Update on FDA's COA Qualification Program, ISTAND Program, and Patient-Focused Drug Development Initiative

Clinical Outcome Assessment Program
Annual Meeting
April 16th, 2026

Agenda

- Introductions
- CDER DDT Qualification Programs
  - COA Qualification Program
  - Innovative Science and Technology Approaches for New Drugs (ISTAND) Program
- Patient-Focused Drug Development Initiative
- Q&A

Introductions

Presenters

- **David Reasner**, Division Director, Division of Clinical Outcome Assessment, OND|ODES, CDER
- **Vanitha Sekar**, Division Director, Division of Biomedical Informatics, Research, and Biomarker Development, OND|ODES, CDER
- **Robyn Bent**, Director, Patient Focused Drug Development, CDER

Moderator

- **Michelle Campbell**, Associate Director, Stakeholder Engagement and Clinical Outcomes, OND|ON, CDER

Panelist

- **Selena Daniels**, Deputy Division Director, Division of Clinical Outcome Assessment, OND|ODES, CDER

Clinical Outcome Assessment DDT Qualification Program (COA QP)

David S. Reasner, PhD

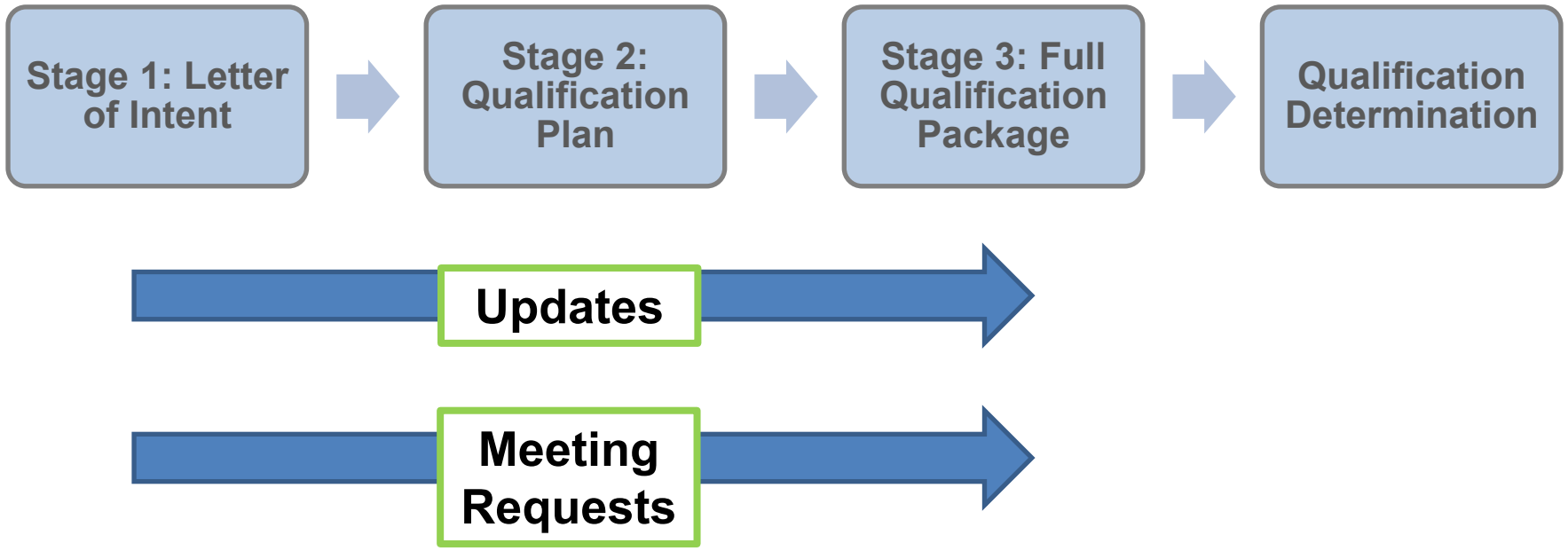
Director, Division of Clinical Outcome Assessment
Office of Drug Evaluation Sciences, Office of New Drugs
CDER, FDA

COA DDT Qualification Program (COA QP)

- **COA QP - Stages**
- **COA QP - 2025 Metrics**

COA QP Stages

DDT Process:
COA Qualification Stages



Each of the three milestone submissions should be a stand-alone package.

DDT Process: COA Qualification Timeframes

Qualification Stage	Timeframe
Letter of Intent (LOI)	3 months (calendar days)
Qualification Plan (QP)	6 months (calendar days)
Full Qualification Package (FQP)	10 months (calendar days)

CDER conducts a reviewability assessment, and the review begins when a reviewable memo issues.

DDT Process: Opportunities for improved processes

Qualification Stage	Opportunities
Letter of Intent (LOI)	LOI Stage QRT
Qualification Plan (QP)	Asynchronous Review
Full Qualification Package (FQP)	Reviewability Limits

COA QP 2025 Metrics

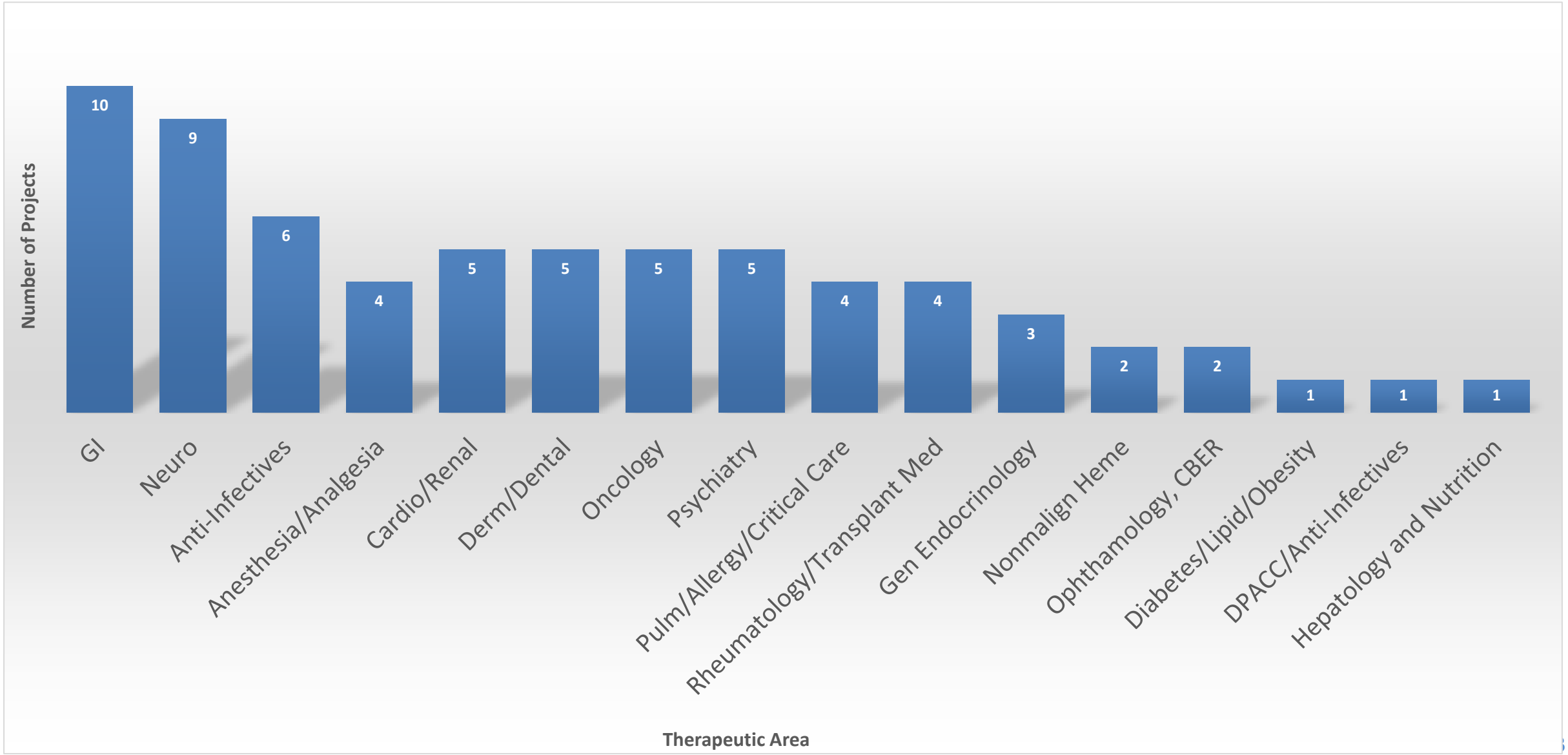
Number of COA QP Projects

- As of December 31st, 2025, the total number of projects in the program was 67
- Pre-LOI Meetings, information requests, interim submissions (e.g., interim briefing document), etc.

