



Docket No. APHIS-2018-0034  
Regulatory Analysis and Development, PPD  
Animal Plant Health and Inspection Service (APHIS)  
U.S. Department of Agriculture  
4700 River Road, Unit 118  
Riverdale, MD 20737-1238

July 30, 2018

Notice of Intent to Prepare an Environmental Impact Statement; Movement and Outdoor Use of Certain Genetically Engineered Organisms (“Notice”)<sup>1</sup>

Submitted electronically to <http://www.regulations.gov/#!docketDetail;D=APHIS-2018-0034>

*Overview*

The Institute for Agriculture and Trade Policy (IATP)<sup>2</sup> appreciates this opportunity to comment on the “Notice.” IATP last wrote to APHIS on June 17, 2017, concerning the Proposed Rule: Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms (Docket No. APHIS–2015–0057)<sup>3</sup> (“Proposed Rule”). Following industry objections and to industry applause,<sup>4</sup> USDA withdrew the Proposed Rule on November 7, 2017, leaving in place the current 20-year-old system for determining whether APHIS will regulate a specific genetic modification to a plant. Although USDA is apparently developing the programmatic EIS in advance of a new Proposed Rule, IATP urges USDA to draft the EIS to be consistent with the following step of the withdrawn Proposed Rule:

If APHIS determines that the GE plant is a noxious weed, it would endeavor to gauge the direct or indirect injury or damage it could cause to crops, livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment. APHIS would make the results of this evaluation publicly available and share both the evaluation and the information on which it is based with the Environmental Protection Agency (EPA) and the U.S. Food and Drug Administration (FDA), as warranted. (Federal Register / Vol. 82, No. 12 / Thursday, January 19, 2017 / Proposed Rules, p. 7011)

The determination of such “direct or indirect injury or damage” for the Proposed Rule is dictated by the requirements of the Plant Protection Act of 2000, specifically in the definition of “noxious weed,” (7 USC 7702, para 10). APHIS must demonstrate that it has considered the scale and variety of “direct or indirect injury or damage” in finalizing a future Proposed Rule, if it is to comply with the statute.

APHIS has chosen to issue the Notice in advance of issuing a new Proposed Rule, whereas a draft EIS would normally be issued after a Proposed Rule, since the EIS is a decision-making tool to

IATP.ORG

2105 FIRST AVENUE SOUTH

MINNEAPOLIS, MINNESOTA

55404

(612) 870-0453

FAX (612) 870-4846

110 MARYLAND AVE NE, SUITE 307

WASHINGTON, D.C.

20002

(202) 543-8602

FAX: (202) 543-0978

guide regulators on the impact of a proposed governmental action, such as a Proposed Rule. In anticipation of a new Proposed Rule that complies with the mandate to determine “direct or indirect injury or damage” resulting from GE plants and the agronomic practices required by the engineered traits of those plants, IATP advises APHIS to require of commercial applicants at least the following categories of information in the programmatic EIS:

- Outline the potential impacts of taking no action to regulate GE plants, per the “no action” alternative requirement of the EIS provision of the National Environmental Protection Act;<sup>5</sup>
- Describe APHIS’s understanding of the method/s used to identify non-target/off-target mutations of gene editing and characterize the risks associated with those mutations;<sup>6</sup>
- Submit field trial information on gene flow outcrossing to open pollinated plants and to wild plants to verify that there is no “kill switch failure” in GE plant design;<sup>7</sup>
- Submit field trial information and data on pesticide use and impacts from GE plants designed and patented to resist proprietary pesticides;
- Document the extent to which bioinformatic tools accurately predict the traits expressed from gene-edited plants and the use of whole genome sequencing by GE plant developers to analyze off-target or non-target mutations of those plants;<sup>8</sup>
- Document agronomic and economic impacts of “superweed” resistance to GE plants under conventional crop land management practices;<sup>9</sup>
- Describe actual or potential risks to plant health, of GE techniques, e.g. risk of disease susceptibility associated with specific gene deletions or gene silencing more generally;<sup>10</sup>
- Assess potential decreases in biodiversity resulting from enhanced invasiveness of GE plants, as anticipated for stacked trait varieties in the 2007 APHIS EIS for Introduction of Genetically Engineered Organisms;<sup>11</sup>
- Develop a programmatic EIS section for biosafety controls on gene drives for pest control generated from CRISPR Cas9 and other techniques.<sup>12</sup>

The EIS docket should remain open and be periodically updated so that the public understands what studies and data APHIS is using to assess environmental impacts of GE plants.

