U.S. FOOD & DRUG ADMINISTRATION

WELCOME

We'll begin the meeting promptly at 9:00am.

U.S. FOOD & DRUG ADMINISTRATION

Public Meeting on the Recommendations and Proposed Enhancements for PDUFA VII

Tuesday, September 28th, 2021

Note: A video recording and transcription of today's meeting will be published on the FDA website after this meeting.

Graham Thompson

Center for Drug Evaluation and Research, FDA

Meeting Moderator, Decision Support and Analysis Team

AGENDA

- Welcome and Introduction
- Opening Remarks
- PDUFA Background and Overview of Recommendations
- CBER Review Support
- Pre-Market Review
- Regulatory Decision Tools
- Post-Market Safety
- **Break**
- Chemistry, Manufacturing and Controls
- Digital Health and Informatics
- Finance and Hiring
- **Lunch**
- Public Stakeholder Perspectives
- Public Comment
- Closing

Janet Woodcock

FDA

Acting Commissioner

PDUFA
Background and Reauthorization Process

Andrew Kish

Center for Drug Evaluation and Research, FDA

FDA Lead Negotiator for PDUFA VII

Basic PDUFA Construct

- Congress directed FDA to establish a user fee program for the process for the review of human drug applications. Fee funds are added to non-fee appropriated funds and are intended to increase staffing and other resources to speed and enhance review process.
- User fees pay for services that directly benefit fee payers*
- Fee discussions with industry focus on desired enhancements in terms of specific aspects of activities in "process for the review of human drugs"
    - What new or enhanced process will the FDA want or industry seek to include in the next 5 years?
    - What is technically feasible?
    - What resources are required to implement and sustain these enhancements?
    - **No discussion of policy** (e.g., FDA does not discuss what its policy decisions will be in guidance)
- Fee discussions also include mechanics of user-fee program (e.g., how fees are collected, fee types, products covered by each fee)
- Medical product user fee programs must be reauthorized every 5-years. PDUFA is the oldest user fee program at FDA.

** OMB Circular A-25; direct benefit distinguishes user fees from tax*

PDUFA Performance commitments and fee funding have evolved since 1992

PDUFA | *1993-1997*
Added funds for pre-market review; reduced backlog and set predictable timelines (goals) for review action

PDUFA II (FDAMA) | *1998-2002*
Shortened review timelines, added review goals; added process and procedure goals; added some funding

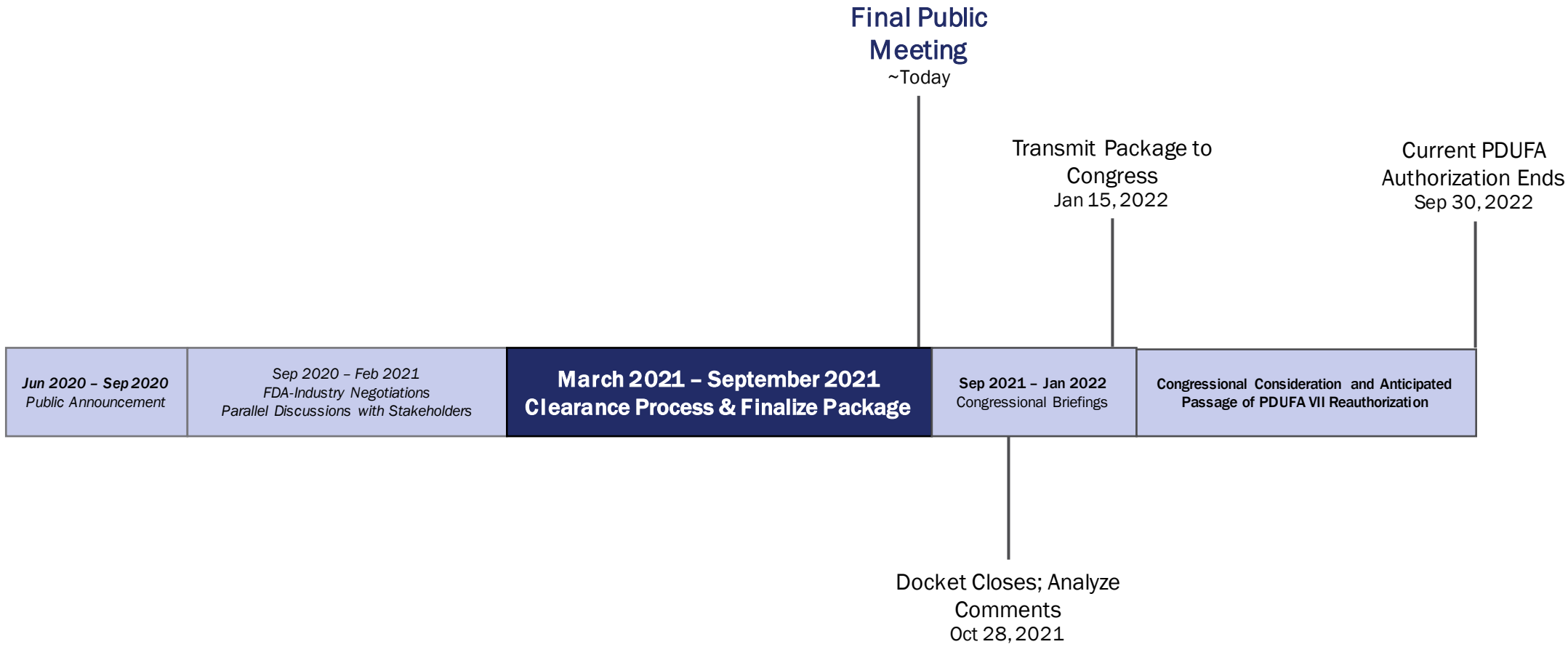
PDUFA III (BT Preparedness & Response Act) | *2003-2007*
Significantly added funding; increased interaction in first review cycle (GRMPs); allowed limited support for post-market safety

