Welcome to the BsUFA III Interim Public Meeting

Darlese Solorzano, MS, MBA, Program Manager of the BsUFA III Regulatory Science Pilot Program, OPQAIII|OPQ|CDER|FDA

Disclosures

- No financial disclosures

- This presentation represents the views of the speaker(s) and not necessarily those of FDA

Agenda

Time	Event (and Proposed Speakers / Panelists)
9:00 – 9:15am	**Welcome and Introduction** (Darlese Solorzano)
9:15 – 9:30am	**The Role of Regulatory Science at the FDA and Impetus for the BsUFA III Regulatory Science Pilot Program** (Steve Kozlowski)
9:30 – 10:15am	**Pilot Program Overview:** Establishing the regulatory science pilot program and summary of stakeholder input (Emanuela Lacana and Darlese Solorzano)
10:15 – 10:30am Break	
10:30am – 12:00pm	**Research Progress Awardee Presentations*** (Moderated by Darlese Solorzano) Research Progress updates by Regulatory Impact 1 & 2: •Priority A: FDA/OTS-Landscape Analysis (Dr. Jeffry Florian) •Priority B: FDA/OPQ-Model Development and Verification of Stability Data (Dr. Uriel Ortega-Rodriguez and Dr. Mari Lehtimaki) •Priority C: FDA/OPQ-Bioassay (Dr. Carole Sourbier) •Priority D: AMCP/ BBCIC - Improving the Efficiency of Regulatory Decisions for Biosimilars (Dr. Cate Lockhart) •Priority E - FDA/OTS- Translating Clinical Pharmacology Biosimilars (Dr. Lakshmi Manasa Sakuntala Chekka) •Q&A/Panel with Presenters **Presentation selections based on stakeholder input from Jan 22, 2025 SBIA meeting*
12:00 – 1:15pm	**Lunch and In-Person Poster Session**
1:15 – 1:45pm	**Poster session Q&A** *(virtual and in-person)* with awardees who did not present (Moderated by Darlese Solorzano)
1:45 – 2:00pm	**Pilot Program Interim Evaluation and Next Steps** (Sarah Yim) •Interim ROI and lessons learned from 3 years of the Pilot Program •FDA's preliminary thoughts on the role of regulatory science in biosimilar development
2:00 – 3:00pm	**Industry Reactions and Panel Discussion:** (Moderated by Susan Winckler from the Reagan-Udall Foundation) •Current perspectives about the role of regulatory science in biosimilar development •Discussion questions and audience Q&A Panelists: •AAM (Cory Wohlbach) •Biosimilar Forum (Juliana Reed) •PhRMA (Sean Hilscher) •FDA (Emanuela Lacana and Sarah Yim)
3:00 – 3:10pm	**Conclusion and Close Out** (Emanuela Lacana and Darlese Solorzano)

Todays Presenters & Panelist

Steven Kozlowski, MD
Acting Chief Scientist
Office of the Chief Scientist
Office of the Commissioner (OC)
FDA

Darlese Solorzano, MS, MBA
Program Manager
CDER BsUFA III Regulatory Science Pilot Program
Office of Pharmaceutical Quality Assessment IIII (OPQAIII)
Office of Pharmaceutical Quality (OPQ) |CDER|FDA

Emanuela Lacana, PhD
Deputy Director
Office of Therapeutics Biologics and Biosimilars (OTBB)
Office of New Drugs (OND) |CDER|FDA

Jeffry Florian, PhD
Associate Director
Division of Applied Regulatory Science (DARS)
Office of Clinical Pharmacology (OCP)
Office of Translational Sciences (OTS) | CDER | FDA

Uriel Ortega-Rodriguez, PhD
Research Scientist
Office of Pharmaceutical Quality Research (OPQR)
Office of Pharmaceutical Quality (OPQ)| CDER | FDA

Mari Lehtimaki, PhD
Interdisciplinary Scientist
Office of Pharmaceutical Quality Research (OPQR)
Office of Pharmaceutical Quality (OPQ)| CDER | FDA

Carole Sourbier, PhD
Senior Research Biologist
Office of Pharmaceutical Quality Research (OPQR)
Office of Pharmaceutical Quality (OPQ)| CDER | FDA

Cate Lockhart, PharmD, PhD
Executive Director
Biologics and Biosimilar Collective Intelligence Consortium (BBCIC)

Lakshmi Manasa Sakuntala Chekka, PharmD, PhD
Visiting Associate
Division of Applied Regulatory Science (DARS)
Office of Clinical Pharmacology (OCP)
Office of Translational Sciences (OTS) | CDER | FDA

Sarah Yim, MD
Director
Office of Therapeutics Biologics and Biosimilars (OTBB)
Office of New Drugs (OND) |CDER|FDA

Ashutosh Rao, PhD*
Division Director
Office of Pharmaceutical Quality Assessment IIII (OPQAIII)
Office of Pharmaceutical Quality (OPQ) |CDER|FDA

Michelle Stafford, MS*
Statistical Analyst
Office of Biostatistics (OB)
Office of Translational Sciences (OTS) | CDER | FDA

* Invited Subject Matter Experts to the research panel discussion.

Todays Scientific Poster Panelist

Diane McCarthy, PhD
Senior Scientific Director
Global Biologics U.S Pharmacopeia (USP)

Reza Nejadnik, PhD
Associate Professor
University of Iowa College of
Pharmacy

Anna Schwendeman, PhD
Larry and Ann Hsu Professor of Pharmaceutical Sciences
University of Michigan, Ann Arbor

Anne De Groot, MD
Chairman of the board and CMO
EpiVax, Inc.

Tongzhong Ju, MD, PhD
Senior Pharmaceutical Scientist
Office of Pharmaceutical Quality Research (OPQR)
Office of Pharmaceutical Quality (OPQ)| CDER | FDA

Daniela Verthelyi, MD, PhD
Supervisory SBRBPAS Expert
Division Director
Office of Pharmaceutical Quality Research (OPQR) IV
Office of Pharmaceutical Quality (OPQ)| CDER | FDA

Yow-Ming Wang, PhD
Associate Director for Biosimilars
Office of Clinical Pharmacology (OCP)
Office of Translational Sciences (OTS) CDER|FDA

Kristina Howard, DVM, PhD
Research Veterinary Medical Officer
Division of Applied Regulatory Science (DARS)
Office of Clinical Pharmacology (OCP)
Office of Translational Sciences (OTS) | CDER | FDA

Invited Industry Panelist

Juliana M. Reed
Executive Director
Biosimilars Forum

Sean Hilscher
Senior Director of
Science and Regulatory Advocacy
PhRMA

Cory Wohlbach
Global VP
Biosimilars Regulatory Affairs
Teva
AAM Representative

Moderated by:
Susan C. Winckler, RPh, Esq
Chief Executive Officer
Reagan-Udall Foundation for the FDA

Ground Rules & Housekeeping

No policy or guidance will be made today.

Step out and take breaks as needed (Kiosk open) but refrain from calls etc. that could be distracting.

The public meeting is being recorded and will be made available post meeting on the Biosimilars | Science and Research | FDA website.

For Questions and Answers (Q&A):

Virtual and In-Person Attendees: please use the QR Code provided for questions.

All questions should include the name of the panelist the question is being addressed to.

The State of Biosimilars at FDA

Approvals and Programs

74
Approved Biosimilars to **19** Reference products

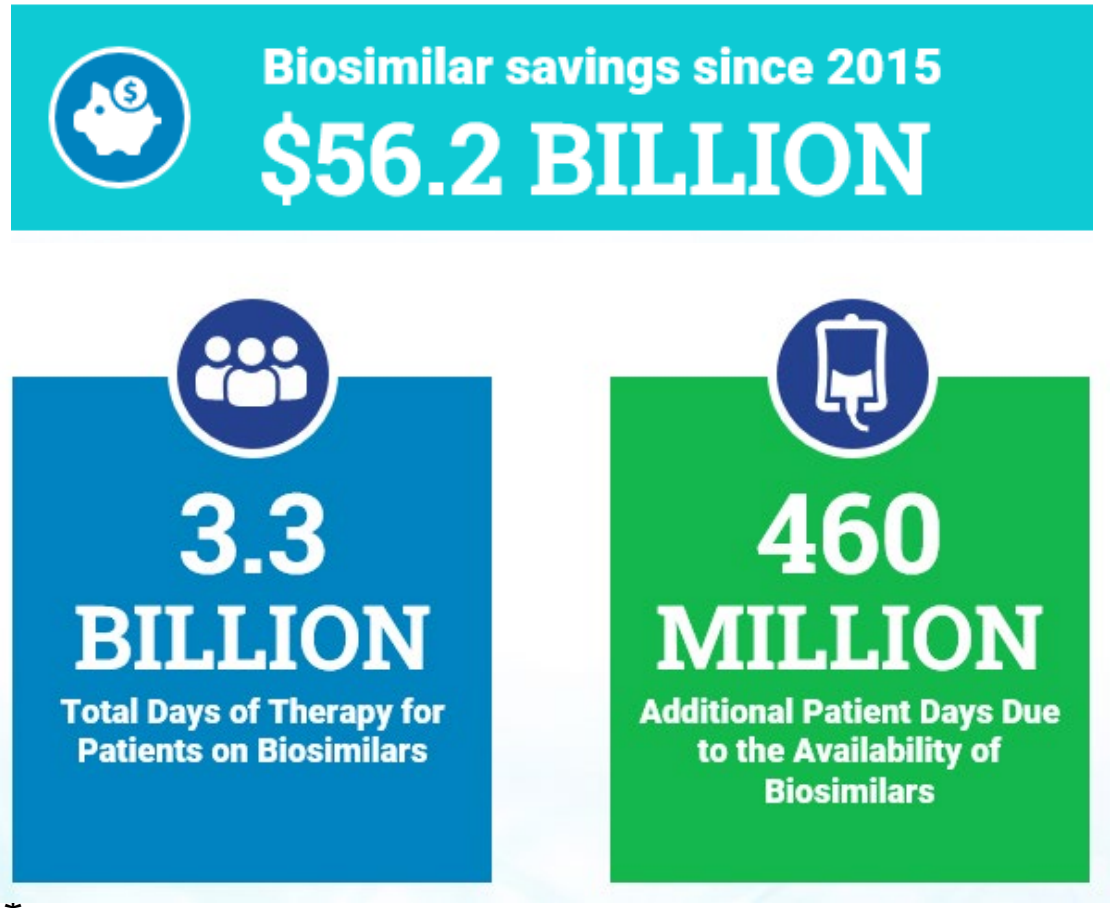
27
Interchangeable biosimilars

53
Currently Marketed to **16** different reference products

129
BS development programs for 63 reference products

***As of September 16, 2025**

As a result….



*Source AAM / 2025 U.S. Generic and Biosimilar Medicines Savings Report
https://accessiblemeds.org/resources/blog/2025-savings-report/

BsUFA III Regulatory Science Commitment

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development.

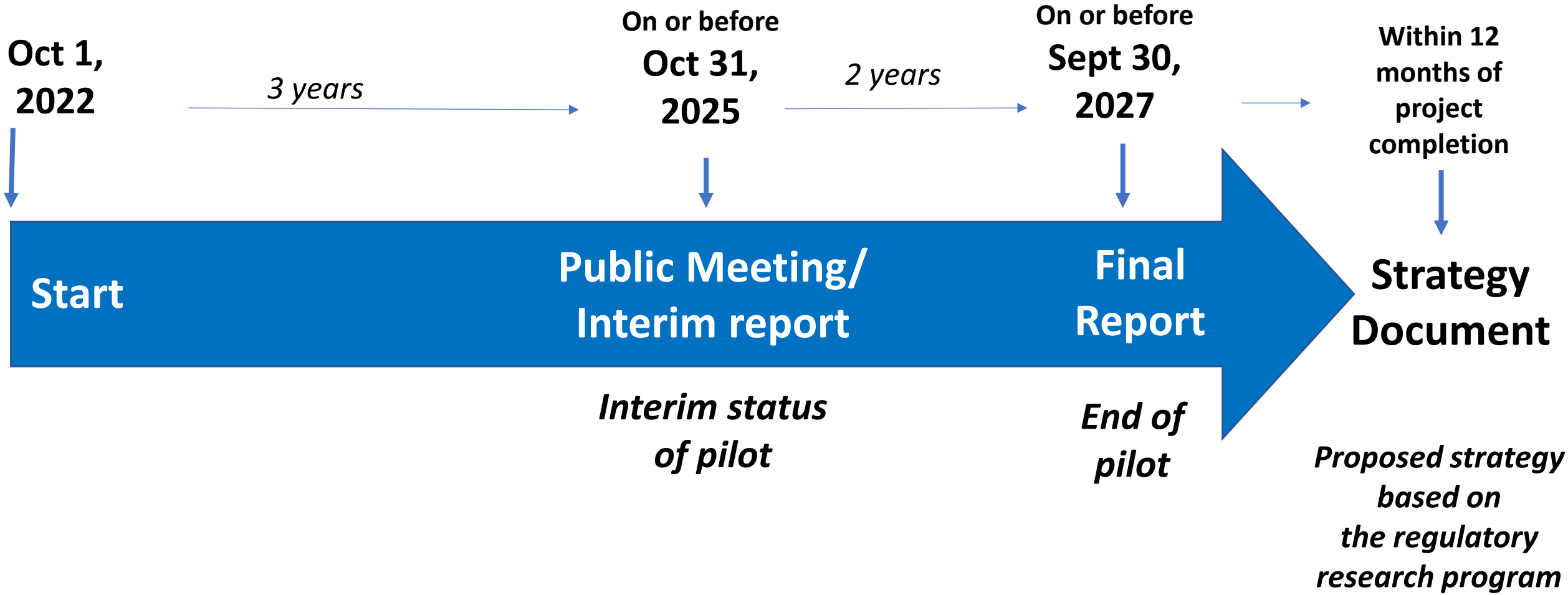
FDA will pilot a regulatory science program to facilitate ways to

(1) improve the efficiency of biosimilar product development and

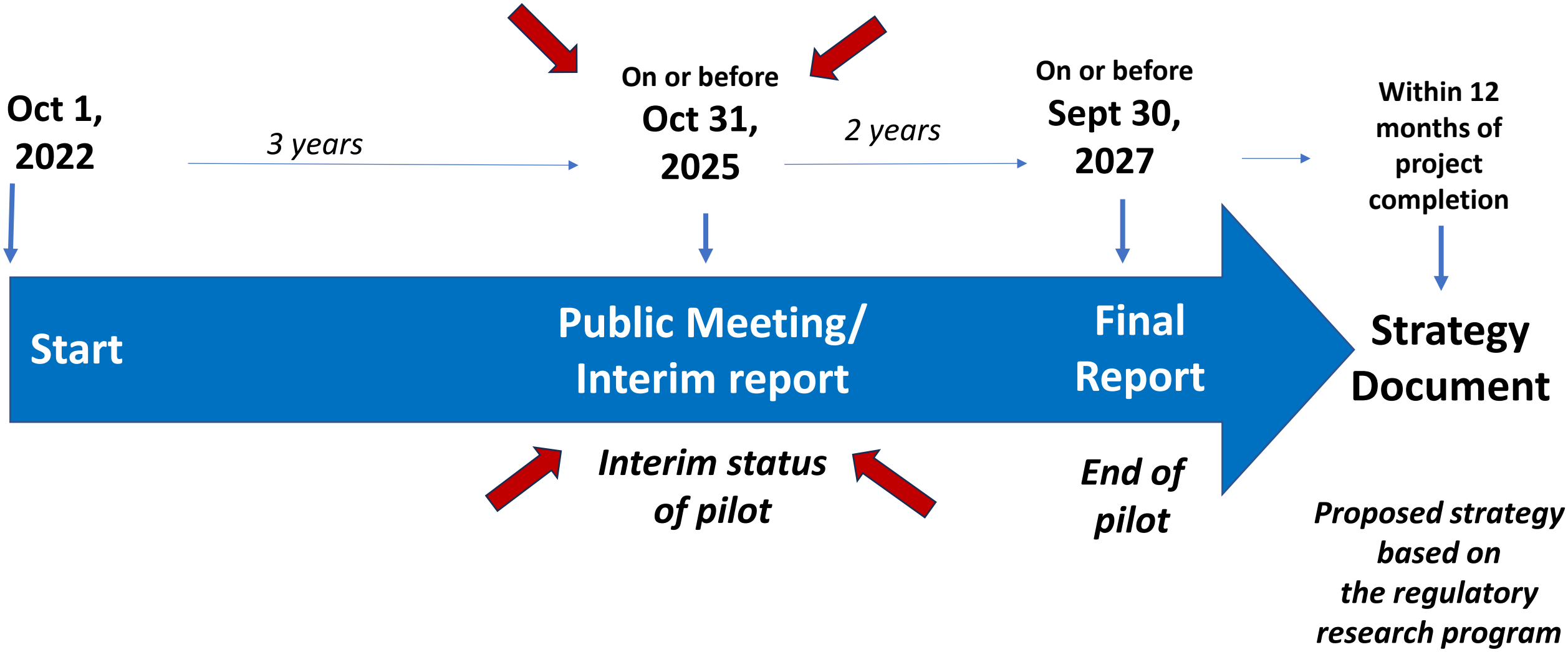
(2) advance the development of interchangeable products

Commitment Letter

Regulatory Science Pilot Program Deliverables



Regulatory Science Pilot Program Deliverables



The Goal of the BsUFA III Interim Public Meeting

- To meet the BsUFA III commitment to review the progress of the pilot program aims or demonstration projects.
  - Note, interim report was published June 2025: BsUFA III Regulatory Science Pilot Program Interim Report

- To solicit input on future research priorities.

Thank you!

Regulatory Science at the FDA

BsUFA III Regulatory Science Pilot Program Interim Meeting

Steven Kozlowski, MD,

FDA Acting Chief Scientist

FDA Priorities

JAMA

Viewpoint

Priorities for a New FDA

Martin A. Makary, MD, MPH;
Vinay Prasad, MD, MPH

Published Online: June 10, 2025
doi: 10.1001/jama.2025.10116

- Accelerating Cures
- Unleashing AI
- Healthier Food for Children
- Harnessing Big Data
- Financial Toxicity

Financial Toxicity

"Financial toxicity harms patients. No one took an oath to treat a patient and then ruin their life financially."

BIOSIMILAR BIOLOGICAL PRODUCT REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027

"FDA will use its power to address costs. These include expediting generic medications and massively streamlining the burden to develop biosimilar compounds.

E. REGULATORY SCIENCE TO ENHANCE THE DEVELOPMENT OF BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCTS

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development.

(1) advancing the development of interchangeable products, and

(2) improving the efficiency of biosimilar product development.

Objectives of a Regulatory Science Program

- Improve healthcare and access for patients by enabling efficient and cost-effective product development
- Enhance regulatory decision-making by addressing information gaps and encouraging use of innovative methodologies

GDUFA Regulatory Science: Proven Benefits for Generic Development

- Research that supported generic synthetic peptides that references an rDNA origin RLD, generic abuse-deterrent opioids, and in vitro bioequivalence approach for several products
- Staff in the reg science program supported pre-application scientific advice and product-specific guidance.

Science, Applied Science, Translation Science, and Regulatory Science

Science is the pursuit and application of knowledge and understanding of the natural and social world following a systematic methodology based on evidence.[1]

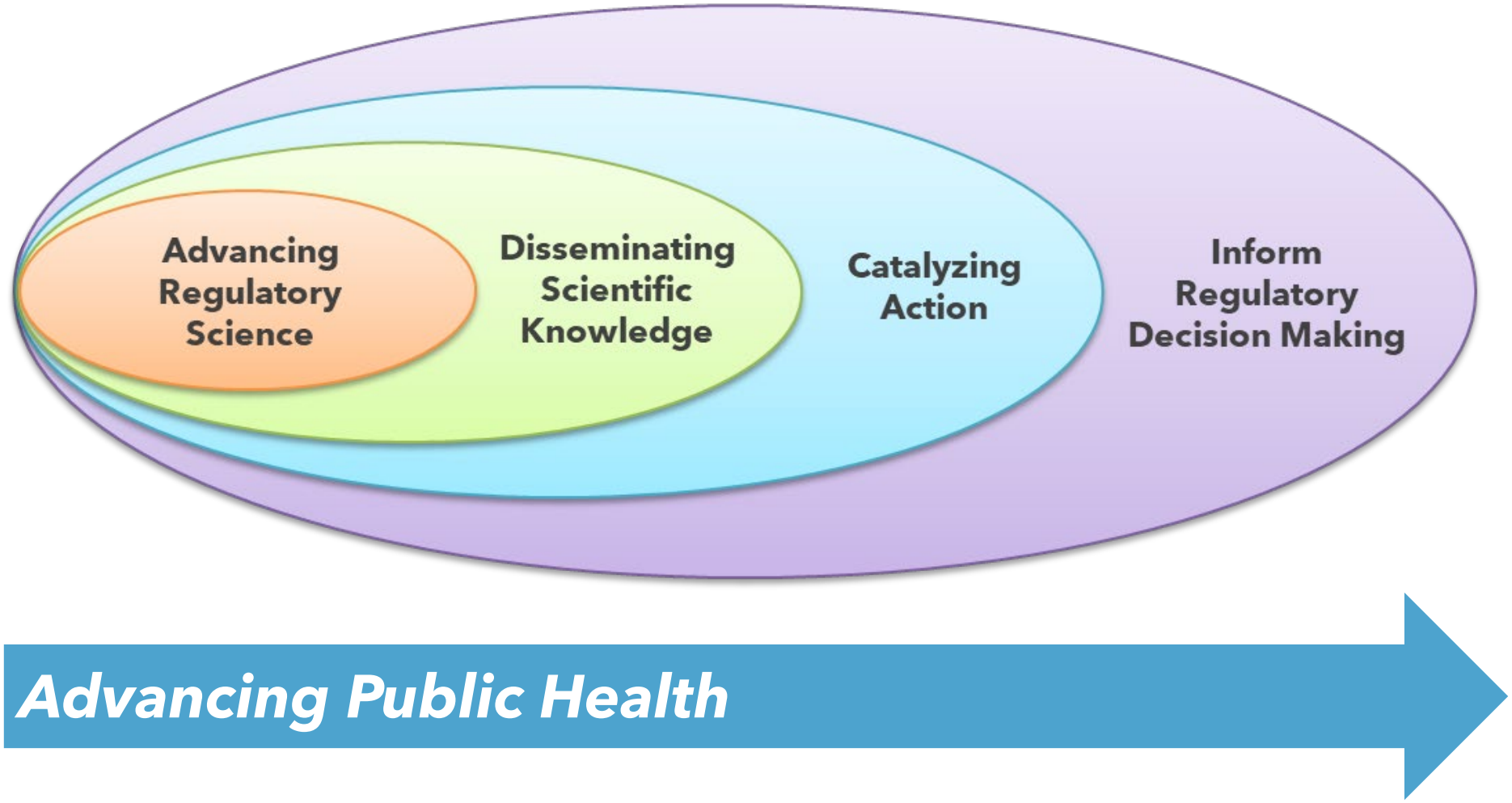
Applied research results in technology and innovation discovery.[2] New knowledge acquired from applied research has specific commercial objectives in the form of products, procedures or services. And, beyond products, technology and innovation can also be used in regulatory science.

Translational science is the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public – from diagnostics and therapeutics to medical procedures and behavioral changes. [NCATS]

Regulatory science is the science of developing tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products. [FDA]

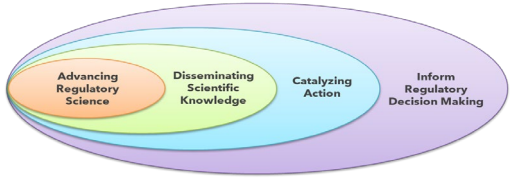
1-https://sciencecouncil.org/about-science/our-definition-of-science/
2-https://www.researchgate.net/publication/304364627

Metrics for Assessing Regulatory Science Research



Outcomes of Interest for Regulatory Science Research Projects | FDA

Metrics for Impact



ADVANCE PUBLIC HEALTH			
Advancing Regulatory Science	**Disseminating Scientific Knowledge**	**Catalyzing Action**	**Inform Regulatory Decision Making**
Alignment with FDA regulatory science priorities	Scientific publications and citations in literature	Adoption/ adaptation of findings by stakeholders	Development or change in: - Reference materials/ standards
Enhancement of FDA resources/ expertise/ capacity	Presentations at conferences, meeting, FDA Advisory Committees	Adoption/ adaptation of findings in advocacy	- Surveillance strategies - Guidelines/guidance
Facilitation of strategic relationships with expert groups	Incorporation into training and/or education curriculum	Technology transfer to stakeholders	- Regulations - Compliance/ enforcement strategies
Building FDA preparedness for rapid response health emergencies and new developments in emerging regulatory science	Medica coverage	Subject of professional society meeting	- inspection/sampling strategies
	Data-sharing with public	Catalyst for future research	- External communication strategies
		Improvements in consumer understanding	- Labeling
		Adoption for use into medical practice	- Agency policy

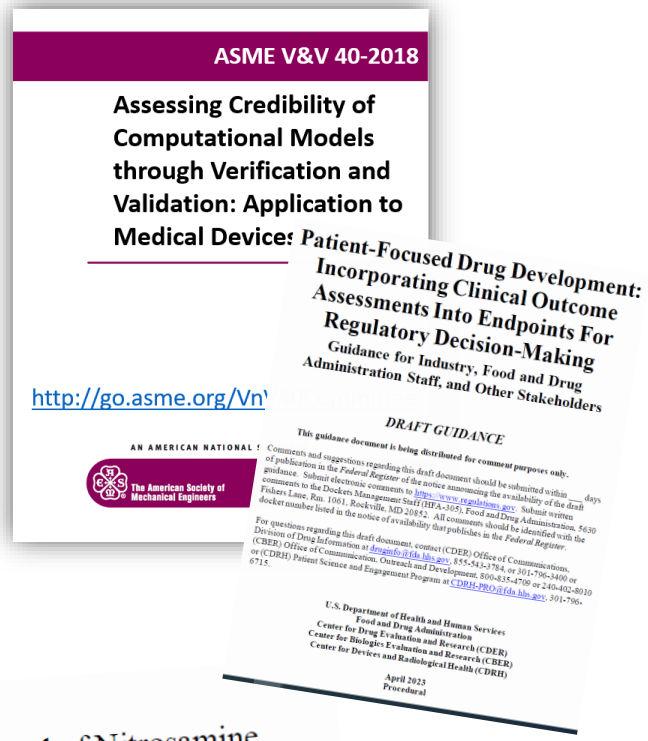
Outputs from regulatory science that can directly inform regulatory decision-making:

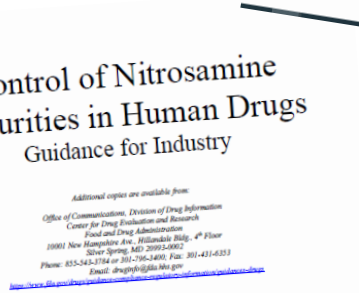
Tools, Standards, Guidance

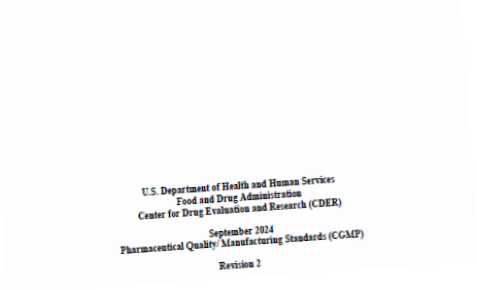
- **Guidance documents** represent FDA's current thinking on a topic. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.

