



Welcome!

Progress on Modernizing the Regulatory System for Biotechnology Products

—Third Public Meeting—

March 30, 2016

9:30 AM – 3 PM

University of California at Davis

Davis Conference Center

550 Alumni Lane

Davis, CA 95616



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Instructions for connecting to
UC Davis Guest Wireless (ucd-guest)



- 1** On your mobile device, choose **ucd-guest** from your available wireless networks.
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- 4** Enter the information requested and click **Register**. You will receive an email and/or text message confirming your account.
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Josette Lewis

Associate Director

World Food Center

University of California at Davis

WELCOME & LOGISTICS

Michael J. Firko
USDA APHIS Deputy Administrator
Biotechnology Regulatory Service
Animal and Plant Health Inspection Service
US Department of Agriculture

OPENING REMARKS & AGENDA



Agenda

- Welcome
- Opening Remarks & Agenda
- Modernizing the Regulatory System for Biotechnology
- Review of Public Comments to RFI
- Progress Update
- Regulation of Biotechnology Product Case Studies
 - Products for Human Food and Animal Feed
 - Products for Biomedical Application
 - Microbial Products for Industrial Application
- Short Break
- Breakout Listening Sessions
- Public Comments
- Additional Information



Robbie Barbero

Assistant Director for Biological Innovation

White House Office of Science and Technology Policy

MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS



Background

- June 1986: White House Office of Science and Technology Policy (OSTP) issued The Coordinated Framework for the Regulation of Biotechnology
- February 1992: OSTP issued an update to the Coordinated Framework
- January 2011: Executive Order 13563—Improving Regulation and Regulatory Review
- July 2015: Executive Office of the President (EOP) issued an memorandum directing US Environmental Protection Agency (EPA), US Food and Drug Administration (FDA), and US Department of Agriculture (USDA) to
 - update the Coordinated Framework for the Regulation of Biotechnology by clarifying current roles and responsibilities;
 - commission an expert analysis of the future landscape of biotechnology products to support this effort; and
 - develop a long-term strategy to ensure that the Federal biotechnology regulatory system is prepared for the future products of biotechnology.



2015 Memorandum on Modernizing the Regulatory System for Biotechnology Products

Goals and Guidance

- Federal agencies that regulate biotechnology products should continually strive to improve predictability, increase efficiency, and reduce uncertainty in their regulatory processes and requirements. It is critical that these improvements
 - maintain high standards that are based on the best available science and that deliver appropriate health and environmental protection;
 - establish transparent, coordinated, predictable, and efficient regulatory practices across agencies with overlapping jurisdiction; and
 - promote public confidence in the oversight of the products of biotechnology through clear and transparent public engagement.



Principles Guiding the Regulation of Biotechnology Products*

- The process used to make a product does not determine the safety of or risk posed by the product; rather it is the characteristics of the organism, the environment into which it will be introduced, and the application of the organism that determine risk (or lack thereof) of a biotechnology product
- A risk-based approach to regulation should distinguish between those organisms that require a certain level of federal action and those that do not
- A risk-based approach properly protects public health and the environment against risk, and avoids hindering safe innovations
- Each agency will use its existing statutory authorities and regulatory programs to help ensure the safety of the biotechnology products
- Federal statutes and implementing regulations regulate products based on specific uses, which allows similar products (whether made using biotechnology or not) to be treated similarly by regulatory agencies
- Agencies should seek to operate their programs in an integrated and coordinated fashion
- Although there is some inconsistency in statutory nomenclature, reviews conducted by each regulatory agency is of comparable rigor
- Future scientific developments will lead to further refinements of Federal policies

*Source: 1986 Coordinated Framework for the Regulation of Biotechnology and the 1992 update



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PROGRESS TO DATE



Modernizing the Regulatory System for Biotechnology Products: Progress to Date

- July 2015: Formed the Biotechnology Working Group under the auspices of the Emerging Technologies Interagency Policy Coordination (ETIPC) Committee
- October – November 2015: Request for Information (RFI) posted on the Federal Register
 - 903 comments received
- October 30, 2015: First public meeting at FDA White Oak Campus, Silver Spring, MD
 - USDA/APHIS, EPA, and FDA discussed Federal regulation of biotechnology products
 - Over 300 registered to attend in-person or via webcast
 - 17 oral comments



