non-GE and GE types of Kentucky bluegrass have high weed risk potential and meet the definition of a “noxious weed.” However, APHIS chose not to add either Kentucky bluegrass to the noxious weed list in part 360 because it “can be effectively managed through the use of standard practices used for overall weed management.”²⁶

²² Id. at 60011

²³ Id. at 60012

²⁴ For a discussion of how APHIS reviews plants and plant products to determine if they may be a noxious weed, see Table 1 and the description at 73 FR 60013-14, October 9, 2008.

²⁵ For example, EPA has maintained it has authority to regulate genetically modified plants that do not fall under the jurisdiction of other agencies under the Toxic Substances Control Act (TSCA). (See 66 FR 7905, January 26, 2001) However, rules that describe how EPA would use this authority have not been promulgated, and EPA does not appear to have any experience regulating organisms other than microorganisms under TSCA. EPA may have additional authorities under the Federal Insecticide, Fungicide, and Rodenticide Act to regulate any genetic inserts that can act as a “plant regulator,” but rules along these lines have not been written.

²⁶ Letter of July 8, 2011 addressed to International Center for Technology Assessment and Center for Food Safety

APHIS authority over organisms covered by the PPA

The above sections discussed the issues surrounding whether or not a plant modified with synthetic biology techniques would be a “regulated article” under Part 340 or the PPA. The following sections address specific questions raised concerning APHIS’ authority under the PPA once a product has been determined to be a “regulated article.” It should be noted that some of the authorities described in the sections below, including those that address unintended consequences, apply to any products that are found to meet the definition of a plant pest or noxious weed, regardless of whether or not they were previously regulated.

Does APHIS have authority to require adequate reporting and test data?

The PPA authorizes APHIS to compile information and conduct any investigation considered necessary for the administration and enforcement of the Act,²⁷ including to subpoena the attendance and testimony of witnesses and documentary evidence relating to its administration and enforcement.²⁸ While it is not clear that this authority would cover all information, it is difficult to conceive of information and data that could not be argued to be necessary to make a plant pest or noxious weed determination. Also, as a practical matter, APHIS would probably need a wide range of information to do a National Environmental Policy Act (NEPA) analysis before issuing a permit or making a decision on a regulated product. If the information were not supplied, APHIS would have a basis to take no action or to deny the underlying request. NEPA is discussed in more detail below.

APHIS also has extensive authority to promulgate regulations to require certain tests and reporting with regard to any regulated article. APHIS has the authority to compile information and conduct investigations. Even if it is not a regulated article, information can be obtained when there is a basis for obtaining a subpoena relating to the administration, enforcement or other investigation in connection with the PPA.²⁹ The information could also be voluntarily supplied or APHIS could obtain it from another agency which has authority over the product or organism. This is very broad authority.

In its 2008 proposed rule to include noxious weed authority, APHIS proposed regulations that “would require additional and modified information collections through recordkeeping, reporting, and notifications to APHIS when certain events occur.” The preamble to the proposed rule stated that it was also more specific about the types of records that must be kept for importations, interstate movements and environmental releases, where the current regulations left more of these details to be specified in permit conditions.³⁰ It was also stated that the current application process allows the Administrator to require an applicant to submit any additional information that is needed for adequate evaluation of the application.³¹ APHIS proposed to continue the requirement for applicants to submit reports of all field tests, any unauthorized

²⁷ 7 CFR 7732

²⁸ 7 USC 7733

²⁹ 7 USC 7733(a)

³⁰ 73 FR 60036

³¹ 73 FR 60037

releases, and any additional reports required as individual permit conditions.³² As discussed subsequently herein, failure to comply or provide the requested information can be enforced through civil, criminal and administrative proceedings, as well as not granting the requested permit or other authorization.

Additional reporting, including environmental impacts, is required for regulated articles in situations before it is released from regulation or other oversight. It has been a routine condition imposed by APHIS before authorizing a release into the environment.³³ Reporting could also be required if any plant pest or noxious weed properties are observed after a product of synthetic biology is released from regulation under Part 340.