PDUFA IV (FDAAA) | *2008-2012*
Increased and stabilized base funding; enhanced pre-market review; modernized post-market safety system

PDUFA V (FDASIA) | *2013-2017*
Small increase to base funding; review enhancements increased communication with sponsors; strengthened regulatory science & post-market safety; set electronic data standards

PDUFA VI (FDARA) | *2018-2022*
Modernized the user fee structure; focused on HR and financial management improvement; created capacity planning capability; enhanced use of regulatory tools via benefit-risk, patient-focused drug development, complex innovative trial designs, model informed drug development; enhanced staffing for breakthrough therapy reviews; focused on communication with industry; explored RWE in regulatory decision-making

PDUFA VII Reauthorization Timeline



This public meeting is one of the last steps in the reauthorization process

PDUFA REAUTHORIZATION and REPORTING REQUIREMENTS.

(d) REAUTHORIZATION.—

(1) CONSULTATION.—In developing recommendations to present to the Congress with respect to the goals, and plans for meeting the goals, for the process for the review of human drug applications for the first 5 fiscal years after fiscal year 2017 and for the reauthorization of this part for such fiscal years, the Secretary shall consult with— (A) the Committee on Energy and Commerce of the House of Representatives; (B) the Committee on Health, Education, Labor, and Pensions of the Senate; (C) scientific and academic experts; (D) health care professionals; (E) representatives of patient and consumer advocacy groups; and (F) the regulated industry.

(2) PRIOR PUBLIC INPUT.—Prior to beginning negotiations with the regulated industry on the reauthorization of this part, the Secretary shall—

(A) publish a notice in the Federal Register requesting public input on the reauthorization; (B) hold a public meeting at which the public may present its views on the reauthorization, including specific suggestions for changes to the goals referred to in subsection (a); (C) provide a period of 30 days after the public meeting to obtain written comments from the public suggesting changes to this part; and (D) publish the comments on the Food and Drug Administration's Internet Website.

(3) PERIODIC CONSULTATION.—Not less frequently than once every month during negotiations with the regulated industry, the Secretary shall hold discussions with representatives of patient and consumer advocacy groups to continue discussions of their views on the reauthorization and their suggestions for changes to this part as expressed under paragraph (2).

(4) PUBLIC REVIEW OF RECOMMENDATIONS.—After negotiations with the regulated industry, the Secretary shall— (A) present the recommendations developed under paragraph (1) to the Congressional committees specified in such paragraph; (B) publish such recommendations in the Federal Register; (C) provide for a period of 30 days for the public to provide written comments on such recommendations; (D) hold a meeting at which the public may present its views on such recommendations; and (E) after consideration of such public views and comments, revise such recommendations as necessary.

(5) TRANSMITTAL OF RECOMMENDATIONS.—Not later than January 15, 2022, the Secretary shall transmit to the Congress the revised recommendations under paragraph (4), a summary of the views and comments received under such paragraph, and any changes made to the recommendations in response to such views and comments.

(6) MINUTES OF NEGOTIATION MEETINGS.—

(A) PUBLIC AVAILABILITY.—Before presenting the recommendations developed under paragraphs (1) through (5) to the Congress, the Secretary shall make publicly available, on the public Web site of the Food and Drug Administration, minutes of all negotiation meetings conducted under this subsection between the Food and Drug Administration and the regulated industry.

(B) CONTENT.—The minutes described under subparagraph (A) shall summarize any substantive proposal made by any party to the negotiations as well as significant controversies or differences of opinion during the negotiations and their resolution.

PDUFA
Overview of Recommendations

Areas of Proposed Enhancements in PDUFA VII

CBER Review Support | Enhancing CBER's capacity to guide development and review innovative products such as Cell and Gene Therapies

Pre-Market | Introducing new approaches to improve efficiency and expand communication in the human drugs review program

Regulatory Decision Tools | Continuing application of innovative methods and tools to enhance regulatory decision-making

Post-Market | Ensuring safe use of medicines through continued enhancements to our drug safety system

Chemistry, Manufacturing and Controls | Facilitating manufacturing readiness and use of innovative manufacturing technologies

Digital Health and Informatics | Investing in modern technology and bioinformatics to support enhanced and streamlined drug development and review

Finance | Enhancing financial management and transparency

Hiring and Retention | Focusing on the strategic hiring and retention of world-class technical and scientific staff

Center for Biologics Evaluation and Research (CBER) Review Support

Chris Joneckis

Center for Biologics Evaluation and Research, FDA

CBER Review Support Sub-group Lead Negotiator

Investing in Cell and Gene Therapy

- Significant increase in staff capacity and capabilities in CBER to support the review of cell and gene therapy products.
- Support for numerous public, stakeholder meetings and guidance on topics of interest including: a patient-focused drug development meeting to better understand patient perspectives on gene therapy studies and products; novel and expedited methods and approaches on cell and gene therapy product development; leveraging knowledge.
- Other PDUFA letter sections also support CBER and Cell and Gene Therapy.