Modernizing the Regulatory System for Biotechnology Products: Progress to Date

- January 2016: National Academies of Science announces study called “Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System”
 - Major advances and potential new types of biotech products over the next 5–10 years,
 - Whether potential future products could pose different types of risk relative to existing products and organisms,
 - Areas in which the risks or lack of risk relating to biotechnology are well understood, and
 - What scientific capabilities, tools, and expertise may be useful to the regulatory agencies to support oversight of potential future products of biotechnology
- March 2016:
 - Website established: www.nas.edu/biotech
 - First public meeting announced: April 18 at NAS building in D.C.
 - Provisional study committee announced



Modernizing the Regulatory System for Biotechnology Products: Progress to Date

- November 2015 – March 2016: USDA, EPA, FDA, and EOP reviewed the public responses to RFI
- Ongoing: Updating Coordinated Framework and developing long-term strategy
- March 9, 2016: Second public meeting at EPA, Region 6 Facility, Dallas, TX
- March 30, 2016: Third public meeting hosted by USDA at UC-Davis, Davis, CA
- Spring/Summer 2016: Update to Coordinated Framework will be made available for public comment



US Department of Agriculture / Animal and Plant Health Inspection Service
US Environmental Protection Agency
US Food and Drug Administration

REGULATION OF BIOTECHNOLOGY PRODUCTS



Agency Protection Goals for the Regulation of Biotechnology Products

Agency	Statute	Protection Goals
USDA/APHIS	Animal Health Protection Act (AHPA)	Protect livestock from animal pests and disease risks
USDA/APHIS	Plant Protection Act (PPA)	Protect agricultural plants and agriculturally important natural resources from damage caused by organisms that pose plant pest or noxious weed risks
EPA	Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)	Eliminate unreasonable adverse effects upon man and the environment <ul style="list-style-type: none"> • For environmental and occupational risks, this involves comparing economic, social, and environmental risks and benefits associated with pesticide use • For dietary or residential human health effects, the sole standard is the safety of exposure
EPA	Food, Drug, and Cosmetics Act (FD&C Act)	Ensure dietary exposure to pesticide chemical residues in or on food are safe
EPA	Toxic Substances Control Act (TSCA)	Ensure the manufacture, processing, distribution in commerce, use, or disposal of chemical substances, or any combination of such activities with such substances does not present unreasonable risk of injury to health or the environment
FDA	FD&C Act Public Health Service Act	Ensure food is safe, sanitary, and properly labeled Ensure human and veterinary drugs are safe and effective Ensure there is a reasonable assurance of safety and effectiveness of devices intended for human use Ensure cosmetics are safe and properly labeled Ensure public health and safety are protected from electronic product radiation Regulate tobacco products



Field Trials: Containment vs. Confinement

- **Containment Procedures**

- Prevent exposure of GE plants to the environment
- Probability of release should be near zero

- **Confinement Procedures**

- Ensure GE plants do not persist in the environment
- Probability of persistence should be near zero

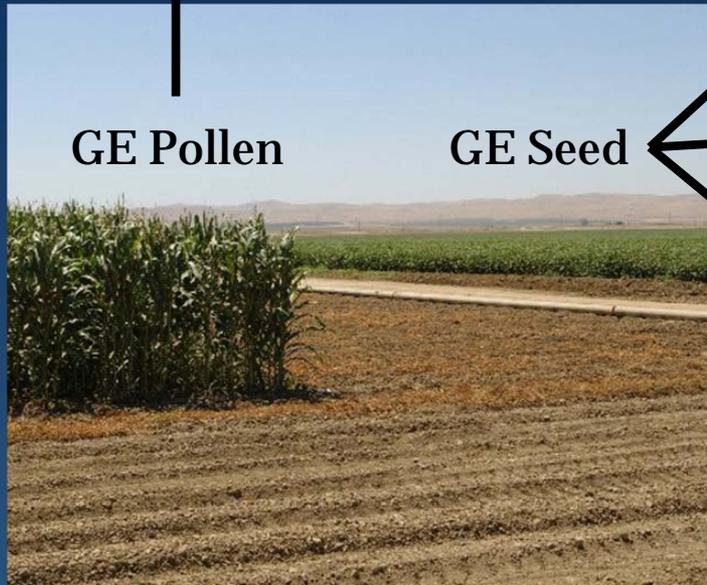


Contained Greenhouse Facility



Confined Field Trials: Maintain GE and Non-GE Plant Separation and Prevent GE Plant Persistence

Maintain appropriate separation distance to sexually receptive plants while pollen is being produced.