- **Consensus standards** are typically technical methods for approaches that have matured and are "standardized" by the community.
  - •FDA can recognize consensus standards for use in development and or evaluatic of specific products.

- **Tools** are methods, materials, or measures that can aid product development and regulatory review.
  - •FDA has qualification tool programs for drugs and medical devices
  - •If the tool is a commercial product, standards may not be the most appropriate route.



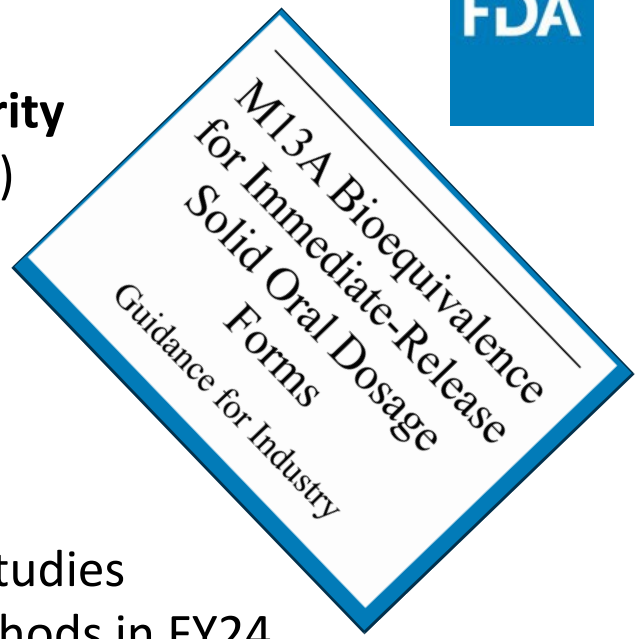




GDUFA Regulatory Science Adds More Value

The need for fed Bioequivalence Equivalence (BE) studies has been an industry priority

- FDA did research and used industry data for a risk-based fed BE (ICH M13A in 2024)
- Over 800 product specific guidance modified to recommend fewer BE studies
- FDA estimate of 200 fewer fed BE studies and $100 Million in lower development costs each year

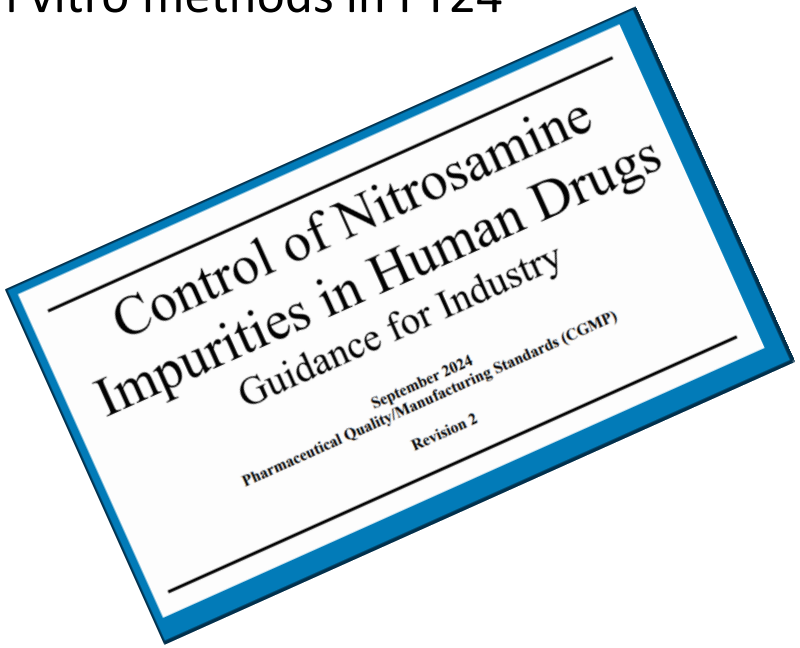


For locally acting complex dosage forms BE can be challenging

- GDUFA FDA research supports development of in vitro alternatives to clinical BE studies
- Alternatives for inhalation products; 20 topical products approved via in vitro methods in FY24

Reformulations to reduce nitrosamine levels

- GDUFA research in OPQ labs demonstrated certain anti-oxidants reduce nitrosamine levels
- External research contracts evaluated the impact of anti-oxidants on drug permeability
- This supported reformulation without new in vivo BE studies
- In September 2024, the FDA revised guidance on the “Control of Nitrosamine Impurities in Human Drugs”



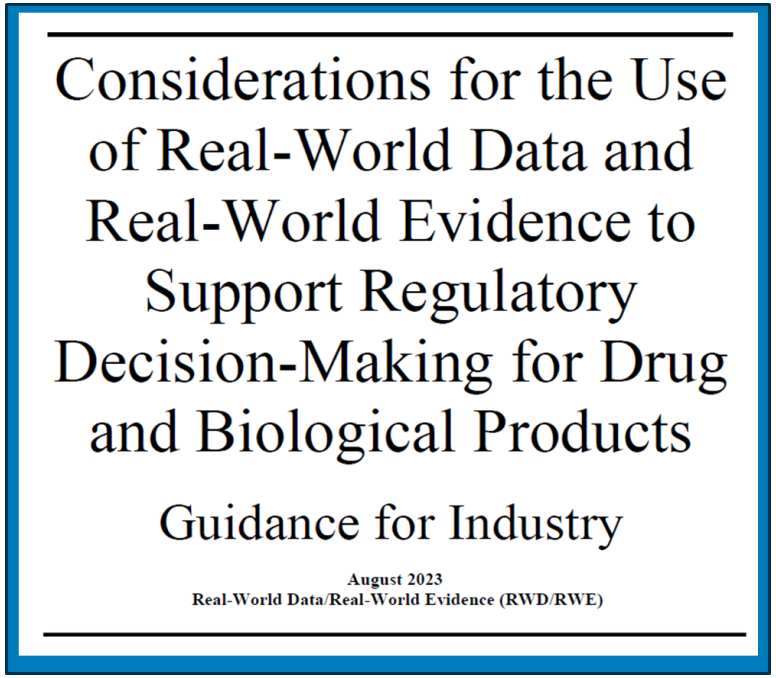
Regulatory Science Across FDA

Office of Regulatory and Emerging Science

Strategic leadership, coordination, and support for innovation in FDA's regulatory science and preparedness research

A project that assessed the ability to decontaminate and reuse respirators that supported the establishment of ASTM E3135-18, the first consensus standard for surface decontamination with UV irradiation.

A project to provide empirically-based recommendations guided by theoretical principles on when real-world evidence (RWE) can substitute randomized control trials (RCTs) and, if so, how to implement… informed the issuance of *guidance*.


Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry

August 2023
Real-World Data/Real-World Evidence (RWD/RWE)

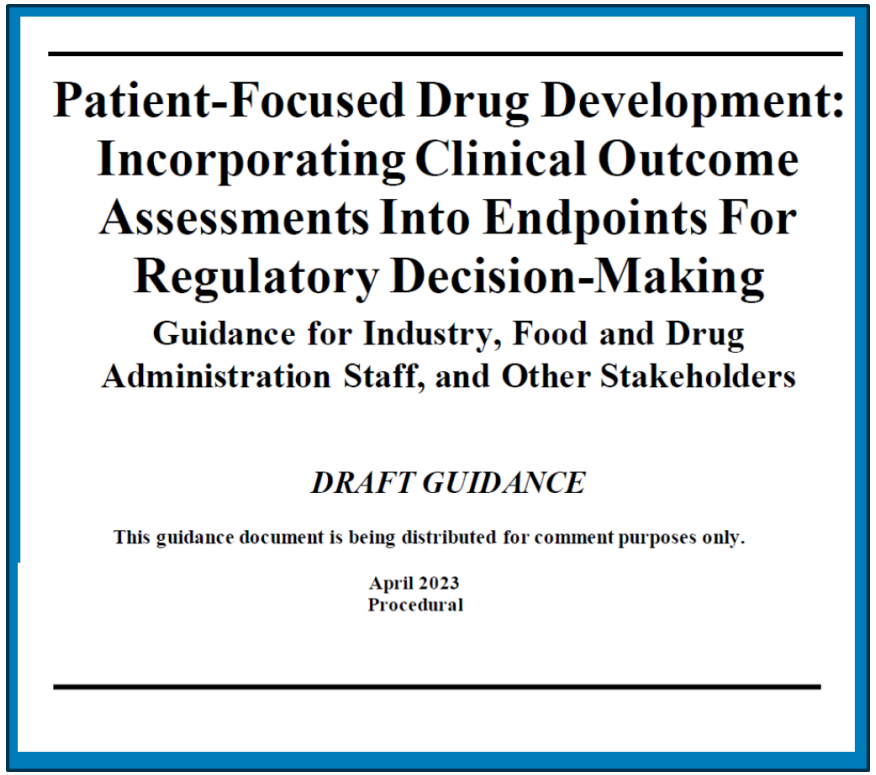
A project to (1) expand biobanks of plasma and PBMC) samples from survivors of Ebola virus disease (EVD) and Marburg virus disease (MVD) as well as vaccine study and control participants; and (2) characterize the natural immunity versus vaccine immunity in EVD and MVD This project supported the development and characterization of a multiplex bead-based immunoassay.

Regulatory Science Across FDA

Centers of Excellence in Regulatory Science and Innovation

Development, Implementation, and Evaluation of an Open Source Software Program for Patient Reported Outcome Measures

Produced guidance Patient-Focused Drug Development



Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

April 2023
Procedural

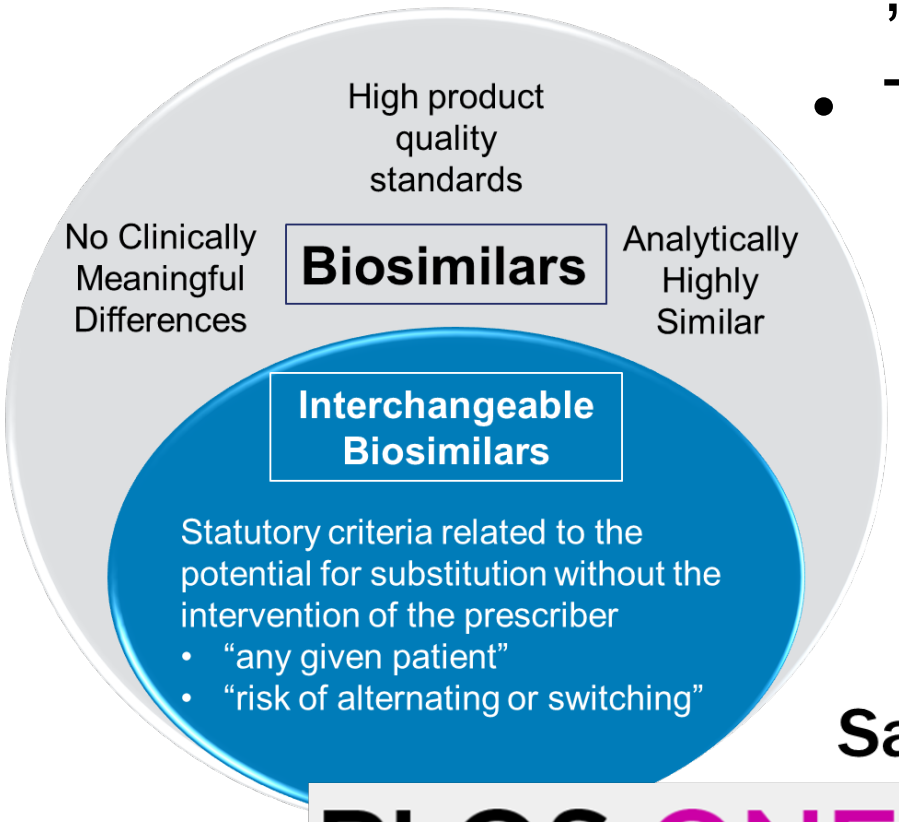
An X-ray Based Online Probe For Real-Time Process Monitoring of Active Pharmaceutical Ingredients in Manufacturing Drug Products

Informed decision making about using X-ray diffraction as a tool in FDA surveillance and oversight of drug quality

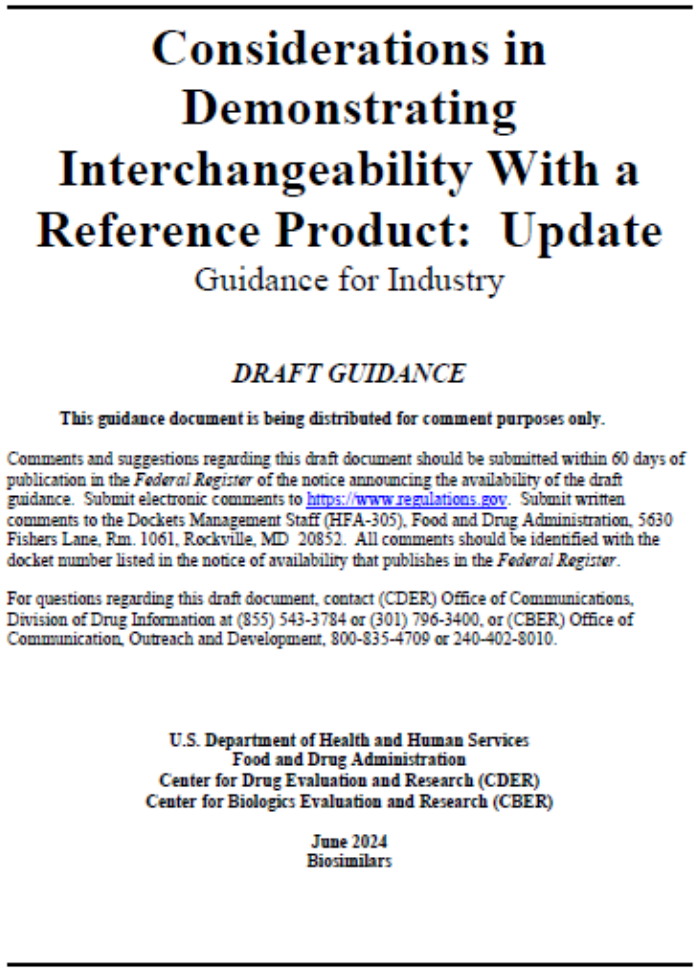
Valley Fever as model for harmonized data for infectious diseases

- Compared **prototype rapid antibody test** to traditional methods
- Publicly available core clinical datasets to speed in vitro diagnostics
- Apply strategy to Lyme Disease (HHS LymeX Innovation Accelerator)

Biosimilars and Interchangeable Biosimilars



- This draft guidance:
  - Outlines a revised approach where switching studies will generally not be needed



Considerations in Demonstrating Interchangeability With a Reference Product: Update

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Communications, Division of Drug Information at (855) 543-3784 or (301) 796-3400, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2024
Biosimilars

PLOS ONE

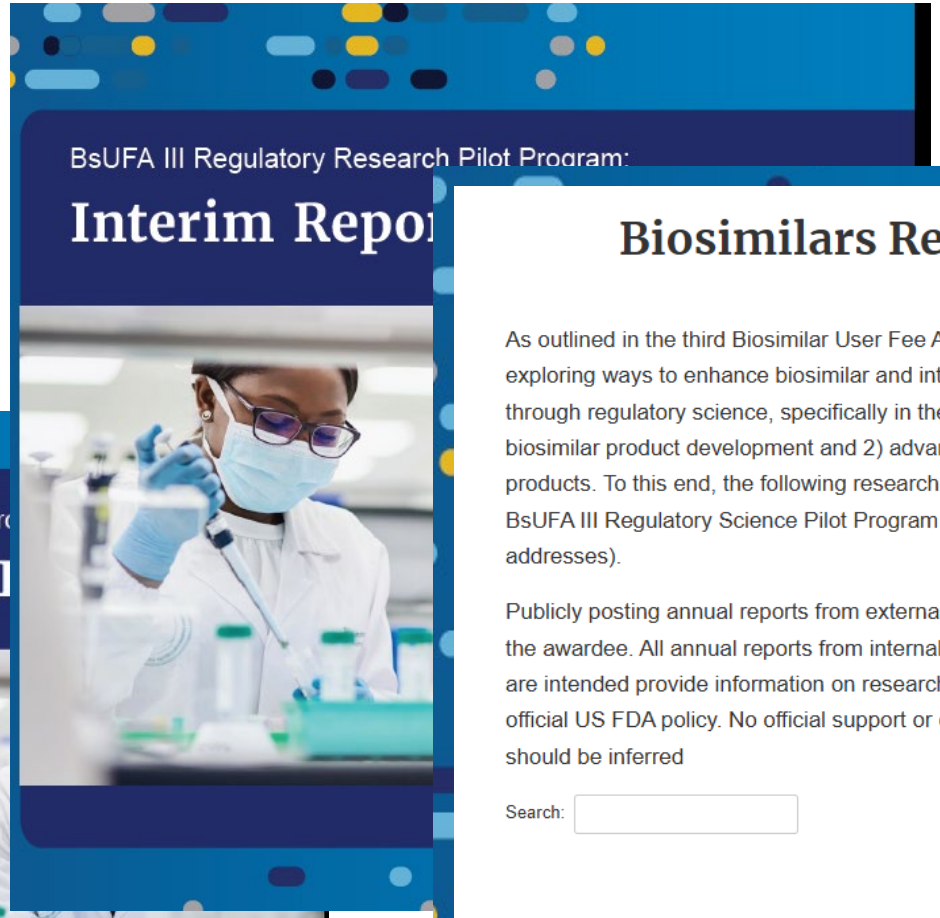
Safety outcomes when swit
biosimilars and referen
A systematic review and meta-analysis

3 October 2023
published online

Thomas M. Herndon[1] , Cristina Ausin[1] , Nina N. Brahme[1] , Sarah J. Schrieber[1] , Michelle Luo[1], Frances C. Andrada[1] , Carol Kim[1] , Wanjie Sun[2] , Lingjie Zhou[2], Stella Grosser[2], Sarah Yim[1], M. Stacey Ricci[1]

[1]Office of Therapeutic Biologics and Biosimilars, Office of New Drugs, CDER, U.S. FDA
[2]Office of Biostatistics, Office of Translations Sciences, CDER, U.S. FDA

Transparent Expectations and Program Status



Biosimilars Research: Awards

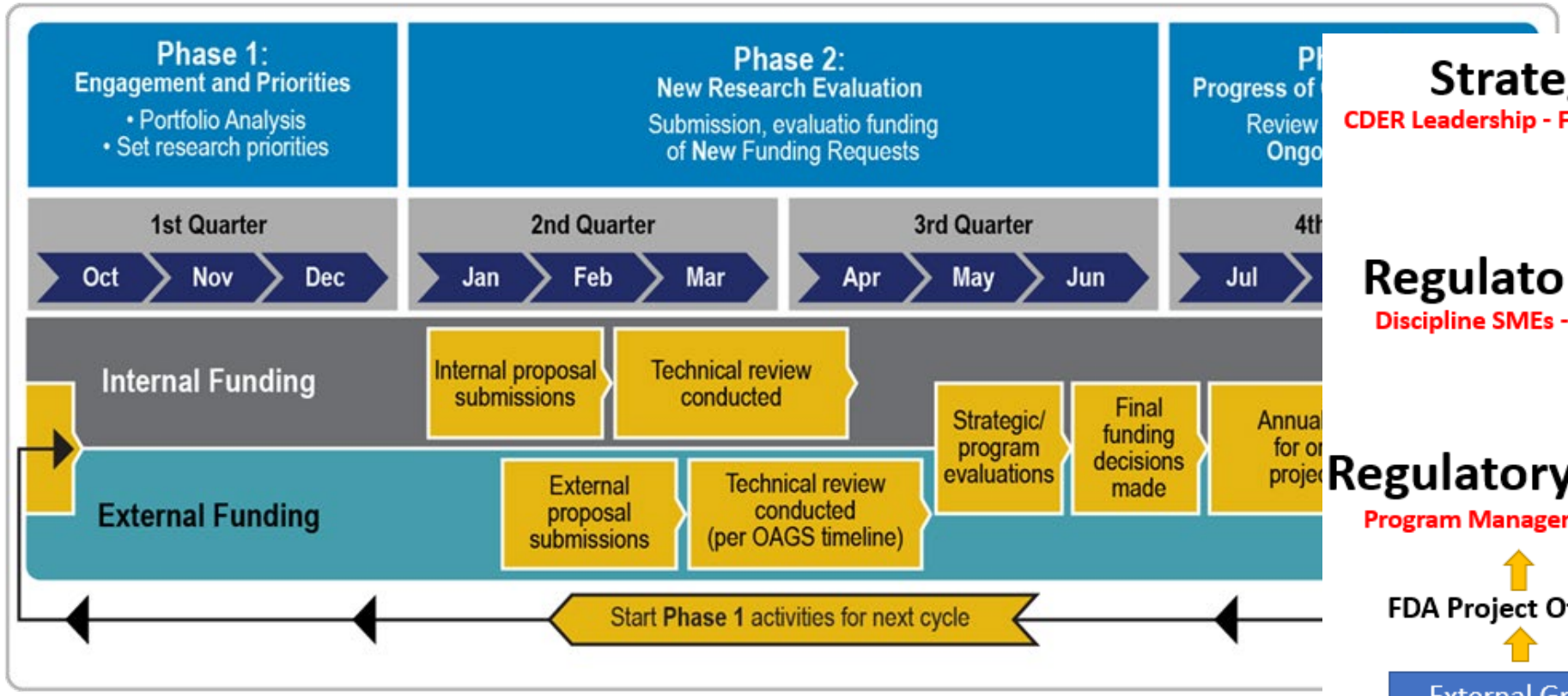
As outlined in the third Biosimilar User Fee Act (BSUFA) commitment letter, FDA is exploring ways to enhance biosimilar and interchangeable biosimilar product development through regulatory science, specifically in the areas of 1) improving the efficiency of biosimilar product development and 2) advancing the development of interchangeable products. To this end, the following research projects were awarded support as part of the BsUFA III Regulatory Science Pilot Program (in order of the research priority the project addresses).

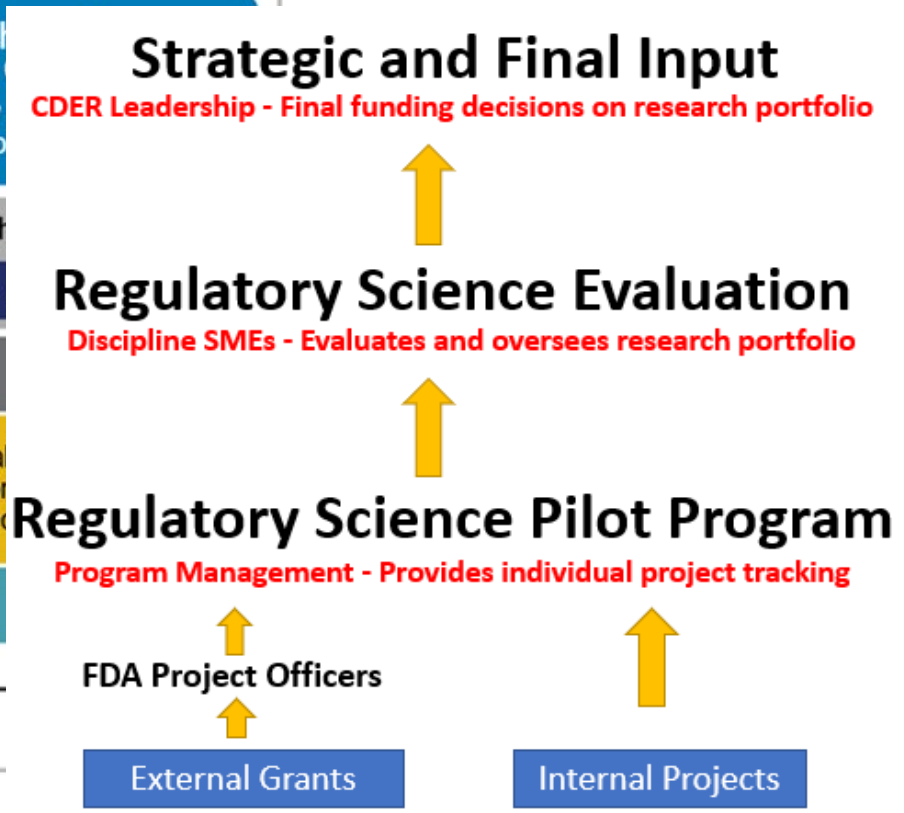
Publicly posting annual reports from external awardees requires written permission from the awardee. All annual reports from internal awardees are posted publicly. These reports are intended provide information on research progress and are not intended to convey official US FDA policy. No official support or endorsement by the US FDA is provided or should be inferred

Search: Export Excel Show 25 entries

Project Title	Awardee	Award Period Start	Anticipated Timeline to Project Outcome(s)	Research Priority
Landscape Assessment of Biosimilar Submissions	OTS/OCP/DARS	May 2023	1 year	Research Priority A: Characterize relationships between product quality attributes with clinical outcomes

Rigorous Skeptical Unbiased Review Process





Predictable Process with Feedback: Priorities → Evaluation → Progress

Technical and Programmatic Evaluations

Final funding decisions require broader leadership review

Broader Stakeholder Input

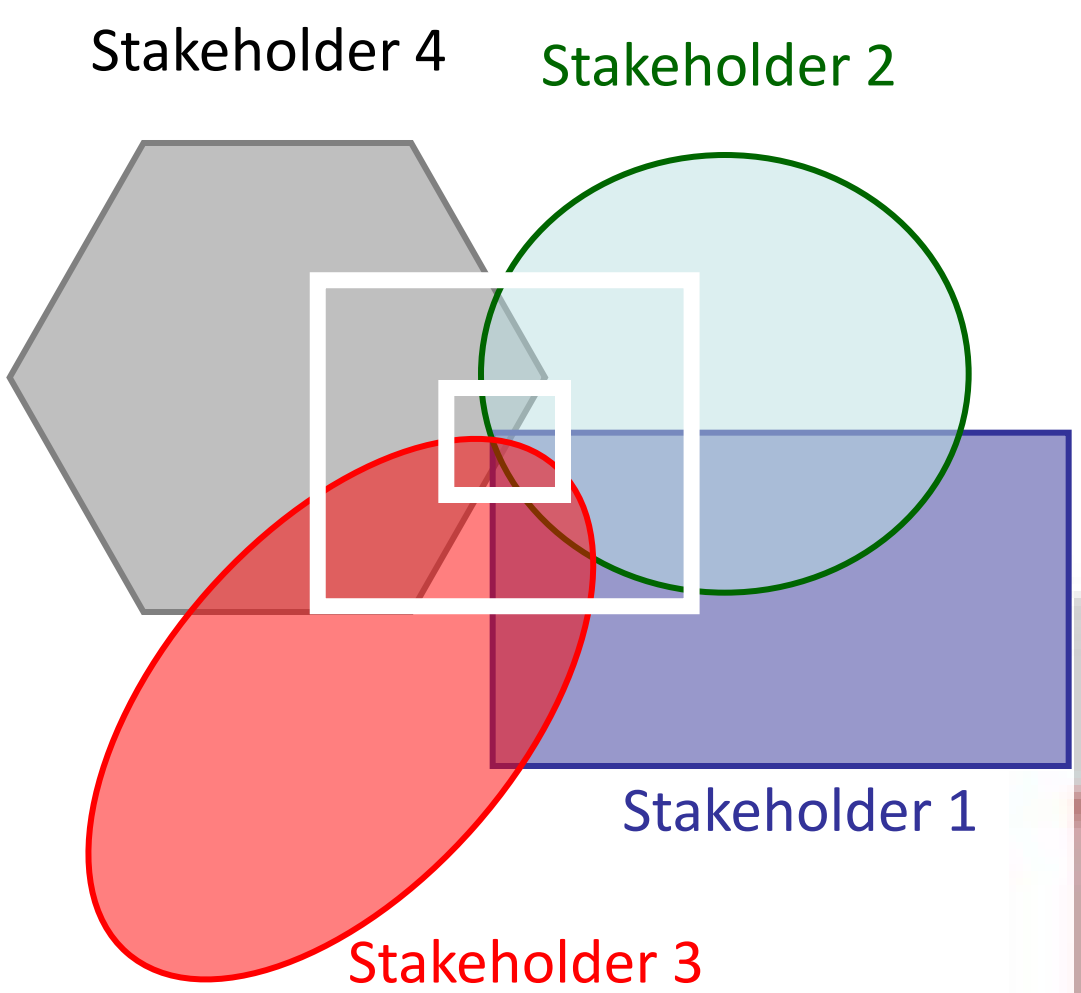
Biosimilar Roundtables | Reagan-Udall Foundation

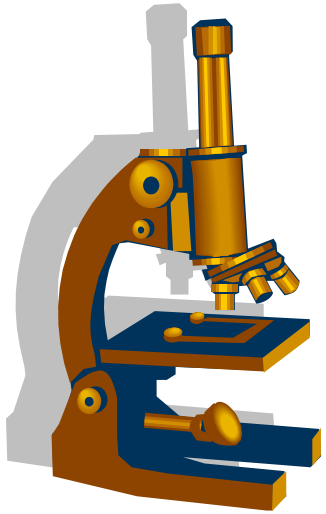
- Need for product class-specific guidance documents providing clarity on common CQAs
- Sharing of FDA experience and information

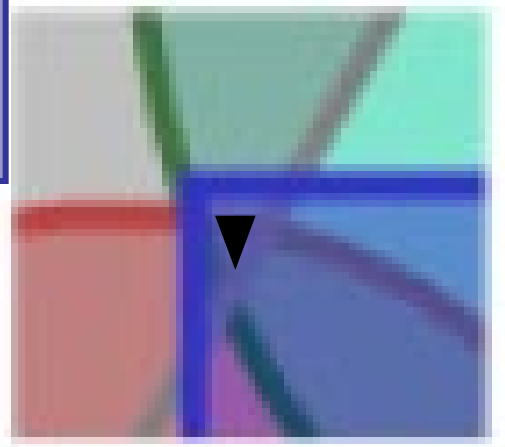
- Commitment Letter – "Project goals should not be specific to a product or product class."
- The need for certain information may vary by stakeholder

Overlay of Regulatory Science Spaces

A. Structure Function
B. Improved Analytical Technologies
C. Assessing and Reporting CQA
D. Efficient Immunogenicity Assessment
E. Leveraging new tools for development
F. User interface with products







Regulatory Research

Planting
Growth &
Benefits

ROI

- Shots on Goal
- Anticipating the Puck

Annual reports and other input are used to evaluate the regulatory impact and return on investment (ROI) of the BsUFA III research portfolio

An Ecosystem - Need engagement from stakeholders

- OTBB/CDER
- BsUFA Regulatory Science Sub-committee
- Rob Lionberger (OGD/CDER)
- Micheal Mair (ORES/OCS)

FDA U.S. FOOD & DRUG ADMINISTRATION

We look forward to your input

Thank you!