Including Allergenics in PDUFA

- Incorporation of new allergenic extract products into the PDUFA program and providing capacity to review those products.
- Allergenic extract products licensed after October 1, 2022, would generally be included in user fees.
- Allergenic extract products licensed before October 1, 2022, and standardized allergenic extract products submitted pursuant to a notification to the applicant from the Secretary of Health and Human Services regarding the existence of a potency test that measures the allergenic activity of an allergenic extract product licensed by the applicant before October 1, 2022, would remain excluded from PDUFA.
- All performance goals, procedures, and commitments apply to the allergenic products included in the PDUFA program under PDUFA VII.

Industry Perspective

Cartier Esham

Biotechnology Innovation Organization (BIO)

Industry Co-Lead Negotiator

Lucy Vereshchagina

Pharmaceutical Research and Manufacturers of America (PhRMA)

Industry Co-Lead Negotiator

Pre-Market Review

Peter Stein

Center for Drug Evaluation and Research, FDA

Pre-market Review Sub-group Lead Negotiator

Establishing performance goals and timelines for post-marketing requirements (PMRs)

- New process, timelines, and performance goals for establishing PMRs during the pre-approval process to ensure timely review and determination of key design features.
- A new process for sponsors to request review of existing PMRs.
- FDA will update relevant MAPPs/SOPs/guidances for the new processes.

Piloting earlier review of some efficacy supplements to expedite patient access

- A new pilot program, the Split Real-Time Application Review (STAR), for certain efficacy supplements that seeks to expedite patient access to novel uses for existing therapies to treat serious conditions with unmet medical needs.
- Accepted STAR applications will be submitted in a "split" fashion, specifically in two parts (with the components submitted approximately 2 months apart), with the goal for FDA to act at least 1 month before the PDUFA goal date.
- Also includes a public-facing webpage, public workshop, and assessment.

Enhancing meeting management

- Two new meeting types to expand communication and feedback during the drug development process:
  - INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs (INTERACT) meeting is intended to facilitate IND-enabling efforts where a sponsor is facing a novel, challenging issue that might otherwise delay progress of the product towards entry into the clinic in the absence of this early FDA input.
  - The new Type D meeting allows for quicker discussion on a narrow set of issues (no more than 2 focused topics) between FDA and a sponsor, such as a follow-up question that raises a new issue after a formal meeting.
- Introduces a new follow-up opportunity sponsors to submit clarifying questions after meetings or a WRO to ensure sponsor's understanding of FDA feedback. This applies to all meeting types.
- Includes a public workshop, training, and updated guidance on best practices in meeting management and communication during between sponsors and FDA during drug development.

Building on the success of the rare disease programs with new pilot

- Well-developed efficacy endpoints, especially those that could apply to other rare diseases with similar manifestations, drive the general advancement of rare disease drug development.
- A new pilot program to advance rare disease drug development by providing a mechanism for sponsor discussions with FDA throughout the efficacy endpoint development process.
- Includes multiple public workshops to discuss topics relevant to endpoint development for rare diseases.
- To promote innovation and evolving science, novel endpoints developed through the pilot program may be presented by FDA, such as in guidance documents, on a public-facing website, or at public workshops as case studies, including prior to FDA's approval for the drug studied in the trial.

Improving predictability in human factors (HFs) and use-related risk analyses (URRAs) reviews

- New procedures and timelines for use-related risk analysis and human factor validation study protocols to advance the development of drug-device and biologic-device combination products.
- Includes guidance on considerations related to combination products.

Investing in improving quality and acceptability of real-world evidence (RWE)

- A pilot program that seeks to improve the quality and acceptability of real-world evidence (RWE) based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements.
- Includes annual reporting on aggregated anonymized information describing pilot submissions.
- A public workshop or meeting to discuss RWE case studies.
- Includes updates to existing RWE-related guidances or new draft guidance, as appropriate, to reflect experience gained in the pilot program.

Industry Perspective

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Industry Co-Lead Negotiator

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Pharmaceutical Research and Manufacturers of America (PhRMA)

Industry Co-Lead Negotiator

BREAK

We'll return promptly at 10:25am (ET).

Note: A video recording and transcription of today's meeting will be published on the FDA website after this meeting.

Regulatory Decision Tools

Theresa Mullin

Center for Drug Evaluation and Research, FDA

Regulatory Decision Tools Sub-group Lead Negotiator

Advancing the patient's voice in drug development and decision-making

Opportunity

- Patient input collected with methodologically-sound clinical outcome assessments (COAs) and endpoints can provide a direct source of evidence regarding the benefits and risks of a drug.
- Patient preference information can inform regulatory decision-making and can advance design/conduct of patient preference studies in high impact areas.
- Studies with quality problems will be minimally useful in regulatory decision making, yielding minimal value for the investment of time and effort to collect this patient experience data.

Proposed Enhancement

- Expanded staff training and outreach to stakeholders with emphasis on Patient-Focused Drug Development methods and tools-related guidance and practice; gathering public input and holding workshops on methodological issues and other issues of greatest interest to public stakeholders.
- Continued work on developing a virtual catalog of standard core COAs seeking support of non-user fee funds.
- Issuing a guidance on use and submission of patient preference information.

Building on the success of the model-informed drug development (MIDD) pilot

Opportunity

- MIDD can improve efficiency in drug development and address residual regulatory uncertainty; the high level of FDA engagement in these meetings have been key.
- PDUFA VI pilot program has been successful; will be managed within the current scope and level of "paired meeting" consultations to remain sustainable.

Proposed Enhancement

- Advance the pilot into a program to further advance and integrate the development and application of exposure-based, biological, and statistical models in drug development and regulatory review.

