August 6, 2019

By Electronic Submission
Docket No. APHIS-2018-0034
Biotechnology Regulatory Services
APHIS
4700 River Road
Riverdale, MD 20737-1238

Re: Comments to Docket No. APHIS-2018-0034 Regarding the Proposed Changes to 7 CFR part 340.

The Center for Science in the Public Interest (CSPI)[1], Environmental Defense Fund[2], the Consumer Federation of America[3] and the National Wildlife Federation[4]… (referred to as "we") appreciate the opportunity to submit comments on the United States Department of Agriculture's (USDA) proposed changes to 7 CFR part 340. We support science- and risk-based oversight by USDA of genetically engineered (GE) plants to ensure they are safe to humans and the environment before they are released for cultivation or restoration. Products produced with genetic engineering present both potential benefits and risks for society. If carefully developed, applied and stewarded, they could increase resilience to stresses caused by climate change and other drivers. Products developed with newer gene editing techniques could increase food and energy security, support biological diversity, improve human health, and sustain community economic development. We support science-based streamlining of the regulatory process to encourage development of these needed innovations; however, the rapid advances in biotechnologies and their resultant products increase the need for effective regulatory oversight that manages potential risks, and for efficient mechanisms that promote transparency and public engagement.

We believe that the proposed changes to USDA's oversight of GE organisms will not provide adequate safeguards for human health and the environment and threaten to undermine consumer support of GE products. In particular, we are concerned that the proposal eliminates

[1] CSPI is a nonprofit education and advocacy organization that focuses on improving the safety and nutritional quality of our food supply. CSPI seeks to promote health through educating the public about nutrition; it represents citizens' interests before legislative, regulatory, and judicial bodies; and it works to ensure advances in science are used for the public good. CSPI is supported by the 600,000 member-subscribers to its *Nutrition Action Healthletter* and by foundation grants. CSPI receives no funding from industry or the federal government.

[2] Environmental Defense Fund (EDF), with over 2.5 million members, is an international non-partisan, non-profit organization dedicated to protecting human health and the environment by effectively applying science, economics, and the law.

[3] Consumer Federation of America is an association of over 250 non-profit consumer organizations that was established in 1968 to advance the consumer interest through research, advocacy and education. Member organizations include local, state, and national consumer advocacy groups, senior citizen associations, consumer cooperatives, trade unions and food safety organizations.

[4] The National Wildlife Federation is America's oldest and largest conservation organization, made up of 52 state and territorial affiliates and representing more than 6 million members and supporters across the nation. NWF's mission is to unite all Americans to ensure wildlife thrive in a rapidly changing world.

USDA oversight of many "traditional" GE plants,[5] which could result in harm to human health, the environment, and/or U.S. agricultural interests. We are also concerned that many of the proposed exemptions from oversight are not supported by the necessary scientific data and analysis that would ensure they will not result in adverse impacts. Finally, we believe that USDA should eliminate the ability for GE plant developers to self-determine whether the regulations apply to them. Instead, USDA should determine whether a GE plant properly qualifies for an exemption from 7 CFR Part 340.

I. Any decision to exempt GE plants from USDA oversight under 7 CRF Part 340 should be based on scientific data and a risk assessment that are both subject to public comment.

A. There is no scientific evidence cited in the proposed rule or the PEIS to support the broad categorical exemptions involving gene editing.

USDA proposes to exempt from regulation any GE plants where the modification is a deletion of any size, a single base pair substitution, or a change that mimics a sequence in the plant's natural gene pool. Those exemptions codify the Secretary of Agriculture's statement that plants that could be developed through traditional breeding would not be regulated because they "are likely to pose no greater risk than their traditionally bred comparators" (84 FR 26519). However, the proposed rule and the accompanying PEIS do not provide any scientific evidence that the GE plants that would qualify for exemptions pose no additional risks that need oversight. Instead, USDA states that "given the accepted safety of traditionally bred plants, and the principle that the use of recombinant DNA does not itself introduce unique risks, it is logical and appropriate to exempt from our regulation plants produced by any method if they could have been produced by traditional breeding" (84 FR 26519).

