USDA Animal and Plant Health Inspection Service
U.S. DEPARTMENT OF AGRICULTURE


# FY 24 Highlights

Bernadette Juarez
BRS Deputy Administrator
November 14, 2024


USDA
APHIS Excellence in Science
Communication Program
2024 Graduation


AGRICULTURAL
OUTLOOK FORUM
CULTIVATING THE FUTURE


USDA


DENIZENS

# 2024 New Staff Members

# Resource Management Services

**Constance Jones**
Management &
Program Analyst

**Bill Kelly**
Senior
Management Analyst

**Briyanna Norman**
Management &
Program Analyst

**Yoomi Shin**
Management &
Program Analyst

# Biotechnology Risk Analysis Programs

*The Plants Branch and the Plant Evaluation Branch*

**Jose Fonseca**
**Biological Scientist**

**Amanda Kenney**
**Senior Biological Scientist**

**James Parr McQueen**
**Biological Scientist**

# Biotechnology Risk Analysis Programs

*The Plants & Insects Branch*

**Tammatha O’Brien**
**Biological Scientist**

**Britany Morgan**
**Biological Scientist**

# Biotechnology Risk Analysis Programs

*The Plants & Microbes Branch*

**Bright Agindotan**
**Senior Biological Scientist**

**Gregg Goodman**
**Branch Chief**

**Rachel Hiles**
**Science Fellow**

**Dharmendra Singh**
**Biological Scientist**

# Regulatory Operations Program

**Ann Gobei-Bacaylan**
**Biological Scientist**

**Jennifer Smith**
**Senior Program and Regulatory Analyst**

# Communications

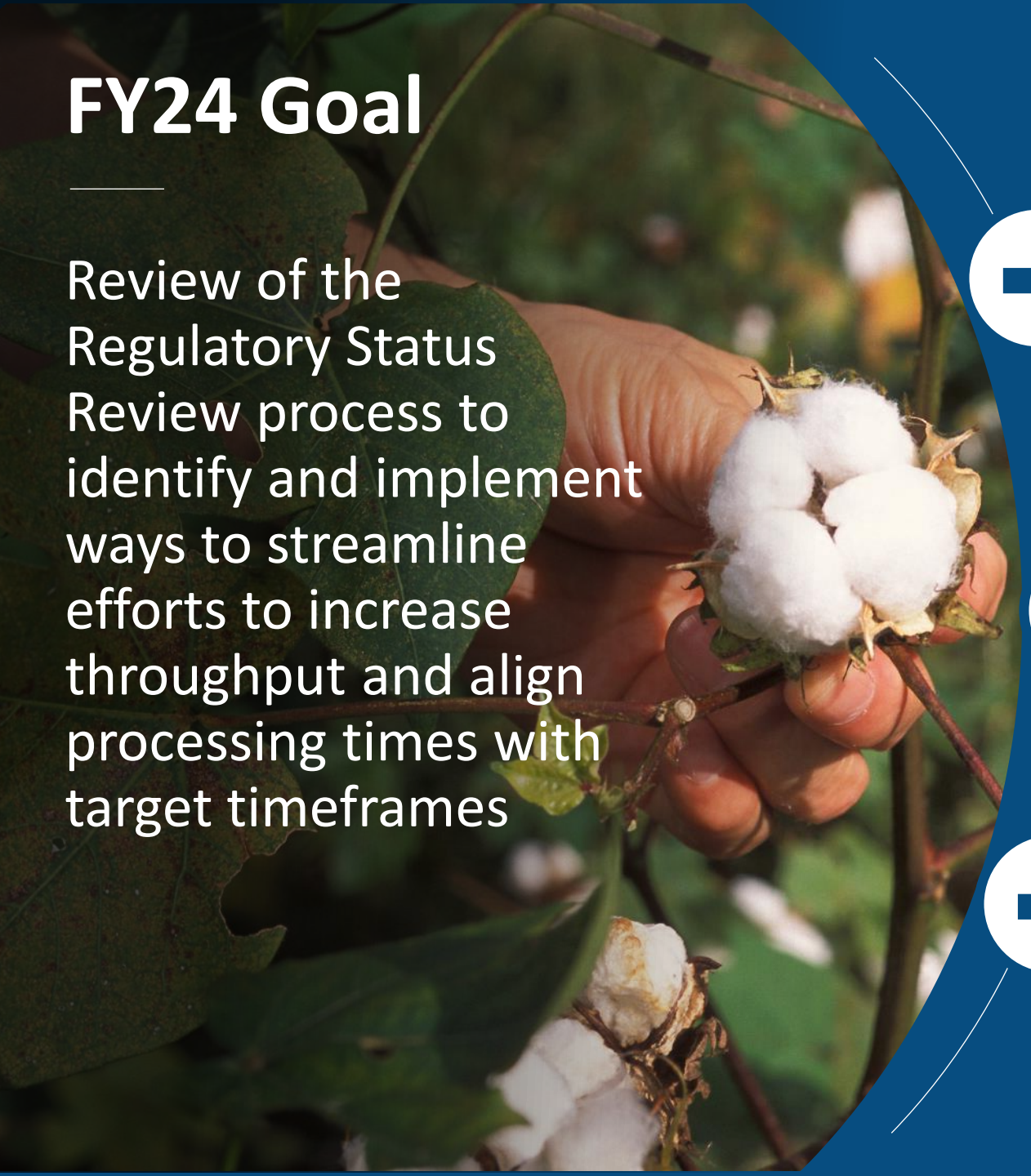
**Dore Mobley**
**Branch Chief**

# Thank You!

# Regulatory Status Review

Michael Stulberg, Ph.D.
Acting Associate Deputy Administrator
BRS Biotechnology Risk Analysis Programs
November 14, 2024

# FY24 Goal

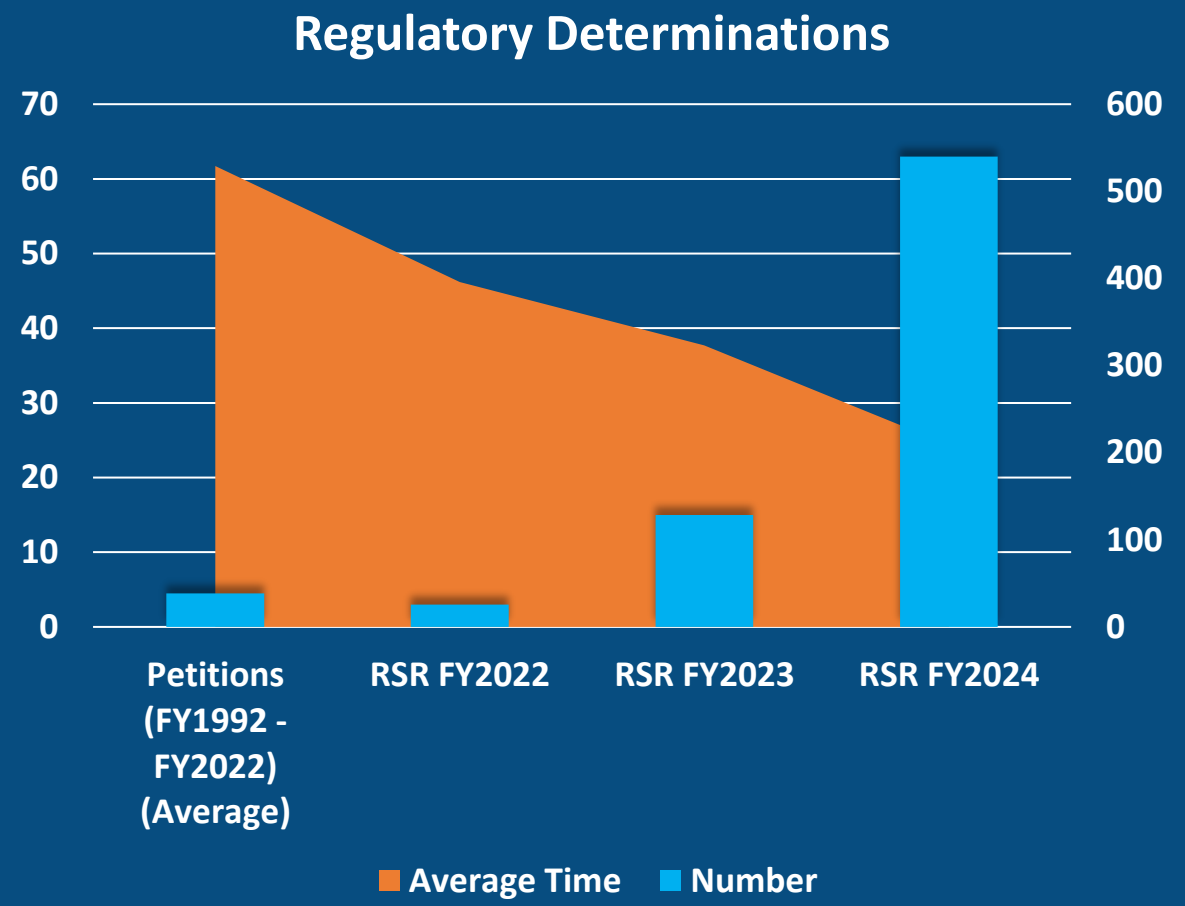


Review of the Regulatory Status Review process to identify and implement ways to streamline efforts to increase throughput and align processing times with target timeframes

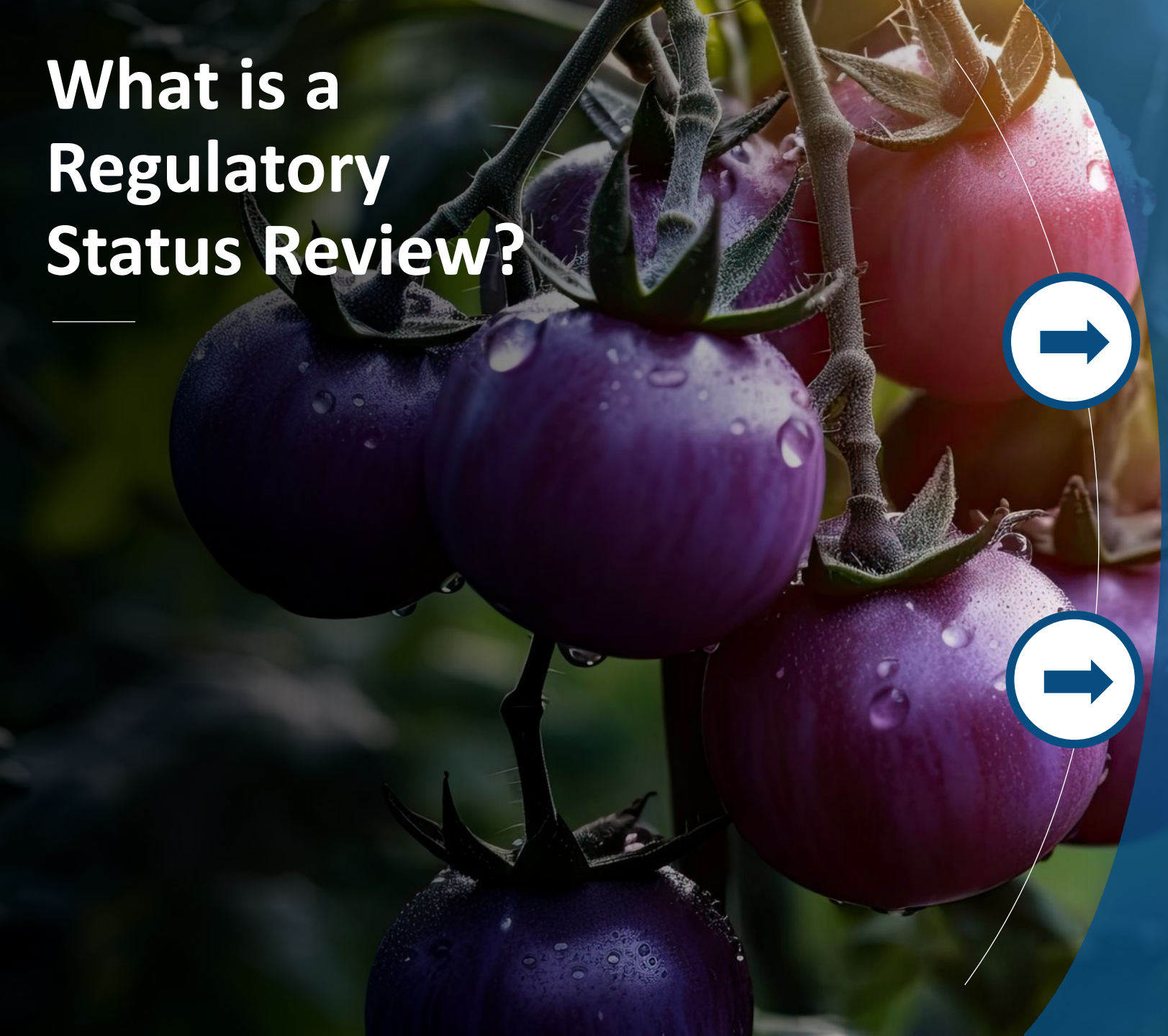
- Develop and implement a new application in APHIS eFile to track pending reviews, data handoffs and coordination
- Clarify and streamline the instructions and templates used to understand a plant's biology
- Evaluate mechanisms of action across biologically-similar plants in a single analysis

# FY24 Goal

Review of the Regulatory Status Review process to identify and implement ways to streamline efforts to increase throughput and align processing times with target timeframes



# What is a Regulatory Status Review?



APHIS review of whether certain modified plants require oversight

Plants that do not require an RSR: exempt from regulation

# Outcomes

*What are the possible outcomes of a Regulatory Status Review?*

1. **No plausible pathway to increased plant pest risk, not subject to regulation**

2. **Plausible pathway, regulate until information shows it is unlikely to pose an increased plant pest risk**

# Regulatory Status Review Process

## 01

### Initial Review

Use publicly available information to identify whether there are plausible pathways to increased plant pest risk

## 02

### No Risk Identified

If no plausible plant pest risk, the plant is not regulated

Findings made public

Completed in 180 days

### Plausible Risk Identified

If APHIS identifies plausible risk, APHIS further evaluates factors of concern with a Plant Pest Risk Assessment (PPRA)

## 03

### Draft PPRA Published

APHIS publishes PPRA in the Federal Register for public comment and considers comments before decision-making

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### Final PPRA Published

No plant pest risk found, not subject to regulation

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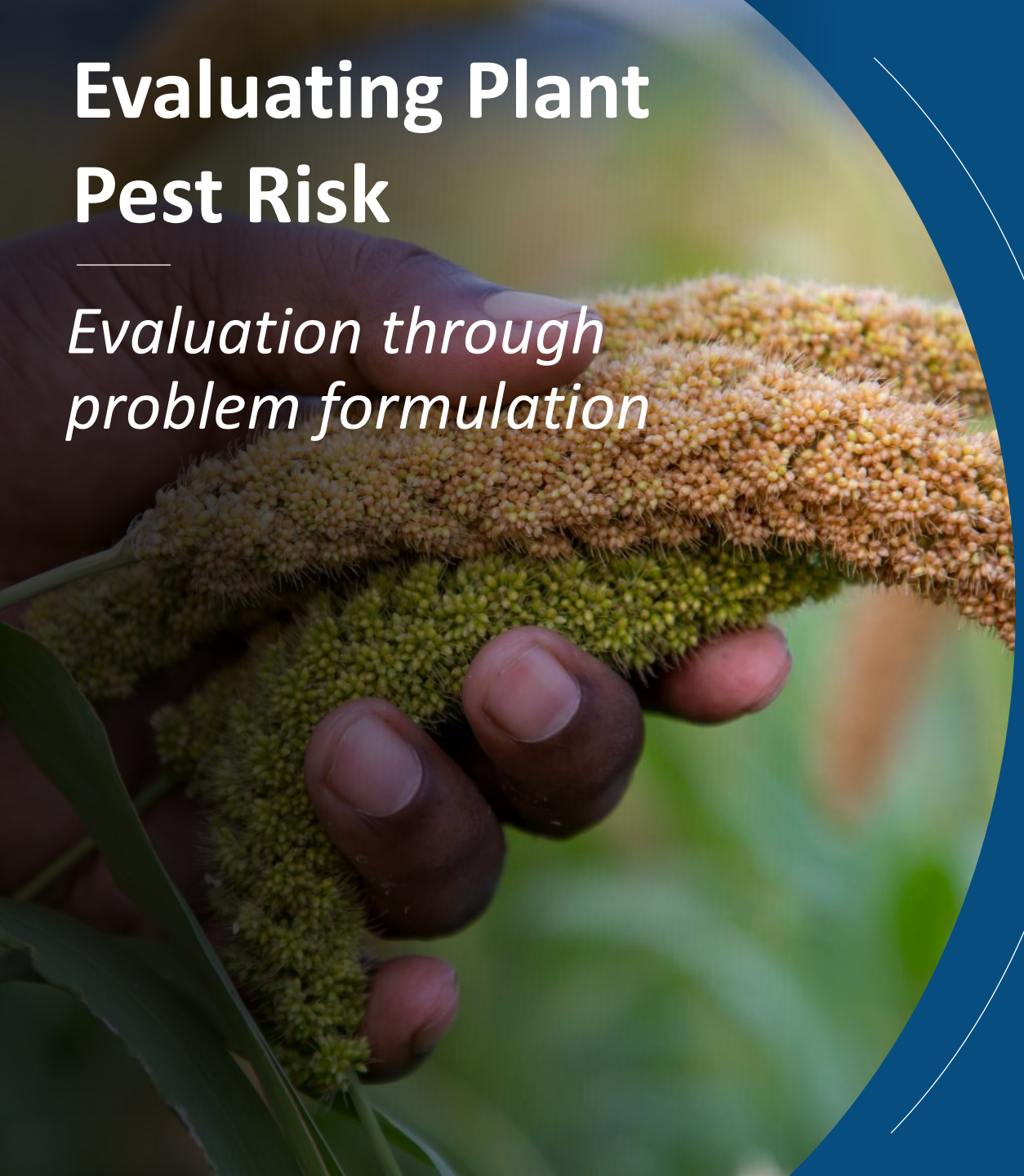
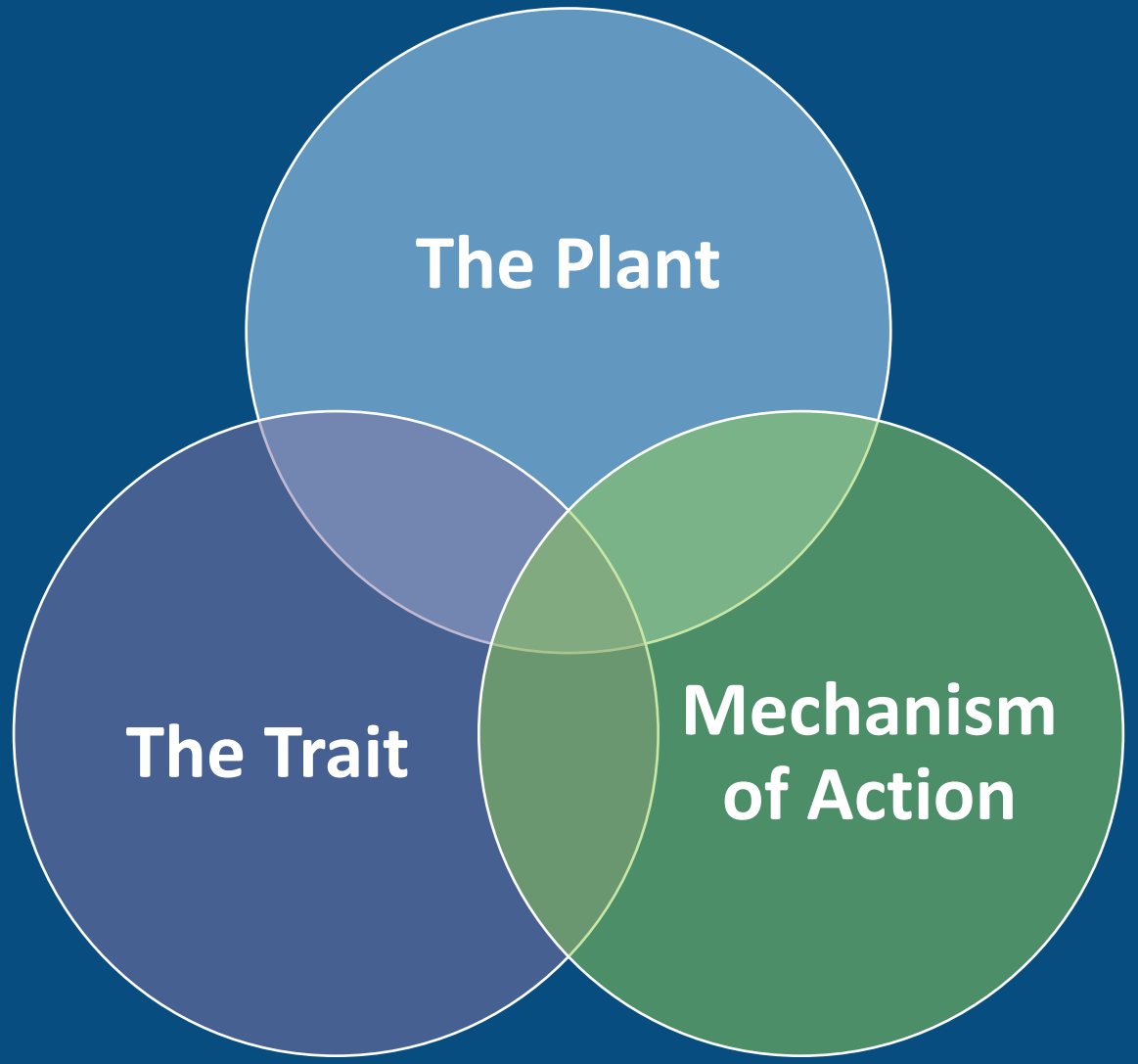
FINISH LINE

FINISH LINE

# Evaluating Plant Pest Risk

*Evaluation through problem formulation*





# Protection Goals

*Plant Pest Risk*

"The potential for direct or indirect injury to, damage to, or disease in any plant or plant product resulting from introducing or disseminating a plant pest, or the potential for exacerbating the impact of a plant pest."