Number of 2025 DDT Submissions

Type	Number (2019)	Number (2020)	Number (2021)	Number (2022)	Number (2023)	Number (2024)	Number (2025)
Letter of Intents (LOIs)	18	22	7	5	**7**	**13**	**8**
Qualification Plans (QPs)	8	15	10	6	**7**	**7**	**4**
Full Qualification Packages (FQPs)	0	2	2	1	**4**	**0**	**2**
Updates	9	9	13	3	**5**	**7**	**3**
Meeting Requests	5	10	13	2	**9**	**5**	**1**
Withdrawal Requests	1	2	0	0	**1**	**0**	**2**

COA DDT Projects by OND Clinical Review Divisions



DDT Projects by COA Type - 2025

COA Type	Number
PRO Measures	42
Other*	9
PerfO Measures	6
ClinRO Measures	5
ObsRO Measures	3
PRO/ObsRO	1
Multi-Component COA	1

*Digital Health Technologies (DHTs) not falling into other categories (e.g., activity monitors)

COA QP 2025 Resources

COAQP Email Listserv

Sign-Up! to the **COAQP Email Listserv** for timely updates and announcements such as:

- Newly qualified COAs
- Updates to existing COAQP resources (e.g., LOI outline edits, etc.)
- COAQP process changes (e.g., switching electronic submission portals)

https://public.govdelivery.com/accounts/USFDA/subscriber/new?topic_id=USFDA_531

Links to Public COA QP Resources

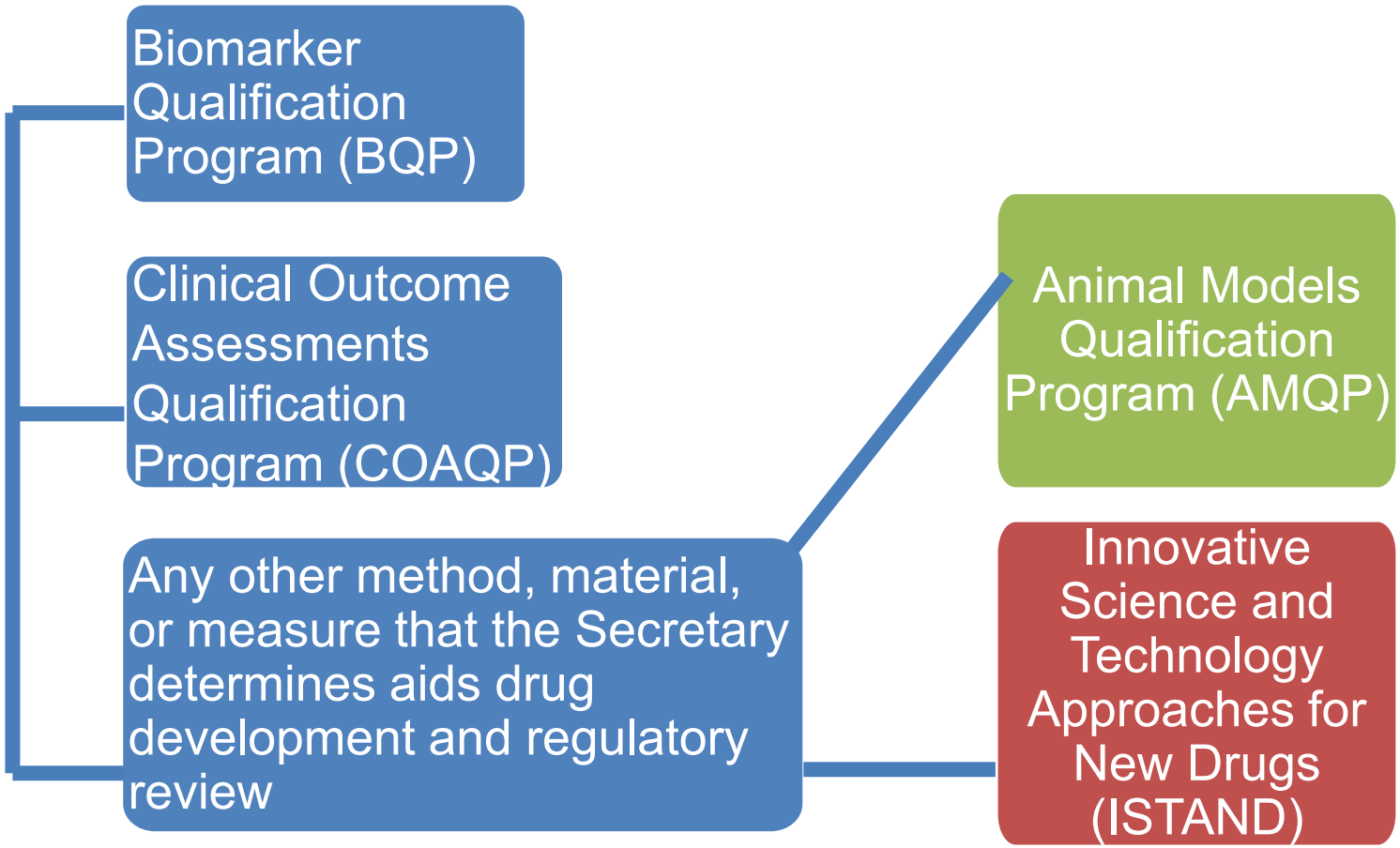
- COA Qualification Program Resources
  - COAQP Orientation Session
- DDT Process Guidance
- Transparency Database

Innovative Science and Technology Approaches for New Drugs (ISTAND) Program

Vanitha Sekar, PhD

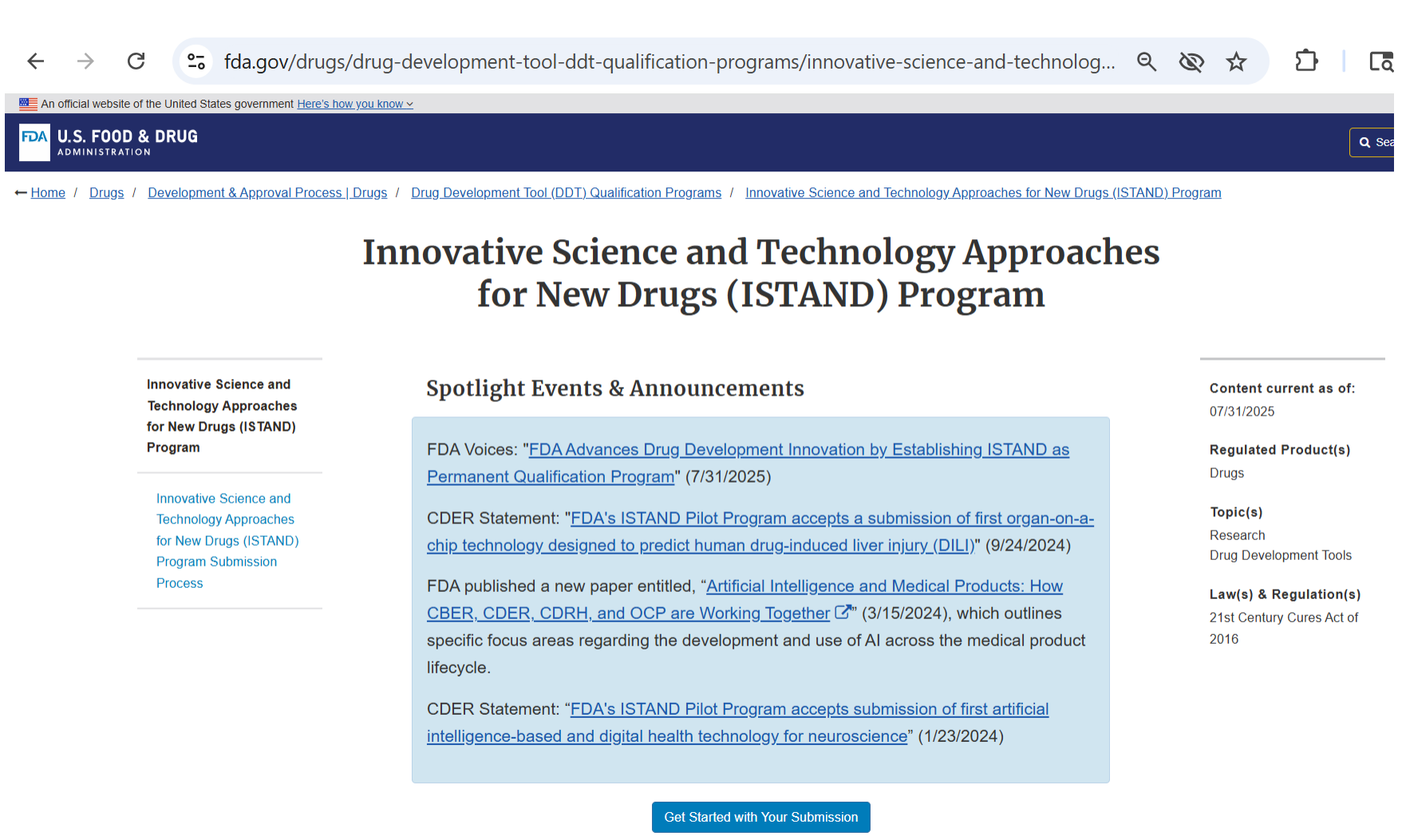
Director, Division of Biomedical Informatics Regulatory Tool Innovation & Biomarker Development
Office of Drug Evaluation Sciences, Office of New Drugs
CDER, FDA

