The Role of the Patient

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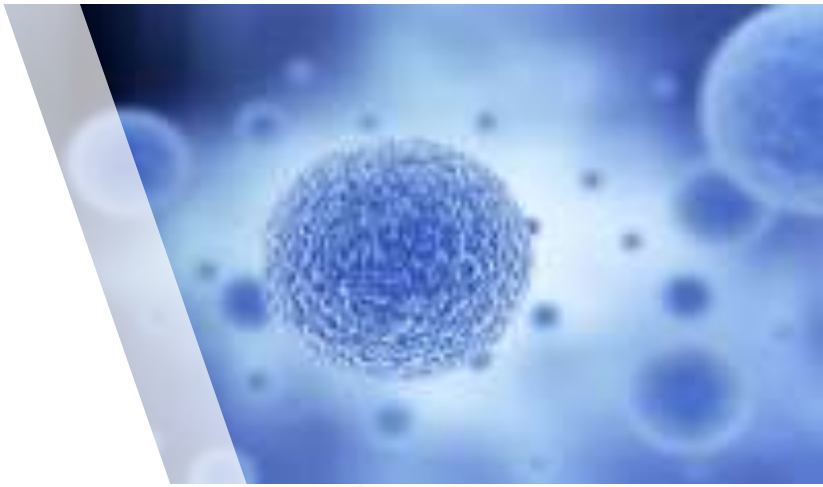
Outline

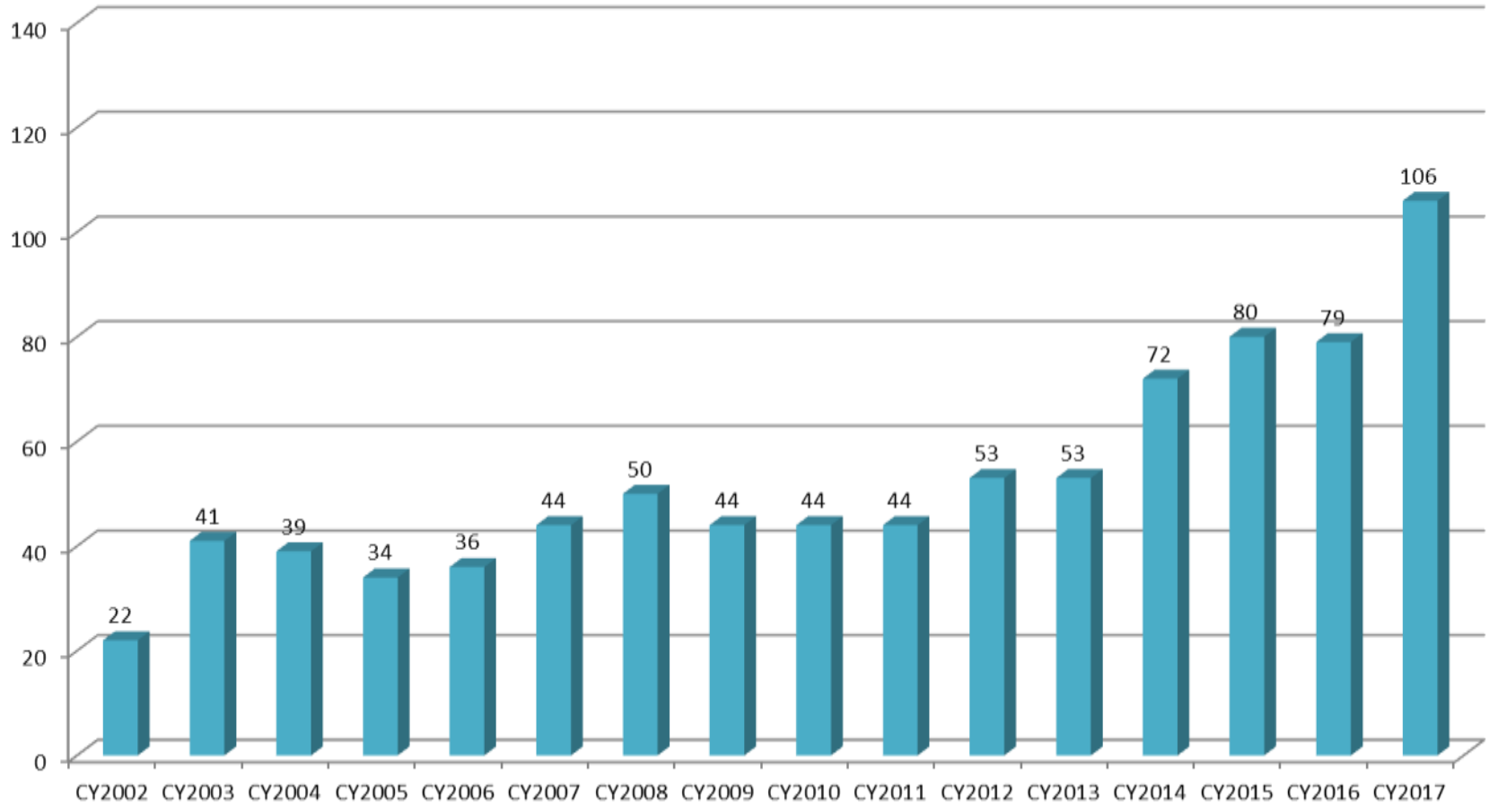
- Introduction
- 21st Century Cures and PDUFA VI
- Patient Affairs Staff Activities
- Other topics
  - Patient comments on guidance
  - Drug Development Tools
  - Individual patient involvement