Pilot Program Overview

Darlese Solorzano, MS, MBA, Program Manager of the BsUFA III Regulatory Science Pilot Program, OPQAIII|OPQ|CDER|FDA

Pilot Program Overview

Developing a Research Roadmap

Establishing Program Decision Making & Operational Oversight

Efficient Targeted Funding & Scientific Review

Current Research Portfolio

BsUFA III Regulatory Science Commitment

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development.

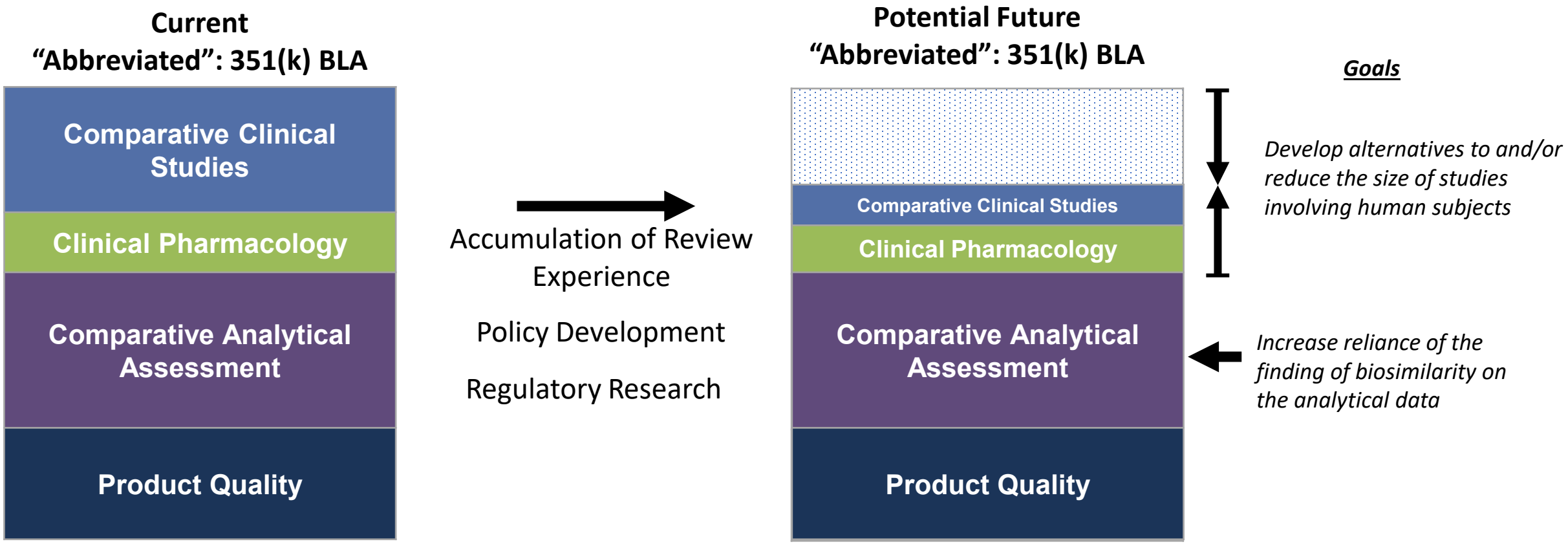
FDA will pilot a regulatory science program to facilitate ways to

(1) improve the efficiency of biosimilar product development and

(2) advance the development of interchangeable products

Commitment Letter

Regulatory Science Pilot Program Goals Focus on Composition of the 351 (k) Data Package



https://www.fda.gov/media/175799/download?attachment

What will inform 'science-based recommendations and regulatory decision-making' at the FDA?

***Knowledge/ information/ methodology that*:**

- Would help FDA apply the current scientific thinking & product-specific regulatory experience more broadly
- Is in alignment with the BsUFA III Commitment Letter
- Would need FDA-specific expertise to obtain
- Could be reasonably obtained through a (set of) research project(s) outcomes and deliverables
- Is not duplicated elsewhere internally or externally of FDA
- Is not product or product-class specific*

Other Important Considerations Included:

- Concerns identified by stakeholders
- Topics that have repeatedly required extensive internal debate across disciplines
- Knowledge or methodology gaps that, when filled, would expand the feasibility of certain biological products entering biosimilar development as reference products (e.g., complex biologics)
- Areas where there is a lack of global regulatory harmonization

* See Guidance for Industry: Questions and Answers on Biosimilar Development and the BPCI Act, September 2021 Biosimilars, Revision 2, Q&A II.2.

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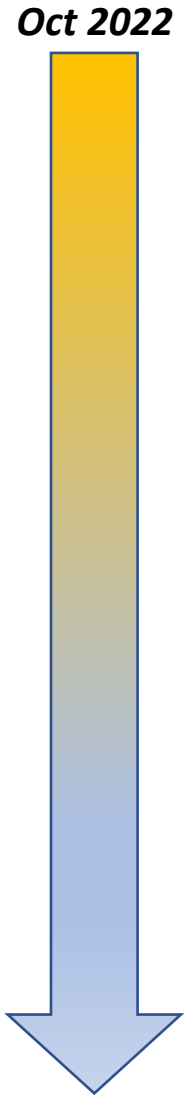
Identified Draft Research Priorities

* See Guidance for Industry: Questions and Answers on Biosimilar Development and the BPCI Act, September 2021 Biosimilars, Revision 2, Q&A II.2.

External Engagement on Pilot Program Roadmap

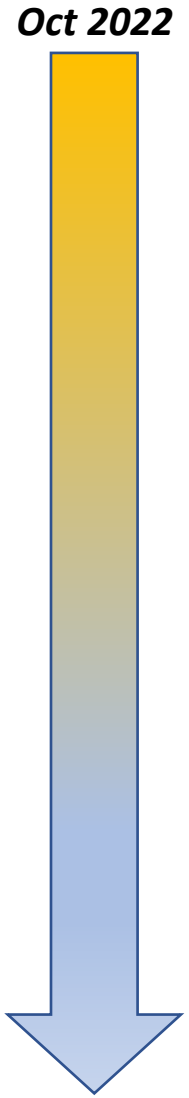


Oct 2022

Publish Draft Research Roadmap Jan 2023

Interim Report and Public Meeting Summer/ Fall 2025

External Engagement on Pilot Program Roadmap



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  - Regulatory Science Pilot Program discussed Feb 2023
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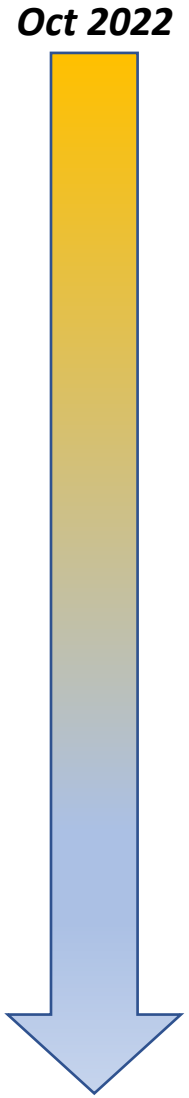
  - Received comments from 7 stakeholder/entities
- **Ten invited talks about the Reg Sci Pilot Program (Spring/ Summer/ Fall 2023)**
  - *External* – Howard University, US Pharmacopeia, Academy of Managed Care Pharmacy x2, White Paper on Recent Issues in Bioanalysis, (WRIB), Biosimilar Forum, **SBIA REDi Conference**, **BAA Day**
  - *Internal* – CDER Research Governance Council, CDER Immunogenicity Review Committee
- **Public SBIA meeting and in-person discussion Oct 2023 - BsUFA III Regulatory Science Pilot Program - 10/16 and 10/26/2023 | FDA**
  - Program updates via SBIA Webinar on Oct 16, 2023, and In-person feedback on Oct 26, 2023
- **Continuous Engagement Meetings as part of BsUFA III #2**
  - Regulatory Science Pilot Program discussed Nov 2023

External Engagement on Pilot Program Roadmap



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Revised BsUFA III Research Roadmap

Regulatory Impact #1: Increase the reliance on analytical data in demonstration of biosimlarity

a. Characterize relationships between product quality attributes (physiochemical or biological) with clinical performance

b. Explore how modernization of analytical technologies could better and/or more efficiently detect relevant quality attributes

c. Define best-practices for assessing and reporting quality attributes

Research Roadmap: *https://www.fda.gov/media/175799/download?attachment*

Regulatory Impact #2: Develop alternatives to and/ or reduce the size of studies involving human participants

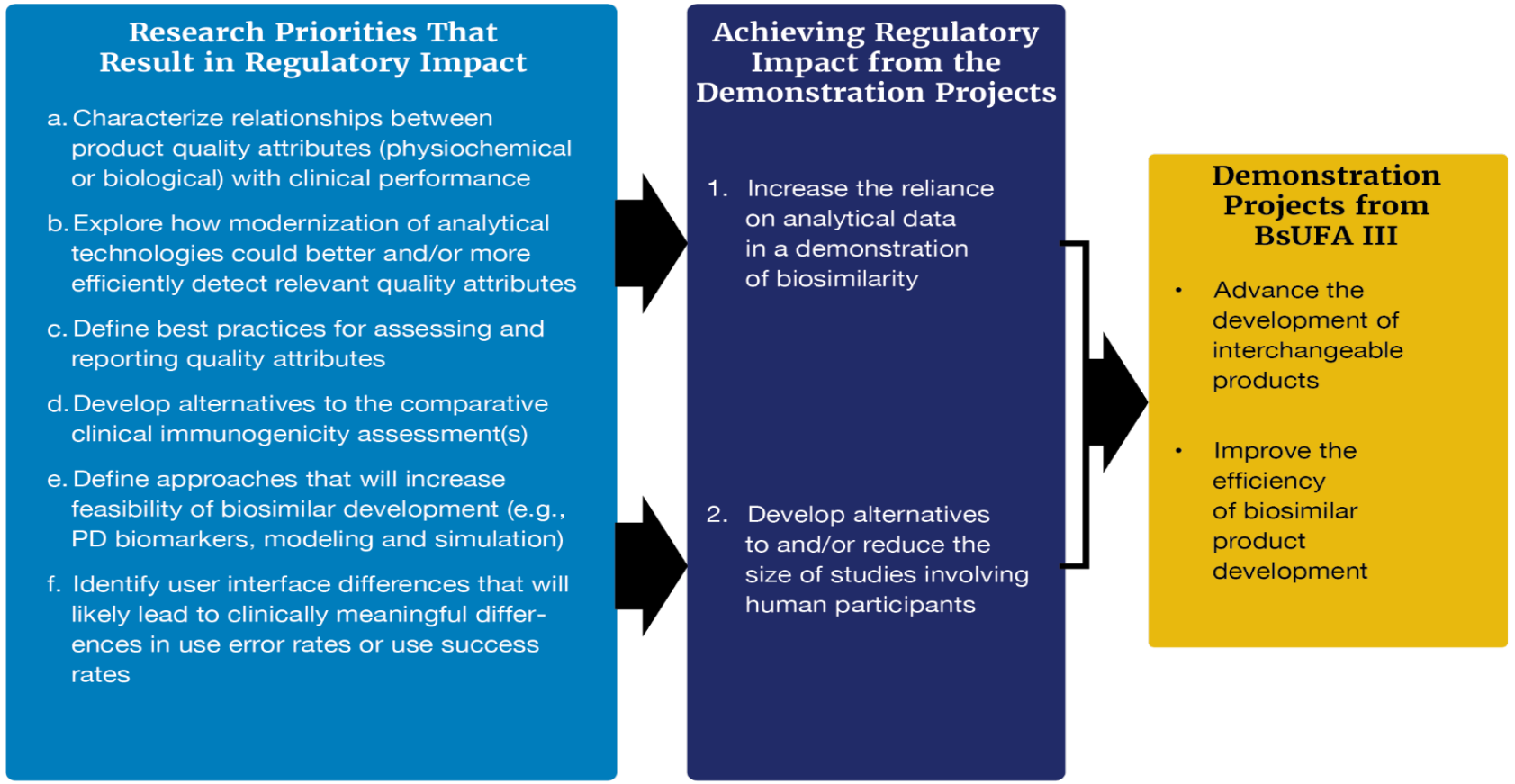
d. Develop alternatives to the comparative clinical immunogenicity assessment(s)

e. Define approaches that will increase feasibility of biosimilar development (e.g., PD biomarkers, modeling and simulation)

f. Identify user interface differences that will likely lead to clinically meaningful differences in use error rates or use success rates

Research Roadmap: *https://www.fda.gov/media/175799/download?attachment*

Research Priorities, Outcome and Impact Reporting Structure



Methods to Consider for Research Conducted as Part of the Pilot Program

- Analytical methods
- Biological assays
- Efficient clinical design (e.g., statistical methods)
- In silico/in-vitro modeling
- MIDD applications
- Machine learning/artificial intelligence
- Pharmacological studies
- RWE/RWD

Pilot Program Overview

Establishing Program Decision Making & Operational Oversight

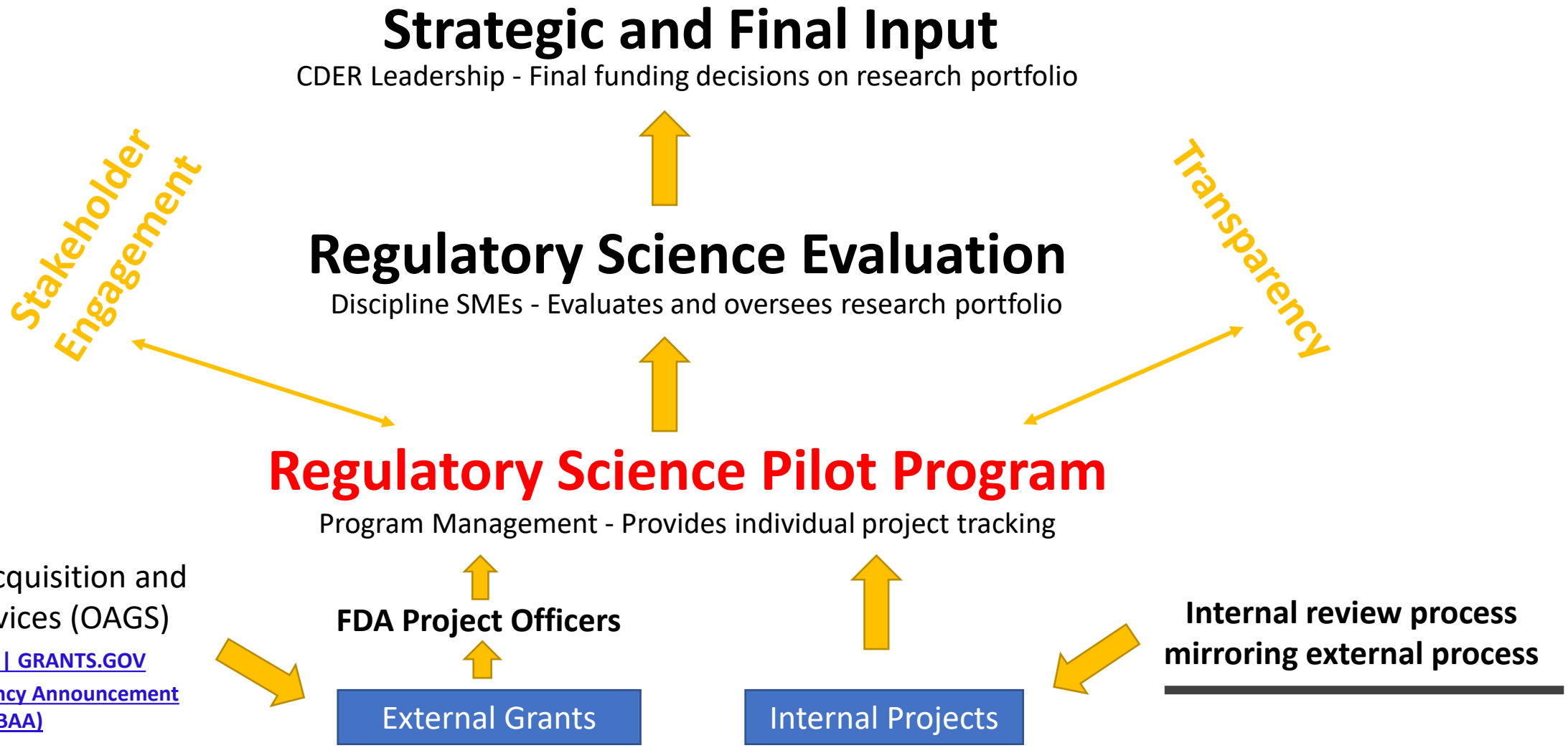
BsUFA III Reg Sci Program Decision Making & Operational Structure

Strategic and Final Input

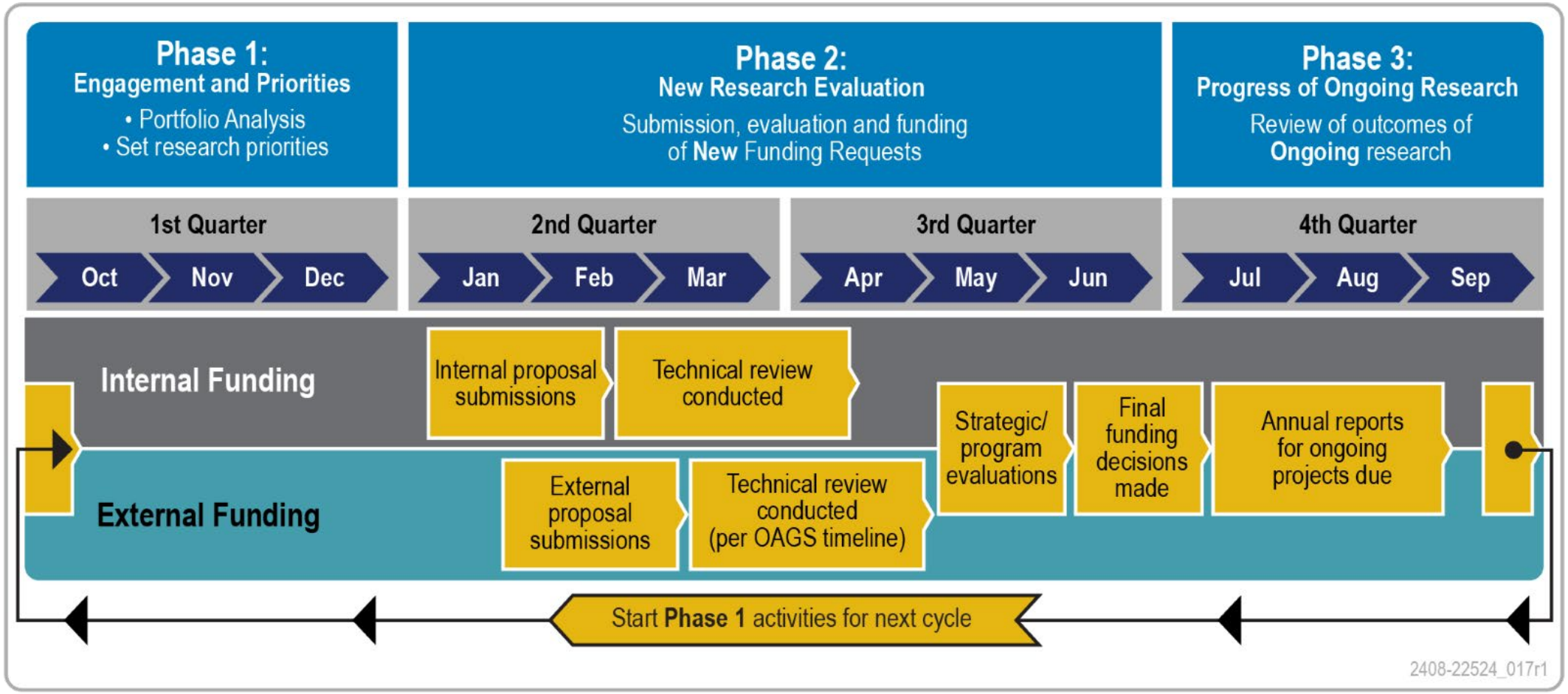
Regulatory Science Evaluation

Regulatory Science Pilot Program

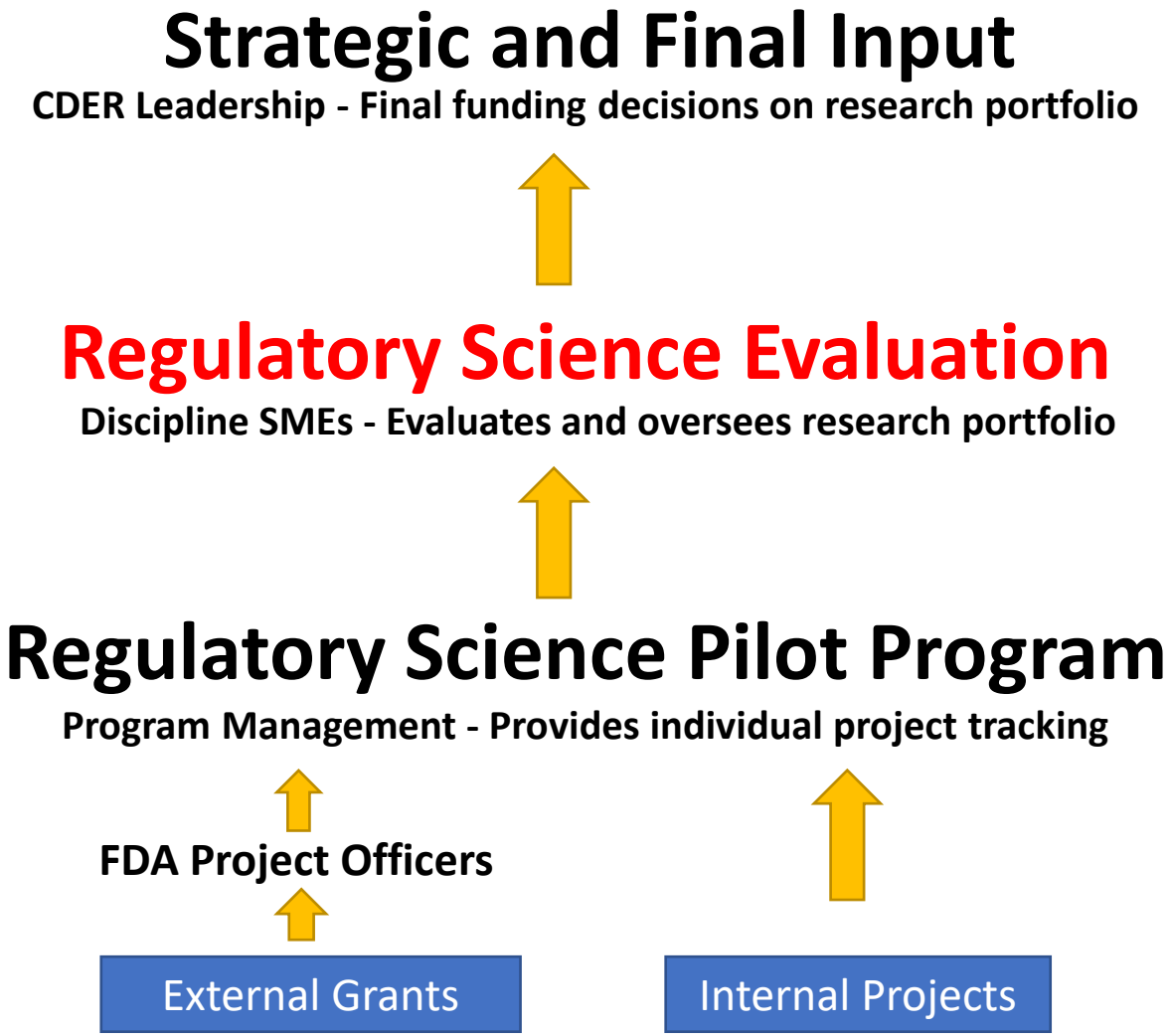
BsUFA III Reg Sci Program Decision Making & Operational Structure



