Environmental Impact Statement; Introduction of the Products of Biotechnology
U.S. Department of Agriculture Animal and Plant Health Inspection Service (APHIS)
Notice of Intent to Prepare an Environmental Impact Statement[1] (EIS)
Docket No. APHIS-2014-0054
81 FR 6225

Kevin Shea, Administrator
Regulatory Analysis and Development
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Submitted Electronically via Federal eRulemaking Portal (http://www.regulations.gov)

Dear Mr. Shea,

The Institute for Agriculture and Trade Policy[2] (IATP) appreciates this opportunity to comment on "reasonable alternatives and possible issues to be evaluated in the environmental impact statement" (Federal Register Vol. 81, No. 24, February 5, 2016, at 6225). IATP understands that the programmatic EIS resulting from the "Notice of Intent to Prepare an Environmental Impact Statement" (Notice) will be consistent with the guidance of the "Coordinated Framework for the Regulation of Biotechnology," (Coordinated Framework) once it has been revised.[3] IATP has submitted comments regarding that revision,x` and the following comment also reflects some of our views on the Coordinated Framework.[4] Furthermore, APHIS is reconsidering amendments to its biotechnology regulations concurrent with developing the agency's programmatic EIS (FR 6226). As a result, IATP will comment on the Notice while taking into consideration the broader policy context of the Coordinated Framework and the statutory basis for the biotechnology regulations.

As indicated throughout the Notice, changes to APHIS biotechnology regulations will apply to a host of new gene modification techniques that are partly illustrated in the Notice's proposed indicative definition of "biotechnology" (FR 6227). IATP agrees with the authors of a 2002 National Research Council report: "before making specific, precedent-setting decisions, APHIS should solicit broad external scientific review well beyond the use of Federal Register notices."[5] The decisions that APHIS will make about a programmatic EIS for current and future genetically engineered (GE) crops certainly qualify as precedent-setting. IATP hopes that APHIS will follow this and other recommendations of the National Research Council report, e.g. regarding the need for APHIS post-market monitoring of GE crops.

Introduction: historical context of the Notice and the APHIS proposed "Take no action" option

The four alternatives that APHIS presents for the design of a programmatic EIS, under the authority of the National Environmental Policy Act (NEPA) and the policy guidance of the yet to be revised 1992 Coordinated Framework, are presented in a remarkable historical context: as of 2012, "a full EIS was never completed for *any* of [more than 80] GE crops on the market; that is, until a [U.S. Supreme] court ordered one for RR [Roundup Ready®] alfalfa."[6] (According to the General Accountability Office, "As of October 2015, USDA had deregulated 118 GE plants."[7]) Instead, APHIS has determined that the deregulated GE crops do not pose a significant environmental risk under the terms of NEPA, and therefore, has filed much less comprehensive Environmental Assessments (EAs) for deregulated GE crops. APHIS EAs delineate the agency's authority over GE crops to distinguish it from that of the Food and Drug Administration and the Environmental Protection Agency. APHIS reviews applicant supplied data and information to develop the EAs for the non-regulated crops.

In the case of a successful 2004 application by Monsanto for deregulation of two of its GE alfalfa "events," the EA stated that "glyphosate would provide a different herbicide mode of action in the growers' crop rotation, which is important in preventing the development of herbicide resistant weeds. Glyphosate is applied like any other post-emergent herbicide used in any other crop. Glyphosate tolerant alfalfa may alter current alfalfa cultivation practices by allowing for reduced herbicide use in comparison to current practices in order to achieve the same crop yield."[8] This and other sections of the EA, which depend on the applicant's optimistic assumptions about how the deregulated GE crop would perform in the field, were spectacularly erroneous. (Weed resistance and pesticide volume increases resulting from deregulated GE crop planting had already been reported when Monsanto applied to deregulate RoundUp Ready® alfalfa.[9])

Unfortunately, herbicide resistant acreage and glyphosate use have increased dramatically since 1995, not only in the United States and not only for GE crops, although herbicide resistance to GE crops accounts for the majority of resistance acreage.[10] Just on the basis of the environmental and economic consequences of herbicide resistance to GE crops designed for use with proprietary herbicides alone, the first alternative APHIS proposes for the EIS, "Take no action" to change existing regulations, is clearly unacceptable.

