Summary

Despite the stated goals to lighten the regulatory burden on small businesses and encourage innovation these proposals do the opposite: they represent a significant expansion in APHIS regulatory authority that will make life more difficult for small companies and impede innovation. If implement as proposed these regulations would result in the closure of my business, the loss of my employees jobs and loss of investment made by 528 members of the general public.

The primary issue with the proposed regulations is the 'catch-all' clause § 340.0 (b) (3) which regulates where:

"The GE organism is a plant that has a plant and trait combination that has not been evaluated by APHIS for plant pest and noxious weed risk in accordance with § 340.4"

This clause is problematic for the following reasons:

1. It introduces process based regulation in violation of the 'product not process' principle of the Coordinated Framework and the recommendations of the National Academy of Sciences
2. This is a significant expansion of APHIS regulatory authority which is not justified by verifiable scientific risks, also in conflict with the principles of the coordinated framework. AHPIS own findings suggest GE plants pose no greater risk than conventionally bred plants
3. It inhibits innovation and disproportionally places the regulatory burden on small companies and academic researchers
4. The full negative impact of this clause has not been properly considered in the economic analysis of the rule
5. The breadth of the clause means many non-agricultural products will become regulated by APHIS which may be unintentional
6. No consideration has been made for grandfathering products which are currently legal to sell and distribute but which will become regulated under the new rules
7. The proposed weed risk assessment methodology is biased towards agricultural crops and is inadequate for the full range of plants which will be regulated by these proposals
8. Excessive regulation which is not aligned with actual risks could hurt USA competitiveness in the field of plant genetic engineering
9. The definition of Genetic Engineering proposed by AHPIS is not aligned with similar definitions being proposed by the FDA

Fortunately the fix should be relatively simple. In the attached pdf document I go into more detail on the background of my company and explain more of the rationale behind the issues listed above. I close my comments by proposing an alternative clause which would address the issues I've identified.

Background on TAXA Biotechnologies

TAXA is a San Francisco based Biotechnology company. We apply genetic engineering technologies to develop new plants for sale direct to consumers. Our guiding principle is the idea that photosynthesis

can provide cleaner, eco-friendly and more sustainable products than alternative chemical manufacturing processes.

We were the first company to use Kickstarter to fund synthetic biology (raising $484k in 2013[i]), the first biotech investment made by the prestigious accelerator Y Combinator[ii] and in the first batch of companies to raise equity investment from the general public under the new title III rules which were implemented in 2016[iii].

Our next product line is Orbella Fragrant Moss. Orbella is a moss which has been genetically engineered to make fragrance using photosynthesis. Unlike flowers it won't senesce and die and unlike traditional fragrance products there are no solvents, phalates or other toxic petroleum products emitted into the air.

Orbella will start shipping in July this year. Initially we have three scents patchouli (earthy), linalool (floral), and geraniol (rose) and we are working to develop several others including lemon and pine. The product is grown by consumers in their home in a glass terrarium and looks like this:

Orbella is currently unregulated by APHIS but if the new rules are implemented as is each flavor will become a regulated organism, which I estimate will change our cost to develop a new flavor from $20,000 to at least $2-4MM. This obviously severely impacts the business case for investing in product development.

I am the CEO of the company and I currently employee three scientists. All of us will lose our livelihoods if the new regulations are implemented as proposed due to the lack of business case for our work with

the increased cost per flavor. **528 members of the general public who invested in my company will also lose their investment.**

Criticism of proposed regulations

Problems with clause § 340.0 (b) (3)

The central problem with the proposed regulations is the 'catch-all' clause § 340.0 (b) (3):

"The GE organism is a plant that has a plant and trait combination that has not been evaluated by APHIS for plant pest and noxious weed risk in accordance with § 340.4"

This catch-all clause is problematic for a number of reasons. First **it introduces process based regulation** as the trigger for regulation is the process of genetic engineering, not the risks inherent in the final product. This stands in opposition to the 'product not process' principle of the Coordinated Framework on Biotechnology, a principle that was upheld by the recent White House review of the Coordinated Framework and which is aligned with the findings of the Council of the National Academy of Sciences[iv]. Indeed the National Academy report issued in May 2016 states: "A tiered process for regulating new crop varieties should focus on a plant's characteristics rather than the process by which it was developed". This clause is clearly process orientated, rather than characteristic focused.

