Biotechnology Regulatory Services (BRS) Annual Stakeholder Meeting

November 15, 2023

Welcome

Doug Grant
Director, Regulatory Operations Programs

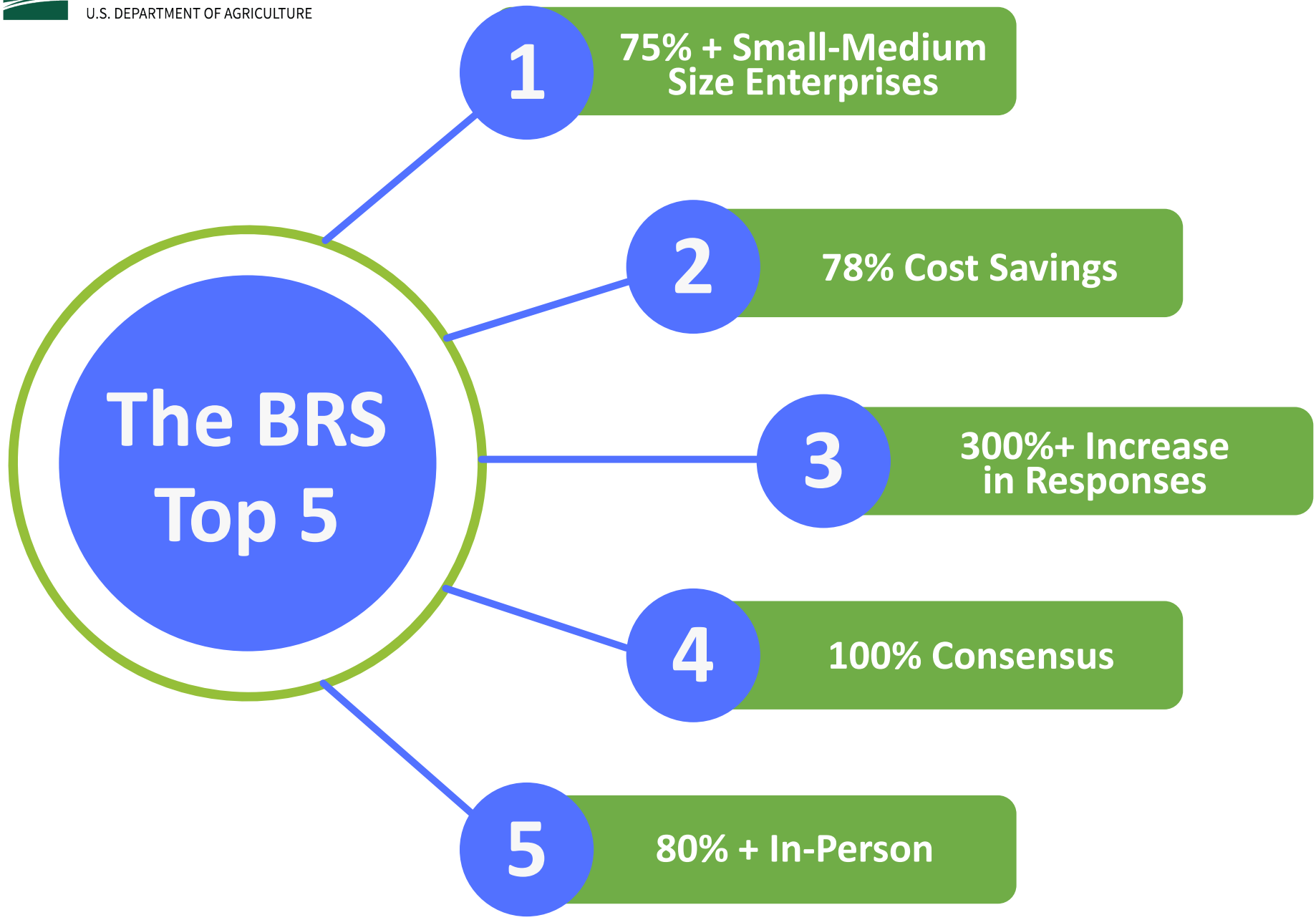
Opening Remarks

Jenny Lester Moffitt
Under Secretary of Agriculture for
Marketing and Regulatory Programs

Some Good News

Bernadette Juarez
BRS Deputy Administrator

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



BRS Workforce Update

Alia Shabazz
Branch Chief
BRS Resource Management Services

BRS Workforce Profile

- **Employee Strength:** 83 as of October 1, 2023
- **Mission Critical Occupations:** Biological Scientists, 52; Administration & Program Management, 13
- **Mission Support Occupations:** 8 occupations, 18
- **Veterans:** 7.22%
- **Retirement Eligibility:** 17 employees are currently eligible to retire and 30 are eligible to retire within 5 years.

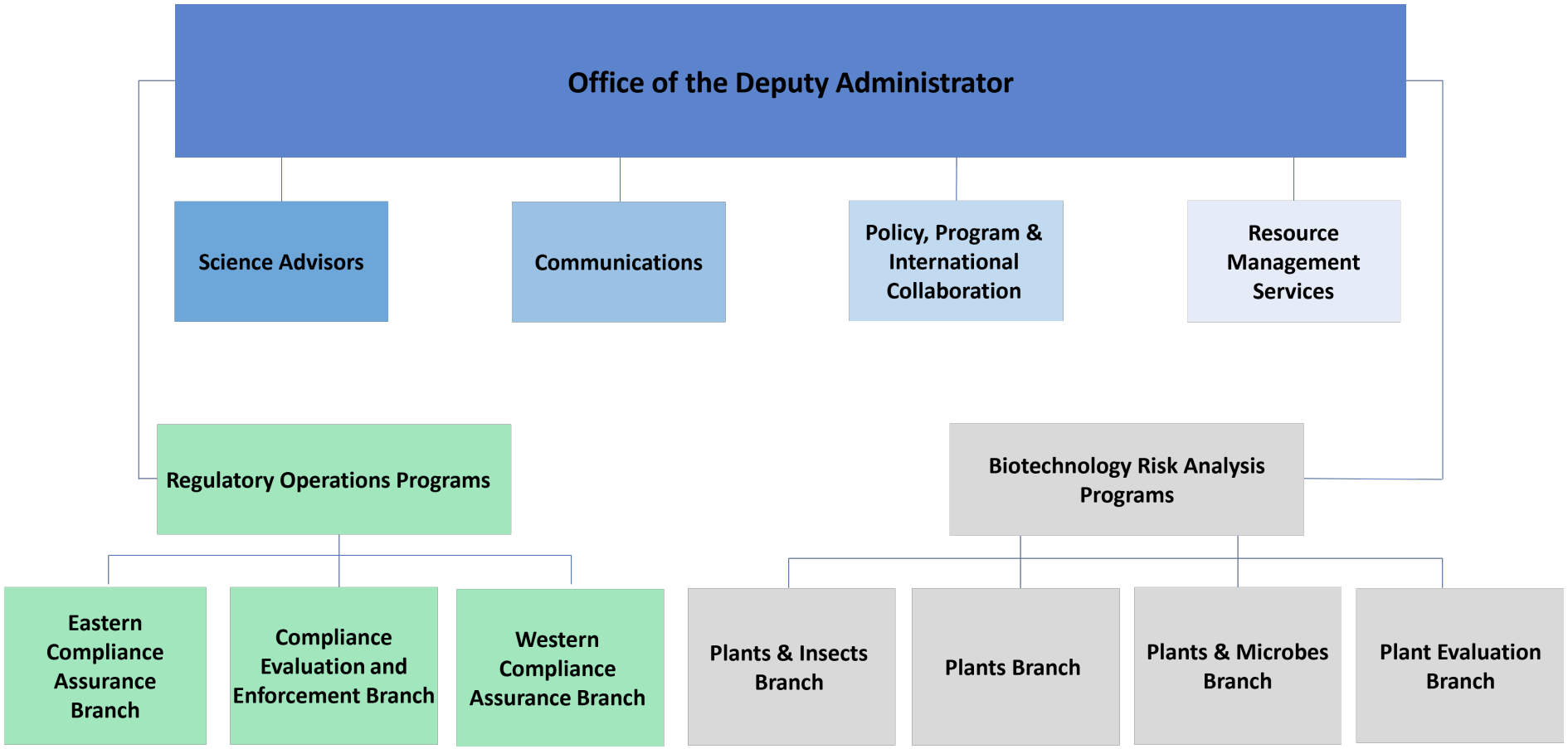
BRS Workforce Forecast

Biotechnology Risk Analysis Programs
Recruit staff with advanced knowledge of microbes and trees

Regulatory Operations Programs
Recruit staff with advanced technical skills and experience using GIS & Satellite imagery

Policy, Program, and International Collaboration Branch
Recruit policy analysts with international knowledge and ability to review and interpret regulations and statutes

Organizational Chart



New Staff: BRAP

Alina Davis, Biological Scientist, Plant Evaluation Branch

- Ph.D. in Biology from the University of Cincinnati
- Postdoctoral research in Texas and Wisconsin in invasive ecology