If USDA is going to allow exemptions, they should be supported by scientific data showing that a specific category of GE plants will not result in plant pest risks.[6] As stated by a US government memo on "Principles for Regulation of Emerging Technologies" issued by the Office of Science and Technology Policy, the Office of Management and Budget, and the US Trade Representative, "Federal regulation and oversight of emerging technologies should be based on the best available scientific information." (Memo dated March 11, 2011). USDA should set forth the scientific evidence supporting its exemption and allow for public comment or

[5] The proposed changes to 7 CFR part 340 define "genetic engineering" to include not just adding a new gene to a plant (which CSPI calls "traditional" genetic engineering) but also gene editing changes made within a plant's own genome. In this comment, when CSPI's discusses gaps in oversight that will be occur if the proposed changes are adopted, CSPI is primarily referring to "traditional" genetic engineering and not gene editing within a plant's own genome.

[6] While USDA's interpretation of their statutory mandate limits it's oversight to plant pest risks, they have regulated GE plants for more than twenty years to address other risks (such as inadvertent introduction to the food supply, economic impacts from gene flow, etc.…). Therefore, CSPI believes that if a GE plant is to be exempt from oversight under 7 CFR 340, there should be scientific evidence that those plants don't pose any of this full range of risks.

else eliminate the exemptions. U.S. consumers and trading partners will not accept unregulated GE products unless the basis for exempting oversight is based on scientific evidence.

B. USDA has not stated whether it has considered potential off-targets impacts from plants covered by the exemptions.

The exemptions for a deletion of any size, a single base pair substitution, and changes mimicking sequences in a plant's natural gene pool, are clearly meant to capture many of the changes made in plants by gene editing tools such as CRISPR, TALENs, and ZFNs. However, those blanket exemptions fail to take into consideration the potential for off-target mutations which could result in potential plant pest risks or impacts on human health, the environment, or agriculture. USDA should spell out the scientific design criteria for limiting off-target mutations that need to be met for a GE plant to qualify for an exemption.

When a plant's DNA is edited, there is a small chance that an off-target mutation could result in a new phenotype with a negative impact. The likelihood of an off-target mutation occurring can depend on the molecule used to make the edit. For example, ZFNs and TALENs result in fewer off-target mutations than CRISPR (Modrzejewski *et al. Environ Evid (*2019) *8:27.* Also, the number of off-target mutations can depend on the plant being edited. A recent review of 1,328 studies/applications of gene-editing in plants found that using CRISPR resulted in off-target mutations at 3% of the predicted off-target locations, but that number increased to almost 9% for edits in rice (Modrzejewski *et al. Environ Evid (2019) 8:27*. Scientific research has shown that the likelihood of off-target edits can be minimized though the use of different experimental techniques, such as "designing guide RNAs [when using CRISPR] that are different from other genomic locations by at least three mismatches in combination with at least one mismatch occurring in the [relevant] region" (Young *et al. Scientific Reports (2019) 9:6729*. Therefore, depending on the gene-editing tool used, the plant being edited, and the design of the guide molecule, the likelihood of off-target mutations will differ.

USDA should modify the proposed gene-editing exemptions so that a GE plant only qualifies if it meets criteria established by USDA that minimize off-target mutations using the current scientific best practices. For example, if off-target mutations are extremely rare with TALEN editing, then plants using that method for a deletion might qualify for one of the exemptions. However, if CRISPR is used, one might need to design the guide RNA as set forth in Young et al. (2019) to qualify for an exemption. USDA could modify the criteria on an annual basis by reviewing the scientific literature on off-target mutations. By doing this, USDA would ensure that only gene-edited plants using state-of-the-art techniques to reduce off-target mutations can take advantage of an exemption.

C. USDA needs to clarify that the exemption for deletions only applies to plants with a single deletion anywhere in the genome, not those with changes made in multiple locations (at the same time or at different times).

The USDA proposal exempts plants where "the genetic modification is solely a deletion of any size." However, many gene-edited plants will be the result of two or more deletions, which could occur during the same gene-editing event or from two or more gene editing events

that occur at different times. Many of those multiple deletions are not possible in nature and should not automatically qualify for an exemption. As stated in a recent article in *Frontiers in Plant Science*, gene editing allows for "altering multiple gene copies in the same target sequence in an organism" and "editing of different genomic sites using different gRNAs in one organism simultaneously or successively in multiplexing approaches," neither of which is possible with conventional breeding nor through naturally occurring mutations." Kawall, *Frontiers in Plant Science*, 10:3389 (2019).