DDT Qualification Programs



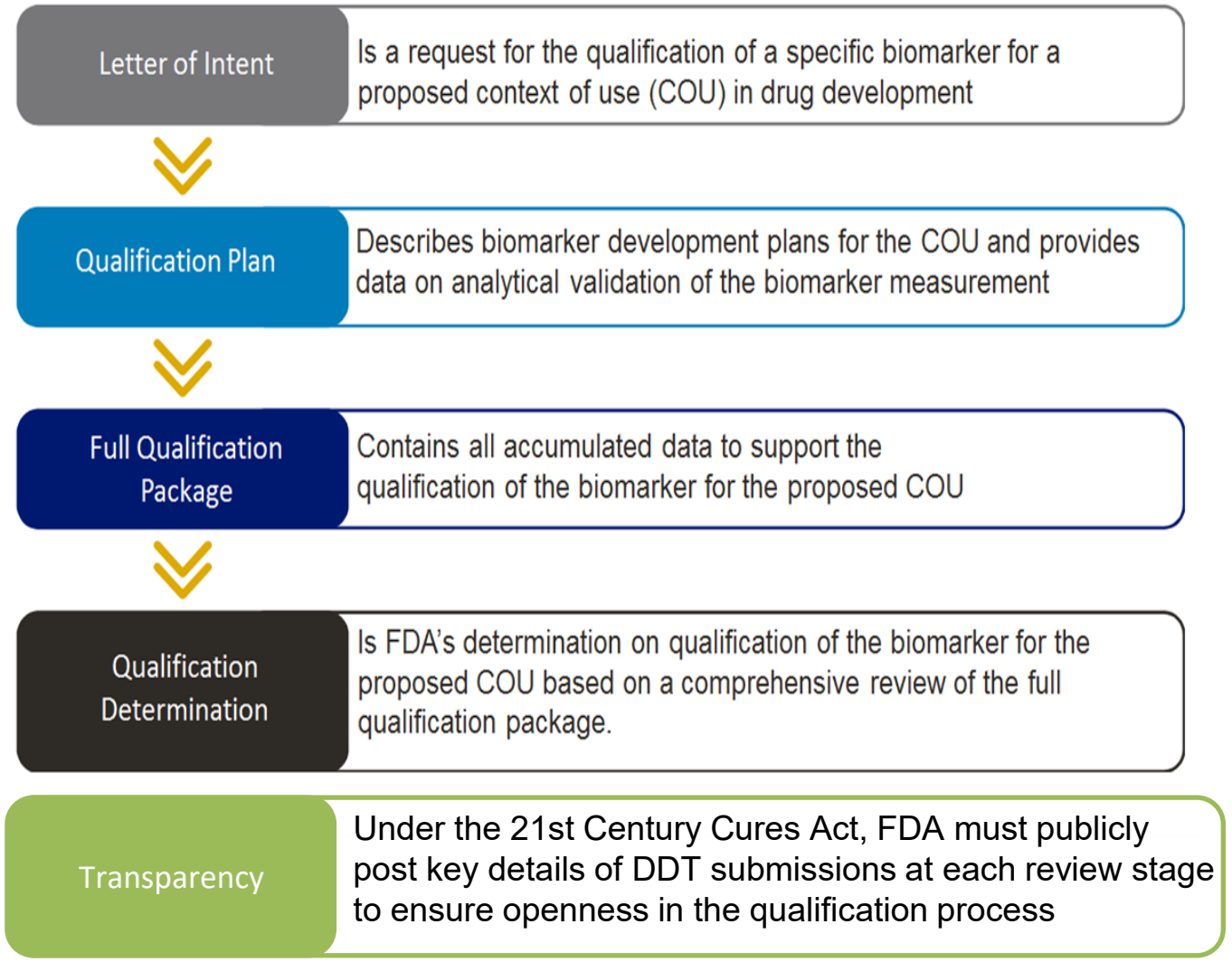
ISTAND Qualification Program

- Recognized that some tools do not fit into biomarker or COA categories, yet can meaningfully support drug development
- ISTAND transitioned to permanent qualification program in July 2025
  - Formalizes support for innovative, science-driven approaches
  - Platform to qualify DDTs that don’t fit as biomarkers or COAs
- Aligns with FDA Initiatives
    - Supports FDA's roadmap to reduce animal testing
    - Support DDTs that incorporate Artificial Intelligence and Machine Learning (AI & ML)
- Follows same process as BQP and COAQP



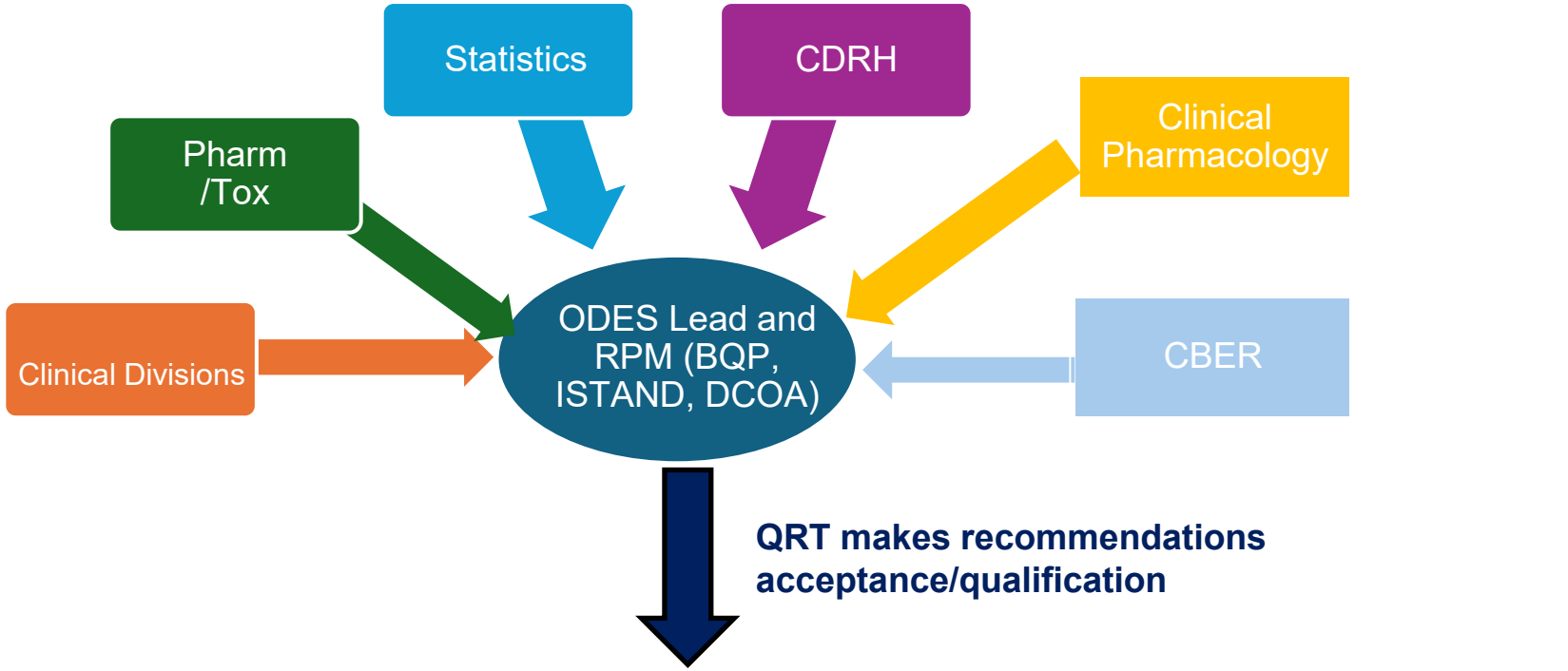
Innovative-science-and-technology-approaches-istand-program

Qualification Steps



Requesters may request pre-meetings for LOI, QP, and FQP submissions for early alignment, especially for complex submissions

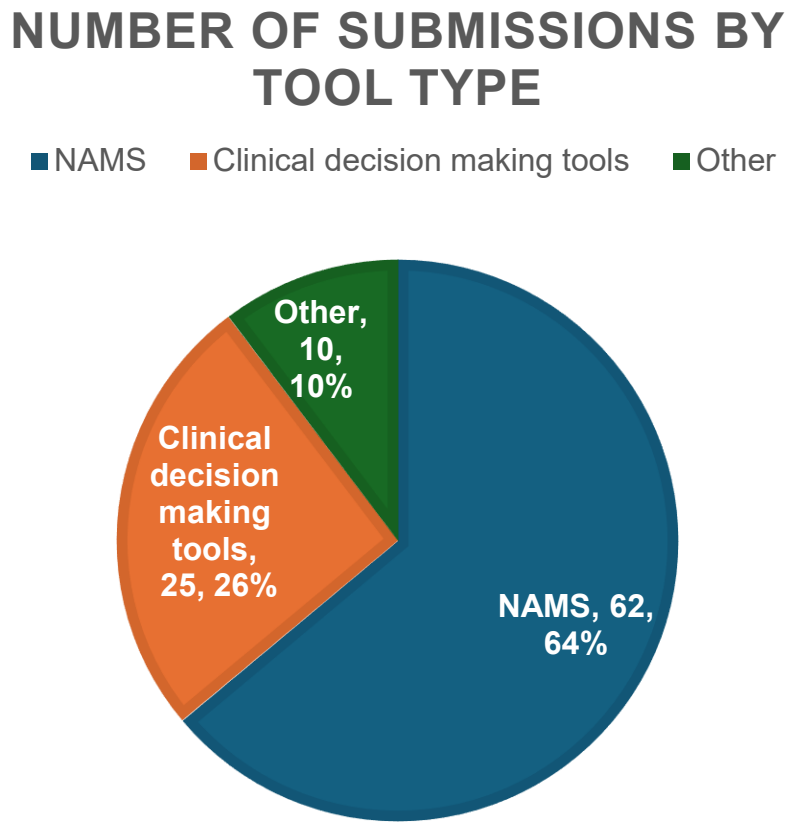
Qualification Review Team (QRT) and DDT Committee