Building on the success of the complex innovative trial designs (CID) pilot

Opportunity

- PDUFA VI CID pilot submissions have spanned a wide range of indications and each proposal raises novel questions and involves computationally intensive analytic techniques and simulations, requiring statistical programming time and expertise to review. With iterative nature of CID simulation and resource demands, sponsors have requested additional meetings and flexibility in timing between meetings.
- Innovative designs are also becoming more common in exploratory and early phase trials; there is increasing interest and use of Bayesian and other novel designs.

Proposed Enhancement

- Advance the pilot into a program with the goal to facilitate the advancement and use of complex adaptive, Bayesian, and other novel clinical trial designs.
- Include a public workshop to discuss aspects of complex adaptive, Bayesian, and other novel trial designs, and guidance on use of Bayesian methodology in clinical trials.

Industry Perspective

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Pharmaceutical Research and Manufacturers of America (PhRMA)

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Post-market Safety

Terry Toigo

Center for Drug Evaluation and Research, FDA

Post-market Safety Sub-group Lead Negotiator

Modernizing and improving REMS Assessments

- Add new REMS review performance goals for review of methodological approaches and study protocols for REMS assessments.
- Update relevant guidances to incorporate REMS assessment planning into the design of REMS.
- Update existing policies and procedures for reviewing methodological approaches and study protocols used to assess a REMS program.
- Develop draft guidance regarding the format and content of a REMS assessment report, including the type of data that can support elimination of a REMS.
- Issue new or update existing policies and procedures to determine if modifications to the REMS or revisions to the REMS assessment plan are needed.

Optimizing the Sentinel Initiative

1. Continued support for the Sentinel Initiative maintenance, training, and transparency.
    - Maintain the quality and quantity of data available through the Sentinel Initiative (Sentinel and BEST) and processes and tools for determining when and how those data are utilized.
    - Support comprehensive training of review staff on the use of Sentinel.
    - Communicate with sponsors and the public regarding general methodologies for Sentinel queries and post study results, study parameters, and analysis code online.
        - Report on the use of Sentinel for regulatory purposes, e.g., in the contexts of labeling changes, PMRs, or PMCs.
        - Report on spending for the Sentinel Initiative in important categories (e.g. data infrastructure, analytical capabilities).

Optimizing the Sentinel Initiative

2. Support for the development of a consistent approach for assessing the outcomes of pregnancies in women exposed to drugs and biological products:
   - Develop a framework describing how data from different types of post-market pregnancy safety studies might optimally be used.
   - Hold a public workshop on post-market safety studies in pregnant women to facilitate determination of the ideal post-market study design(s).
   - Conduct 5 demonstration projects to address knowledge gaps about performance characteristics of different study designs.
   - Develop a guidance or MAPP/SOPP as appropriate to implement a standardized process for determining necessity and type of pregnancy postmarketing studies including PMRs.

Optimizing the Sentinel Initiative

3. Support for development of new methods to support causal inference for product safety questions and advance our understanding of how RWE may be used for studying effectiveness through the use of negative controls
    - Hold a public workshop on use of negative controls for assessing the validity of non-interventional studies of treatment and the proposed Sentinel Initiative projects.
    - Conduct two methods development projects.
    - Publish a report on the results of the development projects.

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Chemistry, Manufacturing, and Controls

Carol Rehkopf

Center for Biologics Evaluation and Research, FDA

Chemistry, Manufacturing, and Controls Sub-group Negotiator

Enhancing communication during review to promote a more efficient and effective process

- More structured Chemistry, Manufacturing, and Controls (CMC) information requests (i.e. Four-Part Harmony), mid-cycle and late-cycle communications, with associated updates to training and FDA procedures.
- Third-party assessment on sponsor and FDA current communication practices through product quality information requests.
- Goal to notify sponsors at least 60 days in advance of BLA Pre-license Inspections and NDA Pre-approval Inspections and no later than mid-cycle when facility inspections for certain applications, not including supplements, need to be inspected during manufacturing. FDA reserves the right to conduct inspections at any time during the review cycle, whether or not it has been communicated to the facility the intent to inspect.

Considering alternative tools to assess manufacturing facilities

- Guidance on FDA's thinking on the use of alternative tools to assess manufacturing facilities named in pending applications beyond COVID-19 pandemic.
- Examples of alternative tools include requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, requesting records and other information directly from facilities and other inspected entities, and, as appropriate, utilizing new or existing technology platforms to assess manufacturing facilities.
- The guidance will incorporate best practices, including those in existing published documents, from the use of such tools during the COVID-19 pandemic.

Facilitating CMC readiness for products with accelerated clinical development

- A new pilot program, CMC Development and Readiness Pilot (CDRP), to facilitate the expedited CMC development of products under an IND application based upon the anticipated clinical benefit of earlier patient access to the products. The goal of the Pilot will be to facilitate CMC readiness for CBER- and CDER-regulated products with accelerated clinical development timelines.
- Includes a new MAPP, a public workshop, and a strategy document that will outline FDA's plans, including proposed timeframes to develop or revise appropriate procedures and other documents.

Advancing utilization and implementation of innovative manufacturing

- A public workshop on the utilization of innovative manufacturing technologies to discuss best practices, case studies, barriers to adoption, and regulatory submission strategies, among other topics.
- After the public workshop, FDA will issue a strategy document outlining specific actions FDA will take over the course of PDUFA VII to facilitate the utilization of innovative manufacturing technologies.