Second, APHIS own findings do not support the identification of risks which would require such broad regulatory coverage. Another principle of the coordinated framework states that only regulation grounded in verifiable scientific risks should be tolerated and APHIS has not identified risks that justify such broad regulatory coverage. Indeed APHIS own submissions in the federal register illustrate that such broad coverage is not warranted: I quote "**GE Plants as a class pose no greater plant pest or noxious weed risk than their counterparts developed through traditional breeding techniques or chemical or radiation-based mutagenesis**." If the plants, as a class, pose no greater risk than unregulated risks then it is not reasonable to regulate them as a class. All of the arguments APHIS is making in the Federal Register to justify excluding genome editing technologies from the definition of a regulated GE plant apply to GE plants as a class: in general there is no difference in risk between conventionally bred plants and GE plants so there should be no difference in regulation at the class level.

APHIS also has a long history in regulating noxious weeds, and as its own comments suggest, APHIS knows that weediness is created by traits such as seed shattering, thorns or seed dormancy. These traits are not simple traits that can be created by inserting a few genes into a plant and introducing such complex phenotypes goes well beyond what's possible with today's technology. **Determining that all GE plants pose noxious weed risk worth regulating is not based in verifiable scientific fasts.**

Third, this clause **inhibits innovation and disproportionally places the regulatory burden on small, innovative companies and academic researchers** who might like to setup such companies. APHIS states that supporting these groups is a goal of the proposed changes. This clause will not help small companies or academic researchers as by their nature these are the groups working on new traits or new plant species as the large companies have locked up all the IP related to typical agricultural plants

and established traits. As a result **this clause regulates all startups working on GE plants even as it reduces the regulatory burden for larger companies**.

I was only able to raise private capital for my company because we had established that there was no APHIS de-regulation process for the products we are developing – these would now be regulated by this clause and I can tell you directly that **it would have been impossible to have raised private capital if this clause was in effect.** Modern investor capital does not support expensive multi-million dollar multi-year de-regulation processes when the alternative is investing in high traction internet businesses. This clause eliminates any toeholds startups can use to establish themselves as a viable company and will therefore be a major drag on innovation using these technologies as small companies are the engine of growth[v].

APHIS states in the Regulatory Impact Analysis that "*A quicker USDA evaluation process and related reduction to firms' regulatory uncertainty may facilitate small companies' ability to raise venture capital*". While it is true that quicker, cheaper and more certain regulatory processes would help startups raise venture capital the new regulations instead add regulatory burden to startups for the reasons discussed in the previous paragraphs: startups are the ones working on new traits and plants. The exception to this is genome editing technologies, however APHIS has already established through the 'Am I regulated' process that Genome editing is not currently regulated so the new regulations do not provide additional certainty there either.

Regulation is costly, particularly to small businesses with limited capital and resources. Costs of regulation include the cost of compliance with record keeping, the cost of preparing regulatory filings, the opportunity cost caused by waiting for a regulatory decision and the cost of complying with other regulations which kick in upon a determination of regulated status such as NEPA. AHPIS estimates[vi] these costs are at least $2.3MM per GE plant. To put that into perspective it currently costs my company $20,000 to develop a new flavor of our fragrant moss. It's clear that, if regulated, regulatory costs drive all business decisions. It should be equally clear why my company would have to close if this clause is implemented as a business plan developed around $20k per flavor cannot support a 5000% increase in costs.

Fourth, the negative impact of this clause has not been considered properly in the economic analysis of the rule. **The economic analysis only models the reduction in cost saved by regulating fewer GE plants with traditional traits, it does not model the cost caused by expanding regulatory authority as proposed**. APHIS knows from the 'Am I regulated' process that there are quite a number of products being developed or in the market that will be impacted by this clause, I am aware of at least five companies who will be directly impact by this rule as I am. To correctly assess the impact of this clause APHIS should consider the cost of regulating these products which would otherwise have no regulatory compliance cost as well as the future economic harm caused by future startups not even starting due to these new compliance costs. To provide APHIS with some numbers to estimate this economic harm I would estimate that this rule will cost my company between $1.4MM (capital invested in the business to date) and $510MM (anticipated annual revenues if we capture 10% of the home fragrance market). It is hard to estimate the total number of future companies that would be similarly affected but because of

advances in DNA sequencing, synthesis and the falling cost of lab automation it can be expected to be a significant number. If we assume that each of the companies I know will be affected employees five scientists, each on a salary of $70,000, then **this clause means a loss of $17.5MM in salaries per year.**

As already discussed such a broad, catch-all clause is not required to protect against plant pest and noxious weed risks. The marginal benefit of the broad clause over a better clause focused on specific risks is therefore minimal.

