



POLICY & ACTION FROM CONSUMER REPORTS

Comments of Consumers Union to the Office of Science and Technology Policy on Clarifying Current Roles and Responsibilities Described in the Coordinated Framework for the Regulation of Biotechnology; Request for Public Comment Docket No. FDA-2015-N-3403

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November 1, 2015

Summary

Consumers Union, the policy and mobilization arm of Consumer Reports,¹ welcomes the opportunity to comment to the Office of Science and Technology Policy (OSTP) on the proposed update to the Coordinated Framework for the Regulation of Biotechnology to clarify the current roles and responsibilities of the Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and United States Department of Agriculture (USDA), consistent with the objectives described in the July 2, 2015, memorandum issued by the Executive Office of the President (EOP).²

Primarily, we urge OSTP to make clear to EPA, FDA, and USDA that they should consider all products meeting the July 2015 EOP memorandum's definition of "biotechnology products" to be subject to a required assessment of any potential health and environmental risks. This definition includes all the newer technologies used in biotechnology, such as those of gene editing or gene silencing. For EPA, FDA, and USDA to achieve the Administration's stated goal to "ensure public confidence in the regulatory system,"³ plants, animals, and microbes that are modified using these technologies should be required to undergo full assessments for human

¹ Consumers Union is the policy and mobilization arm of Consumer Reports. Consumers Union is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers and to empower consumers to protect themselves. It conducts this work in the areas of food and product safety, telecommunications reform, health reform, financial reform, and other areas. Consumer Reports is the world's largest independent product-testing organization. Using more than 50 labs, auto test center, and survey research center, the nonprofit organization rates thousands of products and services annually. Founded in 1936, Consumer Reports has over 7 million subscribers to its magazine, website, and other publications.

² Memorandum for Heads of Food and Drug Administration, Environmental Protection Agency, and Department of Agriculture Regarding Modernizing the Regulatory System for Biotechnology Products, Executive Office of the President, July 2, 2015 (July 2015 EOP Memorandum) (online at: www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf).

³ Office of Science and Technology Policy, *Clarifying Current Roles and Responsibilities Described in the Coordinated Framework for the Regulation of Biotechnology*, request for public comment (Sept. 22, 2016) (81 Fed Reg. 65414).

health and environmental safety, and any biotechnology products sold to the consumer should be labeled as such. In areas where the agencies do not feel they have the statutory tools or authorities needed to carry out these assessments or require this labeling, the agencies should request appropriate statutory changes from Congress.

Please see the following more detailed comments on specific questions posed by OSTP.

1. *What additional clarification could be provided regarding which biotechnology product areas are within the statutory authority and responsibility of each agency?*
2. *What additional clarification could be provided regarding the roles that each agency plays for different biotechnology product areas, particularly for those product areas that fall within the responsibility of multiple agencies, and how those roles relate to each other in the course of a regulatory assessment?*
3. *What additional clarification could be provided regarding communication and, as appropriate, coordination among agencies, while they perform their respective regulatory functions, and for identifying agency designees responsible for this coordination function?*

The draft document should make it explicitly clear that EPA, FDA, and USDA should consider all products meeting the July 2015 EOP memorandum's definition of "biotechnology products" to trigger regulation of those products, in order to ensure adequate assessment of any human health and environmental impacts. As the July 2015 EOP memo states, "'Biotechnology products' refers to products developed through genetic engineering or the targeted or in vitro manipulation of genetic engineering of organisms, including plants, animals, and microbes."⁴ This definition includes the newer technologies of biotechnology, such as those of gene editing (including sequence-specific nucleases, meganucleases, zinc finger nuclease, CRISPR-Cas system, TALENs, and oligonucleotide directed mutagenesis) or gene silencing (including RNAi, RNAi pesticides, and RNA-dependent DNA methylation).

FDA

We note that FDA's definition of "modern biotechnology" is similar to the July 2015 EOP memo's definition of "biotechnology products."⁵ We also note that the National Strategy for Modernizing the Regulatory System for Biotechnology Products (National Strategy) includes under the "future activities" heading: "FDA intends to clarify its policy for the regulation of products derived from genome editing techniques," including by updating its Guidance for Industry 187 "to clarify how developers of animals produced using emerging technologies (e.g., genome editing) may meet applicable statutory and regulatory requirements."⁶

⁴ July 2015 EOP memorandum.