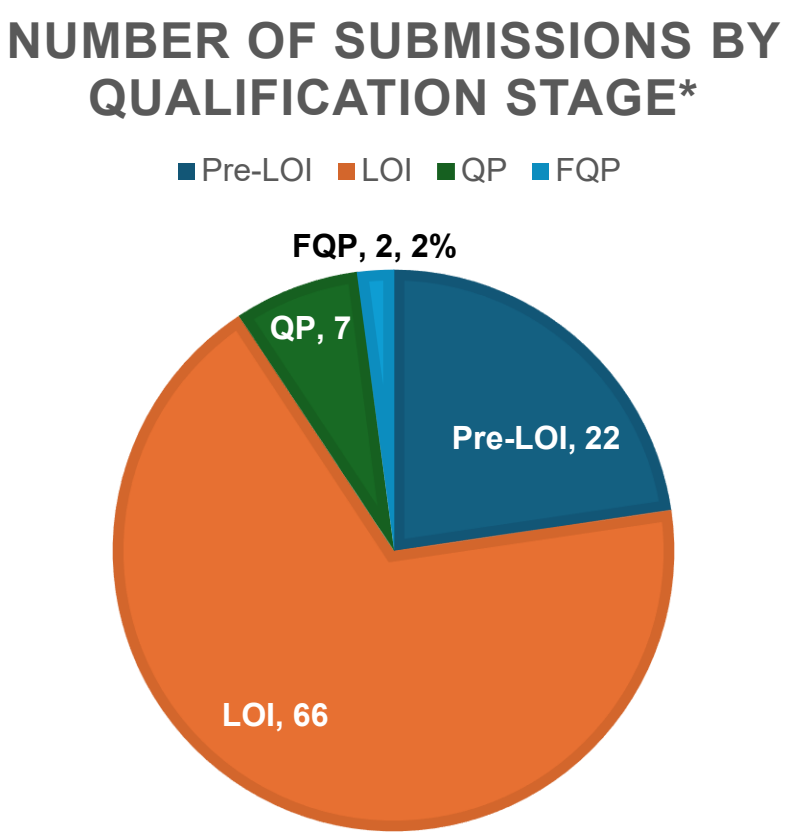


ISTAND REVIEW PROCESS

Review pauses if an information request (IR) is issued

ISTAND Program Progress



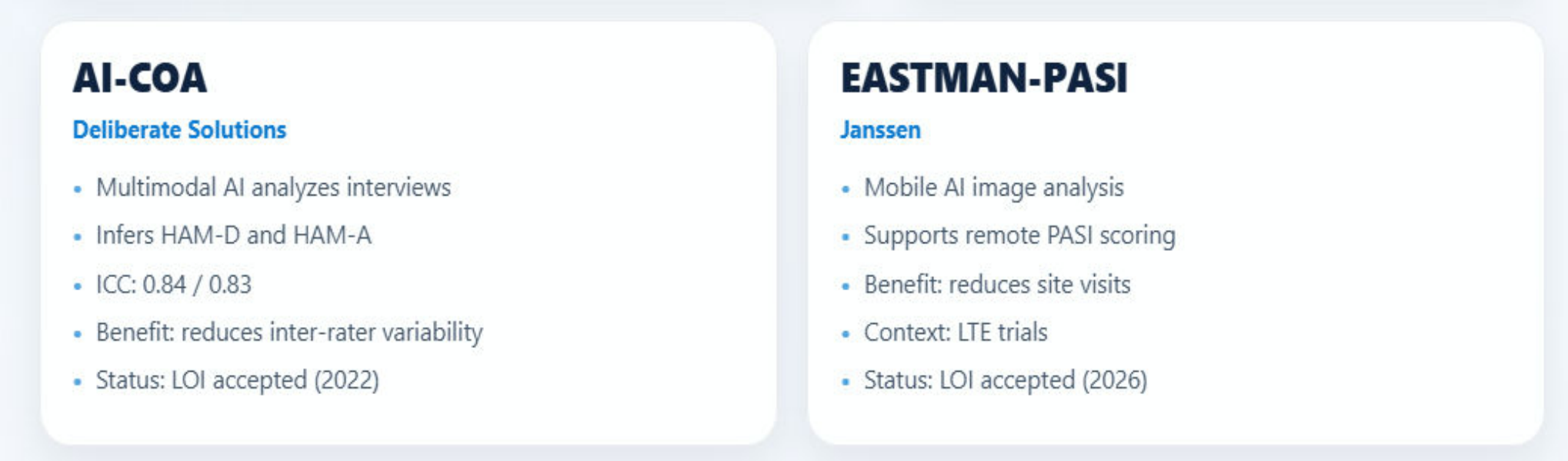


* As of 04/08/2026, ISTAND has accepted 18 LOI and 3 QP submissions.

ISTAND Snapshot: Observations from Disclosed Submissions

- Review Timelines Are Shortening
  - Average LOI decision time reduced by ~ >50% in 2025 compared to prior years
  - Reflects increased experience with Novel alternative methods (NAMs) and maturation of ISTAND program
- Early Alignment with Regulatory Expectations Is Important
  - Early engagement with ISTAND program can facilitate successful submissions
- Submissions Represent a Range of Organization Types
  - Accepted technologies include large pharmaceutical companies, biotechnology/NAM developers, and academic or non-profit institutions
- Context of Use Is a Primary Determinant of Acceptance
  - Acceptance is driven by scientific rationale, drug development need and regulatory relevance
  - Clear articulation of the regulatory decision supported is essential
- Current Technology Trends in ISTAND
  - In vitro NAMs with greater representation of micro physiologic systems (MPS) technologies
  - Technologies address regulatory-relevant safety and pharmacology endpoints
  - In silico, algorithmic and AI/ML approaches (usually clinical applications)

ISTAND -Technology-based COA tools (1 of 2)



- Recent ISTAND Acceptances Demonstrate Innovative Approaches to COA Measurement
- These examples use AI-enabled methods to improve measurement quality and trial feasibility
- Both tools build on established COAs and apply technology to make assessment more consistent or practical
- Not a brand-new endpoint, but rather a potentially better way to capture an existing one

ISTAND - Technology-based COA tools (2 of 2)

Key distinctions

- Replicate existing COAs, not new instruments
- Often use AI or machine learning
- Require strong analytical validation

Implication

- The technology is new, but the clinical concept remains familiar
- The regulatory question is whether the tool measures the established assessment credibly and usefully

