Viewpoint: Here's why the EPA needs to relax regulations that make it harder for farmers to access pest-resistant biotech crops

Plant pests and disease have a massive global impact, causing the loss of 20–40% of crop production and costing over USD 220 billion. These losses can threaten food security, contribute to climate change, and create financial burdens on farmers.

For example, citrus greening disease, first detected in Florida orchards in 2005, caused over $1 billion in annual losses by 2008. The disease has now spread to most citrus-producing states in the US, where it kills trees within 3 to 5 years and still has no effective cure. Recently, several potential genetic solutions for citrus greening disease have emerged, but new regulations could make it harder for them to reach the market.

Citrus greening disease, and the regulatory hurdles facing the industry in curbing it, is a microcosm of similar issues throughout US agriculture.

The use of CRISPR — a relatively new tool that can make small, precise changes to an organism's DNA — allows scientists and plant breeders to respond quickly to constantly evolving agricultural pests by creating a wider variety of disease resistant crops. The problem is that EPA regulation of CRISPR-edited crops may be too burdensome for most to reach the market, depriving farmers of important tools to protect their crops' health.

In 2023, the US Environmental Protection Agency (EPA) passed controversial new regulations making it harder for farmers to get new crops that resist disease and help safeguard agricultural production. The new rule changes regulation of disease- and pest-resistant crops that EPA calls plant-incorporated protectants (PIPs). EPA regulates PIPs including crops with biotech traits that do things like create a toxin that kills pests, or strengthen the plant's immune system for fighting disease; however EPA does not regulate any PIPs with traits created using only conventional breeding.

EPA overregulation of PIPs decreases innovation of new pest- and disease- resistance and plant regulator traits, and hurts the ability of US agriculture to continue growing crop yields. Without these innovations, farmers are left with fewer tools to prevent production loss, especially those growing specialty crops like fruits, vegetables, and nuts that are already more difficult to innovate. Improvements in crop genetics have contributed roughly half of historical yield gains, and biotechnology is an increasingly important tool. Continuing to increase crop yield growth can help decrease food prices, limit greenhouse gas emissions from food waste, and reduce deforestation.

Regulatory overreach

Historically, EPA has applied PIP oversight to a narrow range of traits, but the new rule has a dramatically wider scope. EPA has registered over 100 PIPs so far, with the majority being genetically modified insect-resistant Bt crops — mostly corn, cotton, and soy. Bt crops have been cultivated in the US for decades and have improved pest control, increasing crop yields and reducing pesticide use. Outside of Bt crops, EPA has registered PIPs including RNAi for rootworm control in maize; viral coat proteins for disease resistance in papaya and plum; defensin proteins to fight the bacteria that cause citrus greening disease; and a gene for resistance to the fungal-like pathogen that causes potato late blight.

In addition to pest- and disease-resistance traits, EPA's new rule could also make it harder for plant regulators to reach the market. Plant regulators can encompass a broad range of crops with changes in traits like plant height or flowering time, which are not primarily pest- or disease-resistance traits and require different regulation.

Such a wide-ranging regulatory scope runs counter to previous EPA regulatory practices for PIPs. In 2001, when EPA exempted conventionally-bred PIPs, the agency effectively stopped regulating most disease resistance and plant regulator PIPs without genes from other species because they were all made using conventional breeding. The new rule, however, provides no exemptions for disease resistance or plant regulator traits if they are made using gene editing, meaning EPA could apply full regulatory oversight. This amounts to a large category of products that are often very unlikely to have negative effects on non-target organisms. For example, many plant regulator traits are crucial for increasing crop yields. Pushback on the new rule from industry includes the concern that traits such as short stature in wheat plants could be regulated by EPA as a PIP if they were created using gene editing, even though the same trait created using conventional breeding would be exempt.

The two new categories of exemptions in the rule aim to capture PIPs that EPA considers low risk, particularly those that could have been created using conventional breeding. However, these categories — "loss-of-function PIPs" and "PIPs created through genetic engineering from a sexually compatible plant" — neglect to include many low-risk disease resistance traits that should not be subject to EPA PIP oversight. To make matters worse, USDA also determines exemptions by what could have been achieved using conventional breeding, but the two agencies use different definitions.

In addition, the submission requirements for some PIPs that the agency deems low risk are far too extensive. In order to get EPA confirmation of exemption for "PIPs created through genetic engineering from a sexually compatible plant," the applicant must submit information on the biology of the plant, pesticidal trait, molecular characterization, and history of safe use. EPA reviews the application, and notifies the applicant of the product's regulatory status within 90 days of submission. The component of molecular characterization requiring nucleic acid sequence comparison in particular could be more difficult for PIPs in specialty crops where genomes are less thoroughly sequenced.

In comparison, the submission requirements for other PIPs that the agency deems low risk are more limited. Requirements for self-determination of exemption for these "loss-of-function PIPs" are relatively

simple, and could be worthwhile for transparency purposes. In order to get a self-determined exemption for “loss-of-function PIPs,” the applicant must submit information including name and contact information, identity of the recipient plant, unique identifier for the native gene from NCBI, and trait type; this information will be added to a public database of PIPs submitted to EPA. The time involved in receiving this exemption is also minimal because the electronic portal automatically responds to the applicant confirming receipt, after which the exemption is valid.

Minimal submission requirements could support transparency for stakeholders while keeping the burden of regulation low. Transparency is important to build stakeholder trust and to ease trade between countries with different regulations. Even for gene edited crops with genetic changes that “could have been made using conventional breeding,” definitions and regulations still vary across countries. Minimal submission requirements focused on plant, trait, and mechanism of action — such that re-submission is not required for slightly different genetic changes with the same result — makes agency notification of exempt products more appropriate.