Products at the Center for Biologics Evaluation and Research (CBER)



- Allergenics
- Blood Products
- Human Tissues and Cellular Products
- Gene Therapies (including CRISPR/Cas9)
- Vaccines (preventative and therapeutic)
- Xenotransplantation Products
- Devices Related to Biologics

All Investigational New Drug Applications for Gene Therapy Products, CY 2002-2017



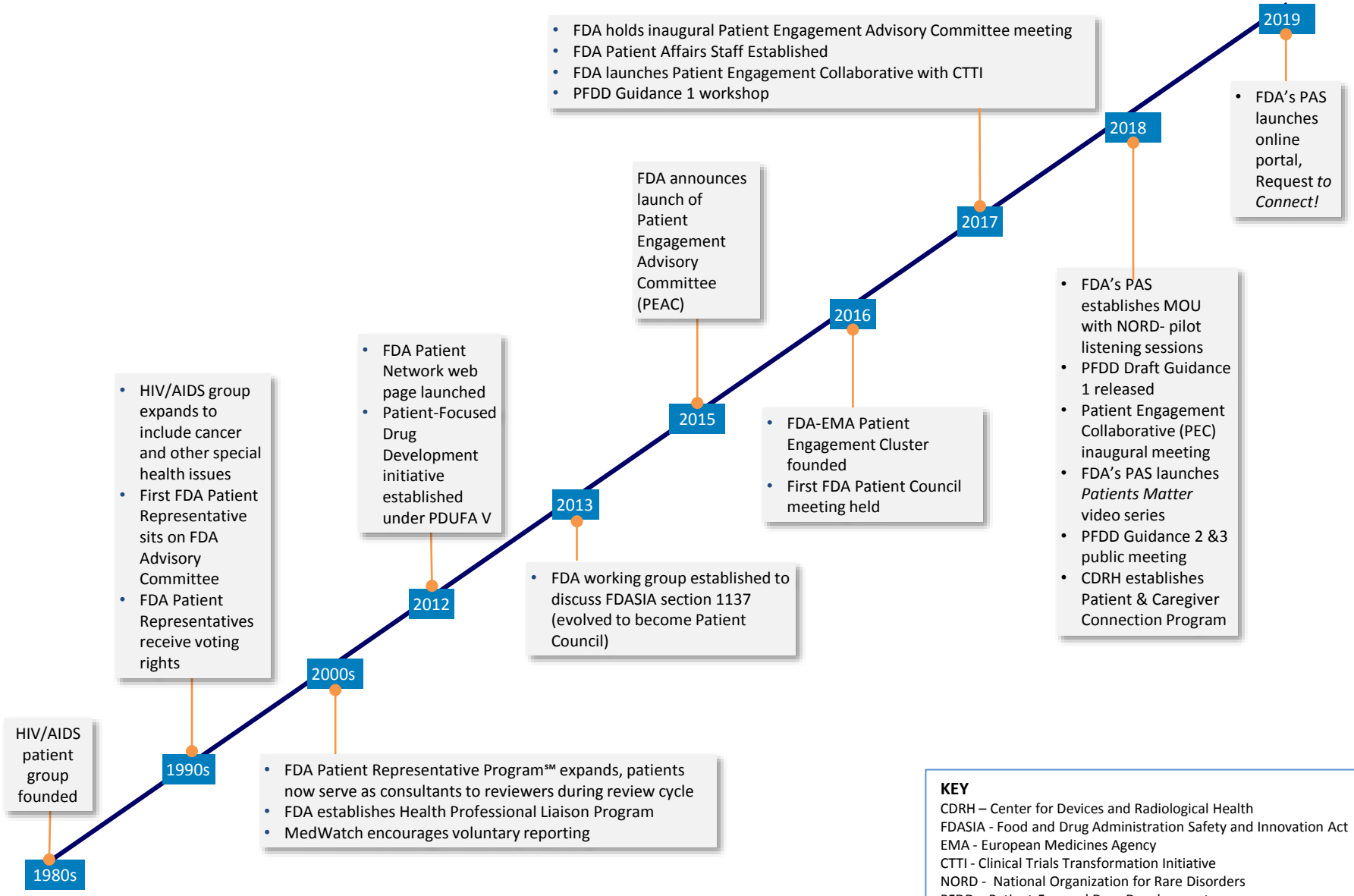
Yearly submissions to the Center for Biologics Evaluation and Research