# Risk Equation

Exposure **x** Adverse Consequence **=** Risk

# Initial Review

Plausible pathways to increased plant pest risk

**Plant Reference Document (PRD)**

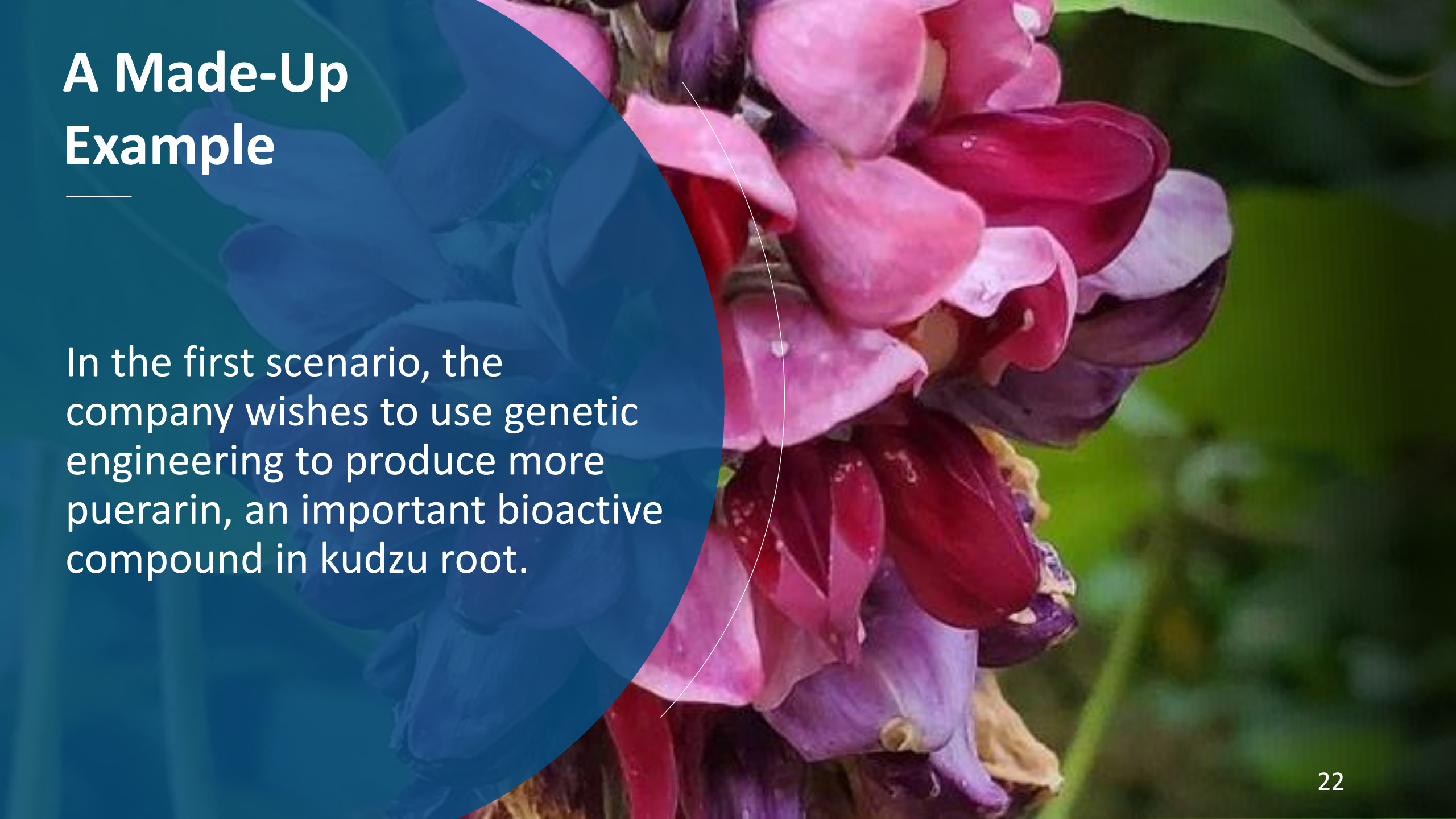
**Mechanism of Action Description (MOAD)**

# A Made-Up Example

Roots of *Pueraria* spp. are used as herbal supplements or a root tea, and a company wants to use genetic engineering to expand how they can use the plant for their business.

# A Made-Up Example

In the first scenario, the company wishes to use genetic engineering to produce more puerarin, an important bioactive compound in kudzu root.



# A Made-Up Example

The company submits a Regulatory Status Review of *Pueraria montana* genetically engineered to overexpress a *C*-glycosyltransferase of isoflavone biosynthesis.

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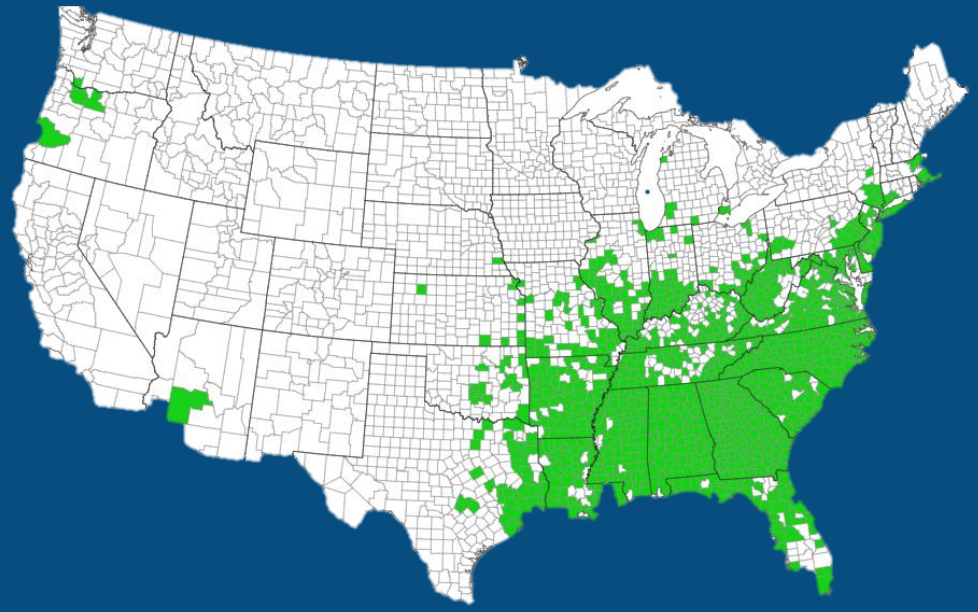
# Plant Reference Document

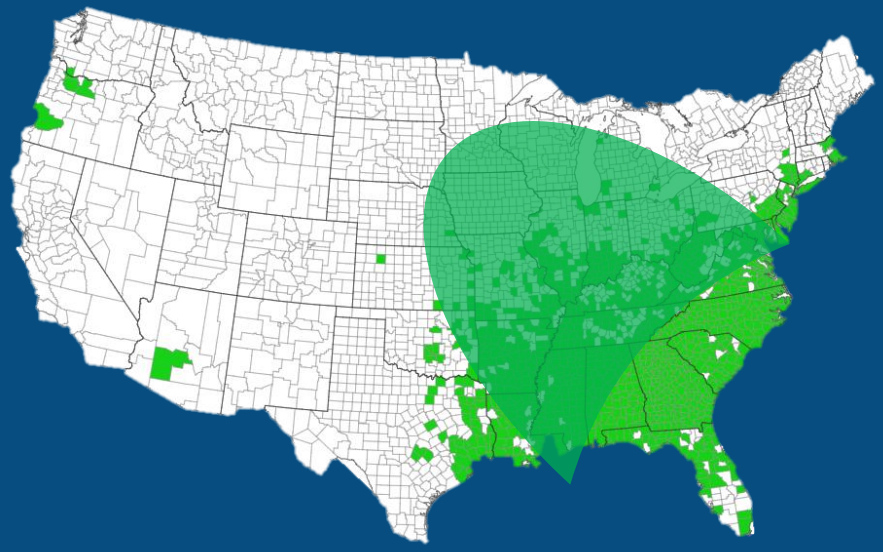
*Why do we need a plant reference document?*



*https://www.eddmaps.org/, accessed 11/6/2024*

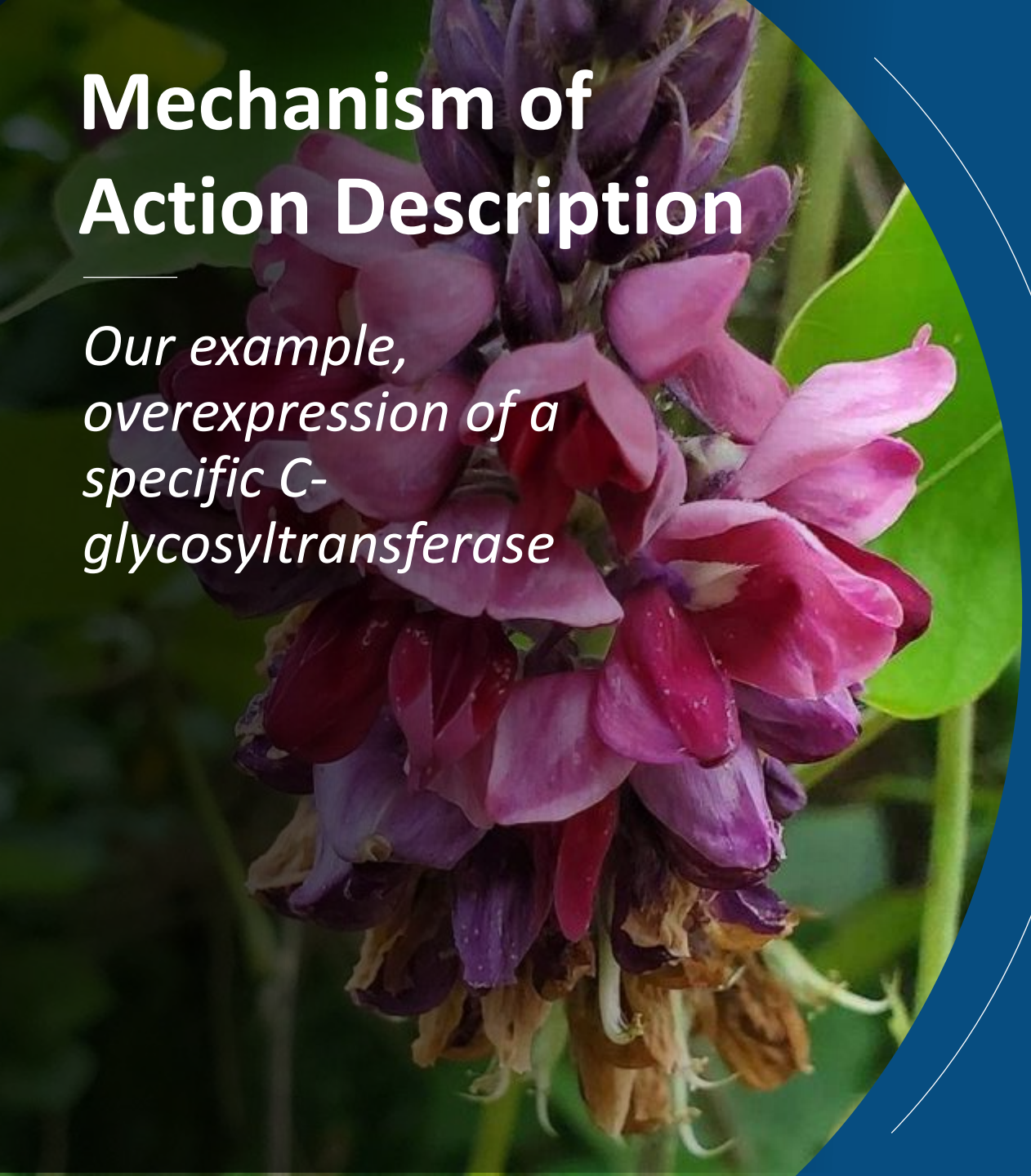
- Information about comparator plants
- Where the plant grows and climatic suitability
- Abiotic and biotic stresses of the plant, sexually compatible relatives, and its reproductive life cycle
- Potential to cause harm

# Mechanism of Action Description



*https://www.eddmaps.org/, accessed 11/6/2024*

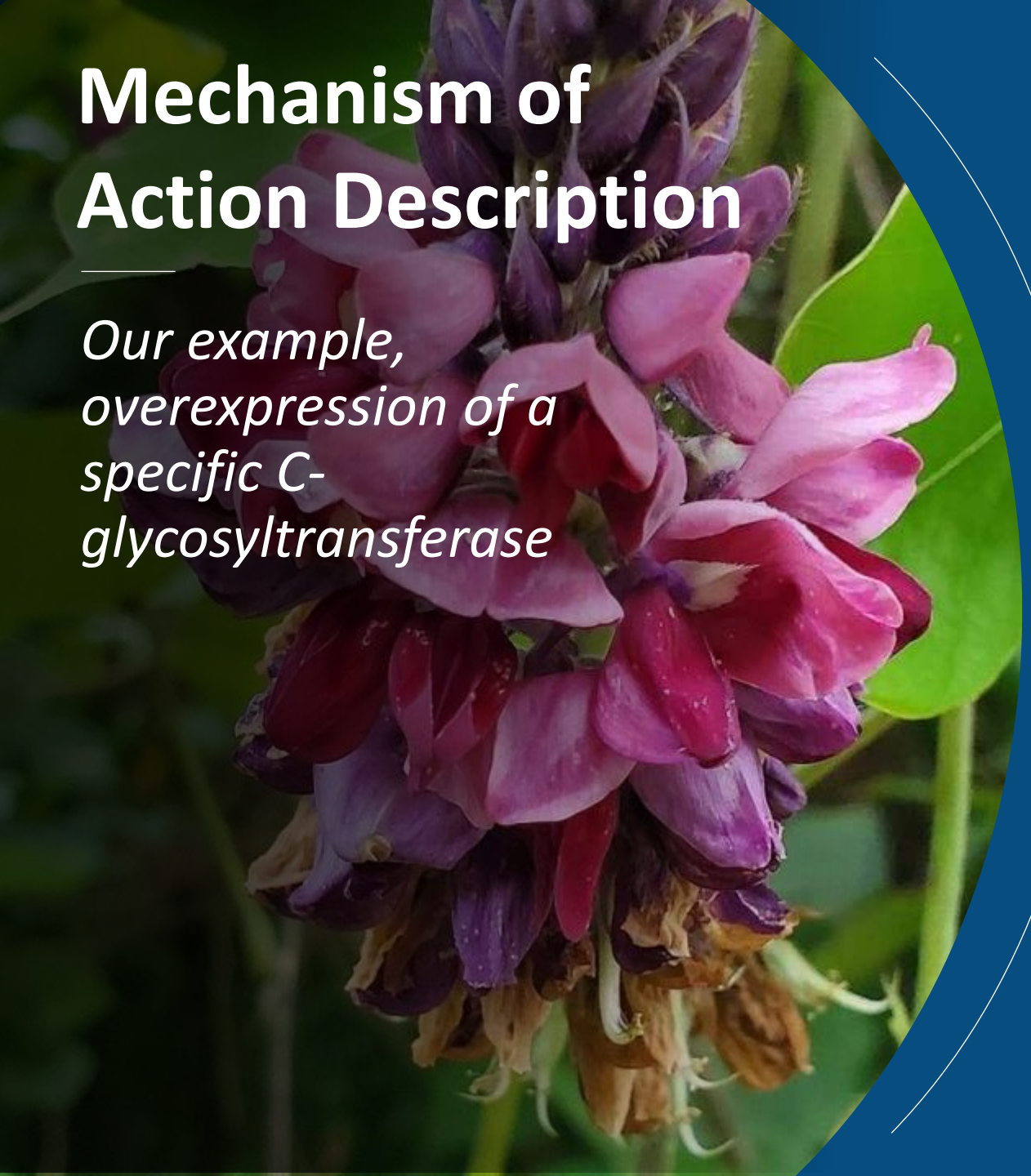
- How does the modification affect plant physiology
- Which biological properties or consequences may change
- Could the occurrence of the plant change
- Potential for changes in occurrence or consequences to cause harm



# Mechanism of Action Description

*Our example, overexpression of a specific C-glycosyltransferase*

This C-glycosyltransferase is near the end of a biosynthetic pathway and is the last step in puerarin biosynthesis.



# Mechanism of Action Description

*Our example, overexpression of a specific C-glycosyltransferase*

This C-glycosyltransferase is near the end of a biosynthetic pathway and is the last step in puerarin biosynthesis.

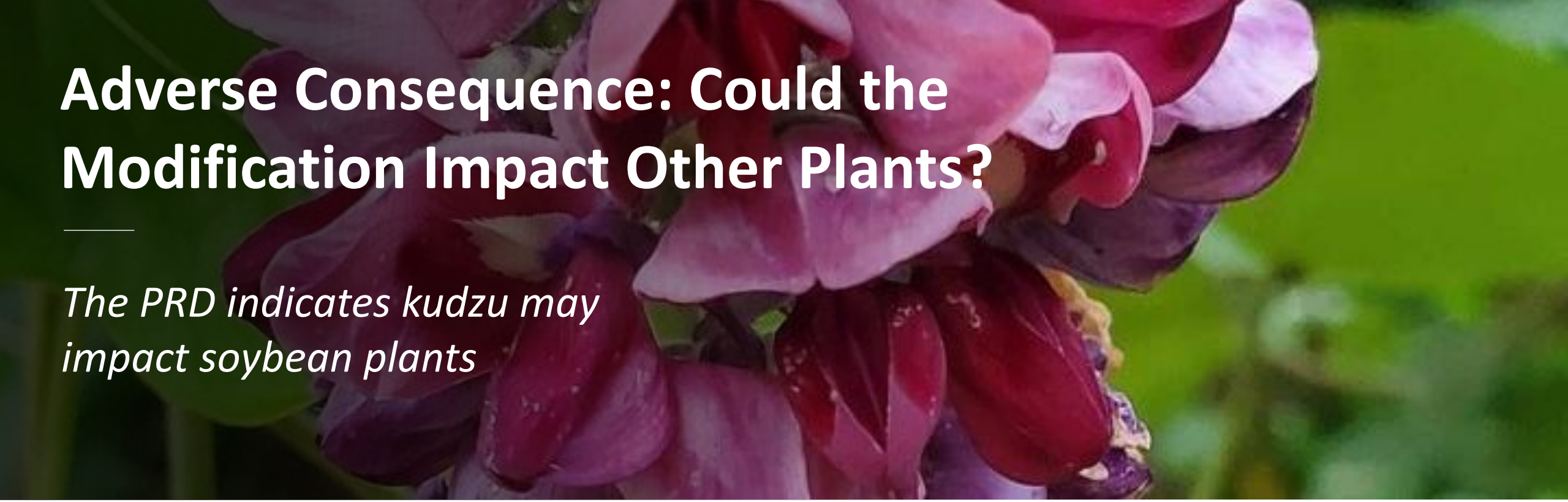
Does increased accumulation lead to any changes in biology or effect on pests, pathogens, or beneficial organisms?

# Exposure: Will the Modification Expand Where the Plant Persists?

*The PRD indicates that cold stress, freeze tolerance, limits occurrence*

**Overexpression of this C-glycosyltransferase is not expected to impact the biology of the plant in a demonstrable way**

**No potential change**



# Adverse Consequence: Could the Modification Impact Other Plants?

*The PRD indicates kudzu may impact soybean plants*

**Increasing levels of puerarin have no documented toxicity to other organisms**

**No plausible pathways to increased plant pest risk**

# Regulatory Status Review Process

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**Findings made public**

**Completed in 180 days**

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# A Second Made-Up Example

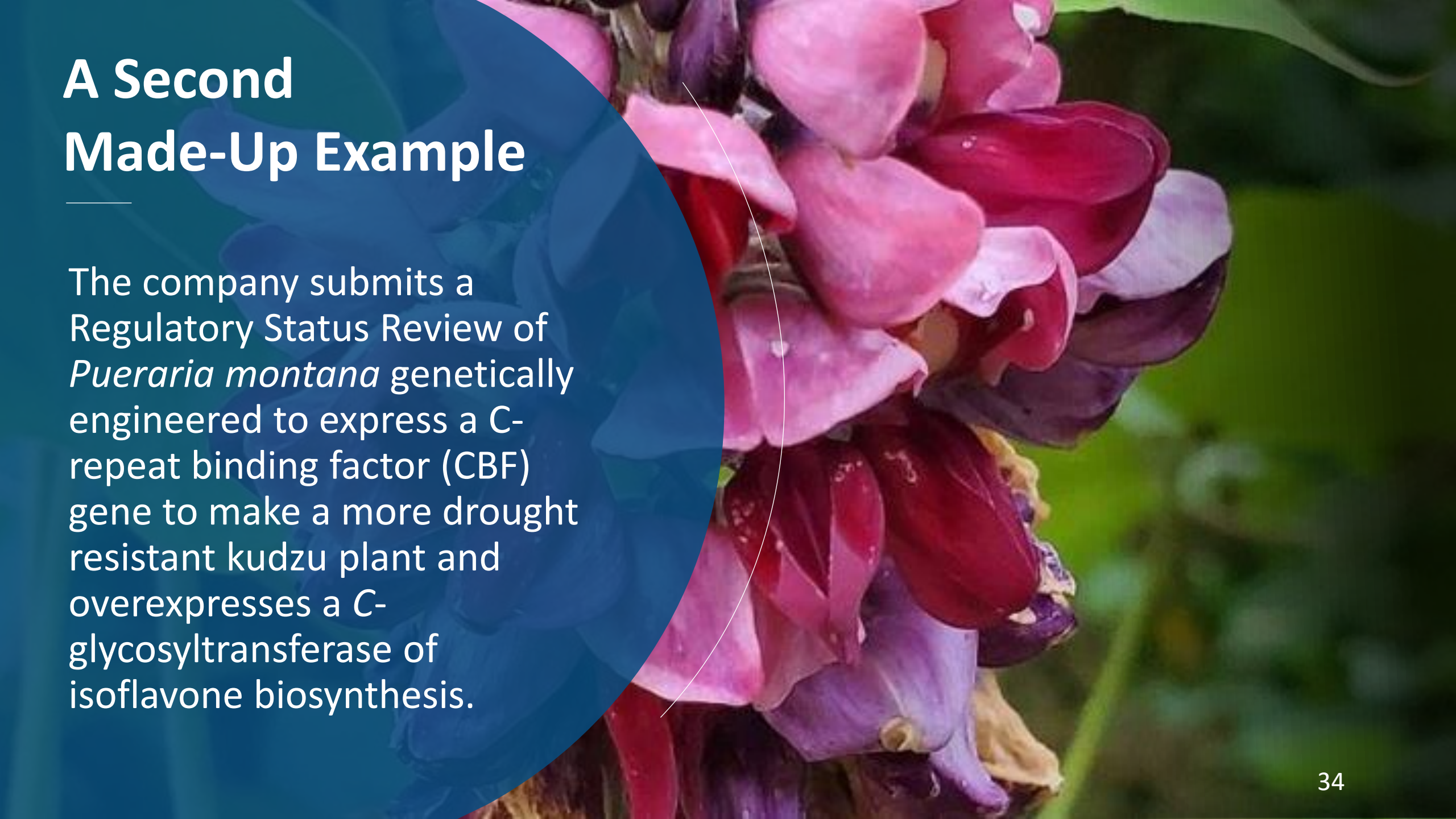
Roots of *Pueraria* spp. are used as herbal supplements or a root tea, and a company wants to use genetic engineering to expand how they can use the plant for their business.