In view of the growing economic and environmental cost of GE crop herbicide resistance, APHIS should regulate GE crops designed to be used with proprietary herbicides as cropping systems and conduct an EIS of such cropping systems to include the potential and historical economic, environmental and public health impacts of the GE crop herbicides. The definition of "noxious weed" in the Plant Protection Act of 2000 (PPA, cited in FR 6226) provides ample authority for APHIS to regulate the GE crop designed to be used with a proprietary pesticide as a cropping system and to conduct an EIS of that cropping system: "The term ''noxious weed'' means 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." (Section

403, paragraph 10)[11] The quantifiable damage of the herbicide resistant weeds to the GE crops and to neighboring conventional and organic crops certainly is an indirect economic and environmental injury resulting from the GE cropping system. Designing the programmatic EIS to include indirect injury from the GE cropping systems, per statute, will help implement the adequate regulation of current and future GE crops designed for use with proprietary herbicides.

Regulatory challenges of "advanced genetic engineering": an example

It is not IATP's purpose to excoriate APHIS for believing Monsanto or other applicant claims for deregulation of herbicide resistant GE crops. Rather, our purpose is to help APHIS design and carry out robust EIS for the GE crops that it has deregulated and for the pending and future applications to deregulate GE crops derived from the far more powerful post-transgenic modification techniques often grouped under the rubric of plant synthetic biology or "advanced genetic engineering."

For example, APHIS has very recently deregulated a GE mushroom modified by the CRISPR Cas-9 technology, enabling multiple genomic manipulations, to resist browning and lengthen shelf life.[12] The April 13 letter informing the product developer that the GE mushroom is not an APHIS "regulated article" states, "APHIS has no reason to believe that the anti-browning phenotype of your white button mushroom would increase the weediness of white button mushroom (*sic)*."[13] To the lay person, including this one, the "weediness of the white button mushroom" is a strange statement because one doesn't associate "weediness" with mushrooms. However, per the aforementioned definition of "noxious weed," pathogenic mold, which could be carried by GE mushroom spoors, is an example of an injury that fits well within this broad definition. The criteria for the programmatic EIS must follow this definition, rather than a regulatory interpretation without an APHIS relevant statutory basis, which deregulates a GE crop on the basis of a comparison of that crop with the risks of a traditional plant breeding variety in terms of their estimated respective potential for "weediness."

The APHIS proposed definitions of "regulated organism" and "biotechnology" and their adequacy for the EIS of post-transgenic techniques applied to plants (and animals)

The APHIS proposed definition for "regulated organism" should be an "organism developed using biotechnology," deleting the rest of the proposed definition. The proposed remaining definition would enable status quo deregulation of GE crops (and animals) derived from CRISPR Cas-9 and other new plant breeding techniques, regardless of which EIS alternative is chosen. According to the April 13 letter and similar previous letters, APHIS considers a GE organism to be a "regulated organism" only if, according to applicant supplied information, the organism is engineered using a "donor organism, recipient organism, vector or vector agent" which is on a list of identified plant pests, is an unknown organism or is determined by the APHIS administrator to be an organism that is or could become a plant pest. The proposed definition of "regulated organism" is wholly inadequate to regulating the environmental risks of 21st century GE techniques.