⁵ Food and Drug Administration, *Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Derived from Genetically Engineered Plants* (Nov. 19, 2015) (online at www.fda.gov/RegulatoryInformation/Guidances/ucm059098.htm).

⁶ EOP, *National Strategy for Modernizing the Regulatory System for Biotechnology Products* (Sept. 2016) (online at www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_national_strategy_final.pdf).

We believe this is a step in the right direction, as FDA is recognizing that genome editing techniques are products of modern biotechnology. That said, we urge FDA to go further, and require safety assessments for plants developed via genome editing techniques and all other techniques of modern biotechnology, instead of having products go through the voluntary safety consultation procedure. Indeed, we think FDA should finalize a rule similar to its 2001 proposal for Premarket Biotechnology Notification,⁷ which would require a premarket safety assessment for genetically engineered (GE) plants rather than a voluntary safety consultation procedure. This requirement would align with FDA’s current requirement for a premarket safety assessment of GE animals, which are regulated as new animal drugs. An update of Guidance for Industry 187 should take this new requirement into account and make clear that all animals produced using newer techniques of modern biotechnology must go through a premarket safety assessment.

EPA

EPA also appears to recognize that it should regulate some products developed with newer biotechnology techniques. EPA plans to update its regulation of biopesticides, including genetically engineered microorganisms and plant-incorporated protectants, as noted under “future activities” in the National Strategy.⁸ This, too, is a step in the right direction, though we urge EPA in clarifying its approach to explicitly require safety assessments of pesticidal products derived from the newer biotechnology techniques such as genome editing and gene silencing.

EPA also regulates a wide range of commercial, industrial, and consumer applications of microbial biotechnology under the Toxic Substances Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act.⁹ TSCA now requires pre-manufacturing EPA review of all new chemical substances. However, when it comes to microorganisms produced by biotechnology, TSCA only considers them to be a “new chemical substance” if they are formed by the deliberate combination of genetic material that was originally isolated from organisms of different taxonomic genera (also called “intergeneric”).¹⁰ “New” microorganisms also include those constructed with synthetic genes that are not identical to DNA that would be derived from the same genus as the recipient, which would then be considered to be “intergeneric” microorganisms.¹¹ This is appropriate, and we urge EPA to be explicit that even a single nucleotide difference in the synthetic gene from a gene found in the same genus as the recipient microorganism should ensure that it is a “new” microorganism.

⁷ FDA, *Premarket Notice Concerning Bioengineered Foods*, proposed rule (Jan. 18, 2001) (66 Fed. Reg. 4706).

⁸ EOP, *National Strategy for Modernizing the Regulatory System for Biotechnology Products* (Sept. 2016) (online at www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_national_strategy_final.pdf).

⁹ 15 U.S.C. 2601-2692, as amended by Pub. L. No. 114-182.

¹⁰ U.S. Environmental Protection Agency, *Toxic Substances Control Act and Genetically Engineered Microorganisms*, presentation at National Academies of Sciences, Engineering, and Medicine public meeting on Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System public meeting (Apr. 18, 2016) (online at nas-sites.org/biotech/wp-content/blogs.dir/78/files/2016/03/3-TSCA-FIFRA-EPA-NAS-meeting-4-18-16-.pdf).

¹¹ *Id.*

In addition, we encourage EPA to define “new microorganisms” as those produced using products of modern biotechnology, regardless of whether the genetic material comes from the same microorganism or from a microorganism in another genera. A study published in 1995 found that genetically engineering the yeast *Saccharomyces cerevisiae* with multiple types of genes found within the same yeast species resulted more than 30-fold increases in the production of a toxic substance, methoxylglycol (MG), such that the level of MG was high enough to cause mutagenic effects in the yeast, an effect that was not seen in the non-engineered yeast.¹² In other words, the process of engineering a yeast with genes from the same genus and species lead to the significant production of a toxic substance. Thus, EPA should make clear in its interpretation of TSCA that any microorganism that is produced via modern biotechnology (e.g., it falls under the definition of “biotechnology products” from the July 2015 EOP memorandum) should be considered a “new” microorganism and therefore a “new chemical substance” that should require a pre-manufacturing review. No microorganism produced via modern biotechnology should be exempt from pre-manufacturing review under TSCA; all such microorganisms should be required to undergo a pre-manufacturing review to prevent them from presenting an unreasonable risk of injury to the health or the environment from their manufacturing, processing, distribution in commerce, use, or disposal.

