Revisions to USDA biotechnology regulations: The SECURE rule

Neil E. Hoffman[a,1]

[a]Biotechnology Regulatory Services, Animal Plant Health Inspection Services, US Department of Agriculture, Riverdale, MD 20737

Edited by Daniel F. Voytas, University of Minnesota, Saint Paul, MN, and approved March 2, 2021 (received for review August 12, 2020)

In keeping with the directive in Executive Order 13874 (Modernizing the Regulatory Framework for Agricultural Biotechnology Products) to adopt regulatory approaches that are proportionate to risk and avoid arbitrary distinctions across like products, the US Department of Agriculture (USDA) revised its biotechnology regulations by promulgating the Sustainable, Ecological, Consistent, Uniform, Responsible, and Efficient (SECURE) rule. Specifically, the SECURE rule 1) establishes exemptions for plants modified by genetic engineering where the modification could otherwise have been made through conventional breeding, 2) uses risk posed by the introduced trait to determine whether an organism is regulated, rather than relying on whether the organism was developed using a plant pest, and 3) provides a mechanism for a rapid initial review to efficiently distinguish plants developed using genetic engineering that do not pose plausible pathways to increased plant pest risk from those that do. As a result of the focused oversight on potentially riskier crops developed using genetic engineering, USDA is expected to improve the efficiency and effectiveness of its oversight program. The reduced regulatory burden is expected to promote innovation by expanding the number and diversity of developers to include smaller businesses and academics and to increase the number and variety of traits being developed through biotechnology.

biotechnology regulations | genetically engineered plants | coordinated framework | SECURE rule | 7CFR340

Innovation—including products improved through biotechnology—is needed to address a wide range of serious worldwide agricultural problems, including how to foster more sustainable agriculture practices, address climate change impacts, and increase productivity to reduce food insecurity (1–3) (https://audaciousproject.org/ideas/2019/salk-institute-for-biological-studies). Recognizing the need for innovation, federal policy for ensuring the safe use of biotechnology products began in 1986 with issuance of the Coordinated Framework for the Regulation of Biotechnology by the White House Office of Science and Technology Policy (OSTP) (4). The 1986 Coordinated Framework (CF) held that three agencies (the Food and Drug Administration [FDA], the US Environmental Protection Agency [EPA], and the US Department of Agriculture [USDA]) had primary oversight responsibilities for biotechnology products and could use existing laws to implement their responsibilities. Furthermore, the CF was "expected to evolve in accord with the experiences of the industry and the agencies, and, thus, modifications may need to be made through administrative or legislative actions" (4).

On 27 February 1992, OSTP issued an update to the 1986 CF (the 1992 CF Update) (5), that "set forth the proper basis for agencies' exercise of oversight authority within the scope of discretion afforded by statute." Key scope principles included the following:

- Scope principle 1: "a determination to exercise oversight . . . should not turn on the fact that an organism has been modified or modified by a particular process or technique." Oversight should "focus 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." In reaching this principle, the 1992 CF Update cites the National Research Council (6) conclusions, 1) "organisms that have been genetically modified are not per se of inherently greater risk than unmodified organisms" and 2) "crops modified by molecular and cellular methods should pose risks no different from those modified by classical methods for similar traits."
- Scope principle 2: "a determination to exercise oversight . . . should be based on evidence that the risk presented by introduction of an organism in a particular environment is unreasonable" [in order to] "ensure that limited federal oversight resources are applied where they will accomplish the greatest net beneficial protection of public health and the environment." A further update to the CF in 2017 (7) elaborated, "To the extent permitted under relevant statutory provisions, following a risk-based approach to regulation, the regulatory system should distinguish between those biotechnology products that require a certain level of Federal oversight and those that do not."