Industry Perspective

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Digital Health and Informatics

Mary Ann Slack

Center for Drug Evaluation and Research, FDA

Digital Health and Informatics Sub-group Lead Negotiator

Expanding capacity in digital health technologies (DHTs)

- Recognizing the potential for DHTs to provide scientific and practical advantages in supporting the assessment of patients by generating information outside of the traditional clinic visit, the agreement increases FDA's capacity and expertise to advise the biopharmaceutical industry in the development and implementation of DHTs and to evaluate DHT outputs including the impact on regulatory initiatives (or regulatory science).
- In addition to expanding capacity in this area, FDA will hold a series of public meetings, conduct issue-focused demonstration projects, and issue new or updated guidances.
- Creation of DHT framework document to guide the use of DHT-derived data in regulatory decision-making, and a newly established committee to support implementation.

Modernizing FDA's data information technology (IT)

- Activities to further enhance transparency of FDA IT activities and modernization plans with regular meetings between FDA and industry IT leadership and maintaining catalogs, standards, and plan updates published to the website. Establishes a Data and Technology Modernization Strategy that reflects the FDA's Technology and Data Modernization Action Plan.
- Resources to accelerate CBER's data and technology modernization to facilitate an efficient review process.
- Resources to monitor and modernize the ESG.
- Demonstration projects to explore how cloud and cloud-based technologies could promote innovation in the drug development and regulatory review process.
- Resources to develop additional expertise, staff capacity, and IT resources to manage the substantial increase in the volume and diversity of bioinformatics and computation biology information and data in regulatory submissions.

Industry Perspective

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Finance

Josh Barton

Center for Drug Evaluation and Research, FDA

Finance Sub-group Lead Negotiator

Maturing the capacity planning function

- Publish an implementation plan outlining continual improvement of the Capacity Planning Adjustment (CPA) and integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes.
- Annual updates on progress made on the activities outlined in the implementation plan and documentation of how CPA funds are used in the annual financial report.
- 3rd party evaluation of the resource capacity planning capability.

Continuing transparency on financial plan and commitments

- Continues the PDUFA VI commitments of publishing a 5-year financial plan and holding a public meeting to discuss the plan and other financial commitments every fiscal year.
- New commitments to share information in 5-year financial plan on the following:
  - Personnel compensation and benefits (PC&B) costs that exceed the funds provided by the PC&B portion of the inflation adjustment. This is related to the new strategic hiring and retention adjustment.
  - FDA's plan for managing costs related to personnel (strategic hiring and retention adjustment) beyond PDUFA VII.

Modifications to fee adjustments

- Modifications to the capacity planning adjustment to clarify the scope of the inputs used in the methodology.
- A new strategic hiring and retention adjustment to provide funding to cover costs for retaining and hiring highly qualified scientific and technical staff for the PDUFA program.
- Enhancements to the operating reserve adjustment to manage financial risks to the program by establishing a minimum amount of available operating reserves to be maintained each year. This minimum amount will start at an amount equivalent to 8 weeks of operations and increase to 10 weeks of operations by FY 2025.

Hiring

Continuing transparency on hiring progress

- Continued quarterly reporting on progress toward meeting annual hiring goals in PDUFA VII on the FDA website.
- A third-party assessment of hiring and retention practices.

Industry Perspective

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LUNCH

We'll return promptly at 12:45pm (ET).

Note: A video recording and transcription of today's meeting will be published on the FDA website after this meeting.

Public Stakeholder Perspectives

Public Meeting on the Recommendations for Prescription Drug User Fee Act (PDUFA) Reauthorization: Commitment Letter Draft Review

September 28, 2021 (via webinar)

Michael T. Abrams, M.P.H., Ph.D.
Public Citizen's Health Research Group

(I have no financial conflicts of interests)

Annual performance measures

Quota and timeline based, focused mostly on pleasing industry with fast reviews

Example: % of NDAs/BLAs acted upon within 10 months of the completed application

❖**Public health indicators should be added and emphasized**

Examples:

1. % of NDAs/BLAs which were rejected because there was a lack of evidence establishing safety or efficacy
2. % of previously approved NDAs/BLAs that were the subject of subsequent FDA warnings or withdrawals during the first several years post approval
3. % of NDAs/BLAs approved with at least two phase 3 randomized, controlled trials demonstrating consistent and robust evidence of safety and efficacy and favorable benefit-risk profiles.
4. % of NDAs/BLAs subject to mandated post-marketing studies where those obligations were fulfilled and confirmed safety and efficacy
5. % of NDAs/BLAs for which the FDA decision regarding approval was concordant with advisory committee recommendations

Formally survey content experts…

- FDA clinical, statistical and other review staff; advisory committee members

❖ **Use the data to derive the following types of performance measures**

1. % of reviewers who had concerns about FDA NDA/BLA decisions related to safety or efficacy
2. % of reviewers who felt they were free from direct or indirect pressure from the regulated industry when reviewing NDAs/BLAs
3. % of reviewers or committee members who felt they had ample time and resources to review the NDAs/BLAs they were assigned
4. % of reviewers or committee members who felt their concerns about NDAs/BLAs were properly ascertained and respected by FDA decision-makers

Recast commitment language

❖**Emphasize FDA's regulatory role and responsibilities**

Example

Commitment letter states: "The goal of the Program is to promote the efficiency and effectiveness of the first cycle review process and minimize the number of review cycles necessary for approval, ensuring that patients have timely access to safe, effective, and high-quality new drugs and biologics."