Ariel Heminger, Biological Scientist, Plants and Microbe Branch

Ph.D. from Virginia Tech in microbial ecology and M.S. in Entomology

Studied biological control agents and invasion biology

New Staff: BRAP

Jaclyn Motyka Corbin, Biological Scientist, Plants Branch

Ph.D. in Biology: Ecology, Evolution and Conservation emphasis from Northern Arizona University

Worked for the US Geological Survey and the US Forest Service

Zachary Schultzhaus, Biological Scientist, Plants and Microbes Branch

Ph.D. in Plant Pathology and Microbiology from Texas A&M University

Worked for the Federal Select Agent Program

New Staff: ROP

Ann Gobei-Bacaylan, Student Intern, Eastern Compliance Assurance Branch

- Undergrad student at the University of California majoring in ecology and evolutionary biology
- Worked with various sea life

Phuong Thanh Le, Biological Scientist, Western Compliance Assurance Branch

- B.S. in biology from UC Davis
- Worked as Agricultural & Standard Inspector for Tulare County Agriculture

Jolene Prochazka, Biological Scientist, Eastern Compliance Assurance Branch

- B.S. in cell and molecular biology and M.S. in integrated biological sciences from University of Minn
- Worked for PPQ as a Plant Health Specialist

New Staff: ROP

Cindy Stuefer Powell, Biological Scientist, Western Compliance Assurance Branch

- B.S. and M.S. in Botany
- Managed various scientific laboratories at the University of Nebraska

Moises Vega, Biological Scientist, Eastern Compliance Assurance Branch

- B.S. in Agriculture from the University of Puerto Rico
- Served in the U.S. Navy and worked with APHIS PPQ

Ashley Fehn, Biological Scientist, Compliance Evaluation and Enforcement Branch

- M.S. in Environmental Management from George Mason University
- Worked for 13 years in the environmental industry

New Staff: PPIC

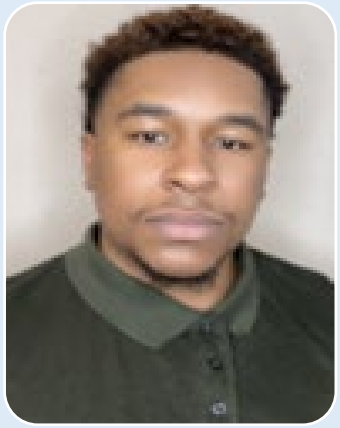
Lakshmanan (Lak) Ramamoorthi, Science Advisor, Policy Program and International Collaboration

- Ph.D. in Food Science and Microbiology from the University of Strathclyde, Glasgow, UK
- Started at USDA with Agricultural Marketing Service, Bioengineered Food Disclosure program

Joseph Tangredi, Program Specialist, Policy Program and International Collaboration

- B.S. in Biology from the University of Nevada Las Vegas and a graduate of the University of San Diego School of Law
- Practiced law for 9 years and has been a FOIA analyst with various agencies of USDA since 2009

New Staff: RMS



David Richardson, Program Assistant, Resource Management Services Branch

- A.A. degree in Business Administration and will earn a B.S. in Business Administration in December 2023 from the University of Maryland
- Previous government experience at the US Postal Service

Promotions

Laura Andrako, Branch Chief, Eastern Compliance Assurance Branch, Regulatory Operations

- M.S. in Plant Pathology from North Carolina State, and B.A. in Environmental Studies from Warren Wilson College
- Has worked in BRS compliance evaluation since 2015

Suma Chakravarthy, Senior Scientific Advisor, Office of the Deputy Administrator

- Ph.D. from Delhi University in India and has several years of research experience at Boyce Thompson Institute and Cornell University
- Served as a Branch Chief, Biotechnology Risk Analysis Programs

Promotions

Samantha Greer, Biological Scientist, Eastern Compliance Assurance Branch, Regulatory Operations Program

- B.S. in Biological Sciences from North Carolina State
- Started with as an intern with APHIS' Animal Care Program and with BRS since 2011

Michael Stulberg, Branch Chief, Plants and Insects Branch, Biotechnology Risk Analysis Programs

- Ph.D. and M.S. in Molecular Biology from Yale University and B.S. in Molecular Biology from Kenyon College
- Has worked for USDA since 2012 at USDA's Agricultural Research Service, APHIS' PPQ, and at BRS as a Senior Biological Scientist

Thank you!

Update on EO 14081

"Advancing Biotechnology and Biomanufacturing Innovation"

Alan Pearson
BRS Assistant Deputy Administrator

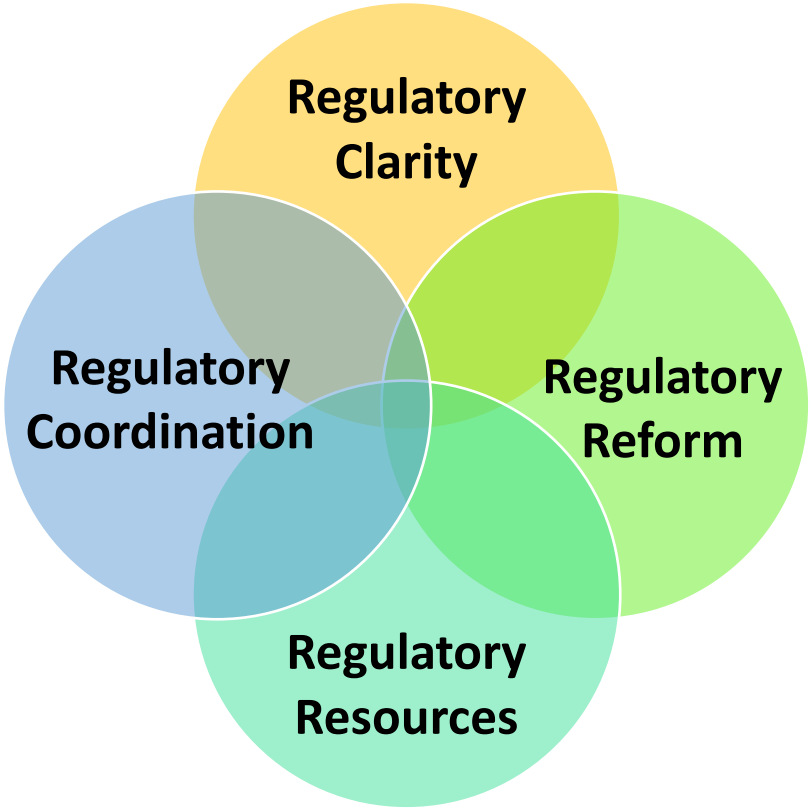
Section 1: Statement of Policy

"Clarify and streamline regulations in service of a science-and-risk based, predictable, efficient, and transparent system to support the safe use of products of biotechnology."

Section 8: Biotechnology Regulation

- Identify ambiguities, gaps, or uncertainties in the Coordinated Framework
- Provide plain-language information regarding roles, responsibilities, and processes on the Unified Website
- Provide a plan with processes and timelines to implement regulatory reform
- Enable developers to submit inquiries about a particular product and promptly receive a single, coordinated response
- Provide an annual progress update

Request for Information
Four Overlapping Themes



- 88 distinct public comments submitted
- Sign-on letter with 6083 signatories

Listening Sessions

- USG Jan 12: 281 attendees, 16 commenters
- BIO Jan 26: 18 commenters
- ASTA Jan 28: 11 commenters
- BPIA Jan 31: 7 commenters

Regulatory Clarity

All Agencies

- Increase regulatory clarity and assistance

BRS

- Clarity regarding Regulatory Status Reviews (RSRs)
- Clarity regarding microbes

Regulatory Coordination

01

Align definitions, exemptions, data and information requirements, & review timelines

02

Clarify jurisdiction and harmonize approaches for microbes

03

Reduce duplicative oversight

04

Establish interagency coordination mechanism

Regulatory Reform
All Agencies

Update regulatory frameworks to account for genome editing and minimize regulation of genome edited products

Streamline regulations and processes, and reduce regulatory burdens and duplicative regulation

Provide more thorough and continuing oversight for biotechnology products based on the entire lifecycle of the production process

APHIS Regulatory Reform

- Expand exemptions
- Meet regulatory timeframes and reduce regulatory burdens
- Streamline procedures and information requirements for interstate movement permits
- Establish a regulatory off-ramp for modified microbes
- Include noxious weed provisions in USDA biotechnology regulations

Regulatory Resources

- Appropriately fund, staff, and train employees to ensure timely and consistent reviews
- Develop streamlined, consistent, science-based permit templates and review processes to ensure reviewers treat similar requests in a similar manner and maintain consistency