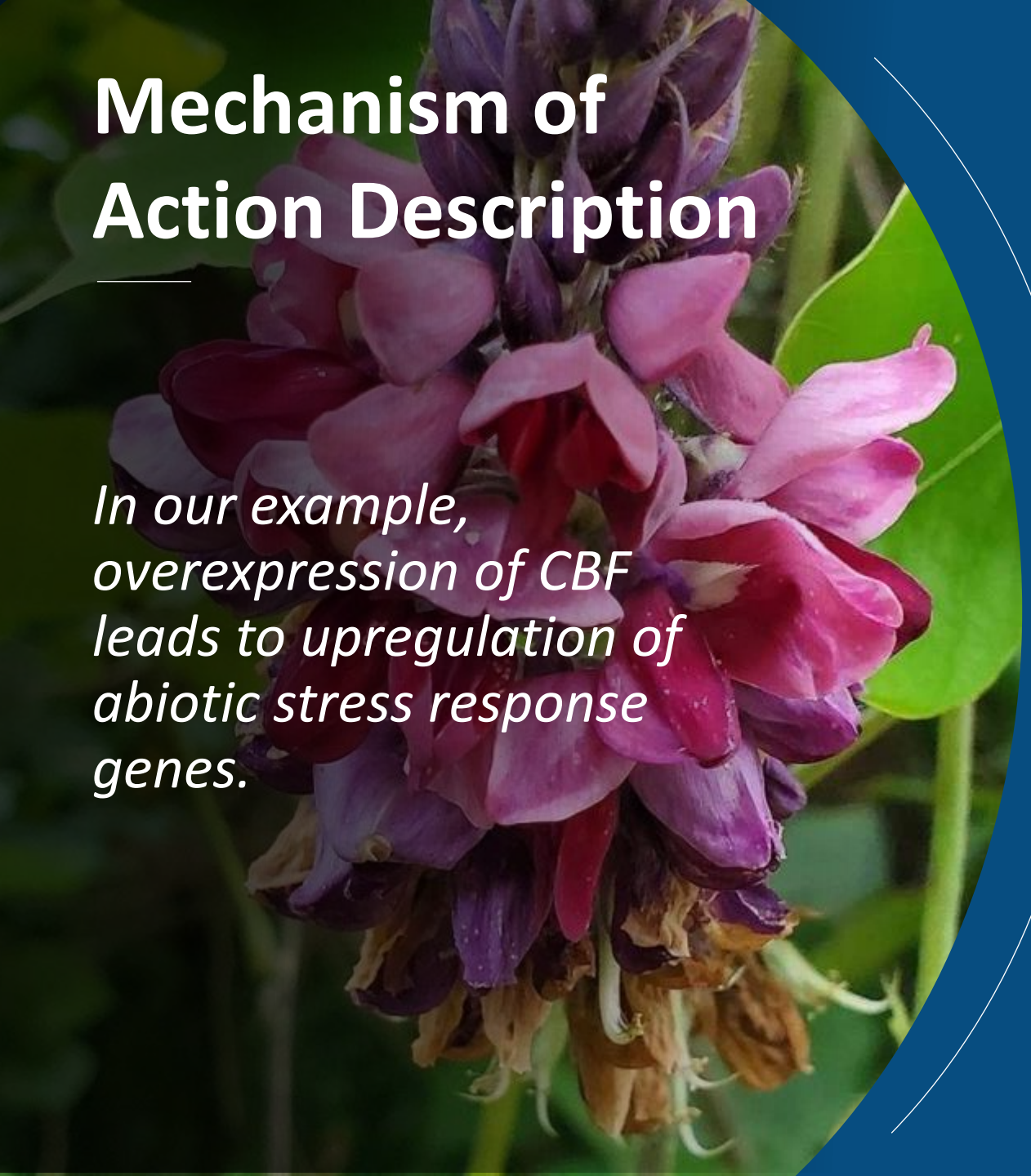
# A Second Made-Up Example

In the second scenario, the company wishes to use genetic engineering to enable these plants to grow in water stressed conditions and produce more puerarin.

# A Second Made-Up Example

The company submits a Regulatory Status Review of *Pueraria montana* genetically engineered to express a C-repeat binding factor (CBF) gene to make a more drought resistant kudzu plant and overexpresses a *C*-glycosyltransferase of isoflavone biosynthesis.





# Mechanism of Action Description

*In our example, overexpression of CBF leads to upregulation of abiotic stress response genes.*

CBF genes are also involved in cold tolerance and early development.

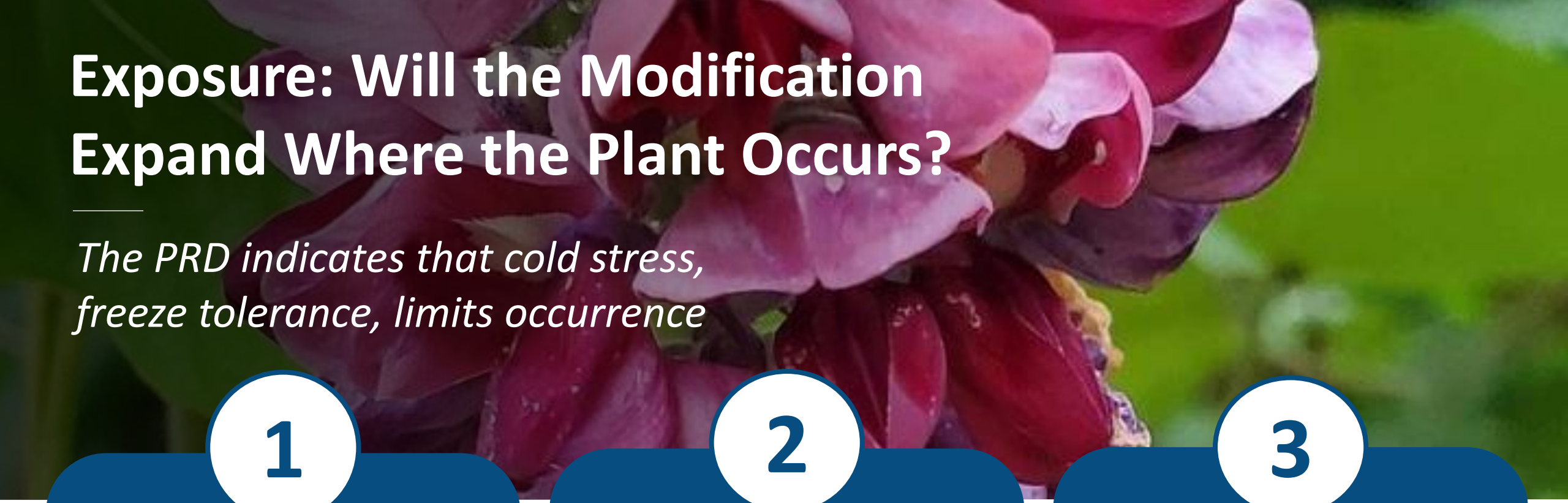
Might these plants also be more tolerant to freezing, or growth inhibition?

# Mechanism of Action Description

*In our example, overexpression of CBF leads to upregulation of abiotic stress response genes.*

Already have the MOAD for a C-glycosyltransferase in kudzu with the phenotype of increased puerarin content

Any interaction between the two MOAs?



# Exposure: Will the Modification Expand Where the Plant Occurs?

*The PRD indicates that cold stress, freeze tolerance, limits occurrence*

**1**

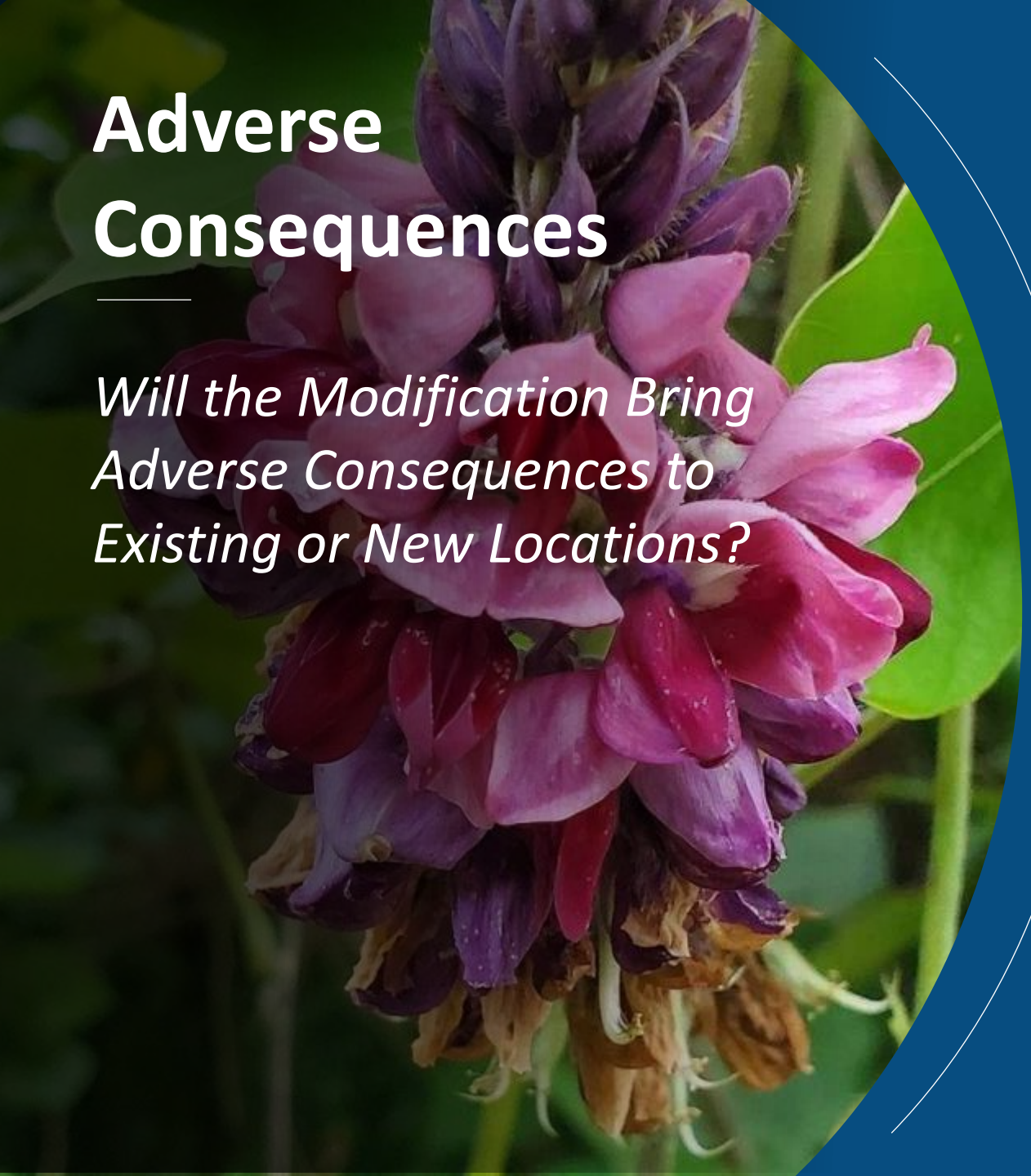
Kudzu has geographical restriction in the United States. What does our PRD indicate about drought and cold tolerance?

**2**

This cold-tolerant kudzu may now grow and occur in areas of the United States where the unmodified cannot grow.

**3**

We look to see if this plant could harm agriculture in a new area.



# Adverse Consequences

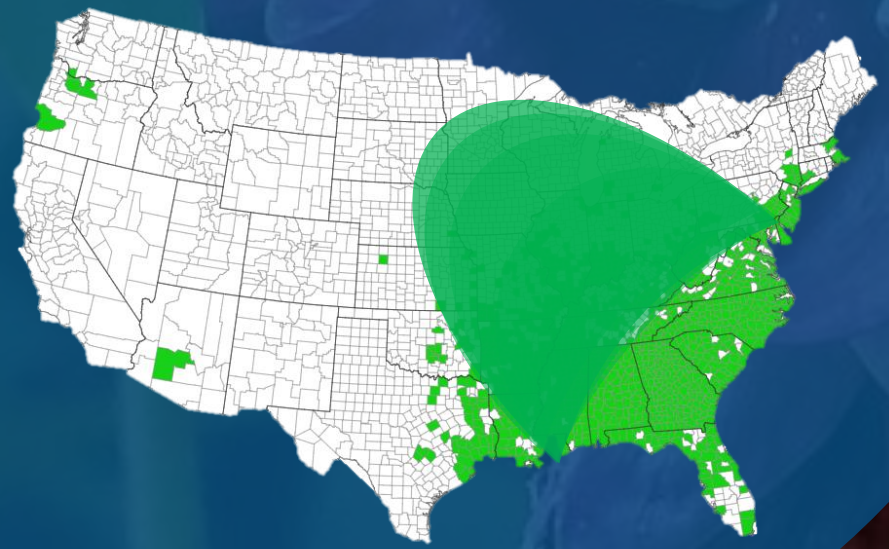
*Will the Modification Bring Adverse Consequences to Existing or New Locations?*

Cold tolerance alone does not bring any adverse consequence that could lead to an increase in plant pest risk.

Kudzu is a host to soybean rust and expanding the occurrence of kudzu could bring increase the abundance of this pathogen in new areas.

# Adverse Consequences

*Plausible pathway to increased plant pest risk*



**Kudzu may grow and occur in new locations and bring soybean rust to new soybean-growing areas**

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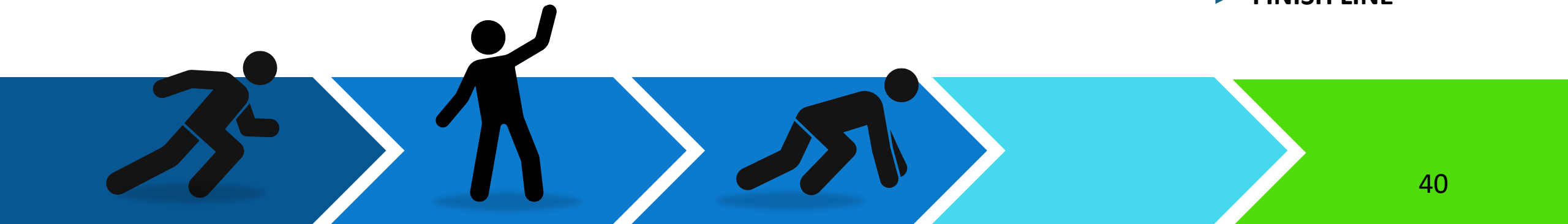

# Initiating a Step 2 Review

In our example, the developer received a letter indicating one plausible pathways to increased plant pest risk:

A change in occurrence leading to increased abundance of soybean rust

# Initiating a Step 2 Review

Customer can submit data to discuss likelihood of each step of the plausible pathway.

- Data supporting how cold tolerant plants will be and whether this is outside comparator variation
- Data and arguments regarding how good a host is the plant for soybean rust and its ability to spread or host the disease

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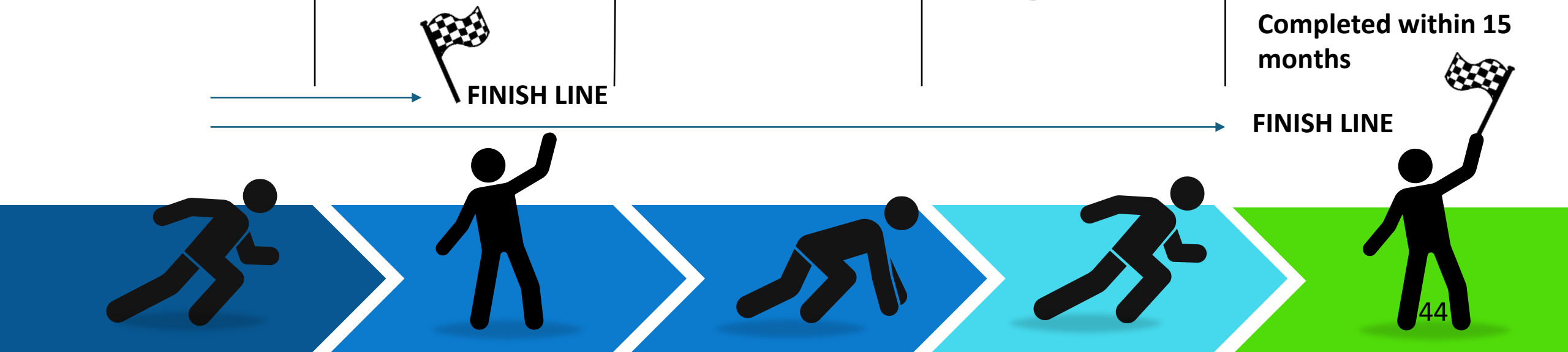


# My Plant is Not Subject to the Regulation

*Now what?*

If you have a permit, email our permit mailbox to inform them of your RSR and how it impacts your permit

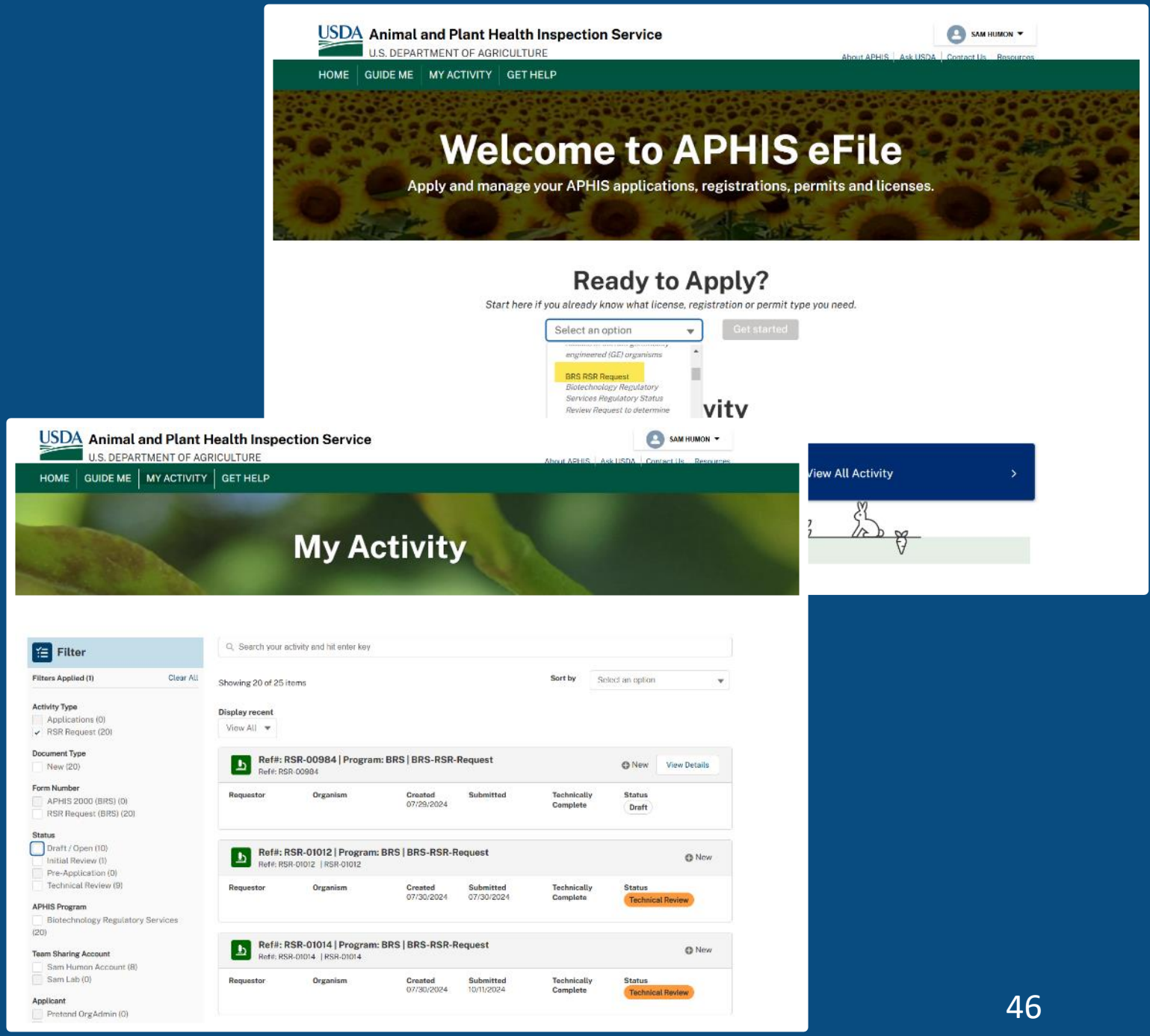
If you seek confirmation that you are using the same plant-trait-mechanism of action, please write to our confirmation of exemption mailbox

**brspermits@usda.gov**

**brs.confirmationrequests@usda.gov**

# Submitting a Regulatory Status Review

*New portal to submit your request through eFile*



# Thank You!

# Permitting Process Updates

Katharine Swoboda Bhattarai, Ph.D.
Biological Scientist
BRS Biotechnology Risk Analysis Programs
November 14, 2024

# FY2024 Permitting Business Process Improvement (BPI) Project

### OBJECTIVE

Re-establish a risk-based and familiarity-based approach for reviewing crop-trait-genotype combinations in permit applications

### GOAL

Restore track record of predictable and timely issuance of permits and confidence in BRS' permitting process

### MEASURABLE TARGETS

- Meet regulatory targets for average days to issue permits
- Issue 95% of BRS permits within the regulatory timeframe

# FY2024 BPI Project Approach

1. Documented the existing permitting process, measured process steps, and identified bottlenecks using Gemba Kaizen "Walk the Line" analysis
2. Identified steps that are duplicative, do not add value, or that can be run concurrently
3. Identified ways to increase consistency of review processes
4. Implemented process improvements to internal APHIS eFile workflow and internal review processes

# FY2024 BPI Process Improvements

- Reduced 3 hand-offs and eliminated 5.5 days from the overall review timeline
- Eliminated duplicative supervisory review for most permits
- Implemented soft enhancements to keep internal APHIS eFile workflow moving forward
- Eliminated the summary letter included in BRS state packages, saving time

# Permitting Flexibilities for Import Permits

- Implemented multi-origin and multi-destination import permits with reusable labels and instructional text for applicants
- Issued 20 import permits with multiple origins or destinations in FY24 = 85 fewer permits submitted in APHIS eFile
- Can be combined with multi-year import and interstate movement flexibility implemented in FY23

# Increased Consistency of Permit Reviews and Communication with Applicants

Clearly identified required information and described how we use it when reviewing permit applications (Permit User's Guide, "Information Requirements for Permit Applications")

