FDA U.S. FOOD & DRUG ADMINISTRATION

Supporting Rare Disease Drug Development: CDER's Rare Diseases Program

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2017 Roadmap for Engaging with the Center for Drug Evaluation and Research

Disclosures

-No Conflicts of Interest
-Nothing to Report
-Opinions expressed are personal and do not reflect those of the FDA

Outline

- Rare Diseases/Orphan Drugs
- Orphan Drug Development
- Special Challenges for Rare Pediatric Diseases
- Rare Diseases Program
- Rare Pediatric Disease Priority Review Vouchers

Rare Diseases/Orphan Drugs

Orphan/rare disease

Affects <200,000 persons in the US

Tend to be challenging drugs to develop

Few patients available for study

Highly diverse group of disorders

~7,000 different disorders

Most are serious, most have unmet medical needs

Affect ~30 million Americans

Collectively, a large public concern

Orphan Drug Act passed in 1983

* 10 years before – 10 drugs approved for Orphan diseases
* Since 1983, 500+ drugs approved (9 in 2016)

Orphan Drug Development

*Clinical Investigations are usually conducted under an Investigational New Drug (IND) application

*Orphan Drug Act does not define separate regulatory standards for the safety and effectiveness of drugs to treat rare diseases

Orphan Drug Development

*Requires at least one adequate and well-controlled trial (§314.126)
*FDA is required to exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards (§314.105)

Special Challenges for Rare Pediatric Diseases

- **Phenotypic** diversity within a disorder adds to complexity, as do **genetic subsets**
- Well defined and validated **endpoints**, **outcome measures**/tools, and **biomarkers** are often lacking
- Lack of **precedent** for drug development

Special Challenges for Rare Pediatric Diseases

- **Ethical** considerations for children in clinical trials
- About **50% of rare disease patients are children**
  - Pediatric research studies should pose **no more than minimal risk** or the risk needs to be justified by anticipated benefit
  - Need to rely on parents to consent
  - Children need to provide **ongoing assent**

CDER Rare Diseases Program

Mission Statement:

- Facilitate
- Support
- Accelerate

…the development of drug and biologic products for the treatment of patients with rare disorders.

Office of Orphan Products Development (OOPD) and OND Rare Diseases Program (RDP)

OOPD

- Administrates ODA
  - Designations
  - Exclusivity
  - Orphan grants
- Device programs
  - Pediatrics
  - Humanitarian Use Device program, Humanitarian Device Exemption
- Advocacy work with RD stakeholders

RDP

- Facilitate
  - communication within CDER/OND review divisions
- Focus
  - On complex regulatory requirements for INDs, NDAs and BLAs
- Develop
  - policy, procedures and advice for RD clinical development in CDER

Office of Orphan Products Development (OOPD) and OND Rare Diseases Program

- Common areas:
  - Coordinate communication across FDA centers and offices
  - Participate in the FDA Rare Disease Council
  - Work with outside stakeholders
  - Enhance Rare Disease information available on FDA website
  - Meet to work on policy issues

Current staff in the Rare Diseases Program

- Jonathan Goldsmith
  - Associate Director for Rare Diseases
- Larry Bauer
  - Regulatory Scientist
- Althea Cuff
  - Senior Regulatory Policy Analyst
- Tracy Cutler
  - Health Scientist Administrator
- Lucas Kempf
  - Medical Officer
- Kathy O'Connell
  - Medical Officer

Rare Diseases Program Projects (1)

Coordinate development of CDER Policies, Procedures and Training

- Several guidances under development
- Continuing involvement with Senior FDA staff re:

  Rare Diseases Program projects
- Review Rare Pediatric Disease Priority Review Voucher requests and developed procedures for review and administration

Assist in development of good science

- Regulatory database adjudication committee for NMEs
- Specific projects/peer reviewed publications

Rare Diseases Program Projects (2)

Work collaboratively with stakeholders

- NIH Collaborations
- Rare Disease Day: Annual Meeting
- Panel Participation in FDA Patient Focused Drug Development Meetings
- Face to Face meetings with patient advocacy groups often in collaboration with PASE and/or OHCA

Rare Diseases Program Projects (3)

- Presentations to stakeholder groups
- Planning Committee for National Organization for Rare Disorders (NORD) Annual Summit
- FDA Rare Disease Council member
- Respond to queries from internal and external stakeholders
- Working Group member of FDASIA Section 1137 – "Patient Participation in Medical Product Discussion"

Rare Diseases Program Projects (4)