Positive Feedback

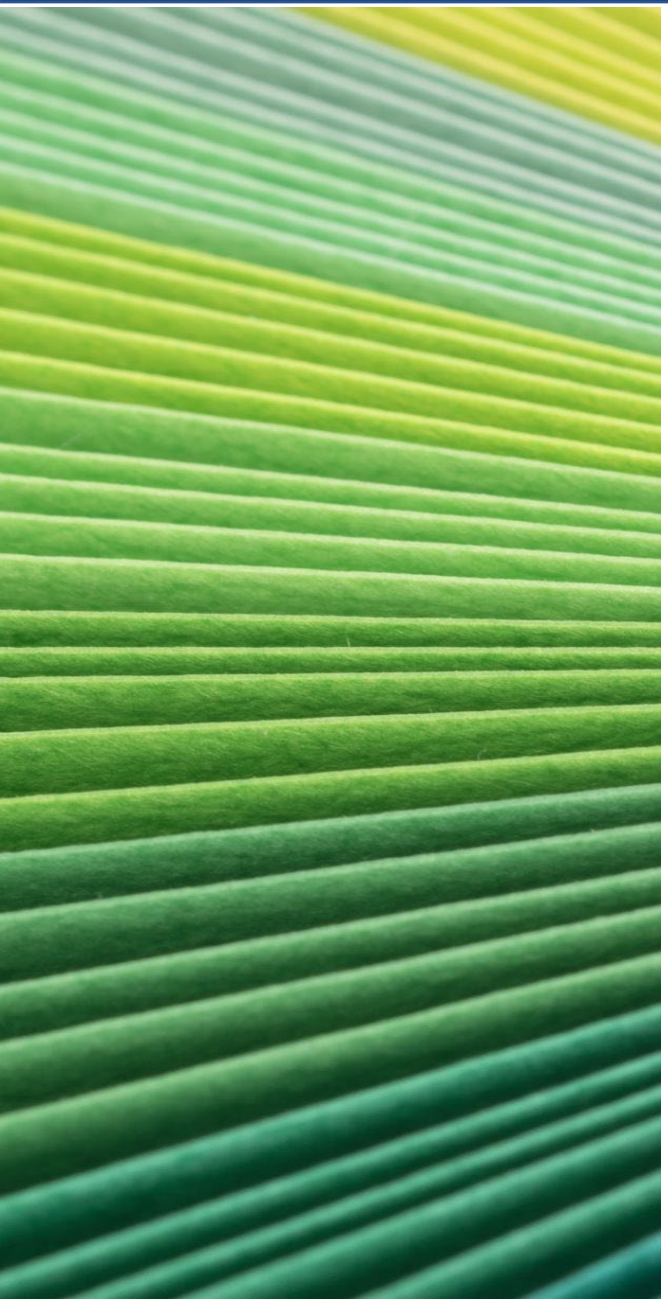
- USDA's revised regulations are "a major advance" and "a positive step towards risk proportionate regulations" for which "USDA APHIS needs to be commended."

- The regulatory agencies "are doing things that are very positive… One of these strengths is the quality of the scientific reviewers and the fact that the agencies encourage informal pre-submission discussions and consultations with researchers and developers."

Thank you!

Proposal to Add Modifications that Qualify for Exemption from Regulation Under 7 CFR part 340

Neil E. Hoffman
BRS Science Advisor



Keeping Pace With Advances in Science and Technology

APHIS may exempt plants with additional modifications achievable through conventional breeding

Proposals will be based on scientific evidence demonstrating that the proposed modification(s) could be achieved through conventional breeding

Scientific Rationale for Exemptions:

Treat Similar Products in a Similar Way

Genetic engineering, in and of itself, does not introduce plant pest risk

Conventional breeding has a history of safe use related to plant pest risk

Exempt plants with certain modifications achievable through conventional breeding

Current Exemptions

A change resulting from cellular repair of a targeted DNA break in the absence of an externally provided repair template (b1);

A targeted single base pair substitution (b2); or

Introduction of a gene known to occur in the plant's gene pool, or a change in a targeted sequence to correspond to a known allele of such a gene or to a known structural variation present in the gene pool (b3).

New Notice

Builds on Notice published in July 2021 that sought to

- Clarify the meaning of “single modification”
- Allow use of an external template to make a deletion

Introduces new modifications related to

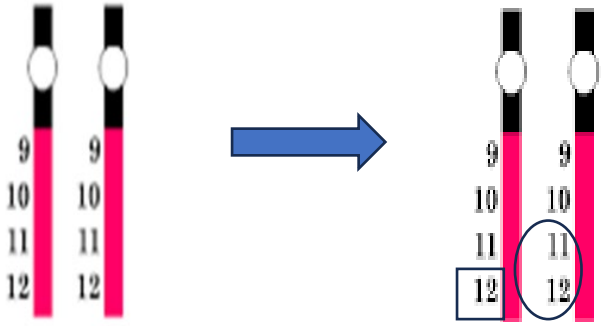
- Loss of function (LOF) modifications
- Polyploid plants
- Multiple edits
- Successive edits

Loss of Function on All Alleles (AM1)

- Would exempt certain plants with loss of function mutations in the same gene across all chromosomes, regardless of how the mutation is generated
- Would apply to modifications without the insertion of exogenous DNA in:
  - A diploid or autopolyploid plant with any combination of loss of function modifications in one to all alleles of a single genetic locus, or
  - An allopolyploid plant with any combination of loss of function modifications in one or both alleles of a single genetic locus on up to four pairs of homoeologous chromosomes

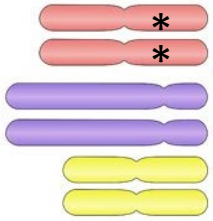
Loss of Function on All Alleles Modifications Need Not be Identical (AM1)

Allows identical or non-identical changes on a pair of chromosomes if the outcome is loss of function

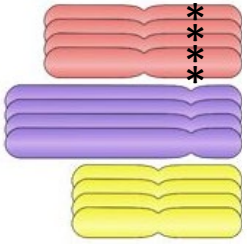


Loss of Function on All Alleles of a Single Genetic Locus (AM1)

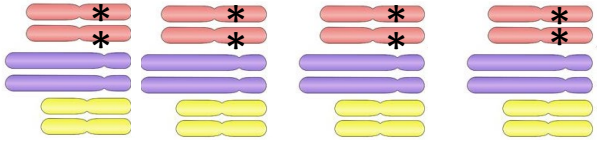
2 sets chromosomes
diploid 2N



4 sets chromosomes
autotetraploid 4N
Homologous c-somes



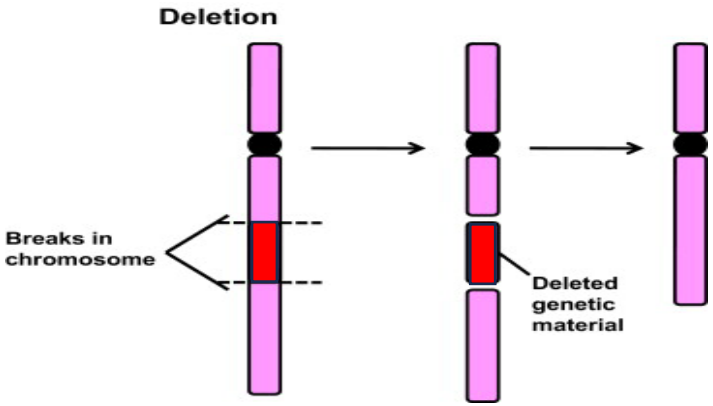
8 sets of chromosomes
Allo-octaploid 8N
Homoeologous c-somes

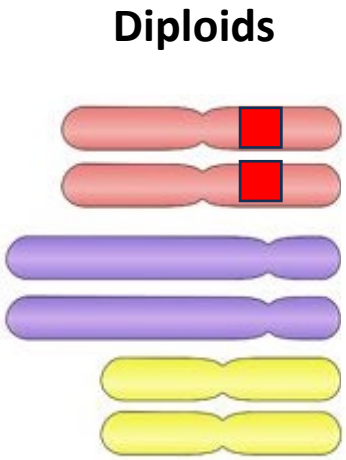


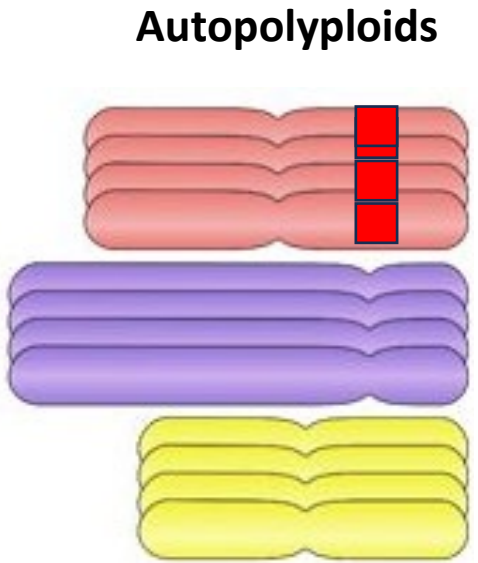
Single Contiguous Deletion of Any Size (AM2)

- Would apply to diploids and autopolyploids plants but not allopolyploids plants
- Would allow a deletion at the same location on two or more homologous chromosomes
- The modification must be a single contiguous deletion of any size, resulting from cellular repair of one or two targeted DNA breaks on a single chromosome or at the same location(s) on two or more homologous chromosomes, without insertion of DNA, or with insertion of DNA in the absence of a repair template

Deletions of Any Size Achieved by Two Breaks (AM2)