Definitions

From the Patient-Focused Drug Development Glossary https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm610317.htm

Patient-focused drug development (PFDD)	Also referred to as ”patient-focused medical product development” A systematic approach to help ensure that patients’ experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into the development and evaluation of medical products throughout the medical product life cycle.
Patient Engagement	Activities that involve patient stakeholders sharing their experiences, perspectives, needs, and priorities that help inform FDA’s public health mission. Such activities may include (but are not limited to):testimony at Advisory Committee meetings; submission to regulations.gov public docket; meetings attended by patients, FDA, and other stakeholders; other correspondence with FDA; interactions through social media; and interactions with or information from patient representatives or patient advocates.

Evolution of Patient Engagement at FDA



KEY

CDRH – Center for Devices and Radiological Health
FDASIA - Food and Drug Administration Safety and Innovation Act
EMA - European Medicines Agency
CTTI - Clinical Trials Transformation Initiative
NORD - National Organization for Rare Disorders
PFDD – Patient-Focused Drug Development
PAS – Patient Affairs Staff

Patient Engagement

Why Patient Input Matters

- Patients are experts in their own experience of their disease or condition
- Can inform medical product development and enhance regulatory decision making to address patients' needs

What Patients Can Tell Us

- Impact and burden or disease/treatment
- Unmet needs
- Benefits and risks of treatment approaches
- Clinical trial participation

When Patient Input Matters

- Drug discovery
- Pre-clinical development
- Clinical development
- Post market: post-approval studies, safety

How Does FDA Receive Patient Input? (1/2)

- **Advisory Committee Meetings**
  - As members or in open session
- **During development as SGE consultant**
- **PDUFAVI/21st Century Cures Act**
- **CBER Science of Patient Input**
- **Public meetings and workshops**

How Does FDA Receive Patient Input? (2/2)