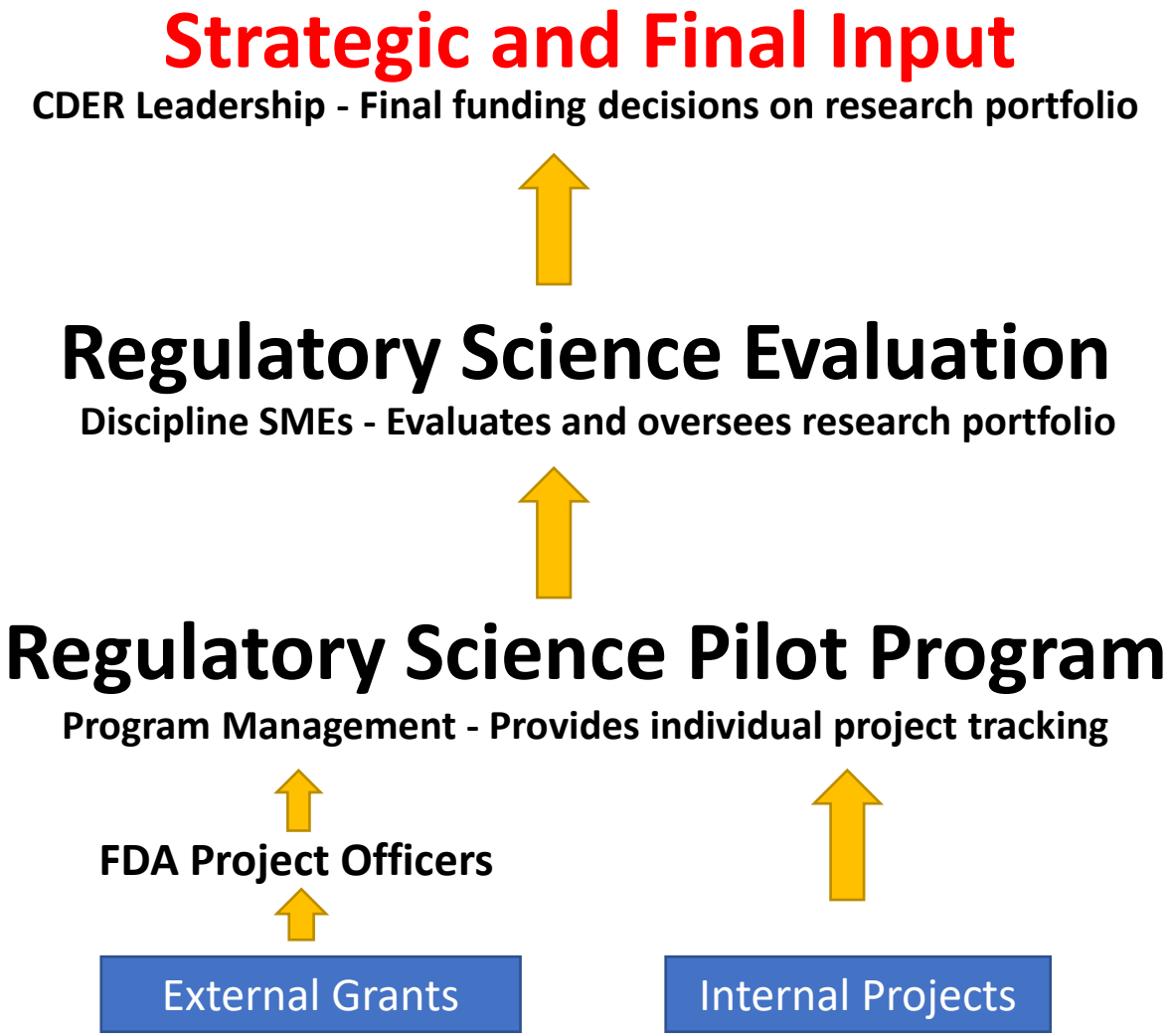
Pilot Program Review Process



BsUFA III Reg Sci Program Decision Making & Operational Structure

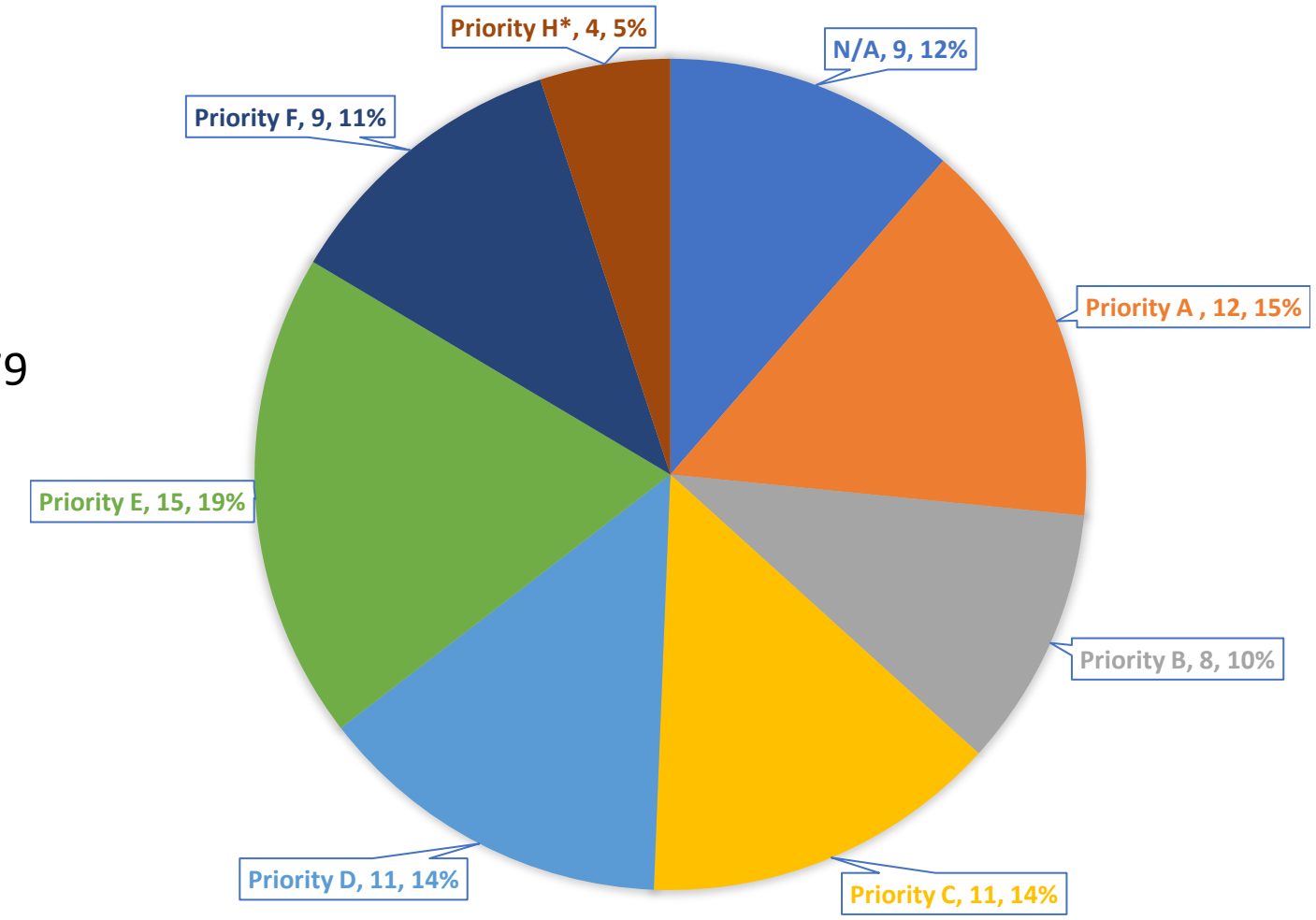


BsUFA III Reg Sci Program Decision Making & Operational Structure

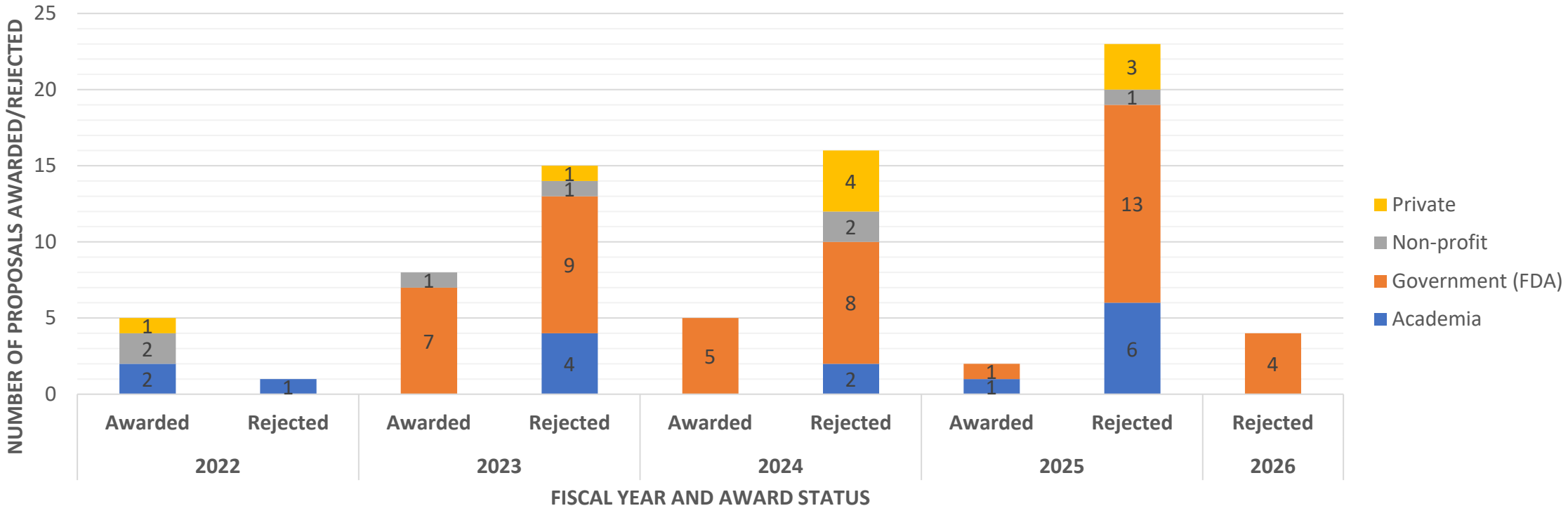


- **Total Number of Proposals Reviewed throughout the pilot program thus far:** 79
- **Total Awarded:** 20
- **Total Rejected:** 59
- *Proposals reviewed under draft research roadmap priorities.

ALL RESEARCH PROPOSALS REVIEWED BY RESEARCH PRIORITY



Research Proposals Reviewed by Organization Type per Fiscal Year



BsUFA III Regulatory Science Pilot Program Roadmap Timeline

August 2022- Development of Research Roadmap

January 2023- Publication of *draft* Research Roadmap

Jan- Dec 2023- Stakeholder Solicitation on *draft* Research Roadmap

January 2024- Publication of *Revised* Research Roadmap

September 2025- ongoing research under the roadmap

Thank You!

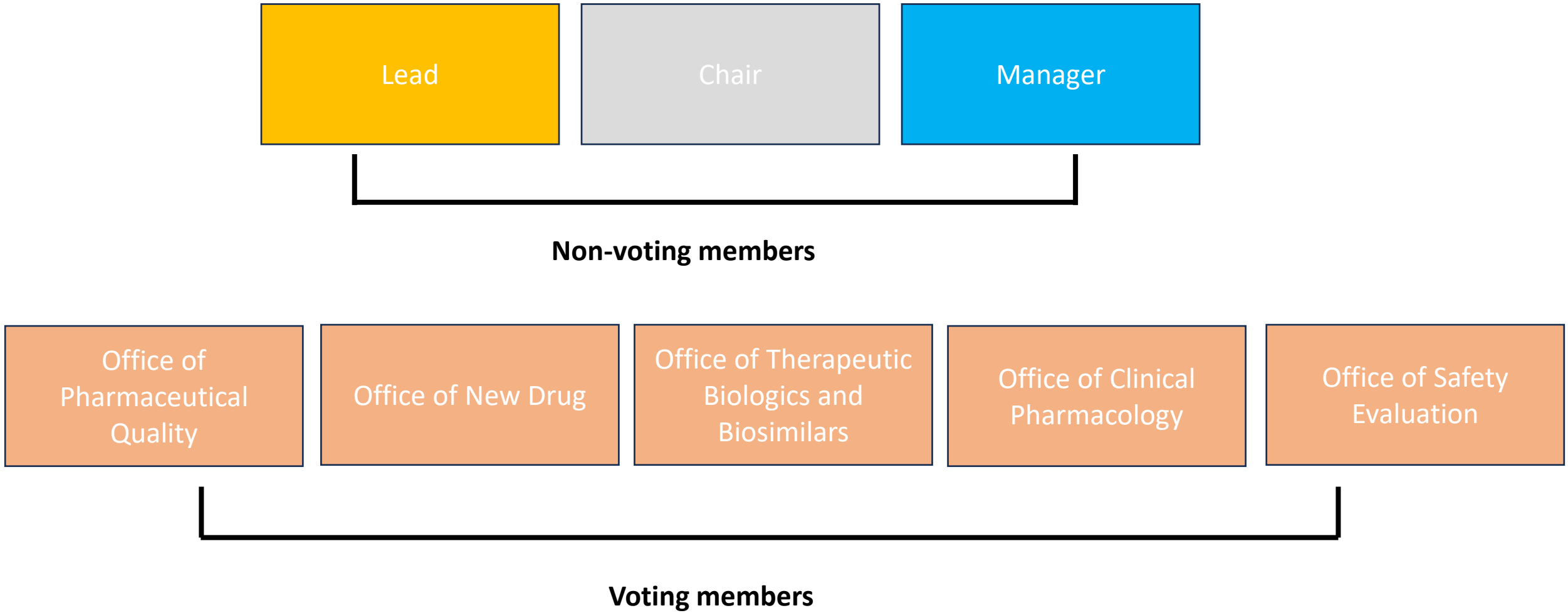
Pilot Program Overview

Emanuela Lacana, Scientific Lead BsUFA III Regulatory Science Pilot Program,
Deputy Director of OTBB|OND|CDER|FDA

Pilot Program Overview

Establishing Program Efficient Targeted Funding & Scientific Review

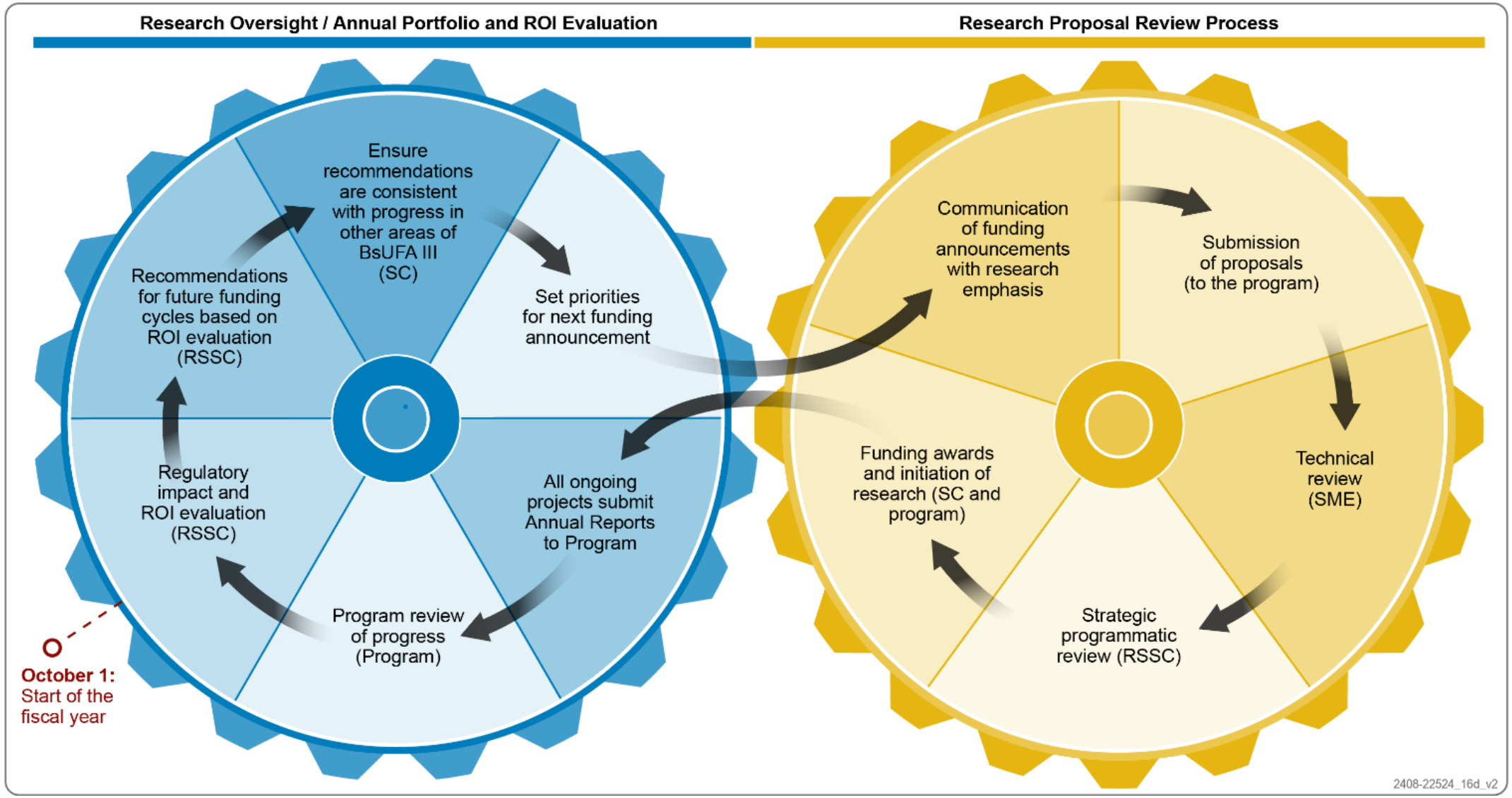
The Regulatory Science Subcommittee (RSSC)



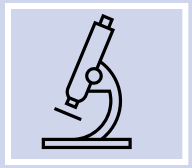
The RSSC roles and functions

- Chair: overall direction, drive decision-making, ensure alignment
- Lead: scientific coordination, monitoring of committee activities collaborate with Chair for the overall program
- Manager: Program and operational leadership
- RSSC members:
  - Provide input and direction on projects and initiatives
  - Reviews proposals and SME recommendations on proposals
  - Scores proposals based on metrics with quantitative values
  - Provides recommendations on funding to CDER leadership
  - Assess regulatory impact and progress review

The review and oversight cycles

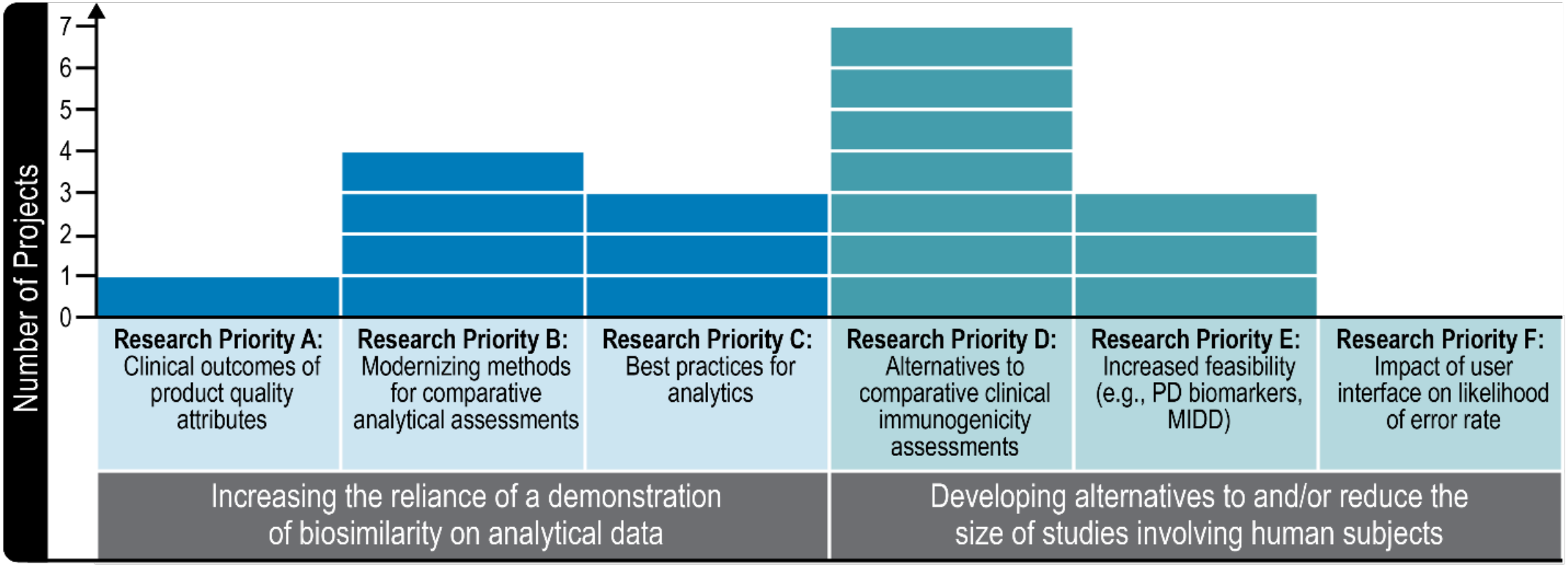


Pilot Program Overview



Current Research Portfolio

Portfolio of research projects



Increasing the reliance of a demonstration of biosimilarity on analytical data: Priorities a-b

- Priority a: Characterize relationship between product quality attributes with clinical performance
    - A landscape assessment of biosimilars submissions correlated analytical results with clinical outcomes using trastuzumab as model across multiple applications
- Priority b: modernization of analytical technology to better and/or more efficiently detect relevant quality attributes
    - Glycosylation: two projects, one aimed at assessing glycoforms in culture media and one at concomitantly identify and quantify N- and O-glycans
    - Comparing MAM vs conventional method to assess quality attributes of adalimumab and etanercept
    - Modeling stability to evaluate minimum data required for biosimilars submission

Increasing the reliance of a demonstration of biosimilarity on analytical data: Priority c

- Define best practices for assessing and reporting quality attributes
  - Characterization and comparability of biosimilar drug products in lyo and liquid formulation, and how formulation impact antibody stability in response to stressors.
  - Analytical characterization of posttranslational modifications in biosimilars and their reference product
  - Enhanced testing capability of bioassays for biosimilars comparisons

Develop Alternative to and/or Reduce the Size of Studies Involving Human Participants: Priority d

- Develop alternatives to comparative clinical immunogenicity assessment
  - In vitro: prediction of immune response using cell-based assays
    - Acceptance criteria and standards for assays measuring innate immune response modulating impurities
    - Addressing fundamental issues for in vitro immunogenicity assays for adaptive immune response
  - In vivo: animal model prediction of adaptive immune response
    - Validation of non-clinical immunogenicity model and production and optimization of humanized mice
  - In silico: Risk prediction for CHO protein immunogenicity

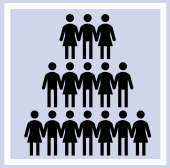
Develop Alternative to and/or Reduce the Size of Studies Involving Human Participants: Priority d

- Develop alternatives to comparative clinical immunogenicity assessment
  - Real world data/evidence to identify differences in adverse immunogenic responses
    - Leveraging real world-data obtained in the U.S. to improve the efficiency of regulatory decision for biosimilars and interchangeable biosimilars
    - Using foreign real-world data to inform interchangeable biosimilars approval

Define Approaches that Will Increase Feasibility of Biosimilar Development (e.g., PD biomarkers, MIDD including AI and/or machine learning): Priority e

- Translating research finding about PD biomarkers into best practices for industry and FDA review staff
- Evidence-based approach to the design of clinical pharmacology studies
- Critical factors for standardization and accuracy of PK assays for PEGylated biosimilars

Pilot Program Overview



Recent stakeholder engagement

Stakeholder involvement

2023

1. Series of public engagements
2. Feedback on the draft roadmap:
    1. Written comments
    2. Two-parts SBIA meeting

2024

1. Final roadmap published
2. Annual reports for all projects published
3. Reagan-Udall round tables, sought feedback from industry on current gaps and challenges facing industry

2025

1. SBIA webinar: Progress report and poll for presentation at interim public meeting
2. Interim report published
3. Interim public meeting September 18

Reagan-Udall BsUFA Regulatory Science Accelerator

Set-up and topics

- Convened participants from industry with diverse levels of experience
- FDA participated only in observing capacity
- Small groups aimed at fostering discussion
- Five round tables on:
  - analytical similarity
  - leveraging analytics to inform further development
  - PK similarity
  - Leveraging PK and or PD to inform further development
  - Immunogenicity risk assessment

Identified challenges

- Reference products lots availability, variability, limited accessibility to data
- CQA, acceptable variability and essential analytical methods
- PK studies dropout rates, integration of immunogenicity
- CQA and methods for emerging drug classes like ADCs

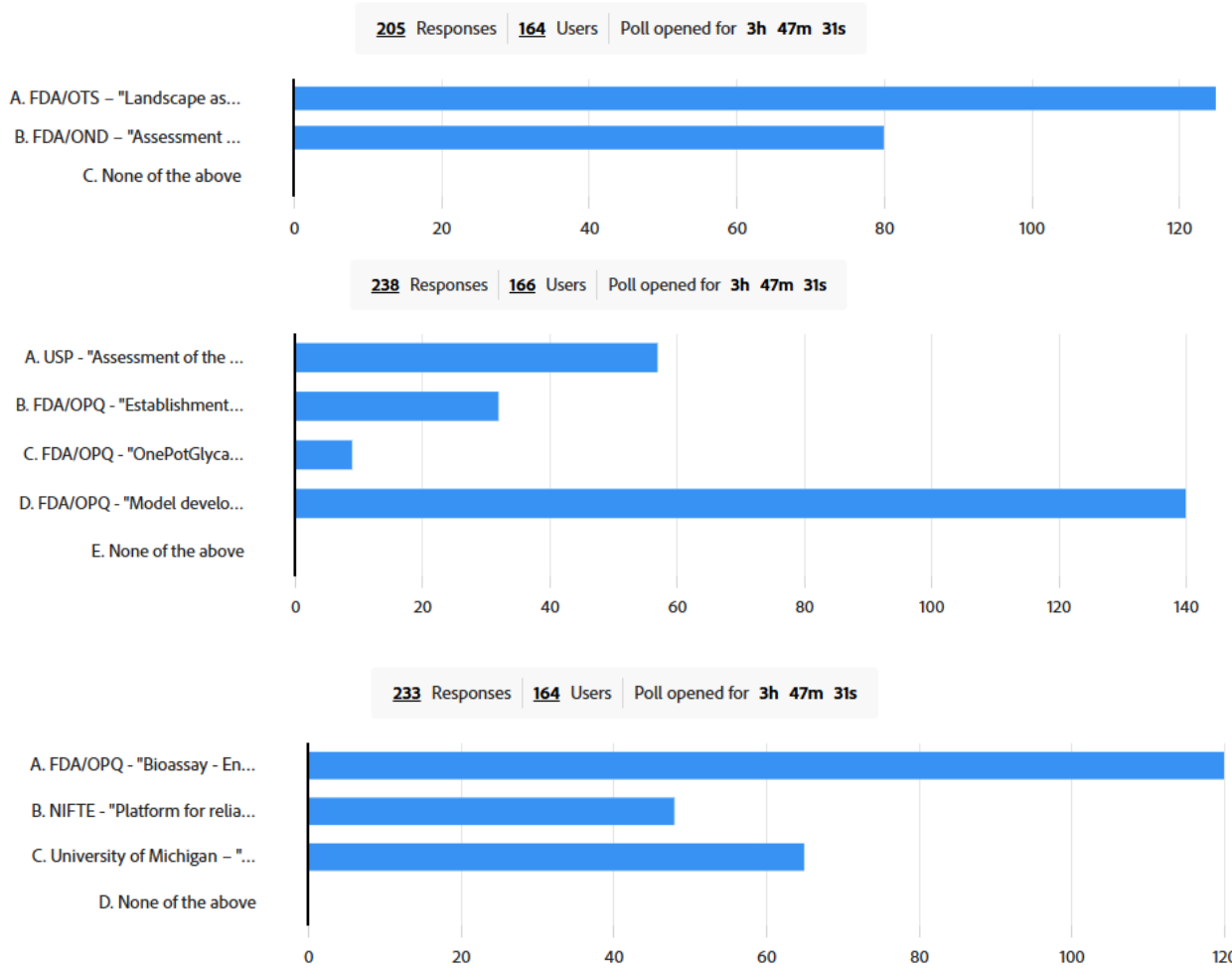
Value of roundtables and suggestions for FDA