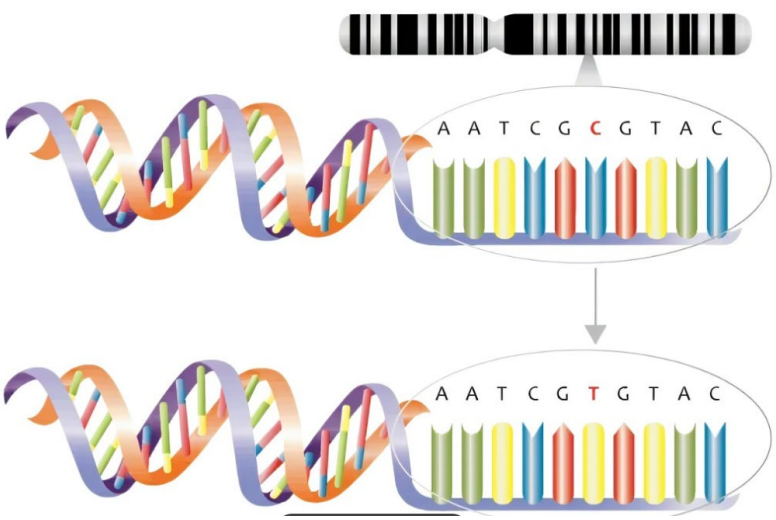


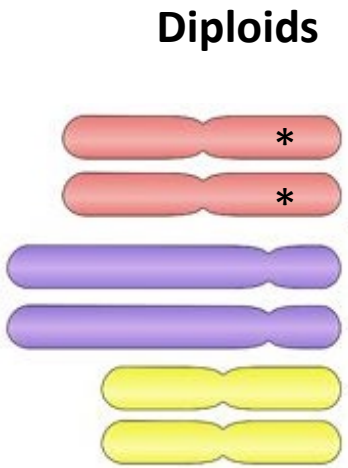


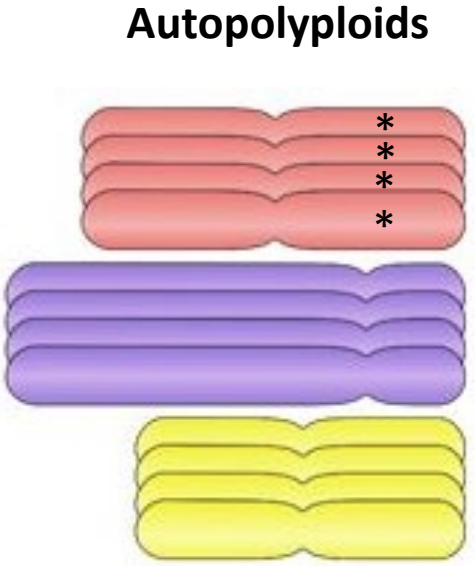
Extends (b)(2) and (b)(3) Exemptions to Autopolyploids (AM3)

- For all alleles of a genetic locus on the homologous chromosomes of autopolyploid
  - Would allow a targeted single base pair substitution (b)(2)
  - Would allow the introduction a gene known to occur in the plant's gene pool or make changes in a targeted sequence to correspond to a known allele (b)(3)

Extends Exemption that Allows a Single Base Pair Substitution (AM3)



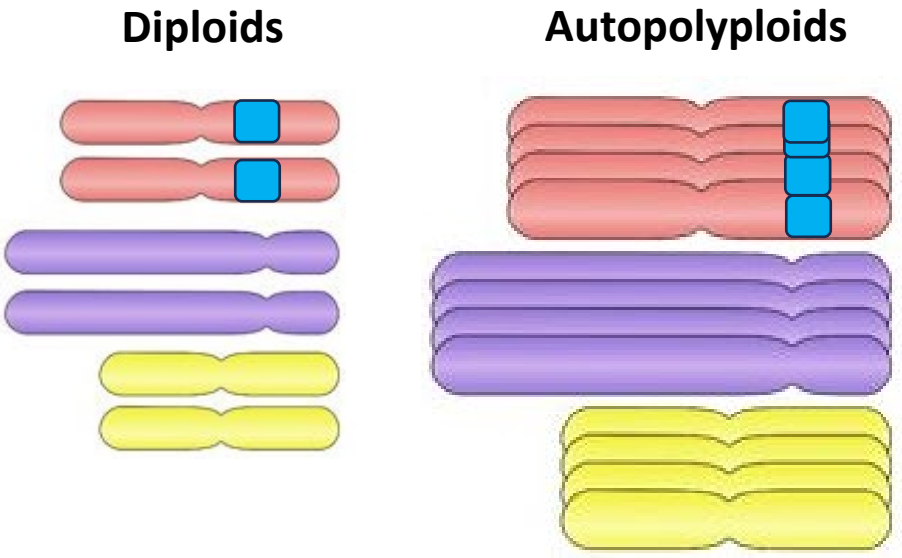




Extends Exemption that Allows the Introduction of an Allele in Gene Pool (AM3)

Current allele

Allele in gene pool

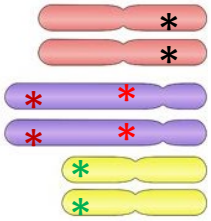


Allows Up To Four Modifications (AM4)

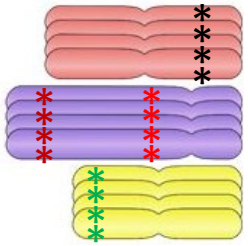
- Would apply to diploids and autopolyploids plants, and to allopolyploids plants with some limitation
- Modifications could be made simultaneously or sequentially
- Each modification must individually qualify for exemption
- Each modification must be made at a different genetic locus
- Allopolyploids could:
  - Contain up to four loss of function modifications in homologous alleles; or
  - Contain up to four (b)(2) or (b)(3) modifications in a single allele

Allows Up To Four Modifications (AM4)

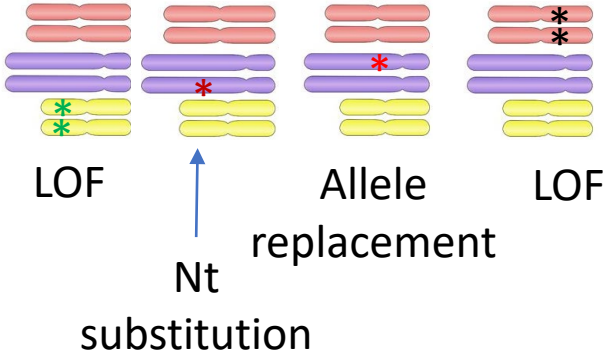
2 sets chromosomes diploid 2N



4 sets chromosomes autotetraploid 4N



8 sets of chromosomes Allo-octaploid 8N

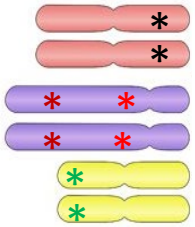


Successive Modifications (AM5)

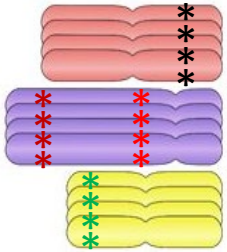
- Would apply to plants that have completed the voluntary confirmation process
- The plant that is the subject of the confirmation response must be produced, grown, and observed consistent with breeding methods appropriate for the species
- If the above criteria are met, the plant could be modified using the exemptions available for under 340.1(b), including any additional modifications that may be finalized through the ongoing notice process

Successive Modifications (AM5)

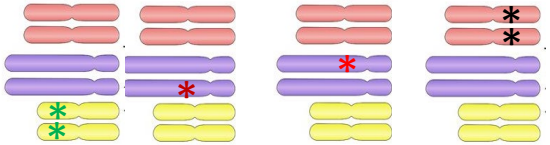
2 sets chromosomes
diploid 2N



4 sets chromosomes
autotetraploid 4N



8 sets of chromosomes
Allo-octaploid 8N



1. Make up to 4 modifications that qualify for exemption under 340.1(b)
2. Confirmation Request-Exempt Status + Plant/Grow/Observe
3. For a modified plant confirmed as exempt, additional four modifications can be made under 340.1(b) exemptions

Thank you!