The Biotechnology Regulatory Services' Deputy Administrator stated in a conference call with stakeholders on June 13, 2019 that this exemption only applies when the gene-edited plant has only **one deletion from a single gene-editing event**. To avoid any misapplication of the exemption by developers, the final rule and the federal register notice accompanying it should include language to make clear the scope of the exemptions.

II. USDA should not eliminate oversight of traditional GE plants.

A. USDA oversight is needed to ensure field trials do not persist and cause adverse impacts to the environment, humans, or agriculture.

USDA states in its proposal that if the new regulations are adopted, it will no longer regulate most of the GE plants it has regulated to date. The impact of the changes will be that traditional GE plant developers (both private developers and academic scientists) will not be required to obtain permits (or file notifications) to conduct field trials and will no longer need to implement any confinement conditions that ensure the GE plants do not persist in the environment when the field trial is complete. USDA states that it "believes that developers would continue to utilize such measures for field testing even in cases where USDA would not require a permit" because it would be in their "best interest" (84 FR 26535).

GE plants have escaped from field trials with USDA oversight in the past and the likelihood of that happening will only increase without USDA oversight, even if developers establish confinement protocols.[7] In 2016, USDA decided to require all GE wheat trials to obtain permits and eliminated the notification option because of several instances where confinement did not work. The GE wheat escaped from trial sites and in some instances caused significant economic impact when foreign governments temporarily banned wheat exports. According to USDA, "bringing GE wheat under permit enables APHIS to create and enforce permit conditions that ensure confinement and minimize the risk that the regulated GE wheat will persist in the environment" (USDA Update Email to Stakeholders July 12, 2019).

The programmatic environmental impact statement (PEIS) states that USDA currently regulates approximately 400,000 to 500,000 acres of confined field trials every year and that the agency expects that number to remain constant if the rule changes (PEIS at page 4-14). USDA also acknowledges that its current confinement requirements "[prevent] undesired cross-

[7] USDA's Biotechnology Regulatory Services has identified several instances of escapes from confined field trials for GE wheat, cotton, corn and bentgrass. See https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/sa_compliance_and_inspections/ct_compliance_history .

pollination or comingling with non-GE crops" (84 FR 26535). Given the large number of field trial acres and the fact that meeting confinement conditions is expensive, it is likely that at least some field trials will be carried out without procedures preventing the release of GE seeds from the test sites. This means that GE field trial material could inadvertently migrate to neighboring fields, leading to possible environmental impacts from the gene flow, such as harm to non-targets from an experimental protein. If the GE plant produces a protein that has not yet been found safe for consumption by humans, there could be food product recalls for fear that the protein could be a potential allergen or toxin. U.S. commodities could also be rejected in export markets if the GE plant is not approved in that export market. Such events could decrease consumer confidence in all GE plants, even ones that are safe to consume.

USDA needs to consider the potential impacts on the environment, food supply, economy, and consumer perceptions if the agency were to no longer oversee most field trials with traditional GE plants (and no other federal agency is taking over that responsibility). In our estimation, such an analysis would support USDA continuing to regulate GE plants' field trials to protect the environment, human health, and U.S. agricultural interests

B. GE plants that produce pharmaceuticals or industrial compounds need to remain regulated by 7 CFR part 340.

Under the current regulations at 7 CFR part 340, USDA requires that any GE plant that produces plant-made pharmaceuticals or industrials (PMPIs) only be grown outdoors after receiving a permit that prevents any escape from the approved planting location. Such plants are not allowed to take advantage of USDA's expedited notification process because there are significant potential risks if the GE plant escaped from the planting site (primarily the risk of unauthorized introduction into the food supply). An example of a PMPI is Ventria Bioscience's engineered rice plants to produce a lactoferrin to combat diarrhea.

