BEYOND THE PLANT PEST TRIGGER: LAW, SCIENCE AND RATIONAL OVERSIGHT OF TRANSGENIC CROPS

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I. INTRODUCTION

A road trip through America's heartland takes on a new dimension when one recognizes that the rising stalks of corn are probably genetically engineered. Genetically engineered (GE) corn, cotton, and soybeans occupied over half the United States arable cropland in 2013, with 90 to 93% of these crops consisting of GE varieties.[1]

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1. JORGE FERNANDEZ-CORNEJO, SETH WECHSLER, MIKE LIVINGSTON & LORRAINE MITCHELL, GENETICALLY ENGINEERED CROPS IN THE UNITED STATES, ERR-162 U.S. DEP'T AGRIC. ECON. RES. SERV., 1, 9 (2014), http://www.beyondpesticides.org/assets/media/documents/USDA_GE[smallpdf.com].pdf.

Federal regulators in the Animal and Plant Health Inspection Service (APHIS) regularly approve GE crops, first for experimental field testing, and then for fully unregulated dissemination.[2] So far, most GE crops are "first-generation" varieties engineered for herbicide resistance (HR), insect resistance (Bt crops), or both.[3] However, increasing numbers of "second-generation" GE crops with value-added traits, such as soybeans with distinctive lipid profiles, low-nicotine tobacco, and high-lysine corn are now becoming available.[4] Studies demonstrate that consumers are willing to pay higher prices for these second-generation products,[5] even though their efficacies are often not well-established. A "third-generation" of GE crops, engineered to produce pharmaceuticals and other non-food products, is now also envisioned.[6]

The spread of first-generation GE crops deepens and reinforces the paradigm of industrial agriculture in the U.S. that began in the post-World War II era.[7] Natural soil replenishment and pest control mechanisms are greatly attenuated on today's industry farms, because ecological cycles are disrupted by large-scale monocultures and the artificial separation of plants and animals.[8] The current system demands the use of copious quantities of chemical herbicides, insecticides, and fertilizers, and is thus facilitated by GE commodity crops that are herbicide-resistant, pest-resistant, or both. Destructive impacts of industrialized agriculture include the reduction of biodiversity engendered by monoculture crops, and

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2. APHIS is located within the U.S. Department of Agriculture (USDA). To date, it has authorized more than 38,000 permits and notifications for the safe importation, interstate movement, and environmental release (field testing) of GE organisms. After some years of field-testing and upon petition, APHIS may grant a determination of "non-regulated status" if it finds that the GE organism is unlikely to pose a plant pest risk. After this determination, the GE organism is no longer regulated. *See Permits, Notifications, and Petitions*, USDA ANIMAL & PLANT HEALTH INSPECTION SERV. (last visited Nov. 27, 2016), https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/ct_submissions_home. Over 100 GE crops have been deregulated since 1987. *See* ANIMAL & PLANT HEALTH INSPECTION SERV., BIOTECHNOLOGY RESEARCH SERVICE STRATEGIC PLAN FY2015-FY2018 at 2, https://www.aphis.usda.gov/biotechnology/downloads/brs_strat_plan_15-18.pdf.

3. *See infra* Section II.A., for a description of GE crops.

4. *See* Fernandez-Cornejo, Wechsler, Livingston & Mitchell, *supra* note 1, at 1. Second-generation traits are often introduced as further alterations within a genetic background already modified for herbicide resistance.

5. *Id.* at 37-38.

6. *Id.* at 1.

7. CAROLYN DIMITRI, ANNE EFFLAND & NEILSON CONKLIN, USDA ECON. RESEARCH SERV., EIB-3: *THE 20TH CENTURY TRANSFORMATION OF U.S. AGRICULTURE AND FARM POLICY*, 1, 6 (2005), https://www.ers.usda.gov/webdocs/publications/eib3/13566_eib3_1_.pdf?v=41055.

8. *Industrial Agriculture: The Outdated, Unsustainable System that Dominates U.S. Food Production*, UNION OF CONCERNED SCIENTISTS, http://www.ucsusa.org/our-work/food-agriculture/our-failing-food-system/industrial-agriculture#.VSFRlDr3U0s (last visited Nov. 27, 2016).

greatly increased levels of air and water pollution, particularly from fertilizer use.[9] GE plants add to these challenges in specific new ways, including adverse impacts from the increased use of toxic herbicides engendered by HR crops, proliferation of herbicide-resistant weeds, and economic damages associated with contamination of organic crops.[10] Concerns about long-term health risks from the pervasiveness of HR crops also persist. For example, an active controversy exists regarding the possible carcinogenicity of glyphosate, the most widely used herbicide in the U.S. and the active ingredient in Monsanto's Roundup products.[11]

In light of these issues, U.S. citizens might reasonably expect that the federal government would exercise stringent, rational governance of the GE crops released on America's farms. It does not. Instead, in 1986, U.S. regulatory agencies adopted the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework), which adopted the position that GE organisms require no particular oversight that cannot be provided under existing statutes.[12] A consequence of this choice is that jurisdiction over GE crops is now spread across three agencies: Department of Agriculture (USDA), Food and Drug Administration (FDA), and Environmental Protection Agency (EPA), with a myriad of overlapping, inconsistent, and inefficiently operating programs that allow significant gaps in oversight.[13] The regulatory scheme is particularly inept in its response to rapid advances in agricultural biotechnology and the underlying, driving science of molecular genetics, which provide new experimental tools enabling the

9. *See id.*

10. NAT'L RESEARCH COUNCIL OF THE NAT'L ACADEMIES, THE IMPACT OF GENETICALLY ENGINEERED CROPS ON FARM SUSTAINABILITY IN THE UNITED STATES, 59-60 (2010) (ebook).

11. The cancer agency of the World Health Organization (WHO) designated glyphosate as a probable carcinogen. *See* Kathryn Z. Guyton et al., *Carcinogenicity of Tetrachlorvinphos, Parathion, Malathion, Diazinon, and Glyphosate*, LANCET ONCOLOGY (2015), http://dx.doi.org/10.1016/S1470-2045(15)70134-8. However, this was contradicted by a co-analysis from the WHO and the U.N.'s Food and Agriculture Organization (FAO), which stated that glyphosate was unlikely to pose a carcinogenic risk from exposure through diet. *See Joint FAO/WHO Meeting on Pesticide Residues, Summary Report* (May 16, 2016), http://www.who.int/foodsafety/jmprsummary2016.pdf?ua=1. An EPA scientific panel will soon meet to consider the issue. *See* Mark Heller, *EPA Panel to Study Whether Glyphosate Causes Cancer*, E&E NEWS (July 26, 2016), http://www.eenews.net/greenwire/2016/07/26/stories/1060040801.

12. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23302 § I(A) (June 26, 1986).

13. Gregory N. Mandel, *Gaps, Inexperience, Inconsistencies, and Overlaps: Crisis in the Regulation of Genetically Modified Plants and Animals*, 45 WM. & MARY L. REV. 2167 (2004).

increasingly sophisticated genomic manipulations associated with second- and third-generation GE crops.[14]

Many scholars and practitioners have called for new approaches to agricultural policy and environmental law to meet these challenges.[15] As a contribution to these efforts, this paper offers a new analysis that addresses the challenges to regulation associated with novel scientific approaches for creating transgenic crops. Section II sets the stage by describing the nature of GE crops and the basis for how the Coordinated Framework functions in agricultural biotechnology.[16] Oversight of GE crops under the Plant Protection Act (PPA) is then described. Under this law, GE plant releases to the environment are regulated only if the new, recombinant plant is created by a particular genetic methodology involving the use of plant pest DNA.[17] From an analysis of how pest DNA is used to create a GE plant, the conclusion reached is that the regulatory scheme under the PPA does not rest on a solid foundation. This is because all GE crops constructed by these techniques use a modified version of the pest DNA that is unable to cause tumors in any plant.[18]

Section III reviews new approaches to the creation of transgenic plants that do not require use of any plant pest DNA, and thus fall outside the scope of the PPA's plant pest trigger as interpreted by APHIS and the courts.[19] This is a significant loophole that further underlines the weakness of the present regulatory scheme. Indeed, developments in the science of plant genetic engineering are now proceeding so rapidly that they threaten to render the framework for oversight obsolete, perhaps within a decade or less. This real prospect of a regulatory vacuum should motivate comprehensive reforms. Substantive discussions that consider the challenges posed by the new technologies have begun in the international arena.[20]

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14. *See* Alex Camacho, Allen Van Deynze, Cecilia Chi-Ham & Alan B. Bennett, *Genetically Engineered Crops that Fly Under the US Regulatory Radar*, 32 NATURE BIOTECHNOLOGY 1087-91 (2014).