The EPA, FDA, and USDA have their own agency-specific regulations, rules, guidance, and policy documents in accordance with their statutory authorities. In the case of USDA, regulations were issued in 1987 (5 y prior to the principles identified in the 1992 CF Update), under the authority of the Federal Plant Pest Act of 1957 and the Plant Quarantine Act of 1912, two acts that were subsumed into the Plant Protection Act of 2000 (PPA, 7 U.S.C. 7701 et seq.), along with other provisions. The regulations held that if an organism was altered or produced through genetic engineering and the engineering process used an organism that was a plant pest or sequences from a plant pest, the developer required authorization for import of the organism into the United States, for its interstate movement, or for its release into the environment (field testing). Since 1987, the regulatory trigger remained unchanged, including through six regulatory amendments (1988, 1990, 1993, 1994, 1997, and 2005) which instituted exemptions from the requirement for permits to conduct activities with certain microorganisms and *Arabidopsis*, instituted a notification process (a streamlined permitting process) and petition process (the process for a plant developed using genetic engineering to attain nonregulated status), and excluded plants engineered to produce industrial compounds from the notification process. The petition process entailed the submission of a dossier (petition for nonregulated

This paper results from the NAS Colloquium of the National Academy of Sciences, "Life 2.0: The Promise and Challenge of a CRISPR Path to a Sustainable Planet," held December 10–11, 2019, at the Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering in Irvine, CA. NAS colloquia began in 1991 and have been published in PNAS since 1995. The complete program and video recordings of presentations are available on the NAS website at http://www.nasonline.org/CRISPR. The collection of colloquium papers in PNAS can be found at https://www.pnas.org/page/collection/crispr-sustainable-planet.

Author contributions: N.E.H. wrote the paper.

The author declares no competing interest.

This article is a PNAS Direct Submission.

[1]Email: neil.e.hoffman@usda.gov.

Published April 30, 2021.

status) that summarized field trial data presenting an argument that the plant developed using genetic engineering did not pose a plant pest risk. On average, the petition process took about 15 mo to complete.

Although biotechnology regulation under the CF has been successful in ensuring that crops developed using genetic engineering, and commercialized over the past 30 y, pose no greater risks for agriculture, the public health, welfare, safety, and environment than do conventional crops (8–11), numerous administrations and the academic community have argued that the current regulation of biotechnology limits innovation by posing a high regulatory burden on transgenic crops that pose little to no risk. For example, Bradford et al. (12) point out that although herbicide- and insect-resistant lines of transgenic corn, cotton, soybean, and canola developed primarily by large companies have been widely grown on a global scale, regulatory barriers have impeded innovation by small companies and academic scientists and have limited the application of biotechnology in nearly all but a few of the largest commodity crops. In 2015, the Obama White House initiated an effort to modernize the CF and directed the FDA, EPA, and USDA to continually strive to improve predictability, increase efficiency, and reduce uncertainty in their regulatory processes and requirements. In two documents the Obama administration concluded that "the costs and burdens [associated with the regulation of biotechnology] have the potential to hamper economic growth, innovation, and competitiveness. These costs and burdens have limited the ability of technology developers, particularly those in small and mid-sized companies and in academic research institutions, to navigate the regulatory process and have limited the ability of the public to understand easily how the safety of these products is assured" (7, 13). In 2019, the Trump White House issued Executive Order 13874, stating that "the policy of the Federal Government is to protect public health and the environment by adopting regulatory approaches for the products of agricultural biotechnology that are proportionate responses to the risks such products pose, and that avoid arbitrary or unjustifiable distinctions across like products developed through different technologies. Any regulatory regime for products of agricultural biotechnology should ensure public confidence in the oversight of such products and also promote future innovation and competitiveness" (14). To this end, FDA, EPA, and USDA—the agencies with primary oversight over biotechnology—were directed to "identify relevant regulations and guidance documents within their respective jurisdictions that can be streamlined to ensure that products of agricultural biotechnology are regulated" [as] "proportionate responses to the risks such products pose" (14).

With these goals of the 1992 CF Update, the 2017 Modernization of the CF, and Executive Order 13874 in mind, USDA recently revised its biotechnology regulations, now called the SECURE (Sustainable, Ecological, Consistent, Uniform, Responsible, Efficient) rule (15). The SECURE rule (15)

1) establishes exemptions for plants modified by genetic engineering techniques where the modification could otherwise be achieved through conventional breeding techniques, ensuring that such plants are treated similarly to conventionally bred plants from a regulatory perspective, consistent with Scope principle 1 from the 1992 CF Update;
2) uses a risk-based approach to determine whether an organism is regulated, rather than relying on whether the organism was developed using a plant pest consistent with Scope principle 2 in the 1992 CF Update; and
3) provides a mechanism for a rapid initial review to efficiently distinguish plants developed using genetic engineering that do not pose plausible pathways to increased plant pest risk from those that do and thus require further evaluation, consistent with Scope principle 2 in the 1992 CF Update.