Break Time

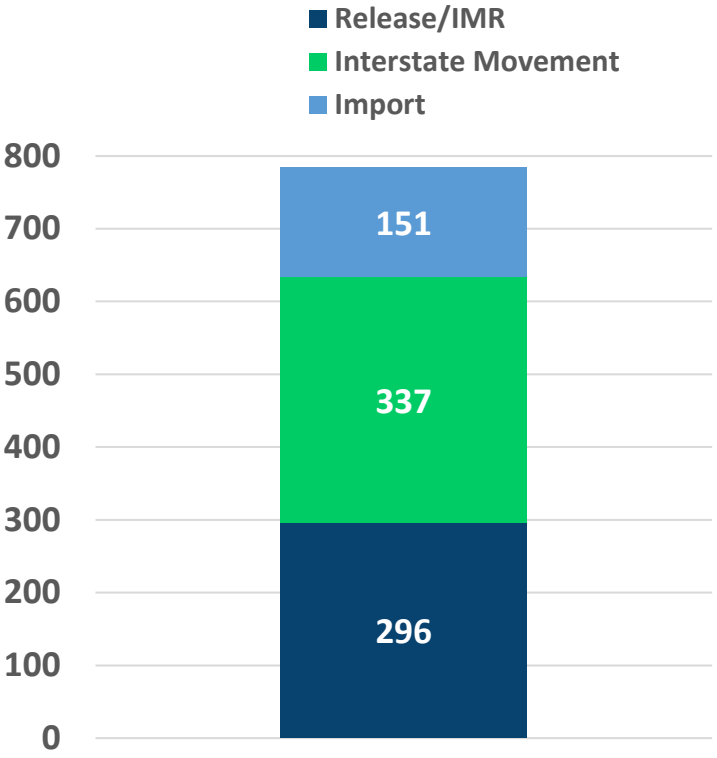
Update on the Permitting Process

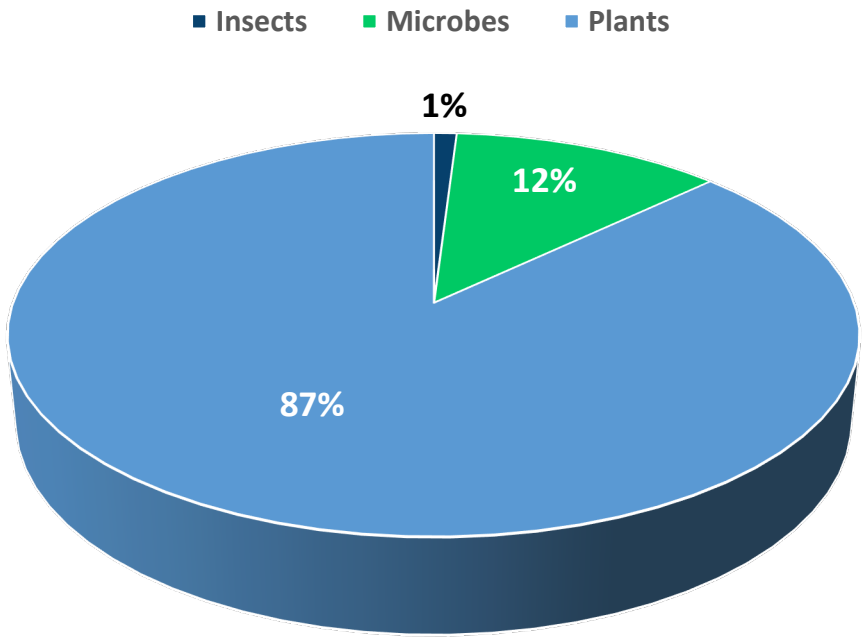
Subray Hegde
Director, BRS Biotechnology Risk Analysis Programs

Permitting: Looking Back and Forward

- FY2023 Permitting at a Glance
- Flexibilities for Permitting
- Tips for Efficient Permit Processing
- FY2024 Permitting Business Process Improvement Project

FY2023 Permitting at a Glance
Permit Types





FY2023 Permitting at a Glance
Average Processing Time (Days)

	From Technical Completeness	From Submission
Import or Interstate Movement	31	50
Release or Interstate Movement and Release	47	87

90% of authorizations were processed within the target timeframe based on technically complete to issuance

Flexibilities: Permit Applications

In Place:

Multi-year interstate movement/import permits for plant species and modified microbes

Completely updated instructional and help text in the application User Interface (UI)

Flexibilities: Permit Applications

In Place:

- Updated Job Aid for Permit Application
- Voluntary Standard Operating Procedures Template
- Revised Draft Guide for Submitting Permit Applications for Microorganisms

- Posted a second draft version to indicate applicants can submit a multiyear (2-3 years) permit application
- Applicant can submit permit applications for the importation and interstate movement of bacteria and fungi at the genus level
- BRS plans to publish a plant pest list in the FY24-25

Flexibilities: Permit Applications

Coming Soon:

Multi-year release permit for annual plant species

Under Review:

Multiple points of origin and/or destinations for import permits

Flexibilities: Permit Applications

Coming Soon:

- Updated Permit User's Guide
- Updated Application and Authorization Detail Pages
- Updated Instructional Text for Sharing Accounts

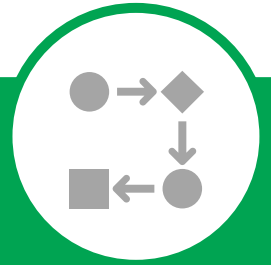
Tips for Efficient Permit Processing

1. Take advantage of pre-consultation meetings
2. Only submit a permit application that contains complete information
3. Monitor your inbox for communications from BRS
4. Respond quickly if action is required before BRS can continue to evaluate your permit application
5. Consult the APHIS eFile Job Aid and Permit User's Guide
6. Consult the voluntary SOP template, as necessary
7. Provide additional information to help BRS review permits, e.g., linked permits

FY2024 Permitting Business Process Improvement Project

OBJECTIVE
Reestablish a risk-based and familiarity-based approach for reviewing crop-trait combinations in the permit applications

GOAL
Restore track-record of predicable and timely issuance of permits and confidence in BRS' permitting process



APPROACH
Identify opportunities to promote consistent reviews, address inefficiencies, implement process changes, and measure progress bi-monthly

FY2024 Permitting Business Process Improvement Project

Completed Steps

- Standardized supplemental permit conditions for importation/interstate movement for plants
- Dedicated staff for permit reviews

Next Steps

- Document current process
- Measure process steps and identify bottlenecks
- Reestablish risk-based and familiarity-based categories of organism-trait combinations for permit reviews
- Set objective criteria for a technically complete permit application
- Improve communications with applicants to expedite response to technical deficiencies

For More Information

APHIS BRS
https://www.aphis.usdourfocus/biotechnology

Revised Regulations
www.ecfr.gov/current/title-7/subtitle-B/chapter-III/part-340?toc=1

Permit User's Guide
www.aphis.usda.gov/biotechnology/downloads/permit_guidance.pdf

APHIS eFile
BRS Permitting Assistant (usda.gov)

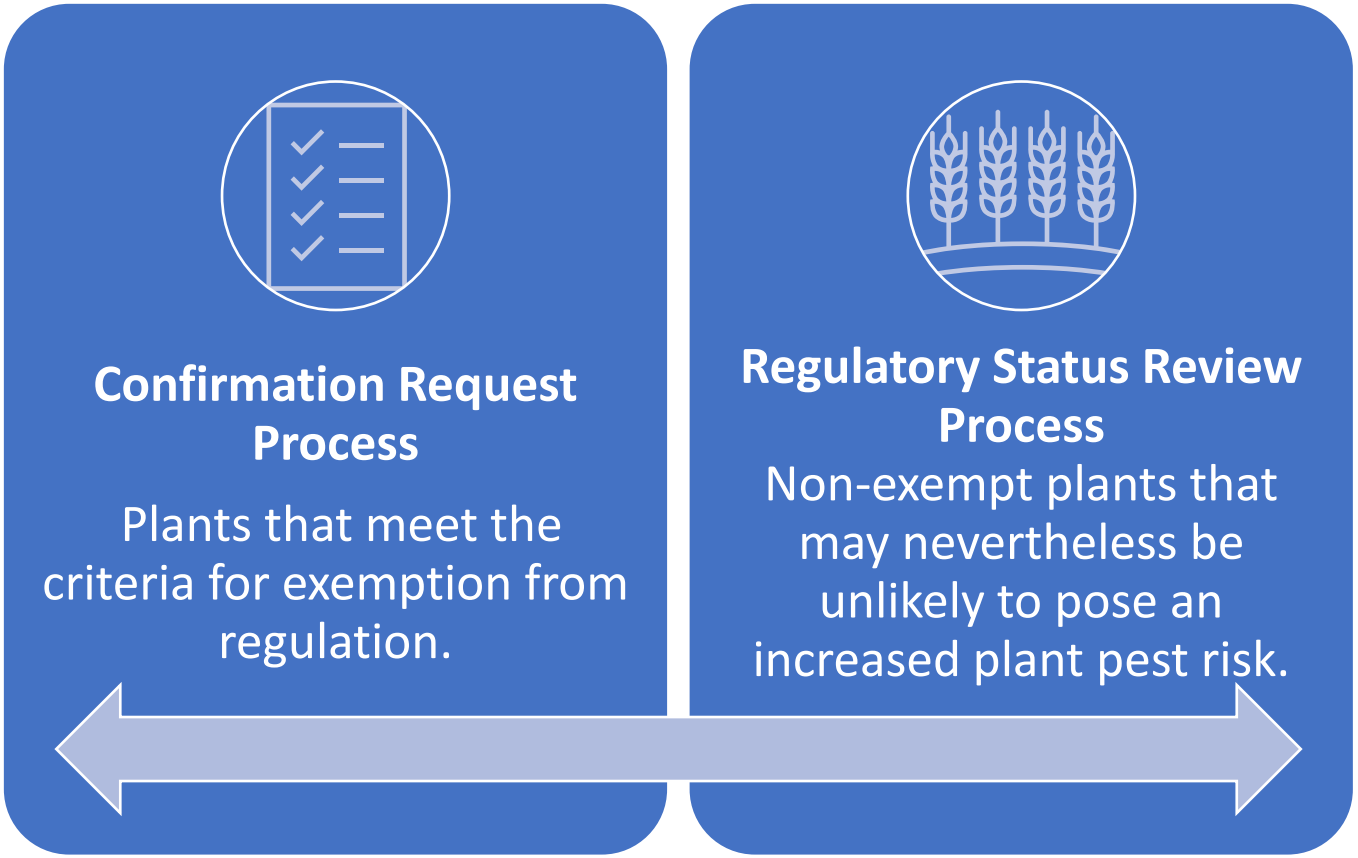
Thank you!