- Clean GE seed from planters and harvesters
- Keep GE separated from non-GE seeds

- Next growing season remove volunteer plants before pollen or seed is produced
- Follow crop planting restrictions

GE seed from test is not used for human or animal food

Confined Field Trials: Considerations

- Is the crop out-crossing or self-pollinating?
- Is it weedy or invasive?
- Are there wild or invasive relatives?
- Can the plant or offspring persist after the test is over?
- Would the trait be expected to change the plant's weediness, invasiveness, or reproductive biology?



Petition Evaluations

- Crop biology and taxonomy
- Any genotypic differences
- Any phenotypic differences
- Field test reports for all releases conducted in the United States
- Relevant experimental data, publications, and other data upon which to base a determination



Petition Process for Non-Regulated Status

- APHIS BRS conducts two evaluations
 - Plant Pest Risk Assessment to determine if the GE organism poses a risk as a plant pest (Plant Protection Act)
 - Environmental Assessment or Environmental Impact Statement to broadly evaluate environmental impacts of APHIS/BRS decision (National Environmental Policy Act (NEPA))



Components of a Plant Pest Risk Assessment

- Create pest or disease problems for agriculture
- Become a weed
- Increase the weediness of sexually compatible plants
- Harm non-target organism (e.g., beneficial, endangered)
- Affect agricultural practices in a way which could create disease and pest problems
- Transmit the genes to organisms with which it does not normally interbreed



Data Needs for MCANs and TERAs

- *Points to Consider* Guidance Document*
 - Taxonomic description of the recipient and donor organisms
 - Detailed construction of the submission microorganism
 - Human health effects information
 - Environmental effects information on submission microorganism
 - By-products, production volume, and use information
 - Worker exposure and environmental release/containment
 - Environmental release protocols
 - Expected survival/dispersion (i.e., environmental exposures)
 - Emergency/contingency protocols

*Source: https://wcm.epa.gov/sites/production/files/2015-08/documents/biotech_points_to_consider.pdf



Plant-Incorporated Protectants

- How EPA Characterizes PIPs
 - Transformation system
 - Characterization of the DNA inserted into the plant
 - Inheritance and stability of genetic insertion after transformation
 - Protein characterization and expression
- How EPA Assesses Human Health Effects of PIPs
 - In vitro* digestibility assay
 - Amino acid homology / toxin and allergen comparison
 - Heat stability
 - Acute oral toxicity
- How EPA Assesses Environmental Effects of PIPs
 - Pesticidal substance expression in the plant
 - Environmental fate of genetic insertion
 - Gene flow
 - Non-target effects

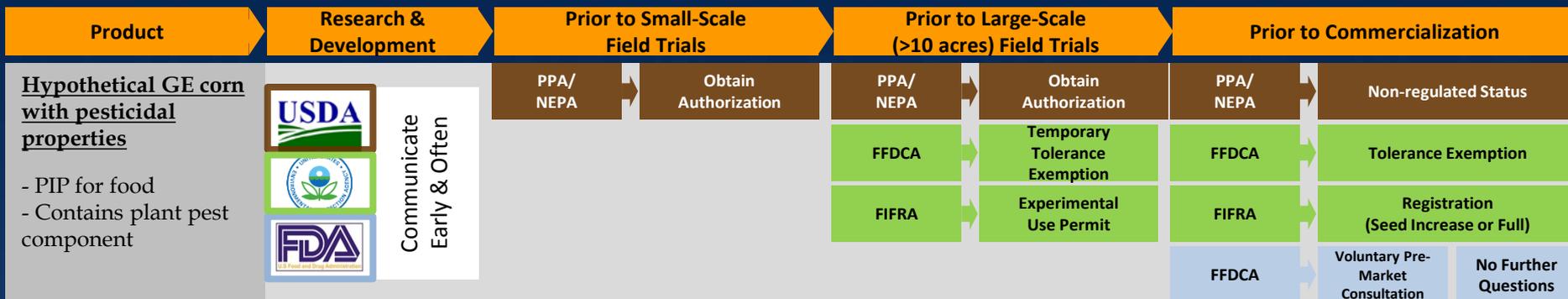


Data & Information Typically Considered as Part of FDA's Voluntary Consultation Program

- What is the crop?
 - What are the human and animal food uses of the crop?
 - What is the purpose or intended technical effect of the modification in the crop?
- Safety assessment components
 - Molecular characterization to aid in identifying what is new/changed in the food that may impact safety/nutrition
 - Safety of newly expressed substances
 - Potential toxicity of newly expressed substances
 - Potential allergenicity of newly expressed proteins
 - Levels of key nutrients, anti-nutrients, and toxicants in food from the plant
- Assessment is performed on a case-by-case basis



