Debrief: Genome-Edited Microbial Workshop, June 5-7:

PSI, Raleigh, NC

Debrief Presentation

June 21, 2023

Phyta BioTech Consulting LLC

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Agenda

- Outcome
- Overview
- Keys in the room
- Focus questions
  - Refined questions
  - Summary of committees
  - Summary of each question (links to flip charts included)
- Discussion transcript
- Recommendations and next steps

Outcome of Genome-Edited Microbial Workshop:

In this workshop, academics, regulators, industry, and NGO partners will work together to

- Learn what are the main concerns from a regulatory agency perspective and discuss how best to facilitate and educate around the permitting process
- Discuss what research is still needed to address gaps/concerns in the literature
- Help to create a more efficient and transparent regulatory framework

Specifically, an aligned "straw person" model which outlines the scope of fundamental research that will generate useful data and insights to help address key uncertainties and concerns surrounding the intentional release of genome edited microbes in the field.

Overview: Pathway for hands-on portion of workshop

5

Note:

- Randomized tables via name tags for day 1.
- Self-chosen tables for day 2

Who is in the room? (KEyS)	Knowledge, Expertise, Skills-Introduction to each other	Day 1
Gap Analysis of current focus areas	Current and Future state: what is the gap?	
	Gap will be phrased as a research proposal	
Gaps and new groups	All teams share gap analysis	
	Which KEyS are needed?	
	Rearrange based on your KEyS	
Steps and timelines	Develop steps to address gap and place on a timeline	Day 2
Challenge group sessions (x2)	A <> B A <> F	
	C <> D B<> D	
	E <> F C<>E	
Report out, align and commit	Commit to following up on projects	

KEyS in the room

Regulatory sciencex4
Biosafety
Plant pathologyx2
Fermentation productsx2
MBAx2
Microbiologyx2
Product safety
Permitting needs
Ag-regulations
Genetics
BioTech
Livestock emphasis

Microbial ecology
Invasive species
Bioinformatics
Social science/history
Stakeholder engagement
Chemistry
Communications
USDA regulatory
Startup company challengesx2
Law/legal
Plant Biology
Plant microbes

Regulatory x6
Health e-commerce
Plant pathology
Shot gun genomics
Fabulous
Microbiology
Regulatory analyst
Global regulatory
Do-er-action oriented
Crop science
Agronomist
Weed evolution
Ecotoxicology

Plant biotech seeds x2
Microbe engineering
Entomology
Microbial
Teacher
Regulatory policy
Consumers x2
Mother
Genome sequencing
Translational context of technologiesx2
R&Dx2
CRISPR expert
commercialization

We considered 6 focus areas…

1. Is the new microbe a plant pest?

2. Does the new microbe have biocontrol properties?

3. What diagnostic tools are best suited to measure the presence of modified microbes in soil after the termination of field experiments?

4. How far do microbes disseminate in a field trial?

5. How long do microbes persist in soil or spread through spores beyond regulated field trials?

6. How best to facilitate and educate stakeholders around the permitting process?

1. Understand the different factors, criteria impacts that USDA considers when they **define a plant pest (decision tree)**

2. Can we have a clear **coordinated definition of biocontrol?** Can we have a standard threshold to determine "biocontrol"? Can we set up an AHPHIS-like plants-for planting model for biocontrol (independent research council as is done for plants)?

3. Is there a **method to devitalize tested microbe** that does not compromise the soil environment? Is it risk-based or hypothesis based that the tested microbe should not persist—what is reasonable and practical LOD?

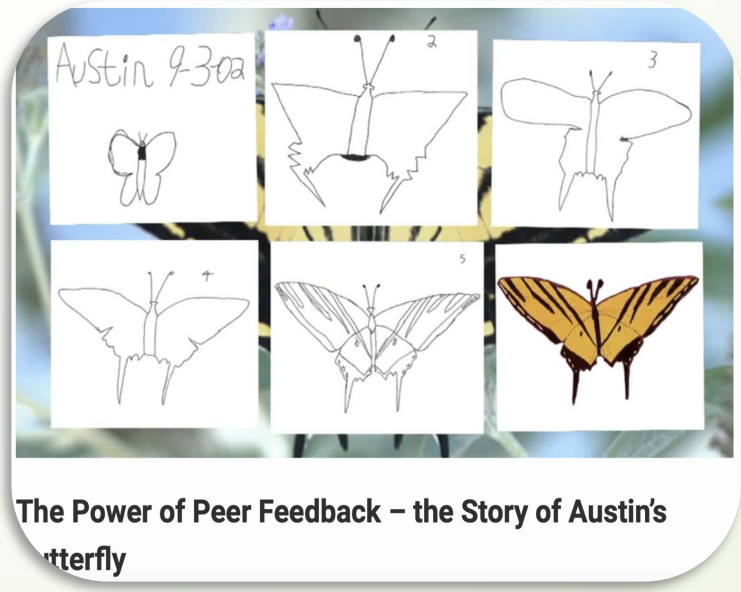
4. What could a **risk-based approach to persistence** look like and what are the most important considerations?