Fifth, the catch-all nature of the clause means that products may be unintentionally pulled into AHPIS regulatory remit that APHIS may not intend or desire to regulate. APHIS depth of experience with GE plants relates primarily to agricultural products, particularly the big export crops. **It is not clear that APHIS intentionally wants to regulate mosses like those my company is developing** which are intended for sale direct to consumers to be grown indoors.

Sixth, there is an issue about grandfathering in the new regulations due to GE plants currently on the market that will be affected by the new regulations. My company has so far developed three flavors of our fragrant moss, Geraniol, Linalool and Patcholi. We are in manufacturing with these mosses and shipment is due to begin in July this year. We also have many more flavors in development and plan to roll out a new one every three months. These mosses are not plant pests and are therefore not currently regulated and we anticipate shipping them to 10,000 customers before the end of the year. They will therefore be widely distributed across the United States. **What will be the status of these mosses once the new rules come into place? Will we still be able to sell the moss? Will our customers, who are average American consumers, become regulated entities because they bought our moss or will there be a grandfathering of existing GE plants?** APHIS knows from the Am I regulated process that other companies will also be affected like this.

Seventh, **the Weed Assessment process** which APHIS has put forward for consideration is inadequate to consider the full range of types of plants which could be regulated by the new rule. **It is heavily biased towards agricultural crops** whereas as I have discussed all kinds of other GE ornamental plants will now become regulated. For example our GE moss neither propagates through seeds not vegetative cloning and thus doesn't fit the 'reproductive potential' section.

Eight, **excessive regulatory burden could threaten American dominance in plant engineering technologies**. One only must look to see what's happening with the debate on genetic engineering humans to see how willing China is to push forward with this technology. One media outlet recently stated "Precision gene editing is still nascent and mostly done on plants, but the technology is moving fast. U.S. scientists are falling behind their counterparts in China, which has fewer ethical quibbles about the research, increasing the pressure to come to a consensus about the best way to proceed."[vii]

Ninth, **the definition of genetic engineering being proposed by APHIS is not aligned with the definition which was also proposed on the last day of the Obama administration by the FDA**. The FDA defines these terms as alterations introduced into the DNA of an organism using modern molecular technologies, such as genetic engineering (also referred to as recombinant DNA technology) and genome editing. Such a divergence in definitions risks further confusing an already confused general

public, inhibits harmonization across the agencies and also illustrates the arbitrary exclusions APHIS is making to its definition in order to try to force a demarcation between genetic engineering from traditional breeding.

A more tightly restricted clause, as I propose below, would still retain all of the benefits of risk management of this clause but be much less restrictive on areas which are not risky.

Alternative clause

Just because some GE plants could (theoretically) pose a noxious weed or plant pest risk does not mean that most or indeed many will pose such risks. Given the high cost of regulation to businesses and innovation in the industry APHIS should regulate only the types of GE plants which may actually pose a plant pest or noxious weed risk and where the benefits of such regulation outweigh the costs created.

APHIS is seeking to create a more focused, risk based regulation of GE plants. As discussed above clause §340.0 (b) (3) is neither focused or risk based but it could easily be. **The fix to these proposals involves regulating only those products of Genetic Engineering which will reasonably present a risk to public health or the environment**. Congress has given AHPIS authority to regulate specifically plant pest and noxious weed risks, so the regulations should only focus on those risks. AHPIS should not introduce process based regulation with a regulatory trigger driven solely by the fact the plant has been genetically engineered.