Case Study: Products for Human Food and Animal Feed



**Note that in many cases, products of biotechnology also have post market monitoring and reporting requirements that will apply but are not depicted here. More information on such requirements are available in relevant agency regulations and guidances.*



Product: Hypothetical GE Corn with Pesticidal Properties

- Typical Major Milestones During Product Development—
USDA/APHIS
 - During R&D phase
 - Notification for interstate movement or import
 - Prior to small- or large-scale field trials
 - Notification or permit for interstate movement, import, or release
 - Fulfill National Environmental Policy Act (NEPA) obligations
 - Confined field trials usually are categorically excluded actions under NEPA
 - Prior to commercialization
 - May petition for non-regulated status
 - NEPA-usually an EA-could be an Environmental Impact Statement (EIS)



Product: Hypothetical GE Corn with Pesticidal Properties

- Typical Major Milestones During Product Development—EPA
 - During R&D phase
 - N/A
 - Prior to small-scale field trials (cumulative plot size <10 acres)
 - N/A
 - Prior to large-scale field trials (cumulative plot size >10 acres)
 - Obtain a temporary tolerance or tolerance exemption for the residues of the pesticidal trait in the food if GE corn will enter the food supply
 - Obtain an experimental use permit (EUP)
 - Prior to commercialization
 - Obtain tolerance or tolerance exemption for the residues of the pesticidal trait in the food if GE corn will enter food supply
 - Register GE corn Plant-Incorporated Protectant (PIP)

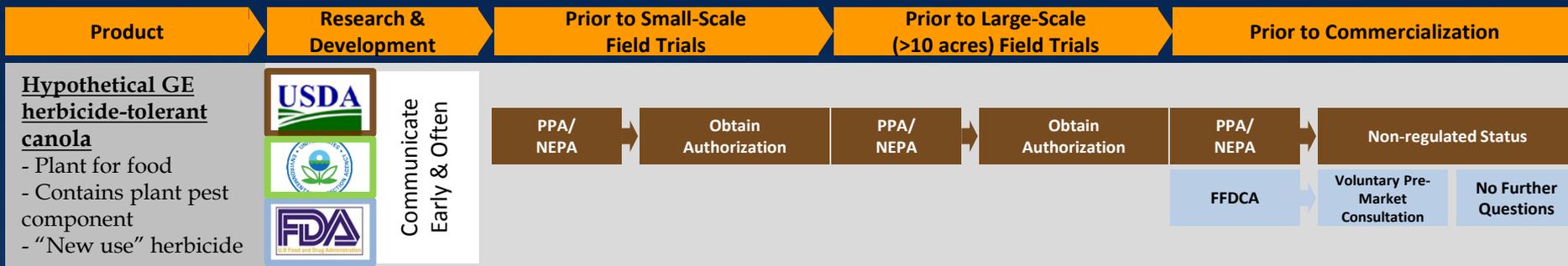


Product: Hypothetical GE Corn with Pesticidal Properties

- Typical Major Milestones During Product Development—FDA
 - During R&D phase
 - N/A
 - Prior to small-scale field trials
 - May provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to large-scale field trials
 - If not already done, may provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to commercialization
 - Developer is strongly encouraged to complete a voluntary consultation with FDA to help ensure any food safety or other regulatory issues are resolved



Case Study: Products for Human Food and Animal Feed



*Note that in many cases, products of biotechnology also have post market monitoring and reporting requirements that will apply but are not depicted here. More information on such requirements are available in relevant agency regulations and guidances.



Product: Hypothetical Herbicide-Tolerant Canola

- **Typical Major Milestones During Product Development—
USDA/APHIS**
 - **During R&D phase**
 - Notification for interstate movement or import
 - **Prior to small- or large-scale field trials**
 - Notification or permit for interstate movement, import, or release
 - Fulfill National Environmental Policy Act (NEPA) obligations
 - Confined field trials usually are categorically excluded actions under NEPA
 - **Prior to commercialization**
 - May petition for non-regulated status
 - NEPA-usually an EA-could be an Environmental Impact Statement (EIS)



Product: Hypothetical Herbicide-Tolerant Canola

- Typical Major Milestones During Product Development—EPA
 - During R&D phase
 - N/A
 - Prior to small-scale field trials
 - N/A (provided Herbicide-X-treated-canola is kept out of the food supply)
 - Prior to large-scale field trials
 - Obtain a temporary tolerance for Herbicide X if Herbicide-X-treated-canola will enter the food supply and Herbicide X residues are not covered by an existing tolerance
 - Obtain an experimental use permit (EUP) for Herbicide X
 - Prior to commercialization
 - Obtain a tolerance for Herbicide X
 - Amend Herbicide X registration