USDA

Unlike FDA and EPA, USDA does not seem to recognize that products of newer techniques of modern biotechnology, such as gene editing or gene silencing technologies, require regulation. At present, USDA has narrowly defined its remit by considering a GE plant, microorganism, or invertebrate to be not regulated as a product of biotechnology unless it contains genetic material from a plant pest. USDA regulates GE plants, microorganisms, and invertebrates with plant pest components under the Plant Protection Act and its associated regulations (specifically, 7 C.F.R. Part 340). As a consequence, there are now over 40 GE plants, including plants developed via gene editing techniques or plants containing the gene for resistance to glyphosate, that are largely considered to be exempt from USDA regulation.¹³ We think this is the wrong approach, and that it is inconsistent with the Administration’s goals in updating the Coordinated Framework.

The National Strategy notes that USDA is in the process of revising its regulations governing how it determines how to regulate GE plants under the Plant Protection Act. We urge USDA, as part of this revision, to make clear that it will require premarket safety assessments for all plants that are produced with modern biotechnology, and not exempt any plants meeting the July 2015 EOP memo’s definition of “biotechnology products” from regulatory oversight.

Engineered animals and insects that might be released into the environment that are pests to or cause disease in livestock are regulated under the Animal Health Protection Act (AHPA).¹⁴

¹² Inose, T. and Murata, K(1995), Enhanced accumulation of toxic compound in yeast cells having high glycolytic activity: a case study on the safety of genetically engineered yeast. *International Journal of Food Science & Technology*, 30: 141–146. doi:10.1111/j.1365-2621.1995.tb01365.x

¹³ USDA Animal and Plant Health Inspection Service, “Am I Regulated Under 7 CFR part 340?” (June 8, 2016) (online at www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated).

¹⁴ 7 U.S.C. 8301 et seq.

AHPA only allows USDA to conduct an animal health risk assessment to determine if GE animals (including insects) present a risk to livestock. Thus, if a company engineered a mosquito to prevent the transmission of avian malaria in wild bird species (as a way to protect a wild bird species from extinction due to spread of avian malaria), AHPA would only allow USDA to consider the impact of that engineered mosquito on livestock species and would not allow it to look at the ecological impact of the release of that GE mosquito on non-livestock bird species, or other animals that might be affected by avian malaria. Clearly, USDA needs statutory authority to allow it to consider the ecological impact of the release of such a GE animal on non-livestock species. In addition, perhaps such statutory authority would allow USDA to seek appropriate input from agencies with expertise in similar environmental assessments, such as EPA.

4. What additional clarification could be provided regarding the mechanism and timeline for regularly reviewing and updating as appropriate, the Coordinated Framework to minimize delays, support innovation, protect health and the environment and promote public trust in the regulatory system for biotechnology products?

To promote public trust in the regulatory system for biotechnology products, it is crucial that the government make very clear that *all* products of biotechnology have undergone a rigorous, independent assessment of potential human health and environmental risks. This means the regulatory trigger for performing a premarket assessment of biotechnology products should be based on the fact that they have been produced by biotechnology and, so, meet the definition laid out in the July 2015 EOP memorandum.¹⁵ In other words, the regulatory trigger should be a process-based one, not one based on the characteristics of the organism.

We note that the recent National Academy of Sciences report on genetically engineered plants stated that without independent governmental assessment of the safety of genetically engineered plants (also known as plants produced via biotechnology), the public perception of safety could be completely eroded:

Without the assurance that there has been some third-party review for safety, consumers' perceptions about the safety of GE food and crops might erode completely. Although consumer confidence should not be the only rationale for a product-approval system, it is important to recognize that it is an important social and economic factor (OSTP, 2015). FINDING: Not having government regulation of GE crops would be problematic for safety, trade, and other reasons and would erode public trust.¹⁶

We urge OSTP to state that federal agencies should consider all genetically engineered organisms to be biotechnology products. OSTP should also state that all these organisms should be required to go through a rigorous mandatory premarket assessment process for potential human health and environmental risks in order to improve public trust in the regulatory process for organisms produced using modern biotechnology techniques.