- Extremely valuable 38%, valuable 50%, neutral 12%
- Experience on usage of non-US comparators
- Catalogue of impurities associated with safety concerns
- Insights on CQAs (e.g, methods, selections, etc.)
- Sufficiency of a one-dose PK similarity study in healthy volunteers
- Experience on the extent of which analytical and clinical PK and CES data contributed to regulatory decision

SBIA Webinar BsUFA III Regulatory Science Pilot Program: Progress Updates

- Presentations
  - Updates on the state of the program
  - FDA investigators presentations'
  - Overview of portfolio
- Webinar evaluation
  - Of the 1442 registrants worldwide, 517 attended, 383 started the evaluation. Of the respondent:
  - 100% found the webinar valuable for them
  - 78% found they learn something new and important
  - 55% found the topic relevant for their work
  - 38% found the information will be valuable to colleagues
  - 44% found that what they learned will have a positive impact on their work
- Polls
  - For each research priority, attendees voted on which project should be presented at the interim public meeting

Poll Results: Priorities A-C

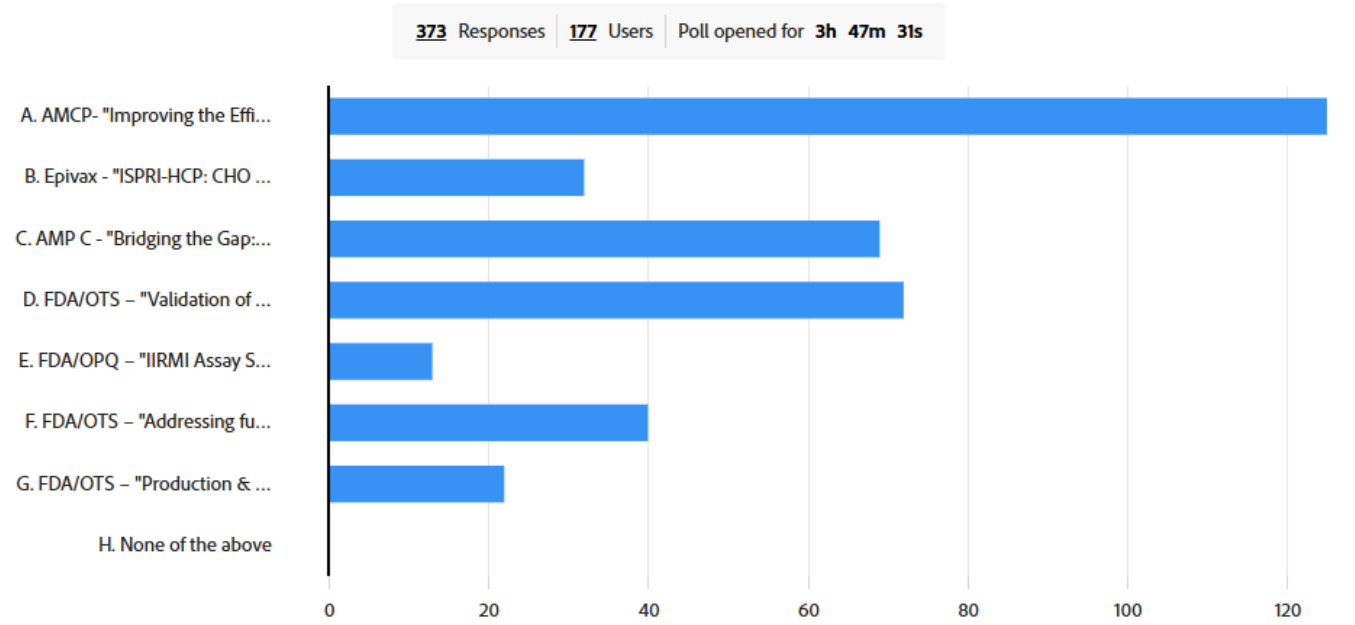


★ Landscape assessment of regulatory submission

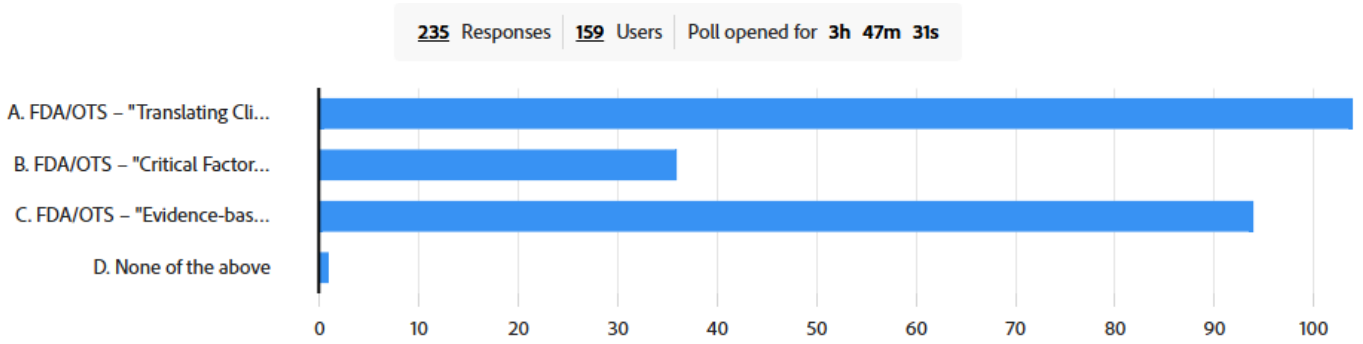
★ Model development and verification to evaluate minimum stability data required for biosimilar submissions

★ Bioassay-enhanced testing capabilities

Poll Results: Priorities D-E



★ Improving the Efficiency of Regulatory Decisions for Biosimilars and Interchangeable Biosimilars by Leveraging Real-World Data



★ Translating Clinical Pharmacology Biosimilar [PD Biomarker] Research Findings into Best Practices for Industry and FDA Review Staff

Thank You!

And Next…

Break Period

Break is from 10:15-10:30am

At 10:30am we will resume for the Awardee Presentations

All questions please submit using the QR code.

Or submit to:
BsUFARegSciProgram@fda.hhs.gov

Q&A Panel with Awardee Presenters

- **For all audience members:** please use the QR code to submit your questions. Please indicate who the question is being addressed to by following this format: *name of presenter: Jane Doe, question.*

U.S. FOOD & DRUG ADMINISTRATION

Landscape Assessment of Biosimilar Submissions

BsUFA III Regulatory Science Pilot Program: Progress Update

Jeffry Florian,
Associate Director,
Division of Applied Regulatory Science,
OCP/OTS/CDER

Disclaimer

- **This presentation reflects the views of the presenter and should not be construed to represent those of the FDA.**

Agenda

- **Background & Methods**
- **Trastuzumab Biosimilar Results**
- **Conclusions**

Aim: Better understand the quality attributes used to compare adalimumab and trastuzumab biosimilars to their reference products

BsUFA III Research Pilot ***Priority A****: Characterize relationships between product quality attributes with clinical performance*

Background & Research Questions

Comparative analytical assessments are foundational in biosimilar development to detect potential differences between products. When differences are present, it is critical to understand:

1. If quality data, combined with clinical PK data, are sufficient to establish biosimilarity between candidates and their reference products (RPs)
2. In cases where differences are present, the steps taken to determine that they do not preclude a determination of highly similar

Methodology*

Comparative Analytical Assessments

- **Collect** structural and functional quality attribute data
- **Evaluate** analytical biosimilarity results
- **Document** resolutions for observed analytical differences

Clinical Pharmacology Studies

- **Collect** clinical pharmacology and immunogenicity data
- **Evaluate** AUC, C_{max}, ADAs and nAbs, and other endpoints
- **Document** instances where endpoints fell outside of acceptance margins

Comparative Clinical Studies

- **Collect** clinical efficacy and safety data
- **Evaluate** treatment differences, response rates, C_{trough}, adverse events, and other endpoints
- **Document** new issues that arose and resolution of residual uncertainty

Analysis Plan

Harmonize attributes and clinical study endpoints → **Visualize similarities & differences** → **Identify patterns in difference resolution** → **Synthesize findings for manuscript**

*Adapted methodology from Guillen et al. (2022)

ADA: Anti-Drug Antibody; AUC: Area Under the Curve; C_{max}: Maximum Concentration; C_{trough}: Trough Concentration; nAb: Neutralizing Antibody; PK: Pharmacokinetic; RP: Reference Product

Trastuzumab Biosimilar Results

Comparative Analytical Assessment

Differences observed across Physico-Chemical/Functional Categories did not preclude a determination of high similarity

Highlighted differences across the Higher Order Structure Physico-Chemical/Functional Category		
Quality Attribute	**No. Biosimilars Evaluated per QA & No. with Differences**	**Resolution Description (n)**
Free thiols	• 4/5 evaluated • 2 showed differences	• Free thiol concentration low (4.1 uM) • Indicative of differences in disulfide bond formation, which may impact the secondary structure, however no change observed in higher order structure (1) • Potentially due to the presence of 2H1L fragments observed in CD-SDS (NR) testing; addressed by monitoring aggregation formation using SEC during release and storage

Highlighted differences across the Post-translational modifications Physico-Chemical/Functional Category		
Quality Attribute	**No. Biosimilars Evaluated per QA & No. with Differences**	**Resolution Description (n)**

Asparagine deamidation	• 3/5 evaluated
	• 3 showed differences
	  ○ 2 Asn 30 (trended lower)
	  ○ 2 Asn 387/392/393 (trended lower)
		• Acknowledged deamidation of Asn 30 in the CDR critical for efficacy; Asn 387/392/393 not in the CDR thus not expected to impact biological function (3)
		• Per a SAR study, the amount of Asn 30 deamidation correlated with a decrease in HER2 binding, with RP lots demonstrating greater amounts of Asn 30 deamidation and lower amounts of HER2 binding compared to biosimilar. Overall, the differences do not significantly impact *in vitro* potency (1)
		• Similar peak profiles for the 3 products with 100% coverage in reduced peptide mapping, and the differences and theoretical masses for all peptides well within 50 ppm and consistent levels of Asp deamidation among lots tested

Methionine oxidation	• 4/5 evaluated
	• 2 showed differences
	  ○ 2 Met 255 (both trended higher)
	  ○ 1 Met 431 (trended higher)
		• Met255 in the Fc region may impact binding to the FcRn
		• Met oxidation levels up to 2.0% are not expected to have a clinical impact; FcRn binding, ADCC, and antiproliferation, as well as the SAR study data, showed no major differences in potency, or in PK

Differences observed across Physico-Chemical/Functional Categories did not preclude a determination of high similarity

Highlighted differences across the Glycosylation Physico-Chemical/Functional Category		
Quality Attribute	**No. Biosimilars Evaluated per QA & No. with Differences**	**Resolution Description**
Galactosylation	• 5/5 evaluation • 1 showed differences	• Per published literature, galactosylation does not affect ADCC; rather it impacts C1q binding and CDC, which is not a mechanism of action of trastuzumab (1)
Sialic acid content	• 3/5 evaluated • 2 N-Glycolylneuraminic acid [NGNA] (trended lower) • 2 N-Acetylneuraminic acid [NANA] (trended above)	• NGNA level small <2%, close to limit of detection (2) • NANA levels small, non immunogenic (2) • Per asialyation studies, no impact on biological activities (1)
Sialyation	• 3/5 evaluated • 2 showed differences (1 trended higher, 1 trended lower)	• Differences in sialylation may impact PK • Per peer review literature, sialylation not expected to impact biological activity of antibodies (1) • Difference (<1.58%), not be expected impact biological activity (e.g., ADCC, PK), and similar FcyRIIIa and FcRn binding (2)
Highlighted differences across Charge Variants Physico-Chemical/Functional Category		
Quality Attribute	**No. Biosimilars Evaluated per QA & No. with Differences**	**Resolution Description**
Charge heterogenicity (basic)	• 5/5 evaluated • 4 showed differences (3 higher, 1 lower)	• Due to C-terminal Lys, which is not expected to have a clinical impact (4) • Characterization studies (i.e., fractionating basic variants and identifying isoforms by peptide mapping) showed no significant impact on potency (3) • Low charge heterogenicity due to C-terminal Lys; difference small
Charge heterogenicity (main)	• 5/5 evaluated • 3 showed differences (all 3 trended lower)	• Due to increased %basic species from presence of C-terminal Lys (2) • Due to increased %basic species from presence of isoAspartate 102 (1) • Due to increased %acidic species attributed to non-consensus glycosylation and partially reduced species; similar distribution of post-translational modifications and each fraction of acidic species has similar biological activities (e.g., proliferation inhibition, ADCC) (1)

Trastuzumab Biosimilar Results

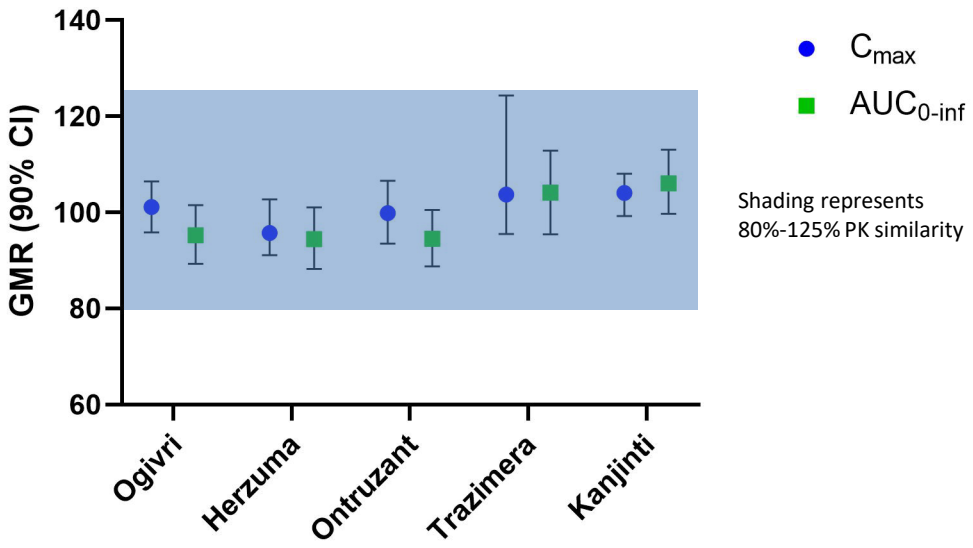
Pharmacology and Comparative Clinical Studies

Sponsors conducted various studies comparing the clinical pharmacology, safety, and immunogenicity of their trastuzumab biosimilars to US RP

- Sponsors each conducted between one and two studies each investigating the comparative PK, safety, and immunogenicity of their products
  - Two products also included pilot PK studies at a single-center with a smaller number of volunteers
  - Five products conducted PK studies in healthy volunteers only while one conducted separate studies for healthy volunteers as well as patients with HER2+ breast cancer

	Ogivri	Herzuma	Ontruzant	Trazimera	Kanjinti
Sample Size	120	70	109	105	157
Observation Period	Day 70	Day 71	Day 56	Day 70	Day 64
1° Endpoints Assessed	AUC extrapolated to infinity ($AUC_{0\text{-}inf}$)				
2° Endpoints Assessed	Maximum concentration (C_{max}), incidence of binding anti-drug antibodies (ADAs)				
Acceptance Margin	90% confidence intervals for the ratios of geometric means within the interval of 80% to 125%				
Incidence of Binding ADAs	3.2% vs. 3.3%	0 (both)	PK Study: 0 (both) CCS: 0.7% (both)	PK Study: 0 vs. 2.9% CCS: 0 (both)	0.6% vs. 1.4%

All trastuzumab products demonstrated no clinically meaningful differences compared to reference products from a clinical pharmacology perspective



- Results of both clinical pharmacology endpoints for all trastuzumab products were within 80-125%
- Incidence and titers of ADAs were low and comparable
- No apparent impact of ADA on PK, activity, or safety endpoints

Observation from Clinical Pharmacology Studies and its Resolution

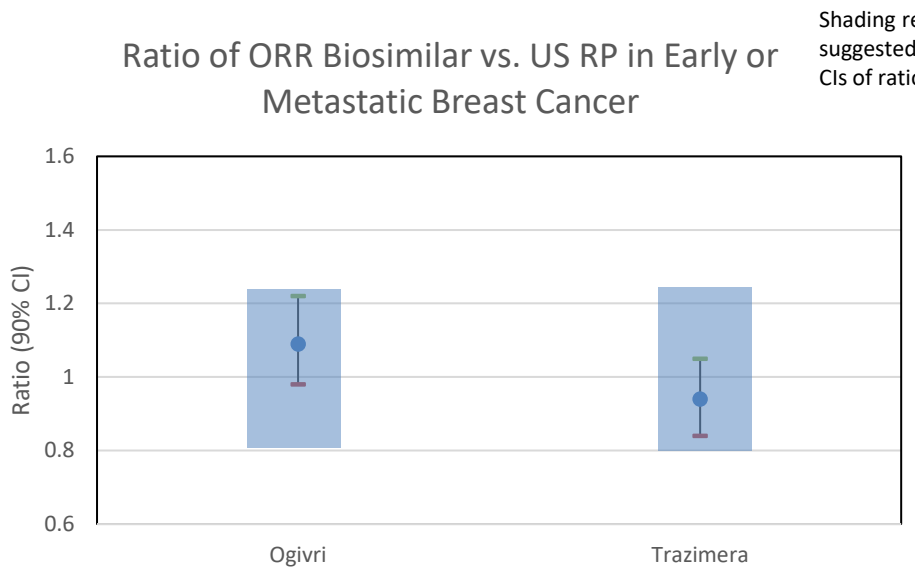
Product	Observation	Resolution Description
Trazimera	In comparative PK study, **higher incidence of pyrexia** reported in biosimilar arm (n=10, 28.6 %) compared to US RP (n=2, 5.7%) and EU RP (n=3, 8.6%).	• Sponsor conducted a follow-up single-dose comparative safety study with larger sample size (n=162): incidence of pyrexia was 6.2% (n=5) in the biosimilar arm vs. 13.6 % (n=11) in the US RP group, which was not statistically significant • Concluded that the differences in the incidence of pyrexia observed in comparative PK study were most likely caused by chance differences due to small sample size

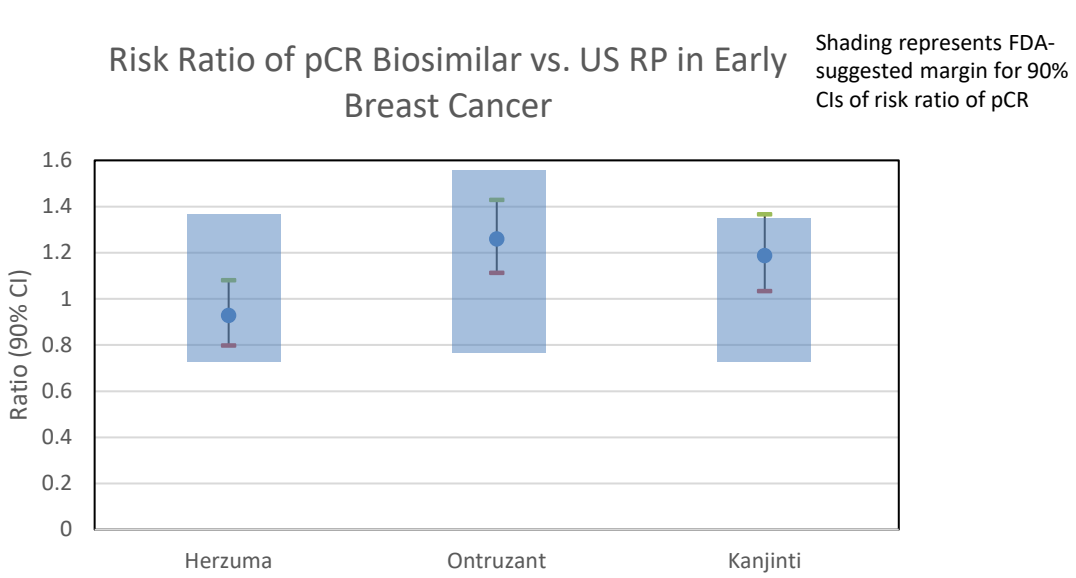
Comparative clinical studies investigated the efficacy, safety, and usability of each biosimilar product versus the RP

- Sponsors investigated the comparative efficacy and/or usability of their products in women with HER2+ breast cancer
  - Three conducted studies in early breast cancer (EBC) while two investigated in metastatic breast cancer (MBC)
  - Four were in the neoadjuvant setting only while one was in both first-line and adjuvant settings
- Primary endpoints were either risk difference (RD) and/or risk ratio (RR) of pathologic complete response (pCR), or overall response rate (ORR)

	Ogivri	Herzuma	Ontruzant	Trazimera	Kanjinti
Study Population	HER2+ MBC in the neoadjuvant setting	HER2+ EBC in both the neoadjuvant and adjuvant settings	HER2+ EBC or locally advanced breast cancer in the neoadjuvant setting	HER2+ MBC in the neoadjuvant setting	HER2+ EBC in the neoadjuvant setting
Sample Size	642	562	875	707	725
1° Efficacy EP	ORR at Wk 24 (assessed by central review)	RR of pCR (assessed by central review)	pCR	ORR at Wk 25, confirmed at Wk 33 follow-up (assessed by central review)	RD and RR of pCR (assessed by local review)
FDA-Suggested Acceptance Margin	90% CI for ratio of ORR within 0.81 - 1.24	90% CI for RR of pCR within 0.74 - 1.35	90% CI of RR of pCR within 0.785 - 1.546	90% CI for the ratio of ORR within 0.80 - 1.25	90% CI for RR of pCR within 0.7586 - 1.3182

Clinical efficacy studies showed no clinically meaningful differences for trastuzumab products compared to the reference product, although primary endpoint results for one product slightly exceeded its pre-specified upper margin





Highlighted Difference and Resolution

Product	Observation	Resolution Description
Kanjinti	Analyses of risk ratio of pCR based on local laboratory assessment resulted in 90% CIs with upper bounds that slightly exceed the pre-defined margin (i.e., >1.3182)	• All analyses of risk difference and risk ratio of pCR based on central laboratory assessment resulted in 90% CIs that were within the predefined margins • Review team considered central assessment for pCR to be acceptable to support the conclusion of no meaningful differences between the biosimilar and reference product. In general, central assessment for pCR is a more reliable method • Applicant was able to obtain sufficient samples for analysis to ensure reliability of this analysis in this study

Conclusions

Conclusions: Landscape Assessment of Biosimilar Submissions

Quality Data

Comparative analytical assessments demonstrated **high structural and functional similarity** between the biosimilar and US-RP for all adalimumab and trastuzumab biosimilars

Analytical differences were observed among various QAs, with different patterns across the different biosimilars. **None of the observations precluded a determination of high similarity**

- In the vast majority of cases, analytical data alone were sufficient to address residual uncertainty

Clinical Data

For all 5 trastuzumab biosimilars, PK similarity was demonstrated for C_{max} and AUC

- In one case, higher pyrexia was observed for the biosimilar compared to the US reference product
- Subsequent single-dose safety study showed no differences in events

Clinical results demonstrated comparable efficacy and safety, although they did not appear to play a role in resolving residual uncertainty from analytical similarity assessments or PK studies

- Efficacy: all primary endpoints were within equivalence margins*
- Safety and Immunogenicity: similar incidence of ADAs/nAbs; rates of AEs considered balanced between treatment groups
- No references in review documentation describing residual uncertainties that comparative clinical efficacy studies resolved

Conclusion: Results from comparative analytical and clinical PK studies typically sufficient to demonstrate that these adalimumab and trastuzumab biosimilars were highly similar to the US-RP except for minor differences that were not clinically meaningful.

Acknowledgements

Funding for this project was provided by the CDER BsUFA III Regulatory Science Pilot Program

CDER Offices including:

- Office of Clinical Pharmacology
- Office of Pharmaceutical Quality
- Office of Therapeutic Biologics and Biosimilars
- Office of Biostatistics

Contractor support from:

- Booz Allen Hamilton

Thank You!

And Next…

U.S. FOOD & DRUG ADMINISTRATION

Use of modeling to support stability in biotechnology regulatory submissions

Uriel Ortega-Rodriguez | Uriel Ortega-Rodriguez@fda.hhs.gov
Mari Lehtimaki | Mari.Lehtimaki@fda.hhs.gov

BsUFA III Interim Public meeting, September 18, 2025

Important Disclaimer!!!