Patient-focused Drug Development (PFDD) meetings

- FDA-led
- Externally-led

FDA/NORD rare disease listening meetings

- Requests can come from a patient, patient organization, or FDA staff

Meetings with patient organizations

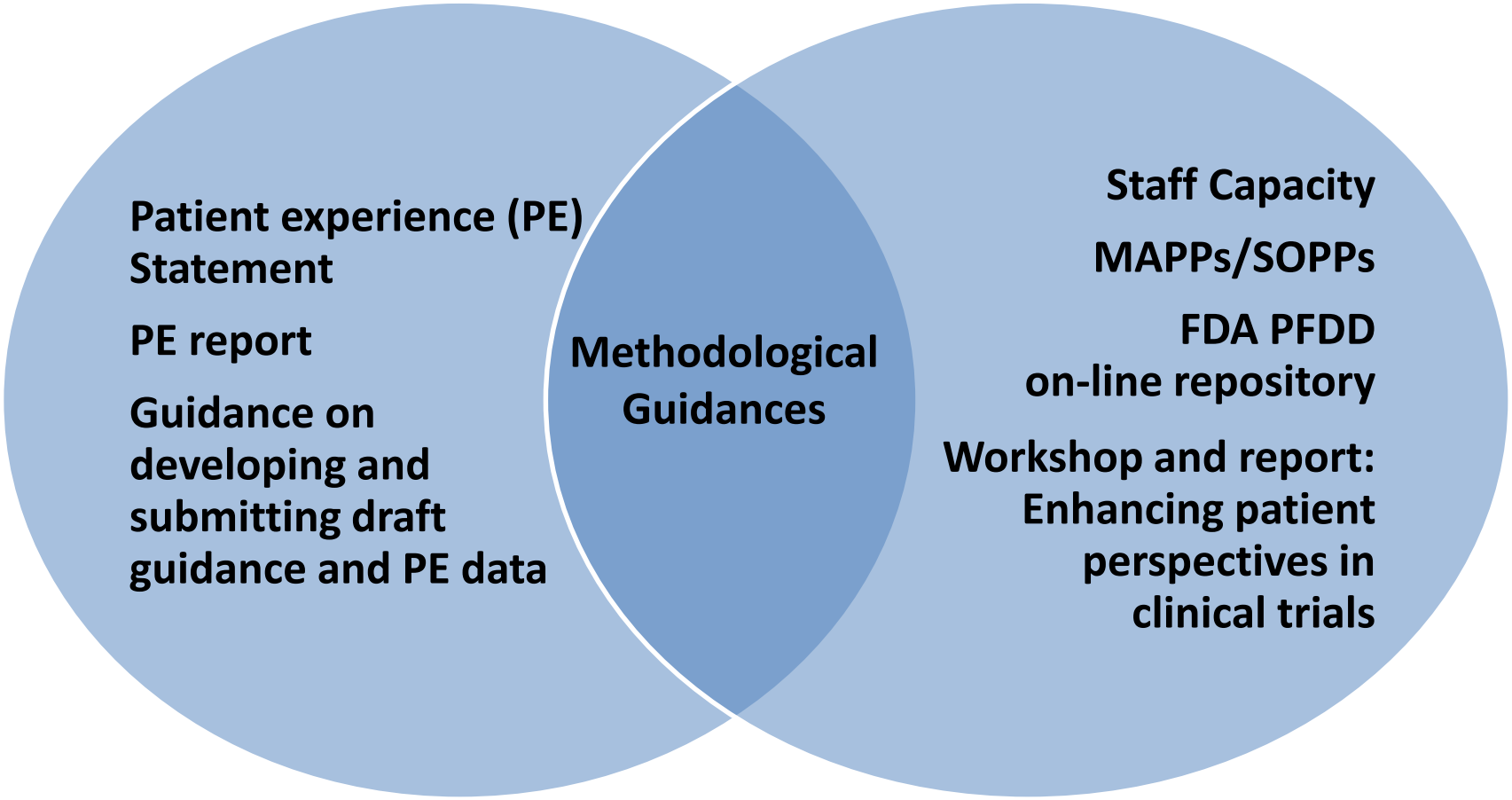
- To request a meeting with CBER: CBERPatientEngagement@fda.hhs.gov

CBER has participated in over 25 PFDDs, patient organization meetings, or FDA/NORD listening sessions since 2013.

Types of work products that patient organizations could submit to FDA

- Meeting reports summarizing the patient perspectives in disease and treatment burden
- Methodologically-sound patient surveys
- White papers or peer-reviewed journal articles describing topics such as background on disease and considerations for clinical trials in a given disease area
- Case examples to address the disease-specific considerations related to medical product development
- Natural history study report
- Proposed draft guidance relating to patient experience data

21st Century Cures vs. PDUFA VI



21st Century Cures Act Section: Patient Experience Data

STATEMENT OF PATIENT EXPERIENCE

IN GENERAL – **Following the approval** of an application that was **submitted** under section 505(b) of this Act or section 351(a) of the Public Health Service Act **at least 180 days after the date of enactment** of the 21st Century Cures Act, the Secretary shall **make public a brief statement regarding the patient experience data and related information**, if any, submitted and reviewed as part of such application. The data and information referred to in paragraph (1) are—(A) patient experience data; (B) information on patient-focused drug development tools; and (C) other relevant information, as determined by the Secretary.