¹⁵ July 2015 EOP memorandum.

¹⁶ National Academies of Sciences, Engineering, and Medicine (2016), *Genetically Engineered Crops: Experiences and Prospects* at 340. Washington, DC: The National Academies Press. doi: 10.17226/23395.

For cases in which there is a lack of necessary tools or authorities, OSTP should urge that agencies seek such tools and authorities from Congress—and, in the meantime, seek whatever expertise may be available currently in other agencies. For example, FDA has decided to regulate GE animals as new animal drugs. FDA, in 2015, approved a salmon that was genetically engineered for a faster growth rate. FDA performed an environmental assessment of the release of this salmon, even though FDA does not have the expertise to perform such environmental assessments. In such a case, agencies with more expertise in this area, such as the EPA or the U.S. Fish and Wildlife Service, should be tasked with doing the environmental assessment. This is particularly important now that there are proposals to release insects such as mosquitoes, Mediterranean fruit flies, Mexican fruit flies, olive flies, or diamond back moths to reduce the population numbers of agricultural pest insects or insects that transmit disease. FDA has decided to review Oxitec’s proposal for a GE *Aedes aegypti*, a mosquito engineered with a lethality gene that is designed to suppress population levels of *A. aegypti*, which transmits the Zika virus, as a medical device and designed to be released in Key West, Florida.¹⁷ Again, we do not think FDA has the expertise to look at the potential environmental impact of the release of engineered *A. aegypti*. In such a case, EPA should be required to help with an ecological assessment of the release of such a GE insect. There is also a proposal to release GE diamondback moths, with a conditional lethality trait, to suppress populations of diamond back moths on brassica crops; such a release is planned in New York.¹⁸ While USDA has the expertise to determine the effect of the release on non-GE diamondback moths, they do not really have the expertise to evaluate the broader environmental impact of the release of such a GE insect. In this case, expertise from EPA should also be tapped to determine the broader environmental impact.

Moreover, take the example of the proposed update’s Case Study #7, a hypothetical GE rabbit engineered to produce recombinant human insulin in rabbit milk. The rDNA construct encoding the recombinant human insulin protein in the genome of the GE rabbit would be regulated as a new animal drug while the human insulin purified from the GE rabbit milk would be regulated as a human drug. We note that in this case study, there is no environmental assessment to deal with the potential problem that might arise if these GE rabbits accidentally were released into the wild. What if these rabbits spread or if local people ate some of these rabbits that have produced this insulin? Or, take the case of a hog engineered to produce vaccines or drugs that could also be accidentally released into the wild. If that happens, the hog may spread in the wild—and there is already a problem with feral hogs in parts of the southern U.S. Again, there should be an environmental risk assessment that incorporates a failure mode analysis (e.g., what happens if things go wrong and the GE organism is accidentally released into the wild).

In sum, to promote public trust in the regulatory system for biotechnology products, it is crucial that the government ensure that *all* products of biotechnology undergo a rigorous,

¹⁷ FDA, “Oxitec Mosquito” (Aug. 5, 2016) (online at www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/ucm446529.htm).

¹⁸ See USDA Animal and Plant Health Inspection Service, *Proposal to permit the field release of genetically engineered diamondback moth in New York* (Oct. 2014) (online at www.aphis.usda.gov/brs/aphisdocs/13_297102r_fea.pdf); USDA Animal and Plant Health Inspection Service, *National Environmental Policy Act Decision and Finding of No Significant Impact; Permit application 13-297-102r, Field release of genetically engineered diamondback moth strains* (2015) (online at www.aphis.usda.gov/brs/aphisdocs/13_297102r_fonsi.pdf).

independent assessment of the human health and environmental safety, and make clear to the public when this assessment has occurred. In areas where the agencies do not feel they have the statutory tools or authorities needed to carry out these assessments or require this labeling, the agencies should request appropriate statutory changes from Congress—and, where possible, seek whatever expertise may be available at other agencies in the meantime.

Thank you for your consideration of our comments.

Respectfully submitted,

A handwritten signature in black ink that reads "Michael Hansen". The signature is written in a cursive style with a large, prominent "M" and "H".

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