- This presentation reflects the views of the authors and does not necessarily reflect the policies of the **U.S. Food and Drug Administration.**

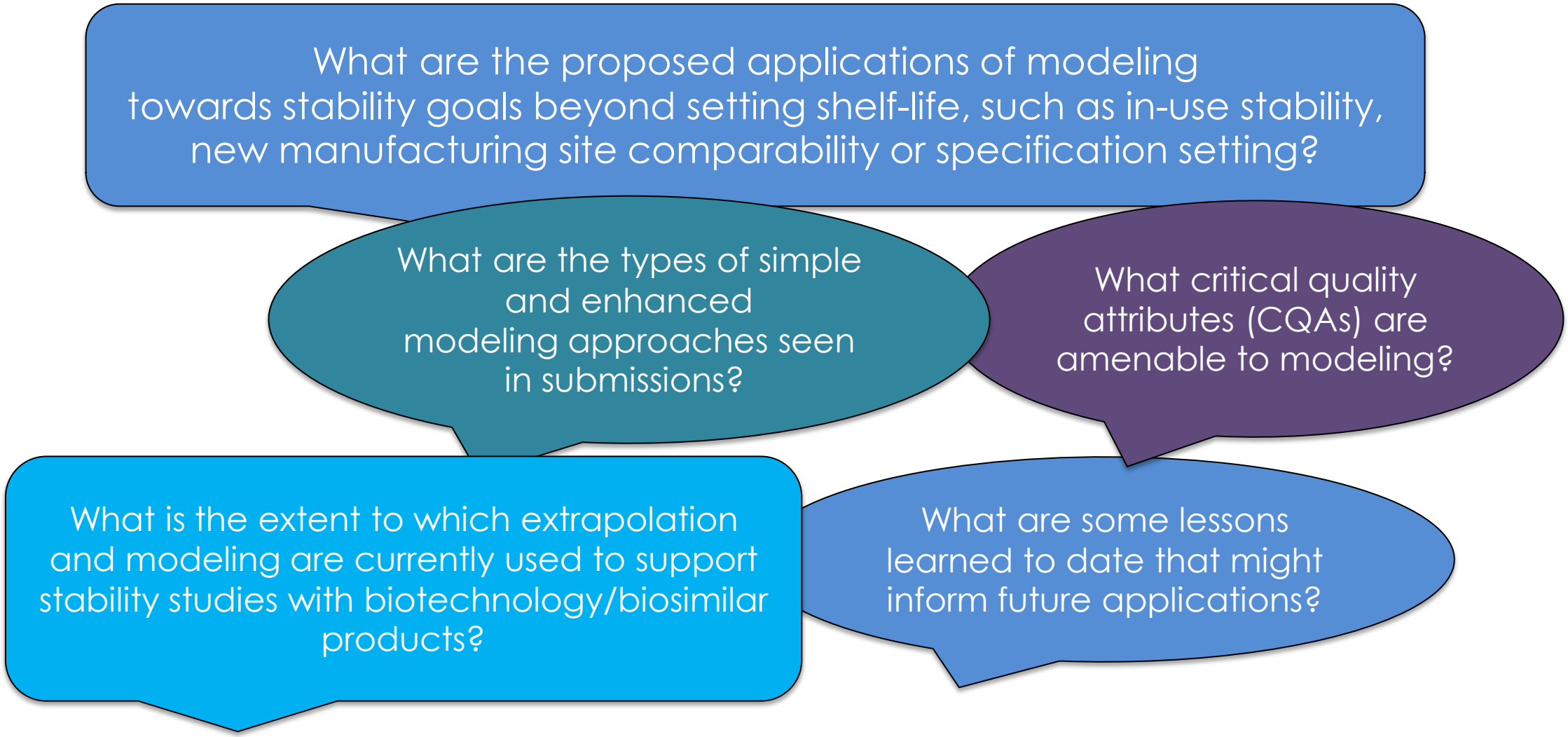
- Any mention of commercial products is for clarification only and is not intended as approval, endorsement, or recommendation.

Current ICH guidelines regarding stability testing

- Covers the generation and submission of stability data for biological and other products
- Typically, shelf-life is determined based on available real-time data.
  - Drives the speed of product development and submission.
  - Long-term Stability studies can be a bottleneck for biosimilar applications.

Hypothesis: Access to biosimilars may be accelerated through predictive stability modeling to estimate shelf-life with limited data!

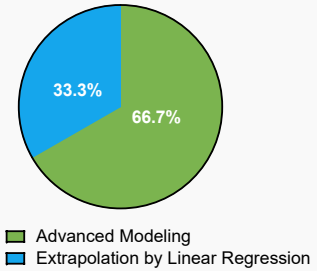
Open questions related to biotechnology stability modeling



Model development and verification to evaluate minimum stability data required for biosimilar submissions

Project Objective: Determine the minimum amount/type of stability data required to accurately predict long term stability and support biosimilar product's shelf-life.

Aim 1: Survey modeling approaches used in Biotechnology regulatory applications using regulatory databases and internal review documents.



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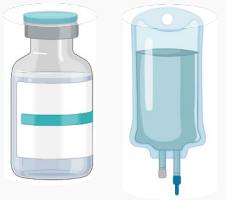
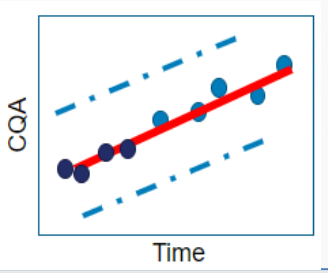


Aim 3: Create predictive models from the data collected using frequentist and Bayesian approaches.



Model development and verification to evaluate minimum stability data required for biosimilar submissions

- CDER is employing a panel of precision analytics to monitor protein degradation and other stability indicating attributes to Inform:
  - On the validity and robustness of models in use for biologic drug products.
  - The suitability of using predictive modeling to support biosimilar comparability
  - What type of stability indicating attributes are amenable to modeling
    - **Support BsUFA Research Priority B: "*Explore how modernization of analytical technologies could better and/or more efficiently detect relevant quality attributes.*"**

Drug Product	Analytic
Trastuzumab Trastuzumab-pkbr	cIEF
	CE-SDS
	SEC-UPLC
	Fc-binding potency
	DLS
	MFI
	MAM
Insulin Lispro 1 Insulin Lispro 2	cIEF
	CE-SDS
	SEC-UPLC
	Potency
	DLS
	MFI
	UHPLC-UV-HRMS

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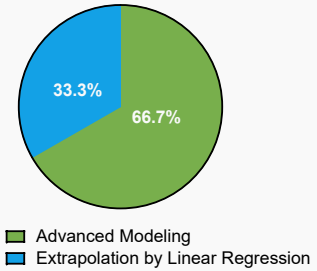

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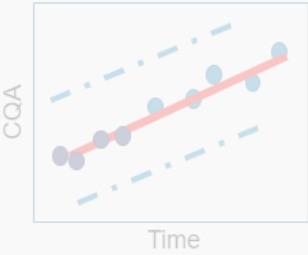
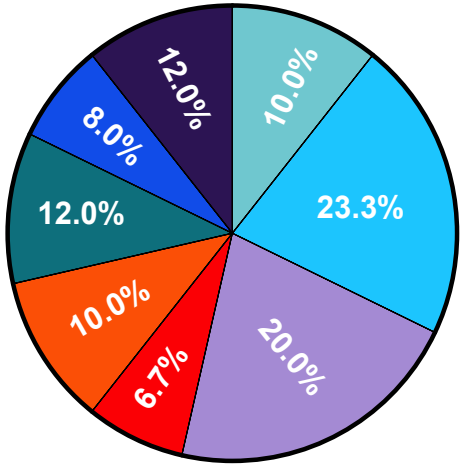


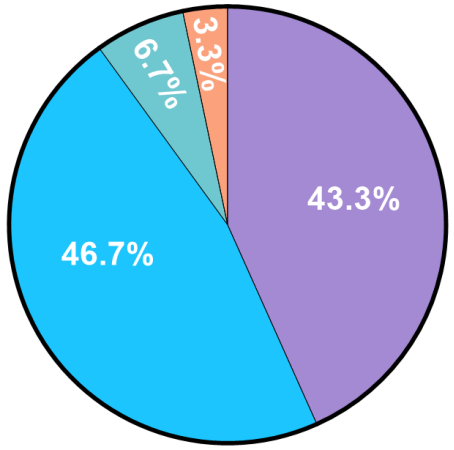
Aim 1 Summary: Comprehensive survey

Stability modeling was used for a variety of CQAs and contexts



- Comparability
- In-process control strategy
- In-use stability
- Setting acceptance criteria
- Setting storage/Shipping conditions
- Shelf-life estimation
- Shelf-life extension
- To support EUA supply

A variety of advanced modeling approaches were used



- Arrhenius equation
- Linear regression analysis
- Bayesian model
- Machine learning algorithms

Ortega-Rodriguez, Lehtimaki, Gutierrez Lugo, Rao. Current landscape of predictive stability modeling in well characterized biotechnology regulatory submissions. Manuscript in preparation

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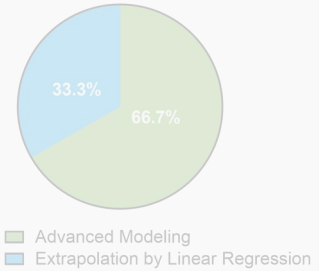

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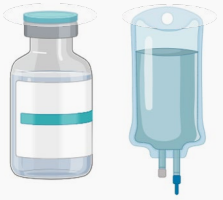

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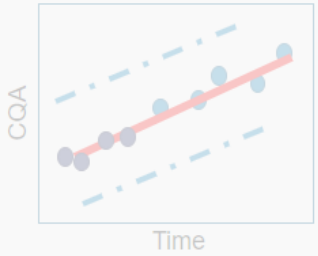
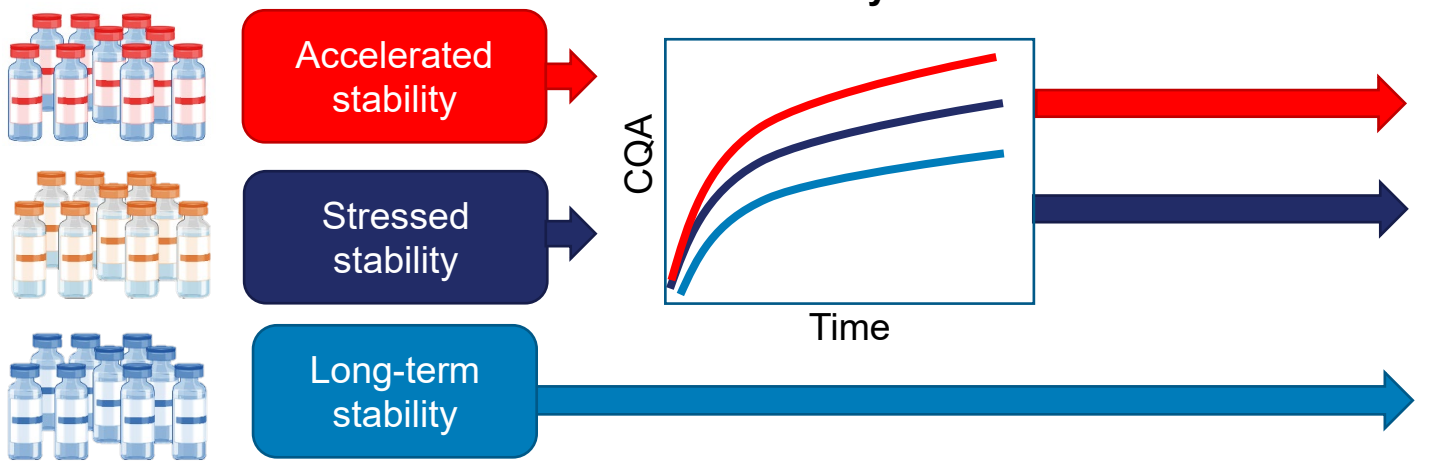
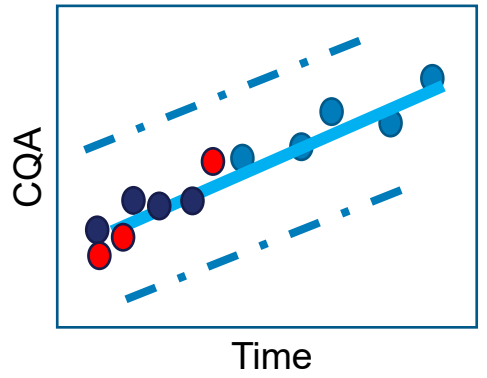


Modeling Outline

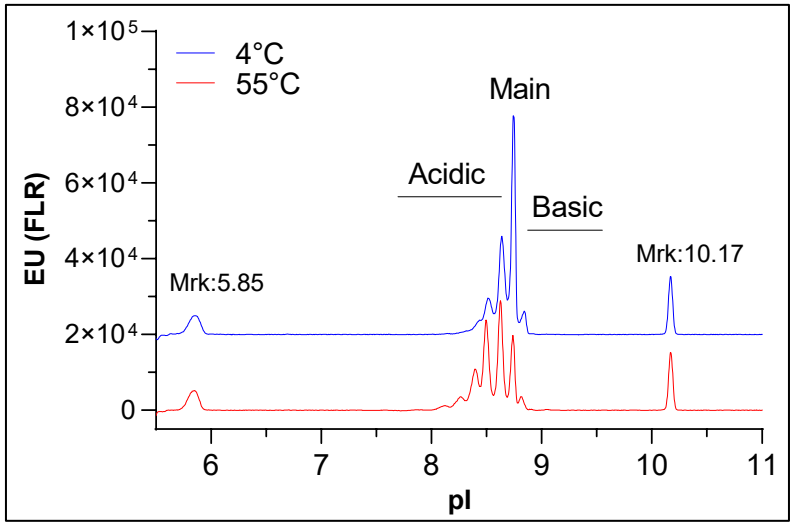




Frequentist and Bayesian models for predicted stability

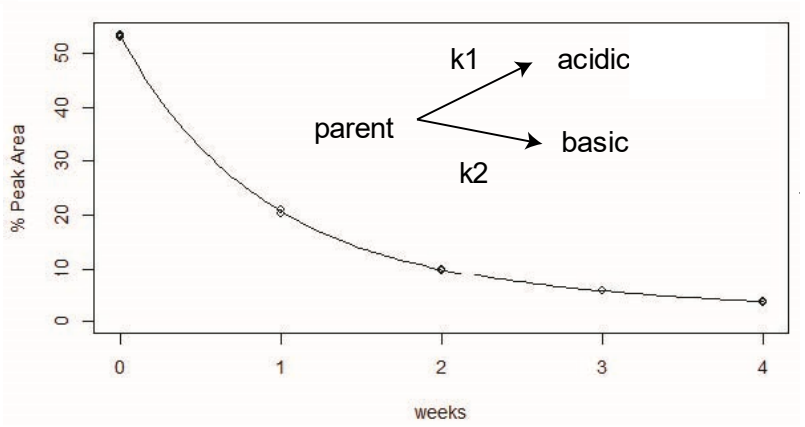
From lab bench to model

Charge Profiles of Trastuzumab Products



Predictive Stability Model

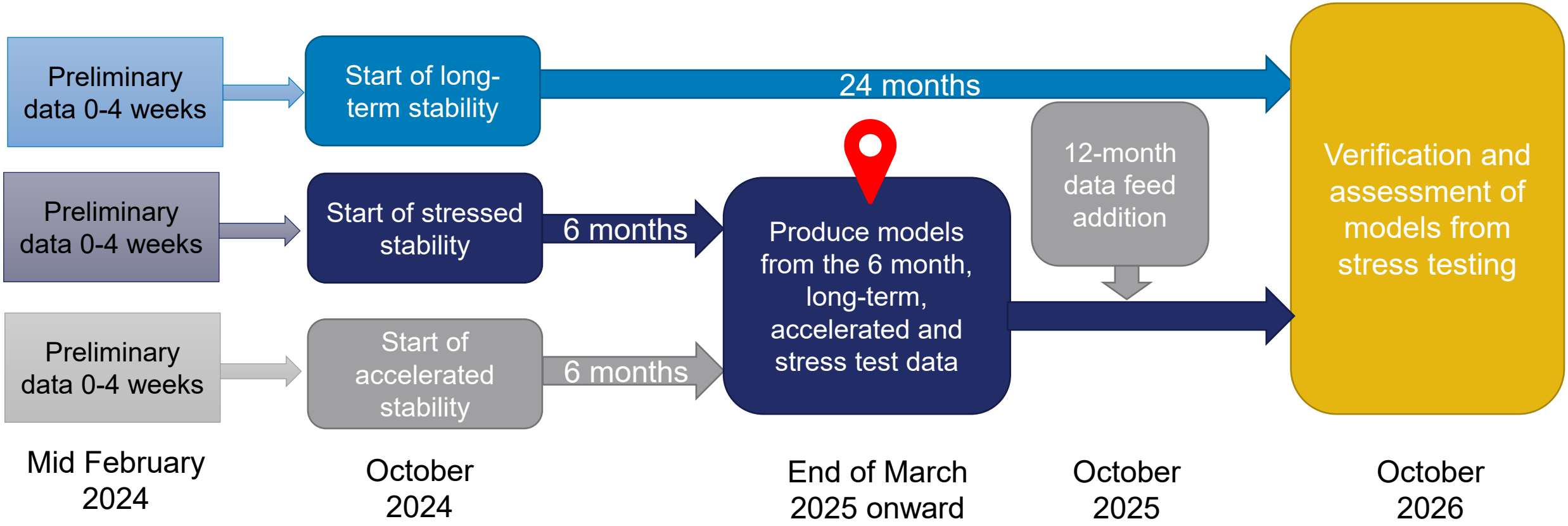
$$\frac{d(parent)}{dt} = \frac{-(k_1 * g\, e^{(-k_1 t)} + k_2 * (1-g) e^{-k_2 t})}{g * e^{-k_1 t} + (1-g) * e^{-k_2 t}} * parent$$



Leveraging Predictive modeling from limited stability data at the time of submission could accelerate the development timeline for biosimilars

Stability Testing of Trastuzumab, Insulin Lispro, and their Biosimilars

Long term sampling: 0, 1, 3, 6, 12 and 24 months
Stressed and accelerated sampling: 0, weekly for 1 month and then monthly for 6 months



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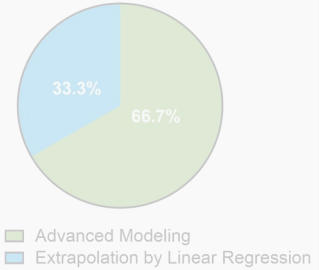

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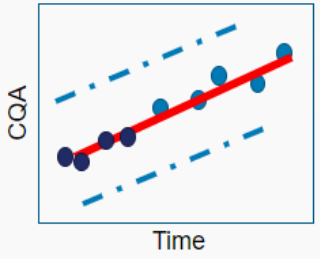


Frequentist VS. Bayesian

Frequentist (the only data available is related to the product at hand)

- Either a decision from a significance test or a confidence interval
- Model – collect data - input data – make inferences

Our approach:
Frequentist models will be used as a framework to build towards and compare the Bayesian approaches for the analytics

Bayesian (applicant has experience with the product or products like it)

- Bayes theorem enables the updating of prior probabilities based on new information
  - Utilize knowledge of the biological process and relevancy of the historical data
- Probability distributions for the identified parameters given observed data.
- Model – collect data – input data – **input historical or related data** – make inferences

Advanced Kinetic Modeling (AKM) for Prediction of Long-Term Stability: Frequentist approach

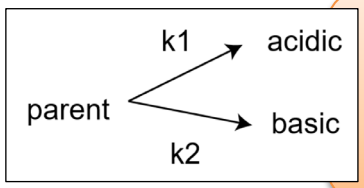
Fit experimental stability data at different temperatures

Screen candidate models

Estimate reaction rate(s) in accelerated & stress conditions

Scale to get the reaction rate for the long-term condition using Arrhenius-based kinetics (where possible)

Predict long-term stability and quantify uncertainty



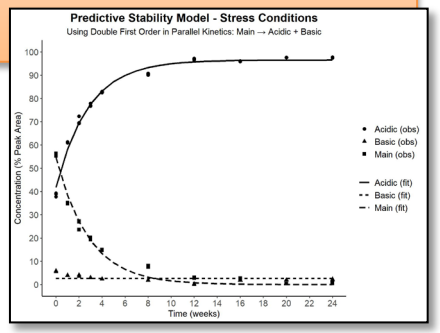
Represent interconversion of measured analytes in **reaction diagrams**

Model each pathway as pseudo-first-order rate laws formulated as a system of ordinary differential equations, or the integrated rate-law for pseudo-first-order kinetics

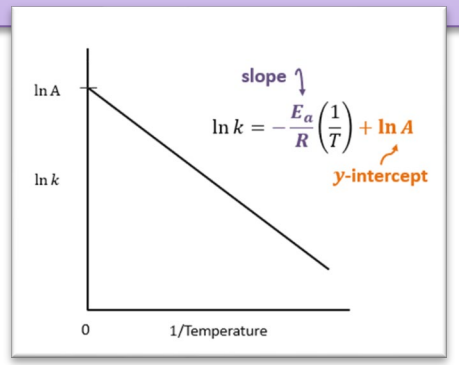
$$\frac{d[A]}{dt} = -(k_1 + k_2)[A]$$

$$\frac{d[B]}{dt} = k_1[A]$$

$$\frac{d[C]}{dt} = k_2[A]$$



The Arrhenius equation is log linear and describes how the rate of the reaction changes with temperature.



Michelle Stafford, CDER/OTS/OB

Acknowledgments: Our Multidisciplinary Team

Analytics Team

***Uriel Ortega-Rodriguez (OPQR)**
***Mari Lehtimaki (OPQR)**
Jordan Pritts (OPQR)
Thomas Biel (OPQR)
Tylee Houchens (OPQR)
Ashwinkumar Bhirde (OPQR)
Carole Sourbier (OPQR)
Sujata Bupp (OPQR)
Yeonjin (Daisy) Yang (OPQR)
Maxwell Korang-Yeboah (OPQR)
Jinhui Zhang (OPQR)
Mack Shih (OPQR)
Seth Thacker (OPQR)
Svetlana Petrovskaya (OPQR)
Garrick Centola (OPQAIII)
Vincent Falkowski
Mamatha Garige
Faiza Tahia
Isabella DeLuna
Mirian Mendoza
Roberto Mendez

Statistics/Modeling Team

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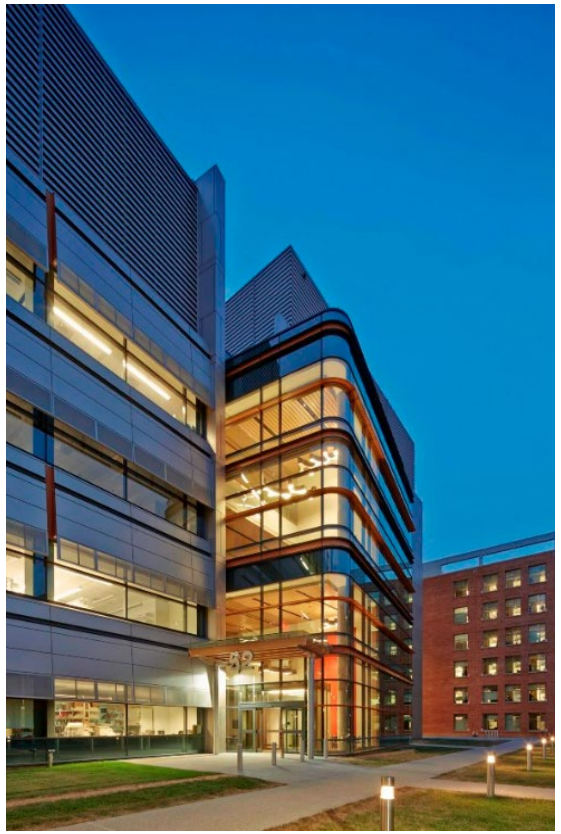
John Bettinger (CBER/OVRR)
Mary Manibusan (OQS)
Alex Viehmann (OQS)



Regulatory and Research Advisors

Ashutosh Rao (OPQAIII)
Thomas O'Connor (OPQR)
Sarah Rogstad (OPQR)
Daniela Verthelyi (OPQR)
Tere Gutierrez (OPQA III)
Shadia Zaman (OPQA III)

Funding Sources

BsUFA III Regulatory Science Pilot Program
Office of Pharmaceutical Quality Research Operating Funds

***Lead Investigators**

Thank You!

And Next…

U.S. FOOD & DRUG ADMINISTRATION

Enhancing Biosimilar Testing Capabilities: The BsUFA Bioassay Initiative

Carole Sourbier, Ph.D.
Office of Pharmaceutical Quality Research
Office of Pharmaceutical Quality
Center for Drug and Research Evaluation

BsUFA III Interim Public meeting – September 18, 2025

Everyone deserves confidence in their *next* dose of medicine.

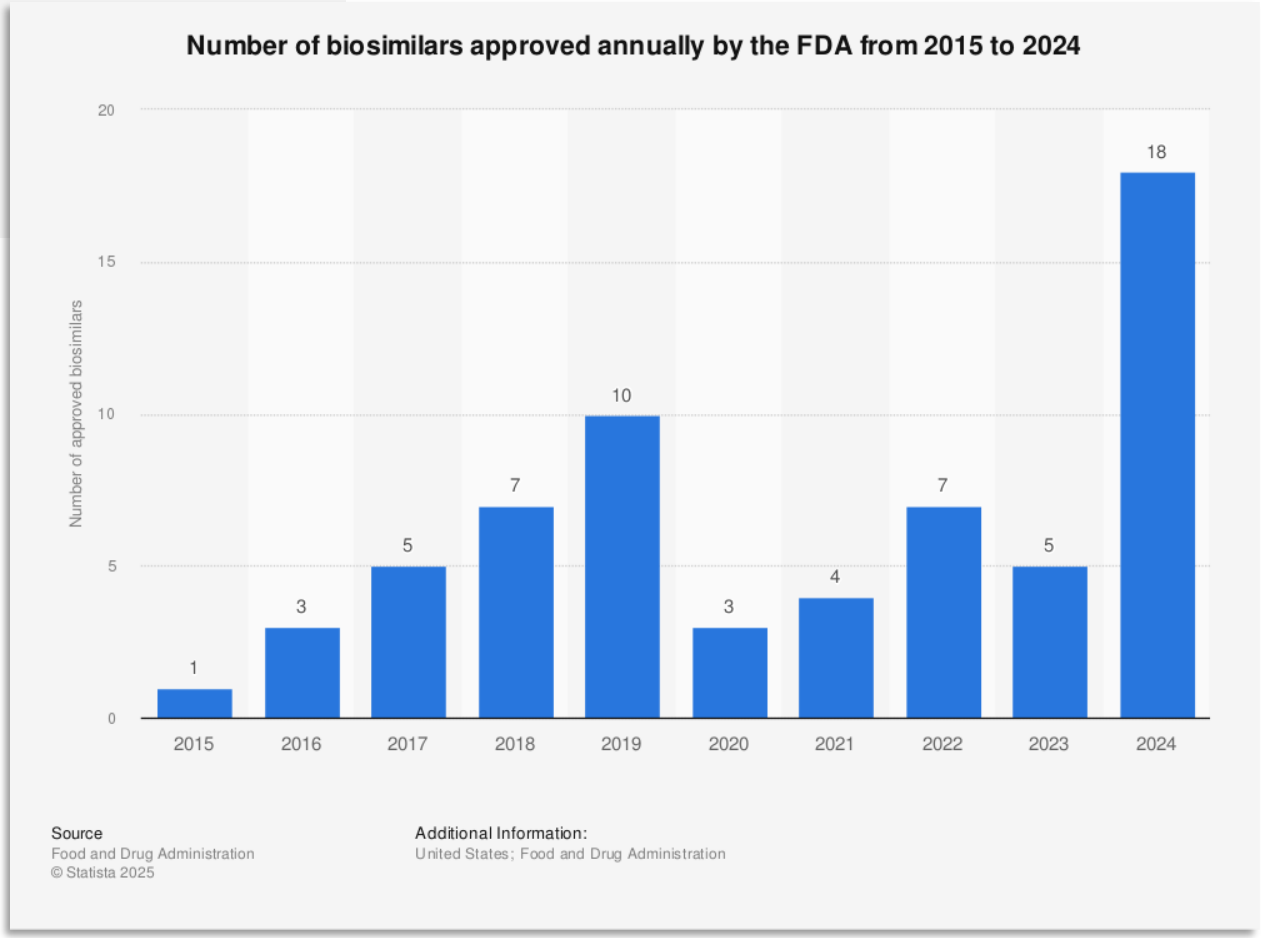
Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

Disclaimer

This presentation reflects my views and should not be construed to represent FDA's views or policies.