15. For a collection of recent scholarship in the field, *see* MARY JANE ANGELO, JASON J. CZARNEZKI & WILLIAM S. EUBANKS II, FOOD, AGRICULTURE AND ENVIRONMENTAL LAW (Envtl. Law Institute, 2013).

16. *See* Coordinated Framework for Regulation of Biotechnology, *supra* note 12.

17. George A. Kimbrell, *Regulating Transgenic Crops Pursuant to the Plant Protection Act, in* FOOD, AGRICULTURE AND ENVIRONMENTAL LAW 1, 281-99 (Mary Jane Angelo, Jason J. Czarnezki & William S. Eubanks II, eds. 2013).

18. Tzvi Tzfira & Vitaly Citovsky, Agrobacterium-*Mediated Genetic Transformation of Plants: Biology and Biotechnology*, 17 CURRENT OPINION BIOTECHNOLOGY 147 (2006).

19. *See* Camacho, Van Deynze, Chi-Ham & Bennett, *supra* note 14, at 1088-89.

20. *See* generally Maria Lusser & Howard V. Davies, *Comparative Regulatory Approaches for Groups of New Plant Breeding Techniques*, 30 NEW BIOTECHNOLOGY 437 (2013).

Section IV confronts the question of how these issues can be best resolved within the framework of the U.S. regulatory system. It is unlikely that Congress will enact changes to the PPA, since oversight of GE organisms has never been part of its rationale for establishing protections against plant pests or noxious weeds.[21] APHIS has also been reluctant to forcefully apply its regulatory authority under the law.[22] However, an alternative and more feasible approach is for the Office of Science and Technology Policy (OSTP) to amend its scope document guiding agencies as to how they should interpret the Coordinated Framework.[23] The new guidance should indicate the importance of a regulatory floor for all transgenic organisms, since without some examination it is impossible for agencies to judge whether new GE crops are substantially similar to existing varieties derived by classical plant breeding.[24] This is particularly relevant when the gene donor organism and the recipient crop plant are from geographically and environmentally disparate regions such that little or no capacity for gene transfer in the wild is plausible. In its new guidance, OSTP should also provide incentives or requirements for APHIS to consult with EPA before approving field trials of new GE crops. This consultation can fruitfully occur in the context of APHIS' required evaluation of whether to prepare an Environmental Impact Statement (EIS) under the National Environmental Policy Act (NEPA).[25] Consultation is justified by the complexity of the new science, comprising a field within EPA's, but not APHIS' expertise, and by the fact that EPA already has a significant role in the oversight of agricultural practices.[26] If successful, this process might have long-term beneficial impacts in fostering interagency collaborations in the food and agriculture fields more generally.

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21. Enactment of the PPA in 2000 repealed or amended nine previous statutes, including the Federal Plant Pest Act and parts of the Federal Noxious Weed Act, 66 Fed. Reg. 21049 (Apr. 27, 2001). For the Congressional findings motivating the laws, *see* 7 U.S.C. § 7701 (2012).

22. *See* Kimbrell, *supra* note 17, at 290-93. *See* also *infra* Section II.C.

23. This bypasses Congress via executive order. *See* Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products Into the Environment, 57 Fed. Reg. 6753-01 (1992) [hereinafter, 1992 Scope Document].

24. "Substantial similarity" to existing varieties from classical plant breeding is one criteria now used for risk assessment of GE crops. *See* NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., ENVIRONMENTAL EFFECTS OF TRANSGENIC PLANTS: THE SCOPE AND ADEQUACY OF REGULATION 83 (2002) (ebook).

25. 7 C.F.R. §§ 372.5(c)(3)(ii), 372.5(d) (1995).

26. *See* Kimbrell, *supra* note 17, at 293-94.

II. REGULATION OF GENETICALLY ENGINEERED CROPS IN THE U.S.

A. Essential Characteristics of GE Crops

Most GE crops in the U.S. are considered to be "first-generation" products, and are distinguished from non-GE crops by the incorporation of one or a few new genes. HR crops incorporate a modified version of a gene already present in all plants, which is essential to the plant's metabolism.[27] The active chemical in Monsanto's Roundup herbicide, glyphosate, is able to attach itself to the natural version of the protein encoded by the essential gene, blocking its required function and thus killing the plant.[28] In contrast, the new, altered protein in the GE plant retains its metabolic function but, because of its slightly altered structure, is no longer susceptible to inhibition by glyphosate.[29] Hence, the GE plant is able to withstand the application of Roundup while surrounding weeds are not. HR crops presently widespread in the U.S. include soybeans, corn, cotton, alfalfa, canola, and sugarbeets.[30]

Bt crops are distinguished by the introduction of a naturally occurring gene from the common soil bacterium *Bacillus thuringiensis* (Bt). This gene encodes a protein that allows the plant to resist predation by insect pests.[31] Proteins of this class form crystalline structures that are toxic to many beetles, mosquitoes, leafworms, moths, and other insect pests. The toxicity of the protein crystals is specific to certain classes of insects, allowing for targeted applications in agriculture depending on which pests are present in a particular area.[32] GE Bt plants incorporate the genes encoding the crystal-forming proteins into their own DNA, and the proteins are

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27. Through the operation of the universal genetic code present in all life, this essential gene encodes a protein known as EPSP synthase. In plants, this protein catalyzes a key step in a metabolic pathway that ultimately produces certain key amino acids essential to the life of the cell. In general, modified versions of genes often encode altered proteins, which may have distinct properties. *See* T. Funke et al., *Molecular basis for the herbicide resistance of Roundup Ready crop*s, 103 No. 35 PROC. NATL. ACAD. SCI. U.S. 13010, 13010-15 (2006).

28. Robert Douglas Sammons & Todd. A. Gaines, *Glyphosate resistance: state of knowledge*, 70 PEST MGMT. SCI. 1367, 1367-77 (2014).

29. One mechanism for glyphosate resistance in weeds is that their EPSP synthase genes naturally acquire similar mutations to those deliberately engineered into the crop plant. *Id.* at 1371. Profligate use of glyphosate has generated more distinct resistance mechanisms than are known for any other herbicide. *Id.* at 1367.

30. *See* FERNANDEZ-CORNEJO, WECHSLER, LIVINGSTON & MITCHELL, *supra* note 1.

31. Liliana Pardo-Lopez, Mario Soberon & Alejandra Bravo, *Bacillus thuringiensis insecticidal three-domain Cry toxins: mode of action, insect resistance and consequences for crop protection*, 37 FEMS MICROBIOL. REV. 3, 3-22 (2013); *see also* Funke et al., *supra* note 27 (noting the relationship of genes to proteins).

32. *Id.* at 4.

then referred to as plant-incorporated protectants (PIPs) by EPA.[33] U.S. crops incorporating PIPs include corn and cotton.[34] Some GE crops have been engineered to incorporate both HR and Bt traits. Such crops are referred to as "stacked cultivars".[35]

Second- and third-generation GE crops also incorporate one or a small number of genes, which are derived from a variety of other organisms depending on what trait is desired. As of September 2013, about 20% of the crops approved by APHIS for deregulation were second- or third-generation. It is likely that this fraction will increase substantially in the near future, since many new products are in development.[36]

B. Coordinated Framework for the Regulation of Biotechnology

In 1986, the Coordinated Framework established the administrative basis for regulating GE plants in the U.S.[37] This document describes how authority is divided among EPA, USDA and FDA for oversight of organisms and foods developed with recombinant DNA techniques.[38] When the Coordinated Framework was released, the context for regulation was still based upon *process*: use of the new gene-splicing techniques itself was intended to be the basis of oversight.[39] However, in the next few years, both the National Academy of Sciences and the National Science Foundation issued

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33. Plant-incorporated protectants (PIPs) are pesticidal substances produced by plants and the genetic material necessary for the plant to produce the substance. *See Biopesticides*, ENVTL. PROT. AGENCY, http://www.epa.gov/pesticides/biopesticides (last visited Nov. 27, 2016). Alternatively, Bt cells in a suitable suspension can be applied directly to the susceptible crop plants as a microbial bioinsecticide. This is an effective approach to pest management that does not require construction of a transgenic crop. APHIS has jurisdiction over the transgenic Bt plants, while EPA regulates the Bt bioinsecticide and the pesticide in the transgenic plant under FIFRA.

34. *See* FERNANDEZ-CORNEJO, WECHSLER, LIVINGSTON & MITCHELL, *supra* note 1.

35. NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., *supra* note 10, at 30.

36. *See* Camacho et al., *supra* note 14, at 1088.

37. *See* 51 Fed. Reg. at 23,302-01. Authority for the Coordinated Framework is provided by the Nat'l Science and Technology Policy, Organization, and Priorities Act of 1976, 42 U.S.C. § 6601 (1976).