How does APHIS identify, assess, and manage risks (including NEPA analyses)?

APHIS can make assessments of various plants, products and organisms to see if they should be regulated as plant pests or noxious weeds under the PPA, as they did for Kentucky bluegrass. However, APHIS would need additional authority to conduct risk assessments on organisms which are not subject to regulation under the PPA or other USDA authority. APHIS can cooperate with other agencies that have authority over the subject organism or product. As previously discussed, this would still leave large gaps with regard to review of many plants produced by synthetic biology techniques.

Part 340.4 requires detailed information to be provided to APHIS when applying for a permit to introduce a regulated article into the environment. APHIS reviews all information provided, including test data and other information it can gather on GE plants, their impact on other plants and the environment. In its NEPA implementing regulations, APHIS has stated that the approval and issuance of permits for genetically engineered species normally require environmental assessments, but not necessarily environmental impact statements.³⁴ The issuance of permits or notifications for confined field releases of genetically engineered organisms and products are categorically excluded,³⁵ unless a confined field release involves new species or novel modifications that raise new issues.³⁶ This would seem to apply to most products of synthetic biology, if they are subject to APHIS regulation.

NEPA requires an analysis of all potential environmental impacts of an agency's actions, not just those which the agency has authority to address. The failure to do a full analysis of all potential environmental impacts under NEPA is reason to enjoin or reverse an agency's action, regardless of whether the agency has authority to address those environmental concerns. It would be in the applicants' own best interests to fully cooperate with APHIS and provide whatever data it had to help APHIS do its NEPA analysis.

APHIS is currently conducting a pilot project regarding draft guidance for the preparation of environmental reports for an environmental assessment (EA) or environmental impact statement

³² 73 FR 60038

³³ See 7 CFR 340.4(f)(8,9, & 10)

³⁴ 7 CFR 372.5(b)(4)

³⁵ 7 CFR 372.5(c)(3)(ii)

³⁶ 7 CFR 352.5(d)(4)

(EIS). The information is used by APHIS as the basis for its NEPA analysis. The report includes information regarding the affected environment where non-modified plants and the modified plant will be grown. According to APHIS, the affected environment can be divided into six main areas: agricultural production, the physical environment, biological resources, human health, livestock health, and socioeconomic.³⁷

An agency cannot circumvent or pick and choose what parts of the environmental analysis to do. It must look at all potentially significant environmental impacts in order to proceed, even if using a categorical exclusion or EA instead of a full blown EIS. An agency does not have to ameliorate all environmental risks in order to comply with NEPA; it only has to identify them. It is possible to do a NEPA analysis that finds a certain action will destroy all or many plants and animals in a certain environment. The agency could choose to pursue that action for any number of reasons and still be in full compliance with NEPA, as long as it accurately identified the significant environmental consequences. NEPA is a procedural statute. It does not require a certain outcome, only that the potential or possible significant environmental impacts be known so an informed decision can be made. It does not require that the alternative with the least environmental impacts be chosen. Furthermore, NEPA bestows no authority on an agency to take action outside of that which Congress has given the agency in its enabling legislation. This can leave an agency in the awkward position of identifying an environmental risk without a basis to take action to prevent it. If APHIS refuses to issue a permit on the basis of a risk for which it has no authority, it would probably lose a legal challenge. The standard would not be whether such a risk was present, but whether APHIS had statutory authority to refuse to issue a permit based on that risk. However, as a practical matter, it is unlikely that a product that has shown significant environmental harm would succeed in the marketplace, and few producers would want to be in the position of suing APHIS in order to promote such a product.

What movements can APHIS regulate by permit?

The PPA prohibits the import, export or interstate movement of a plant pest without a permit and in accord with regulations to prevent the introduction or dissemination of a plant pest.³⁸ APHIS has defined an introduction to include a release into the environment and regulates it as an interstate movement. APHIS can prohibit or restrict the importation, entry, exportation, or movement in interstate commerce of any plant, plant product, biological control organism, noxious weed, article, or means of conveyance when it is necessary to prevent the introduction or dissemination of a plant pest or noxious weed, including that it be accompanied by a permit, a certificate of inspection, and be subject to remedial measures, such as treatments before movement.³⁹ This is very specific and very broad authority. However, as mentioned above, there still needs to be some rational, scientific basis why APHIS believes a product of synthetic biology is, or at least may be, a plant pest or noxious weed.