In contrast, under the former regulations the determination to regulate was based on whether a plant pest or plant pest sequence was used in the engineering process. USDA did not evaluate the risk posed by the modified plant or conduct a risk assessment of the product until a petition was submitted by a developer several years after the plant was subject to USDA oversight, thereby resulting in a substantial regulatory burden from the outset. The plant pest trigger provided a means of capturing most organisms developed using genetic engineering under the regulation because *Agrobacterium* (a plant pest) was used as a vector, or regulatory sequences from *Agrobacterium* or plant viruses were commonly used in genetic engineering. Over time the agency has learned that the presence of plant pest sequences or the use of a plant pest vector to modify a plant is unrelated to the properties (and risk) of the plant. Conversely, the plant pest trigger did not capture plants transformed by biolistics and with DNA lacking plant pest sequences. Thus, the plant pest trigger created a situation where many lower-risk plants developed using a plant pest were subject to regulation, while potentially higher-risk plants created without using a plant pest were not. By further harmonizing with the 1992 and 2017 CF Updates, the SECURE rule will provide more appropriate risk-based oversight of plants and other organisms developed using genetic engineering techniques. This is expected to reduce regulatory barriers, reduce regulatory costs, and stimulate innovation.

Exemptions for Modifications That Could Otherwise Be Achieved through Conventional Breeding

The SECURE rule (15) exempts plants containing a single modification where

1) "the genetic modification is a change resulting from cellular repair of a targeted DNA break in the absence of an externally provided repair template; or
2) the genetic modification is a targeted single base pair substitution; or
3) the genetic modification introduces a gene known to occur in the plant's gene pool or makes changes in a targeted sequence to correspond to a known allele of such a gene or to a known structural variation present in the gene pool."

As described in the preamble to the SECURE rule (15),

> the types of plants that qualify for these exemptions can also be created through conventional breeding. Conventional breeding techniques generally involve the deliberate selection of plants with desirable traits from existing population genetic variation or from new genetic variation created through artificial hybridization or induced mutagenesis. Such techniques include marker-assisted breeding, F1 hybrids, hybridization and selection, tissue culture, protoplast, cell, or embryo fusion, and chemical or radiation-based mutagenesis. Products generated solely using such techniques have a history of safe use and have never been regulated under the part 340 regulations. Although conventional breeding is not risk-free, the risks associated with it are, according to a 1989 National Research Council (NRC) report (6), "manageable by accepted standards." In other words, the types of modifications that can be introduced through conventional breeding have not led to concerns that require oversight from the federal government.

As noted to in the preamble to the SECURE rule (15), the NRC has concluded "that there is no evidence of unique hazards inherent in the use of recombinant DNA techniques with respect to plants, and that crops modified by molecular and cellular methods should pose risks no different from those modified by conventional breeding methods for similar traits (5, 16)." This conclusion formed part of the basis for the Scope principles in the 1992 CF Update:

> New molecular methods for editing genomes have been developed since the NRC studies that can be more specific and precise than those evaluated by the NRC studies, and plants modified by these

new methods should also pose plant pest risks that are no different from plants that are modified for similar traits by conventional breeding methods. Thus, when a plant meets one of the above-listed exemptions, it is not expected to pose plant pest risks greater than the plant pest risks posed by plants modified by conventional breeding methods and thus should rightly not be subjected to regulation under the SECURE rule.

As noted in the preamble to the SECURE rule (15), exemptions in the SECURE rule reflect what can be accomplished through conventional breeding:

> The types of DNA modifications that occur through conventional breeding by mutagenesis are well characterized (17, 18). Among the common outcomes that result from mutagenesis are deletions, insertions, and base pair substitutions (17), which often result from double strand breaks in the DNA followed by natural DNA repair. These types of modifications also occur at a low rate from naturally occurring environmental exposure to ionizing radiation, radical oxygen, chemical compounds, or biological agents such as viruses, or at an elevated rate in response to radiation and chemical-induced mutagenesis. In conventional breeding, these types of DNA modifications are introduced randomly. Individual plants possessing a mutation conferring a useful phenotype are isolated by screening, and random mutations that are introduced and do not convey a useful phenotype are segregated out during backcrossing and/or selection. New plant breeding technologies, such as those used in genome editing, can be used to create targeted double strand breaks in specific parts of the genome that when repaired result in deletions and small insertions, just as from natural environmental exposure or radiation mutagenesis (19). Likewise, new plant breeding technologies can also be used, in a specific, targeted manner, to create base pair substitutions that are similar to the modifications that can be created by random chemical mutagenesis. In other words, the same types of DNA modifications that occur in conventional breeding can also be constructed precisely using new plant breeding technologies (20). The SECURE rule exempts plants generated using plant breeding technologies that have non-templated insertions and deletions and that have a single base pair substitution, because they could otherwise be created by conventional breeding and pose no increased plant pest risk relative to their conventionally bred counterparts.

As mentioned in the preamble to the SECURE rule (15), one of SECURE's exemptions

> applies to the use of new plant breeding technologies to recreate the introduction of a gene, allele of a gene, or structural variation that could otherwise be introduced by natural or human-assisted crosses. Human selection of plants has been used for thousands of years; and crossing has been used to introduce alleles into breeding populations since at least the early 18th century (21). More recently, plant breeders have expanded the source of genetic material that can be used to introduce genetic changes into breeding populations through wide crosses, embryo rescue, and protoplast fusion (22–24), and have increased the rate of introduction of genetic material through marker-assisted and genomic selection (25). All of these approaches are considered conventional breeding methods and are used to expand and guide changes in the gene pool available within a population. However, genetic engineering techniques can also be used to introduce a genetic sequence from any donor source into plants, which cannot be accomplished through conventional breeding. To limit the exemption to what is possible in conventional breeding, the exemption applies only to the introduction of a gene, allele, or structural variant known to occur from a donor source (1) in the same species as the recipient, or (2) in a species compatible via wide crosses, embryo rescue, or protoplast fusion with the recipient species.

The exemptions described above represent the types of DNA modifications that occur within the realm of conventional breeding for any plant species. At the present time, only a single modification qualifies for the exemption because multiple modifications typically result from combining multiple specific traits, and the probability of success decreases as the number of modifications increases. However, the probability of introducing multiple changes may be more likely in one species versus another. Therefore, the SECURE rule contains a process to add additional modifications that are exempt from regulation to allow multiple targeted modifications to plants if such modifications can be accomplished through conventional breeding methods. This process might also allow USDA to expand the types, range, or complexity of modifications eligible for exemption based on experience. USDA can initiate an expansion on its own or in response to requests from the public. This provision ensures the exemptions remain current with advances in plant breeding practices and as information accumulates that more extensive modifications are routinely possible through conventional breeding in a given crop.

Finally, USDA has also created an exemption to dispense with event-by-event regulation. Events refer to separate plant lines that are transformed with identical DNA. They mainly differ in where the DNA inserts into the genome. Separate events were regulated based on the notion that the different position of the insert might result in unintended effects. In the agency's experience, unintended effects are uncommon, and in the course of a normal breeding program plants with unintended effects are discarded during the process of screening for desirable phenotypes and selecting lines for advancement. USDA reaffirms the view made in the 1997 preamble to the 7 CFR 340 rule revision establishing the extension process (26) that "the Agency believes that the differences [in plant pest risk from gene insertion sites, copy number, and genetic background] that may result [in plants qualifying for the extension process] would be of the magnitude observed through traditional crop breeding." Regulating for unintended effects is not consistent with the CF Scope principle to regulate only when the risk presented is unreasonable.

USDA has reviewed separate dossiers for the same plant–trait–mechanism of action (MOA) combination several times. For example, there were eight petitions for altered fruit ripening in tomato with the same MOA, four petitions for glyphosate-resistant corn with the same MOA, four petitions for glyphosate-resistant canola with the same MOA, and three petitions for glyphosate-resistant cotton with the same MOA. To save resources under the previous regulation, USDA created the more streamlined extension process where plants that had sufficient similarity to a previously reviewed plant that was deregulated would be evaluated for similarity and for any new issues that may be relevant to the regulatory decisions. Under the SECURE rule, an exemption has been created, § 340.1(c)(1), for a plant containing a plant–trait–MOA combination that USDA has previously evaluated using either the petition process or the Regulatory Status Review (RSR) process (discussed below) and found not to be regulated. The list of plant–trait–MOA combinations previously evaluated is publicly posted, subject to confidential business information (CBI) claims, to assist developers in determining whether a plant is subject to regulation. This exemption will eliminate event-by-event regulation.