38. *See* 51 Fed. Reg. at 23304. Recombinant DNA molecules are defined as (i) molecules that (a) are constructed by joining nucleic acid molecules and(b) that can replicate in a living cell, i.e., recombinant nucleic acids; (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or (iii) molecules that result from the replication of those described in (i) or (ii) above. NAT'L INST. OF HEALTH, NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES 9 (Apr. 2016).

39. *See* 51 Fed. Reg. at 23304. The process-based context is evident in the regulation of intergeneric combinations, or "deliberately formed microorganisms which contain genetic material from dissimilar source organisms."

reports arguing that regulation should instead be *product-based*.[40] These reports made the argument that no specific, unique harms emerge solely from the use of genetic engineering methods to construct transgenic crops or microbes.[41] Based upon these analyses, administrators envisioned that oversight should be based solely on the intrinsic characteristics and environments of the organisms, and not on the new methodologies by which they are derived. The essential idea was that classical plant breeding techniques such as tissue culture and hybridization also alter the genetic makeup of crop plants, yielding variants that may require regulatory oversight. No fundamental distinction was therefore seen between these earlier methods and the more recent, highly precise approaches to specifically introduce new genes.[42] Of course, recombinant DNA technology allows construction of new GE plants that could never occur naturally or be derived from traditional plant breeding, since genes from any organism in nature can be combined.[43] Nonetheless, the judgment of the expert committees at the time was that no focused oversight of this particular aspect of the technology was warranted.[44]

This early scientific consensus also influenced the decision to regulate GE plants and microorganisms within preexisting statutory frameworks.[45] Guidelines for oversight were developed under the auspices of an interagency working group, the Biotechnology Science Coordinating Committee (BSCC), formed in October of 1985. BSCC is part of the Federal Coordinating Council for Science,

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40. NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., FIELD TESTING GENETICALLY MODIFIED ORGANISMS: FRAMEWORK FOR DECISIONS (1989) (ebook); COMMITTEE ON THE INTRODUCTION OF GENETICALLY ENGINEERED ORGANISMS INTO THE ENVIRONMENT, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., INTRODUCTION OF RECOMBINANT-DNA ENGINEERED ORGANISMS INTO THE ENVIRONMENT: KEY ISSUES (1987) (ebook).

41. *See* NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., *supra* note 40, at 14-15. Findings were based in part on the absence of attributable harms from genetic engineering experiments in many academic, industry and government laboratories. The rationale for an early self-imposed moratorium on recombinant DNA experiment is described in Paul Berg et al., Summary statement of the Asilomar conference on recombinant DNA molecules, 72 PROC. NATL. ACAD. SCI. US 1981, 1981-84 (1975). For the subsequent lifting of the ban *see* W.R. Grace and Co.; Filing of Food Additive Petition 46 Fed. Reg. 40331 (1981).

42. *See* NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., *supra* note 40, at 15; NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., GENETICALLY MODIFIED PEST-PROTECTED PLANTS: SCIENCE AND REGULATION (2000) (ebook). This report reiterated the findings of the 1989 analysis and provided further support for the paradigm of product-based regulation.

43. Genes are made entirely of DNA, and all DNA has the same overall structure. Hence, DNA segments can usually be interchanged without adversely affecting the capacity of the cell to replicate its DNA or to divide into daughter cells.

44. The final scope document released by OSTP in 1992 eliminated the notion of "intergeneric combinations" in its guidelines for agency action. *See* 57 Fed. Reg. at 6753-01; 51 Fed. Reg. at 23,304; *infra* Section IV.

45. *See* Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23308 (June 26, 1986).

Engineering and Technology (FCCSET), a statutory interagency coordinating mechanism managed by the Office of Science Technology and Policy (OSTP) in the Executive Office of the President (EOP).[46] The BSCC-led process produced a scheme by which GE plants and microorganisms used in agricultural biotechnology are regulated under two statutes. First, new regulations were developed by APHIS under the PPA to evaluate all GE plants that fit the statutory definition of a plant pest.[47] Second, new rules were formulated under the authority of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), which is administered by EPA. This statute regulates the manufacture, sale and use of GE plants that incorporate pesticides, and microbial bioinsecticides that are applied in U.S. agriculture.[48] Other important aspects of the Coordinated Framework included a new authority to regulate all GE microbes as toxic substances under the Toxic Substances Control Act (TSCA), which is also administered by EPA.[49] The Coordinated Framework also specified several important roles for the Food and Drug Administration (FDA) in regulating GE foods and animals.[50]

The Coordinated Framework envisioned that EPA, USDA, and FDA work "in an integrated and coordinated fashion, and together should cover the full range of plants, animals, and microorganisms

46. *See* Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,306 (June 26, 1986).

47. 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, 52 Fed. Reg 22908 (proposed June 16, 1987) (to be codified at 7 C.F.R. pt. 340); Genetically Engineered Organisms and Products: Notification Procedures for the Introduction of Certain Regulated Articles and Petition for Nonregulated Status, 58 Fed. Reg. 17044 (proposed Mar. 31, 1993) (to be codified at 7 C.F.R. pt. 340); Genetically Engineered Organisms and Products: Simplification of Requirements and Procedures for Genetically Engineered Organisms, 62 Fed. Reg. 23945 (proposed May 2, 1997) (to be codified at 7 C.F.R. pt. 340).

48. For an overview of FIFRA, *see* STEVEN FERREY, ENVIRONMENTAL LAW 640-47 (Wolters Kluwer Law & Business, 6th ed. 2013). Regulations for transgenic plants engineered to express pesticides are found at Plant-Incorporated Protectants (Formerly Plant Pesticides), Supplemental Proposal, 66 Fed. Reg. 37,855-69 (July 19, 2001) (to be codified at 40 C.F.R. pt. 140).

49. *See* David Markell, *An Overview of TSCA, its History and Key Underlying Assumptions, and its Place in Environmental Regulation* 32 WASH. U. J.L. & POL'Y 333 (2010). For the final EPA regulations governing GE microbes under TSCA, *see* Microbial Products of Biotechnology; Final Regulation Under the Toxic Substances Control Act, 62 Fed. Reg. 17,910 (proposed Apr. 11, 1997) (to be codified at 40 C.F.R pt. 700, 720, 721, 723, 725); At EPA, FIFRA is administered by the Office of Pesticide Programs, while TSCA is administered by the Office of Pollution, Prevention and Toxics (OPPT). The recent amendments to TSCA do not specifically address EPA's authority to regulate GE microbes. Bergeson & Campbell, P.C., *TSCA Reform: An Analysis of Key Provisions and Fundamental Shifts in the Amended TSCA*, NAT'L LAW REV. (May 31, 2016), http://www.natlawreview.com/article/tsca-reform-analysis-key-provisions-and-fundamental-shifts-amended-tsca.

50. The FDA regulates both GE foods that are not exposed to pesticides, and transgenic animals. Transgenic foods are classified as food additives under the Federal Food, Drug and Cosmetic Act (FFDCA), while transgenic animals are classified as new animal drugs. *See* Kimbrell, *supra* note 17, at 286-87.

derived by the new genetic engineering techniques."[51] For example, EPA is the lead agency on pesticide regulation and is expected to coordinate with USDA and FDA in fulfilling its mission.[52] However, in reviewing the multiagency approach of the Coordinated Framework, a study commissioned by the National Research Council (NRC) raised substantial concerns regarding regulatory overlap and failures in interagency communication.[53] These issues may become more acute in light of the fact that increasingly sophisticated scientific methods are becoming employed to create new second- and third-generation GE products.[54] Bringing additional scientific expertise to bear in the oversight process and improving mechanisms for collaboration between agencies are key challenges that must be faced in reimagining the regulatory scheme.

C. The Plant Protection Act

Authority for oversight of GE crops on America's farms is derived from the PPA.[55] This statute authorizes the USDA Secretary to restrict the importation, movement, and means of conveyance of plants, plant products, biological control organisms, plant pests, and noxious weeds to prevent their introduction and interstate movement within the U.S.[56] Reflecting its early origins, the law and its associated regulations address the need to protect U.S. agriculture from invasion of plant pests and noxious weeds from other countries, and classify these harmful organisms into very specific taxonomic categories. Both the plant pest and noxious weed authorities allow petitions for the purpose of adding new organisms.[57] Regulation of transgenic plants was added under the authorities of several of the PPA's precursor statutes, the Federal Plant Pest Act and Federal Plant Quarantine Act, shortly after the

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51. *See* Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23304 (June 26, 1986).