The proposed changes to 7 CFR part 340 would result in "most, if not all, GE PMPI-producing plants that are currently under APHIS permits" allowed to "be grown outdoors without the need for APHIS permits and without APHIS oversight." (84 FR 26518). USDA acknowledges that the resulting "gap in Federal oversight could generate concerns from the general public regarding the safety and wholesomeness of the human or animal food supply, which could adversely impact agricultural interests." The Department further acknowledges that confinement conditions for PMPI-producing plants prevent inadvertent releases with "public health or economic impacts." USDA states that it "has identified two options that have the potential for adequate Federal oversight of outdoor plantings of plants engineered to produce PMPIs." Yet neither of these options will automatically be implemented if USDA finalizes its proposal. The two proposed options are to either have USDA regulate using 7 CFR Part 360, or for Congress to enact a statute addressing oversight of these GE plants.

Given the potential impacts that could arise if a GE plant with a PMPI were inadvertently released from a field, USDA should not go forward with eliminating USDA oversight of this subset of GE plants unless and until another office within USDA or a different federal agency intends to fill the regulatory void. We support USDA's second option, which is to seek a new law from Congress to address these plants. However, such a law should not be limited to GE

PMPI plants, but give USDA authority to regulate all GE plants and the full range of potential impacts (e.g. environmental, economic, etc…).[8]

C. GE plants that produce biological pesticides need to remain regulated by 7 CFR part 340 until the Environmental Protection Agency (EPA) regulates trials of less than 10 acres.

USDA's proposed changes would eliminate any USDA oversight of small-scale field testing of GE plants that produce biological pesticides (called "plant-incorporated protectants" or "PIPs").[9] As stated by USDA, "such plants could be grown outdoors without the need for an APHIS permit and without undergoing APHIS oversight" (84 FR 26518). EPA, which registers PIPs for commercial use, has historically regulated PIP field trials when they exceed 10 acres. USDA states that in the absence of its oversight of small-scale field trials, "EPA may decide to require experimental use permits for **all, some, or none** of such PIPs" (84 FR 26518) (emphasis added). USDA also states that it will work with EPA during any interim period if EPA decides to regulate those small-scale trials.

If EPA does not require permits for experimental plantings of less than 10 acres, those trials will go unregulated, and another category of GE field trials will lack federal oversight. This would pose the same risks as mentioned in section A and B above. Therefore, USDA should not implement its proposed changes to 7 CFR part 340 until there is an assurance that EPA will regulate all PIP-field trials.

D. By withdrawing federal oversight of GE plants, USDA would encourage a patchwork of state regulations that both raises cost for developers and inadequately protects human health, the environment, or the interests of consumers.

USDA states in its proposal that many GE plants that have been regulated by USDA would no longer be regulated if the proposed changes to 7 CFR part 340 are finalized. The PEIS states that under the current system, states are given the opportunity to review proposed permits and request additional permit conditions, and that some states actively participate in that process (PEIS 4-116 and 4-117). In addition, states such as Florida, Oklahoma, Minnesota and Washington issue their own permits for movement or introduction of GE plants (PEIS 4-117).

In the PEIS, USDA states that "In response to the expected reduction in the number of permits issued by APHIS, some states may decide to enact legislation to impose state level regulation on GE organisms" (PEIS 4-119). In fact, this is already occurring. On June 17, 2019, Vermont established a law which requires review of GE traits before they can be sold, distributed, or used in the state (VT Act 83 of 2019). So, one possible result of the USDA

[8] While USDA's regulatory oversight of GE plants involves plant pest risks, those are not the most likely adverse impacts from GE plants. The most likely impacts include but are not limited to development of resistant weeds, development of resistant pests, gene flow to wild relatives, and development of resistant crops. Therefore, it would be best if Congress provided authority to ensure the safety of PMPIs but also provided USDA or another agency authority to manage and minimize the most likely adverse impacts from growing GE plants.