5. **Conduct** a **study** that generates information **on persistence** and spread that's cognizant of IP and generally applicable. Include surrogacy, field work and greenhouse work

6. What **knowledge gaps** do **stakeholders** have around the permitting process? What is the right private-public partnerships fill these education gap to prevent silos?

….and refined the focus areas to 6 questions

New teams formed, made plans, and plans went through two challenge group rounds



- 1 <> 4
- 3 <> 2
- 5 <> 6
- _____
- 1 <> 2
- 4<> 5
- 3<>6

- After first round, teams 1, 2 and 4, 5, felt that their questions were related
- Therefore, the following summaries will be ordered 1,2,4,5,3,6

Projects and Committees with Contact information

1. Define a plant pest

- **Leah Buchman (lead)**
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- **Shade Sabitu**
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- **Rodolphe Barrangou**
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- **Sharon Berberich**
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- **Mike Weeks**
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- **Kellye Eversole**
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- **Randy Deinhammer**
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2. Coordinated definition of biocontrol

- **Leah Buchman (lead)**
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- **Shade Sabitu**
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- **Rodolphe Barrangou**
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- **Kellye Eversole**
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- **Randy Deinhammer**
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4. Risk-based approach to persistence

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- **Kelly Patterson**
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5. Study persistence

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3. Devitalize tested microbe

- B. **Pratyusha Cheneupati (lead)**
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6. Stakeholder knowledge gaps

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- **Kellye Eversol**
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- **Kelly Patterson**
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- **Madeline Maynard**
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Group 1: Understand the different factors, criteria impacts that USDA considers when they define a plant pest (decision tree)

Big Idea: USDA funded validated list related to plant pests that are specific for microbes	Steps: Industry consortium to develop database	Database aspects	Committee (groups 1 and 2)

• Enter microbe name into relational database and outcome would be
  • **Red**-do not work on
  • **Yellow**-need to develop data (data needs to be determined) to deregulate and commercialize
	1. Stakeholders (AgCo tech dev, PPQ, Fed agencies, academic, NGO, etc.) define what qualifiers are relevant to engineered microbes
	2. Develop flow chart steps to examine defined aspects of a plant pest
		• Infection agents-pathogens; non-human
		• Receives DNA from plant pest or org capable of injure; cause damage; cause disease; plant; plant product
		• Impact on: beneficial to plants; non-target orgs
		• Micro-org used to control plant pests or post plant pest risk
		• Orangism0geography of origin
		• Environment--where found/used
		• Host range-plants
		• Dissemination/spread
		• Rhizosphere effects
			• Leah Behman (lead)
			• Shade Sabita
			• Rodolphe Barrangou
			• Sharon Berberich
			• Mike Weeks
			• Kellye E
			• Randy Deinhammer

Link to group 1 flip chart pdf

Group 2. Can we have a clear coordinated definition of biocontrol? Can we have a standard threshold to determine "biocontrol"? Can we set up an AHPHIS-like plants-for planting model for biocontrol (independent research council as is done for plants)?

Big Idea

- Since the current definition of biocontrol is "…intended use to control plant pests and could pose a plant pest risk" think of biocontrol in terms of efficacy: What concentration of microbes or viability is needed to achieve desired efficacy? absence of risk in lieu of efficacy

Consequences

- This may also help us answer the devitalization question
- Self determination by developers as to what the threshold/standard/criteria are

Steps

- 1. combine with group 1 for definition of plant pest
- 2. develop independent research that supports government decision making

Committee (groups 1 and 2)

- Leah Behman (lead)
- Shade Sabita
- Rodolphe Barrangou
- Sharon Berberich
- Mike Weeks
- Kellye E
- Randy Deinhammer

Link to group 2 flip chart pdf

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Group 4. What could a risk-based approach to persistence look like and what are the most important considerations?