52. Plant Insecticides Subject to the Federal Insecticide, Fungicide, and Rodenticide Act; Proposed Rule, 59 Fed. Reg. 60,519-35 (proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pt. 152, 174); Regulations Under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-Incorporated Protectants (Formerly Plant-Pesticides), 66 Fed. Reg. 37,771-37,817 (July 19, 2001) (to be codified at 40 C.F.R. p. 152, 174).

53. *See supra* note 44, Section 4.3, at 155.

54. *See infra*, Section III.

55. 7 U.S.C. §§ 7701-7784 (2012).

56. CONG. RESEARCH SERV., SUMMARIES FOR THE AGRICULTURAL RISK PROTECTION ACT OF 2000. TITLE IV. PLANT PROTECTION ACT, https://www.govtrack.us/congress/bills/106/hr2559.

57. 7 C.F.R. § 360.500; 7 U.S.C. § 7711(c)(2) (2012).

Coordinating Framework was established.[58] These regulations were then imported with no substantive changes into the PPA when it was enacted in 2000.[59] They have not been updated since.[60]

1. The Noxious Weed Authority

The noxious weed provisions of the PPA confer broad regulatory authority. 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 U.S., the public health, or the environment."[61]

On its face, this definition should readily encompass, for example, HR commodity crop seeds that escape to contaminate a nearby organic farm, thereby causing economic damages to that agricultural interest. Showings that the liberal application of herbicides leads to dissemination of damaging HR "superweeds," or increases health risks of farmworkers, would also appear to be cognizable harms accommodated under the statute's mandate to protect the natural resources of the U.S., the public health, or the environment.[62]

However, while a plain reading of the statute suggests that many GE crops could well be regulated as noxious weeds, USDA has yet to affirmatively employ its authority to do so.[63] Specific regulations in the PPA addressing transgenic crops are described only within the bounds of the plant pest authority.[64] This suggests that at the time it formulated the regulations, APHIS chose not to view its mandate to regulate noxious weeds as an appropriate vehicle to

58. *See supra* note 21.

59. Plant Protection Act, Revisions to Authority Citations, 66 Fed. Reg. 21,049 (proposed Apr. 27, 2001) (to be codified at 7 C.F.R. pts. 300-302, 318, 319, 322, 330, 340, 351-56, 360, 361, 371, 372, 380; 9 C.F.R. pts. 1-3, 11, 49-54, 70-75, 77, 79, 80-82, 85, 89, 91, 92, 94-99, 101-109, 112-18, 122-24, 145, 147, 151, 156, 160-62, 166, 167); Plant Pest Regulations; Update of Current Provisions, 66 Fed. Reg. 51,340 (proposed Oct. 9, 2001) (to be codified at 7 C.F.R. pt. 340).

60. On October 9, 2008, USDA published a proposal to amend the regulations for GE crops under the PPA. *See Importation, Interstate Movement, and Release Into the Environment of Certain Genetically Engineered Organisms*, 73 Fed. Reg. 60008-48 (proposed Oct. 9, 2008) (to be codified at 7 C.F.R. pt. 340). However, the proposed rule was withdrawn on March 4, 2015. *Importation, Interstate Movement, and Release Into the Environment of Certain Genetically Engineered Organisms*, 80 Fed. Reg. 11598 (proposed Oct. 9, 2008) (to be codified at 7. C.F.R. pt. 340).

61. 7 U.S.C. § 7702(10) (2012). Current regulations enumerate over 100 distinct varieties of noxious weeds that are regulated under the statute. 7 C.F.R. § 360.200 (2012).

62. *See* Kimbrell, *supra* note 17, at 292-93, for further description of harms that are arguably included within the agency's statutory mandate.

63. *Id.* at 292.

64. 7 C.F.R. § 340.2 (2016); *see also infra*, Section II.C.2.

oversee GE crops. The agency did later propose new rules, apparently envisioning application of the noxious weed authority to this end, but those rules were withdrawn in early 2015.[65] Further, in *International Center for Technology Assessment v. Johanns* (*Johanns*),[66] the D.C. Circuit clearly stated that APHIS is under no obligation to add to the list every plant that fits the statutory definition.[67] Instead, the court emphasized that, in responding to petitions to add new noxious weeds, APHIS retains discretion that is constrained only by the need to provide a reasoned explanation based upon sound science.[68] From the withdrawal of the proposed rule and the court's decision in *Johanns*, it appears that general application of the noxious weed authority to all GE plants may be unlikely in the near future. However, extension of the authority in particular, well-justified cases could be possible.[69] Any choice at all to regulate under the noxious weed authority would certainly mark a significant moment in the evolution of the PPA.

2. The Plant Pest Authority

The primary basis for regulation of GE crops in the U.S. derives from their classification as plant pests under the PPA. Plant pests are defined as follows:

> 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.[70]

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65. *See id.*

66. Int'l Ctr. for Tech. Assessment v. Johanns, 473 F. Supp. 2d 9 (D.D.C. 2007). This is the only case that addresses application of the PPA's noxious weed authority to GE plants.

67. *Id.* at 26.

68. *Id.* at 26-27.

69. For example, in March of 2014, the Center for Food Safety (CFS) petitioned USDA to regulate several multiple herbicide resistant plants as noxious weeds. At the time of publication, USDA-APHIS had not yet responded to the petition. CTR. FOR FOOD SAFETY, COMMENTS ON USDA APHIS'S PROPOSED PLANT PROTECTION ACT APPROVAL OF DOW'S 2, 4-D-RESISTANT CORN AND SOY; NOXIOUS WEED PETITION (2014), http://www.centerforfoodsafety.org/files/cfs-24-d-corn-and-soy_legal_3_11_2014_final_77612.pdf.

70. 7 C.F.R. § 340.1 (2016).

GE crops are not likely to come within this definition, since they are not infectious agents or substances, nor are they parasitic.[71] It has been argued that GE crops could be classified as plant pests based upon the indirect injuries that they cause to organic agriculture (economic damages from contamination) and to biodiversity (transgenic pollution).[72] However, this claim was rejected in a case involving Roundup Ready (RR) alfalfa, in which a panel of the 9th Circuit Court of Appeals emphasized that these harms, while significant, are not plant pest harms within the meaning of the PPA.[73] Instead, the court upheld the agency's claim that only direct or indirect physical damage or destruction of plants is a protected injury.

If transgenic crops by their nature do not constitute plant pests, then why are they regulated under the PPA? Remarkably, oversight is based instead on the fact that the new genes are introduced by using the plant pest *Agrobacterium tumefaciens*.[74] *Agrobacterium* is common in many soils and is the causative agent of crown gall disease, which generates damaging tumors in many plants.[75] The mechanism of tumor formation involves the transfer of certain genes from the bacterial cell into the plant.[76] In 1983, it was demonstrated that the oncogenic (tumor-generating) genes of *Agrobacterium* could be replaced by other genes of interest,[77] offering an approach to plant transformation that now provides the most common and efficient method for generating new GE crops.[78] In the laboratory, the DNA of desired, external genes is combined with a larger *Agrobacterium*-derived DNA that is able to integrate into the plant chromosome. This newly engineered DNA is incorporated into the living *Agrobacterium* cells, which are then co-cultivated with cells

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71. Parasitic plants possess specific root structures that connect them to another plant, through which they acquire nutrients and thus damage the capacity of the host to fully flourish. *See* Daniel L. Nickrent and Lytton J. Musselman, *Introduction to Parasitic Flowering Plants*, THE PLANT HEALTH INSTRUCTOR (2010), http://www.apsnet.org/edcenter/intropp/pathogengroups/pages/parasiticplants.aspx.

72. Center for Food Safety v. Vilsack, 718 F.3d 829 (9th Cir. 2013).

73. *Id.* at 839-41.

74. E.W. Nester, Agrobacterium*: Nature's Genetic Engineer*, 5 FRONTIERS IN PLANT SCIENCE 1 (2015), http://journal.frontiersin.org/article/10.3389/fpls.2014.00730/full.

75. *Id.* at 1, 10.

76. Mary-Dell Chilton et al., *Stable Incorporation of Plasmid DNA into Higher Plant Cells: the Molecular Basis of Crown Gall Tumorigenesis*, 11 CELL 263, 263 (1977).

77. A. Hoekema et al., *A binary plant vector strategy based on separation of the Vir- and T region on the* Agrobacterium tumefaciens *Ti plasmid*, 303 NATURE 179, 179-80 (1983).

78. While the natural range of *Agrobacterium* is restricted to dicotyledonous plants (a subset of all flowering plants), it has been possible to find conditions in the laboratory that allow infection of many more species. This considerably expands the scope of the technology. "Transformation" means introduction and stable uptake of DNA into cells. *See* Tzfira & Citovsky, *supra* note 18.

or tissues harvested from the crop of interest.[79] Transgenic shoots are later recovered for generation of new, stable crop lines.