Revised internal review processes for assessing application completeness

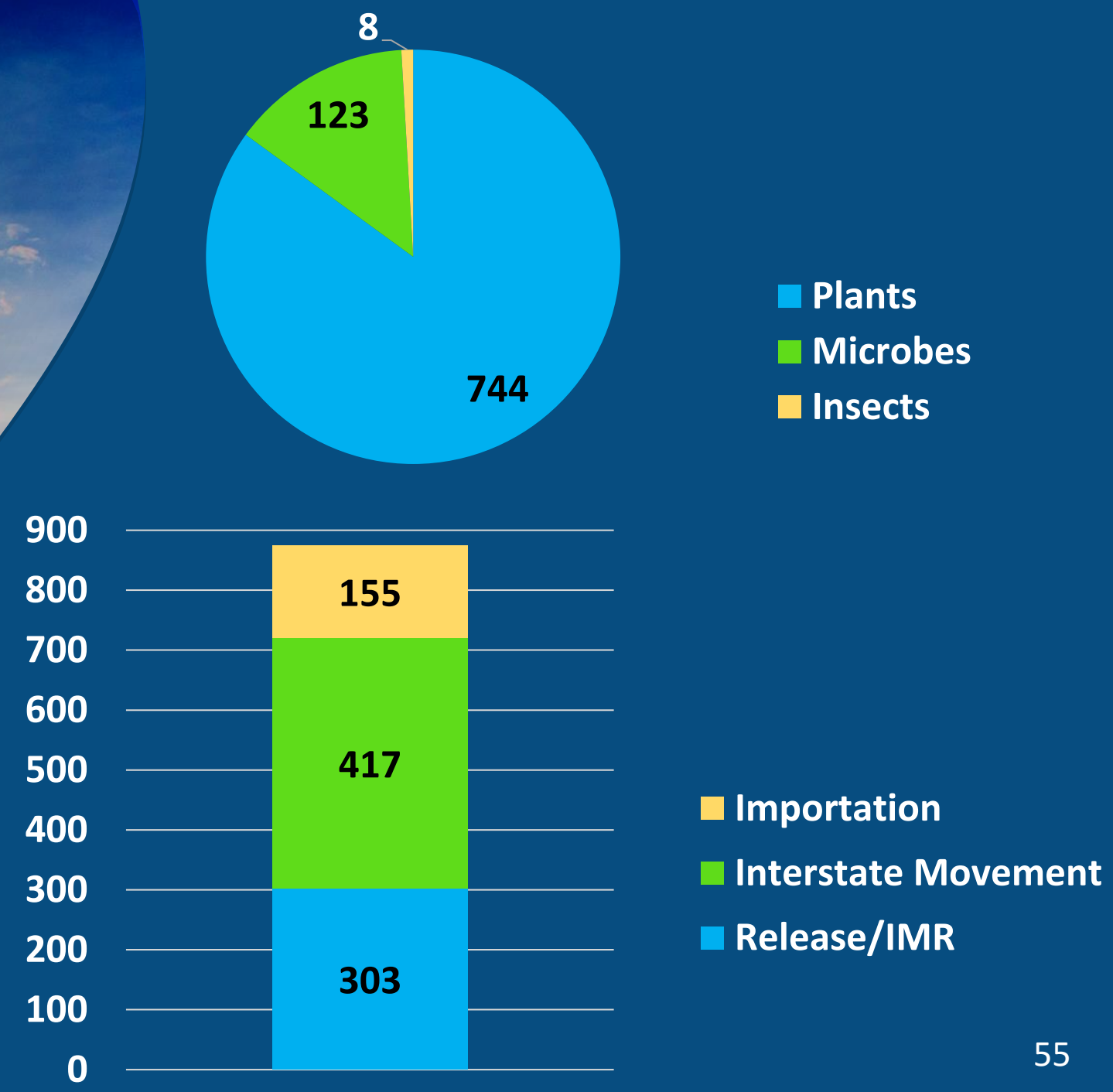
Updated a document designed to help applicants identify additional federal and state requirements that may apply to their permit

# Increased Consistency of Permit Conditions

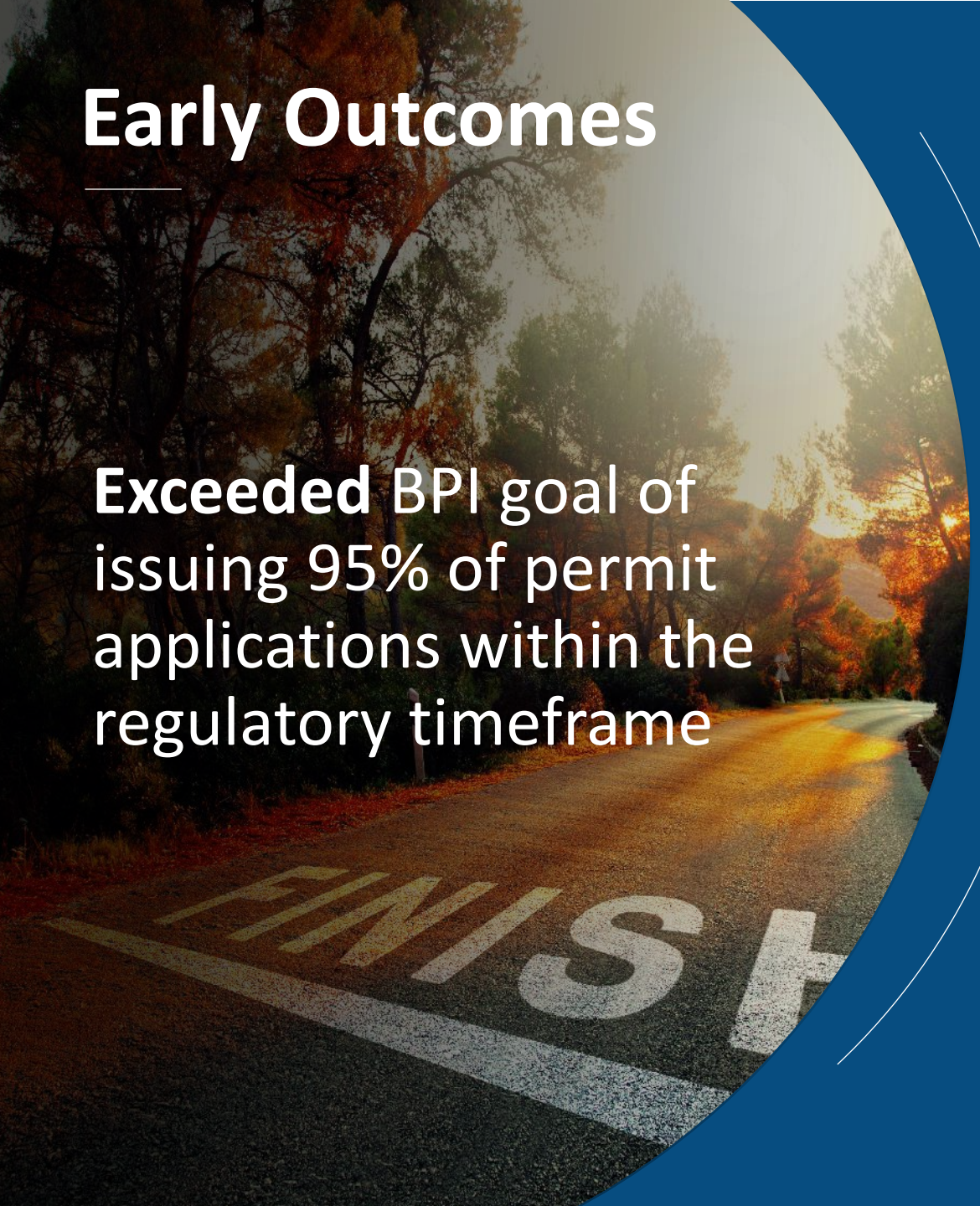
- Standardized permit conditions for certain permit categories
- Included sample standard conditions for corn/soybean releases in the Permit User's Guide
- Will continue standardizing conditions

# Early Outcomes

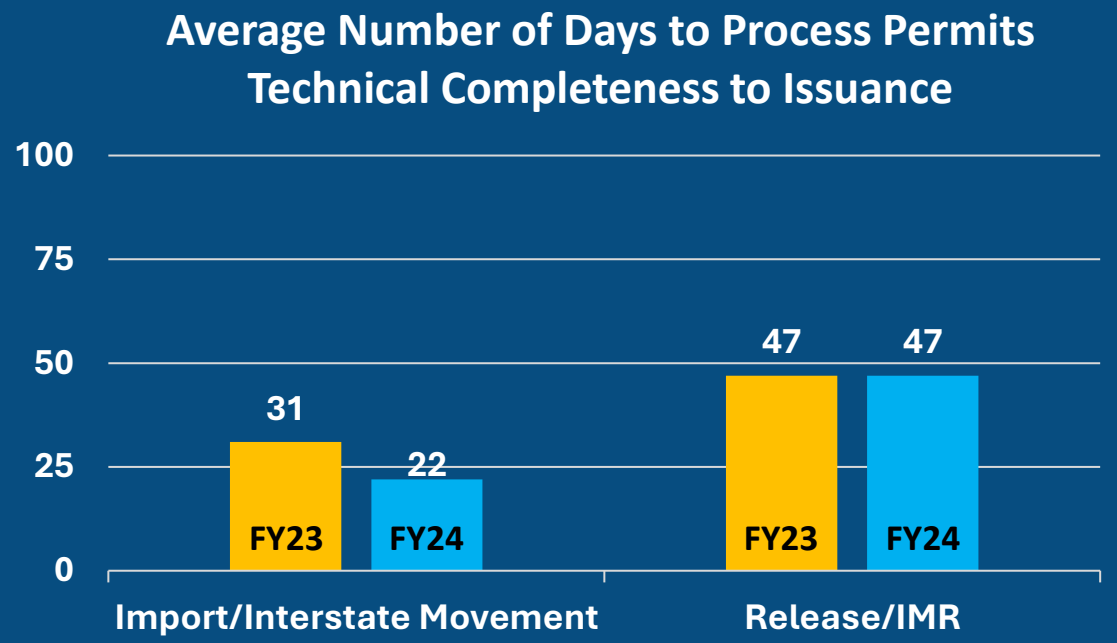
Issued 875 permits in FY2024

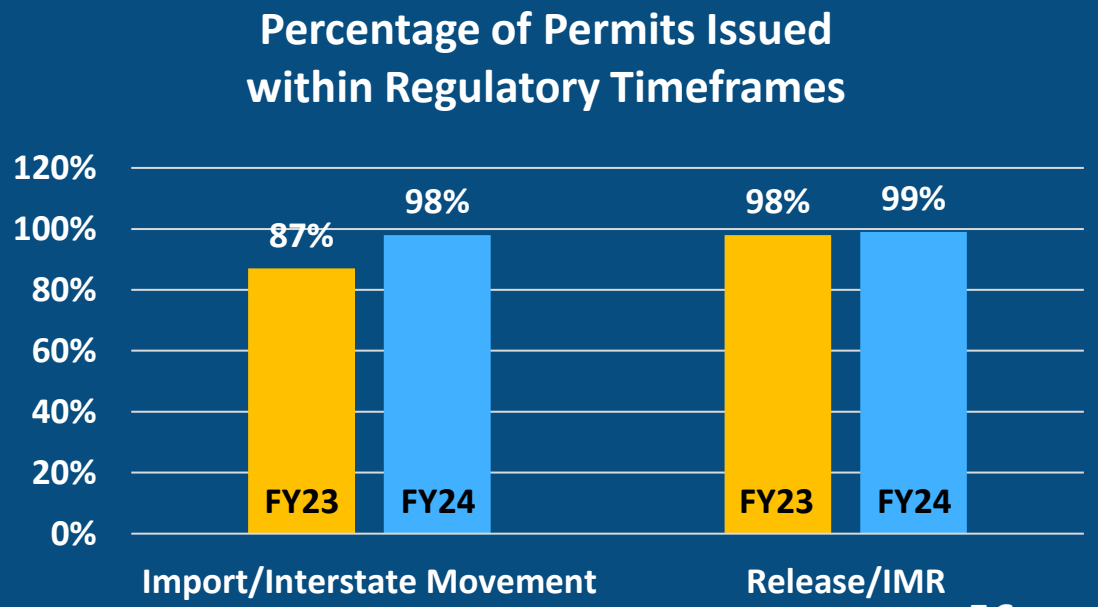


# Early Outcomes



**Exceeded** BPI goal of issuing 95% of permit applications within the regulatory timeframe



# Early Outcomes

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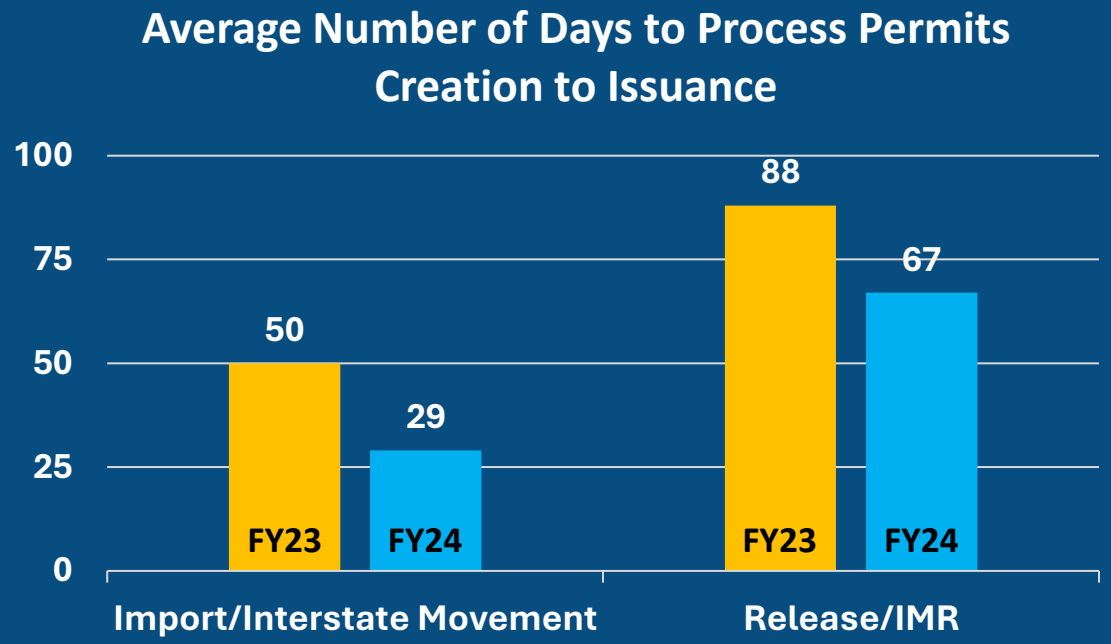


# Next Steps

*FY2025 BPI Project*

- Build on permitting gains going forward
- Measure and monitor impacts of implemented initiatives and course correct as needed
- Continue to implement process improvements that increase efficiency and consistency

# For More Information

- APHIS BRS Website
- Revised Regulations
- Updated Permit User's Guide
- APHIS eFile

# Thank You!

# International Engagement and Capacity Building Initiatives

Chessa Huff-Woodard, Esq.
Branch Chief
BRS Policy, Program, and International Collaboration
November 14, 2024

# Engagement with Future Developers and Regulators

- University of Brussels
- Cochran Fellows
  - South America
  - Africa
- Michigan State University

# Bilateral Engagement

- Japan
- Korea
- Pakistan
- Thailand
- India
- Taiwan
- Colombia
- EU

# Multilateral and Organizational Engagement

- Multilateral Engagements
  - Trilateral Technical Working Group
  - Asia-Pacific Economic Framework
  - Like-Minded Group
  - Association of Southeast Asian Nations
- Organizational Engagements
  - Organization for Economic Cooperation and Development
  - Cartagena Protocol meetings, including the Ad Hoc Technical Expert Group on Risk Assessment

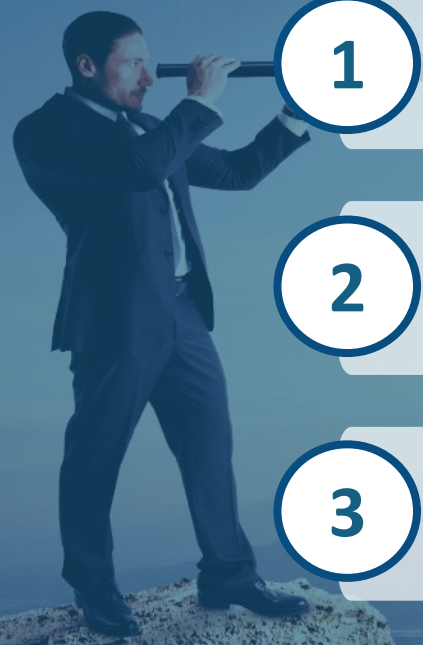
# Multilateral Engagements


Asia-Pacific Economic Cooperation
High Level Policy Dialogue
on Agricultural Biotechnology

Like-Minded Group

Innovative Genomics Institute
16 countries, FAO, IICA

# Looking Ahead



1. World Trade Organization: Technical support
2. Asia-Pacific Economic Cooperation: Policy approaches and regulatory cooperation document
3. Like-Minded Group: Increasing engagement
4. Outreach on novel products
5. Supporting OECD efforts that promote harmonization

# Thank You!

USDA Animal and Plant Health Inspection Service
U.S. DEPARTMENT OF AGRICULTURE

# Inspection and Compliance Update: FY24 Business Process Improvements

Phillip Mason, Ph.D.
Branch Chief, Western Compliance Assurance Branch
BRS Regulatory Operations Programs
November 14, 2024

# Regulatory Operations Objectives & Goal

Modernize BRS' inspection, compliance, and enforcement processes to reflect experience, knowledge, and the revised regulations

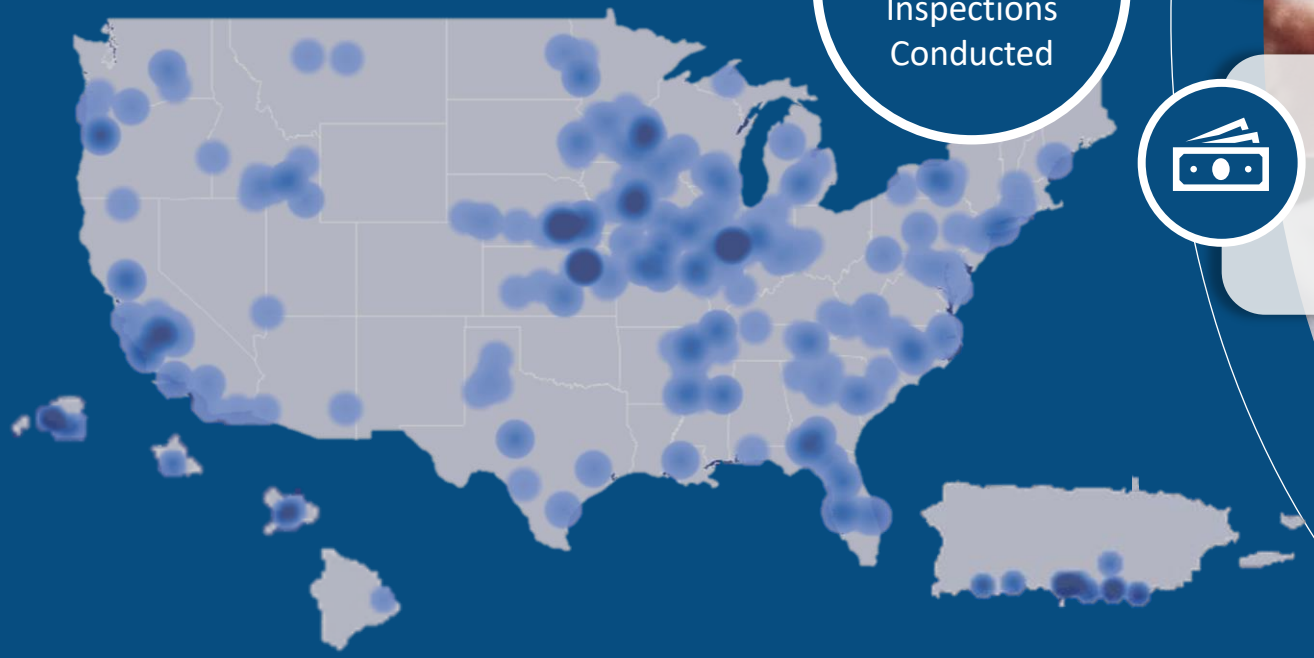
## Measurable Targets

**Issue 95 percent of noncompliance notices within 14 days of completing an inspection in FY2024**

**Reduce the time from completing an inspection to issuing any noncompliance notice from 48 days on average in FY2023, to 14 days on average in FY2024**

# Challenge

Optimize BRS resources and protection goals by emphasizing inspections of higher-risk trials



**542**
Inspections Conducted

**Refreshed risk-based inspection selection model**

**Reduced repeat travel to the same field location to inspect similar trials under separate permits**

# Challenge

Complex review processes caused delays in notifying permittees of noncompliance

1

**Rapidly Resolve Clearly Compliant Inspections**

- Reduced 2 handoffs and 9 tasks

2

**Improve Communication Between Inspection and Compliance Teams**

- Sped up handoffs to Evaluation Team
- Reduced 2 handoffs

3

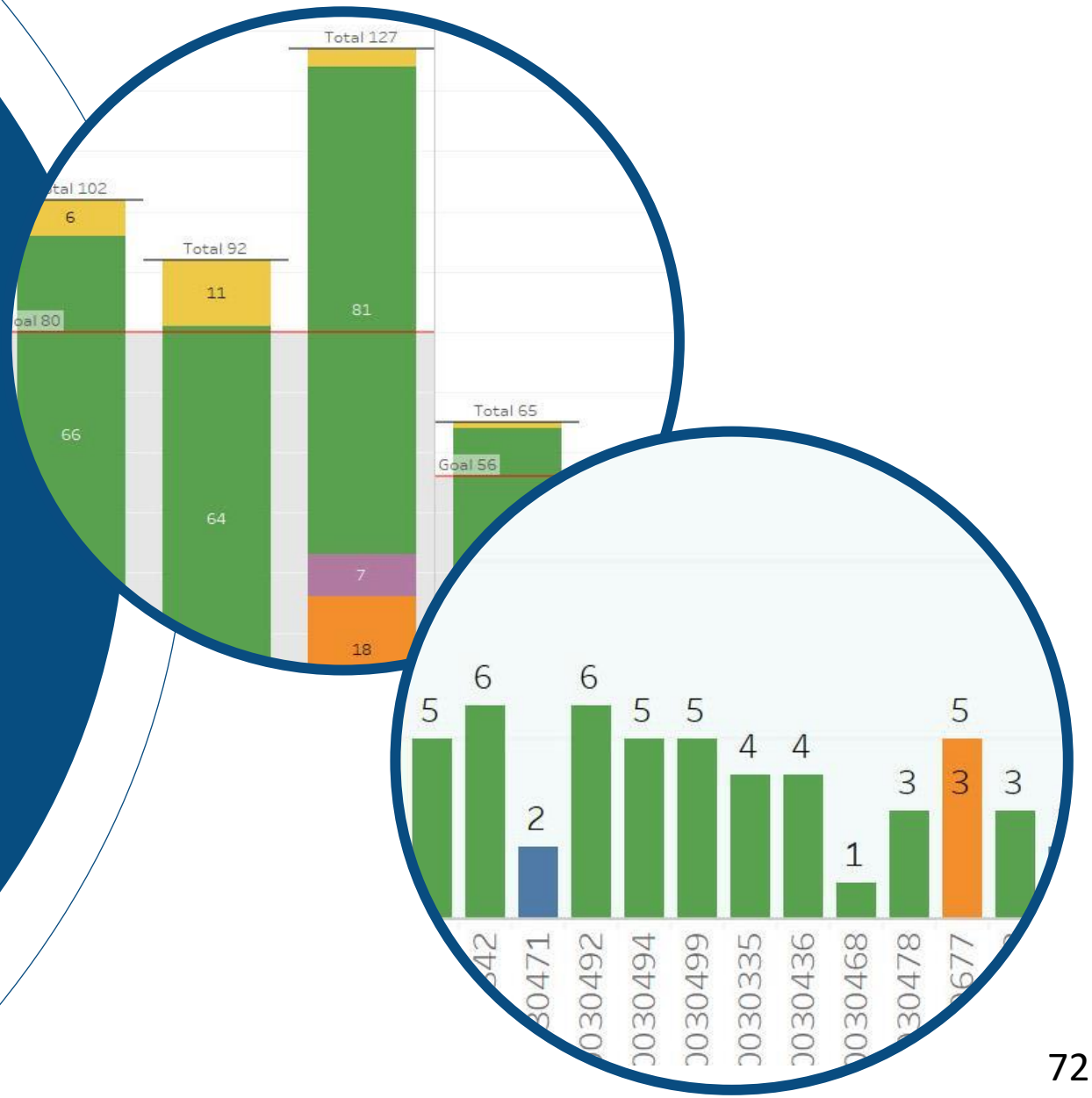
**Use Standard Templates to Collect Information During Inspections**