IATP notes that in the *Draft Programmatic Environmental Impact Statement: Introduction of Genetically Engineered Organisms* of 2007, APHIS described a sixth month long public consultation process that included stakeholder meetings, surveys and written comments in response to a 2004 Notice for an EIS.<sup>13</sup> Given the greater complexity and variety of application of genome editing techniques, IATP urges APHIS to at least offer as many opportunities for public input into the current draft EIS process. It is regrettable that APHIS did not respond affirmatively to a request to extend the deadline for the 30-day comment period to this Notice.

#### *National Environmental Policy Act requirements for the Environmental Impact Statement*

The programmatic Environmental Impact Statement (EIS) that APHIS will finalize in response to stakeholder comments should inform the risks of GE plants to be regulated under any future Proposed Rule. The Notice states, “Under the provisions of the National Environmental Policy

Act of 1969 (NEPA), as amended (42 U.S.C. 4321 *et seq.*), Federal agencies must examine the potential environmental impacts of proposed Federal actions and alternatives.”

But the Notice requests commenters to give their views on matters far beyond what NEPA authorizes. In addition to the bulleted categories of information in the Notice, APHIS states, “We will also examine socioeconomic considerations, such as the potential impacts of crop plants that are GE organisms on the domestic economic environment, international trade, and coexistence among all forms of U.S. agriculture—conventional, biotechnology-based, and organic—and on market demand for food, feed, fiber, and fuel.” NEPA does not require APHIS to request nor for commenters to present information from such a broad range of considerations for an EIS. Indeed, the Notice’s minimal comment period of 30 days for the EIS makes the task of commenters exceedingly difficult, even if the terms of the Notice were tailored only to NEPA requirements.

Rather than basing the programmatic EIS on broad “socio-economic considerations,” in addition to the NEPA and PPA requirements, IATP urges APHIS to apply the NEPA criteria as the framework for the EIS for GE plants, including agricultural plants derived from newer genetic engineering techniques, such as CRISPR Cas9. The EIS should illustrate how APHIS would regulate new genetic engineering techniques according to each of these NEPA requirements:

- (i) the environmental impact of the proposed action; (ii) any adverse environmental effects which cannot be avoided should the proposal be implemented; (iii) alternatives to the proposed action; (iv) the relationship between local short-term uses of man’s environment and the maintenance and enhancement of long-term productivity; and (v) any irreversible and irretrievable commitments of resources which would be involved in the proposed action should it be implemented, (42 USC 4332, para C).

The scientific literature reports off-target effects of CRISPR engineered plant modifications.<sup>14</sup> For example, contrary to the precision generally claimed for genome editing, in crops of greatest commercial interest, there are the highest number of off-target mutations:

In maize, which has the largest genome and greatest number of annotated genes among the eight species that were analyzed, only 30% of the transcription units could be targeted by specific gRNAs. The lack of specific gRNAs for so many maize genes probably reflects the genome complexity (duplication events) and genomic sequence context. It is therefore anticipated that wheat and barley, with even larger genomes than maize, may present similar challenges for CRISPR/Cas9-mediated genome editing ([Xie et al., 2014](#)).<sup>15</sup>

The programmatic EIS should summarize both this literature and the literature that identifies potential hazards that are associated with the off-target effects. One researcher stated, “We feel it’s critical that the scientific community consider the potential hazards of all off-target mutations caused by CRISPR, including single nucleotide mutations and mutations in non-coding regions of the genome.”<sup>16</sup> This advocacy comes from a medical researcher, but APHIS should advocate for the study of potential hazards in genome edited agricultural plant research. One research group emphasized that research to understand the off-target effects of plant genome

editing is not yet advanced: “The quest for better understanding of off-target effects has led to unique approaches to detection of off-targets resulting from CRISPR RNA-guided nucleases which as of yet have not been applied to plant systems.”<sup>17</sup> The programmatic EIS should outline what is known about the off-target effects and associated hazards, both actual and potential, in plant systems. If the EIS fails to acknowledge the incipient state of understanding of off-target mutations of the plant genome, APHIS will join the industry boosterism for new genetic engineering techniques and turn its back on the state of plant genome research.