GE crops are thus considered "regulated articles" because some of the donor DNA comes from a plant pest.[80] However, the tumor-promoting genes of all *Agrobacterium* strains used in laboratory GE plant derivations have been removed, rendering the bacteria disabled. Indeed, in the RR alfalfa case, the court ruled against the plaintiff's assertions that GE alfalfa is a plant pest in part because the pest DNA used was disabled.[81] The court stated that the Agrobacterium "can no longer injure other plants *once the bacterium's genetic material is inserted into the genetic structure of conventional alfalfa*."[82] The reality, however, is that the lack of oncogenic DNA in the *Agrobacterium* strain means that no plant pest-related injury is possible *at any stage* of the process—and this is true for any GE crop constructed with this technology.[83] This could form the basis for a challenge to the regulations as outside of the authority of the statute, in which the question to be litigated would be whether an engineered *Agrobacterium* lacking oncogenic sequences is a plant pest within the meaning of the PPA.[84] Regulation of GE plants under the plant pest authority of the PPA, the sole present basis for all GE crop regulation in the U.S., thus, rests on highly uncertain grounds.

III. THE MUSHROOMING REGULATORY LOOPHOLE

Administrative oversight may languish, yet science continues to advance. This dynamic is now provoking new concerns that even the existing weak regulatory paradigm may not endure much longer. Novel techniques increasingly enable the creation of GE plants

79. Sylvester Anami et al., *Higher plant transformation: principles and molecular tools*, 57 INT. J. DEV. BIOL. 483, 483 (2013).

80. 7 C.F.R. § 340.1 (1997). Gene(s) of interest may be taken from any organism, but all GE crops generated using *Agrobacterium* are regulated because all have the *Agrobacterium* DNA sequences necessary to insert the foreign DNA.

81. *See* Vilsack, 718 F.3d 829 at 840-41.

82. *Id.* (emphasis added).

83. The recombinant DNA manipulations are carried out using the common laboratory bacterium Escherichia coli, and the DNA segment containing the gene of interest is then introduced into a modified *Agrobacterium* strain that lacks the oncogenic DNA, prior to infection of the plant cells. *Agrobacterium* cells that have plant pest properties are not present at any stage of the genetic engineering process. *See* Tzfira & Citovsky *supra* note 18, at 147.

84. A modified *Agrobacterium* with oncogenic sequences removed is obviously "similar to" the natural organism that is a plant pest, and is also "infectious" in the sense that part of its DNA is transferred to the crop plant. However, the DNA that is transferred is not the oncogenic segment, but the new external gene, which may not "cause disease or damage . . ." *See infra*, Section II.C.2 for the regulatory definition of "plant pest"; *See* discussion *infra* Part IV.

without any use of *Agrobacterium*, and thereby allow developers to circumvent regulation entirely.[85] As suggested, APHIS could respond by asserting its noxious weed authority to ensure some oversight,[86] but it has chosen not to do so. Instead, private and public entities seeking to avoid regulation are invited to send the Biotechnology Regulatory Services (BRS) bureau of APHIS a brief letter describing the transformation method, the DNA constructs used, the donor and recipient organisms, and the new genetic trait that they seek to introduce.[87] APHIS considers these inquiries and usually responds rapidly with an even briefer letter, often within just a few months. A reply affirming the firm's view ends the matter, assuring no regulation. Twenty-six such inquiries were made between 1994 and 2012; of these, 22 were ruled outside the scope of regulation.[88] Thirty more determinations of nonregulated status were then made publicly available by APHIS between 2013 and March 2016.[89] Some of these inquiries come from small private firms and public sector institutions, suggesting that GE seed developers lacking deep pockets are deliberately adopting the new technologies to avoid oversight.[90] It is apparent that the continued viability of the U.S. regulatory scheme for GE crops is now wholly dependent on how rapidly the new approaches can be brought on line at sufficiently low cost to compete with the well-established *Agrobacterium* technology. Given the sharp, recent increase in the number of inquiries to BRS, and a parallel recent rise in scientific publications and patent applications,[91] this timeframe could be quite short.

A. New Approaches for Delivering Foreign DNA into Plants

Since *Agrobacterium* is used to deliver foreign DNA into plant cells (the *transformation* process), the most direct challenges to regulation come from the invention of new delivery techniques. The most common alternative, which has been available for some time,

85. *See* Camacho et al., *supra* note 14, at 1088.

86. *See supra* Section II.C.2.

87. *See Biotechnology Regulatory Services (BRS)*, USDA ANIMAL & PLANT HEALTH INSPECTION SERV., http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/biotechnology?1dmy&urile=wcm%3Apath%3A/ (last visited Nov. 27, 2016).

88. *See* Camacho et al., *supra* note 14, at 1090.

89. *See Petitions for Determination of Nonregulated Status*, USDA ANIMAL & PLANT HEALTH INSPECTION SERV., https://www.aphis.usda.gov/biotechnology/petitions_table_pending.shtml (last visited Nov. 27, 2016).

90. *See* Camacho et al., *supra* note 14, at 1088.

91. *See* Maria Lusser, Claudia Parisi, Damien Plan & Emilio Rodríguez-Cerezo, *Deployment of New Technologies in Plant Breeding*, 30 NATURE BIOTECHNOLOGY 231, 231 (2012).

is biolistics.[92] DNA containing the gene of interest is attached to the surface of a very small, metal sphere (a "microparticle"), which is fired at high speed into the plant cell.[93] The break in the plant cell wall from the microparticle bullet is repaired by natural processes, and the DNA then integrates into the plant chromosome.[94] A broad range of plants, including all common commodity crops in the U.S., have been successfully transformed with this approach.[95] The success of biolistics in any particular application, however, and its efficacy as compared to *Agrobacterium*, depend on a wide range of experimental variables that have to be optimized in each case. Most of the time, biolistics results in the integration of many copies of the desired genes into the chromosome, which often has deleterious effects on the consequent properties of the GE plant.[96] This explains why *Agrobacterium* has been the method of choice to date, although the recent regulatory approvals by APHIS of many biolistics-derived GE plants demonstrate that these hurdles are increasingly surmountable.[97]

Other direct gene transfer systems that bypass the need for *Agrobacterium* have also been developed. One set of methods involves the preparation of protoplasts, which are plant cells lacking the rigid exterior cell wall.[98] This makes the uptake of DNA much easier to accomplish, by techniques involving treatment with chemical reagents or application of electric fields. Although only a small number of plants, most notably tobacco, have so far been successfully transformed by this approach, ongoing work holds potential to expand the number of applications.[99] Alternatively, DNA has been introduced using viruses that have a broad host range and are capable of infecting many plants.[100] In this case, the delivery system may be regulated under the PPA as a plant pest, since plant viruses are an enumerated category under the statute.[101] However, modification of the virus to eliminate its pathogenic

92. J.C. Sanford, F.D. Smith and J.A. Russell, *Optimizing the Biolistic Process for Different Biological Applications*, 217 METHODS ENZYMOL 483, 483-85 (1993).

93. Nigel J. Taylor & Claude M. Fauquet, *Microparticle Bombardment as a Tool in Plant Science and Agricultural Biotechnology*, 21 DNA AND CELL BIOLOGY 963, 964 (2002).

94. *Id.* at 971-72.

95. *Id.* at 967.

96. *Id.* at 972.

97. *See* Camacho et al., *supra* note 14.

98. Jeffrey A. Townsend et al., *High frequency modification of plant genes using engineered zinc finger nucleases*, 459 NATURE 442, 442 (2009).

99. J. Shen et al., *Isolation, Culture and Transient Transformation of Plant Protoplasts* 63 CURRENT PROTOCOLS IN CELL BIOLOGY. 2.8.1, 2.8.1-2.8.2 (2014).

100. Ira Marton et al., *Nontransgenic Genome Modification in Plant Cells*, 154 PLANT PHYSIOLOGY 1079, 1079 (2010).

101. *See supra* Section II.C.2.

properties while maintaining its capacity as a gene delivery vehicle is also possible, as demonstrated for *Agrobacterium*.[102] This would threaten jurisdiction under the PPA. Finally, there is potential for delivering not an external gene, but instead, its encoded protein enzyme directly into a plant cell—where it is then capable of modifying the DNA of the plant to create a GE organism.[103] Given so many new developments in recent years, it seems unlikely that the ingenuity of plant genetic engineers has been fully exhausted. Further regulation-threatening technologies are almost certainly in the pipeline.