What kind of labeling is required?

³⁷ Draft Guidance for Preparing Environmental Reports, NEPA Pilot Project, APHIS, Biotechnology Regulatory Services, July 2011, p.4. Available at www.aphis.usda.gov/biotechnology/nepa_pilot_documents.shtml

³⁸ 7 USC 7711

³⁹ 7 USC 7712

Marking and identity requirements for importations of regulated articles under part 340 are contained in 7 CFR 340.7. Additional requirements with regard to labeling could be required for importations and interstate movements. But that would only apply to “regulated articles” or other products and organisms subject to the PPA. There is no authority to require labeling for marketing purposes, such as certifying that a product does or does not contain any ingredient that is a product of synthetic biology.

What precautionary measures can APHIS require for field tests and how can it enforce them?

APHIS has the authority to require precautionary measures for field tests of regulated articles.⁴⁰ Such precautions would not have to be limited to direct actual damage to plants. It could encompass indirect injury and damage to plants under the plant pest definition and environmental damage under the definition of a noxious weed. For example, an indirect injury or damage to plants has included regulation of mites and beetles that adversely impact honey bees that are considered necessary for pollination of many crops. The mites are considered an indirect plant pest because they reduce the pollination done by honeybees which reduces the yield from the plants and thereby injures or damages the plants.⁴¹ In programs of this nature APHIS usually has the support of the affected industry and has not been challenged in court regarding how far it can go regarding such indirect effects.

There are many ways APHIS can enforce its regulations and the precautionary measures it applies to field tests. APHIS can use civil, criminal and administrative proceedings. It is not solely reliant on often overloaded U.S. Attorney’s offices to take civil or criminal action for what may be viewed as a relatively low priority. For example, civil penalties up to \$250,000 per violation or twice the gross gain or loss for any violation can be assessed through administrative proceedings in front of the Department’s own Administrative Law Judges.⁴² The Secretary can also seek an injunction to stop violations or compel compliance.⁴³ In addition, a permit can be withdrawn for failure to comply with one or more conditions listed in the permit, and a request for a new permit can be denied for failure to comply with a previously issued permit.⁴⁴

The PPA allows the Secretary to obtain a warrant to enter any premises in the United States to conduct investigations or make inspection and seizures concerning any product, article, plant or means of conveyance regulated under the Act.⁴⁵ The Secretary can also cooperate with foreign and domestic Federal, State, and local government agencies, entities, organizations, associations and other persons to carry out the Act.⁴⁶

⁴⁰ There is nothing in the PPA that limits the Secretary’s discretion with regard to how to define what constitutes a “field test.”

⁴¹ See 7 CFR part 322

⁴² 7 USC 7734(b)

⁴³ 7 USC 7735(2)

⁴⁴ APHIS outlined the possible consequences of failure to comply with its regulations as “including denial of future permits; revocation of current permits; destruction, treatment and removal of GE organisms; issuance of penalties; and a means to settle alleged civil violations prior to the issuance of an administrative complaint.” (73 FR 60025). Also see 7 CFR 340.4(g)

⁴⁵ 7 USC 7731

⁴⁶ 7 USC 7751(a)

In addition, as discussed below regarding remedial measures for unintended events, APHIS can order the owner to treat, apply other remedial measures to or destroy plants, products and articles to prevent the dissemination of a plant pest or noxious weed. If the owner fails to take the action, APHIS can enforce the order in court or take the action and collect the cost of the action from the owner.

What authority does APHIS have to regulate the full life cycle?

APHIS has broad authority over any “regulated article” until it is deregulated. It can also re-regulate a product after it has been deregulated, if the organism or product exhibits any plant pest or noxious weed properties. As discussed above, the real question is whether it is a “regulated article” under Part 340 or otherwise subject to the PPA. APHIS also has broad discretion regarding its regulatory authority, including to regulate or exempt small field trials.