Regulatory Off-Ramps for Plants

Michael Stulberg
Branch Chief, BRS Biotechnology Risk Analysis Programs

Suma Chakravarthy
BRS Science Advisor

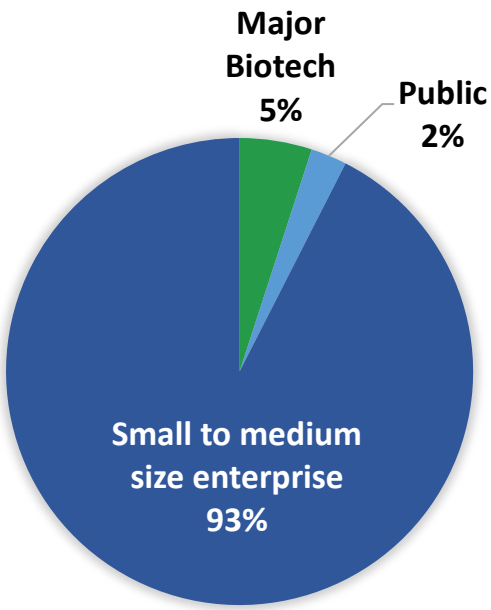
Main Pathways to Safely Commercialize Agricultural Biotechnology Products



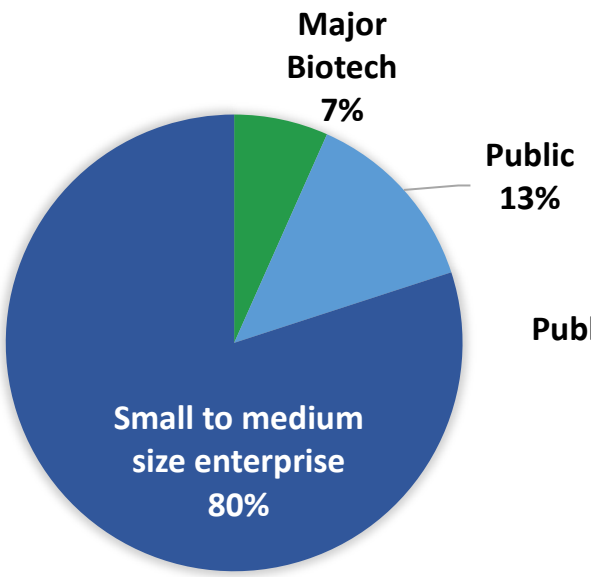
How Are These Processes Performing?

Facilitating Growth in the Bioeconomy

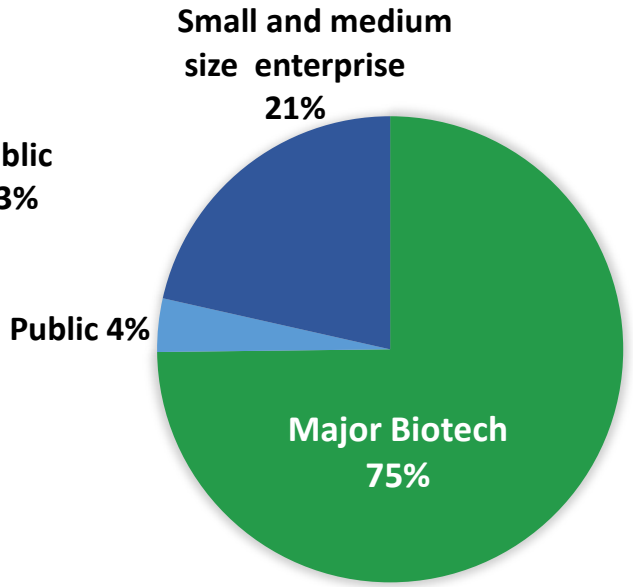
REVISED REGULATIONS
FY23 COMPLETED
CONFIRMATION REQUESTS



REVISED REGULATIONS
FY23 COMPLETED
REGULATORY STATUS REVIEWS



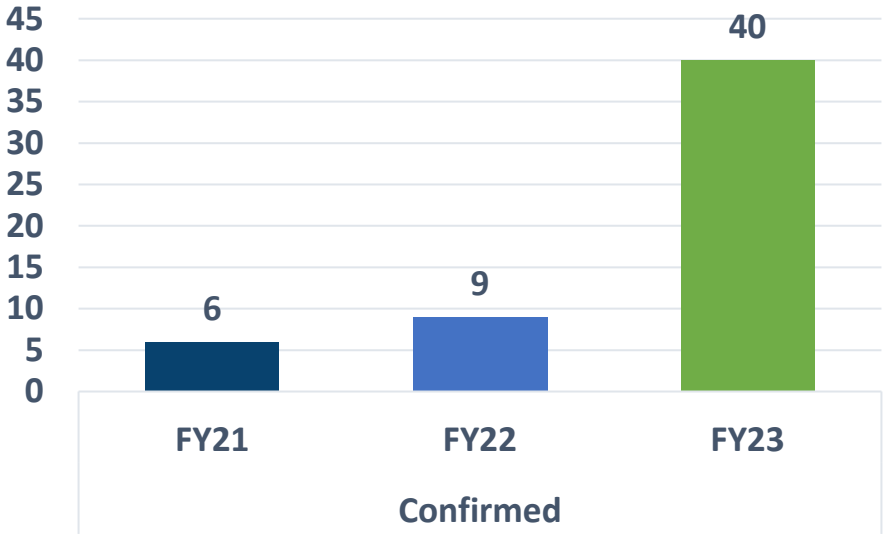
LEGACY REGULATIONS
COMPLETED PETITIONS



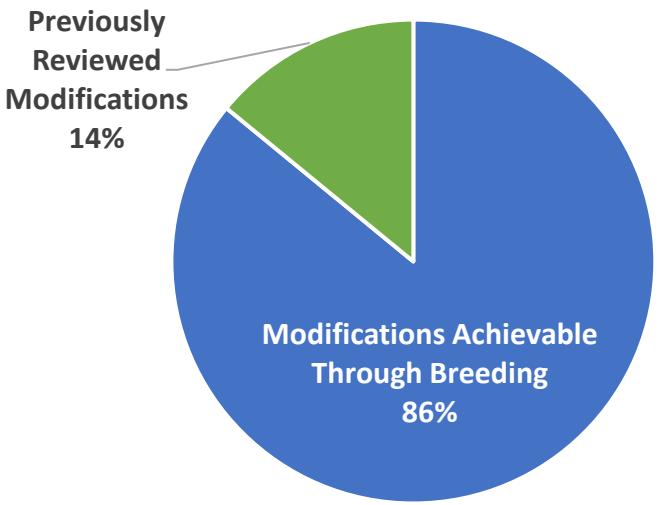
As of Oct 1, 2023

Timely Responses to Increased Number of Confirmation of Exemption Requests (CRs) in FY23

40 Timely Responses in FY23



CRs Mostly Equivalent to Conventional Breeding in FY23



FY23 Confirmation of Exemption Responses

12 Crop Varieties

1 Tomato

1 Potato

1 Apple

1 Sorghum

1 Cotton

1 Citrus

2 Brassica Juncea

2 Corn

3 Rice

8 Pennycress

9 Soybean

10 Blackberry

Regulatory Status Review Process

1

Initial review problem formulation to identify whether there are plausible pathways to increased plant pest risk

2

Plant Pest Risk Assessment (PPRA) determines likelihood and consequence of any plausible pathways to plant pest risk identified in the initial review

FY23 Completed Regulatory Status Reviews

15 Crop Varieties

Transgene | Genome Edited

Ohalo Genetics Potato Altered Nutrition

Simplot Potato Improved Product Quality & Disease Resistance

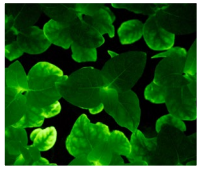
Infinite Enzymes Corn Enzyme for Potential Detoxification