B. The Blurred Line Between Transgenic and Non-Transgenic Plants

Other aspects of the new biotechnology-based plant breeding techniques challenge the existing regulatory paradigm because they threaten to eliminate any clear distinction between plants that are transgenic and those that are not. For example, in contrast to the use of *Agrobacterium* in first-generation applications, where control of gene placement in the plant chromosomes was not possible, new site-specific mutagenesis approaches allow for highly targeted and usually much more limited modifications.[104] These techniques make it possible to knock out or modify specific plant gene functions by introducing targeted changes, insertions, and/or deletions of DNA at specific positions.[105] The recently approved bruise-resistant apple is an example of a GE crop created by this approach.[106] Further, in many of these methods, the external recombinant DNA molecules and proteins are introduced solely for the purpose of modifying existing plant genes, and are then removed before propagation of

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102. *See supra* Section III.A.

103. *See* Susana Martin-Ortigosa et al., *Mesoporous Silica Nanoparticle-Mediated Intracellular Cre Protein Delivery for Maize Genome Editing via* loxP *Site Excision*, 164 PLANT PHYSIOLOGY 537, 537 (2014).

104. Yuriko Osakabe & Keishi Osakabe, *Genome Editing with Engineered Nucleases in Plants*, 56 PLANT CELL PHYSIOL. 389, 389-90 (2015). There are many distinct approaches, but the common idea is that the newly introduced DNA does not itself encode a desired function (such as a plant-incorporated protectant), but rather encodes an enzyme system, such as a zinc-finger nuclease (ZFN), that is capable of specifically modifying the pre-existing DNA of the plant cell. After the enzyme has done its work, its gene is eliminated during further cell propagation, so that the final stable line lacks any integrated transgene.

105. Some techniques rely on ribonucleic acid (RNA) to silence specific plant genes or to cause epigenetic modification of the plant genome. These approaches are known, respectively, as "reverse breeding" and "RNA-dependent DNA methylation" (RdDM). *See* Lusser et al., *supra* note 91, at 232.

106. For a recent APHIS press release on bruise-resistant apples, *see Questions and Answers: Arctic Apple Deregulation*, USDA ANIMAL & PLANT HEALTH INSPECTION SERV. (2015), http://www.aphis.usda.gov/publications/biotechnology/2015/faq_arctic_apples.pdf.

the new, stable plant line. This avoids stable integration of a transgene into the genome, while generating a precisely modified nontransgenic plant. Indeed, with this technology, it is virtually impossible to later distinguish whether the final engineered plant has been derived from genetic engineering approaches or from classic plant breeding.[107]

Another challenge arises from techniques known as cisgenesis and intragenesis, by which genetic engineering methods are used to alter plants using a source gene pool that is drawn from plants with some capacity to interbreed with the plant that is modified.[108] These approaches employ *Agrobacterium* or biolistics to introduce the new DNA, but in the case of cisgenesis, the resulting transgenic organism could also have been produced using classical plant genetics.[109] In transgenesis, more varied combinations of genes and regulatory elements are introduced, making generation of the resulting plant by classical approaches unlikely. In both approaches, the transgenes are again segregated out in subsequent strain propagation, so that the new plants are not transgenic but are instead the progeny of a GE plant.[110] It is of interest to note that cisgenesis and transgenesis were developed in part to quell anxiety about GE crops, since surveys have repeatedly shown that many consumers are more comfortable with traditional plant breeding than with recombinant DNA approaches—even when the resulting products are indistinguishable.[111]

Two other developments complicate the regulatory picture. First, using traditional plant breeding methods, it is now possible to graft the vegetative component of a non-GE plant (the scion) onto the rootstock of a GE plant.[112] This raises the question of whether the fruit of this plant should be considered a GE food. Second, a suspension of non-tumor generating *Agrobacterium* can be used to infiltrate non-germline plant tissues (usually leaves) to enable high local expression of an external gene that is not inherited by the plant's progeny.[113] Again, this raises questions regarding the meaning of "plant pest" and the extent to which only transient GE modifications should be regulated.

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107. Nancy Podevin, Yann Devos, Howard Vivian Davies & Kaare Magne Nielsen, *Transgenic or Not? No Simple Answer!,* 13 EUR. MOLECULAR BIOLOGY ORG. REPORTS 1057, 1057 (2012).

108. *See* Lusser & Davies, *supra* note 20, at 441.

109. New *Agrobacterium* vectors that eliminate the possibility of introducing any plant pest DNA into the plant chromosome have been developed for some cisgenesis applications. This introduces yet another regulatory wrinkle. See *id.* at 442.

110. *See id.* at 443.

111. *See* Podevin et al., *supra* note 107, at 1057.

112. *See* Lusser & Davies, *supra* note 20, at 444.

113. This is one of three approaches collectively termed "agro-infiltration." *See* Lusser et al, *supra* note 91, at 232.

IV. BEYOND THE PLANT PEST TRIGGER

Driven by scientific breakthroughs, the landscape of agricultural biotechnology has expanded tremendously in the nearly thirty years since the Coordinated Framework was established, exposing the inadequacies of a regulatory system built on laws not designed to accommodate such advances. The clear threat of further devolving to a condition where there is effectively no oversight at all should now lend substantial impetus for reform. Arguments for change should focus on emphasizing particular aspects of the present system that are relevant to all GE products, and that have potential to resonate across the broadest possible political spectrum. These arguments are essentially economic. One clear approach is to emphasize the imbalance between the weak U.S. oversight of GE products and the much stronger regulation abroad, particularly in the European Union (EU) and South America.[114] In most foreign jurisdictions, GE organisms are regulated under a process-based framework in which the essential criterion is whether its genetic material was produced in ways that could not occur naturally.[115] An active international debate is underway with respect to what the scope of oversight should be, with many key unresolved issues focused on the new plant breeding techniques that blur the lines between transgenic and non-transgenic products.[116] The U.S. has yet to substantively participate actively in these exchanges. However, the outcome of the discussions could clearly have important impacts on the development of international trade agreements.[117] U.S. corporations seeking foreign markets for GE products, and U.S. consumers desiring access to international goods, clearly each have a stake in establishing common international norms.[118]

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114. *See* Podevin et al., *supra* note 107, at 1060.

115. *Id.* It is noteworthy that only the U.S. and Canada have adopted product-based regulatory frameworks.

116. *See* Lusser & Davies, *supra* note 20; *supra* Section III.

117. Provisions of the Trans-Pacific Partnership (ustr.gov/tpp) may work against the regulation of GE products. This could cause substantial disruption as it would create a block of Pacific nations operating under rules substantially opposed to the EU and South America. *See* Adam Needelman, *Whose Century is it?: The Trans-Pacific Partnership, Food, and the 21st Century "Trade Agreement"*, INST. FOR AGRICULTURE & TRADE POLICY (Aug. 27, 2014), http://www.iatp.org/files/2014_08_22_TPP_AN_0.pdf.

118. For a discussion of the problems of "asynchronous" regulation between the EU and others, *see* Alexander J. Stein & Emilio Rodriguez-Cerezo, *International trade and the global pipeline of new GM crops*, 28 NATURE BIOTECHNOLOGY 23, 23-25 (2010).

The large and growing market for organic agricultural products may also offer impetus to reexamine the regulatory structure. Consumer demand for organics continues to expand,[119] yet achieving a reasonable balance between agricultural biotechnology proponents and organic farmers has been elusive.[120] Contamination of organic crops with GE seeds is a problem in many agricultural sectors, and threatens to cause substantial economic disruption given that the value of the organic produce may be completely eliminated by these incidents.[121] Recognition of these genuinely competing interests and the threats to the lucrative organic farming industry from continued, unregulated GE crop proliferation might also help motivate a fresh look at the regulatory framework.

A. Broadening Regulatory Scope by Executive Authority

Identifying a few areas of common concern among stakeholders is clearly necessary, but where in the government might advocates of more robust oversight most effectively focus their efforts? To imagine how the U.S. could enact a more rational, science-based system of oversight for GE crops, it is well to begin by recognizing that the present regulatory architecture was created almost entirely by the executive branch, with no direct input from Congress. In passing the National Science and Technology Policy, Organization, and Priorities Act (NSTPOPA) of 1976,[122] legislators did establish OSTP within the EOP, and also provided that appointment of the OSTP Director be subject to the advice and consent of the Senate.[123] By establishing this typical level of involvement for the creation of new executive agencies, Congress, of course, retained the right to oversee the Director's activities.[124] The Director also is

119. Organic foods have recently experienced double-digit growth rates and presently represent about 4% of the U.S. food supply. *See Organic Agriculture: Overview*, USDA, http://www.ers.usda.gov/topics/natural-resources-environment/organic-agriculture.aspx (last updated June 2, 2015); *see* also Stephanie Strom, *Paying Consumers to Go Organic, Even Before the Crops Come In*, N.Y. TIMES (July 14, 2016), http://www.nytimes.com/2016/07/15/business/paying-farmers-to-go-organic-even-before-the-crops-come-in.html?_r=0; *Big food companies underwriting switch to organic*, GREENWIRE (July 15, 2016), http://www.eenews.net/greenwire/stories/1060040348/print.