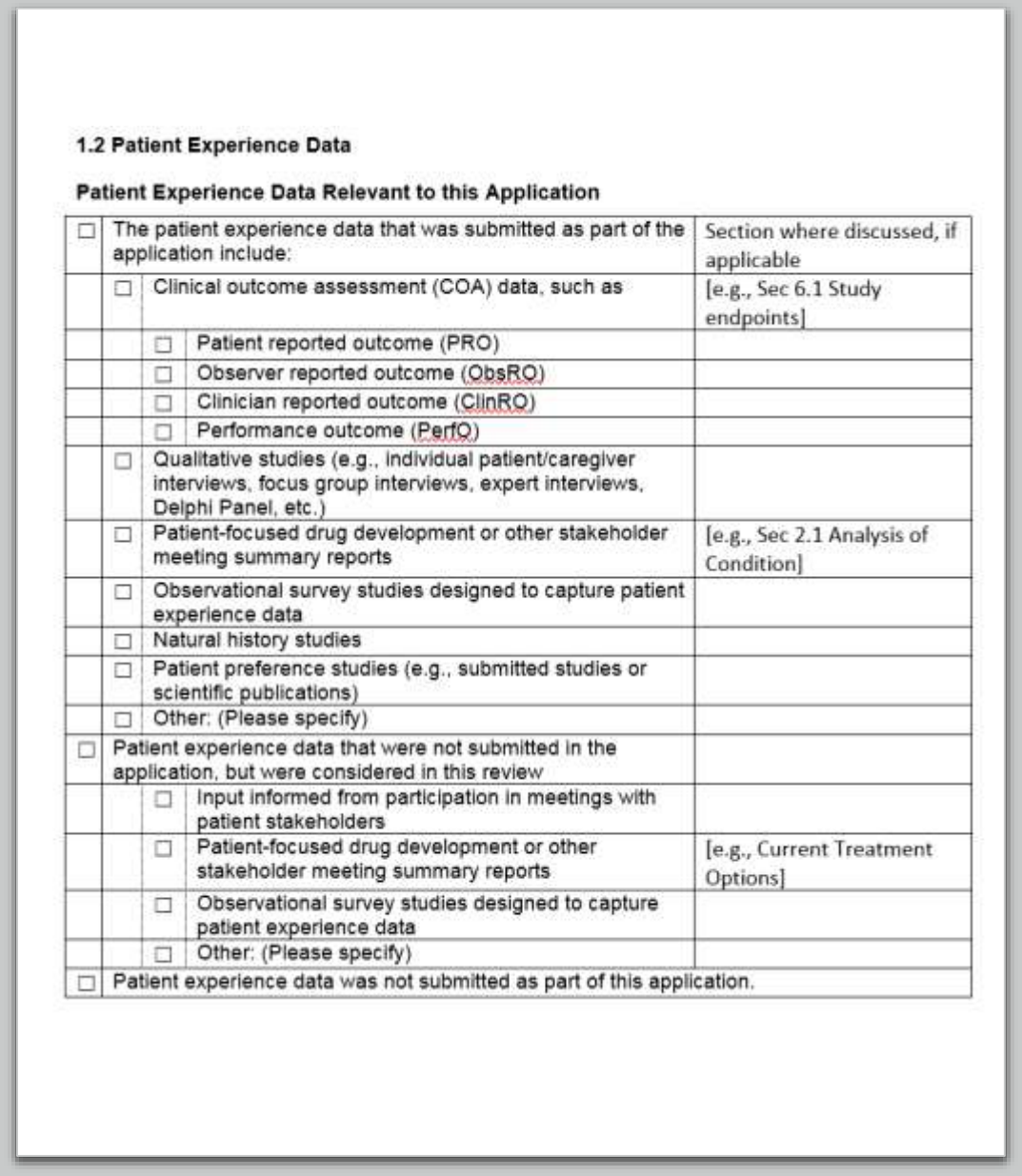
PATIENT EXPERIENCE DATA

For purposes of this section, the term 'patient experience data' includes data that are collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and are intended to provide information about patients' experiences with a disease or condition, including—(A) impact (including physical and psychosocial impacts) of such disease or condition, or a related therapy or clinical investigation*; and (B) patient preferences with respect to treatment of such disease or condition.

*As amended by FDARA Section 605

CBER Clinical Review Memo Template

- July 19, 2018, CBER implemented an updated clinical review memo template
  - Executive Summary Section 1.2 indicates what kind of PE data submitted and where it is discussed



1.2 Patient Experience Data

Patient Experience Data Relevant to this Application

			Section where discussed, if applicable
☐	The patient experience data that was submitted as part of the application include:		
	☐	Clinical outcome assessment (COA) data, such as	[e.g., Sec 6.1 Study endpoints]
		☐ 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	[e.g., Sec 2.1 Analysis of Condition]
	☐	Observational survey studies designed to capture patient experience data	
	☐	Natural history studies	
	☐	Patient preference studies (e.g., submitted studies or scientific publications)	
	☐	Other: (Please specify)	
☐	Patient experience data that were not submitted in the application, but were considered in this review		
		☐ Input informed from participation in meetings with patient stakeholders	
		☐ Patient-focused drug development or other stakeholder meeting summary reports	[e.g., Current Treatment Options]
		☐ Observational survey studies designed to capture patient experience data	
		☐ Other: (Please specify)	
☐	Patient experience data was not submitted as part of this application.		