Such language should be modified by adding that a primary Program goal is to protect public health by minimizing the probability that unsafe or ineffective drugs or biologics enter the market.

Further modifications to the language should be made stating that ensuring the quality of the NDA/BLA is ultimately the responsibility of the sponsor, not of the FDA.

Reaffirm the commitment to substantial evidence

The draft commitment letter encourages fast approval at the expense of careful approval

For example:

- Under a section "K. Enhancing regulatory science and expediting drug development" it is suggested that the Agency is responsible for:

  "…ensuring the sustained success of the breakthrough therapy program, continuing early consultations between FDA and sponsors on the use of new surrogate endpoints as the primary basis for product approval…and exploring the use of real-world evidence for use in regulatory decision-making."

❖ **Such pronouncements and goals should be clarified by explicit language which:**

1. Limits surrogate endpoint use to those that have been scientifically validated and deemed by the majority of the medical community to be predictive of clinically meaningful outcomes.
2. States that RWE should not substitute for well-designed, randomized controlled trials (RCTs).
3. Affirms at least two phase 3 RCTs as the usual standard for demonstrating substantial evidence of effectiveness.

Regulatory capture of the Agency

The draft commitment letter states: "FDA's philosophy is that timely interactive communication with sponsors during drug development is a core Agency activity to help achieve the Agency's mission to facilitate the conduct of efficient and effective drug development programs."

- **Because such interactive communications established under PDUFA have resulted in collaborations between the Agency and sponsors that have compromised the integrity of NDA/BLA reviews — evident during the review for aducanumab — the commitment letter should be modified to include provisions that:**

1. Characterize the FDA's primary role as being a gate-keeper, watchdog, and judge of industry products (to assert and codify its objectivity and independence)

2. Establish procedures that separate (with a firewall between) staff involved in pre-NDA/BLA-submission interactions with sponsors from staff who formally review those applications for regulatory decision-making purposes

3. Require FDA staff training on how to minimize the risk of regulatory capture of the Agency by sponsors

Using the commitment letter the FDA should also aim to…

1. Request an increase in their discretionary drug/biologic regulatory budget
2. Eliminate closed meetings with industry during reauthorization negotiations
3. Implement the National Academies' public health framework for regulatory oversight of opioids
4. Maintain in-person manufacturing facility inspections as the standard
5. Commission objective studies that quantify the avoided or realized harms resulting from NDA/BLA approval decisions
6. Minimize reliance on REMS mandates in lieu of premarket resolution of safety concerns

Thank you. For more information:

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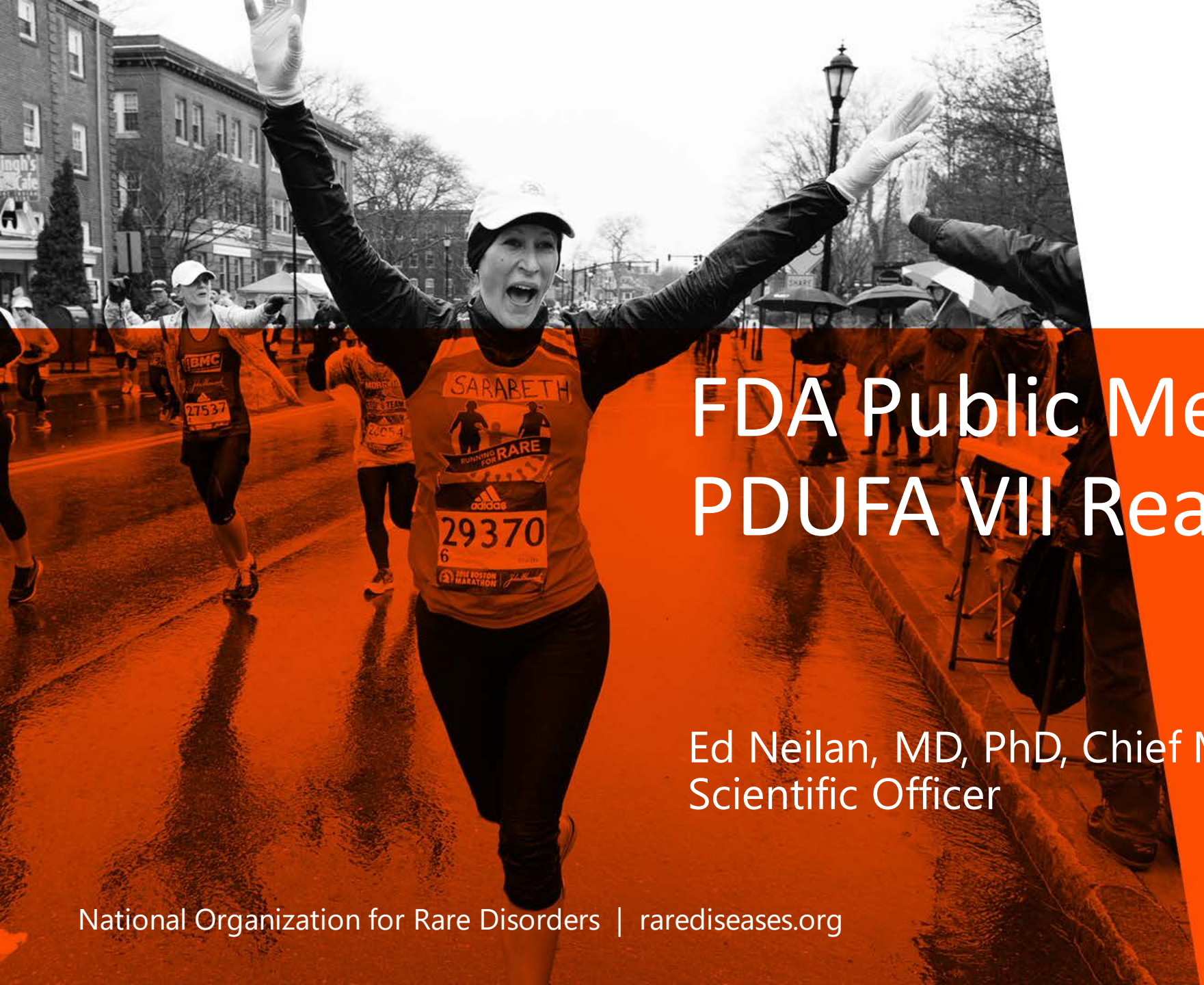
EVERYLIFE FOUNDATION FOR RARE DISEASES