120. *See* CENTER FOR FOOD SAFETY, A REPORT BY THE CENTER FOR FOOD SAFETY: MONSANTO V. U.S. FARMERS (2005), http://www.centerforfoodsafety.org/reports/1401/monsanto-vs-us-farmers.

121. *See* Kimbrell, *supra* note 17, at 284-86.

122. 42 U.S.C. § 6601 (2012).

123. *Id.* § 6612.

124. The role of the Director "is to provide, within the Executive Office of the President, advice on the scientific, engineering, and technological aspects of issues that require attention at the highest levels of Government." *Id.* § 6613.

obligated to keep Congress informed of the OSTP's work in yearly Science and Technology Reports.[125] However, Congress's monitoring role has remained just that: the key decisions to regulate GE organisms based on the risks of the product rather than the process, and within the context of existing statutes, were made by OSTP and then implemented in the agencies quite independently of the legislative branch. Indeed, on its own initiative, Congress has never revealed an intent or belief that GE organisms should be subjected to any oversight other than that which presently operates—or indeed to any oversight at all. Although many commentators have suggested that Congress should amend the PPA to address the regulatory shortfalls described above,[126] given its manifest lack of interest, not to mention the difficulties of negotiating an issue as divisive as genetic engineering in such a politically polarized body, it seems highly unlikely that statutory revisions will be forthcoming.

Those seeking more thorough oversight of GE organisms also should not expect assistance from the judicial branch. In addition to the discretion that appellate courts have granted APHIS with respect to its interpretation of the noxious weed and plant pest authorities of the PPA,[127] a complaint directed at the Coordinated Framework itself was also turned aside.[128] In this early case, plaintiffs sought to enjoin operation of the Coordinated Framework by asserting that the definitions employed were incomplete and inexact, and that ecological harm could ensue from the inadequate oversight of potentially dangerous GE organisms. The court denied the plaintiff's claim on standing grounds, and in so doing emphasized that the Coordinated Framework plainly did not impose any limitations or requirements for future regulations, but served merely as an organizing, enabling document that agencies could rely on in formulating those regulations.[129] This rationale would surely also determine the outcome of any challenges to the 1992 Scope Document.[130] OSTP guidelines apply only to agency discretion

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125. *Id.* §§ 6614-15.

126. *See*, e.g., Sheryl Lawrence, *What Would you do with a Fluorescent Green Pig: How Novel Transgenic Products Reveal Flaws in the Foundational Assumptions for the Regulation of Biotechnology*, 34 ECOLOGY L. Q. 201, 281-82 (2007) (arguing that existing laws create a regulatory *infra*structure too inflexible to address the spectrum of unforeseen risk potentials); Mary Jane Angelo, *Regulating Evolution for Sale: An Evolutionary Biology Model for Regulating the Unnatural Selection of Genetically Modified Organisms*, 42 WAKE FOREST L. REV. 93, 155-56 (2007) (suggesting that a completely new legal approach drawing on the principles of evolutionary biology should be considered).

127. *See* 7 C.F.R. § 360.2 (2016) (noxious weed authority); 7 C.F.R. § 330 (2016) (plant pest authority).

128. Found. on Econ. Trends v. Johnson, 661 F. Supp. 107 (1986) [hereinafter, Johnson].

129. *Id.* at 110.

130. *See* 1992 Scope Document, *supra* note 23.

within the scope of preexisting statutory authority, and do not "displace[ ] agencies' duties under applicable statutes, nor provide[ ] additional authority not available under applicable law."[131] Therefore, challenges would fail because of the necessarily highly attenuated link between these general principles and any actual injury sustained by a plaintiff. As in *Johnson*, plaintiffs would simply be redirected to challenge the agency action as a violation of a particular statute or of the Administrative Procedures Act (APA).[132]

Since Congress is highly unlikely to revise the PPA, and direct challenges to the OSTP Scope Document also do not provide a viable approach, the best option to effect broader regulatory oversight of GE crops is for the President to exert executive authority through the OSTP Director, to introduce limited changes to the 1992 Scope Document. Taking this path avoids the need to overcome Congressional paralysis, and, if properly formulated, could redirect how oversight is conducted to move APHIS away from its permissive culture and, perhaps, its strict adherence to the plant pest standard.[133] As with the present authority, an amended Scope Document similarly would not face a serious judicial challenge. Pushback from Congress is, of course, possible, but, especially given its general disinterest in the subject, should be mitigated if the new policy is carefully formulated to lie clearly within existing statutory authorities and to balance stakeholder interests.

B. Amending the 1992 Scope Document

The 1992 Scope Document provides final guidance for all planned introductions of biotechnology products into the environment, and indicates that agencies must apply their oversight authorities in a manner consistent with the risk-based principles contained therein.[134] A bedrock principle of the Scope Document is that oversight must be *product-based*, with characteristics and risks evaluated in the context of the environment into which it is introduced. It may not be *process-based*, because biotechnology "processes do not *per se* pose risks to human health and the environment."[135] These notions are consistent with regulation in the

131. *Id.* at 6753.

132. *See Johnson*, 661 F. Supp. 107, 110.

133. APHIS' permissive culture is revealed in its expediting of the requests to BRS to avoid regulation (*See* Lusser et al., *supra* note 91), and its withdrawal of the rulemaking that envisioned a more robust interpretation of the noxious weed authority (*See supra* note 64).

134. *See* 1992 Scope Document, *supra* note 23, at 6757.

135. *Id.* at 6756 (emphasis added).

context of existing statutes.[136] They are firmly embedded in the work of all three primary agencies that oversee GE products and organisms, and are almost certainly not susceptible to change.

Two other principles in the Scope Document also have profound influence on the regulatory environment. First, oversight must be based on evidence that the risk presented by environmental release for a particular application is unreasonable.[137] Second, organisms with new traits conferring no greater risk to the environment than the parental organisms should not be subject to greater oversight than the unmodified organism.[138] The first of these principles, of course, relies on the appropriate exercise of agency discretion for its effective implementation. The second principle is that of familiarity—the notion that agencies may take guidance from their experience with evaluating the behavior of similar organisms in the past.

The principle that biotechnology oversight should be based on product and not process does not imply that no new regulatory attention is needed. As cogently stated immediately after the 1992 Scope Document was issued, "The fact that the process of genetic engineering does not always produce risky organisms does not imply that the risky organisms that it does produce present no new or unique types of risk."[139] This insight offers key perspective on how APHIS is failing in its mission to properly oversee the environmental release of transgenic plants. First, nothing in the 1992 Scope Document suggests that APHIS should limit its regulation to GE plants that are plant pests or are created with the use of technology that employs plant pests. Second, the 1992 Scope Document is entirely consistent with the notion that APHIS' regulation should protect against all types of harms, not just those that cause injury to plants. Importantly, APHIS is an outlier compared to both EPA and FDA in both of these areas. Under TSCA, EPA regulates almost all engineered microorganisms,[140] not just a limited subcategory causing certain harms, and it has at least some authority to consider hazards outside the main focus of decision-making, including

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136. If biotechnology *were* held to pose inherent risks, new statutes would almost certainly be required to protect the public from its consequences. The choice to regulate within existing statutes, which may well have been driven by internal agency dynamics, thus effectively demands a finding that the technology is inherently safe. *See* Peter Mostow, *Reassessing the Scope of Federal Biotechnology Oversight*, 10 PACE ENVTL. REV. 227, 240-43 (1992).

137. *See* 1992 Scope Document, *supra* note 23, at 6756.

138. *Id.*

139. *See* Mostow, *supra* note 136, at 242.

140. EPA has retained use of the term "intergeneric microorganism" for its authority under TSCA. *See supra* note 52.

environmental effects.[141] EPA's authority to consider hazards of PIPs is also broader than that adopted by APHIS over transgenic plants generally.[142] Similarly, FDA regulates all transgenic animals, although its authority to consider hazards is limited to those impacting human and animal health.[143]

There is little doubt that APHIS could choose to employ its noxious weed authority to regulate all transgenic plants, thus bringing its practices in line with those of FDA and EPA. Instead, APHIS' choice to operate within an extremely narrow scope implies that it is ignoring possible hazards not related to plant pest harms to plants. OSTP cannot amend the 1992 Scope Document to directly require APHIS to broaden its regulatory scope, because it lacks authority to substitute its judgment for that of the agency in the area of its Congressional mandate. However, OSTP may certainly review the effectiveness of any agency's approach and revise its guidance as it deems necessary. Indeed, the 1992 Scope Document envisioned changes in regulatory structure as needed to accommodate advances in scientific knowledge.[144] To this end, an effective step that OSTP can take to encourage APHIS to broaden its regulatory scope is to require consultation with EPA for all inquiries to BRS, and considerations for field releases under notifications or permits.