ANALYTICAL VALIDATION

Performance and reliability

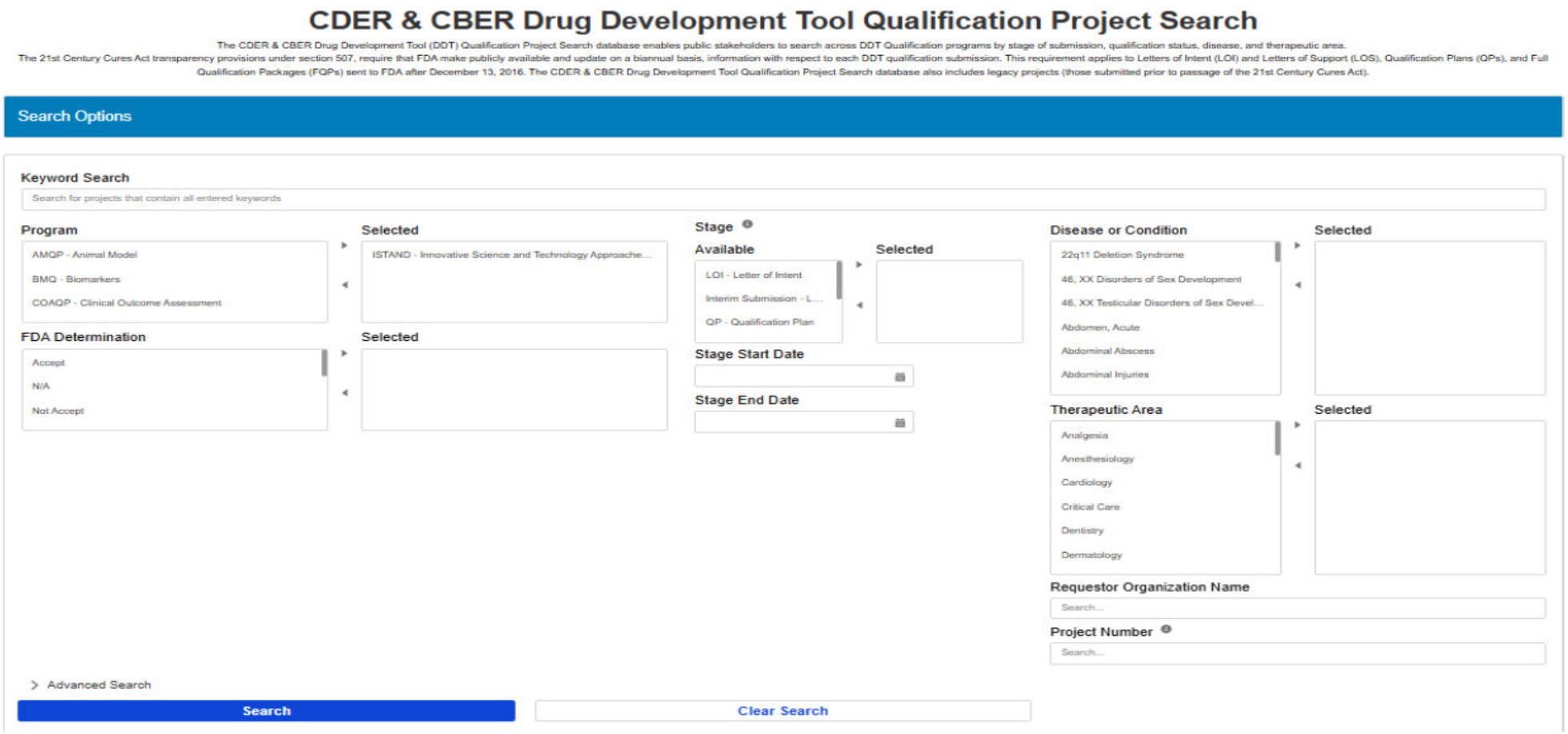
AI / ML

Credibility and transparency

CLINICAL UTILITY

Meaningful change and usability

DDT Transparency Database



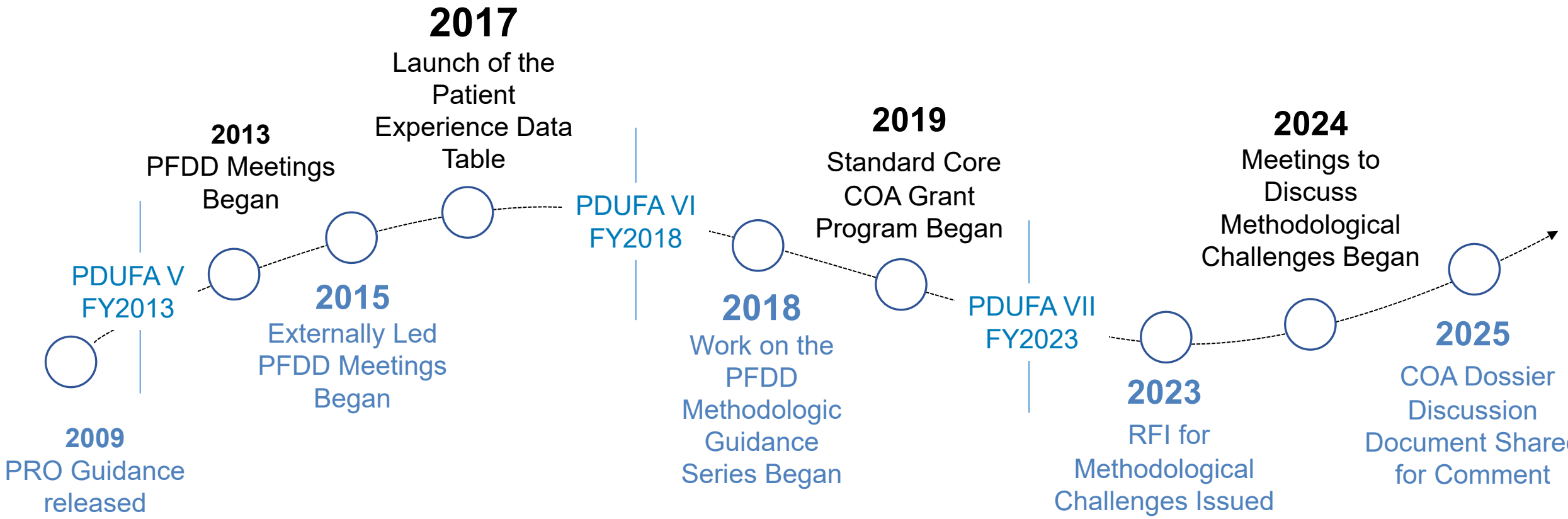
[DDT Transparency Database]