There are few estimates of the cost of regulatory compliance under the new rule, but many stakeholders are concerned. The rule itself estimates a reduction in registration costs for newly exempt products from $472–886k per product, but does not cite typical registration costs for non-exempt products for comparison. A fact sheet from the American Seed Trade Association cites a biotech-specific regulatory cost of up to $3 million and 3 years per non-exempt edit, but does not cite the comparative reduction in costs for newly exempt edits. The same source cites the cost and time under the Canadian regulatory system as $0. Agricultural industry groups and researchers have raised concerns that EPA regulation of gene edited PIPs will be too expensive and time consuming, and thereby decrease innovation from small developers (like university labs and start-ups) and in specialty crops (which comprises most fruits, vegetables, nuts, and more).

A coalition of organizations — including US agricultural associations for both row and specialty crops, and industry and research associations — wrote a letter to the US House and Senate Committees on Agriculture Leadership opposing higher regulatory burdens for gene edited crops than their conventionally-bred equivalents, and requesting that Congress direct EPA to withdraw the rule. In addition, academics and plant breeders commented on the draft rule with concerns about the narrowness of exemption categories. These efforts to withdraw the rule will likely continue into 2024 as Congress continues to negotiate a spending package and a bipartisan farm bill.

How to make EPA PIP regulations more effective

The new EPA PIP rule should be changed in four ways to make regulation more proportional to risk, adaptable to future technologies, supportive of innovation — especially by small developers and in specialty crops — and a more efficient use of resources.

First, the USDA and EPA rules for biotech crop regulation ought to use the same definition of conventional breeding. Both agencies base exemptions on the type of genetic change and whether it could have been made using conventional breeding, but use different definitions. In the new PIP rule, EPA defines very narrow PIP exemptions by loss of function or added genetic material from a sexually compatible plant. In

comparison, USDA's 2020 SECURE rule has one similar exemption category — addition or recreation of a gene present in the plant's gene pool — but also two additional categories that together are more inclusive than EPA's loss of function exemptions. Considering USDA has had years of experience with these definitions of conventional breeding, EPA should follow USDA's lead and change their definitions of conventional breeding in PIP regulation to match.

Second, EPA should narrow the scope of plant regulators and disease resistance traits that are subject to PIP regulation. The new rule did nothing to change the definition of plant regulator PIPs, which has been overly capacious since it was written. The definition of plant regulator includes a physiological mode of action and the intention to change the rate of growth or maturation "or otherwise altering the behavior of plants or the produce thereof". This could include changes in traits like plant height or flowering time, which would not reasonably be considered protectants or fit within the scope of EPA's authority to regulate pesticides.

In 1994, EPA proposed, but never finalized, a rule exempting many types of plant regulator and disease resistance traits, such as those that inhibit pests from attaching to the plant's leaves. This would have focused oversight on PIPs that have a generalized toxic mechanism of action, which are the most likely to have undesired effects on non-target organisms. EPA must revive that proposed rule today.

Third, EPA ought to reduce the number of levels of exemptions in the rule. Currently there are four levels of exemption (one of which is full exemption) that all have different requirements, adding confusion to the process. If a category of traits is considered low risk, then it should be exempt; if not, it should be subject to full oversight.

In order to incorporate flexibility and consider different levels of risk within non-exempt products, EPA could have a two-tiered system of review similar to USDA's: a first tier to assess any possible pathways for risk, and a second to assess the likelihood and degree of risk. Narrowing EPA regulation to just PIPs that have a generalized toxic mechanism of action would prioritize oversight of products with the most potential for risk.

It's important to note that premarket regulations are not the only regulations that apply to PIPs, though they do inhibit innovation the most. Other post-market regulations protect farm workers, the environment, livestock, and consumers from negative impacts of pesticides, including a requirement to report any negative effects of a product to EPA — whether a conventional chemical pesticides or PIP — for the entire time the product is on the market.

Fourth, EPA should create a way to continue adapting PIP regulations in the future. The rule should leave room for both the agency itself and stakeholders to propose a broader scope of new exemptions that could be added to the rule. Currently, the final rule says that any new categories of exempt PIPs added "would be required to fall within the previously defined scope of exempt PIPs, i.e., those that can be created through conventional breeding". This means that new exemptions could not be for categories of PIPs like those with non-toxic modes of action, which are not defined by whether the genetic change could be created using conventional breeding. Continuing to compare new genetic changes to what could be achieved through conventional breeding unnecessarily limits innovation and is a poor proxy for risk

potential.

Ultimately, EPA regulation of PIPs — like all regulation of biotech crops at EPA, FDA, and USDA — should be based on the traits of the product and the risks they pose, rather than the method of genetic engineering. A wide variety of authorities acknowledge that the processes of gene editing and genetic modification do not introduce any new or unique risks compared to conventional breeding.

In EPA's case, risk-based regulation could be accomplished by limiting PIP oversight to those that have a generalized toxic mechanism of action. This change would capture some but not all genetically modified traits, and potentially a small number of conventionally bred and gene edited traits. In addition, it would be a more effective way to focus regulatory attention on PIPs that have greater risk potential.

In contrast, the current rule's exemptions capture a much smaller number of PIPs and maintain unnecessary regulation over many that EPA itself acknowledged in proposed 1994 regulation have very low risk potential.

The downsides of overregulation here are substantial: leaving farmers with less tools to fight pests and diseases and increase yields, thereby increasing food waste, greenhouse gas emissions, and deforestation.

Emma Kovak is a senior Food and Agriculture Analyst at Breakthrough. Find Emma on X @EmmaKovak

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