

# 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***

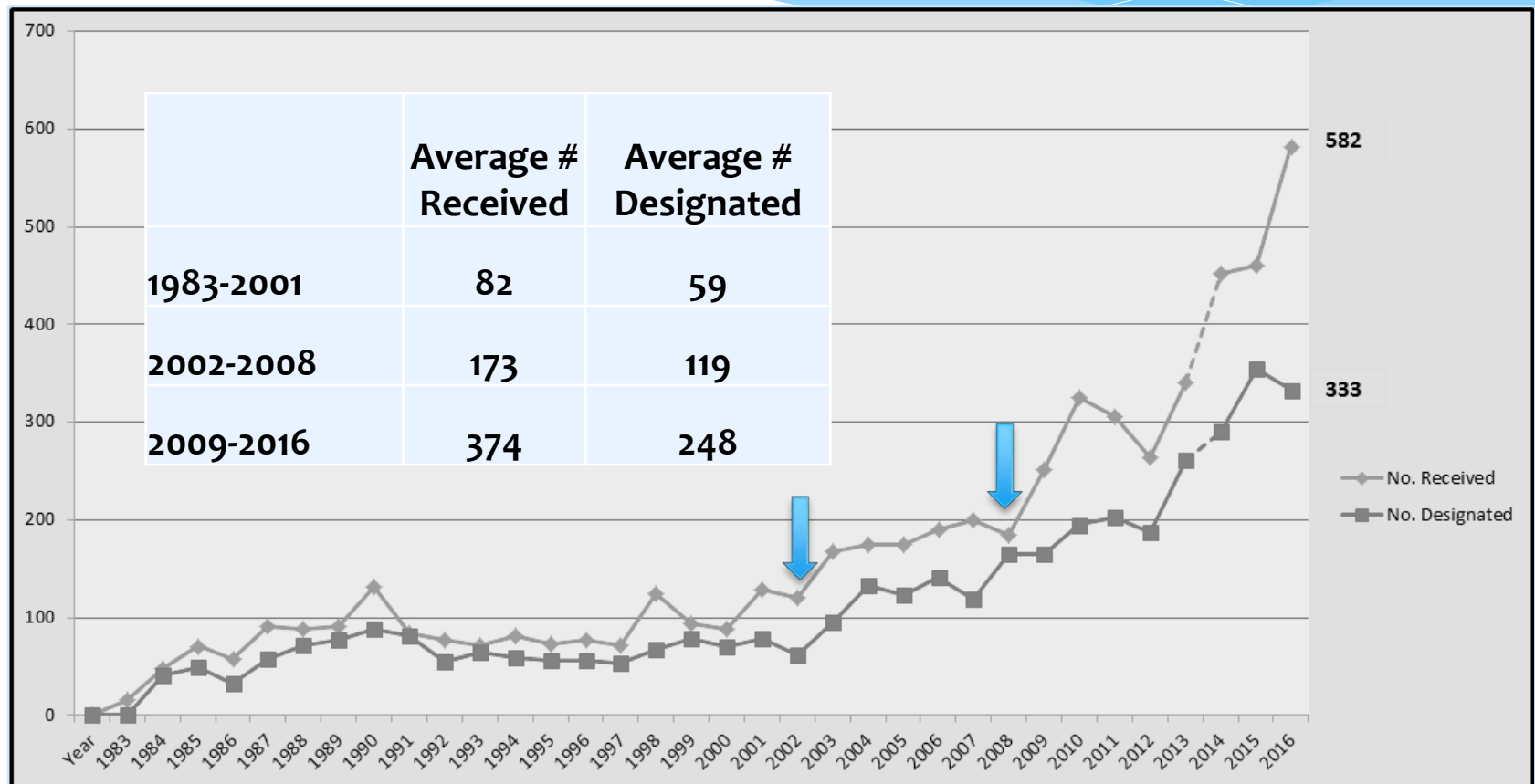
- Annual Rare Diseases Training Course for FDA Review staff
- Recurring Introduction to Rare Disease Drug Review Course for New Reviewers
- Attend milestone (pre-IND, EOP2, pre-NDA, etc) review division meetings for rare diseases
- Presentations to numerous professional societies

# 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



# 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