As noted in a recent editorial in *Nature*, "What is new is the advent of CRISPR . . . because it make gene drives much easier to create and could dramatically accelerate the timeline for a potential release—accidental or intentional . . . efforts to understand the ecological consequences of a gene drive should be made an urgent priority."[14] The ability of gene drives to copy the CRISPR edited DNA from one chromosome to another in every generation means that "newly introduced DNA will speed through a population exponentially faster than normal."[15] The APHIS proposed definition of "regulated organism" would allow the agency to not conduct the detailed EIS required to understand the "ecological consequences of a gene drive," to say nothing of the documented and potential off-target effects alterations of the genome and gene regulation. In terms of the *Nature* editorial, the APHIS proposed definition of "regulated organism" fails the CRISPR gene "driving" regulatory test.

The Coordinated Framework, although it is a policy statement and not a statutory obligation, orders APHIS and other federal agencies to facilitate trade in products of modern biotechnology. In order to enhance the likelihood that trade in products of modern biotechnology will be accepted by U.S. trading partners, APHIS should substitute for its proposed definition of "biotechnology" the definition for "modern biotechnology" agreed to by the governments and international organizations of the Codex Alimentarius Commission. The United States helped to develop and supported the Codex definition of "modern biotechnology." Codex standards and guidance documents are presumed to be authoritative in the World Trade Organization's Agreement on Trade-Related Sanitary and Phytosanitary Measures, which apply to all WTO members, including the United States. The Codex definition states,

> Modern biotechnology means the application of: i) In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles; or ii) fusion of cells beyond the taxonomic family that overcome natural physiological reproductive or recombinant barriers and that are not techniques used in traditional breeding and selection.[16]

This is a straightforward, accurate and widely agreed definition that leaves neither product developers nor the public in doubt about the scope of the definition, as the proposed APHIS definition could: "Such techniques include, but are not limited to" (FR 6227) is an open-ended definition that may result in confusion and even litigation concerning the boundaries of the agency's regulatory understanding of "biotechnology."

Trade in the products of modern biotechnology vs. risk analysis of the risks identified in the processes of the transgenic and post-transgenic GE crops (and animals): the second APHIS identified policy option for a programmatic EIS

Dr. Christoph Then, a biosafety researcher with the non-governmental organization Test Biotech, advises:

> Unintended side effects [of CRISPR and other post-transgenic techniques] will depend on the intended changes, the length of the nucleotide, its biological

> properties and its selectivity, the cells, the species and the additional steps applied in the laboratory. Consequently, each plant or animal derived from these techniques needs to undergo a detailed risk assessment, taking into account all relevant technical steps of the process.[17]

This advice is followed by numerous examples of risks identified in regulatory correspondence and the scientific literature for oil rapeseed derived from oligonucleotides and CRISPR Cas-9 derived soybeans. However, the 1992 Coordinated Framework forbids APHIS from evaluating risks identified in the scientific literature at the various steps in the process of making the transgenic and post-transgenic products. The Coordinated Framework, "describes a risk-based, scientifically sound approach to the oversight of planned introductions of biotechnology products into the environment that focuses on the characteristics of the biotechnology product and the environment into which it is being introduced, not the process by which the product is created."[18]

The edict to regulate the product, and not the process by which the product was created, was trenchantly criticized by Federal and independent scientists before the Council on Competitiveness finalized the Coordinated Framework in 1992, after the interagency Biotechnology Science Coordinating Committee could not agree on the terms of the Framework.[19] As FDA scientist Dr. Linda Kahl wrote to her supervisor in January 1992 of the draft Coordinated Framework:

> I believe that there are at least two situations relative to this document in which it is trying to fit a square peg into a round hole. The first square peg in a round hole is that the document is trying to force an ultimate conclusion there is no difference between foods modified by genetic engineering and foods modified by traditional breeding practices. This is because of the mandate to regulate the product not the process. The processes of genetic engineering and traditional breeding are different, and according to the technical experts, they lead to different risks. There is no data that addresses the relative magnitude of the risks—for all we know, the risks may be lower for genetically engineered food than for foods produced by traditional plant breeding. But the acknowledgment that risks are different is lost in the attempt to hold to the doctrine that the product and not the process is regulated.[20]

Regrettably and remarkably, the technical experts were ignored in the process of finalizing the Coordinated Framework. APHIS is still trying to pound that square peg of trade policy derived doctrine to regulate products only into the round hole of performing science-based risk assessment according to the risks identified in the technical steps of the processes that produce GE crops (and animals). Not surprisingly, this forcing of science to increase trade in products of biotechnology, irrespective of process specific risks identified in the scientific literature, produces many regulatory contradictions and contortions.