Promote consistency and innovation in review

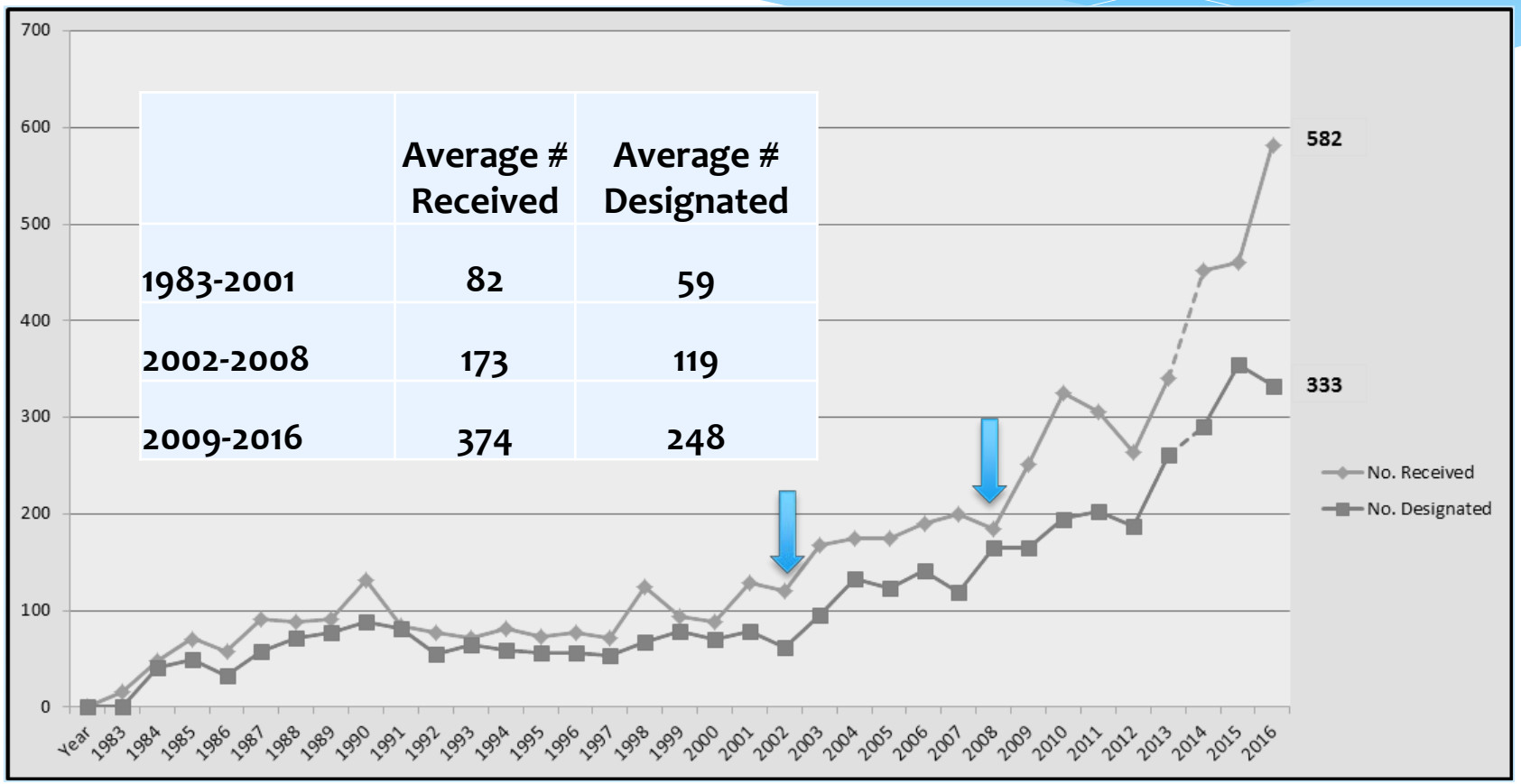
- Annual Rare Diseases Training Course for FDA Review staff
- Recurring Introduction to Rare Disease Drug Review Course for New Reviewers
- Attend milestone (pre-IND, EOP2, pre-NDA, etc) review division meetings for rare diseases
- Presentations to numerous professional societies

Rare Diseases Program Projects (5)

EMA/FDA Rare Disease Cluster

- Global interest in rare disease drug development from patients/families, non-profit patient advocacy stakeholder organizations, drug developers and regulatory authorities
- Enhanced interactions between FDA and the EMA could provide important opportunities for scientific exchange and potential harmonization
- Monthly meetings to discuss topics