One potential problem that could arise is if APHIS tried to regulate a release into the environment of a product that did not involve the potential of an interstate movement. As a response to comments to its proposed regulations in 1986, APHIS’ justification for the regulation of releases into the environment was, in part, because “[l]iving organisms do not acknowledge State lines.” While that is probably true of pollen of plants that can be carried on the wind and seeds that can be distributed by wind, water, birds and other animals, it may not be true of all products of synthetic biology. If a product can be produced that does not pose such a potential for natural interstate distribution after release into the environment, the basis for regulation of the release under Part 340 might be successfully challenged. However, if remedial measures are required in such a situation, the Secretary could still declare an extraordinary emergency and take action, if necessary.

An additional issue that could be of interest, is what kind of authority might there be to regulate the resulting biomass after the alcohol fuel base is extracted from a modified plant. Such biomass would probably go to a fermenter/refinery for incineration, which would fall under the authority of another agency, most likely EPA. If, however, the resulting biomass were to be used for something else, such as animal feed, it is possible that both the FDA and USDA might have some interest and authority to regulate it.

What authority does APHIS have to address unintended events?

There are many options available to APHIS to prevent dissemination of and eliminate a plant pest or noxious weed that is new to or not widely prevalent. These authorities could be used on any organism when there is “reason to believe” it is a plant pest or noxious weed, whether or not it was previously regulated. Generally, APHIS would first look to a state to quarantine the individual field or area with a specified buffer around it to contain the organism or product. If a state is unwilling or unable to place and enforce the desired quarantine, the Federal government could cooperate with the state to help provide the needed resources,⁴⁷ or it could quarantine the entire state.⁴⁸ The entire state is quarantined in such a situation because there is no violation of

⁴⁷ 7 USC 7751

⁴⁸ 7 USC 7714

the Federal quarantine until a quarantined product or article moves across a state line, unless an extraordinary emergency is declared. The declaration of an extraordinary emergency allows the Secretary to take action intrastate to prevent the artificial movement of the pest or weed. In order to declare an extraordinary emergency, the Secretary must find that a state is not taking adequate measures to eradicate or contain the plant pest or noxious weed.⁴⁹ The chosen action and decisions are independent of whether the product or organism was previously regulated.

APHIS can cooperate with⁵⁰ or order the owner of any product, article or means of conveyance to take the necessary remedial measures to control or eradicate a plant pest or noxious weed that is new to or not widely prevalent in the United States.⁵¹ If the owner does not take the ordered measures, the Secretary can take the owner to court to force compliance,⁵² or APHIS can take what action is deemed appropriate and recover the cost of the action from the owner.⁵³ This, of course, assumes that the responsible entity is still in existence and not bankrupt. Other types of liability are not currently covered and would probably be governed by common law principles, such as torts.

APHIS is specifically authorized to hold, seize, quarantine, treat, apply other remedial measures to, destroy or otherwise dispose of any product, article or means of conveyance which is moving into or through the United States or interstate if there is reason to believe it is, or was at the time of the movement, infested or infected by a plant pest or noxious weed.⁵⁴ However, the articles cannot be destroyed or returned to origin unless there is no less drastic action that would prevent the dissemination of the plant pest or noxious weed.⁵⁵ If an extraordinary emergency is declared, such remedial measures can also be taken intrastate.

APHIS is authorized, but not required, to pay compensation for economic losses incurred as a result of its actions under an extraordinary emergency. Payment of compensation is not authorized for actions ordered by a state or other authority, or for actions taken before the declaration of an extraordinary emergency. It should also be noted that this authority is greater than just paying the fair market value (FMV) of the goods or products destroyed. It can also include collateral and incidental economic losses incurred as a result of the destruction, such as lost profits. For example, if an infected grove of mature fruit producing trees is destroyed, in addition to paying the FMV of the trees, the Secretary is authorized to pay for the economic losses that would be incurred until the replacement trees reach producing maturity. While the Secretary is authorized to pay compensation, it is a discretionary authority that is not required to be paid. It is also limited by available funds.⁵⁶