# Challenge

Develop tools to track process times

1. **Create new APHIS online permitting interface fields**
   - Auto-populate, if applicable
   - Track metric data
2. **Build Dashboard**
   - Time in process
   - Scheduled inspections timeline
   - Inspection outcomes
   - Totals per month
3. **Future**
   - Automate data tracking
   - Publish searchable reports and dashboards online

## Examples of our Inspection Visuals



# Challenge

Develop a strategy to quickly identify and assess noncompliance trends

## Actions

1. Created new categories that describe the nature of each incident
2. Prepared training on assigning categories to incidents to promote consistency
3. Developed reports, charts, and dashboards to automate analysis

# Challenge

Reduce recurrence of noncompliance in regulated field trials

- Developed a strategy for progressive enforcement for repeated noncompliance
- Increased proactive engagements based on compliance trends
- Enhanced cross-collaboration with APHIS' Investigative and Enforcement Services

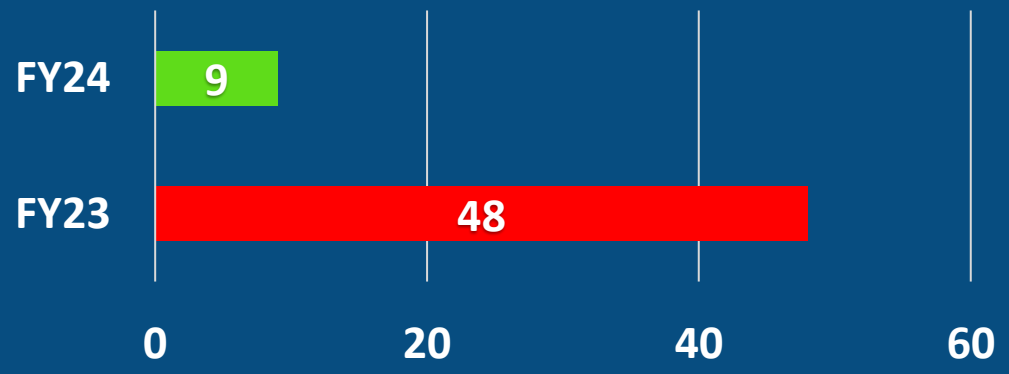
# Results

## Percentage of Noncompliance Notices Issued within 14 Days

FY23 15%

FY24 85%

## Average Number of Days to Send Noncompliance Notices



# Next Steps

1. Analyze inspection data from updated inspection selection protocol and refine, as appropriate
2. Measure and monitor impacts of implemented initiatives
3. Implement additional BPI process improvements

# Acting on Your Feedback

*Guide to Submitting Reports and Notices*

**Annual In Season/Post-Termination Volunteer Reports**

Monitoring Period End Date is not a required field anymore

**Field Test Reports**

Defaulted to "No"

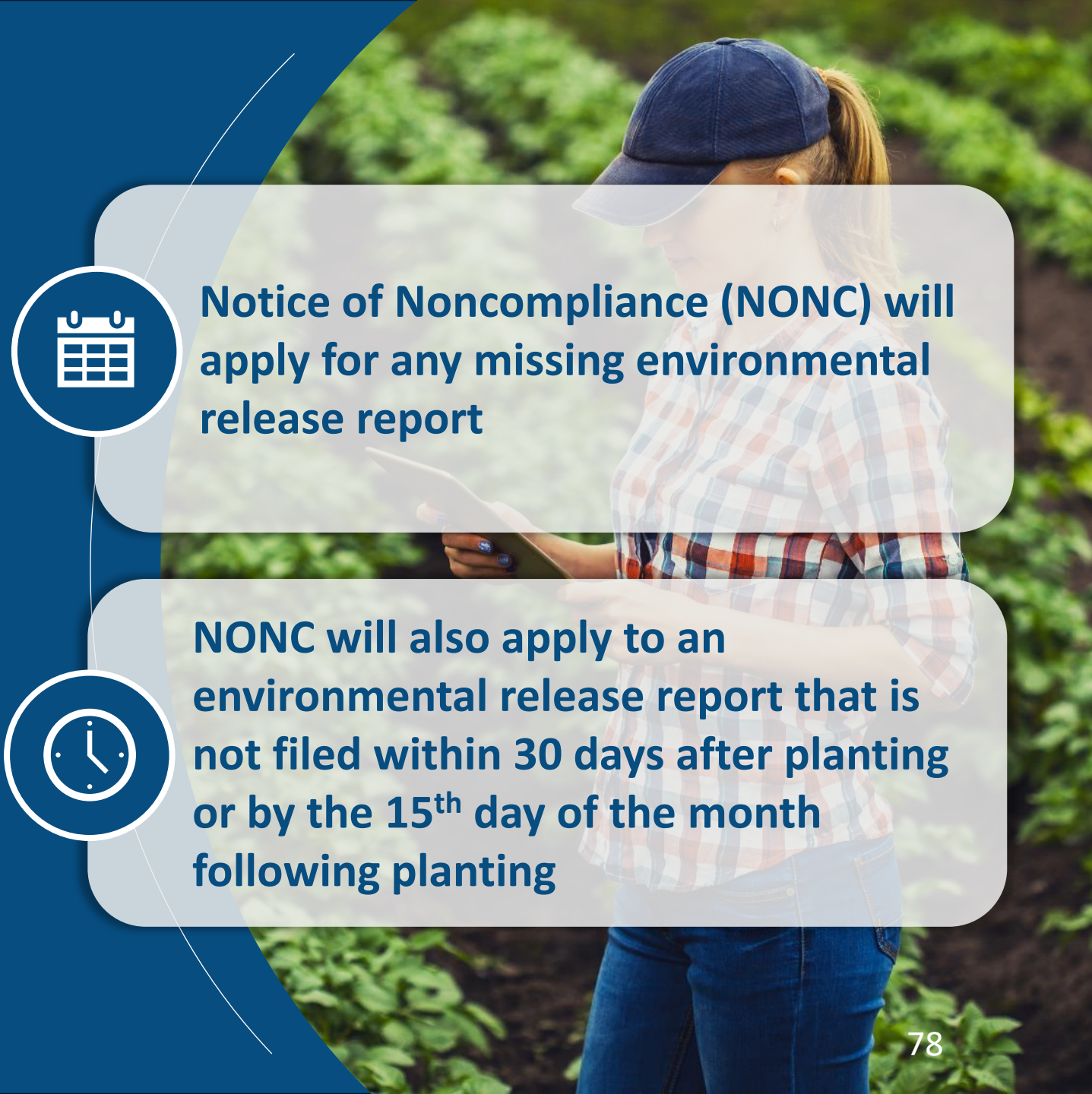
- Unexpected Effects
- Deleterious Effects
- Any Planting Material Still Growing

**No Planting Submission in Planting/Release Report**

- No Unique ID required
- No Release Date required

# Environmental Release Report Due Date Change

Based on feedback received from stakeholders, the due date for environmental release reports has now changed from 15th day of the month following planting to within 30 days after planting.



**Notice of Noncompliance (NONC) will apply for any missing environmental release report**

**NONC will also apply to an environmental release report that is not filed within 30 days after planting or by the 15th day of the month following planting**

# Thank You!

# BRS Efforts to Improve Oversight of Modified Microorganisms

Zachary Schultzhaus, Ph.D.
Biological Scientist
BRS Biotechnology Risk Analysis Programs
November 14, 2024

# Modified Microorganisms

*2024 Projects*

**1**

**PERMITTING**
Streamlining Processes and Improving Efficiency

**2**

**REGULATORY CLARITY & COORDINATION**
Interactive Tool

**3**

**STAKEHOLDER OUTREACH & FUTURE AIMS**
Request for Information

# Streamlining Microbial Permitting

*Microorganism permitting needs differ from plants*

- Greater variety of tools for modification
- Faster turn-around time for new modifications
- More modified species overall

**More Information:**
*Draft Guide for Submitting Permits for Microorganisms Developed using Genetic Engineering*

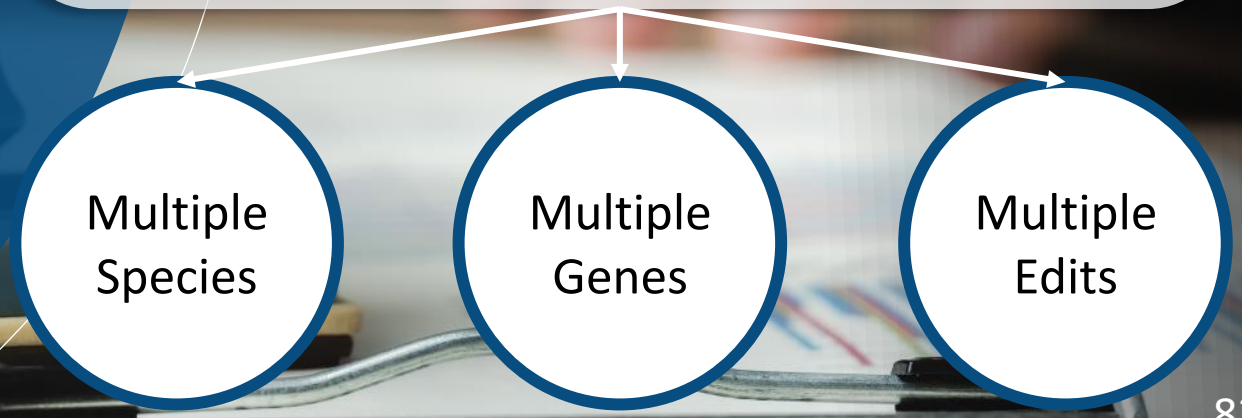
# Streamlining Microbial Permitting

*Permitting application refinements*

**Three-year permits for interstate movement and importation**

**Interstate movement between contained facilities only (excluding greenhouses)**

- May submit a single permit for multiple species within a kingdom
- A single construct submission may cover:




**More Information:**
*Draft Guide for Submitting Permits for Microorganisms Developed using Genetic Engineering*

# Interactive Tool

Assists users with understanding regulations for modified microorganisms by using a series of questions that lead to regulatory requirements based on product, activity, and organism

**Available now on the Unified Website**

- **Regulatory outcomes – what is needed (and what may not be)**
- **Links to guidance documents, data requirements, and direct agency contacts**

# Request for Information

## *Steps for publication*

### May 2020

***Update to APHIS Biotechnology Regulations***

Comments on the proposed rule requested APHIS develop a similar process to evaluate the regulatory status of microorganisms based on their plant pest risk

### September 2022

***Executive Order 14081 on Advancing Biotechnology***

Commenters expressed concerns about clarity regarding the regulation of modified microorganisms, and desire for exemptions regulatory pathways for commercialization for these organisms

### May 2023

***BRS Draft Guide for Submitting Permit Applications for Microorganisms***

BRS published a draft guide to assist applicants with applying for permits for microorganisms

### November 2023

***BRS Initiates the Development of RFI***

BRS initiates the development of an RFI to obtain input specifically focused on identifying pathways to commercialization for products containing modified microorganisms

# Request for Information

*Format, Publication, and Comments*

**Format**

Background (introduction and motivation)

Six guiding questions for respondents

**Date**

Published in the Federal Register July 2, 2024

60-day open comment period: Jul 2-Sep 3, 2024

**Response**

50 comments were received

- 28 individuals (18 anonymous)
- 12 businesses
- 7 non-profit organizations or associations
- 3 universities

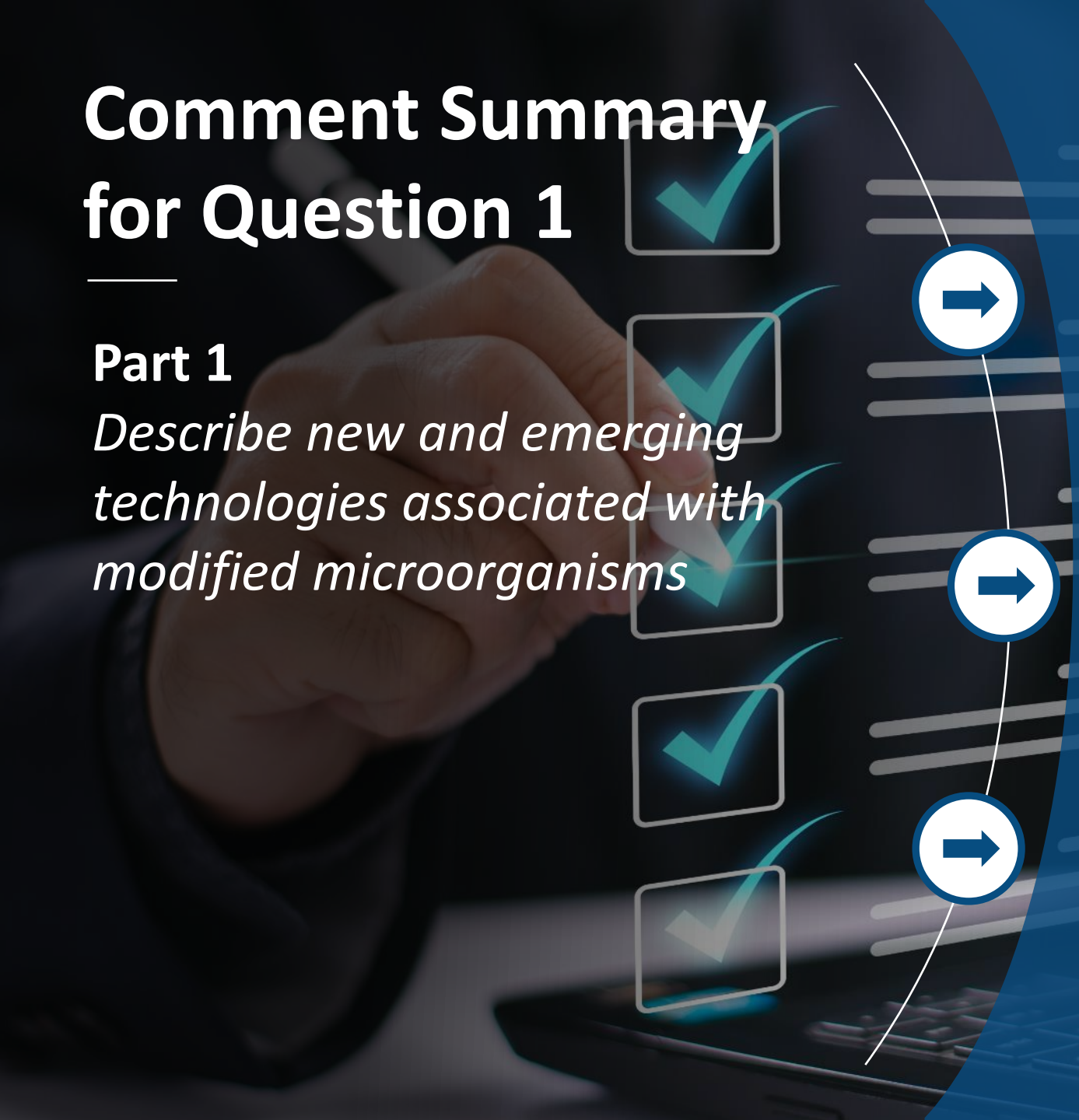
**Review**

- Established a BRS team to review comments
- Extracted responses to specific questions
- Identified themes and common recommendations (including support and opposition)

# Comment Summary for Question 1

**Part 1**

*Describe new and emerging technologies associated with modified microorganisms*

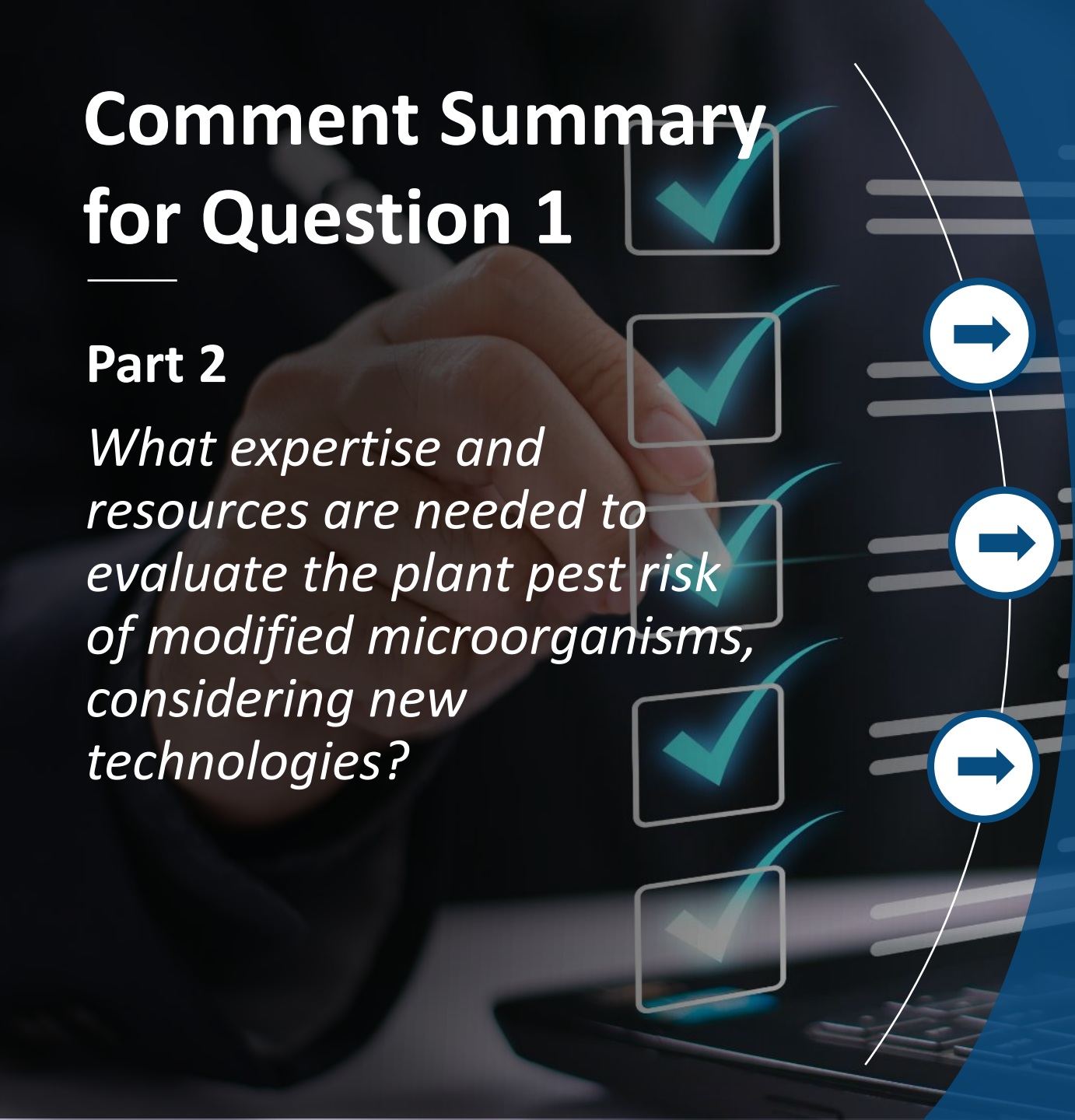


- Advanced tools to edit and modify genomes - CRISPR, base alteration, RNA silencing
- In situ microbial tools – bioremediation, probiotics, biocontrol, plant growth promotion, modification of whole communities
- Synthetic biology – biomaterials, pharmaceuticals

# Comment Summary for Question 1

**Part 2**

*What expertise and resources are needed to evaluate the plant pest risk of modified microorganisms, considering new technologies?*



- Microbial ecology (including plant microbiomes)
- Computational and synthetic biology
- Genetics (phylogenetics, genomics, and evolutionary genetics)

# Comment Summary for Question 2

*Describe areas where the clarity and/or efficiency of regulations governing modified microorganisms could be improved*

- Definitions (e.g., plant pest risk, biological control)
- Resources for understanding how to fulfill requirements
- Update permit analysis and conditions (devitalization, persistence, PPQ alignment)
- Collaborate with other agencies to discuss and mitigate regulatory overlap issues

# Comment Summary for Question 3

**Part 1**

*Describe features of a modification that changes plant pest risk*

- Consider the product and intent, rather than development process
- Biological features – dormancy, gene transfer, plant harm
- Tiered approach – group modified microorganisms by risk category
- Ecological impact – perform holistic assessment on environment, plants, and human health

# Comment Summary for Question 3

**Part 2**
*What should be considered when determining whether modifying a biocontrol organism results in it posing a plant pest risk?*

- Biological features (mechanism, specificity)
- Consider the context in which the organism is used (establishment)
- Discuss risk among Coordinated Framework

# Comment Summary for Question 4

*How should APHIS regulate modified microorganisms with multiple uses to ensure efficient and appropriate oversight?*

- Nearly every microorganism can have multiple impacts – Identify leading agency based on purpose of use
- Establish Memoranda of Understanding with other agencies in the framework
- Perform a holistic assessment beyond plant pest risk in the absence of a coordinating office

# Comment Summary for Question 5

*Should APHIS consider risk-based exemptions for certain types of modified microorganisms (examples)?*

Five comments did not support exemptions because of the novelty of modified microorganisms

Eighteen other respondents laid out criteria for exemptions

- **Familiarity** – history of use, purpose, common in agricultural locations (establishment), known changes/effects of modifications
- **Coordination** – apply same exemptions as for plants, use Tier 1 list published by EPA's Office of Pollution Prevention and Toxics

Respondents asked for public communication of decisions about plant pest risk of microorganisms

# Common Themes

*Recommendations*

1. **Coordinated Framework: Centralized portal for submitting applications to obtain decisions for genetically modified microorganisms/products**
2. **Transparency: Communicate and explain methods for determining the plant pest risk of microorganisms. SOP examples for field trials.**
3. **Permits: Collaborate with PPQ for conditions when the modification does not change the plant pest risk. Establish a clear pathway for scaling up field trials (encourage data collection).**
4. **Look to exemptions and Regulatory Status Review processes already developed for plants**

# RFI Next Steps

1. Further response analysis
2. Compile resources provided (literature)
3. Identify ways to act on comments
4. Discuss improvements with other programs and agencies
5. International outreach

# Thank You!

# Final Exemptions

Neil Hoffman, Ph.D.
BRS Science Advisor
November 14, 2024

# Overview

- What we heard that was most influential
- Where we ended up
- Practical tips on how to apply the exemptions
- What is required for submitting an exemption
- What to do if a permit or RSR includes plants that now qualify for exemption

# Existing and Proposed Exemptions

1

**Current Exemptions**

1 targeted modification
- (b)(1) - indel
- (b)(2) - single nucleotide substitution
- (b)(3) - gene in the gene pool

2

**Update Exemptions**

(b)(4) update the modifications that are achievable through conventional breeding based on science and breeding advances