NORD®
National Organization for Rare Disorders

FDA Public Meeting on PDUFA VII Reauthorization

Ed Neilan, MD, PhD, Chief Medical and Scientific Officer

NORD, an independent nonprofit, is leading the fight to improve the lives of **rare disease patients and families.**

We do this by supporting patients and organizations, accelerating research, providing education, disseminating information and driving public policy.

Advancing Development of Drugs for Rare Diseases

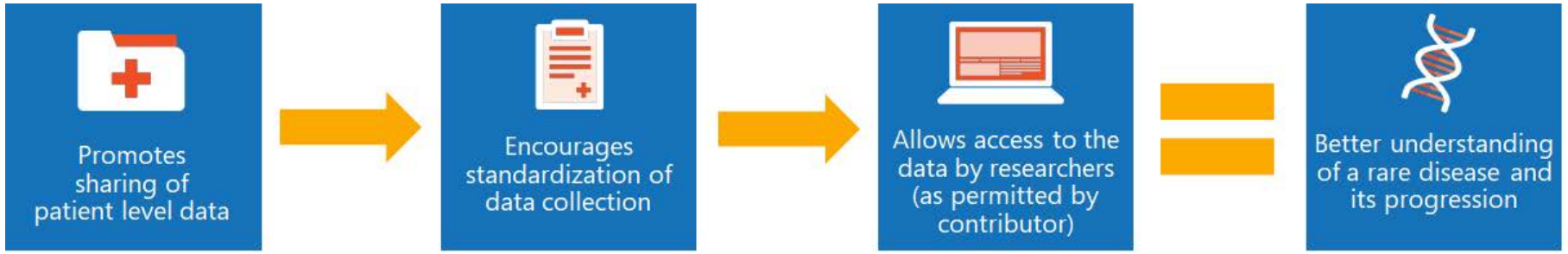
- Rare Disease Endpoint Accelerator (RDEA) Pilot Program

- Rare Disease Cures Accelerator Program
  - Data Analytics Platform

FUNDED BY FDA, C-PATH and NORD TO LAUNCH RARE DISEASE DATA ANALYTICS PLATFORM

Posted by Lisa Sencen

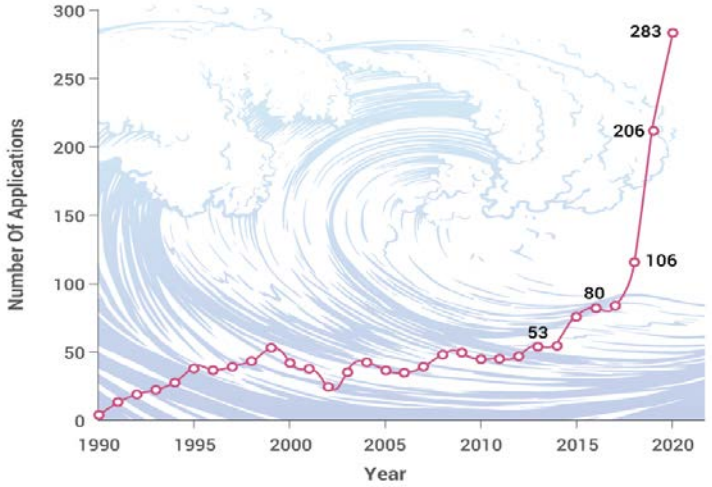
CRITICAL PATH INSTITUTE | NORD® National Organization for Rare Disorders