USDA will not consider off-target mutations when evaluating whether a plant meets a criterion for an exemption. Off-target mutations are unintended mutations that arise during genome editing when the targeting component of the editing nuclease is not as specific as intended. With current editing technology, the number of off-target edits is below the baseline mutation rate in many cases (27–33), and the technology continues to improve (34). Beyond this, plant breeders make changes to a population of organisms and select those of interest. If an adverse off-target mutation occurred in an individual, breeders would not select that individual for advancement in the breeding pool. Finally, plants have a high degree of tolerance for mutation. For example, a sequence comparison of two of the most widely used inbred lines in maize revealed that the two lines have nearly 10 million single-nucleotide polymorphisms between them (35). The tolerance of plants to mutation combined with selection during the breeding process has meant that very high rates of mutation induced through chemicals or radiation could be safely used in breeding for decades (36, 37). By comparison, off-target

https://doi.org/10.1073/pnas.2004841118

mutation rates are typically below background levels of mutation, orders of magnitude below that created through radiation and chemical mutagenesis, and therefore fall within an acceptable level of risk.

Confirmation Letters

USDA has included provisions in the SECURE rule for developers to voluntarily request a confirmation that a plant is exempt from the regulation. USDA anticipates that "many developers whose plants fall within an exemption will request confirmation letters because the letters will help them market their plant products domestically and internationally. For developers not seeking confirmation letters, no submission of information to USDA is required. Except in unforeseen circumstances, written responses will be provided within 120 days of receiving a confirmation request containing sufficient detail to determine whether the plant meets one of the exemptions in § 340.1" (15). Guidance for parties requesting confirmation is posted on the USDA website (https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/confirmations/confirmation-process).

New Regulatory Trigger

The old rule regulated any organism that was altered or produced through genetic engineering that was itself a plant pest, or that was engineered using a vector agent that was a plant pest, such as *Agrobacterium*, or that was engineered to contain sequences derived from a plant pest, such as T-DNA borders, the nopaline synthase (nos) terminator, or cauliflower mosaic virus 35S promoter. Although the SECURE rule similarly regulates organisms developed using genetic engineering that are themselves plant pests, other organisms developed using genetic engineering that are not themselves plant pests are regulated only if 1) they pose a plant pest risk or 2) they contain plant pest sequences that are capable of producing an infectious agent that causes plant disease or that encode a compound that is capable of causing plant disease or 3) they are plants that encode a product intended for pharmaceutical or industrial use. For plants modified through genetic engineering that do not meet one of the express regulatory exemptions, the SECURE rule contains a new risk-based feature called Regulatory Status Review (RSR) to evaluate the plant–trait–MOA combination of a plant for plant pest risk to determine whether the plant is subject to regulation. The RSR process is not mandatory. Some developers may elect to forgo this analysis and request a permit and can elect to request an RSR later. If a plant–trait–MOA combination is not covered by an exemption or has not completed the RSR the plant remains subject to the SECURE rule.

RSR

For plants that do not qualify for an exemption, SECURE applies a concept proposed in 2002 by the NRC (16), that "for environmental risk, regulatory oversight should be designed to winnow the potentially riskier transgenic crops from the less risky ones before a substantial regulatory burden is imposed on the less risky ones." Consistent with the CF's position that oversight should be risk-based and scientifically sound, the RSR uses problem formulation and risk assessment to evaluate the characteristics and risk of the plant prior to a formal determination to continue to exercise oversight. The RSR approach is triggered by the fact that genetic engineering is used and in this regard is process-based. However, because this process is designed to evaluate risk prior to a formal determination to continue to exercise oversight, it is consistent with principles of the CF.

In problem formulation, an explicitly stated problem and approach for analysis is defined (38). In the case of the RSR, the problem formulation consists of identifying whether a plausible pathway to increased plant pest risk exists and if so, to address the area(s) of concern. USDA will request additional data only when needed to address the identified problem. When problem formulation is not used, there is a tendency to conduct experiments that often are not warranted by a predicted concern, leading to collection of data not needed for a regulatory decision. Thus, problem formulation is a measure that aims to mitigate data collection in reference "to vague assertions without providing specific predictions about things of concern" (39).