Patient Experience Data Considered in Gene Therapy Applications

Luxturna

- Visual Function Questionnaire (page 58 of BLA Clinical Review Memorandum)
  - Patient reported outcome (PRO)
  - developed by National Eye Institute of NIH
  - 25 questions pertaining to daily living

- Publicly accessible: https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/approvedproducts/ucm589507.htm (Approval History files: "Clinical Review, December 16, 2017")

21st Century Cures Act and PDUFA VI User Fee Goals

Patient-Focused Drug Development Provisions and Guidance Development

PDUFA VI goals:

Enhancing Incorporation of Patient's Voice in Drug Development and Decision-Making (1/2)

Revise MAPPs and SOPPs as needed to incorporate an increased patient focus in FDA public meetings; staff training re processes, tools, and methodologies

Repository of information on publicly available tools and ongoing efforts

Available at: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579400.htm

Public workshop to gather experiences and recommendations of patients and caregivers on approaches to enhance engagement in clinical trials convened with Clinical Trials Transformation Initiative (CTTI)

View webcast: http://fda.yorkcast.com/webcast/Play/d27bdc602ae74a1e9fbe66e7a405f5df1d

Enhance staff capacity to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions

PDUFA VI goals:

Enhancing Incorporation of Patient's Voice in Drug Development and Decision-Making (2/2)

Develop a series of guidance documents to focus on approaches and methods to bridge from initial patient-focused drug development meetings to fit-for-purpose tools to collect meaningful patient and caregiver input for ultimate use in regulatory decision making

Prior to the issuance of each guidance, FDA will conduct a public workshop to gather input from the public

21st Century Cures Act

Patient-Focused Drug Development

Public statement of patient experience data used in clinical review

Report on patient experience data

Issuance of guidance documents addressing methodological approaches to collecting, analyzing, and submitting patient experience data

- Plan for guidances document published May 2017https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM563618.pdf

Guidance on developing and submitting draft guidance and PE data

- Draft published Dec. 2018 https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM628903.pdf

PDUFA VI & 21st Century Cures Act Guidances

FDA's PFDD Guidance Series: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm610279.htm

Suite of Guidances on Collecting Patient Experience Data and Using It in Drug Development

Guidance 1

- Approaches to collecting comprehensive and representative input from patients and other stakeholders on burden of disease and current therapy (Draft June 2018)

Guidance 2

- Processes and methodological approaches to development of holistic sets of impacts that are most important to patients (Oct 15-16, 2018)

Guidance 3

- Approaches to identifying and developing measures for an identified set of impacts which may facilitate collection of meaningful patient input in clinical trials (Oct 15-16, 2018 workshop)

Guidance 4

- Methods and Technologies for Clinical Outcome Assessments (Workshop TBD in 2019)

FDA Patient Engagement Initiatives*

Initiative	FDA-led Patient-Focused Drug Development (PFDD) Meetings	Externally-led PFDD Meetings	NORD MOU Pilot Listening Sessions	Patient Engagement Collaborative (PEC)	Patient Engagement Advisory Committee (PEAC)	Patient Representative Program (PRP)
Purpose	Public meetings that systematically obtain the patient perspective on specific diseases and their treatments	To allow patient organizations to identify and organize patient-focused collaborations to generate public input on other disease areas, using the process established through FDA-led PFDD meetings as a model	Pilot listening sessions in rare diseases to inform FDA staff of disease and treatment burden in rare diseases	A forum to discuss and share experiences on patient engagement in medical product development and regulatory discussions	Provides advice to the Commissioner or designee, on complex issues relating to medical devices, the regulation of devices, and their use by patients in a public advisory committee meeting	FDA Patient Representative ℠ consultants provide direct input to inform the Agency's decision-making associated with medical products for drugs, biologics, and medical devices in a public advisory committee meeting or as part of agency-directed assignments
Medical Product Type Covered	Biologics, Drugs	Biologics, Drugs	Biologics, Devices, Drugs	Biologics, Devices, Drugs	Devices	Biologics, Devices, Drugs

*This list is not inclusive of all FDA Patient Engagement Initiatives.