3

**5 Proposed Exemptions**

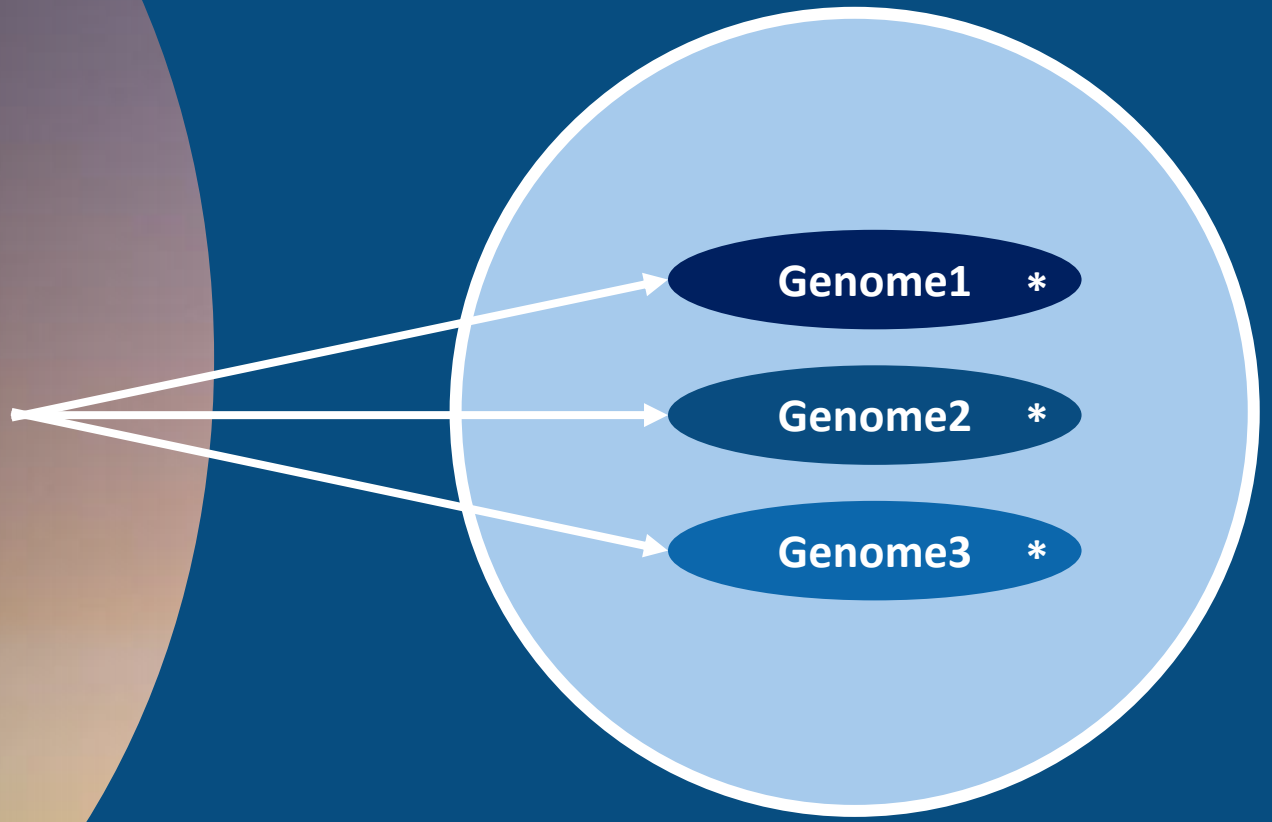
- Flexibility in making indels
- Deletion of any size
- Polyploids
- Simultaneous and sequential modifications

# What We Heard from Stakeholders

- The proposed exemptions are too complicated
- Exemptions should apply equally to polyploids
- 4 simultaneous or sequential modifications are overly limiting
- Sequential modifications should not “require” a “voluntary” confirmation (CR)

# What We Heard from Stakeholders

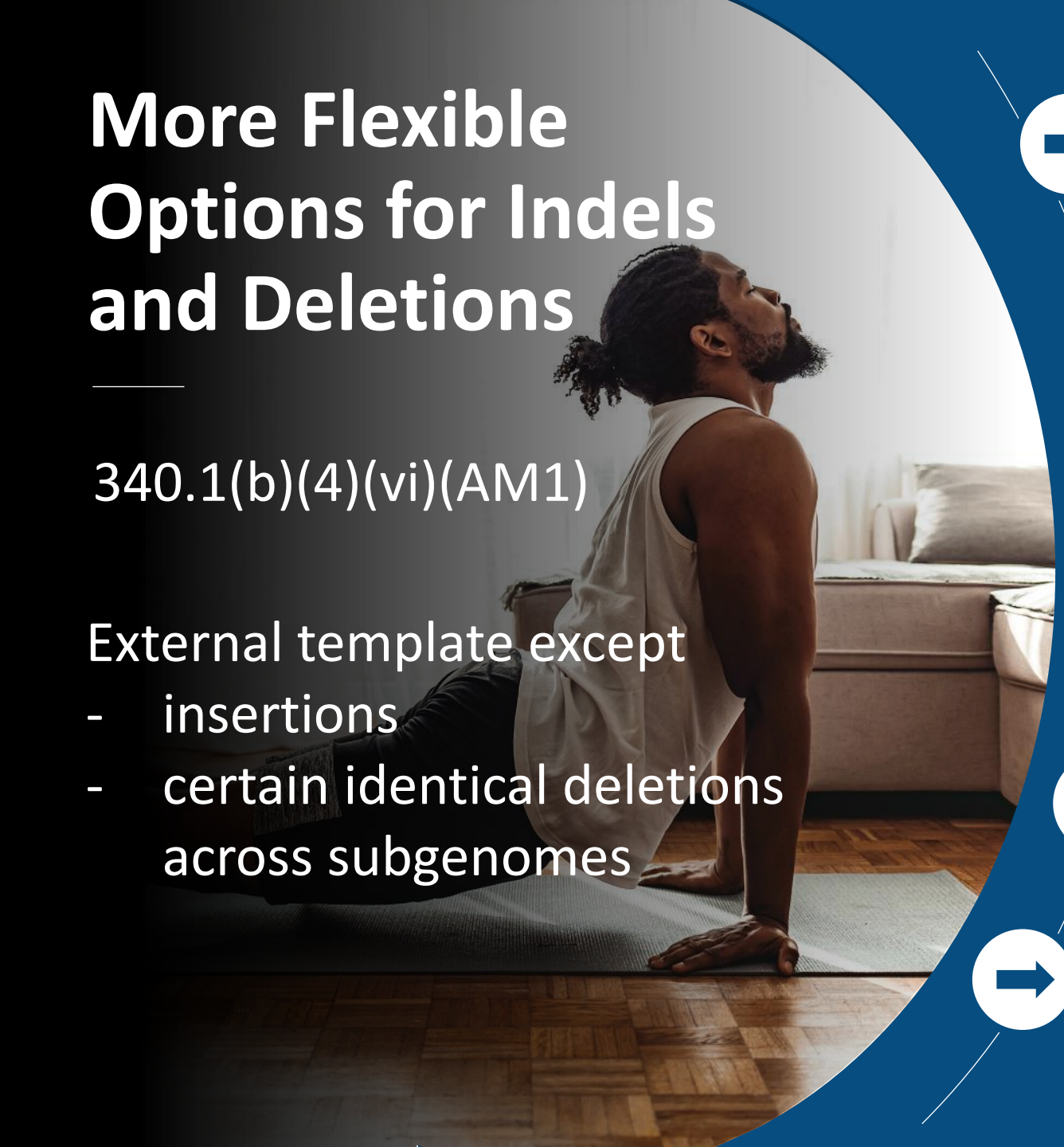
Identical modifications
Across subgenomes of allopolyploids
By conventional breeding



# Where Did We End Up?

- ✕ No distinctions between polyploids
- ✕ No distinction for GOF or LOF
- 2 Five proposed exemptions to two final exemptions

# More Flexible Options for Indels and Deletions



340.1(b)(4)(vi)(AM1)

External template except
- insertions
- certain identical deletions across subgenomes

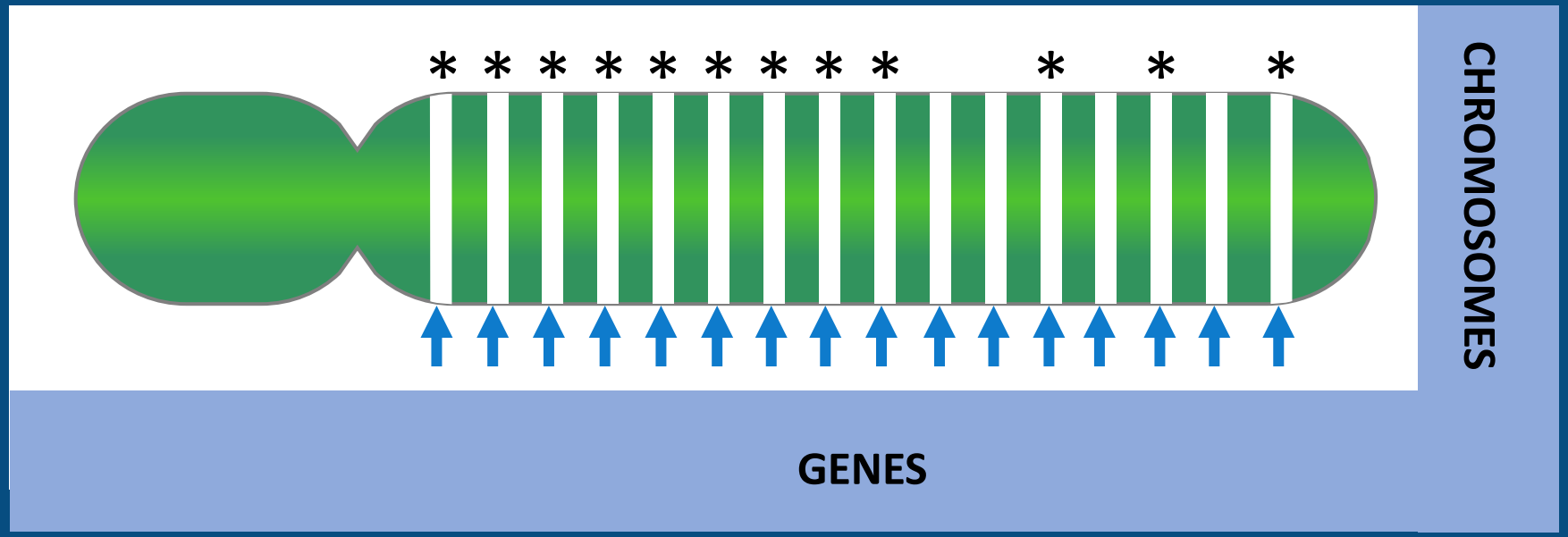
- More than one cut
- Single contiguous deletion of any size
- “GOF from natural repair” means NO use of template
- Silent mutations ok
- Functionally equivalent modifications to alleles counted as single modification
- No foreign DNA in final product

# 340.1(b)(4)(vi)(AM2)- 12 (b) Type Modifications Simultaneously or Sequentially

Applicable to any plants not subject to 7 CFR part 340 confirmation, petition, or RSR processes




## Only 1 Modification/Gene



# Confirmation Request (CR) Process Remains Voluntary

No hypothetical plants for CR process

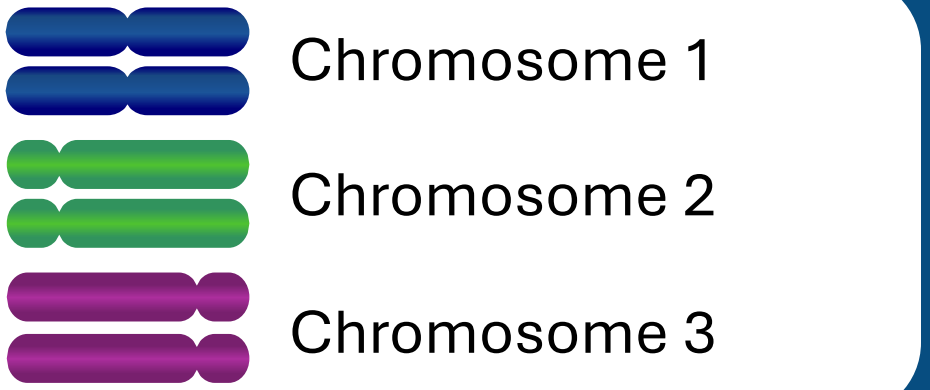
**Intended Phenotype**

**Genotype**

**Viability**

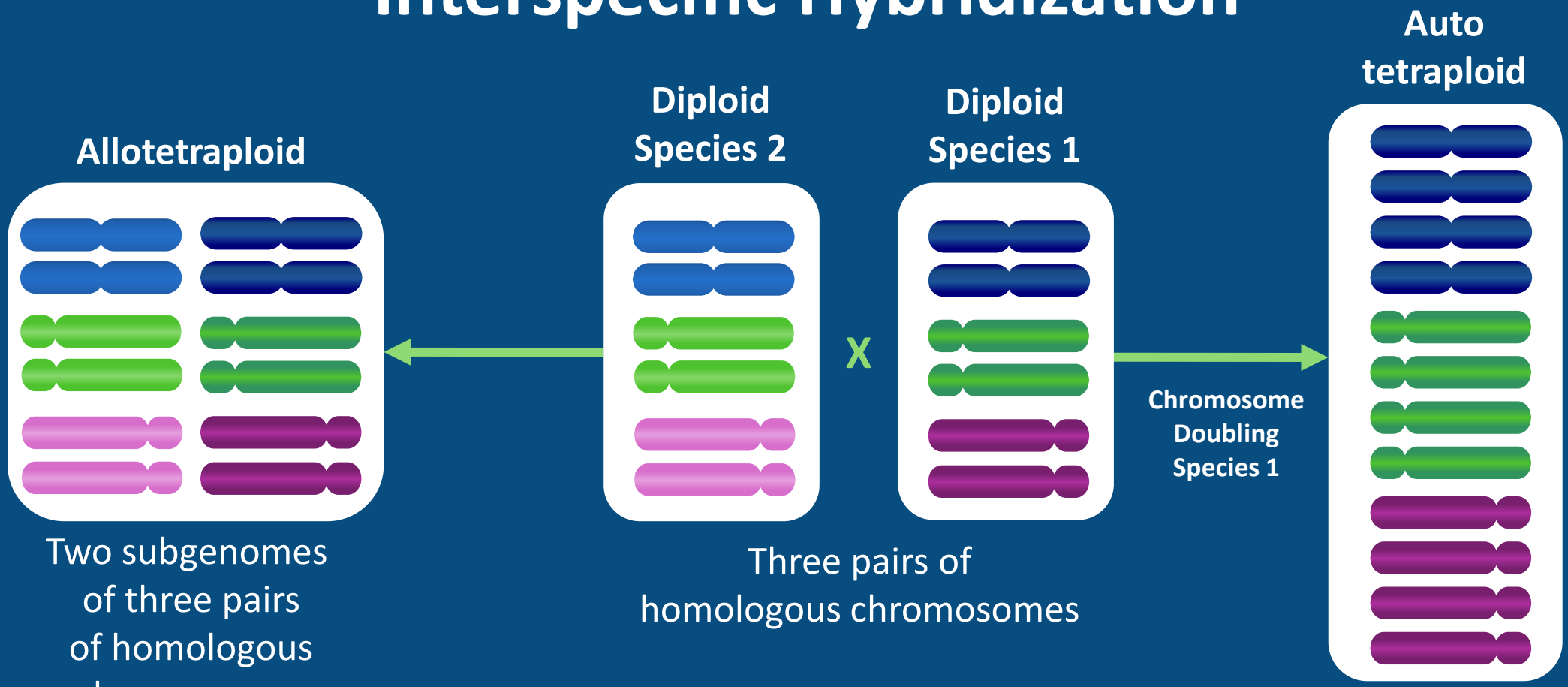
# Hypothetical Plant with Three Chromosomes

**Diploid**

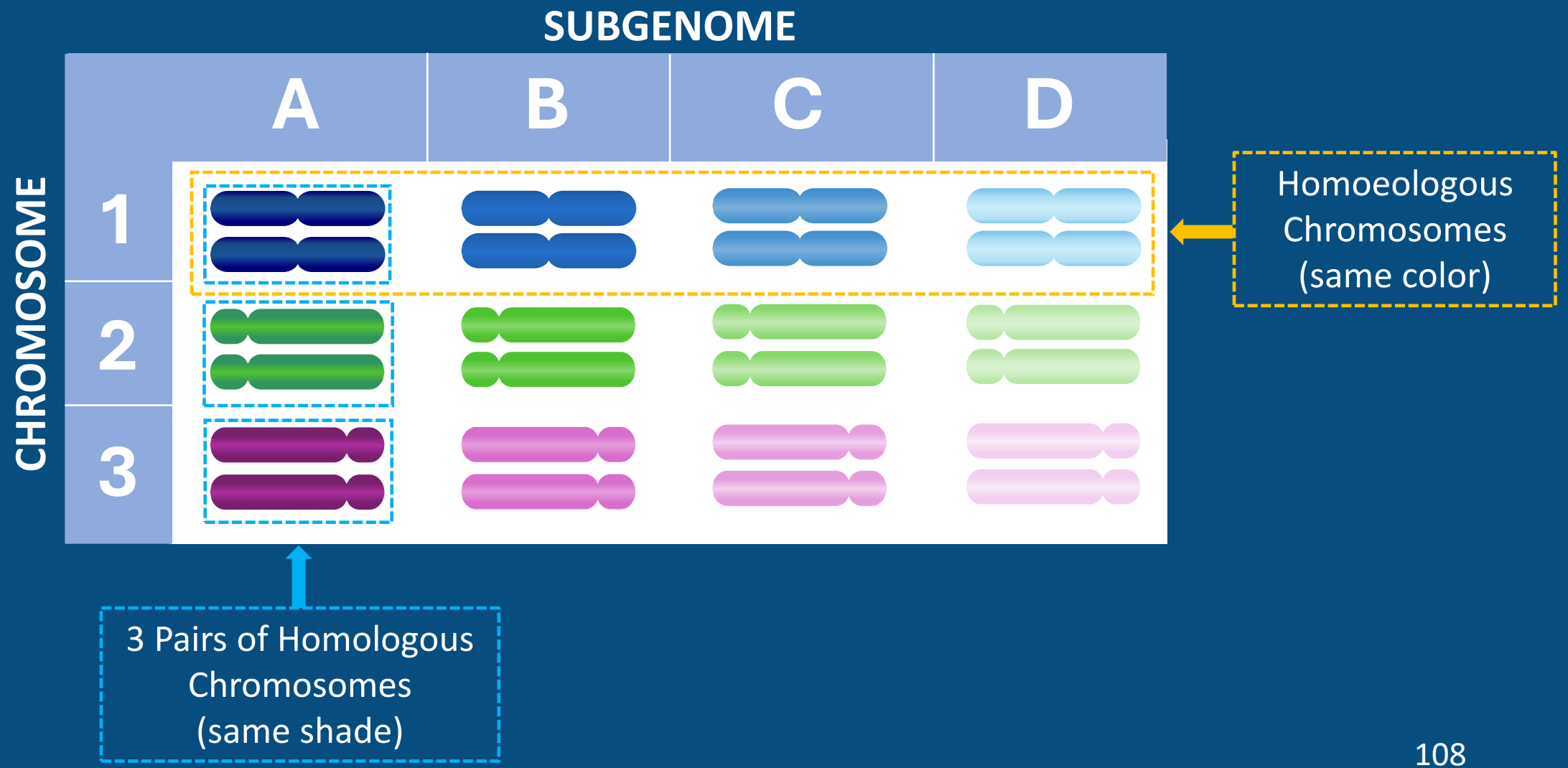



One pair of
homologous chromosomes
for each chromosome

# Interspecific Hybridization



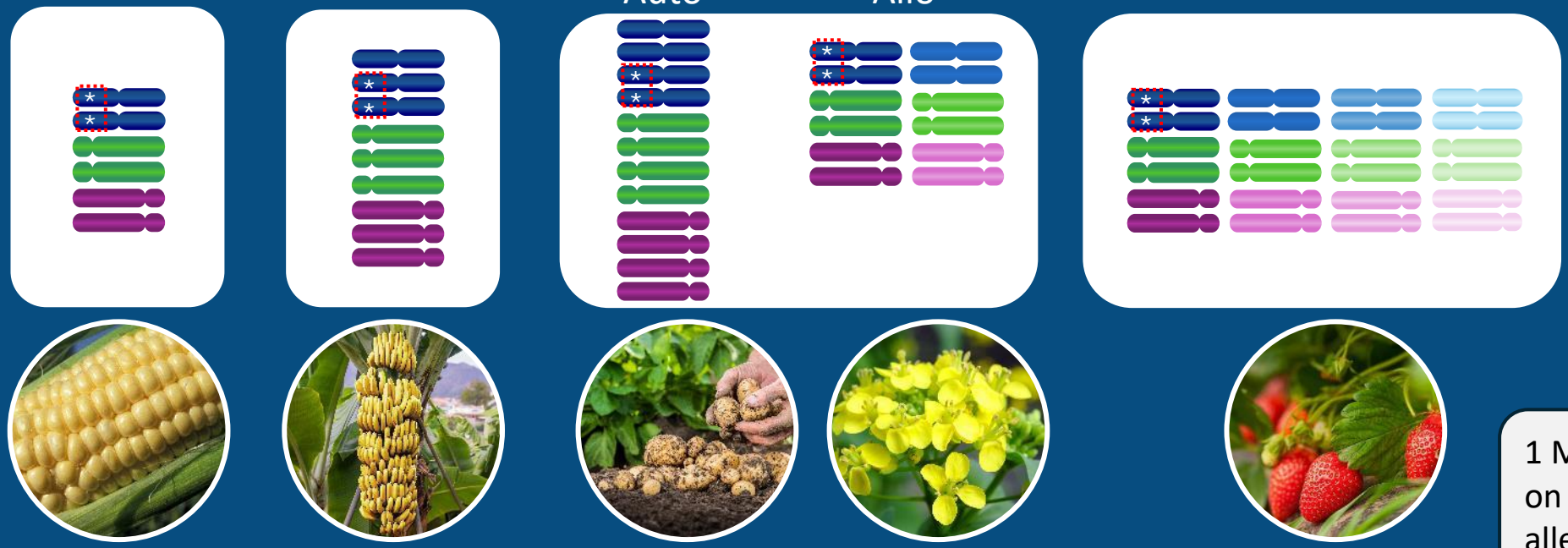
# Allopolyploid



# (b)(1)-A targeted DNA break with no repair template (i.e., an indel modification)

Only one cut - No external template - One pair of homologous chromosomes

**Diploid 2N** | **Triploid 3N** | **Tetraploid 4N** (Auto, Allo) | **Allo-octaploid 8N**

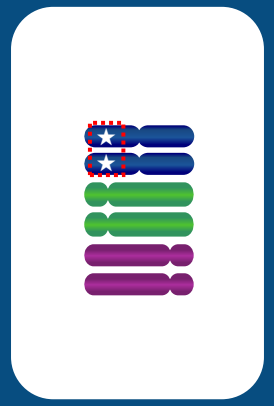


1 Mod.=1 Indel (*) on one or both alleles

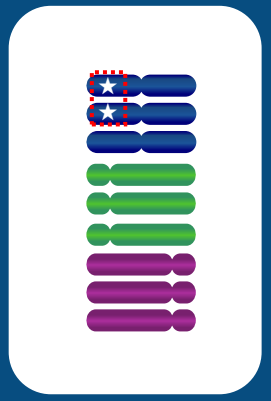
# (b)(2)-A targeted single base pair substitution

External template allowed - One nucleotide change - One pair of homologous chromosomes