[9] PIPs that are currently grown in the US include corn and cotton seeds engineered with genes from *bacillus thuringiensis* to produce biological toxins that act as pesticides on certain insects.

proposal is that there will be a patchwork of state regulations of GE plants with each state having different requirements. This will raise the cost of carrying out confined field trials and commercial release by public and private seed developers and could lead to "forum shopping," where seed developers conduct their field trials in states with lax regulation or no regulation at all. A state patchwork of oversight is less desirable than uniform oversight by USDA because it is less likely to ensure that GE plants are safe before entering the market. Therefore, continuation of USDA oversight is a better option for ensure safety and consumer confidence.[10]

III. USDA should eliminate the self-determination option in the proposed regulations and should subject all GE plants to either the "Am I regulated?" or the "Regulatory Status Review" processes.

The USDA proposed rule would allow the GE plant developer to self-determine whether they qualify for an exemption. This procedure is problematic for several reasons. First, there is an inherent conflict of interest because developers have financial incentives to determine themselves exempt. While some developers will diligently determine the regulatory status of their GE plant, others may not. Second, if self-determination is allowed, neither USDA nor the public will know which GE plants are released into the environment and entering the food supply. This lack of transparency could have market and/or trade, impacts as U.S. consumers will not know which GE plants are entering the food supply and other countries will not know which products produced in the U.S. need regulatory approval by their governments. Finally, if developers can self-determine whether they are regulated, the international Cartagena Protocol's requirement that countries list all GE organisms released into the environment in the Biosafety Clearinghouse will be impossible for the U.S. to satisfy. Therefore, the USDA, not the developer, should decide whether a GE organism needs regulation. USDA should eliminate self-determination and require USDA to determine whether a GE plant is regulated using the existing "Am I regulated?" procedure. If USDA disagrees and allows for self-determinations, USDA should require the developer to submit those self-determinations to USDA, both for USDA's information and so USDA can make them publicly available.

IV. USDA should publish on its website a complete list of all GE organisms released into the environment in the U.S.

Throughout the proposal, USDA identifies the information it will make available to the public. For example, USDA says that it will publish a list of all plant-trait-mechanism of action (MOA) combinations that it has reviewed (including all GE plants that have obtained non-regulated status under the current 7 CFR 340) so that future developers can use that list to take advantage of the exemption in 7 CFR 340.19(c). USDA also states that it will provide the results of any regulatory status reviews if USDA identifies a potential plant pest risk and conducts a plant pest risk assessment (PPRA) (7 CFR 340.4(b)(3)). However, the proposed rule does not state that USDA will make public the results of any inquiries by developers confirming their qualification for exemptions under 7 CFR 340.1(d), and USDA has no way to make public

[10] We want to make clear that we are not suggesting that USDA or Congress should preempt states from oversight of GE plants. Preemption would only be appropriate if USDA conducted comprehensive science-based oversight of GE plants that addressed their potential impacts to human health, the environment, and agriculture.

developer self-determinations that it does not receive. Finally, the proposal also does not state whether permits issued under 7 CFR 340.5 will be made publicly available, (and whether there will be an opportunity for the public to comment on proposed permits).

In addition to providing the information currently set forth in the proposed rule, USDA should establish on its website a single list of all GE organisms that are being released into the environment. That list should include all plant-trait-MOA combinations, all regulatory status reviews, all permitting, and all USDA confirmations of developers' self-determinations of an exemption. With a complete and accurate list of all GE organisms that have been released into the environment, food industry stakeholders and the public will be able to determine which GE plants have entered the food supply. A transparent and comprehensive list will provide helpful information if any food safety and environmental threats materialize. This information will also be important for international trade because it may prevent unnecessary trade barriers from being constructed based on inaccurate information about which GE plants may be entering a country without the proper regulatory approval. It will improve consumer confidence about GE plants because consumers will realize that their existence is not being hidden from them. To be as useful and as transparent as possible, the list should include information about the plant, the type of modifications or edits performed, the changed traits, a summary of data about the benefits of the traits, and any testing for safety concerns.

V. USDA should incorporate the Plant Protection Act's "noxious weed" authority into 7 CFR Part 340.

We support broadening the scope of 7 CFR Part 340 to include "noxious weed" concerns. USDA should use all its potential regulatory authorities that Congress included in the Plant Protection Act to ensure GE plants do not harm the environment and/or agricultural interests. The Plant Protection Act defines "noxious weed" to mean:

> 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.