Center for Biologics Evaluation and Research (CBER) Resource Needs

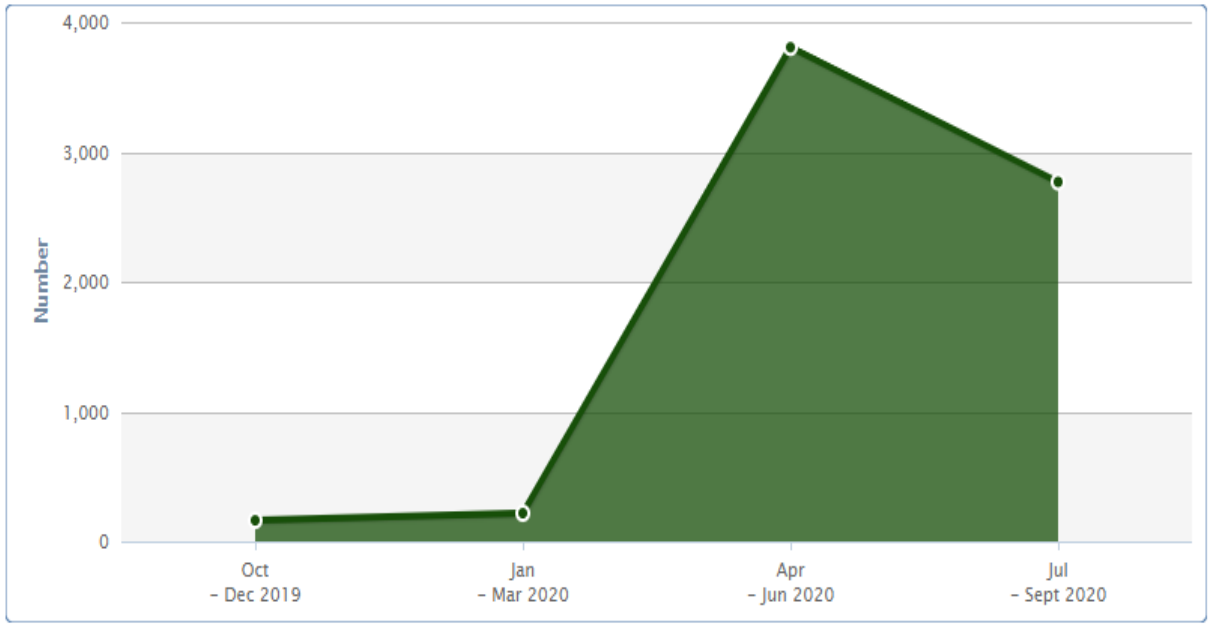
- 6,954 INDs received by CBER in FY2020
- 228 new FTE's provided in PDUFA VII
- Modernization of IT infrastructure

Gene Therapy IND Applications Per Year 2009-2019



*Source: Pink Sheet, Scientific Wave Pushes CBER Into Brighter Light, March 26, 2020

FY 2020 CBER INDs



Source: https://www.accessdata.fda.gov/scripts/FDATrack/view/track.cfm?program=cber&status=public&id=CBER-All-IND-and-IDEs-recieved-and-actions&fy=2020

FDA NOTE (9/29/21): Following the public meeting, NORD provided this revised slide to correct the previously inaccurate figure of new FTEs from 123 to 228.

Strengthening PFDD Efforts

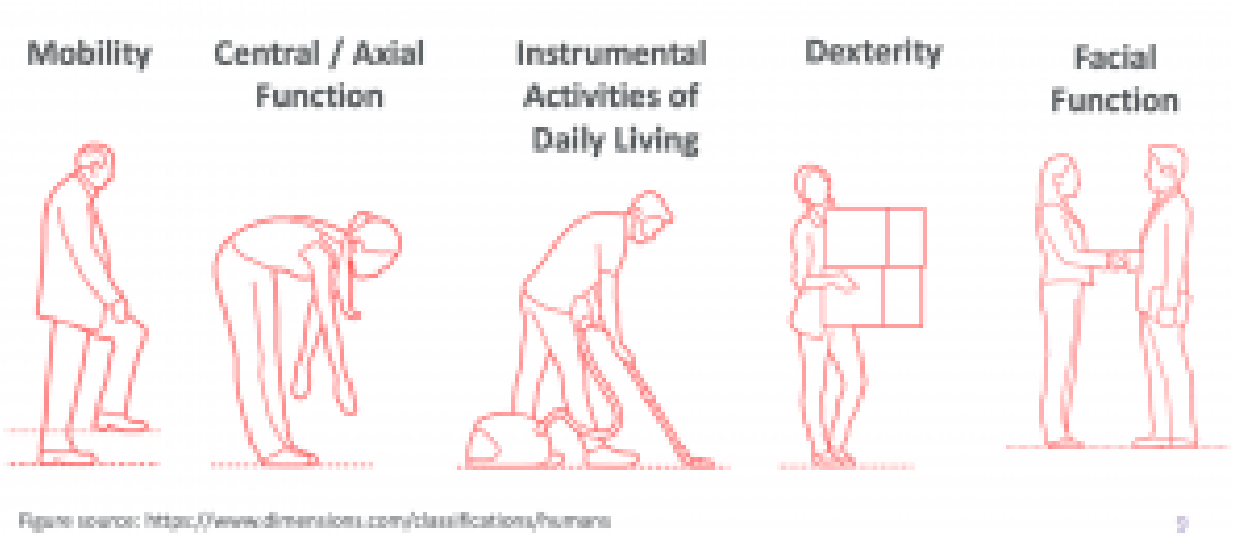
- PDUFA VII – COA Goal
- Rare Disease Clinical Outcome Assessment Consortium – with C-Path
- NUCOAT-Northwestern-NORD Project

NORD
National Organization for Rare Disorders

CRITICAL PATH INSTITUTE

NUCOAT
Northwestern University Clinical Outcome Assessment Team

CDER Pilot Grant Program: Standard Core Clinical Outcome Assessments (COAs) and their Related Endpoints



Advancing Drug Development Utilizing Lessons Learned from the COVID-19 Pandemic

- Decentralized Clinical Trials
- Advancing Real-World Evidence
- Enhancing Use of Digital Health Technologies

Thank you!

Public Comment

Public Commenters

Robert Falb
Alliance for Regenerative Medicine

Brad Jordan
Flatiron Health

Paul Melmeyer
Muscular Dystrophy Association

Jerry S. Roth
Hill Dermaceuticals

Dru West
USA Patient Network

Kim Witczak
WoodyMatters

Diana Zuckerman
National Center for Health Research

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South Medical Economic Institute

U.S. FOOD & DRUG ADMINISTRATION

THANK YOU