According to the Notice's second proposed policy option for a programmatic EIS, APHIS would evaluate the process of producing a post-transgenic GE crop, but only for the purpose of exempting it from regulation. "For example, some possible candidates to be

exempted from regulation might be: a) Plant products of biotechnology in which the genetic modification was obtained through a process of biotechnology including nucleotide deletions, single base pair substitutions or other modifications that could reasonably be expected to be obtained through mutagenic techniques that have commonly been used for plant development since the early 1900s" (FR 6227). Even in this provisional indication of possible candidates for regulatory exemption, there is an attempt to historicize the new plant breeding techniques of gene editing, as if they were techniques of traditional plant breeding.

For the exempted candidates, no EIS would be required. Indeed "under this second alternative, APHIS proposes to eliminate the notification procedure (currently 7 CFR 340.3), as APHIS anticipates that many organisms currently regulated under the notification procedures would not be regulated nor subject to further review under this alternative" (FR, 6227-6228). No longer subject to notification requirements, GE crop developers of the exempted products would be free to manage their field trials without disclosure of data to APHIS nor, indeed, to the owners of fields adjacent to the field trials. Such an exemption strategy harmonizes with that of the transatlantic industry New Breeding Technologies (NBT) Platform's legal taxonomy of post-transgenic engineering techniques to exempt them from regulation.[21]

For example, Zinc Finger Nuclease Technology (ZFN), one of the most common gene editing techniques, has been designed for the express purpose of avoiding designation as a Genetically Modified Organism (GMO) under EU law.[22] Notwithstanding the claims for the precision of ZFN and other gene editing techniques, "ZFN technology is known for its non-specific binding to non-target DNA and thus results in a significant level of off-target mutations in the genome."[23] Given the extent and variety of off-target mutations resulting from the application of ZFN and other NBT techniques, APHIS should design the programmatic EIS so as to enable the regulation of NBT techniques to prevent the off-target mutations from resulting in "noxious weeds" or "plant pests" per the PPA.

In sum, the second EIS option APHIS proposes is wholly unsatisfactory for the purpose of carrying out the agency's statutory obligations under the PPA. IATP urges APHIS to work with other agencies with statutory obligations to regulate GE crops and animals to convince the White House offices that requiring agencies to follow a policy to pound the square peg of regulating only the end product of the GE process into the round hole of the science required for proper risk assessment will force agency scientists to ignore off-target mutations reported in the scientific literature. A policy that permits studied regulatory ignorance could result eventually in trade damaging rejection of crops with off-target mutations. According to a recent United Nations Food and Agriculture Organization survey, respondent governments reported 198 incidents since 2009 of low-level presence of GE crops unapproved for import in their countries. One hundred and thirty-eight of those incidents have occurred since 2012.[24] It would be a major strategic error for the United States to rely on its current deregulatory regimes and the agricultural market access terms of the Trans-Pacific Partnership Agreement to increase trade in yet to be quantified "low-level presence" of products of modern biotechnology[25] while the body of scientific literature illustrating the risks specific to NBTs grows.

Given the large number of post-transgenic "events" awaiting deregulation by commercial applicants,[26] the budgetary austerity for regulatory agencies and the Congressional majority's antipathy to regulation, under the guise of "reform,"[27] the default APHIS response to plant synthetic biology varieties very well could be to continue the process of deregulation, including de facto commercial applicant self-regulation of field trial notifications. The lack of effective bio-containment mechanisms to prevent Horizontal Gene Transfer of the post-transgenic crops alone should counsel APHIS to abandon the second proposed EIS alternative.