If the proposed action is not to develop an EIS that presumes the regulation of genome edited plants, the programmatic EIS should describe as an alternative to the proposed action how APHIS will evaluate and publish the potential hazards of those off-target mutations as they are identified in the greenhouse laboratory and in field trials. The EIS should describe how APHIS will require developers to mitigate adverse environmental impacts. For example, APHIS should require GE crop developers to verify, in field trials, techniques that prevent or reduce off-target mutations identified in the laboratory.<sup>18</sup> In order to enable public review of such field trial results, the EIS should outline the reasons that APHIS will not grant commercial applicants’ claims of Confidential Business Information (CBI) for field trial studies and data, since indiscriminate granting of CBI claims has impeded biosafety innovation.<sup>19</sup>

APHIS should not structure the EIS to endorse the views of scientist-entrepreneurs who understand plant modification without a transgene as a permit to commercialize a GE plant without an EIS and further regulation. Apparently, the current APHIS practice of deregulating most gene-edited plants have led some scientists to make not only deregulatory claims for the eventual commercialization of their research, but also demands for commercialization of products with no regulator study of their environmental impacts. For example, a Chinese research team recently wrote:

Because these transgene-free base edited herbicide-resistant watermelon plants are genetically identical to those bred via traditional mutagenesis, no extra regulations should be applied to these transgene-free base-edited mutants (Huang et al. 2016). Without fitness cost associated with the base-edited point mutations, this non-GM herbicide-resistant watermelon is now ready for immediate field application.<sup>20</sup>

While this peer-reviewed article may reflect a naïve understanding of the U.S. petition for deregulation system, the USDA bears part of the responsibility for narrowing the scientific evaluation of risk by the trade related doctrine of “substantial equivalence” between traditional plant breeding and GE plant breeding.

Secretary Sonny Perdue has already signaled the orientation of any future Proposed Rule on GE Plants in his “Statement on Plant Breeding Innovation” of March 28: “With this approach, USDA seeks to allow innovation when there is no risk present.” That approach prejudices risk so narrowly, according to the trade-related substantial equivalence doctrine that it cannot be assessed scientifically: “Under its biotechnology regulations, USDA does not regulate or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques as long as they are not plant pests or developed using plant pests.”<sup>21</sup> Because GE plant breeding no longer depends on a transgene vector that can introduce plant

pest, APHIS is in danger of becoming a rubber stamp on petitions to deregulate new GE plant varieties, regardless of the environmental risks documented in the scientific literature.

APHIS currently grants most petitions for deregulation of GE agricultural plants:

To date, APHIS has issued more than 18,000 authorizations for the environmental release of GE organisms in multiple sites, primarily for research and development of improved crop varieties for agriculture. Additionally, APHIS has issued more than 12,000 authorizations for the importation of GE organisms, and nearly 12,000 authorizations for the interstate movement of GE organisms. APHIS has, to date, denied slightly more than 1,500 requests for permits or notifications, many of which were denied because APHIS ultimately decided the requests lacked sufficient information on which to base an Agency decision (FR 7008).

Given the falling cost of developing GE plants for commercialization with new GE techniques, APHIS will be under industry pressure to issue more authorizations more rapidly. APHIS is unlikely to receive adequate funding to risk assess commercialization applications of GE plants on a case by case basis under current and projected Congressional Budget Office constraints.<sup>22</sup> As a result, the programmatic EIS becomes a critical guide for APHIS to assess not only the case by case risks of GE plants, but also the long-term environmental impact of intensified use of new GE plant varieties on the conservation and regeneration of the natural resource base of U.S. agriculture, including soil health, water quality and availability and biodiversity impacts under the climate of more frequent and more adverse extreme weather events. In sum, the programmatic EIS must be as scientifically robust as possible to serve as a decision-making tool for APHIS under intense budgetary pressure and industry pressure for commercialization of their individual products, regardless of their cumulative impact on the natural resource base of U.S. agriculture.

IATP hopes that these brief comments will assist APHIS in drafting a robust programmatic EIS. We also urge APHIS to offer public meeting and survey opportunities with adequate notice to foster public input to this critical document.

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<sup>1</sup> <https://www.regulations.gov/document?D=APHIS-2018-0034-0001>

<sup>2</sup> The Institute for Agriculture and Trade Policy (IATP) is a nonprofit, 501(c)(3) nongovernmental organization, headquartered in Minneapolis, Minnesota, with offices in Washington, D.C. and Berlin, Germany.