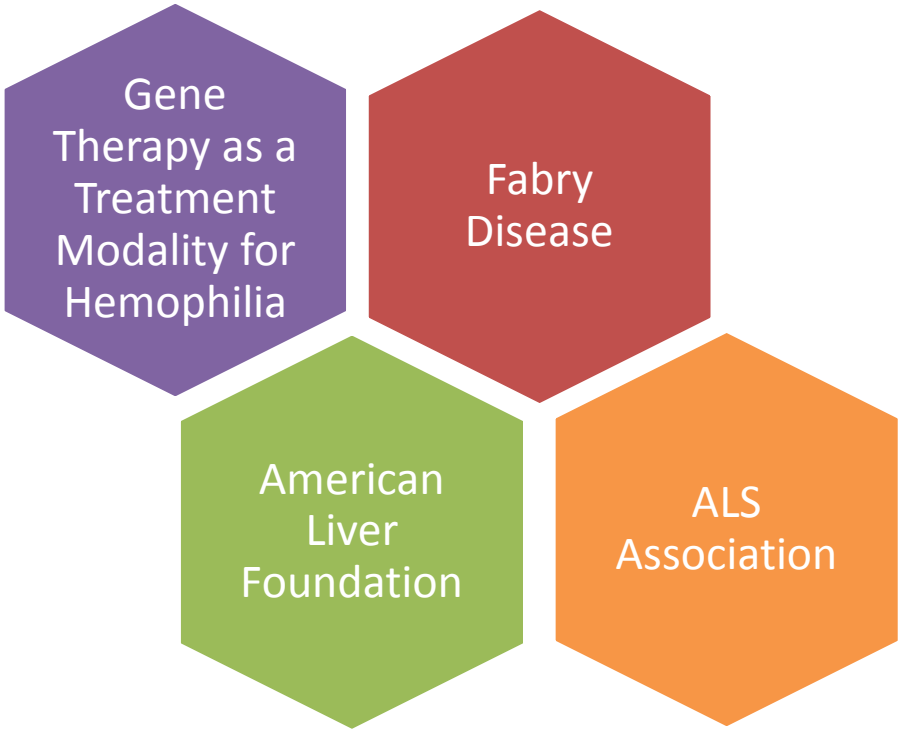
Complete table available at https://www.fda.gov/ForPatients/PatientEngagement/ucm611467.htm

Rare Disease Listening Sessions

- FDA Patient Affairs Staff (PAS) in partnership with National Organization for Rare Diseases (NORD) (pilot program)
  - Inform regulatory decision making
  - Provide a starting point to inform early stage research & development
  - Educate review staff about rare diseases or specific segments of non-rare diseases
  - Help patients and their advocates understand the FDA's mission and work

Rare Disease Listening Sessions

Public reports:
https://wwwfda.gov/ForPatients/PatientEngagement/ucm625092.htm



Gene Therapy as a Treatment Modality for Hemophilia

October 23, 2018

Topics discussed

- Risks and benefits of gene therapy
- Safety monitoring
- Measuring success
- Other considerations

Participants

- 7 patients and caregivers who are segments of the following groups:
  - adults with hemophilia enrolled in a clinical trial
  - adults with hemophilia not enrolled in a clinical trial
  - caregivers to children with hemophilia

Suite of Gene Therapy Draft Guidance Documents

July 2018

https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/default.htm

- Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)
- Testing of Retroviral Vector-Based Gene Therapy Products for Replication Competent Retrovirus (RCR) during Product Manufacture and Patient Follow-up
- Long Term Follow-up After Administration of Human Gene Therapy Products
- Human Gene Therapy for Hemophilia, on Gene Therapy Products Intended for Treatment of Hemophilia
- Human Gene Therapy for Retinal Disorders
- Human Gene Therapy for Rare Diseases

Public Comments

- A number of patient groups provided comments
- Comments are considered in finalization of the guidance documents

How FDA can work with individual patients

- Patient engagement is not limited to a patient's or caregiver's affiliation with a patient organization.