U.S. FOOD & DRUG ADMINISTRATION

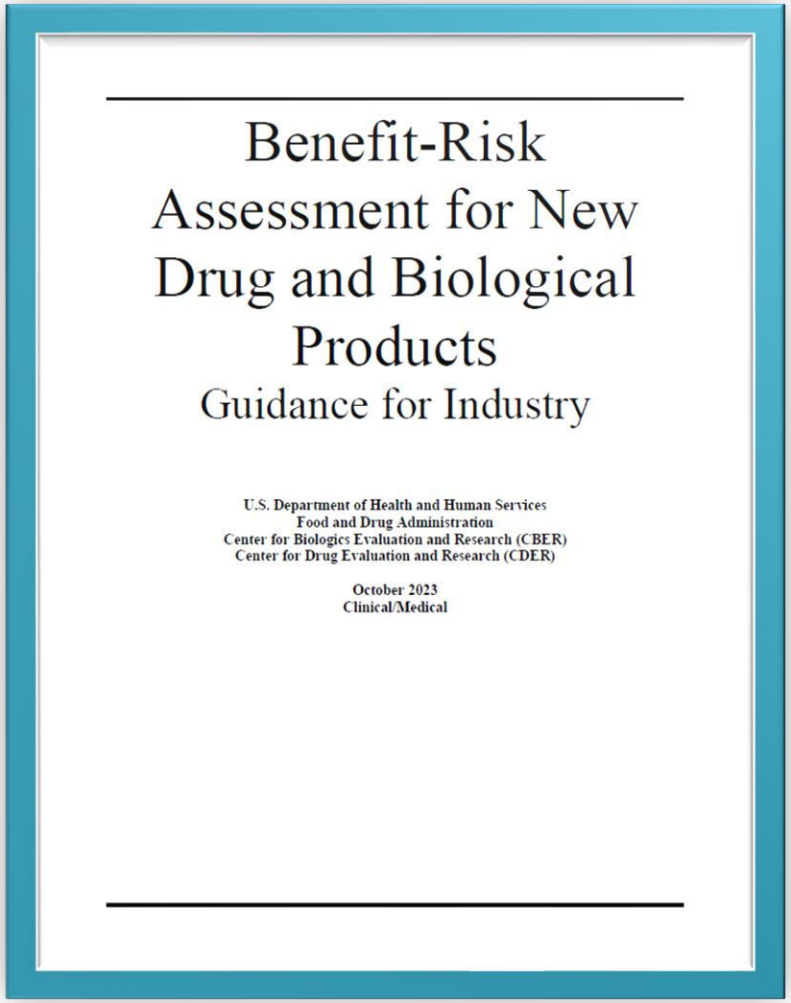
Patient-Focused Drug Development

April 2026

Patient Focused Drug Development



Benefit Risk



Benefit-Risk Assessment for New Drug and Biological Products

Guidance for Industry

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

October 2023
Clinical/Medical

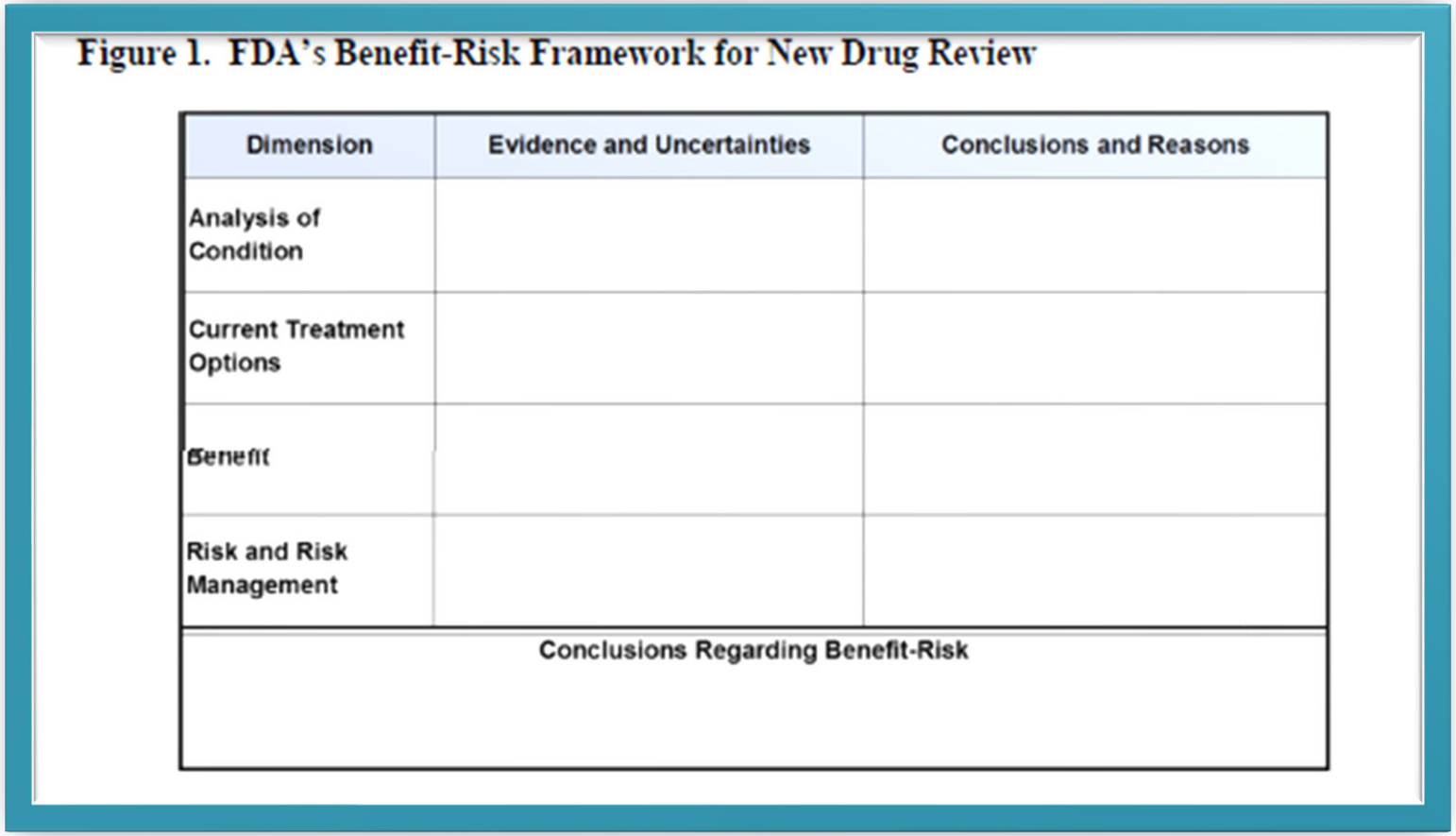


Figure 1. FDA's Benefit-Risk Framework for New Drug Review

Dimension	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition		
Current Treatment Options		
Benefit		
Risk and Risk Management		
Conclusions Regarding Benefit-Risk		

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/benefit-risk-assessment-new-drug-and-biological-products

Methodologic Guidance Documents

GUIDANCE 1
Collecting comprehensive and representative input

01

GUIDANCE 2
Methods to Identify What is Important to Patients

02

GUIDANCE 3
Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcome Assessments (COAs)

03

GUIDANCE 4
Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making

04

https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

Guidance Topics At A Glance

Collecting Comprehensive & Representative Input

- Whom do you get input from, and why?
- How do you collect the information?

Status:
Issued Draft Guidance in June 2018 and
Final Guidance in June 2020

PFDD Guidance 1 — 01

PFDD Guidance 2 — 02

PFDD Guidance 3 — 03

PFDD Guidance 4 — 04

Guidance Topics At A Glance

Methods to Identify What is Important to Patients

- What do you ask, and why?
- How do you ask non-leading questions that are well-understood by a wide range of patients and others?

Status

- Issued Draft Guidance in October 2019 and Final Guidance in February 2022

PFDD Guidance 1 — 01

PFDD Guidance 2 — 02

PFDD Guidance 3 — 03

PFDD Guidance 4 — 04

Guidance Topics At A Glance

Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments

- How do you decide what to measure in a clinical trial and select or develop fit-for-purpose clinical outcome assessments (COAs)?

Status

- Issued Draft Guidance in July 2022 and Final Guidance in October 2025

PFDD Guidance 1 — 01

PFDD Guidance 2 — 02

PFDD Guidance 3 — 03

PFDD Guidance 4 — 04

Guidance Topics At A Glance

Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making

- Once you have a COA measurement tool and a way to collect data using it, what is an appropriate clinical trial endpoint?