In proposing this I am guided by the National Academy of Sciences who state that regulation should be based on the novel characteristics, not the process of genetic engineering:

"*In determining whether a new plant variety should be subject to safety testing, regulators should focus on the extent to which the novel characteristics of the plant variety (both intended and unintended) are likely to pose a risk to human health or the environment, the extent of uncertainty about the severity of potential harm, and the potential for human exposure – regardless of whether the plant was developed using genetic-engineering or conventional-breeding processes."*

Plant Pest Risks

With plant pest risks APHIS correctly identifies that regulatory elements, such as 35S or NOS, do not pose a risk but that the risk comes from encoding infectious material or encoding genes that create pathogenic compounds. These risks are well captured by § 340.0 (b) (2).

Noxious Weed Risks

Instead of § 340.0 (b) (3) APHIS should develop a more refined clause to protect against noxious weed risks. As AHPIS mentions most farmers have tried to breed traits associated with noxious weeds out of their crops. While conceivably someone could attempt to create a noxious weed from a plant, it is unclear why someone would do that except for a malicious intent, and a malicious actor will go ahead independent of the regulations. Assessing all GE plants for noxious weed risk is therefore excessive regulation.

A more refined clause would look like the following:

- *"The GE organism is a plant that is listed as a noxious weed according to list maintained on AHPIS website"*
- "*The GE organism is a plant that is listed as a weed according to a list maintained on APHIS website and which has been engineered with a trait that provides a known mechanism for increased noxiousness. These mechanisms would include only traits which:*
    - *Increase competitive growth ability (eg enhanced nitrogen fixation, photosynthesis or pest resistance)*
    - *Increase reproductive ability (eg increased viable seed production)*
    - *Increase spread or persistence of plant (eg increased dormancy)*
    - *Increase stress tolerance (eg drought, salt tolerance)*
    - *Increase agricultural impact*
    - *Increase impact on beneficial organisms*
    - *Increase other abiotic impact (eg hydrology, fire risk, soil quality etc)"*
- *"The GE organism is a plant which has been engineered with a gene drive or other genetic mechanism that promotes the inheritance of a particular gene to increase its prevalence in a population"*

These definitions are sufficient to protect against noxious weed risks because current and foreseeable genetic engineering techniques are not capable of turning a plant which is not a weed into a noxious weed. For a GE plant to become a noxious weed it requires the plant to already have weediness characteristics and to be engineered with a trait which increases that: critically the baseline plant matters and the regulations should reflect that.

Thus I would propose determining regulatory risk based on the following matrix:

	Trait has no impact on weediness	Trait increases weediness	Gene Drive
Noxious Weed	Regulate	Regulate	Regulate
Weed	Don't regulate	Regulate	Regulate
Non-weed	Don't regulate	Don't regulate	Regulate

AHPIS surely has enough experience to determine the taxa of plants which could reasonably present a noxious weed risk if engineered with certain traits. Perhaps APHIS could go even deeper to determine the type of traits which would increase weediness of specific weeds. Such a focused regulation would align the regulation with the actual risks of the plants, rather than regulating the process of genetic engineering per-se. This process would also allow APHIS to update the regulations based on new understand or scientific developments, as recommended by the White House review of the Coordinated

Framework. This focused regulation would also free up innovation to take place in areas which present a very low risk, such as ornamental plants for consumers.

Conclusion

Crucially APHIS should not regulate all products just because they are genetically engineered. Having APHIS review product ideas is fine, so long as the review is completed within 90 days, **it is the designation of an organism as being regulated that causes problems**. For small companies even lighter regulation which doesn't require field trials imposes significant costs and hurts innovation due to NEPA requirements, the length of time it takes APHIS to take decisions and compliance costs. APHIS should only regulate GE plants for noxious weed risk where there is a justifiable scientific risk.

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[i] https://www.kickstarter.com/projects/antonyevans/glowing-plants-natural-lighting-with-no-electricit/description
[ii] https://techcrunch.com/2014/08/11/glowing-plant-is-one-of-y-combinators-very-first-biotech-startups/
[iii] https://wefunder.com/taxa
[iv] https://www.nap.edu/catalog/23395/genetically-engineered-crops-experiences-and-prospects
[v] https://steveblank.com/2016/06/23/intel-disrupted-why-large-companies-find-it-difficult-to-innovate-and-what-they-can-do-about-it/
[vi] APHIS-2015-0057-0002.pdf
[vii] https://theoutline.com/post/1093/there-are-people-who-want-to-make-gene-editing-a-human-right