A plain reading of that definition would support USDA carrying out noxious weed assessments to address potential impacts to the environment, public health, and "other interests of agriculture." This could include impacts of unapproved GE plants on farmers of non-GE plants, impacts of resistant weeds on the environment (because farmers need to kill them with additional herbicides), and economic impacts from potential trade disruptions if farmers grow GE plants that are not yet approved in export markets.

USDA proposed adding the "noxious weed" authority to 7 CFR Part 340 in its proposed revisions announced in both 2008 and 2017, and its rationale for inclusion at that time is still valid. As stated in the 2017 proposal:

> "Advances in genetic engineering have also made the need to evaluate GE plants for noxious weed risk more pressing […].

> In more recent years, there has been an increasing diversity of both agronomic and non-agronomic traits engineered in plants. There has also been an increased use of plants in genetic engineering that, in their unmodified state, are known to possess weedy traits.
>
> Moreover, APHIS' current regulatory structure, which entails evaluating such plants solely for plant pest risk, is not sufficient to properly identify all risks that these plants present to other plants and plant products….Thus, APHIS considers it both **appropriate and necessary to begin to evaluate GE plants for noxious weed risk."** (82 FR 7009-10, emphasis added).

USDA now is reversing course without any explanation about why its analysis from 2017 is no longer applicable. Therefore, USDA should incorporate its "noxious weed" authority into 7 CFR part 340 and interpret that authority broadly to manage the wide range of potential impacts of GE plants.

VI. USDA should provide additional opportunities for public participation in the proposed regulations, such as opportunities to comment on regulatory status reviews which involve novel plant-trait-mechanism of action combinations.

In the USDA proposed rule, the public is given the opportunity to comment on a subset of the regulatory status reviews USDA conducts – only where USDA determines from its initial review that there are potential pest plant risks and a PPRA is needed. For other USDA regulatory decisions under 7 CFR 340 – the permit decisions and the many "regulatory status reviews" that USDA determines do not need a PPRA – there is no opportunity for public comments. This denies the public the ability to provide USDA with potentially important information relevant to whether a GE plant has potential risks. Information provided by the public can help ensure that USDA's decisions take into consideration all available data and analysis, not just what is submitted by the developer. This is particularly important since USDA has stated that its "regulatory status reviews" will likely be completed without any actual field data on how the plant-trait-MOAs perform in the environment. Therefore, USDA should provide the public with the opportunity to comment on all GE plants undergoing "regulatory status review" and on any issued permits. For similar reasons, USDA should maintain and make public a complete and accurate list of all GE organisms that have been released into the environment.

VII. The elimination of USDA oversight for most GE plants could lead to trading partners determining when U.S. farmers can grow and export those GE plants.

If the changes to 7 CFR part 340 are finalized as proposed, the ability of farmers in the U.S. to grow GE plants could be impacted by the laws and regulations of nations that have agricultural trade with the United States. First, even if most GE domesticated plants are no longer regulated by USDA, that does not mean our trading partners will not regulate their introduction into their countries. U.S. farmers may not be able to grow new GE plants until those export countries have approved them. Therefore, the time and cost savings envisioned by the USDA proposal may not materialize if the GE plant will be exported to a country that requires government approval or adds additional layers of review as a result of this proposal.

Secondly, if a GE plant is not regulated by USDA but is regulated by another country, that country will no longer have the USDA approval to support that country's regulatory process. Under USDA's proposal, U.S. trading partners would become the regulators of "first impression" on the safety of a GE plant. This could slow down a foreign government's approval of a GE plant developed in the U.S. because that country cannot rely on a US government decision that the GE plant is safe to grow. Finally, if GE plants can be grown by farmers in the U.S. without USDA oversight, the chance for adventitious presence of unapproved GE plants will increase. This could lead to the loss of export markets or significant economic impacts if a GE plant grown in the U.S. is rejected when it arrives at a foreign port. Therefore, reducing oversight in the U.S. may not benefit seed developers and farmers as envisioned by the proposed changes to 7 CFR part 340.

We appreciate the opportunity to provide this comment to the USDA. We would welcome the opportunity to meet with the staff at USDA's Animal Health and Plant Inspection Service to discuss the issues addressed in this letter in more detail if that would be helpful.

Sincerely,

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