Biocontainment of Horizontal Gene Transfer in post-transgenic agricultural plants: a major EIS evaluation challenge

The potential for Horizontal Gene Transfer (HGT) from deregulated post-transgenic GE crops, typically as a result of pollen or seed dispersal, poses a major regulatory challenge to APHIS, not the least because there are no reliable means to bio-contain the novel DNA and RNA sequences in post-transgenic plants. Three European Commission Scientific Committees, in their 2015 "Preliminary Opinion [on] Synthetic Biology Risk Assessment Methodologies and Safety Aspects," stated, "Currently available safety locks used in genetic engineering such as genetic safeguards (e.g. auxotrophy and kill switches) are not yet sufficiently reliable for SynBio. Notably, SynBio approaches that provide additional safety levels, such as the genetic firewalls, may improve containment compared with classical genetic engineering. However, no single technology solves all biosafety risks and many new approaches will be necessary."[28]

The Preliminary Opinion, as well as the Presidential Commission for the Study of Bioethical Issues in synthetic biology, assume multiple genetic safeguards will be required to solve biosafety risks.[29] However, as one biosafety research team noted, "the higher the complexity of a biosafety device, the more prone it may be to disturbance and failure" because of multiple physiological burdens placed on the microbial host by the multi-device safeguard.[30] The same researchers state that building a genetic firewall against HGT from combinations of DNA or RNA not found anywhere in nature "could lead to an effective semantic containment within decades; however, this would not stop a refactored microbe from competing at the physiological level with natural flora and fauna during environmental release."[31]

In view of the very long timeline forecast by biosafety researchers to achieve biocontainment of HGT from synthetic biology plants, and the lack of publicly reviewable field trial data on whether such plants will result in "noxious weed" injury to non-GE crops and/or wild plants, APHIS should initiate an EIS for any applicant petition for deregulation of a GE crop that lacks documented reliable bio-containment mechanisms. Testing to produce publicly available data about such a mechanism would occur in a bio-secure greenhouse in which field conditions could be simulated to determine the effects of the applicant's new GE crop on surrounding non-GE crops.

Evidence to be used in the programmatic EIS: the fourth proposed alternative considered

Under the fourth proposed alternative, "APHIS would not have a dedicated regulatory scheme to specifically regulate any products of biotechnology that may pose plant pest or noxious weed risks and therefore would not require consultation nor prescribe methods or practices related to any products of biotechnology" (FR, 6228). Instead APHIS would maintain biotechnology expertise to provide voluntary consultations to industry which "might facilitate commercialization of the products of biotechnology by providing an objective analysis of plant pest or noxious weed risks using APHIS risk analysis processes" (FR, 6228). This approach might reduce the legal basis for possible successful litigation concerning APHIS non-enforcement of the PPA as regards plant biotechnology. The fourth alternative would shift responsibility and liability for the safety of biotechnology products entirely to the biotechnology product developers. However, IATP does not understand how this fourth alternative could advance the design of a programmatic EIS.

IATP is concerned that the design of the programmatic EIS not reprise the APHIS EA's near total dependence on information and data supplied by commercial applicants and/or from scientists or consultants whose work has been funded by the commercial applicants. IATP is aware that past agency EA's have been documented to be non-compliant with NEPA's "sound science" standards.[32] It would be a misuse of APHIS authorities and resources if the programmatic EIS unduly depended on data and information supplied by commercial applicants and/or their funded scientists and consultants.