**Diploid 2N**



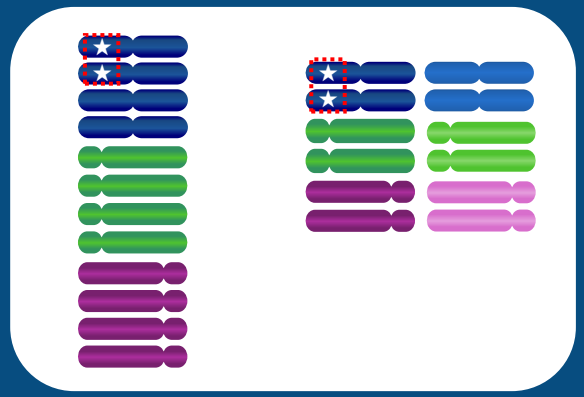
**Triploid 3N**



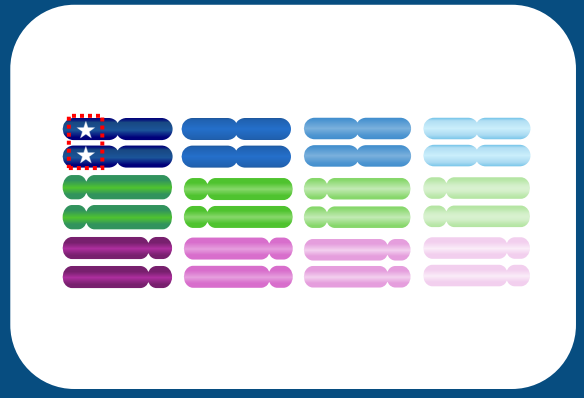
**Tetraploid 4N**

Auto

Allo



**Allo-octaploid 8N**

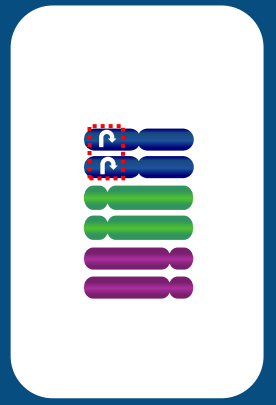


1 Mod.= 1 SNS (★ ) on one or both alleles

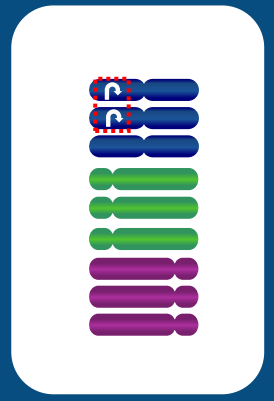
# (b)(3)-Introduction of gene or structural variant from the plant's gene pool

External template allowed - No limit on edits to recreate gene - One pair of homologous chromosomes

**Diploid 2N**



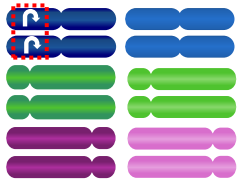
**Triploid 3N**



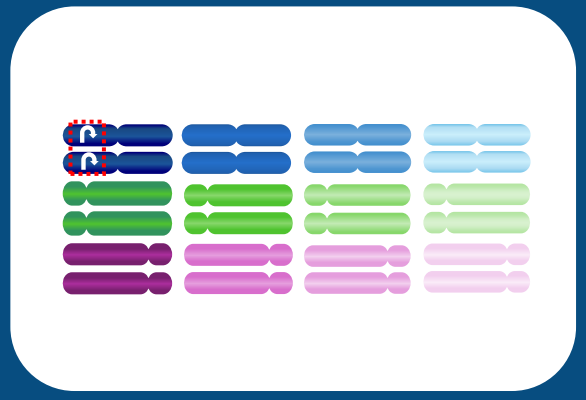
**Tetraploid 4N**

Auto

Allo



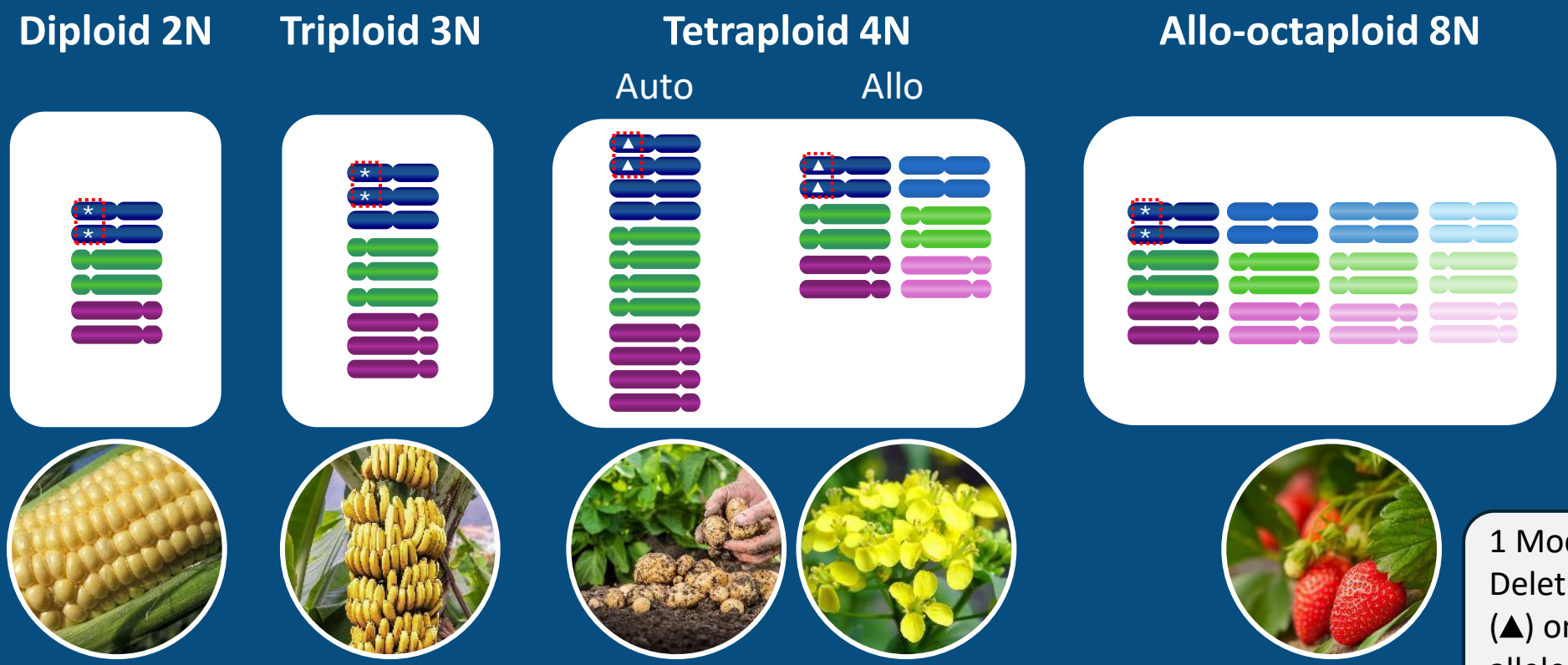
**Allo-octaploid 8N**



1 Mod.= 1 allele addition or replacement (↷) on one or both alleles

# AM1- A targeted indel modification or deletion of any size

Single targeted location - Indels on both alleles need not be identical - External repair template for deletions



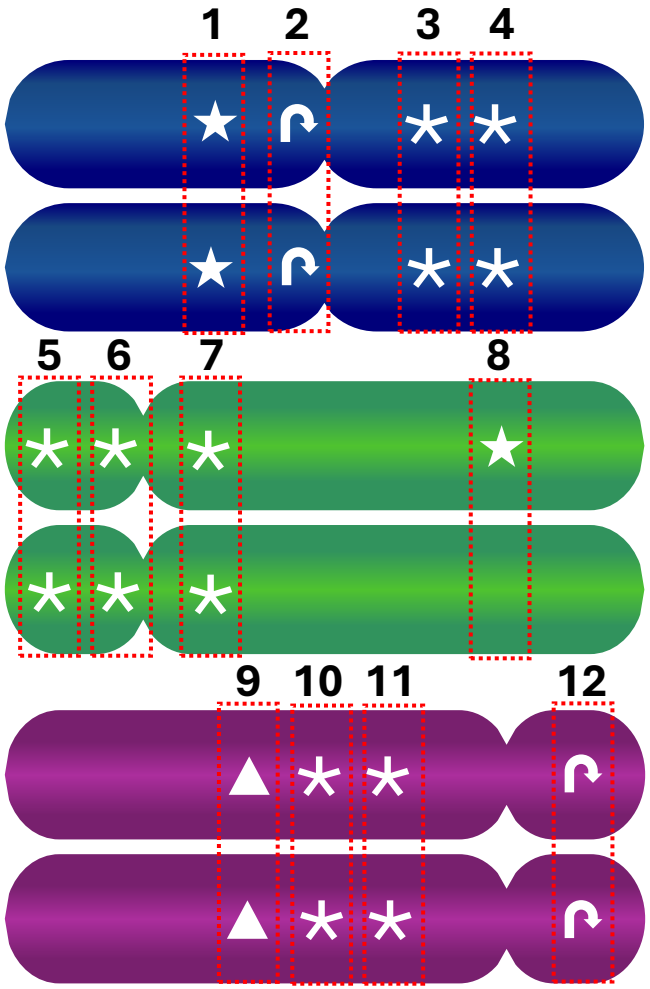
# AM2 Up To Twelve Modifications

## Diploid 2N

Mod: 4
Loci: 4

Mod: 4
Loci: 4

Mod: 4
Loci: 4




**One modification on one or both alleles**

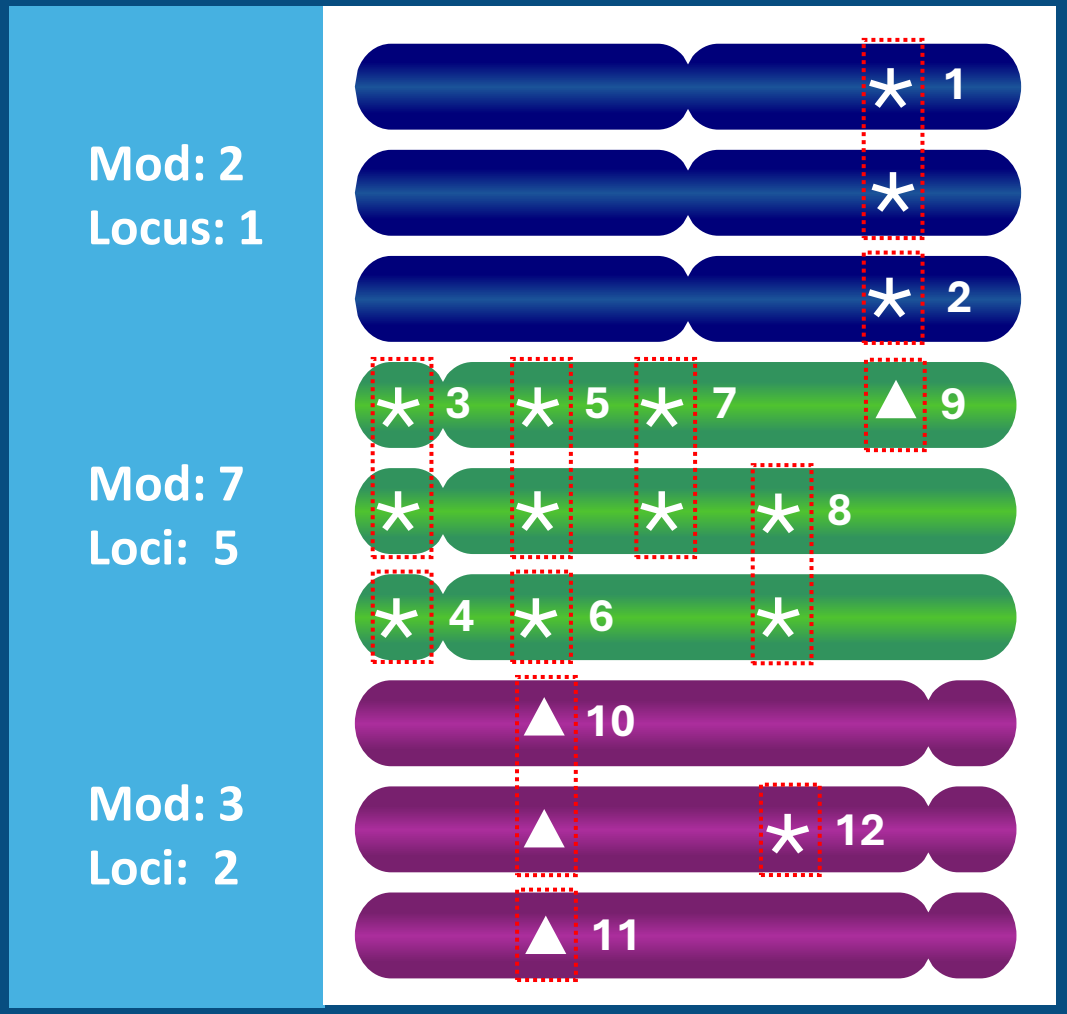
- ∗ Indel (AM1)
- ▲ Deletion of any size (AM1)
- ★ Single base pair substitution-(b)(2)
- ↷ Allele replacement-(b)(3)

AM2: AM1(8), ((b)(2))(2), ((b)(3))(2)

1. (b)(2) (base pair substitution)
2. (b)(3) (allele replacement)
3. AM1 (indel)
4. AM1 (indel)
5. AM1 (indel)
6. AM1 (indel)
7. AM1 (indel)
8. (b)(2) (base pair substitution)
9. AM1 (deletion)
10. AM1 (indel)
11. AM1 (indel)
12. (b)(3) (allele replacement)

# AM2 Up to Twelve Modifications

**Triploid 3N**




AM2: AM1(12)
1. AM1 (indel)
2. AM1 (indel)
3. AM1 (indel)
4. AM1 (indel)
5. AM1 (indel)
6. AM1 (indel)
7. AM1 (indel)
8. AM1 (indel)
9. AM1 (deletion)
10. AM1 (deletion)
11. AM1 (deletion
12. AM1 (indel)

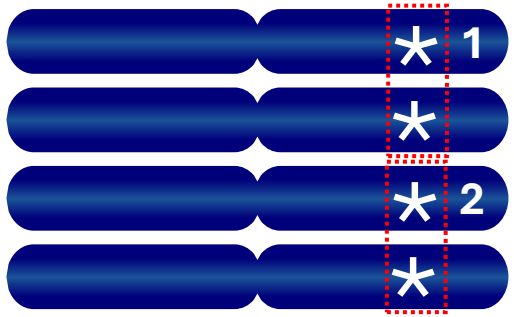
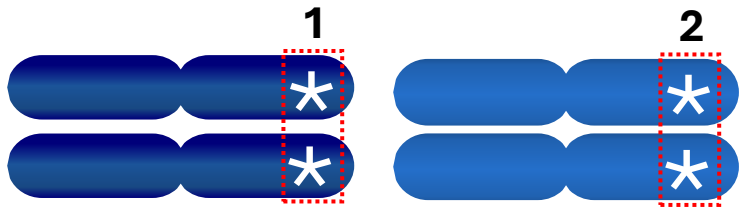
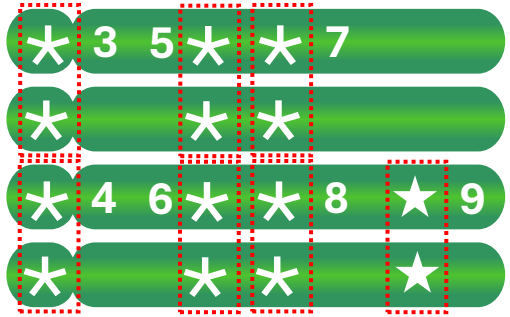
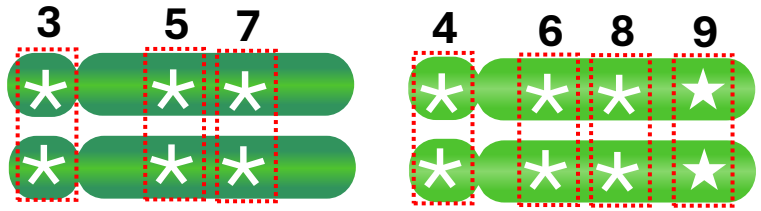
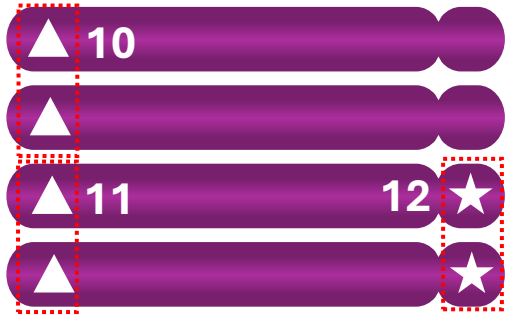
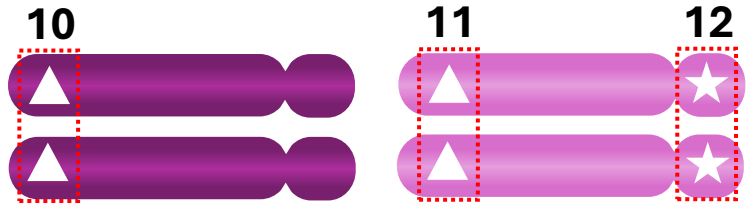
**One modification on one or both alleles**

* Indel (AM1)
▲ Deletion of any size (AM1)

# AM2 Up To Twelve Modifications

**Tetraploid 4N**

AM2:
AM1(10), ((b)(2))(2)

| | Autopolyploid | Allopolyploid |
|---|---|---|
| Mod: 2<br>Locus: 1 |  |  |
| Mod: 7<br>Loci: 4 |  |  |
| Mod: 3<br>Loci: 2 |  |  |

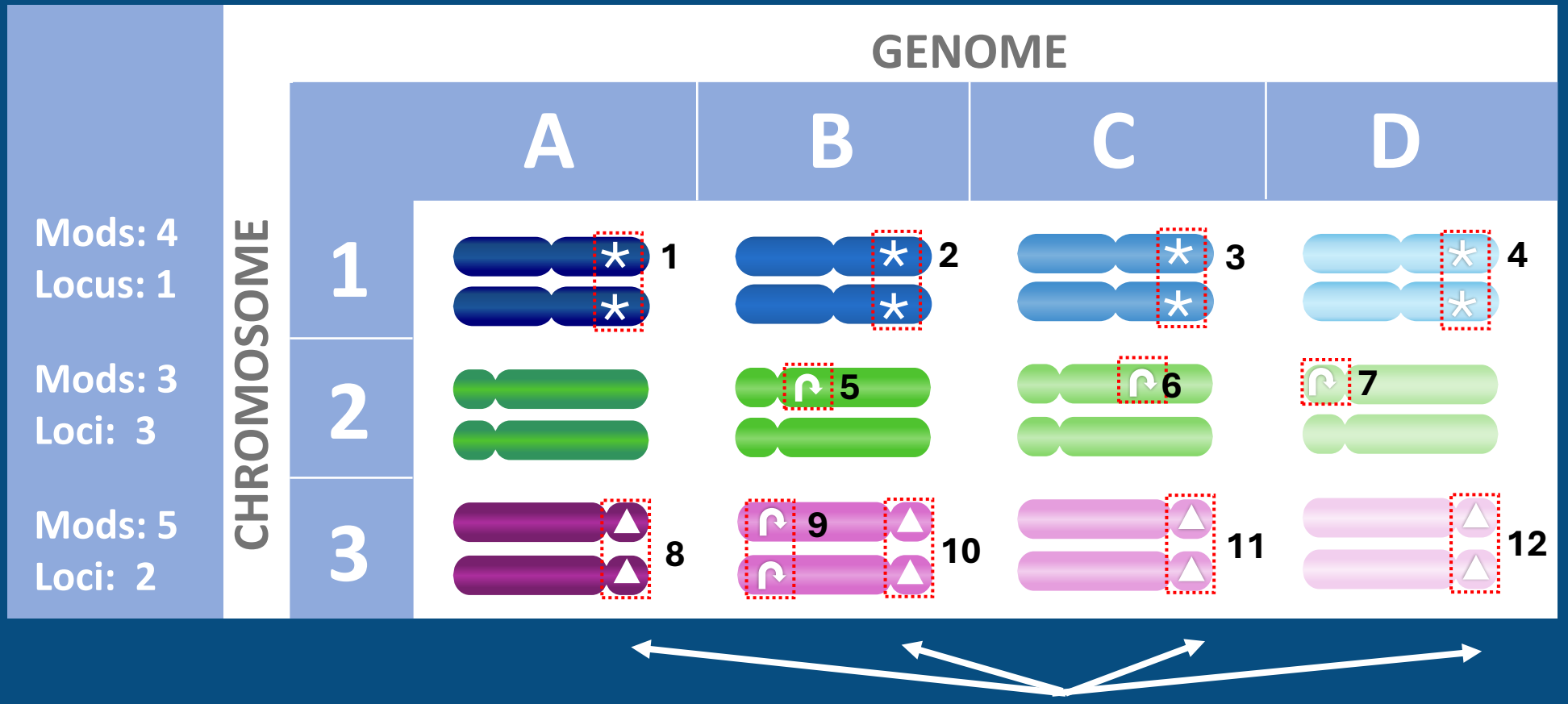
**One modification on one or both alleles**

- ✶ Indel (AM1)
- ▲ Deletion of any size (AM1)
- ★ Single base pair substitution-(b)(2)

# AM2 Up To Twelve Modifications

**Allo-octaploid 8N**

AM2:
AM1(8), ((b)(3))(4)




**One modification on one or both alleles**

* Indel (AM1)

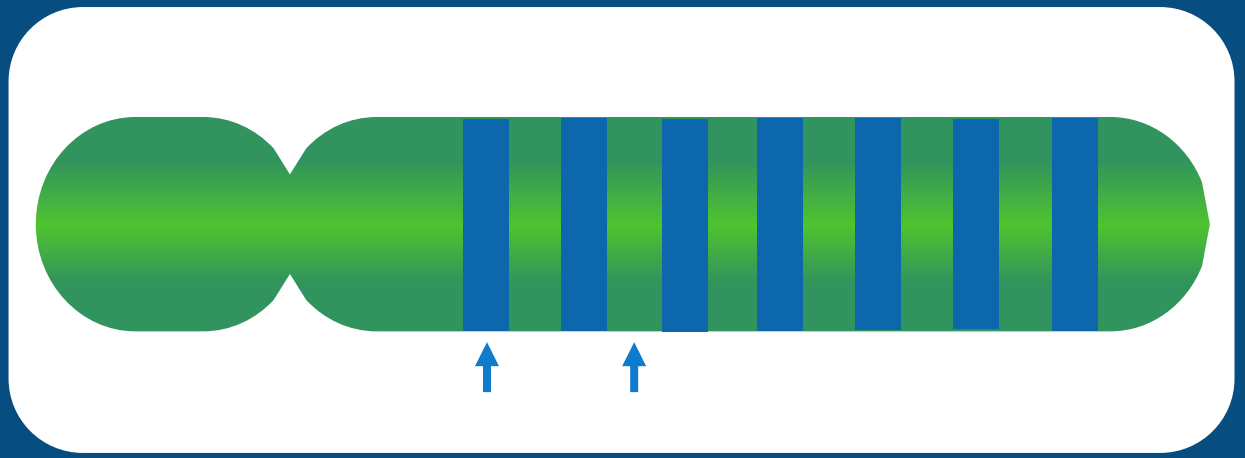
▲ Deletion of any size (AM1)

Allele addition or replacement (b)(3)

*Note: An external repair template cannot be used to make an AM1 modification across subgenomes when the desired outcome requires making the exact indel or deletion*