Expanding CDER's Bioassay Capabilities

Background



- ✓ Biosimilars are rapidly becoming a major product class submitted to FDA.
- ✓ **Cell-based bioassays** measure critical quality attributes (**CQA**) central to product potency and can be used to perform comparative analytical assessments of biosimilars.
- ✓ Current gaps exist in standardized control strategies for **insulin and mAb products**.

https://www.statista.com/statistics/1186585/number-biosimilar-drugs-approved-each-year-fda-us/

Expanding CDER's Bioassay Capabilities

Defining the need

- ✓ Need for consistent, harmonized testing approaches across laboratories
- ✓ Reducing inconsistencies and unnecessary testing burdens
- ✓ Ensuring unbiased, rapid assessment capabilities
- ✓ A bioassay program relevant to OPQ regulated products will have impact across the pharmaceutical lifecycle.
- ✓ Leveraging a drug product's critical quality attributes (CQA) to make crucial regulatory decisions on quality, safety and efficacy.

1. **Insulin Potency Bioassay/s**
2. **Antibody Function Bioassay/s**

➢ **Supportive of BsUFA III Research Priority C: Define best practices for assessing and reporting quality attributes**

Goals of the Bioassay Initiative

Aim 1: Validate bioassays for insulin and mAbs products

1. Insulin bioassay using an in-cell western assay derived from USP <121>
2. Fc effector function assay using Surface Plasmon Resonance (SPR)

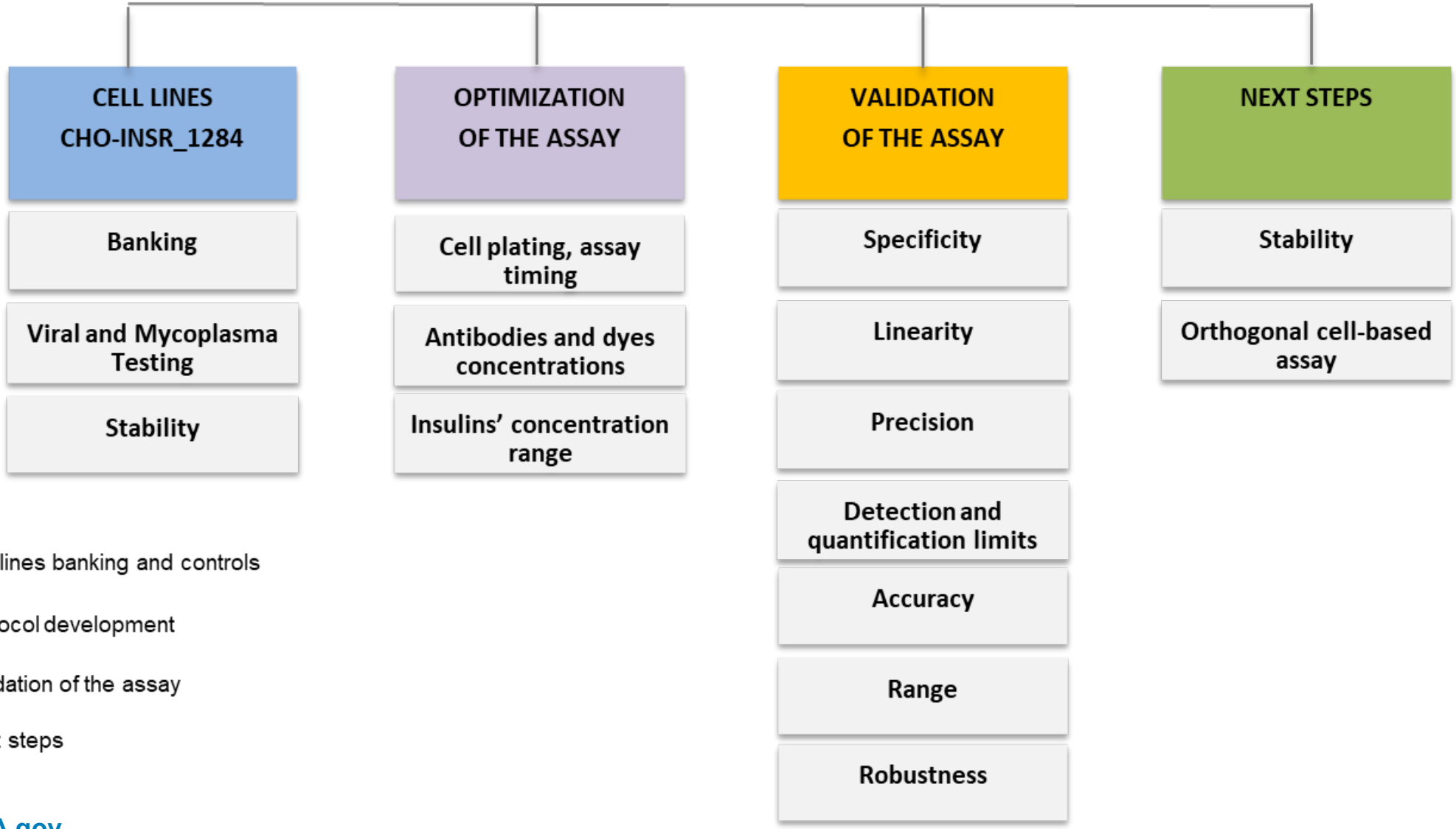
Aim 2: Leverage existing validated bioassays with international standards

1. Cross-validation using reference standards
   - Harmonization across laboratories

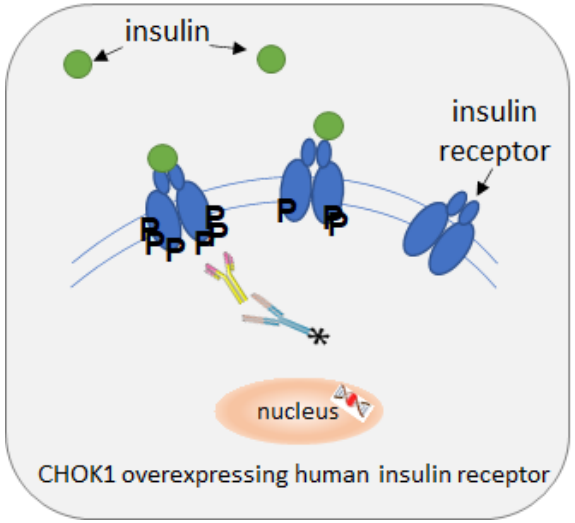
Aim 3: Perform stability studies and develop orthogonal assays for comprehensive quality assessment

1. Accelerated/stress stability studies
2. Orthogonal assays:
   - Insulin bioassays using luciferase reporter systems
   - Fc effector function using a cell-based ADCC assays

Project Overview – Insulin Bioassays

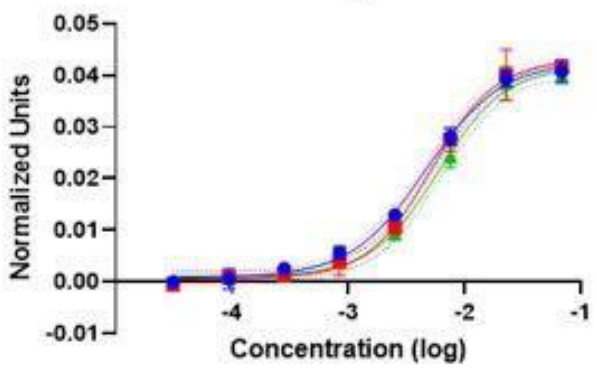


Current Progress – Insulin Bioassays



5 days

Glargine, Aspart, or Lispro



- ✓ Primary cell-based in-cell western (ICW) bioassay successfully validated for insulin glargine, insulin aspart and insulin lispro
- ✓ Protocol published
  PMID: 37104015, DOI: 10.3390/mps6020033
- ✓ Orthogonal testing: stable reporter cell line developed, qualification of the assay ongoing

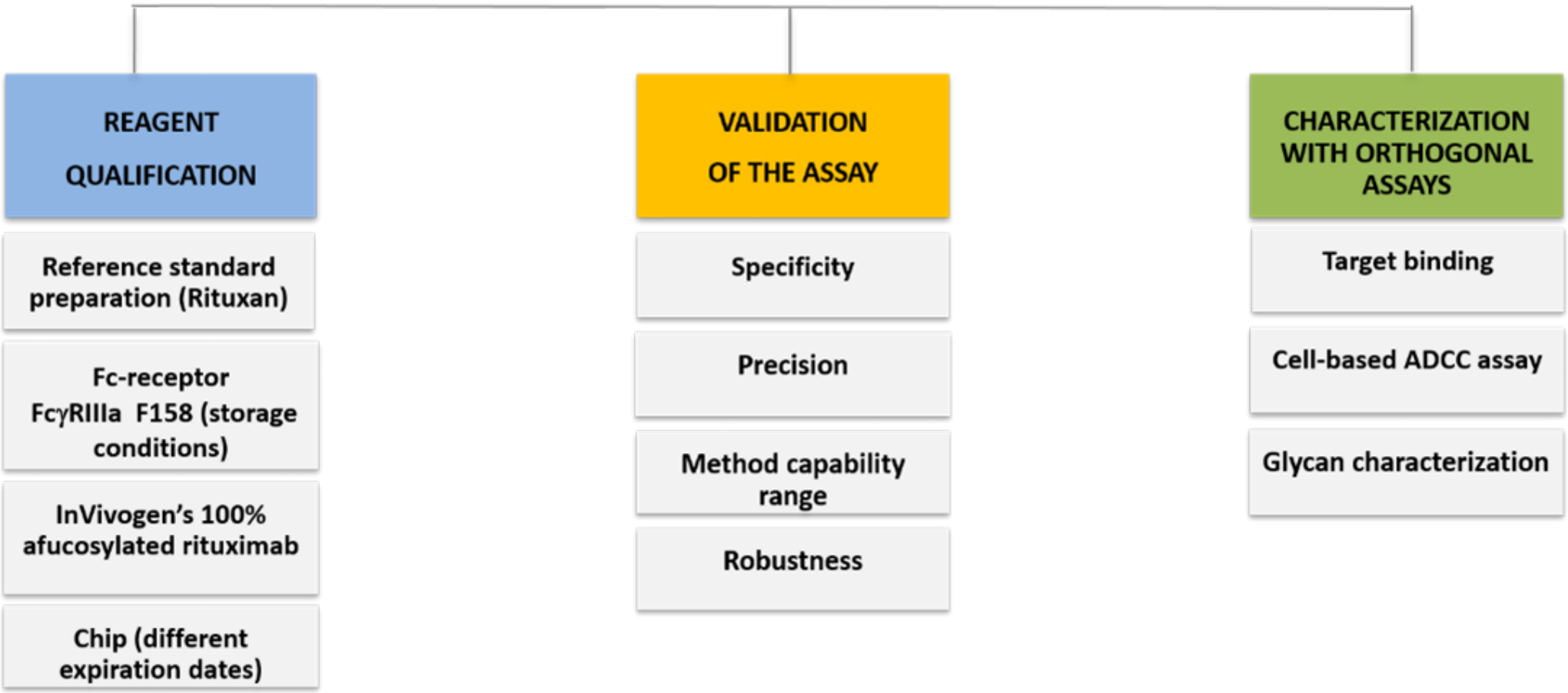
Current Progress – Insulin Stability Studies

- ✓ Heat stress stability studies completed on three insulin products (lispro, aspart, glargine)
- ✓ Photostability studies ongoing

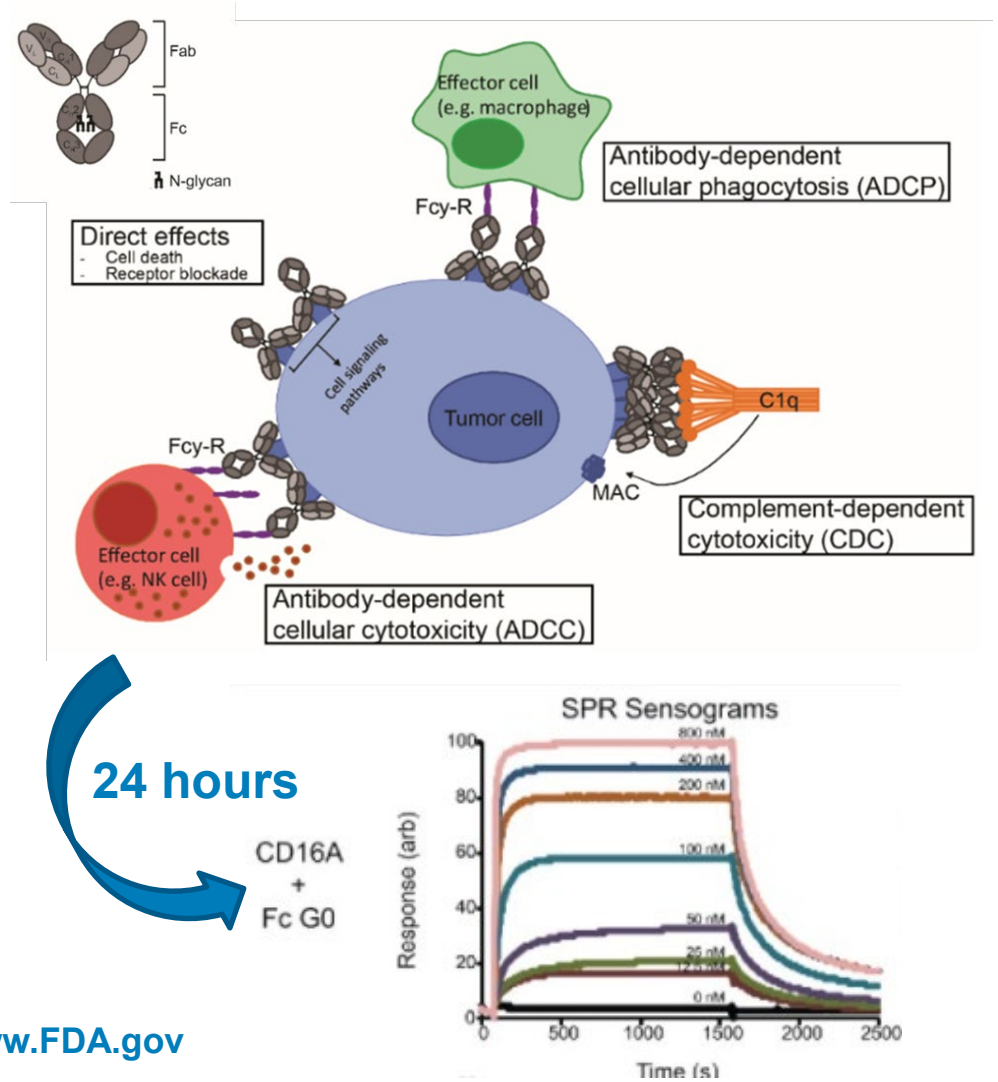
Thermal stability study

	40°C	Bioassay (ICW)	Content (HPLC)	Impurities	HMW (SEC)
Lispro	0 (control)	pass	pass	pass	pass
	1 month	pass	pass	***fail***	***fail***
	3 months	pass	***fail***	***fail***	***fail***
Glargine	0 (control)	pass	pass	pass	pass
	1 month	pass	pass	pass	pass
	3 months	pass	***fail***	***fail***	***fail***
Aspart	0 (control)	pass	pass	pass	pass
	1 month	pass	***fail***	pass	pass
	3 months	pass	***fail***	***fail***	***fail***

Project Overview– Fc effector function Assays

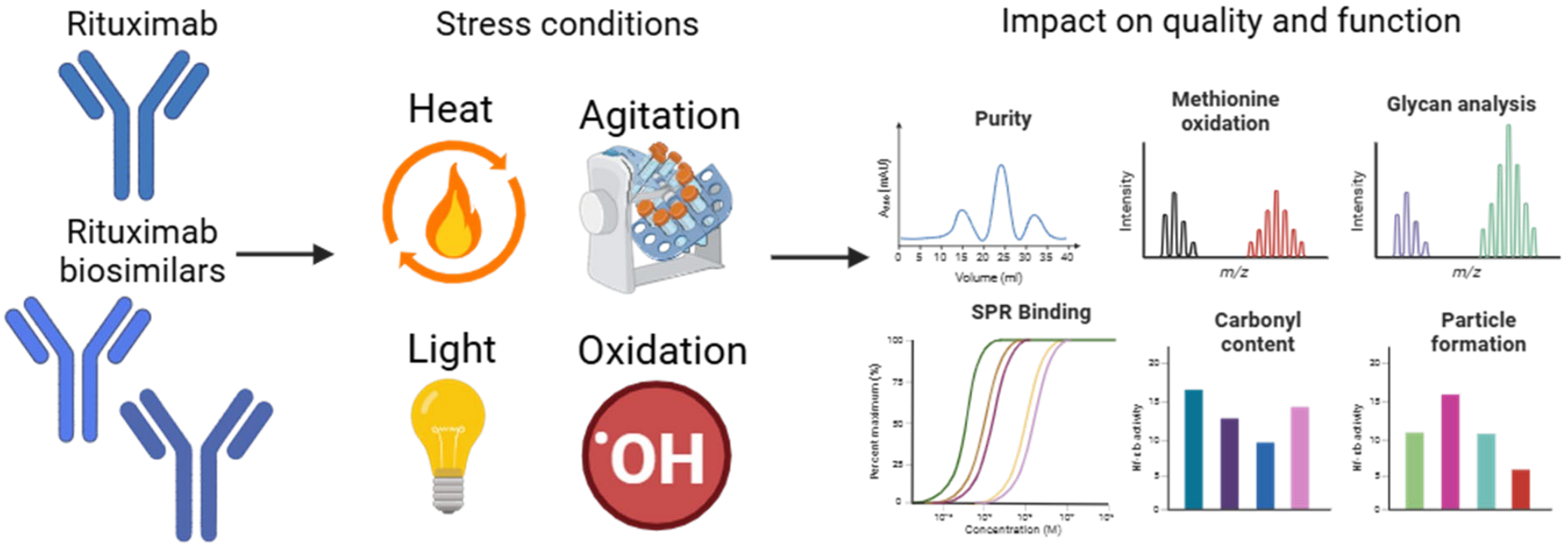


Current Progress – Fc effector function Assays



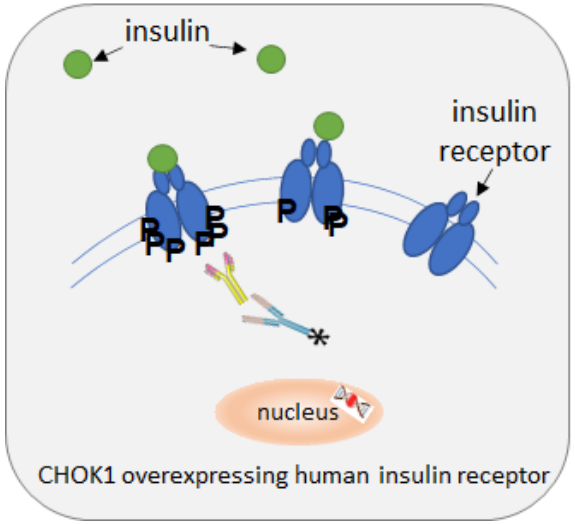
- ✓ SPR assay successfully validated for rituximab
- ✓ Method is in the process of being published
- ✓ Orthogonal testing: Commercial ADCC cell-based assay has been established using FcR Jurkat reporter cells

Current Progress – Fc effector function Stability Studies



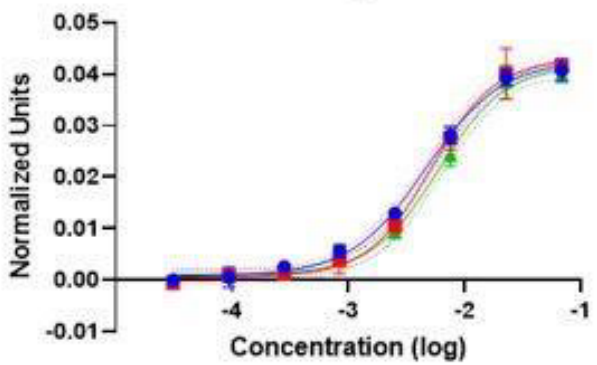
- ✓ Stability study using 6 stresses and 6 analytics completed for Rituxan® (Reference standard)
- ✓ Stability studies ongoing for Biosimilar 1 and Biosimilar 2

Applications and Impact: Insulin Biosimilars



5 days

Glargine, Aspart, or Lispro



Applications

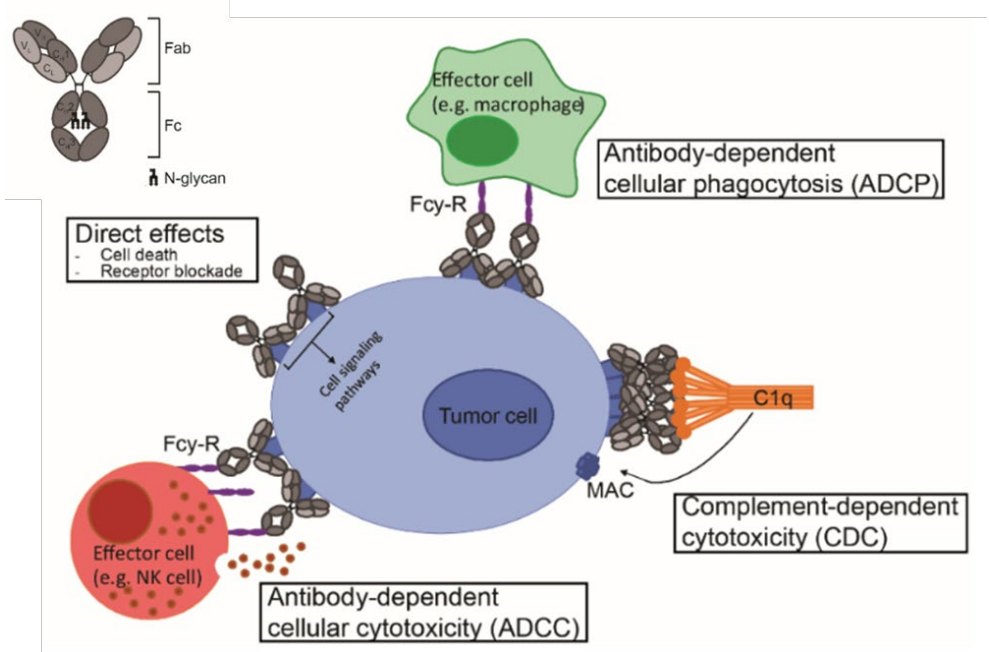
The validated ICW assay is available for:

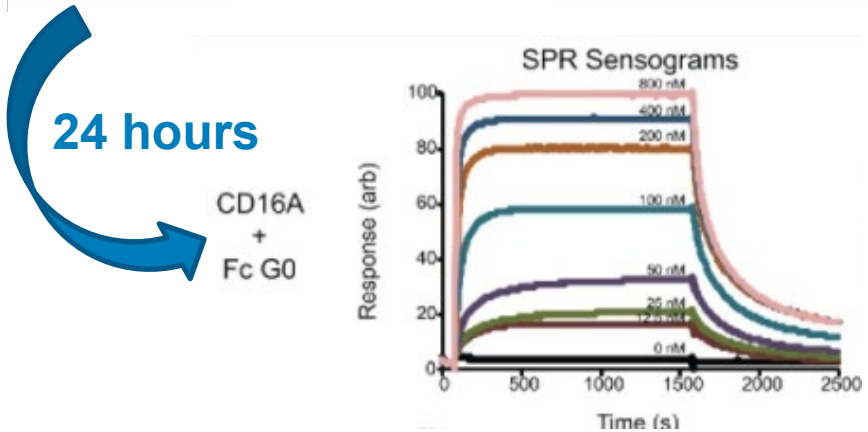
- Assessment of the functional activity of insulin products and related biosimilars.
- Testing of insulin Glargine, Lispro, and Aspart, and is amenable to be extended to other insulins.

Regulatory Impact:

- Available technology to address surveillance or pre-licensure review of Biosimilar BLAs
- As a proof of principal, the validated ICW was successfully implemented in regulatory applications, including two insulin biosimilar BLA assessments and a citizen complaint investigation.

Applications and Impact: Fc effector function





Applications

A validated FcR bioassay is available for:

- Screening the FcR binding and signaling characteristics of most mAbs, Fc-fusion proteins and related biosimilars.
- Investigating the potential role of any identified differences in determining potential safety signals of the product under established or undesired states.

Regulatory Impact:

- Available technology to address surveillance, pre-licensure review of Biosimilar BLAs
- Discussions with OQS to support quality surveillance of biotechnology products with Fc effector function

Next Steps & Future Directions

Immediate Priorities:

- Complete qualification of orthogonal assays for both insulin and mAb projects
- Finalize stability studies and data analysis
- Obtain reference standards for cross-validation studies

Communication & Dissemination:

- Technical reports and publications planned for Year 3
- Presentations at scientific conferences to share findings

Looking Forward – Broader Impact

- Benchmark standards across laboratories
- Enhanced resources for biosimilar development
- Continued advancement of regulatory science supporting biosimilar innovation

- Delivering valuable outcomes that advance insulin and mAbs biosimilar product development while ensuring product quality and public health protection

Bioassay Regulatory Science Program

Initiative Leads

Carole Sourbier

Gerald Feldman & Ashutosh Rao

Funded by the CDER BsUFA III Regulatory Science Pilot Program

Insulin Bioassay Group – Lead Carole Sourbier

Sujata Bupp
Morgan Hudson-Davis
Jinhui Zhang
Daniel P. Magparangalan
Ilan Geerlof-Vidavsky
Alicia Hoover
Connie Ruzicka
Patrick Faustino
**Mamatha Garige, Brian Roelofs*

FcyR Bioassay Group – Lead Tao Wang

Silvia Bacot
Jordan Pritts
Nozomi Sakakibara
Guozhang Zou
Patrick Faustino
Paul Dell, Jessica Dement-Brown
Jenni Swisher & Gunther Boekhoudt
Venkat Simhadri
**Gerald Feldman (former Lead)*


FDA
U.S. FOOD & DRUG
ADMINISTRATION

Thank You!