Status

- Issued Draft Guidance in April 2023

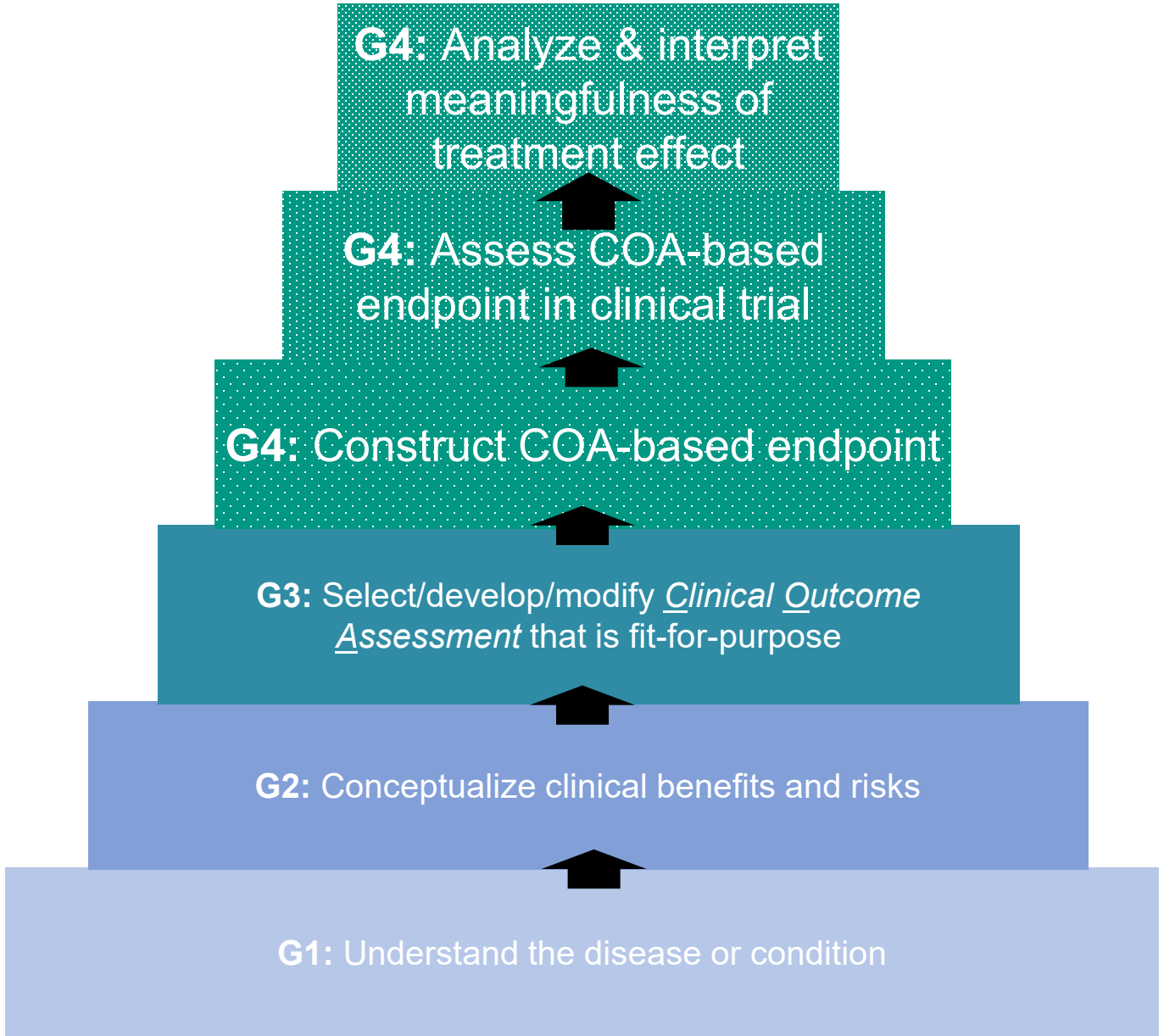
PFDD Guidance 1 — 01

PFDD Guidance 2 — 02

PFDD Guidance 3 — 03

PFDD Guidance 4 — 04

Using COAs in Clinical Research



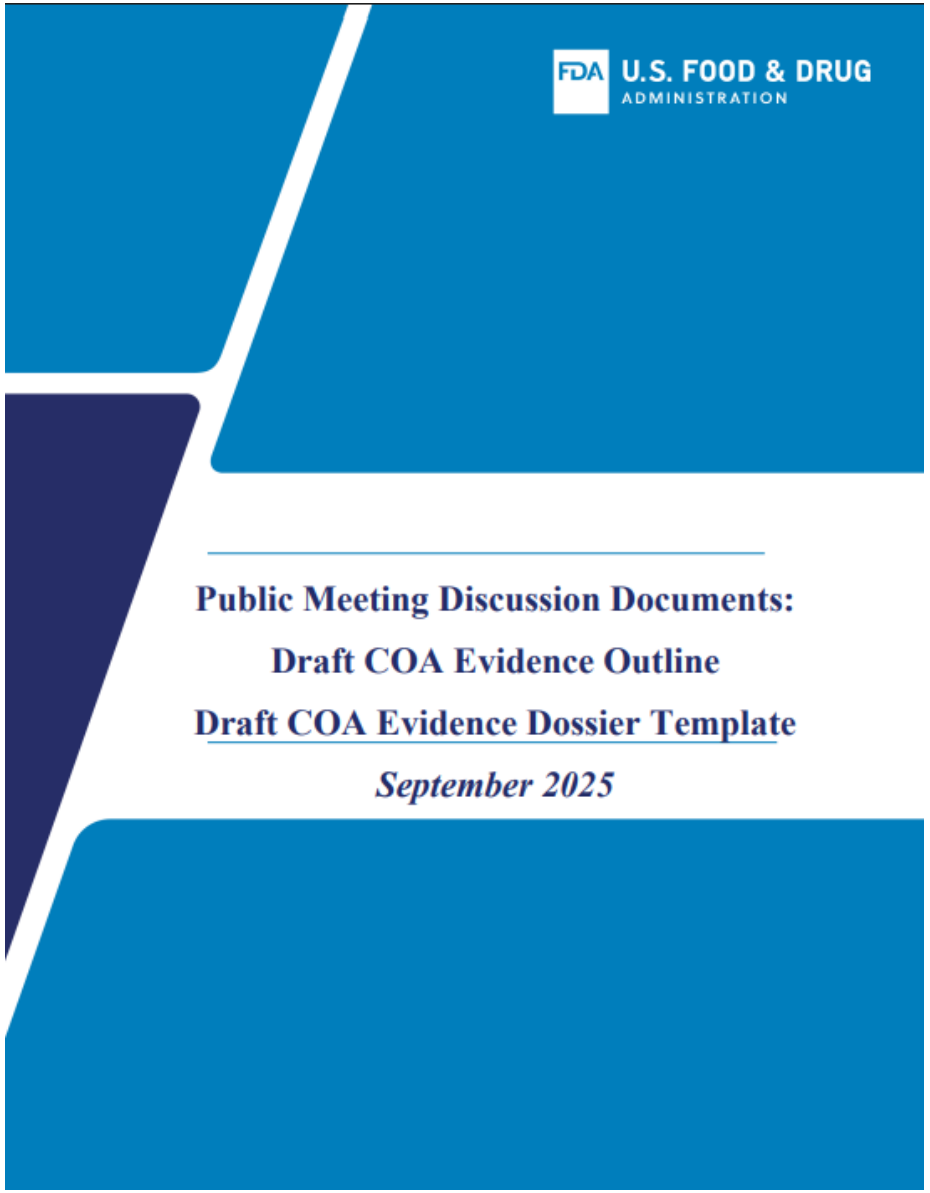
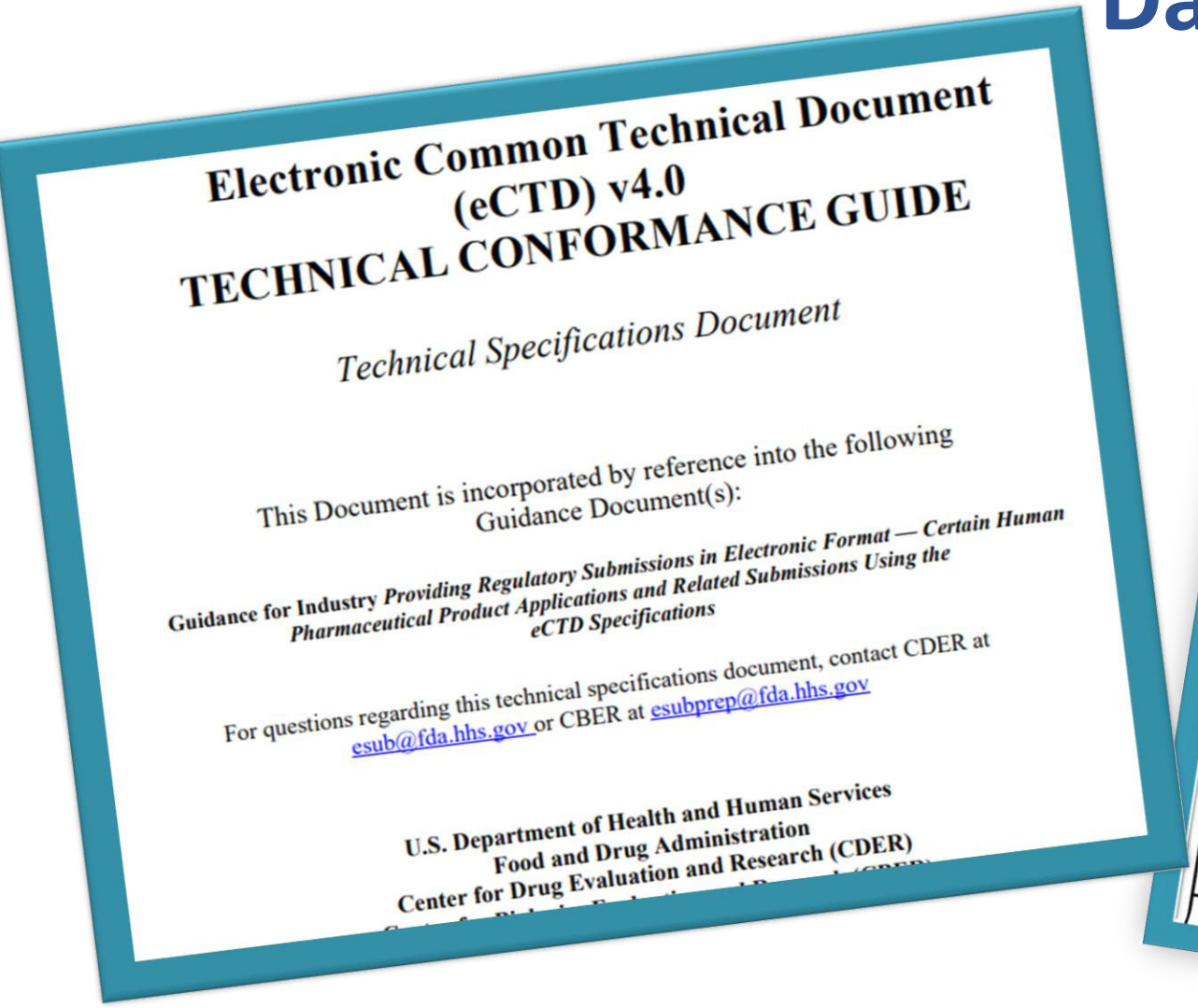


Table mapping the 2009 Appendix to the current draft documents

2009 PRO Appendix Section	*Draft 1* COA Dossier Section
I. Instrument	IV. Description and Justification for COA Appendix A
II. Targeted Claims	II. Context of Use Information
III. Endpoint Model	II. Context of Use Information
IV. Conceptual Framework	III. Meaningful Aspect of Health (MAH) IV. Description and Justification for COA (*if concept of interest (COI) is different from MAH*)
V. Content Validity	IV. Description and Justification for COA
VI. Assessment of Other Measurement Properties	IV. Description and Justification for COA V. Description and Interpretation of COA-based Endpoint(s) Appendices E, F, G, I
VII. Interpretation of Scores	V. Description and Interpretation of COA-based Endpoint(s)
VIII. Language Translation and Cultural Adaptation	IV. Description and Justification for COA
IX. Data Collection Method	IV. Description and Justification for COA Appendix B
X. Modifications	*Not a standalone section. Evidence should be provided in IV.C., as appropriate/as needed* Appendix A
XI. PRO-Specific Plans related to Clinical Trial and Analysis	II. Context of Use Information V. Description and Interpretation of COA-based Endpoint(s) Links and directions to specific portions of submission(s)
XII. Key References plus Appendix A: User Manual Appendix B: Item Tracking Matrix Appendix C: Transcripts	Appendices B, C, D, J

https://www.fda.gov/drugs/news-events-human-drugs/patient-focused-drug-development-workshop-2-discuss-methodologic-and-other-challenges-related