Zeakal Soybean Increased Oil and Protein

Suntory Flowers Limited Chrysanthemum Altered Flower Color

Moolec Science Safflower Altered Seed Oil Profile

Inner Plant Soybean Fluorescent Reporter



Inner Plant Soybean Fluorescent Reporter

Inner Plant Tomato Fluorescent Reporter

Donald Danforth Teff Reduced Lodging

Bayer Corn Reduced Lodging

University of California Davis Walnut altered for disease resistance

Light Bio Petunia Altered Appearance

G.T. Research Hemp with Altered Cannabinoid Profile

Ohalo Genetics Potato with Altered Tuber Sugar Profile

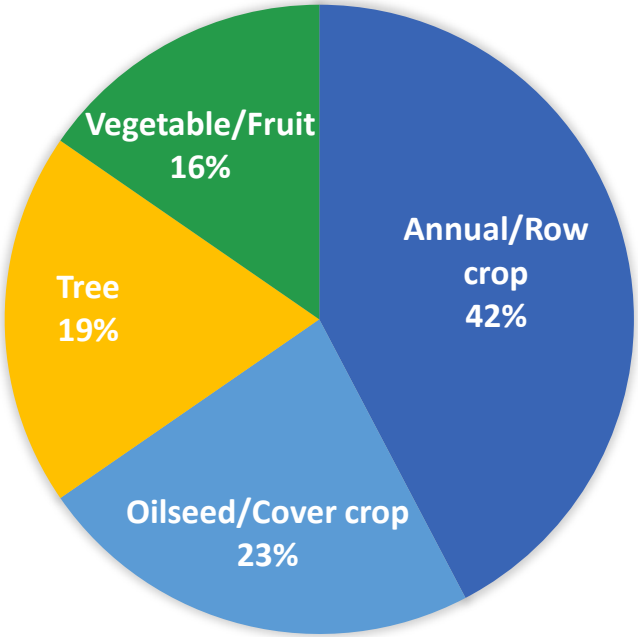
Diverse plants and traits not seen in the legacy regulations

FY23 RSR Actions

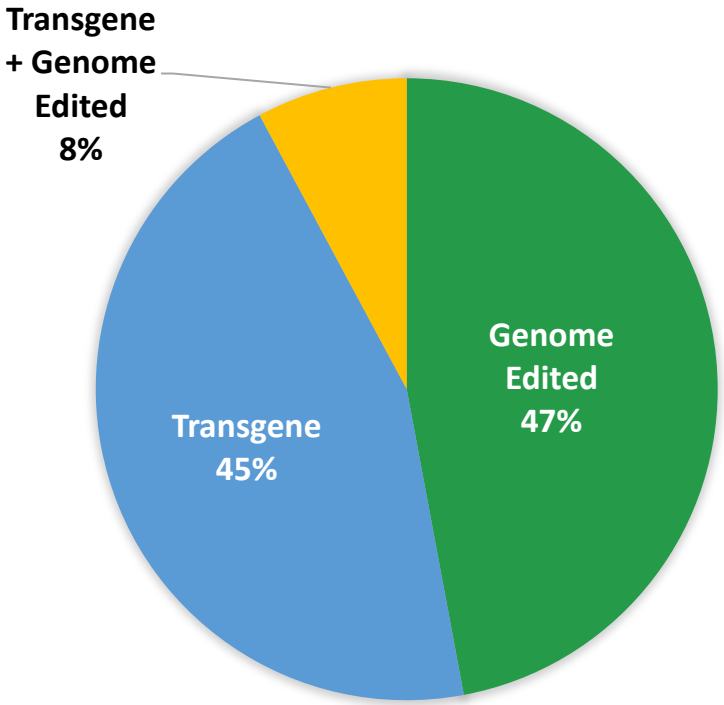
- Completed 21 Initial Reviews in FY23 relative to 3 in FY2022. Ongoing work for 2 RSRs in Step 2.
- Nearly 20% were completed within the regulatory timeframes.
- Dedicated staff for RSRs and Senior Advisor Support.
- Creation of new Plants and Insects Branch.
- Developing IT platform for RSR management.
- By gaining experience, BRS has reduced handoffs and made other process refinements.
- Obtained approval to pilot test A.I. to scan literature for writing documents.

A Snapshot of Pending Requests

PLANTS



RSR REQUESTS



As of October 26, 2023

Addressing the Pending RSRs

Goals for FY24

- Completion
- Percentage of on-time completion
- Cross-training staff members in the RSR review process

Evaluation of RSR Process

- Continue implementing efficiency gains realized in FY2023
- Forming a team to collect and implement process improvement ideas to gain efficiency

Suggestions for Developers

Plant-MOA Information

- For plants we are not familiar with, can also submit publicly available data related to the plant's biology
- Can submit more information regarding MOAs that cite publicly available data

Tips for Avoiding Returned Initial Submissions

- Include/annotate all inserted nucleotide sequence, including spacer sequence
- Avoid drawing conclusions about the plant pest risk of the modified plant and
- Do not include non-publicly available data outside what is required

Thank you!

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

Compliance and Inspection Updates

Laura Andrako
Branch Chief, BRS Eastern Compliance Assurance Branch

Regulatory Operations Programs (ROP) Statistics, Outcomes, and Projects

- APHIS eFile upgrades and other improvements
- Inspection data
- Compliance outcomes
- Overview of noncompliance
- New projects

APHIS eFile Upgrades

Stakeholder APHIS eFile Users

- Improved Reporting Experience
  - Improved XML uploads, tables
  - Ability to create, upload, larger reports
- Ability to delete supporting documents before submission
- Centralized method to check compliance status before issuing new permits

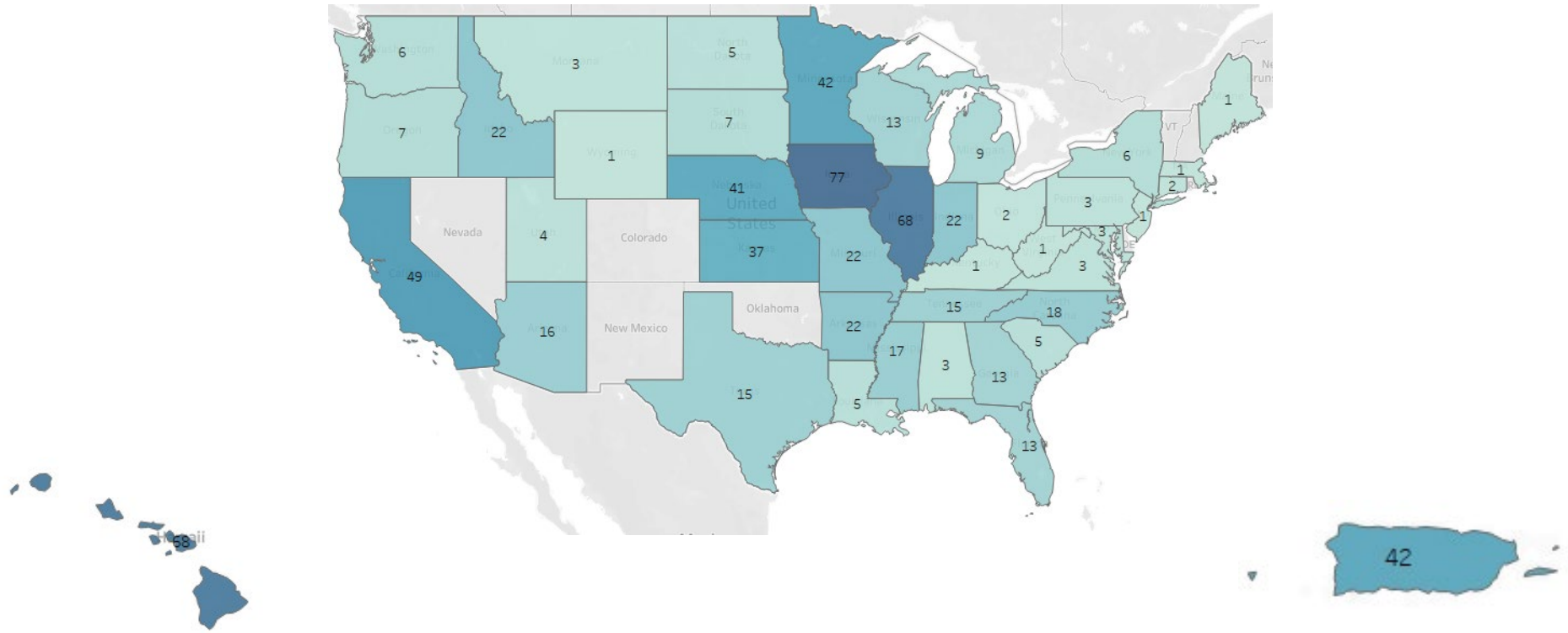
Other FY 2023 BRS Improvements

Draft Guide for Submitting Data for Reports and Notices in APHIS eFile (available for public comments through Dec. 11, 2023)

Onboarding and training of four new BRS inspectors

Proactive compliance assistance – 17 engagements

FY 2023 Conducted 711 Inspections



In-Person Inspections

In FY 2023, 80% of inspections were in-person (571 of 711)