EPA's expertise in genetic engineering and its existing authorities to regulate microbial biopesticides and PIPs provide a strong basis for interagency consultation with APHIS. EPA operates a Biotechnology Office to oversee intergeneric microorganisms under TSCA,[145] and the molecular genetics methods used in microbe engineering and reviewed in this office also provide the basis for the new plant transformation techniques. No such expertise exists at APHIS, suggesting that the consultation process can be productive in identifying hazards that would otherwise be overlooked. Such hazards might include defects in the construction of the organism, such as unwitting modification of untargeted DNA,[146] and in how it interacts with its environment. It is essential that OSTP develop the

141. Sarah Carter et al., J. CRAIG VENTER INSTITUTE, *Synthetic Biology and the U.S. Biotechnology Regulatory System: Challenges and Options* 20-22 (2014), http://www.jcvi.org/cms/research/projects/synthetic-biology-and-the-us-biotechnology-regulatory-system/overview/.

142. *See supra* note 33.

143. *See* Kimbrell, *supra* note 17; *see supra*, Section III.

144. *See* 1992 Scope Document, *supra* note 23, at 6760.

145. *See Regulation of Biotechnology under TSCA and FIFRA*, ENVTL. PROT. AGENCY, http://www.epa.gov/biotech_rule/ (last visited Nov. 27, 2016).

146. Eva Sirinathsinghji, *Beware the Changing Face of Genetic Modification*, INST. OF SCIENCE IN SOC'Y (2013), http://www.i-sis.org.uk/Beware_the_Changing_Face_of_Genetic_Modification.php.

scientific justification for this consultation in detail, because the 1992 Scope Document also specifies that oversight should be exercised only "when the value of the reduction in risk obtained by additional oversight is greater than the cost thereby imposed."[147] It is unlikely that OSTP would find sufficient support among stakeholders to remove this principle from the revised guidance.

EPA exercises rigorous oversight over transgenic microorganisms under TSCA. It requires that initial small-scale field trials first be subjected to the approval of a TSCA Experimental Release Application (TERA), while manufacture or import for commercialization requires approval of a Microbial Commercial Activity Notice (MCAN).[148] While TERAs are regularly approved by EPA,[149] very few MCAN submissions are successful,[150] EPA's record thus stands in stark contrast to the permissive approval of environmental releases of transgenic plants by APHIS. This suggests that interagency collaboration with EPA may positively influence the regulatory culture at APHIS. It is important to note, however, that the level of EPA regulatory activity on intergeneric microorganisms has been low, but may increase if the promise of synthetic biology is realized.[151] Interagency consultations with APHIS would also tax EPA resources, and would likely require budget increases to expand the infrastructure and personnel conducting oversight.

A productive basis for EPA consultation could be at the level of NEPA review, since for each notification or permitting application APHIS must decide whether to grant an exception to the exclusion

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147. *See* 1992 Scope Document, *supra* note 23, at 6753.

148. ENVTL. PROT. AGENCY, MICROBIAL PRODUCT OF BIOTECHNOLOGY SUMMARY OF REGULATIONS UNDER THE TOXIC SUBSTANCES CONTROL ACT (2012), https://www.epa.gov/sites/production/files/2015-08/documents/biotech_fact_sheet.pdf.

149. For a list of approved TERAs from 1998 to the present, *see TSCA Biotechnology Notifications Status*, ENVTL. PROT. AGENCY, https://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/tsca-biotechnology-notifications-status#mcan.

150. This approval was for a bacterial strain that improves nitrogen fixation in alfalfa. See ENVTL. PROT. AGENCY, FACT SHEET: COMMERCIALIZATION OF SINORHIZOBIUM (RHIZOBIUM) MELILOTI, RMBPC-2 (2012), http://www.epa.gov/biotech_ rule/pubs/factdft6.htm. *See also supra* note 145, at 34-35. More recently, EPA has approved TERAs for engineered bacteria useful in detecting the presence of land mines and unexploded ordnance in soils, and for other purposes. See, e.g., TSCA EXPERIMENTAL RELEASE APPLICATION APPROVED FOR PSEUDOMONAS PUTIDA STRAINS, ENVTL. PROT. AGENCY, https://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/tsca-experimental-release-application-approved-0 (last visited Nov. 27, 2016).

151. Synthetic biology is a rapidly developing field that transforms the scale of microbial engineering by enabling wholescale redesign of biological functions and chemical synthesis of large segments of DNA. Applications that may lead to environmental release include nitrogen-fixing bacteria, biopesticides, and engineered algae for biofuels production. For a comprehensive assessment of regulatory implications at EPA, USDA-APHIS, and FDA, s*ee supra* note 145.

for field releases.[152] Exceptions are granted for actions that have the potential for significant environmental impact.[153] Because such impacts may extend beyond plant pest harms, and environmental harms and human health impacts are protected under the broad noxious weed authority, all applications would undergo the new interagency review process. This consultation would include the preliminary inquiries to BRS inquiring whether a GE product is regulated.[154] The essential notion is that, by mandating interagency review, OSTP eliminates the possibility of cursory oversight that examines only the capacity for plant pest harms. The interagency consultation requirement should then be the subject of a new rulemaking by APHIS.[155] This rule may make clear, if APHIS insists, that environmental releases still could be limited to those encompassing plant pest harms. However, findings of broader risks across many products, during consultations, would exert substantial pressure to remotivate APHIS to reconsider expansion of its noxious weed authority.

Robust oversight of GE microorganisms and GE foods in the agricultural sector is clearly less effective when entire categories of GE plants are exempt from any oversight at all. The joint mission of USDA, EPA, and FDA is compromised by APHIS' unwillingness to apply its authority, and this invites OSTP to reinvigorate its own mandate in the biotechnology sector. In general, the application of executive authority can be an effective tool to advance regulatory goals, enabling the President to put his stamp on policy, and helping agencies to solve problems that implicate multiple jurisdictions.[156] It is encouraging that the Obama administration, recognizing that new advances in biotechnology must be accounted for, has finally begun a process to update the Coordinated Framework to clarify agency roles.[157] This process includes commissioning of an external, independent analysis of the future landscape of biotechnology products, and recognizes the need to improve coordination

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152. *See* 7 C.F.R. §§ 372.5(c)(3)(ii), 372.5(d) (1995).

153. Exceptions can be granted for field releases that involve new species or organisms or novel modifications that raise new issues. Many of the new plant breeding techniques described in Section III may raise such issues. *Id.* § 372.5(d)(4).

154. *See supra* Section III.

155. An alternative to a formal rulemaking could be an OSTP-mediated memorandum of understanding (MOU) between APHIS and EPA that would allow APHIS access to EPA's expertise.

156. Jody Freeman & Jim Rossi, *Agency Coordination in Shared Regulatory Space*, 125 HARV. L. REV. 1131, 1174 (2012). This article recommends a comprehensive executive branch effort to promote stronger interagency coordination and to improve coordination instruments.

157. EXEC. OFFICE OF THE PRESIDENT, MEMORANDUM FOR HEADS OF FOOD AND DRUG ADMINISTRATION, ENVIRONMENTAL PROTECTION AGENCY, AND DEPARTMENT OF AGRICULTURE (2015), https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf.

among agencies. Therefore, improved prospects for better regulation of transgenic crops under the PPA may at last be on the horizon.

V. CONCLUSION

All contemporary regulation of GE plants in the U.S. rests on an incorrect premise. The engineered *Agrobacterium* strains used to create GE plants cannot induce tumors, and are fully disabled with respect to their capacities to cause plant pest harms. Today, even this fundamentally flawed basis for oversight is increasingly threatened by the emergence of new plant transformation methods. It is clear that a strong normative basis for strengthening GE plant regulation exists based on the precautionary principle, and that practical economic considerations are present that also should unite stakeholders. Nonetheless, the capture of APHIS by private interests, legislative gridlock at the Federal level, and political polarization engendered by activists on both sides renders meaningful change difficult. The best approach to break this gridlock is for OSTP to amend its 1992 scope guidance document to better incorporate evolving innovations in agricultural biotechnology, domestic interests in organic farming, and international norms for regulation of GE organisms. The new guidance should include a regulatory floor ensuring some review of all new GE plants, and incentives for consultation to bring EPA's expertise in molecular genetics to bear on APHIS' review of new plant products. These changes can be manifested in revised regulations under the PPA, without the need for changes in the statute. Development of a model for interagency collaboration in this context should be carried out with a view toward eventually integrating all authorities for GE governance within a single umbrella.