One source of concern for modified plants is the potential for “gene flow,” the unintended mixing of modified plant genes with conventional seeds or grain. On March 29, 2007, APHIS published a notice entitled “Policy on responding to Low-Level Presence of Regulated

⁴⁹ 7 USC 7715

⁵⁰ 7 USC 7751

⁵¹ 7 USC 7714(b)(1)

⁵² 7 USC 7735(2)

⁵³ 7 USC 7714(b)(2)

⁵⁴ 7 USC 714

⁵⁵ 7 USC 7714(d)

⁵⁶ 7 USC 7715(e)

Genetically Engineered Plant Materials.”⁵⁷ This notice described how APHIS responds when low levels of regulated GE plant materials occur in commercial seeds or grain that may be used for food or feed. APHIS proposed to “establish criteria under which the occurrence of a low level presence (LLP) of GE plant materials in seed or grain may not be cause for agency remedial action.”⁵⁸ It should be noted that this was a statement of policy and not a statement of the extent of its authority under the PPA.

Is there a clear pathway to commercial use for products of synthetic biology?

Currently, the only clear pathway to commercial use is for regulated articles under Part 340. As noted previously, this is currently limited to GE organisms developed with a known plant pest. It does not appear to include most products of synthetic biology, such as a chloroplast modified with a gene gun and inserted into an alcohol feedstock plant. This may change if APHIS chooses to try and use the “unknown organism” provision in the definition of “regulated article” and can successfully defend that decision in court.

APHIS could develop additional pathways to commercialization if it broadened its regulations by using the noxious weed authority and possibly some other areas.⁵⁹ But there has to be some rational scientific basis or theory to regulate the organism or product, before there can be a pathway to commercialization. Therefore, the most important question, again, is whether the organism or product is a “regulated article” under part 340.

If it is not regulated by APHIS or any other agency, there are no barriers to commercialization and it can take whatever pathway its owner desires.

Conclusion

APHIS has stretched its authority under the PPA to regulate the products of genetic engineering under part 340 with regard to plant pests. However, the regulations only cover products of synthetic biology if a plant pest is used in the process. There has not been a legal challenge regarding APHIS’ authority to promulgate Part 340 and the definition of what constitutes a “regulated article.” It is not clear where such a line may be drawn if and when such a challenge should occur, and there is a significant possibility that the entire scheme of regulation under Part 340 could be struck down. If APHIS were to lose such a challenge, it could take many years to get additional legislative authority or to promulgate new regulations. Products of synthetic biology would not be regulated by APHIS or would be in a regulatory limbo until new legislation could be passed or regulations promulgated. The remedial provisions of the PPA could still be brought to bear on unintended events when there is “reason to believe” the organism or product is a plant pest or noxious weed, whether or not it was previously regulated.

APHIS could take action to use its noxious weed authority to broaden its authority under Part 340. However, it is not clear that such action would significantly increase its authority over the

⁵⁷ 72 FR 14649-14651

⁵⁸ 73 FR 60025

⁵⁹ The PEW Initiative on Food and Biotechnology outlined options for additional methods for regulation by various agencies in its Issues in the Regulation of Genetically Engineered Plants and Animals (April 2004)

products of synthetic biology. If pre-market regulation of such technology is desirable, the authority to regulate may need to come from other agencies or from new legislation.

If additional legislative authority is sought, it is important to include authority to address new situations in the fastest possible time frame, to minimize direct and indirect damages, including environmental damages, and not have to wait for action by Congress for authority or appropriations. In order to achieve those objectives, any new legislation should include authority to cover release into the environment and criminal, civil and administrative enforcement mechanisms, including civil penalties assessed through administrative proceedings. It should include being able to order remedial actions and the ability to take action and recover the cost from the owner, especially if the initial action ordered is not followed promptly. In addition, it should include the ability to cooperate with foreign and domestic governmental units at all levels, as well as organizations and individuals. And last, but not least, a funding mechanism that will allow immediate remedial action without having to seek specific new appropriations before action can be taken.