Submission of Patient Experience Data



Electronic Common Technical Document (eCTD) v4.0
TECHNICAL CONFORMANCE GUIDE

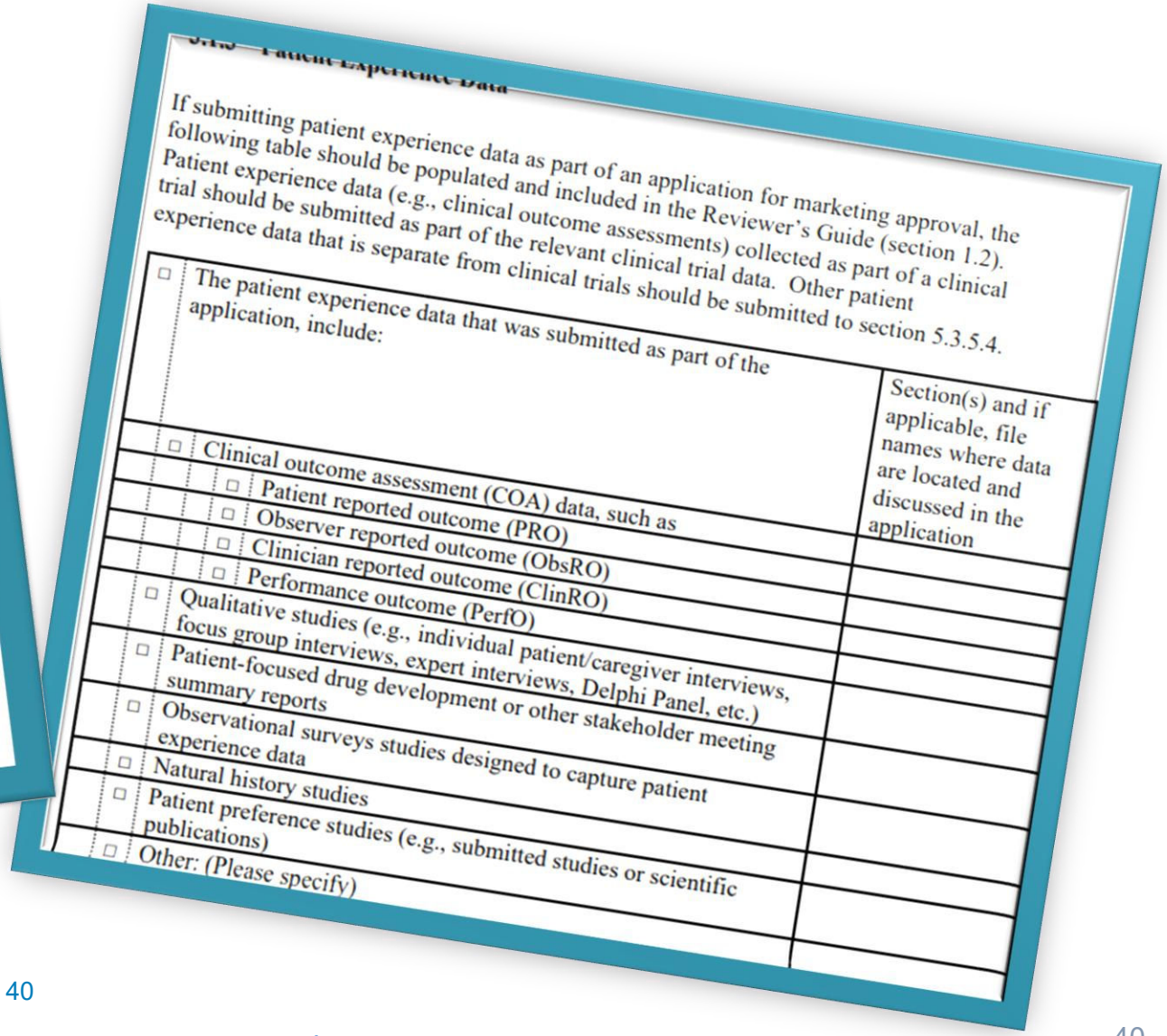
Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry ***Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications***

For questions regarding this technical specifications document, contact CDER at esub@fda.hhs.gov or CBER at esubprep@fda.hhs.gov

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



If submitting patient experience data as part of an application for marketing approval, the following table should be populated and included in the Reviewer's Guide (section 1.2). Patient experience data (e.g., clinical outcome assessments) collected as part of a clinical trial should be submitted as part of the relevant clinical trial data. Other patient experience data that is separate from clinical trials should be submitted to section 5.3.5.4.

☐ The patient experience data that was submitted as part of the application, include:	Section(s) and if applicable, file names where data are located and discussed in the application
☐ Clinical outcome assessment (COA) data, such as	
☐ Patient reported outcome (PRO)	
☐ Observer reported outcome (ObsRO)	
☐ Clinician reported outcome (ClinRO)	
☐ Performance outcome (PerfO)	
☐ Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	
☐ Patient-focused drug development or other stakeholder meeting summary reports	
☐ Observational surveys studies designed to capture patient experience data	
☐ Natural history studies	
☐ Patient preference studies (e.g., submitted studies or scientific publications)	
☐ Other: (Please specify)	

https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd

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Patient Focused Drug Development Meetings

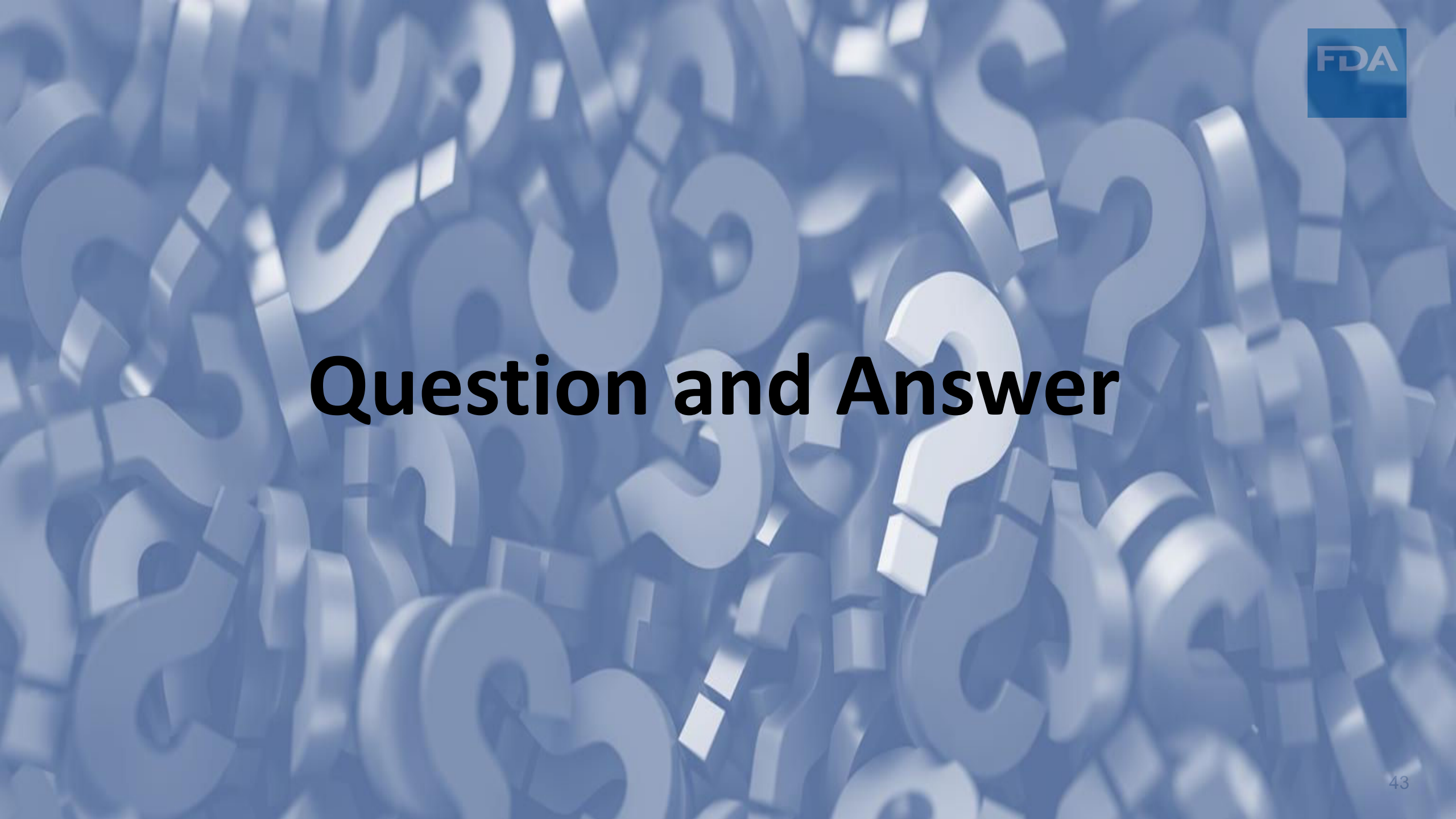
- Increasing discussion of how FDA is using patient experience data
- Internal notifications
- Website that highlights upcoming EL-PFDD meetings

Disease or Condition	Organization Submitting LOI	Organization Contact	Anticipated Meeting Date
Infertility and Advancing Therapeutic Solutions for In Vitro Fertilization (IVF)	Alliance for Fertility Preservation	Joyce Reinecke jreinecke@a4fp.org	March 26, 2026
Central Nervous System Disseminated Coccidiomycosis (Meningitis)	MYCARE Foundation	Rob Purdie rpurdie@fightfungus.org	April 14, 2026
Genetic Cardiomyopathies	Hypertrophic Cardiomyopathy Association	Hypertrophic Cardiomyopathy Association support@4hcm.org	April 23, 2026
Diamond-Blackfan Anemia Syndrome (DBAS)	The Styrke Foundation for Rare Disease and Treatment	Anne Yang ayang@styrke.org	May 1, 2026
Down Syndrome-Associated Alzheimer's Disease (DS-AD)	National Down Syndrome Society	National Down Syndrome Society pfdd@ndss.org	June 2, 2026
Maternal Alloimmunization and Hemolytic Disease of the Fetus and Newborn (HDFN)	Maternal Alloimmunization Foundation	Stephanie McCary stephaniemccary@alloimmunization.org	July 20, 2026
Spinal Cord Injury (SCI)	Spinal Cord Injury Perspectives Initiative	Gabriela Ocampo gocampo@nasciconsortium.org	September 29, 2026
Fanconi Anemia (FA)	Fanconi Cancer Foundation	Andrea Ronan communitysupport@fanconi.org	October 3, 2026

Other PFDD Activities

1. Training and Outreach
   - Internal
   - External
2. Identifying and Addressing Methodologic Issues
   - Public Meetings to discuss methodological issues in Patient Focused Drug Development

     September 2025 meeting
3. COA and PPI Development
   - Core Sets of Clinical Outcome Assessments Grant Program
   - Patient Preference Guidance
4. Report on how FDA uses Patient Experience Data in Regulatory Decision Making


Question and Answer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