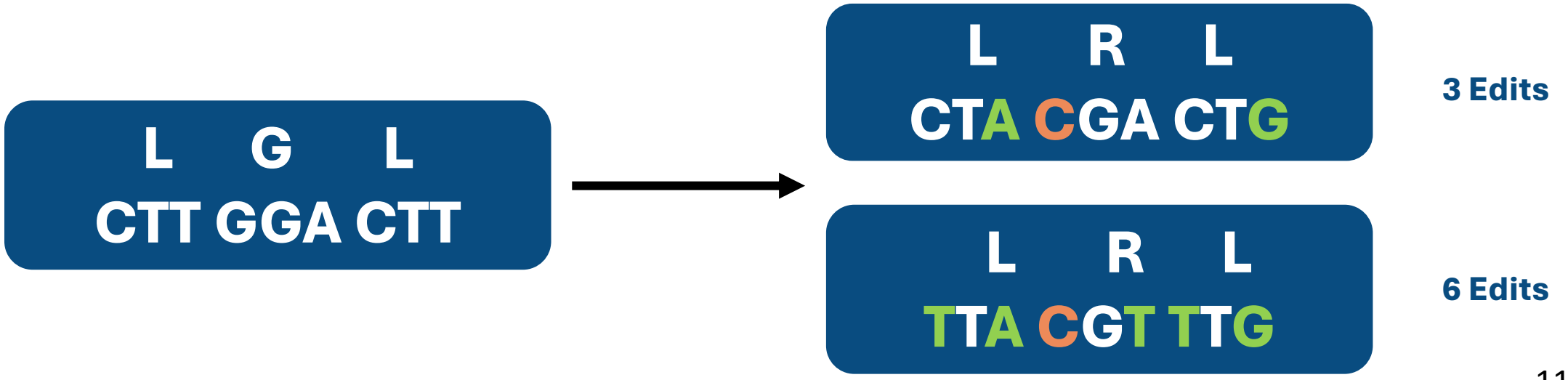
# When Multiple Edits Count as One Modification

Two guide RNAs cut out a portion of a gene or deletion of any size (AM1)



# When Multiple Edits Count as One Modification

One edit functional while other edits have no additional effect. (AM1) or (b2)



# When Multiple Edits Count as One Modification

Gene in gene pool is inserted into the genome or existing gene is edited several times to correspond to a gene/sv in the gene pool (b)(3)

*Nature Genetics (2015) 47: 1494*

***T. aestivum*** **4D hexose transporter: G144; V387**

***T.aestivum Lr67*****: R144; L387**

***T. Aestivum*** **4A hexose transporter: G144; V387**

***T. Aestivum*** **4B hexose transporter: G144; V387**

# Voluntary Confirmation Request Process

*b1-b3*

- Requestor's name, contact information, and email address
- The plant's common name, genus, species, and, if relevant, subspecies
- Plant's ploidy
- Claimed exemption and why the plant qualifies:
  - (b)(1), (b)(2), (b)(3), (AM1), (AM2) or (c)
  - When claiming (AM2), list each modification and number of each (e.g., AM2: (AM1)(10), (b2)(2))

# Voluntary Confirmation Request Process

*b1-b3*

Trait description

Describe genetic modification (type and targeted gene)

Method used to:

1. Make modification
2. Verify modification(s)
3. Reduce/verify modifications to similar sequences
4. Verify absence of foreign DNA

# Voluntary Confirmation Requests

*Additional information for b3*

1. Include the donor organism or the organism on which the modification is based

2. Demonstrate the modification exists in the gene pool

3. The resulting modification is consistent with the original genetic context

# Voluntary Confirmation Requests

*Helpful **optional** information*

1. Function of modified gene and consequences of altered function
   Images of phenotype
2. Molecular Characterization Data
3. DNA sequence of the modification with alignments to the unmodified sequence

# How to Revise Permits and RSR to Remove Exempt Plants

brspermits@usda.gov

rsrrequests@usda.gov

## PERMITS

Pending Application → Remove exempt plants

Permit Issued → Contact BRS to withdraw the permit

## RSRs

BRS will notify submitters of plants that potentially meet the criteria in the notice → Request a consultation

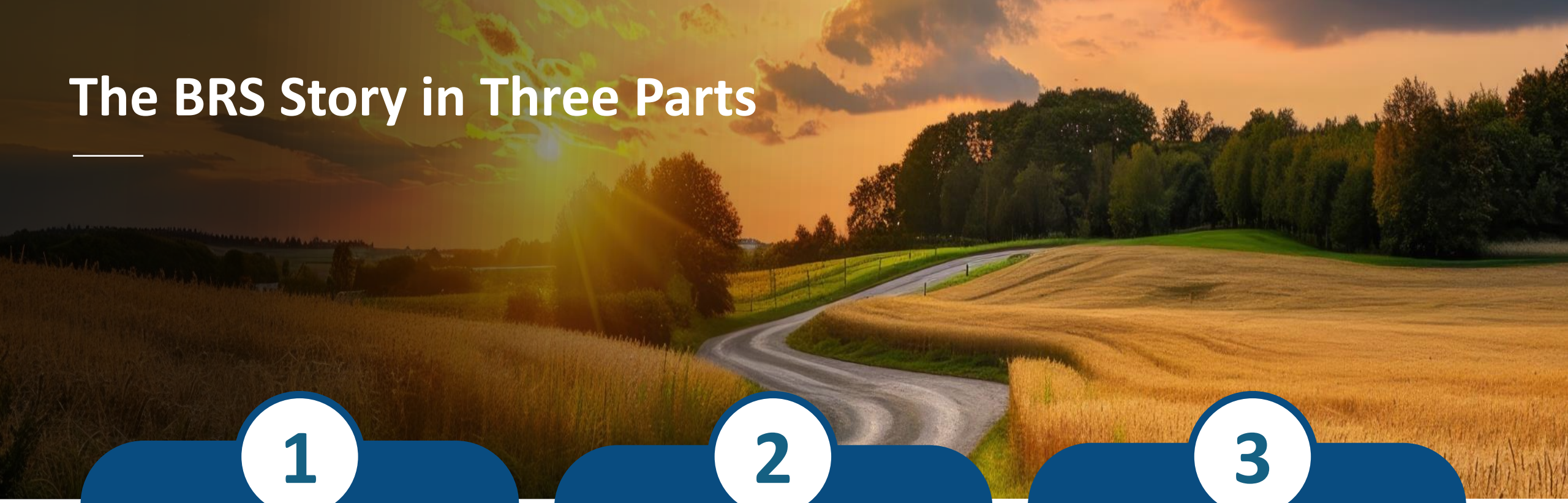
# Thank You!

USDA Animal and Plant Health Inspection Service
U.S. DEPARTMENT OF AGRICULTURE

# APHIS eFile: A BRS Permitting Story

Kham Vongpaseuth, Ph.D.
Biological Scientist
BRS Biotechnology Risk Assessment Programs
November 14, 2024

# The BRS Story in Three Parts



1

**BEGINNING**
Exposition

2

**MIDDLE**
Rising Action

3

**END**
Resolution

# The Beginning: Exposition

*How did we get here?*

**1987**

Paper applications for the movement of products of biotechnology

**2006**

Electronic applications emerge (ePermits)

**2021**

APHIS eFile replaces ePermits

# The Middle: Rising Action

*Challenge Presented*

Bugs and some functionality issues emerged

- Inability to handle large amounts of data
- User Challenges
- Sharing Accounts
- Handling of CBI
- PDF generation, formatting
- External and internal workflow blockers

# The Middle: Rising Action

*Challenge Accepted*

Upgrades:

- March 2022 (project Magnus)
- April 2023 (project Surge)


**Improved user interface which impacted how things are built and displayed on APHIS eFile portal**

**Allowed reliable XML upload of large data to create applications, and self reports**


**Allowed reliable PDF generation of large applications, permits, and self reports**

# The Middle: Rising Action

*Challenge Response*

**1868**

**The number of work items closed out in 3.5 years since APHIS eFile go-live**

**58%**

**The percent of closed work items improving the user experience**

**1068 work items**

# The End: Resolution

*Where are we now?*

**A decently functioning permitting system**

You can make use of flexibilities and system know-how to enhance your customer experience

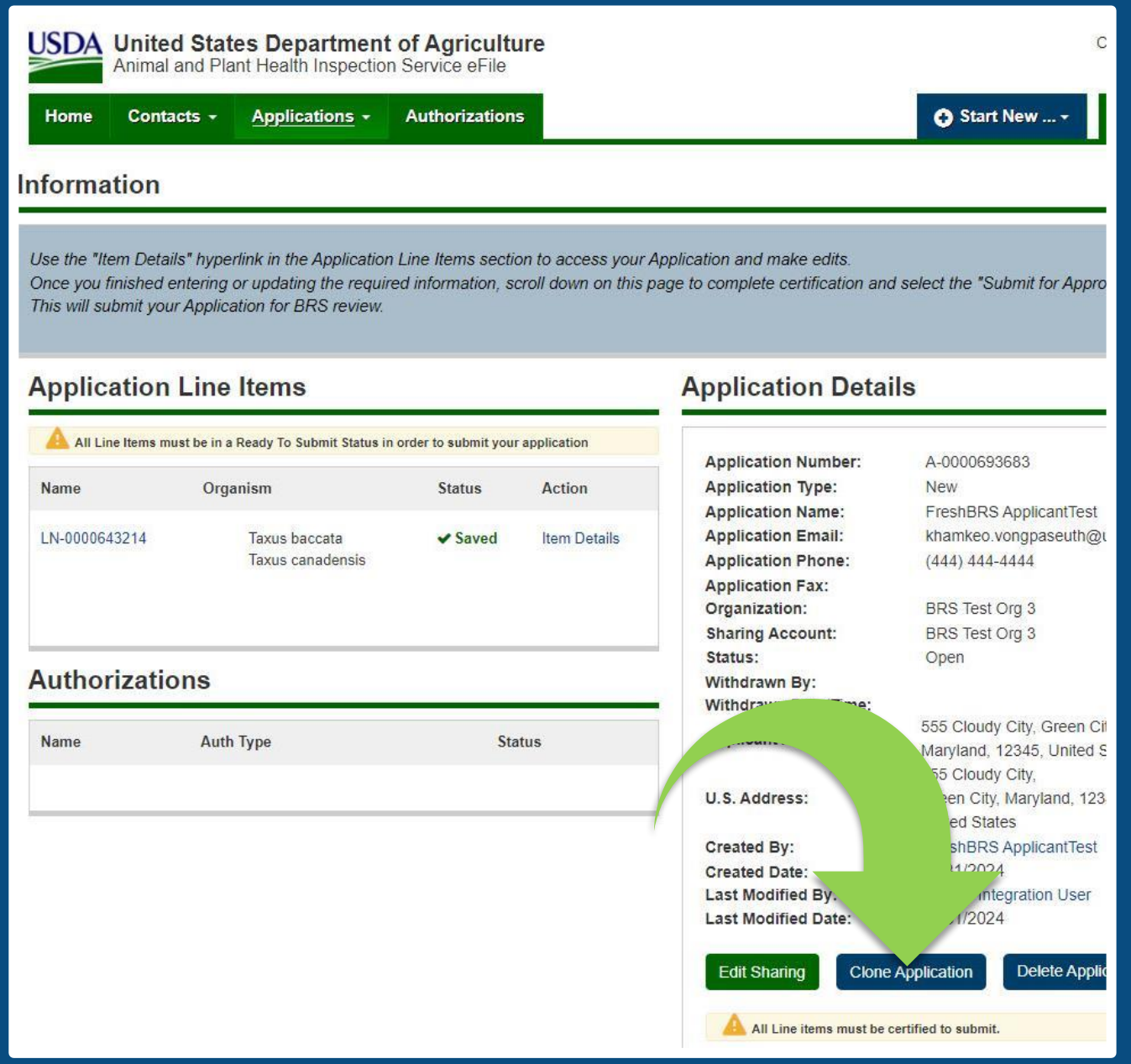
Will collectively refer to “flexibilities and system know-how” as “short cuts”

# Application Shortcuts

*Starting*

**Cloning an application saves time**

- Repetitive clicks
- Large amounts of information carry over from existing applications

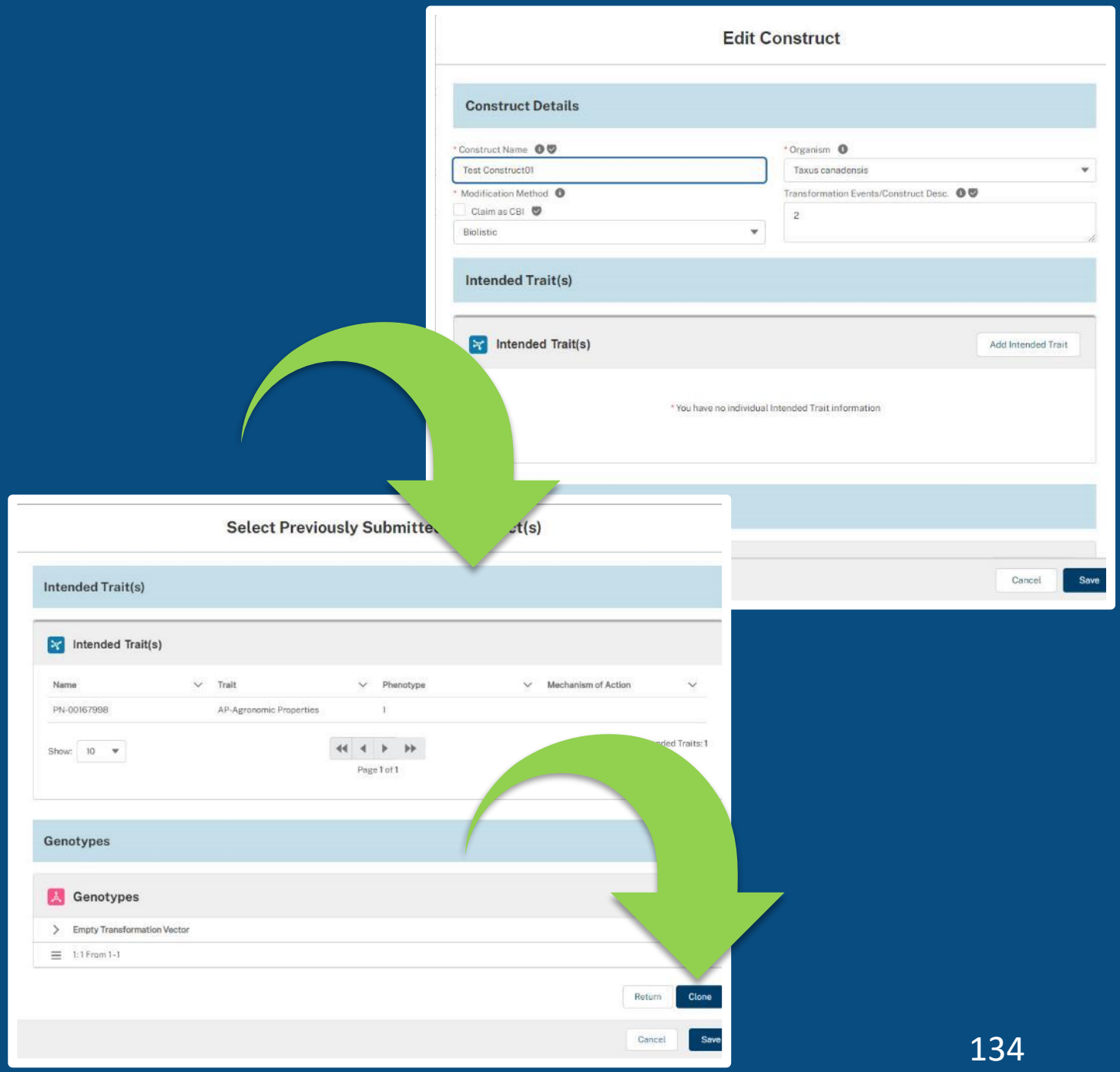


# Application Shortcuts

*Drafting*

**Cloning a construct/previously submitted construct (PSC) saves time**

- Fewer clicks
- Eliminates creating multiple constructs that contain similar genetic elements



# Application Shortcuts

*Starting and Drafting*

**Advanced cloning strategy**

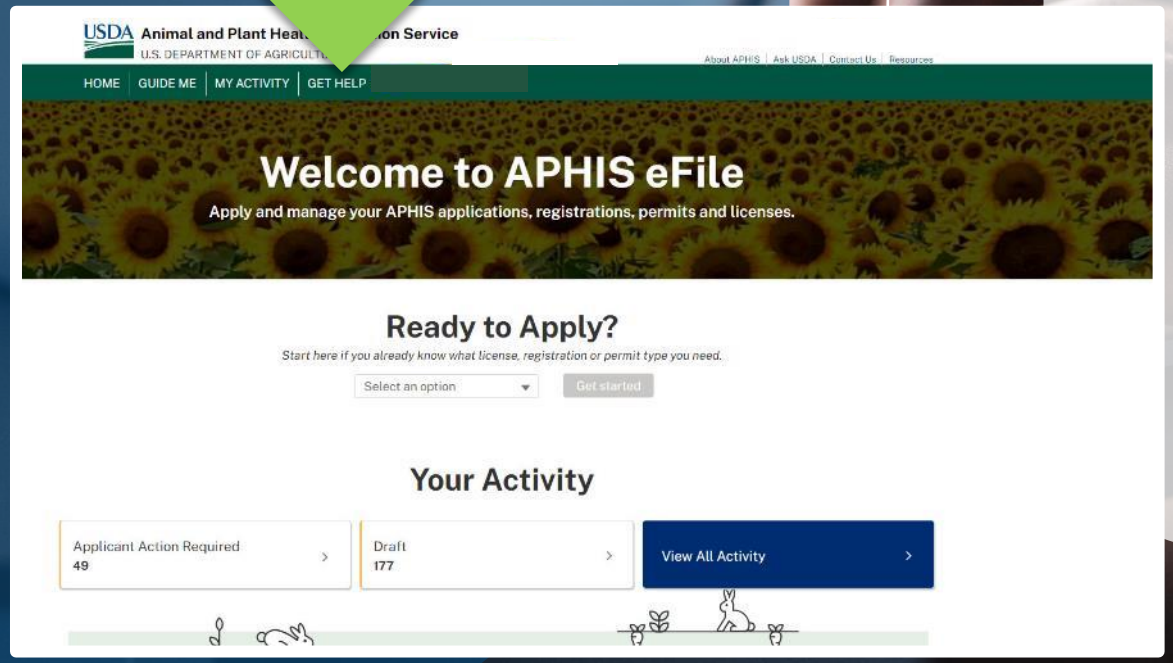
Common scenario: researcher submits application for one organism and a certain set of constructs, but now needs to submit another application for another organism using the same constructs

**Clone both the application and constructs/PSCs to save time/clicks**

1. Clone application
2. Add new organism
3. Clone PSCs
4. Reassociate PSCs with new organism
   - Repeat steps 3-4 as many times as necessary
5. Delete old organism
6. Fill out rest of application as necessary and submit

# Managing Challenges

*Strategies to get help*



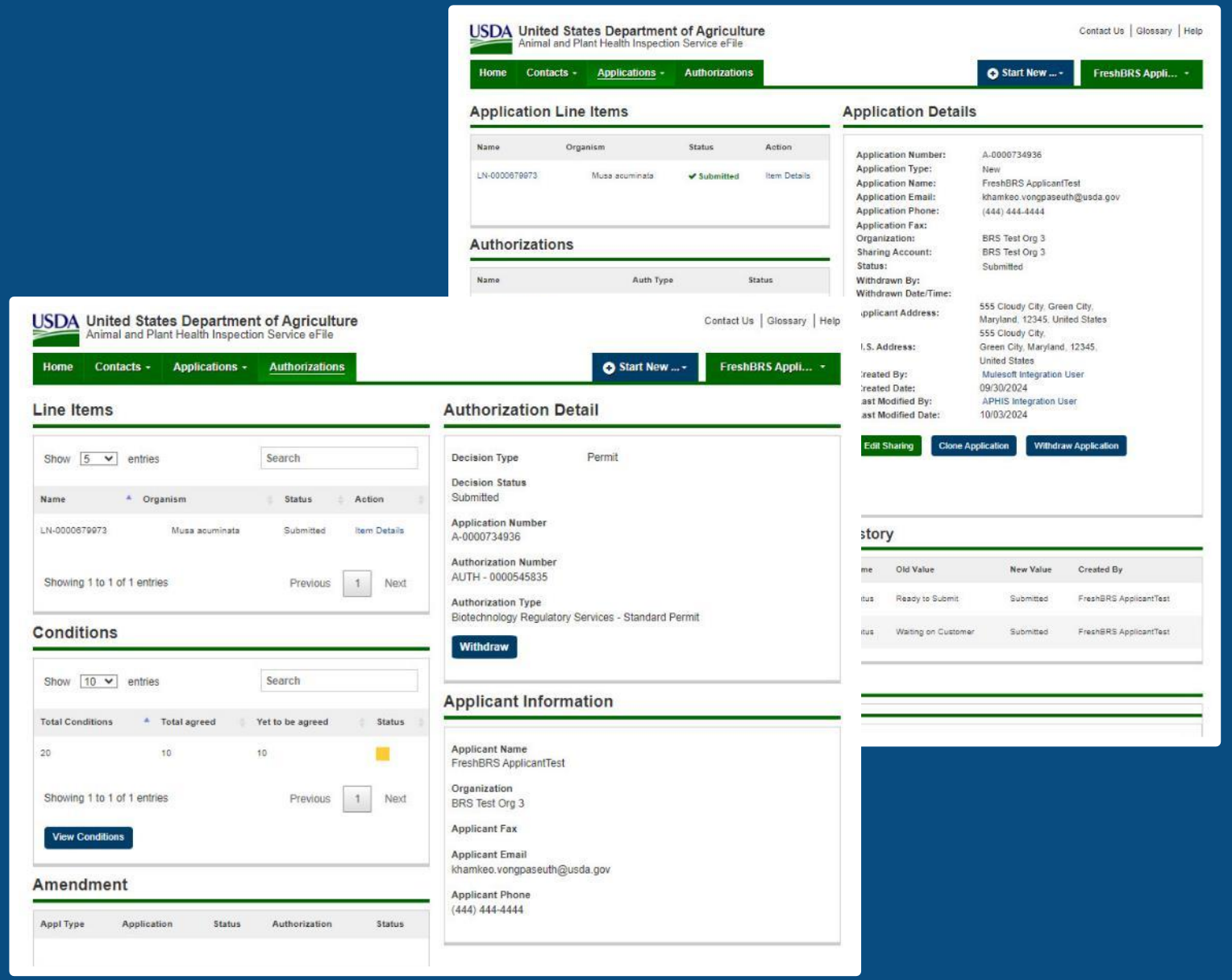

## APHIS eFile Help Wizard

- Request help from BRS (and any other APHIS program)
- Two primary features:
  - Identifies common challenges and associated solutions
  - Creates help tickets for routing to the appropriate APHIS help desk

# The Final Resolution

*This isn't really the end*

- Continued investment to improve user experience
- Planned work items include a complete redesign of the application and authorization detail pages to improve utility

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# Acknowledgements


**BRS Team**

Briyanna Norman
Megan Dexter
Eddie Serrano
Heather Brown
Becky Fletcher
Sarah Prewitt
Tina Gouin
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Samantha Greer

**Aleut Team**

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**AFS Team**

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Danielle Lane
Phillip Pascal
Megan Ingram
Katherine Edelblut

**And a lot of others I'm forgetting….**

**…and thank you to our stakeholders!**

# Thank You!