<sup>3</sup> [https://www.aphis.usda.gov/brs/fedregister/BRS\\_20170119.pdf](https://www.aphis.usda.gov/brs/fedregister/BRS_20170119.pdf)

<sup>4</sup> "BIO Statement on USDA Withdrawal of 340 Biotech Rules," Biotechnology Innovation Organization. November 7, 2017. <https://www.bio.org/press-release/bio-statement-usda-withdrawal-340-biotech-rules>

<sup>5</sup> <https://www.law.cornell.edu/cfr/text/39/775.11>

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<sup>6</sup> For a review of such mutation detection methods in use, see Julia Zischewski, Rainer Fisher and Luisa Bortesi, "Detection of on-target and off-target mutations generated by CRISPR Cas9 and other sequence specific nucleases," *Biotechnology Advances*, January-February 2017.  
<https://www.sciencedirect.com/science/article/pii/S0734975016301586>

<sup>7</sup> Oliver Wright, Guy-Bart Stan and Tom Ellis, "Building-in biosafety for synthetic biology," *Microbiology* 159, July 2013. <https://www.ncbi.nlm.nih.gov/pubmed/23519158>; Anna J. Simon and Andrew D. Ellington, "Recent advances in synthetic biosafety," *F1000Research*, August 31, 2016.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5007755/>

<sup>8</sup> Sarah Z. Agapito-Tenfen, "Biosafety aspects of genome editing techniques," Biosafety Briefing, Third World Network and African Biodiversity Centre. November 2016.  
[https://www.researchgate.net/publication/310800841\\_Biosafety\\_aspects\\_of\\_genome-editing\\_techniques](https://www.researchgate.net/publication/310800841_Biosafety_aspects_of_genome-editing_techniques)

<sup>9</sup> Ian Heap, "Increase in Unique Resistant Weeds for the USA", Slide 5, in International Survey of Herbicide Resistant Weeds. [www.weedscience.org](http://www.weedscience.org). Accessed June 15, 2017. The international Survey identified 160 unique weed resistant cases in the United States as of June 2017.

<sup>10</sup> Ricarda Steinbrecher, "Inherent risks and the need to regulate: New Plant Breeding Techniques," Econexus, December 2015 at 6. <http://www.econexus.info/sites/econexus/files/NBT%20Briefing%20-%20EcoNexus%20December%202015.pdf>

<sup>11</sup> [https://www.aphis.usda.gov/brs/pdf/complete\\_eis.pdf](https://www.aphis.usda.gov/brs/pdf/complete_eis.pdf)

<sup>12</sup> Virginie Orgogozo, Baptiste Morizot and Christophe Boete, "Agricultural pest control with CRISPR-based gene drive: time for a public debate," *Embo reports*, June 2017.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452019/>

<sup>13</sup> *Op cit*.

<sup>14</sup> E.g. Gregory Ladics et al, "Genetic basis and detection of unintended effects in genetically modified plants," *Transgenic Research*, February 26, 2015.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4504983/> "CRISPR gene editing can cause hundreds of unintended mutations," *Phys.org*, May 29, 2017. <https://phys.org/news/2017-05-crispr-gene-hundreds-unintended-mutations.html> Heidi Ledford, "CRISPR gene-editing produces unwanted DNA deletions," *Nature*, July 16, 2018. <https://www.nature.com/articles/d41586-018-05736-3>

<sup>15</sup> Luisa Bortesi and Rainer Fischer, "The CRISPR Cas9 system for genome editing and beyond," *Biotechnology Advances*, January-February 2015.  
<https://www.sciencedirect.com/science/article/pii/S0734975014001931>

<sup>16</sup> Cited in "CRISPR gene editing can cause hundreds of unintended mutations."

<sup>17</sup> Jeffrey D. Wolt et al, « Achieving Plant CRISPR Targeting That Limits Off-Target Effects," *The Plant Genome*, September 29, 2016. doi:10.3835/plantgenome2016.05.0047

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<sup>18</sup> E.g. Qiuang Zhang et al, «Potential high-frequency mutagenesis introduced by CRISPR/Cas9 in *Arabidopsis* and its prevention,” *Plant Molecular Biology*, February 23, ,2018. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5978904/>

<sup>19</sup> Kaare M Nielsen, “Biosafety Data as Confidential Business Information,” *PLOS Biology* 11(3) (March 2013), 1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3589341/>

<sup>20</sup> Linjian Jiang et al., “Engineering herbicide resistant watermelon though CRISPR Cas9-mediated base-editing,” *Plant Cell Reports* May 2018. <https://doi.org/10.1007/s00299-018-2299-0>

<sup>21</sup> “Secretary Perdue Issues Statement on Plant Breeding Innovation,” U.S. Department of Agriculture, Press release 0070.18. March 28, 2018. <https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation>

<sup>22</sup> E.g., Jim Tankersley, “How the Trump Tax Cut Is Helping to Push the Federal Deficit to \$1 Trillion,” *The New York Times*, July 26, 2018.