The EIS should not allow evidence for the EIS to include unpublished studies and data, and studies and data claimed as Confidential Business Information (CBI), since information pertaining to public and environmental health is not a CBI protected trade secret. The routine granting of broad CBI claims impedes the robust peer-reviewed science that should be determinative of Federal science-based decision-making. According to one biosafety researcher, CBI claims often

> marginally serve their legitimate purpose to protect commercial interests and unnecessarily limit transparency and public peer review of data submitted to specifically regulatory authorities. CBI and proprietary claims also restrict access to transgene sequence data, transgenic seeds, and other GMO materials, which precludes the development of independent research and monitoring strategies. In the long run, such claims are counterproductive to the safe and responsible commercial development of GM technology as they hinder the accumulation of biosafety data in the open, peer-reviewed literature, which is needed for both public and scientific consensus-building on safety issues and for improvements to the risk-assessment procedure itself.[33]

In 2004, a National Academy of Sciences report recommended various measures to make data and information submitted to Federal agencies concerning GE foods publicly accessible for peer review: "Collect and make publicly available key compositional information on essential nutrients, known toxicants, anti-nutrients, and allergens of commonly consumed varieties of food" and "Remove compositional information on GE foods from proprietary domains to improve public accessibility."[34] APHIS should heed the advice of the NAS report concerning transparency of the information as it determines

the information requirements for the programmatic EIS. IATP does not see how the fourth, wholly voluntary alternative approach to products of biotechnology can result in a scientifically robust EIS.

IATP further urges the agency not to limit its consideration of comments to the numerous "potential impacts" listed in the Notice (FR 6226). Requests for "potential impacts" often result in econometric speculation and environmental computer modeling whose results depend on unrealistic or even "heroic" policy assumptions about regulatory costs and benefits.[35] There is a historical economic and scientific record of GE crop performance and crop system risks that APHIS can and should use to help design its programmatic EIS for the post-transgenic crops.

We urge APHIS to ensure that the EIS incorporates information and analysis representative of plant, environmental and public health risks identified in the literature, rather than find legal reasons not to regulate the GE crops and consequently not to perform and EIS for those crops. According to one research team, "Synthetic biology and other new genetic engineering techniques will likely lead to an increase in the number of genetically engineered plants that will not be subject to review by USDA [U.S. Department of Agriculture], potentially resulting in the cultivation of genetically engineered plants for field trials and commercial production without prior regulatory review for possible environmental or safety concerns."[36]

For the commercialization applicant, one of the advantages of receiving an APHIS letter stating that the applicant's product is not subject to APHIS regulation is that the applicant does not have to disclose whether or not it is holding field trials. As a result, there are no field trial data for the unregulated product that can be independently evaluated for an EIS. "'We don't know how to test for it [genetic material in the unregulated plants],' says Carol Mallory-Smith, a weed scientist at Oregon State University. "It's a big discussion out here in seed country.'"[37] The discussion is likely to grow bigger as genes from the unregulated post-transgenic modified crops outcross to non-GE crops (and wild plants), causing market disruptions for non-GE growers and exporters. The design of the EIS should not allow CBI barriers to identifying the unregulated but commercially transgressive genetic material. In sum, the fourth alternative makes it highly unlikely that APHIS will obtain the data and information required for a robust EIS.

The third alternative: possible regulation of modern biotechnology with a robust programmatic EIS, subject to provisos

IATP believes that the third option APHIS has proposed holds substantial promise, with the following provisos

1. That APHIS change the proposed definition of "regulated organism" and "biotechnology," as IATP proposes above;
2. That the programmatic EIS apply to cropping systems for GE crops designed to be used with proprietary herbicide or pesticides, in order to evaluate direct and indirect injury of GE cropping systems, per the PPA definition of "noxious weed;"

3. That the programmatic EIS be designed to evaluate risks in the post-transgenic plants and animals at each step in the process of creating a biotechnology product, in order to enable risk analysis of the non-target genomic mutations resulting from the application of post-transgenic techniques;
4. That the programmatic EIS include measures to ensure that reliable biocontainment means be incorporated in each GE crop to prevent Horizontal Gene Transfer; and
5. That information and data, including field trial data, reviewed by APHIS in issuing an EIS be from published studies or be publicly available, and not be withheld from peer review as a result of CBI claims by commercial applicants. Since all DNA and RNA sequences in products of biotechnology have been patented with severe penalties for patent violations, there is little justification for APHIS to grant CBI claims for data and information whose evaluation in a robust EIS is required in order to regulate within the parameters of the PPA.