Predicting the Future of Rare Disease Drug Development: Orphan Designation



	Average # Received	Average # Designated
1983-2001	82	59
2002-2008	173	119
2009-2016	374	248

Rare Pediatric Disease (RPD) Priority Review Vouchers (PRV)

-Established by the 2012 FDA Safety and Innovation Act (FDASIA) [Section 908]
-Provides an incentive to encourage the development of drugs and biologics for the prevention or treatment of rare pediatric diseases
-Upon marketing approval, the sponsor for a RPD drug may be eligible for a voucher redeemable for a priority review for a subsequent marketing application that would have otherwise received a standard review

RPD PRVs

Voucher eligibility:

- A rare pediatric disease "…is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years…" with greater than 50% of the disease affected US population in this age group
- Is a rare disease or condition as defined in section 526 of the FD & C Act
- Relies on clinical data from pediatric population(s) in doses intended for use in that population

RPD PRVs (2)

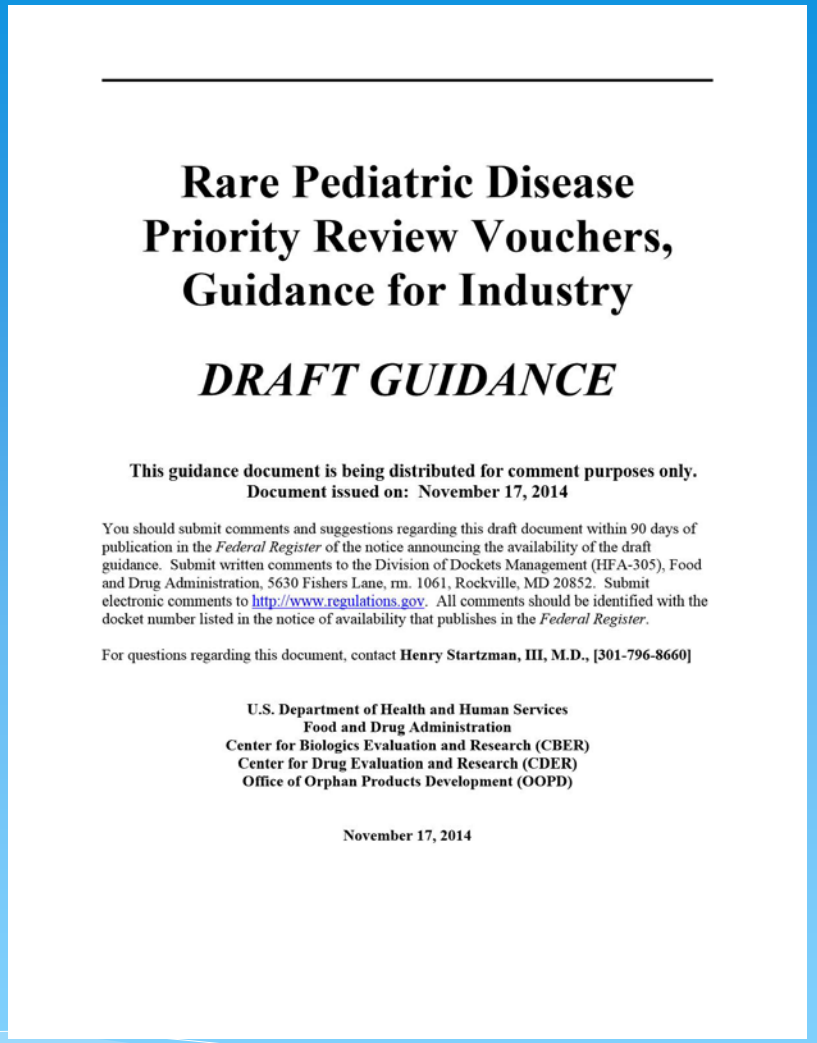
Voucher eligibility:

- The candidate drug or biological product contains no active ingredient (including any ester or salt of the active ingredient) that has been previously approved in any other application
- Does not seek approval for an adult indication in the original rare pediatric diseases product application
- FDA deems eligible for priority review

RPD PRVs (3)

* 10 Vouchers have been awarded to date
* They have sold for up to $350 million dollars
* 3 have been redeemed for priority reviews

Resources



Rare Pediatric Disease Priority Review Vouchers, Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: November 17, 2014

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. 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 document, contact **Henry Startzman, III, M.D., [301-796-8660]**

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)
Office of Orphan Products Development (OOPD)

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http://www.fda.gov/RegulatoryInformation/Guidances/ucm423313.htm

Thank you very much for your attention!

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Rare Diseases Program/OND/CDER/FDA