Product: Hypothetical Herbicide-Tolerant Canola

- Typical Major Milestones During Product Development—FDA
 - During R&D phase
 - N/A
 - Prior to small-scale field trials
 - May provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to large-scale field trials
 - If not already done, may provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to commercialization
 - Developer is strongly encouraged to complete a voluntary consultation with FDA to help ensure any food safety or other regulatory issues are resolved



Products for Human Food and Animal Feed

Questions & Answer Session



Case Study: Products for Biomedical Application



**Note that in many cases, products of biotechnology also have post market monitoring and reporting requirements that will apply but are not depicted here. More information on such requirements are available in relevant agency regulations and guidances.*



Product: Hypothetical GE Rabbit

- Typical Major Milestones During Product Development—FDA
 - After animal lineage is established
 - Initiate discussion of GE rabbit with CVM
 - Open an investigational new animal drug (INAD) file with CVM
 - Submit data and information pertaining to GE rabbit lineage to INAD
 - Prior to clinical trials activities related to recombinant insulin
 - Obtain an investigational new drug (IND) exemption from CDER
 - Prior to commercialization
 - Submit a new animal drug application (NADA) for rDNA construct in the rabbit
 - Submit EA or claim a categorical exemption
 - Submit a new drug application (NDA) for recombinant insulin
 - Submit EA or claim a categorical exemption
 - Demonstrate GE rabbit and recombinant insulin meet safety and effectiveness standards



Data & Information in GE Animal INAD and NADA Submissions*

- Investigational New Animal Drug (INAD)
 - INAD file should include information about the GE animal, e.g., species of animal under study, introduced gene(s), intention of modification, including any gene product(s) produced
 - In general, INAD regulations specify:
 - Labeling and record-keeping requirements
 - Animal disposition
 - NCIE Notice, prior to shipping any GE animals
 - Environmental considerations
- Recommended process for submitting data for GE animal New Animal Drug Application (NADA)
 - Product identification
 - Molecular characterization of the construct
 - Molecular characterization of the GE animal lineage
 - Phenotypic characterization of GE animal
 - Genotypic and phenotypic durability assessment and durability plan
 - Food/feed safety and environmental safety assessments
 - Effectiveness/claim validation

*See GFI 187 for more information

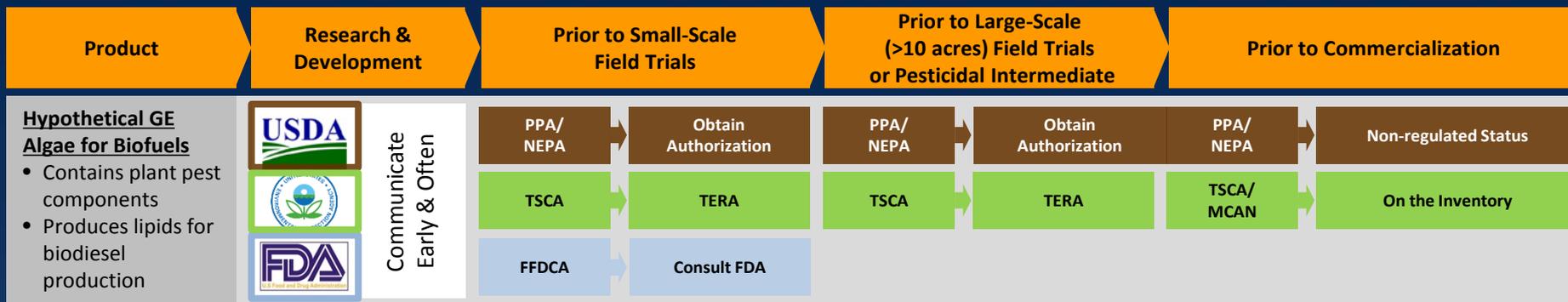


Products for Biomedical Applications

Questions & Answer Session



Case Study: Microbial Products for Industrial Application



**Note that in many cases, products of biotechnology also have post market monitoring and reporting requirements that will apply but are not depicted here. More information on such requirements are available in relevant agency regulations and guidances.*