Evaluation	Engagement	Assessment	management	Committee
•Low, reduced risk frameworks •define persistence •consider agencies' POV •exemptions or modifications that don't need persistence data? •genus/species/population groupings?	•engage stakeholders •recognize variability •solicit input from stakeholders (public, industry, users, NGOs early) •preliminary best practices grounded in existing frameworks-greenhouse as model	•conduct environmental impact studies to determine concerns •review literature and gaps •study design	•address knowledge gaps to provide evidence of risk-based approach •Establish best practices/enforcement by third party/neutral org •establish controls to mitigate risks (use existing frameworks?) •test in different environments (greenhouse, in situ field trials, commercial use) •establish rules based on study	•Ellen Lentz (chair) •Kelly Patterson

Link to group 4 flip chart pdf

5. Conduct a study that generates information on persistence and spread that's cognizant of IP and generally applicable. Include surrogacy, field work and greenhouse work

Collect available info on	Develop protocols	Greenhouse-->Field	Guideline	Committee
•Literature search/organization •methods •quantitation •Surrogacy •consider studies already underway (DOE, EPA)	•Predictive studies from gh to extrapolate to field •microbiome or single strain •expert panel (and stakeholder) to develop •application method •barcoding or other tracking •LOD •USDA/EPA review and provide comments	•cost effective •successful studies provides appropriate data to use surrogate •confidentiality and IP •define the accetable lower level? (Population decline? •conduct study	•expectation that agencies will adapt to produced data	•Ellen Lentz •Tammy Zimmer •Vera Bonardi •Helen Harrison

Link to group 5 flip chart pdf

Group 3. Is there a method to devitalize tested microbe that does not compromise the soil environment? Is it risk-based or hypothesis based that the tested microbe should not persist—what is reasonable and practical LOD?

Devitalization	Persistence	Committee
• depends on application method and concentration • explore: hold off devitalization if it is determined that concentration/amount of microbe is decreasing • explore flexibility iwth devitalization-method and time • Meet with USDA to discuss devitalization method • should not be too laborious	• work with USDA to determine persistence definition • consider: cost/burden • consider: third party (like farmers CRO) • Neutral source to generate data/methodology for all parties	• B. Cheneupati • Randy Deinhammer

Link to group 3 flip chart pdf

6. What knowledge gaps do stakeholders have around the permitting process? What is the right private-public partnerships to fill these education gaps to prevent silos?

Stakeholders	BRS needs	Developer roles	Determine scope	Committee
• Define via stakeholder map • BRS, PPQ EPA, etc • when to bring in public-what information would look like? • engage NGOs • NAS • CAST • Farmers/consumers	• what is information regulators need to make a decision? • Checklist • Rapid response system for technical questions (FAQ)	• Provide basic science info to BRS staff (microbial • Educate BRS and NASDA on product development pipelines • Joint company meetings with USDA and EPA	• Plant pest criteria/biocontrol out of scope • Biotech query to confirm out of scope • Developers and BRS are most focused on this	• Annie • Natasha • Kellye E. • Kelly Patterson • Madeline Maynard

Link to group 6 flip chart pdf

Report out discussion

- Which questions should be combined or have dependencies….
  - Biocontrol and plant pests.
  - **Q1&2**—choosing of model organisms can address those dependencies-frame as safety
    - Mechanisms for creating definitions—who—how about industry associations? Might need to go into farm bill with appropriations
    - US does not require efficacy data—so be careful not to create precedence: providing data for absence of risk at certain doses (not efficacy for safety)
    - Labels—where would they be housed? –first find existing definitions and don't create new one
    - Similar to FDA—stage gate processeses—groups 3,4,5—build arguments that it is there, but it is safe
    - Indirect plant pest risk is easier for microbial product to address—so adverse affect reporting with ability to react post market could be a better solution
    - Policy question follow up: testing in place by the developer shows it no longer is there does not require devitalization
  - **Q6**-Importance in education of regulators about product development process
    - Stakeholders are similar to q1&2
    - Stakeholder mapping exercise would be the appropriate next step
  - **Q3**: is devitalization the right route or will it disrupt our understanding?
    - "kill switch" wasn't a major part of discussion but should continue to be discussed—public bidding process to get idea on how to do this. Maybe an LOD value would not require a kill switch

Recommendations and next steps

- Share debrief with all workshop participants
- Contact leads to ensure they are working on scheduling their team
- Who was not at the 'Hands on' who would have been helpful?
  - NGOs?
  - ?
- A follow up "workshop" could be a remote event, reporting out progress and developing next steps
- ´When inviting for a workshop, expect 50-70% positive responses. Don't be afraid to "over-invite"

Appendix

Attendees

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