As noted in the preamble to the SECURE rule (15),

> in the first step in RSR, USDA evaluates the characteristics of a plant developed using genetic engineering relative to an appropriate comparator plant to identify whether a plausible pathway to increased plant pest risk exists. If USDA does not identify a plausible pathway to increased plant pest risk in the first step, USDA will find that the plant is unlikely to pose an increased plant pest risk and the plant will not be subject to further regulation, i.e., no permits are required for the importation, interstate movement, or environmental release of the plant. If USDA does identify a plausible pathway to increased plant pest risk, USDA will identify the area(s) of concern to the developer and the developer may: 1) elect to take no further action, 2) obtain a permit to move or release the plant, or 3) request that USDA complete the second step in the RSR process. In the second step, USDA will complete a more detailed evaluation of the identified factors of concern to determine the likelihood and consequence of the plausible increased plant pest risk. If USDA finds the plant developed using genetic engineering is unlikely to pose an increased plant pest risk, the plant will not be subject to further regulation. If USDA does not make such a finding, the plant will remain regulated.

As noted in the preamble to the SECURE rule (15),

> one benefit of the RSR process is that it provides a means to assess the plant pest risks of the plant prior to imposing a substantial regulatory burden. In the first step of the RSR, USDA considers the plant-trait-MOA combination based on the following types of information: 1) biology of the plant, 2) genotype of the modified plant with respect to the modified trait and the differences from the genotype of the comparator plant (e.g., sequence differences in the region(s) targeted for engineering between the modified plant and its comparator), and 3) a description of the new trait and available information on the MOA in the modified plant. The trait information should include a description of the intended and any observed phenotype(s) of the plant. By having an understanding of the plant's biology, any existing impacts of the plant, the genetic trait to be inserted into the plant, and the MOA, USDA is able to conduct a review based upon a large body of scientific publications, as well as USDA's knowledge and experience.

By incorporating problem formulation into the RSR process, information from field tests would be unnecessary for completing the first step of the RSR. Accordingly, field test information is generally not an applicable requirement for the first step. A developer may submit, or USDA may request, field test information, as needed, when the second step of the RSR is required. "This approach would not preclude developers from providing information from field tests that they consider pertinent to our analysis at any time during the process. For example, if a developer requested a re-review of a plant developed using genetic engineering that USDA had previously considered to be subject to regulation, field test information demonstrating a lack of plant pest risk could be provided in support of that request (15)." USDA expects that the RSR process will be an effective means to winnow the potentially riskier plants developed using genetic engineering from the less risky ones without imposing substantial regulatory burdens on the less risky ones, as proposed by (16).

Will the SECURE Rule Promote Innovation?

The exemptions of the SECURE rule went into effect on 17 August 2020. The RSR process will begin for corn, soybean, cotton, potato, tomato, and alfalfa on 5 April 2021 and all crops on 1 October 2021. Although it is still too early to know the extent to which SECURE will spur innovation, it seems likely to do so based on a comparison of statistics under the previous part 340 regulations. Under

Table 1. Comparison of AIR and petition process with respect to organizational use, number of organizations, and number of crops

	AIR		Petition	
	Total no. of submissions	% of Total	Total no. of submissions	% of Total
Government	3	1.7	1	0.6
Academic	48	27.7	5	3.0
Small biotechnology companies	110	63.6	38	22.9
Major plant biotechnology companies	12	6.9	122	73.5
	173	100.0	166	100.0
Total nonregulated status	168		128	
No. of organizations	73		19	
No. of crops	54		10	

Total number of submissions includes pending, completed, and withdrawn applications as of 4 August 2020. APHIS stopped accepting AIR inquiries on 17 June 2020. For petitions, the time span begins in 1992. For AIR, 2010. Major plant biotechnology companies include any of the following: AgrEvo, Aventis, BASF, Bayer, Ciba Geigy, Corteva, Dekalb, Dow, Dupont, Mycogen, Monsanto, Novartis, Pioneer, Syngenta, and Zeneca. Small biotechnology company includes any private business other than those listed as a major plant biotechnology company. This list includes some large companies, such as Altria, where biotechnology represents a small component of their business. Total nonregulated status decisions since 1992 (petitions) or 2010 (AIR). Number or organizations submitting petitions or AIR inquiries since 1 January 2011. Number of types of crops in petition and AIR submissions since 1 January 2011.