Open Raceway Pond Facility for Algae Cultivation



Photo courtesy of AzCati



Product: Hypothetical GE Algae for Biofuels

• Typical Major Milestones During Product Development— USDA/APHIS

–During R&D phase

- Notification for import or interstate movement

–Prior to small- or large-scale field trials

- Notification for interstate movement, import, or release
- Fulfill NEPA obligations
 - Confined field trials usually are categorically excluded actions
 - Exceptions for new species or novel modifications that raise new issues (most likely an EA)

-Prior to commercialization

- May petition for non-regulated status.
- NEPA-usually an EA-could be an EIS



Product: Hypothetical GE Algae for Biofuels

• Typical Major Milestones During Product Development—EPA

– During contained R&D phase (e.g. lab development)

- No reporting requirements
- Technically qualified individual (TQI) assigned
- Recordkeeping and other good laboratory practices (GLP) required

– Prior to small-scale field trials

- Submit a TSCA experimental release application (TERA) at least 60 days before field work
- Obtain TERA approval

– Prior to large-scale field trials

- Submit a TSCA experimental release application (TERA) if the initial TERA did not cover all project phases
- Obtain TERA approval

– Prior to commercialization

- Submit microbial commercial activity notice (MCAN) at least 90 days prior to initiation of manufacture, importation, or use
- Submit a notice of commencement to have GE alga added to the TSCA inventory



Product: Hypothetical GE Algae for Biofuels

- Typical Major Milestones During Product Development—FDA
 - During R&D phase
 - N/A
 - Prior to small-scale field trials
 - May provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to large-scale field trials
 - If not already done, may provide information for consideration and initiate consultation about food safety and other FDA-related regulatory issues
 - Prior to commercialization
 - Developer is strongly encouraged to consult with FDA to help ensure any food safety or other regulatory issues are resolved



Microbial Products for Industrial Application

Questions & Answer Session



Short Break

- We will proceed to breakout listening sessions at the end of this break.



BREAKOUT LISTENING SESSIONS



Breakout Listening Sessions

Governance

- What is the role of stakeholders outside of government? How can the regulatory agencies engage non-governmental stakeholders as participants in the governance of biotechnology?
- Is there a role for other government agencies or offices (for example, non-regulatory agencies or offices) in the governance of biotechnology?

Education, Communication, & Outreach

- What are the needs of various stakeholders for understanding and accessing information on regulatory agency activities? What specific information is needed? How could this information be delivered?
- How should information be presented for various stakeholders to make regulatory agency activities clear and understandable?

Improving Regulatory Certainty

- What specific aspects of regulatory processes or procedures can regulatory agencies improve to make regulatory oversight for products of biotechnology more transparent, coordinated, predictable, and efficient while continuing their primary role(s)?
- What specific information can regulatory agencies, or other agencies and offices, provide to biotechnology product developers, especially small businesses, to assist in their efforts to navigate the regulatory system?



Reporting Back on Governance Listening Session

- TBD



Reporting Back on Education, Communication, & Outreach Listening Session

- TBD



Reporting Back on Improving Regulatory Certainty Listening Session

- TBD



Moderator: Robbie Barbero

Assistant Director for Biological Innovation

White House Office of Science and Technology Policy

PUBLIC COMMENT



Public Comment

- TBD



ADDITIONAL INFORMATION



Additional Information

- **1986 Coordinated Framework for Regulation of Biotechnology**
 - https://www.aphis.usda.gov/brs/fedregister/coordinated_framework.pdf
- **1992 Update to Coordinated Framework: Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products Into the Environment**
 - https://www.whitehouse.gov/sites/default/files/microsites/ostp/57_fed_reg_6753__1992.pdf
- **2015 EOP Memo and Blog post: Modernizing the Regulatory System for Biotechnology Products**
 - https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf
 - <https://www.whitehouse.gov/blog/2015/07/02/improving-transparency-and-ensuring-continued-safety-biotechnology>
- **Other Relevant Policy Documents**
 - “Improving Regulation and Regulatory Review”, Executive Order 13563, January 18, 2011.
 - <http://www.gpo.gov/fdsys/pkg/FR-2011-01-21/pdf/2011-1385.pdf>
 - “Principles for Regulation and Oversight of Emerging Technologies”, Memorandum for the Heads of Departments and Agencies, March 11, 2011.
 - <https://www.whitehouse.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf>
 - “Identifying and Reducing Regulatory Burdens”, Executive Order 13610, January 10, 2012.
 - https://www.whitehouse.gov/sites/default/files/docs/microsites/omb/eo_13610_identifying_and_reducing_regulatory_burdens.pdf