*all PPQ and State inspections were in-person

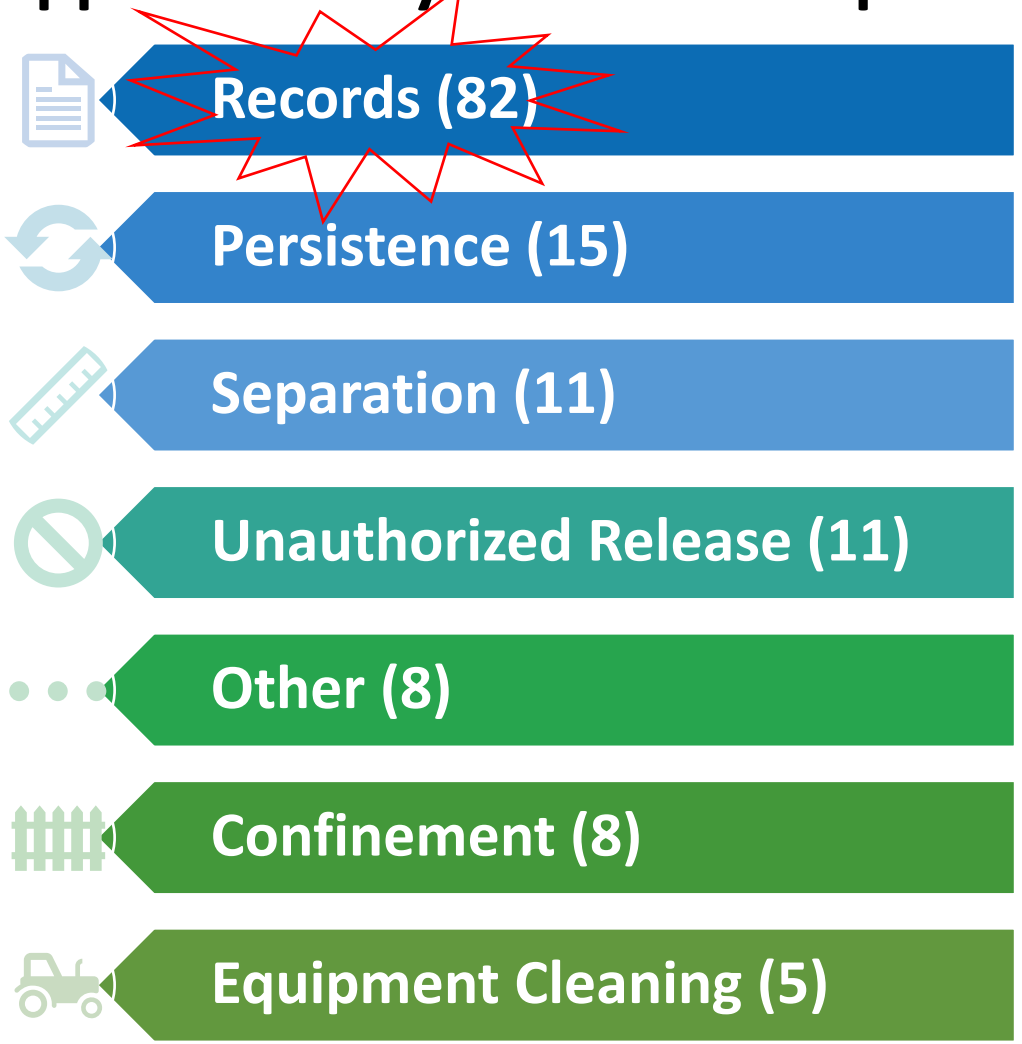
Compliance Inspection Outcomes

Notices sent in FY 2023

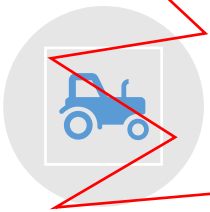
Compliant	Notice of Noncompliance	Pending Outcomes
591	119	1

Noncompliance Documented During Inspection

Approximately 140 Noncompliances



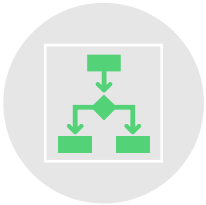
Records



Equipment Cleaning Records (56)

Volunteer Monitoring Records (9)

In-season Monitoring (6)



Multiple Types (5)

Shipping Records (3)

Plant Reports (3)

Equipment Cleaning Records

What we can improve

- Early and clear notice for new information requirements in supplemental permit conditions
- Proactively monitor inspection trends and communicate across inspectorate

What you can improve

- Recovery/disposition of material
- Complete list of equipment used and cleaned

Records Review

Records help verify what has been done so far

Planting information (acreage, location, constructs), shipping information

Separation, confinement

Equipment cleaning

Preventing persistence after trial termination

FY24 ROP Projects

Address Public Comments on Draft Guide for Reports and Notices

- Publish Final Guide

Business Process Improvement (BPI)

- Re-evaluate risk-based inspection selection process based on experience and familiarity
- Streamlining internal inspection procedures
- Update enforcement strategy

Data-driven Proactive Compliance Assistance

Thank you!

Exploring Regulatory Off-Ramps for Modified Microbes

Chessa Huff-Woodard
Branch Chief
BRS Policy, Program, and International Collaboration

Exploring Regulatory Off-Ramps: Modified Microbes

- Continue to address stakeholder feedback
- Begin developing a contemplated framework that enables commercialization of modified microbes

Stakeholder Engagement: Microbes

24 Mar

- Publish a Request for Information

24 July

- Review and Analyze Comments

24 Sep

- Develop Contemplated Regulatory Framework
- Address actionable non-regulatory solutions, in coordination with PPQ and EPA under the EO

Thank you!

International Engagement

Jessica Mahalingappa
BRS Associate Deputy Administrator

Bilateral Engagements

Support for Foreign Affairs Agencies

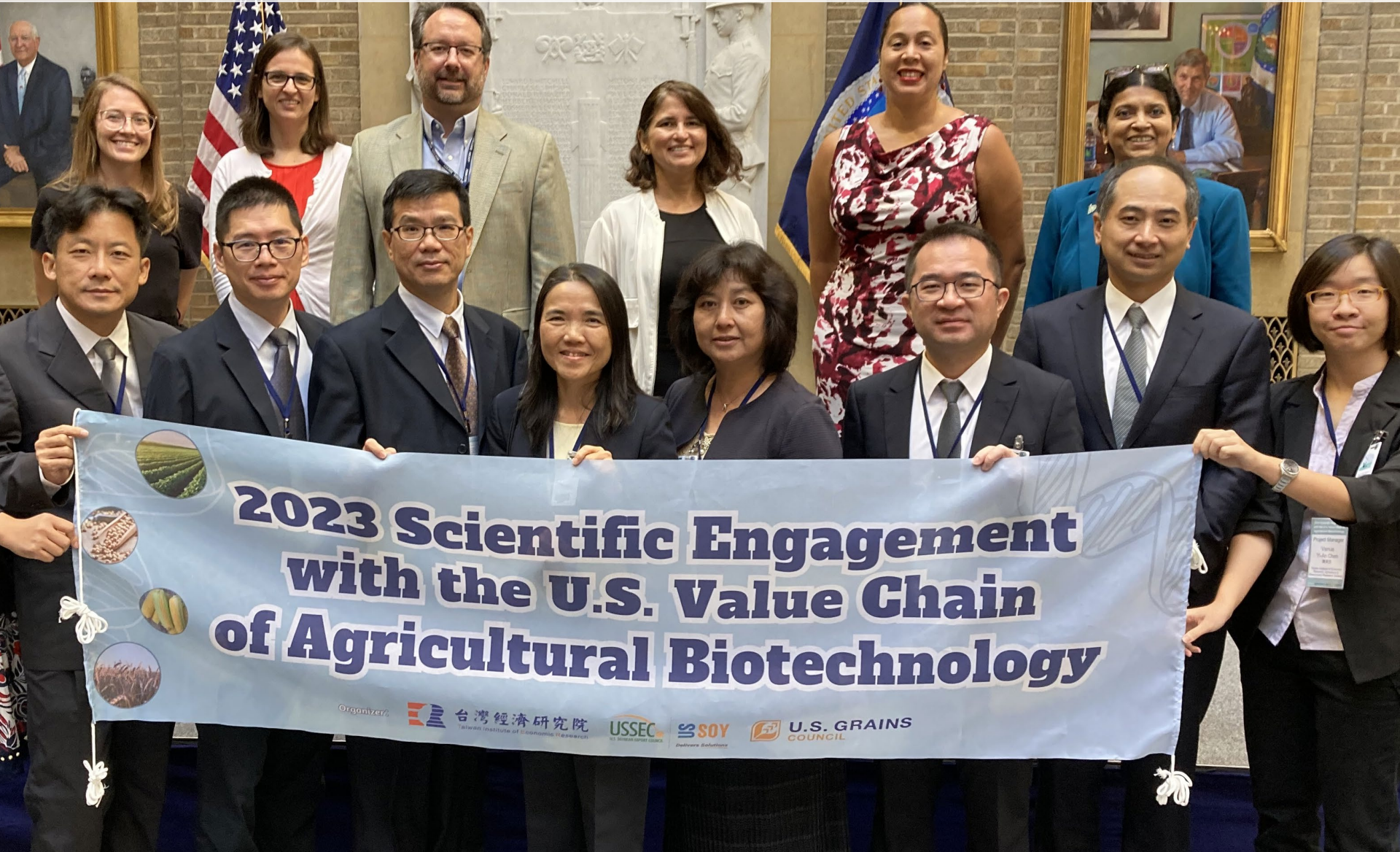
Multi-Lateral Engagement

Tri-lateral Technical Working Group

Inter-American Institute for Cooperation in Agriculture

Asia-Pacific Economic Cooperation

Thank you!


2023 Scientific Engagement
with the U.S. Value Chain
of Agricultural Biotechnology
Organizer:
台灣經濟研究院
Taiwan Institute of Economic Research
USSEC
SOY
U.S. GRAINS
COUNCIL

Questions & Answers

Final Remarks

Bernadette Juarez
BRS Deputy Administrator

Thank you for joining us today!