Drug development, regulation, or safety

- Patient Representative Program
- NORD Rare Disease Listening Sessions
- Public meetings, workshops, PFDDs, Advisory Committee meetings
- Comments on guidance and rule making
- MedWatch reporting

Advancing efforts to strengthen FDA-patient community relationship

- Patient Engagement Collaborative

Opportunities for one-on-one interaction or for addressing patient-specific needs:

- FDA Request to Connect
- Expanded Access program

Patients Matter: How CBER Brings the Patient Voice into Rare Disease Product Development

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Patient Engagement @ CBER

Activities involving patient stakeholders sharing their experiences, perspectives, needs, and priorities to help inform FDA's public health mission.

Products CBER regulates

- Allergenics
- Blood and blood products
- Gene therapy products
- Human tissue and cellular products
- Vaccines
- Xenotransplantation
- Certain medical devices

CBER engagement with individuals with rare diseases and caregivers*

Patient-Focused Drug Development meetings:

- Alpha-1 antitrypsin deficiency
- Alport syndrome
- Amyotrophic lateral sclerosis
- Barth syndrome
- Charcot-Marie-Tooth
- Cystic fibrosis
- Duchenne muscular dystrophy
- Epidermolysis bullosa
- Friedreich ataxia
- Hemophilia A and B, von Willebrand & other heritable bleeding disorders
- Hereditary angioedema
- Juvenile idiopathic arthritis
- Pachyonychia congenita

Patient group meetings:

- Angelman syndrome
- Biliary atresia
- Microtia and atresia
- Myotonic dystrophy
- Pemphigoid and pemphigus
- Progressive familial intrahepatic cholestasis
- Sanfilippo syndrome
- Sickle cell anemia
- Wilson disease

NORD/FDA Listening Sessions:

- Congenital hyperinsulinism
- Fabry disease
- Hemophilia and gene therapy

*Examples of CBER patient engagement activities between 2013 and 2019

Share your knowledge and health experiences with CBER

Patients provide an important and unique perspective that is critical for consideration as part of the regulatory process. We highly value patient engagement and its contribution to the development of biological products.

Impact of the disease and its treatment

- chief complaints (most bothersome signs/symptoms)
- burden of living with and managing a disease or condition
- impacts from disease or condition on activities of daily living and functioning

Perspectives about current and potential treatment approaches

- expectations of benefits
- tolerance for harms or risks
- patient preference
- unmet medical needs

Clinical trial considerations

- e.g., views on gene therapy
- burden of participating in clinical studies
- risk tolerance

How to provide your unique perspective to CBER

- Participate in FDA Advisory Committee meetings
- Submit comments on guidance documents and proposed rules to regulations.gov
- Attend product meetings upon invitation of the product developer
- Attend FDA public meetings in person or via remote access
- Participate in a NORD/FDA listening session
- Interact with FDA via social media
- Become an FDA patient representative
- Coordinate an externally-led Patient-Focused Drug Development meeting: https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm
- Patient groups can request a meeting with CBER by emailing: CBERPatientEngagement@fda.hhs.gov

CBER's Patient Engagement groups

CBER Patient Engagement Workgroup

- Staff share knowledge and input on CBER's patient engagement activities

CBER Rare Disease Coordinating Committee

- Facilitates and advances the development and timely approval of safe and effective biologics to improve the lives of children and adults with rare diseases

Science of Patient Input (SPI) Initiative

- supports incorporation of patient perspectives into CBER's regulatory framework

Agency-wide coordination

CBER works closely with patient engagement staff across the FDA to maximize opportunities for CBER staff to hear the patient's voice. This includes participation in:

- Regular cross-center coordination meetings
- Public workshops
- Patient-Focused Drug Development meetings
- FDA's Patient Representatives program
- FDA's Patient Engagement Collaborative
- NORD/FDA Listening Sessions
- Guidance development

Resources

- **CBER Website** https://www.fda.gov/biologicsBloodVaccines/default.htm
- **Learn About FDA Patient Engagement** https://www.fda.gov/forpatients/patientengagement/default.htm
- **Patient-Focused Drug Development** https://www.fda.gov/drugs/developmentapprovalprocess/ucm579400.htm

Presented at Rare Disease Day at the National Institutes of Health, February 28, 2019, Bethesda, MD

Summary

FDA is committed to bringing the promise of innovative, safe and effective new therapies to those in need of them, as quickly as possible.

Contact Information

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Public Access to CBER

- **CBER website:**
  http://www.fda.gov/BiologicsBloodVaccines/default.htm
- **Phone: 1-800-835-4709**
- **Consumer Affairs Branch (CAB)**
  Email: ocod@fda.hhs.gov
- **Manufacturers Assistance and Technical Training Branch (MATTB)**
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