the legacy approach, USDA maintained an "Am I Regulated?" process (AIR process), which provided a voluntary mechanism for developers to obtain USDA's opinion about whether a plant or organism met the legacy definition of a "regulated article" and thus was subject to regulation. Under the previous regulations, USDA maintained a petition process by which a developer could submit data and information to demonstrate a plant developed using genetic engineering was not a plant pest and should not be regulated. To evaluate the types of users of the two processes, they were grouped into four categories: 1) government, 2) academic, 3) major biotechnology companies (AgrEvo, Aventis, BASF, Bayer, Ciba Geigy, Corteva, Dekalb, Dow, Dupont, Mycogen, Monsanto, Novartis, Pioneer, Syngenta, and Zeneca), and 4) small biotech companies which also includes large companies where biotechnology is not a major focus.

The distribution of these four types of users for the petition process and the AIR process (Table 1) shows just under 75% of the submissions to the petition process were from the major biotechnology companies, whereas just under 7% of the submissions to the AIR process were from this group. In contrast, small biotechnology companies represented 23% of the petition submissions but over 63% of the AIR submissions. The contrast was even greater for academic developers. They submitted just 3% of the petitions but nearly 28% of the AIR inquiries. Since 2011, there have been 19 distinct entities that submitted petitions and 73 distinct entities that submitted an AIR inquiry, nearly a fourfold difference in the number of users in favor of the AIR process. Likewise, for the number of different organisms, the difference was greater than fivefold in favor of the AIR process; 54 different plants were considered through AIR inquiries since 2011, compared to 10 different plants that were submitted through the petition process over the same time period.

Based on this, it is reasonable to expect that the regulatory burden easing aspects of the SECURE rule will also contribute to innovation by increasing the number and diversity of developers using plant biotechnology and the number of crops and traits under development. Whelan et al. (40) recently analyzed the effect of Argentina's decision not to consider some genome-edited organisms to be genetically modified organisms. They observed an increase in the diversity of developers coming mostly from small and medium enterprises and public institutions, an increase in the types of traits and organisms developed, and a decrease in the time it takes products to enter the market from the bench. Thus, it may be reasonable to expect even a further increase in innovation from the exemptions compared to the AIR process.

Conclusions

USDA has substantially revised its biotechnology regulations to further harmonize regulatory oversight with concepts originally stated in the 1992 CF Update. In so doing, USDA has made the regulations more risk-proportionate, science-based, product-based, and streamlined. Exemptions have been created to make the regulation of plants developed using genetic engineering more comparable to that of plants developed using conventional breeding, and to recognize the plant–trait–MOA combinations that USDA previously evaluated and found not regulated. The regulations contain an RSR process that can be initiated prior to permitting requirements and collection of field data. It is reasonable to expect that these changes will stimulate innovation through a reduction in regulatory costs and regulatory barriers that will ultimately result in a broader array of private and public developers using biotechnology.

Data Availability. There are no data underlying this work.

ACKNOWLEDGMENTS. I acknowledge others on the Animal and Plant Health Inspection Service team who contributed to writing The SECURE rule: Sid Abel, Edward Belfar, Gwen Burnette, Michael Firko, Mary Fleming, Doug Grant, Michael Gregoire, Ron Hardman, Subray Hegde, Andrea Huberty, Chessa Huff, Ed Jhee, Bernadette Juarez, Donna Lalli, Ben Karzmanski, Kayla Knilans, Sally McCammon, Michael Olson, Alan Pearson, Joanne Serrels, Ibrahim Shaqir, Rebecca Stankiewicz Gabel, and John Turner. Special thanks to Fan Li Chou at USDA and interagency reviewers, in particular Courtney Higgins at the Office of Management and Budget, for valuable feedback on the rule. I thank Bernadette Juarez, Alan Pearson, Subray Hegde, Mary Fleming, and Sally McCammon for critically reviewing the manuscript. The findings and conclusions in this publication are those of the author and should not be construed to represent any official USDA or US Government determination or policy.

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