Under the third alternative, "APHIS proposed regulations would substantially increase oversight and resources over those currently used to regulate GE organisms" (FR 6228). Notwithstanding the increasing scientific and technological complexity of the post-transgenic techniques and their capacity to accelerate genomic manipulations through populations of plants and animals, the third alternative offers the possibility of adequate and effective regulation. IATP agrees with APHIS that under the outlined terms of the third alternative, the current petition system for deregulation and the current notification system for field trials of new GE crops should be ended, since all crops will be regulated according to the risk "analysis triggers" for "noxious weeds" and "plant pests," as defined in the PPA. IATP anticipates that there will be strong industry resistance to the proposed third alternative for the programmatic EIS. This resistance could include Congressional denial of resources necessary for the agency to carry out its statutory obligations.

Conclusion

IATP looks forward to the opportunity to comment on a draft programmatic EIS developed under the outline presented for the third alternative. Again, IATP appreciates the opportunity to comment on this Notice and hopes that our comment aids the agency as it faces the difficult tasks of regulating the proliferation of post-transgenic GE crops (and animals) whose developers are applying for and will apply to deregulate under the current regulatory regime.

Respectfully,

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Senior Policy Analyst

[1] https://www.federalregister.gov/articles/2016/02/05/2016-02247

[2] The Institute for Agriculture and Trade Policy (IATP) is a nonprofit, 501(c)(3) nongovernmental organization, headquartered in Minneapolis, Minn., with an office in Washington, D.C. Our mission states,

"The Institute for Agriculture and Trade Policy works locally and globally at the intersection of policy and practice to ensure fair and sustainable food, farm and trade systems."

[3] http://www.gpo.gov/fdsys/pkg/FR-2015-10-16/pdf/2015-26311.pdf

[4] http://www.iatp.org/files/2015_11_24_RevisedCoordinatedFramework.pdf

[5] *Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation*, National Research Council, 2002, 10.

[6] Kristina Hubbard and Neva Hassanein, "Confronting coexistence in the United States: organic agriculture, genetic engineering, and the case of Roundup Ready alfalfa," *Agri. Hum Values* (2013) 30:325-335. DOI: 10.1007/s10460-012-9394-6. See "Monsanto et al. v. Geertson Seed Farms, U.S. Supreme Court, October Term, 2009. http://www.centerforfoodsafety.org/files/09-475.pdf

[7] "Genetically Engineered Crops: USDA Needs to Enhance Oversight and Better Understand Unintended Mixing with Other Crops," General Accountability Office, March 2016, GAO 16-241, 4-5. http://www.gao.gov/assets/680/675791.pdf

[8] USDA/APHIS Environmental Assessment: Monsanto Company and Forage Genetics International Petition 04-110-01p for Determination of Non-regulated Status for Roundup Ready® Alfalfa Events J101 and J163, October 2004, 12. https://www.aphis.usda.gov/brs/aphisdocs/04_11001p_pea.pdf

[9] E.g. Michael DK Owen and Ian Zelaya, "Herbicide Resistant Crops and Weed Resistance to Herbicides," *Pest Manag Sci* 61:301–311 (2005) DOI: 10.1002/ps.1015

[10] Ian Heap, "International Survey of Herbicide-Resistant Weeds," Weed Science Society of America, February 7, 2016. http://weedscience.org/ and Charles Benbrook, "Impact of genetically engineered crops on pesticide use in the U.S.—the first sixteen years," *Environmental Science Europe*, September 28, 2012. http://enveurope.springeropen.com/articles/10.1186/2190-4715-24-24

[11] https://www.aphis.usda.gov/plant_health/plant_pest_info/weeds/downloads/PPAText.pdf

[12] J.R. Pegg, "APHIS clears new gene-edited mushroom," *Food Chemical News*, April 15, 2016.