And Next…

Evaluating Real-World Data for Biosimilar Regulatory Assessments

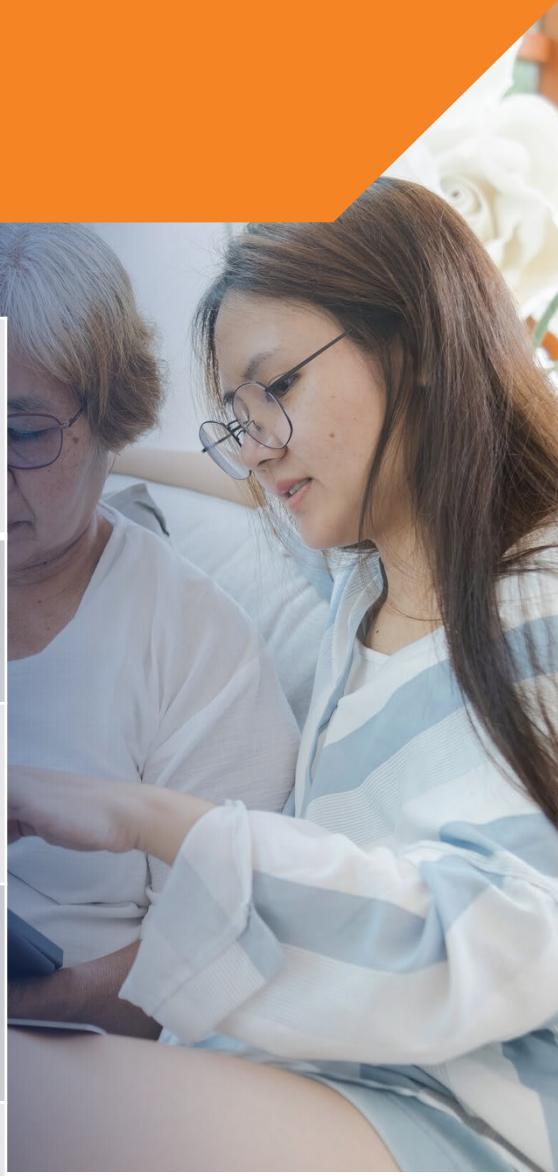
Catherine M. Lockhart, PharmD, PhD
Chief Science Officer, Academy of Managed Care Pharmacy
Executive Director, Biologics & Biosimilars Collective Intelligence Consortium

AMCP Research Institute™

BBCIC Biologics & Biosimilars Collective Intelligence Consortium

Award # 1U01FD007757-01

Project Title:	Improving the Efficiency of Regulatory Decisions for Biosimilars and Interchangeable Biosimilars by Leveraging Real-World Data
Grant ID:	1 U01 FD007757-01
Principal Investigator:	Catherine M. Lockhart, Pharm D, PhD - BBCIC
Co-Investigators:	Cheryl N. McMahill-Walraven, PhD (CVS Clinical Trial Services) Djeneba Audrey Djibo, PhD (CVS Clinical Trial Services) Pamala A. Pawloski, PharmD (HealthPartners Institute)
Others:	Julia Marsh (BBCIC), Scott Myers (PearlDiver), Steven Asche (HealthPartners Institute), Terese DeFor (HealthPartners Institute), Xi Wang (CVS)



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Award # 1U01FD008041-01

Project Title:	Bridging the Gap: Using Foreign Real-World Data to Inform Interchangeable Biosimilar Approvals
Grant ID:	1 U01 FD008041-01
Principal Investigator:	Catherine M. Lockhart, Pharm D, PhD - BBCIC
Co-Investigators:	Dr. Gianluca Trifirò - Professor of Pharmacology, University of Verona Dr. Jesper Hallas -Professor of Clinical Pharmacology, University of Southern Denmark
Others:	Julia Marsh (BBCIC), Scott Myers (PearlDiver)

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Collective Intelligence Consortium

RWD in Regulatory Applications

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Collective Intelligence Consortium

RWD in Regulatory Applications

- Literature Review

Most Common

Antineoplastics = 60

Coagulation disorders = 15

Enzyme replacement = 9

Most drug evaluations (n=136, 83.4%) deemed RWD was fit for purpose

A total of 14 (8.6%) studies reported the RWD was included in drug labeling

No RWD used for biosimilar approvals

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RWD Fitness for Purpose

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Data Source Characteristics

- **United States**

Data Source	National, commercial health plan	Regional integrated delivery network	Multi-payer, national claims database
Data Type	claims and enrollment; some EHR	claims linked to EHR	Multi-payer claims
Population Size	>44 million patient-lives	>4 million patient-lives	>170 million patient-lives
Data Lag	~11 weeks	Claims: ~3 months; EHR: 1 day	~20 months
Average Follow-Up Time	2 years	5 years	9 years
Geographic Region	All 50 states and territories	Midwestern U.S.	All 50 states

- **Europe**

Data Source	Denmark	Italy
Data Type	Comprehensive Registries	Claims + Medical Records
Population Size	Inhabitants of Denmark	Inhabitants of the Veneto Region of Italy (e.g., >4 million in 2021)
Data Lag	Variable	Variable
Average Follow-Up Time	Time of Residence	Time of Residence
Geographic Region	Denmark	Veneto Region of Italy (Verona)

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Data Source Assessment - Considerations

	Strengths	Considerations
United States	Readily identify patient cohorts	Some variables (e.g., race/ethnicity, other SDoH) may not be available or incomplete
	Exposures readily available	Disease progression measures may be unavailable
	Broadly representative population	Laboratory values may be unavailable or incomplete
	Reflects real-world patient care	Data lag and follow-up time vary
Europe	Extremely rich data, especially in Denmark	Patients switch drugs very quickly due to tender
	Representative population nationally (Denmark) or regionally (Italy)	My require access to specific data sets (e.g., claims vs provider-level data)
	Follow-up not reliant on insurance coverage	Process to request specific data can be long
	Data available beyond claims	Population and treatment patterns may differ

Data Quality:
Ensuring the data is accurate, complete, consistent, and timely is crucial for fitness for purpose.

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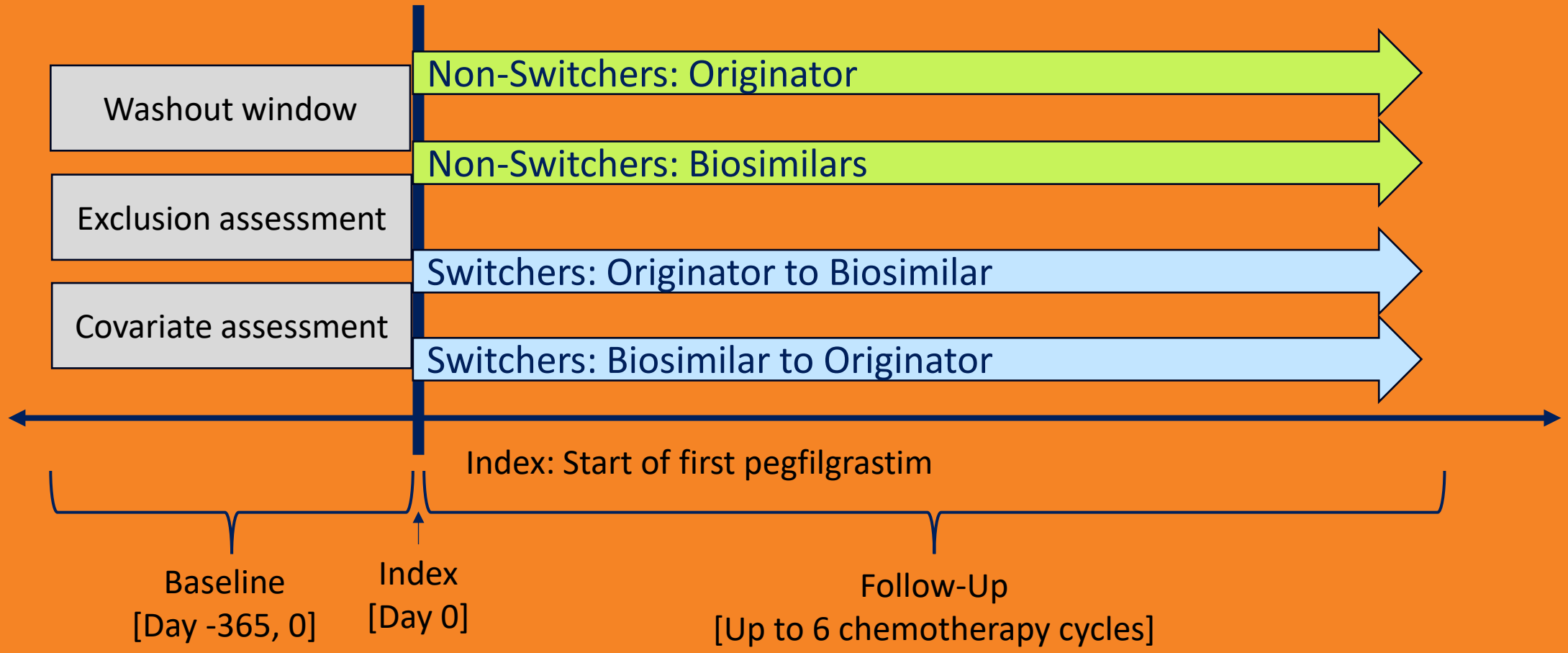
Test Emulation – Breast Cancer



Pegfilgrastim

- Likely observable outcomes (FN)
- Widely used

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Fit For Purpose RWD – Test Emulation

YES!

- Common conditions, relevant populations
- Readily identify patient cohorts
- Measurable exposures and outcomes
- Assessed switching patterns and outcomes
- Wide use of reference products
- Reflective of patient care
- Large volume of RWD available
- Internal consistency

but…

- Algorithm needed to identify cohorts
- Some effectiveness outcomes may be unavailable
- Treatment patterns varied across sites
- Routine patient care may not reflect clinical trials (e.g., multiple switching)
- Sample size matters

Key Considerations: Selecting appropriate data sources and robust study design is essential to success

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135

Summary + Recommendations

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Summary + Recommendations

- RWD can be meaningful and appropriate for biosimilars
- Biosimilars are unique with extensive reference product experience
- Data selection and fitness-for-use assessment is imperative
- Appropriate study design to generate evidence relevant for regulatory purposes
- Continue advancing data linkage and enrichment, and algorithm development
- More work is needed to define relevant outcomes available in RWD
- Broader education is needed on nuances of available RWD
- Promote wider acceptance of RWD as a valuable source

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Thank You!!

Thank You!

And Next…

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CENTER FOR DRUG EVALUATION & RESEARCH
OFFICE OF CLINICAL PHARMACOLOGY

Translating Clinical Pharmacology Biosimilar Research Findings into Best Practices for Industry and FDA Review Staff

Lakshmi Manasa Sakuntala Chekka, PharmD, PhD
Visiting Associate
Division of Applied Regulatory Science
Office of Clinical Pharmacology/OTS/CDER

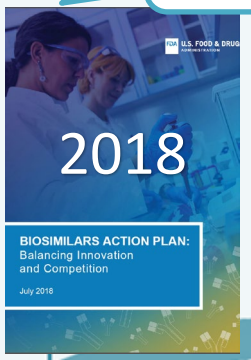
Disclaimer

This presentation reflects the views of the presenter and should not be construed to represent FDA's view or policies

Journey of Biosimilars

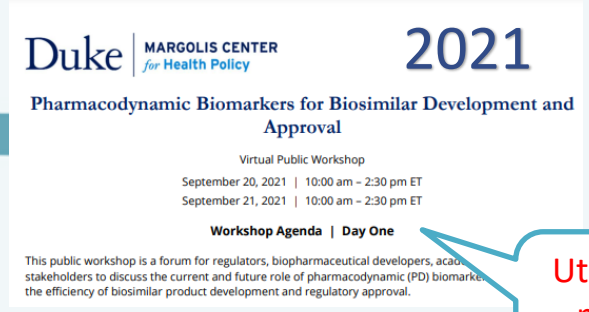
BPCI Act 2010

Biologics Price Competition and Innovation Act: Abbreviated licensure pathway for biosimilars or interchangeable products



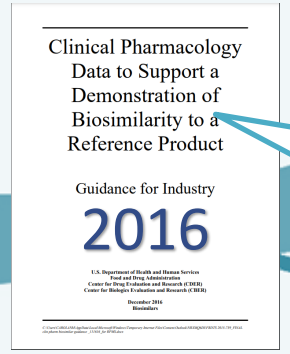
Improve accessibility of biologics/ biosimilars

Evidentiary considerations for PD biomarkers; FDA pilot clinical studies



Utility of PD biomarkers multiple stakeholder perspectives

Re-evaluating the need for comparative clinical efficacy studies



Role and considerations for using clinical pharmacology data to demonstrate biosimilarity

Project Overview

- **Goal:** Closeout of bioanalytical and omics-related project activities from the 'Pharmacodynamic Biomarkers for Biosimilar Approval' project - multi-year initiative supporting FDA's Biosimilars Action Plan

- **Project Focus:** Translating clinical pharmacology biosimilar research findings into best practices for industry and FDA review staff

Specific Aims

Aim-1:

Finalizing reports and publishing manuscripts for bioanalytical and proteomic activities conducted as accompaniment to previously completed FDA-led clinical studies

Aim-2:

Developing and discussing best practices for bioanalytical and proteomic assays at internal meetings and seminars for reviewer education

Premise of the PD Biomarkers for Biosimilar Approval Project

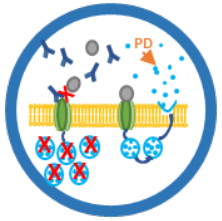
- FDA Clinical Pharmacology Guidance* outline that biosimilars may be approved based on clinical pharmacokinetic (PK) and pharmacodynamic (PD) biomarker data without a comparative clinical efficacy study (CES).
- PK/PD studies can provide sufficient clinical evidence of safety (immunogenicity) and biosimilarity with reduced sample size, smaller study duration, and increased sensitivity compared to clinical outcome measures and may be conducted in healthy participants.
- Develop an evidentiary framework and standards to use PD biomarkers in a biosimilar development program
- Explore methodologies to identify and characterize previously known and novel PD biomarkers for biosimilar development

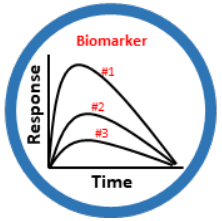
* US FDA Guidance: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product <https://www.fda.gov/media/82647/download> (2015).
* US FDA Guidance: Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product. <https://www.fda.gov/media/88622/download> (2016).

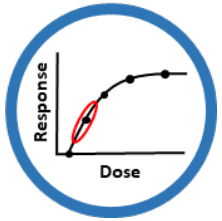
FDA Action to Fill Information Gaps

Under FDA's Biosimilars Action Plan, FDA has conducted targeted/applied research to fill information gaps, inform best practices and evaluate new methodologies

Characterize known PD biomarkers



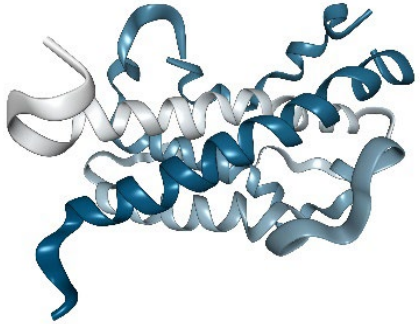




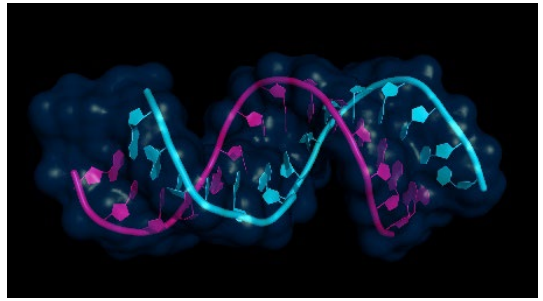
Therapeutic Class	Biomarker Data Availability	Type of Biomarker(s)
PCSK9 Antagonist	Readily available	Surrogate endpoint and biomarker tied to MOA
IL-5 Antagonist	Some availability	Biomarkers that are tied to MOA, direct-relationship with endpoint
Interferon β-1a	Limited availability	PD biomarkers that are linked to biological activity and/or MOA

Explore the use of new technologies to identify PD biomarkers or assess multiple biomarkers simultaneously

Proteomics



Small-RNA transcriptomics



Major project milestones achieved

Public Workshop

Duke | MARGOLIS CENTER *for* Health Policy

Pharmacodynamic Biomarkers for Biosimilar Development and Approval

Virtual Public Workshop

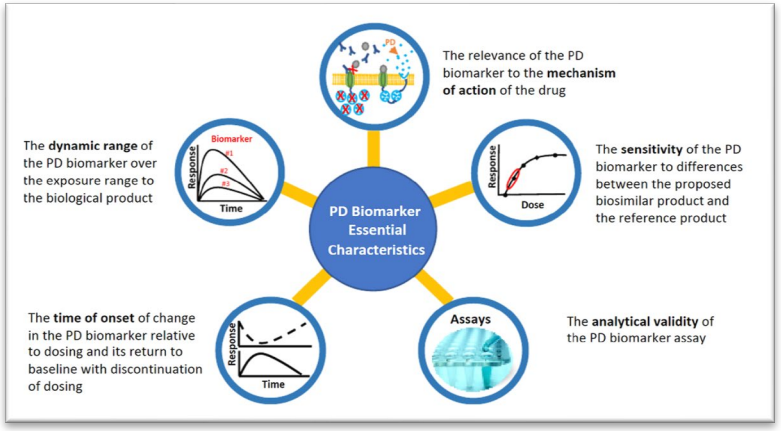
September 20, 2021 | 10:00 am – 2:30 pm ET

September 21, 2021 | 10:00 am – 2:30 pm ET

Workshop Agenda | Day One

This public workshop is a forum for regulators, biopharmaceutical developers, academic researchers, and stakeholders to discuss the current and future role of pharmacodynamic (PD) biomarkers in improving the efficiency of biosimilar product development and regulatory approval.

Evidentiary Framework
Strauss DG et.al. *CPT* 2023



Three clinical trials

Considerations for Use of Pharmacodynamic Biomarkers to Support Biosimilar Development – (I) A Randomized Trial with PCSK9 Inhibitors

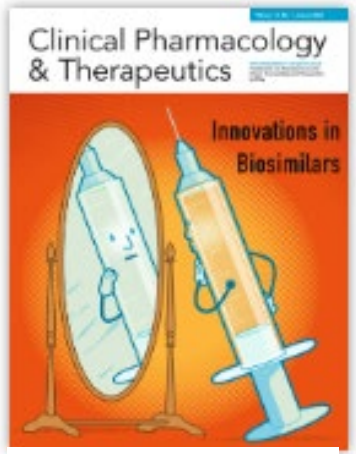
Morasa Sheikhy, Sarah J. Schrieber, Qin Sun, Victoria Gershuny, Murali K. Matta, Jane P.F. Bai, Xiulian Du, Giri Vegesna, Aanchal Shah, Kristin Prentice, Colleen Nalepinski, Issam Zineh, Yow-Ming Wang, David G. Strauss, Jeffry Florian ... See fewer authors

Considerations for Use of Pharmacodynamic Biomarkers to Support Biosimilar Development – (II) A Randomized Trial with IL-5 Antagonists

Victoria Gershuny, Qin Sun, Sarah J. Schrieber, Murali K. Matta, James L. Weaver, Ping Ji, Morasa Sheikhy, Cheng-Hui Hsiao, Giri Vegesna, Aanchal Shah, Kristin Prentice, Jennifer Deering, Yow-Ming Wang, David G. Strauss, Jeffry Florian

Considerations for Use of Pharmacodynamic Biomarkers to Support Biosimilar Development – (III) A Randomized Trial with Interferon Beta-1a Products

Jeffry Florian, Victoria Gershuny, Qin Sun, Sarah J. Schrieber, Murali K. Matta, Anthony Hazel, Morasa Sheikhy, James L. Weaver, Paula L. Hyland, Cheng-Hui Hsiao, Giri Vegesna, Ryan DePalma, Aanchal Shah, Kristin Prentice, Carlos Sanabria, Yow-Ming Wang, David G. Strauss



Volume 113, Issue 1
Innovations in Biosimilars
January 2023
Pages 71-79

Pilot studies to fill information gaps, inform best practices, and demonstrate methods, standards and approaches for biomarker selection and characterization. Used modeling and simulation to estimate PD parameters when therapeutic dose data is unavailable.

Major Project Milestones Achieved

Proteomic Studies

Clinical Pharmacology & Therapeutics

Article | Full Access

Evaluating the Utility of Proteomics for the Identification of Circulating Pharmacodynamic Biomarkers of IFNβ-1a Biologics

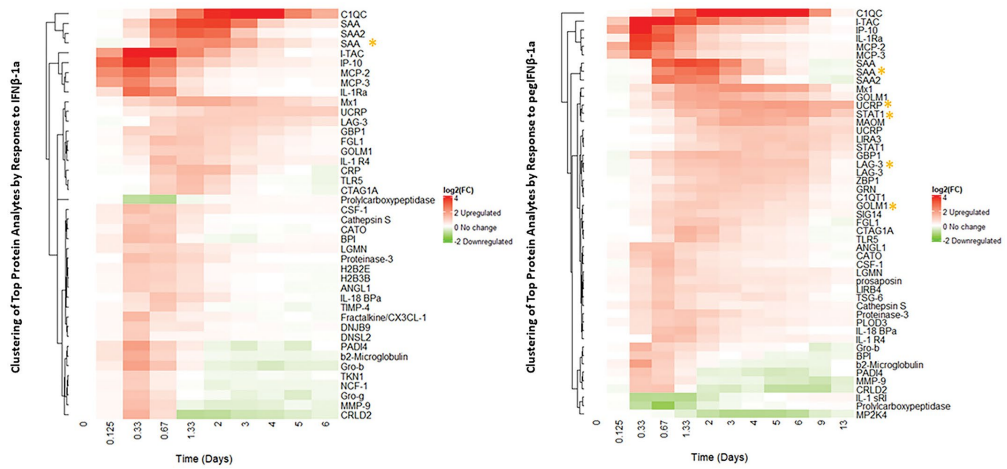
Paula L. Hyland, Lakshmi Manasa S. Chekka, Deepti P. Samarth, Barry A. Rosenzweig, Erica Decker, Esraa G. Mohamed, Yan Guo, Murali K. Matta, Qin Sun, William Wheeler, Carlos Sanabria, James L. Weaver, Sarah J. Schrieber, Jeffry Florian, Yow-Ming Wang, David G. Strauss

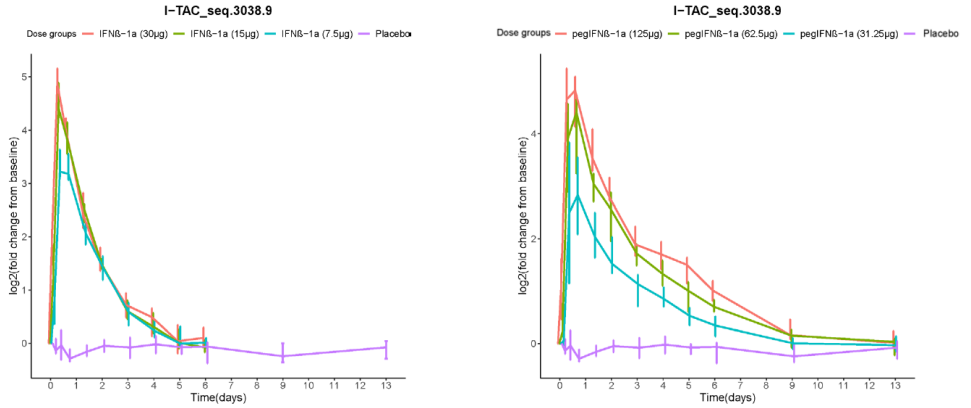
Characterization of Proteomic Pharmacodynamic Biomarkers of IFNβ-1a Biologics to Inform Potential Utility in Biosimilar Development

Lakshmi Manasa S. Chekka, Deepti P. Samarth, Yan Guo, Esraa G. Mohamed, Erica Decker, Murali K. Matta, Qin Sun, William Wheeler, Carlos Sanabria, Joel Wommack ... See all authors

First published: 04 July 2025 | https://doi.org/10.1002/cpt.3754

IFNβ-1a **pegIFNβ-1a**





Several new differentially expressed proteins with good magnitude of response

Evaluated variability at therapeutic *vs.* lower doses, dose-response and sensitivity, return to baseline

Progress and Outcomes

Aim-1 Finalizing reports and publishing manuscripts

Progress:

- Bioanalytical methods development and validation reports completed for all drugs and PD biomarkers
- Proteomics sample analysis, data analysis, and methods reports completed for all three clinical studies

Outcomes:

- One bioanalytical manuscript submitted for publication
- One proteomics manuscript published, one proteomics and one transcriptomics manuscript submitted

Aim-2 Developing and discussing best practices

Progress:

- Presentations and best practice documents were prepared and have been discussed at internal Office of Clinical Pharmacology meetings

Outcomes:

- Best practices for bioanalytical and proteomics methods have been discussed at internal meetings (e.g., reviewer training seminars, scientific interest groups) for reviewers to utilize in review of biosimilar submissions.

Lessons Learned

Regulatory Uncertainty

Sponsors may pursue traditional development paths due to uncertainty about biomarker acceptance, potentially delaying more efficient approaches.

Trial design and challenges

- Variability and sensitivity: PD biomarkers may be more variable than drug concentrations, requiring larger sample sizes and higher doses to distinguish from placebo responses.
- Parameter optimization: Appropriate PD parameter selection (AUEC vs ΔPD_{max}) through pilot studies and modeling/simulation can achieve sufficient sensitivity at therapeutic doses.

Technical Limitations

- Bioanalytical methods development for PD biomarkers requires additional time and resources.
- Proteomics and small-RNA transcriptomics may face limited adoption in biosimilar development due to resource intensiveness, cost, and technical complexity. Additionally, small-RNA transcriptomics faces platform-specific biases.

Reduced regulatory reliance on CES

- Use of PD biomarkers may not offer increased efficiency (beyond comparative analytical and PK data) in development for all biosimilar programs
- PD biomarkers have greatest utility in cases where systemic exposure is not available or where use of the approach can be agreed on early in development

Regulatory Impact

- Research from this multi-year project, designed based on strategic priorities and goals outlined in the BAP, has helped inform FDA's understanding regarding the potential and limitations regarding use of PD biomarkers for biosimilar development.
- FDA is better positioned to provide timely feedback to sponsors regarding use of PD biomarkers, novel analytical methods (e.g., omics approaches), and bioanalysis for biologics and PD biomarkers that may be included as part of a biosimilar development program.

Funding and Acknowledgements

Funding Source: CDER BsUFA III Regulatory Science Pilot Program

Acknowledgements:

- Numerous staff, contractors, and fellows from Division of Applied Regulatory Science (DARS)
  - Project Lead – David Strauss
  - Clinical Studies – Jeffry Florian and Victoria Gershuny
  - Genomics and Molecular Biology Lab – Paula Hyland
  - DARS Bioanalytical Team – Murali Matta and Ryan DePalma
- Office of Clinical Pharmacology
  - Therapeutic Biologics Program – Yow Ming Wang and Qin Sun
- Office of Therapeutic Biologics and Biosimilars
  - Sarah Yim, Kimberly Maxfield, and Sarah Schrieber

Thank you!

Panel Discussion with Presenters

- **For all audience members:** please use the QR code to submit your questions. Please indicate who the question is being addressed to by following this format: *name of presenter: Jane Doe, question.*

Break for Lunch and Poster Session

Break is from 12:00-1:15pm

All audience members are encouraged to review the scientific posters.

At 1:15pm we will resume for the Poster Session Panel Q&A.

All questions please submit using the QR code.

Or submit to:
BsUFARegSciProgram@fda.hhs.gov

Poster Session Q&A

- **For all audience members:** please use the QR code to submit your questions. Please indicate who the question is being addressed to by following this format: *name of presenter: Jane Doe, question.*

Thank You!

And Next…

Pilot Program Interim Evaluation and Next Steps

Industry Reaction and Panel Discussion Q&A

- **For all audience members:** please use the QR code to submit your questions. Please indicate who the question is being addressed to by following this format: *name of presenter: Jane Doe, question.*

Thank You!