[13] https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-321-01_air_response_signed.pdf

[14] "Driving test," *Nature*, August 4, 2015. http://www.nature.com/news/driving-test-1.18118

[15] Christoph Then, "Synthetic gene technologies used in plants and animals for food production," Test Biotech, 2016, fig. 2, p. 10. http://www.testbiotech.org/en/node/1597

[16] "Principles for Risk Analysis of Foods Derived from Modern Biotechnology," in *Foods derived from modern biotechnology*, World Health Organization and Food and Agriculture Organization of the United Nations, 2nd edition, 2009, 2. ftp://ftp.fao.org/codex/Publications/Booklets/Biotech/Biotech_2009e.pdf

[17] Then, *Op cit.*, 7.

[18] https://www.whitehouse.gov/sites/default/files/microsites/ostp/57_fed_reg_6753__1992.pdf

[19] http://www.sourcewatch.org/index.php/Coordinated_Framework_for_the_Regulation_of_Biotechnology

[20] Dr. Linda Kahl, Food and Drug Administration compliance officer in a letter to Dr. James Maryanski, FDA Biotechnology Coordinator, January 8, 1992, in "FDA scientists discuss various concerns," documents produced in the discovery process of Alliance for Bio-Integrity v. FDA. http://www.biointegrity.org/

[21] "The regulatory status of plants resulting from New Breeding Technologies," NBT Platform, July 11, 2013. http://www.nbtplatform.org/background-documents/legal-briefing-paper---the-regulatory-status-of-plants-resulting-from-nbts-final-.pdf

[22] Ricarda Steinbrecher, "Genetic Engineering in Plants and the 'New Breeding Techniques (NBTs)': Inherent risks and the need to regulate," Eco Nexus, December 2015, 3. http://www.econexus.info/sites/econexus/files/NBT%20Briefing%20-%20EcoNexus%20December%202015.pdf

[23] Ibid.

[24] "Technical consultation on the low-level presence of genetically modified (GM) crops in international food and feed trade," United Nations Food and Agriculture Organization, March 2014, 15. http://www.fao.org/fileadmin/user_upload/agns/topics/LLP/AGD803_6_Report_En.pdf

[25] Steve Suppan, "The TPP SPS chapter: not 'a model for the rest of the world'," Institute for Agriculture and Trade Policy, November 12, 2015. http://www.iatp.org/files/2015_12_03_TPP_SPS_SS.pdf

[26] Andrea L. Halweg Edwards et al., "The emergence of commodity-scale genetic manipulation," *Current Opinion in Chemical Biology* (2015) 28: 150-156. http://dx.doi.org/10.1016/j.cbpa.2015.07.009

[27] Regulatory Reform Legislation: 114th Congress, George Washington University. https://regulatorystudies.columbian.gwu.edu/regulatory-reform-legislation-114th-Congress

[28] http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_048.pdf at 6.

[29] http://bioethics.gov/node/172

[30] Oliver Wright, Guy-Bart Stan and Tom Ellis, "Building-in biosafety for synthetic biology," *Microbiology* 159 (July 2013), 1223.

[31] Ibid, 1227.

[32] e.g. Bill Freese and Martha Crouch, "Comments to USDA APHIS on Draft Environmental Assessment and Draft Plant Pest Risk Assessment for Dow AgroSciences Petition (09-349-01p) for Determination of Nonregulated Status of Event DAS-68416-4: 2,4-D-!and glufosinate-resistant soybean," Center for Food Safety, September 11, 2009. http://www.centerforfoodsafety.org/files/cfs-24-d-soy-science-comments-final-9-11-12_11171.pdf

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