Rare Diseases: Landscape and Overview

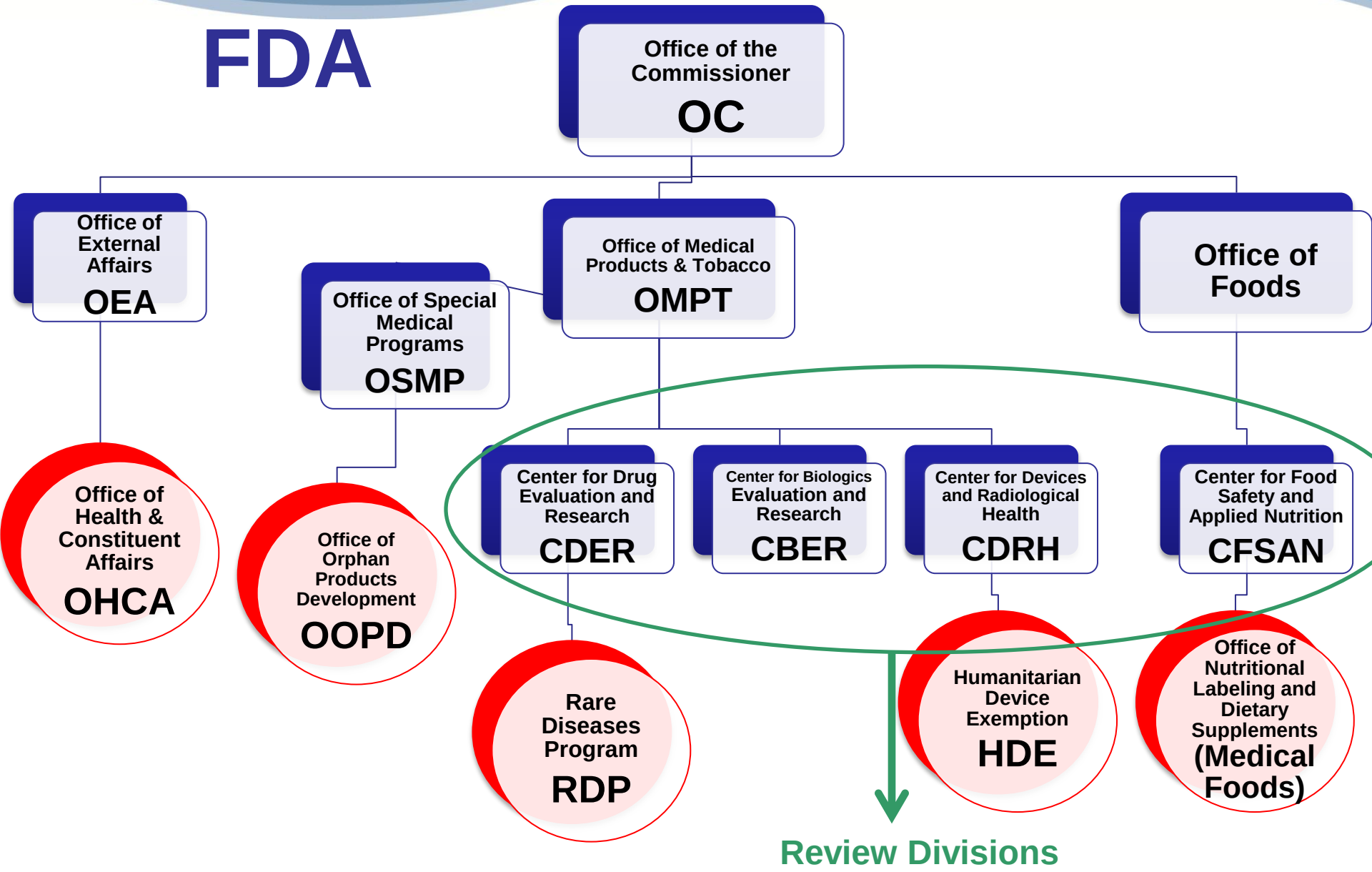
Katherine Needleman, MS, PhD, RAC
Director, Orphan Products Grants Program
FDA/OOPD

Symposium: Best Practices in Clinical Study Design for Rare Diseases
April 29 & 30, 2013

Outline

- Background
  - FDA and its Organization in relationship to rare diseases
  - ODA
- Where are we now and how far have we come?
  - OOPD and its Programs
  - Collaborations
- Where are we going?
  - New Things on the Horizon – FDASIA

FDA



For Complete FDA Organizational Chart: :http://www.fda.gov/downloads/AboutFDA/CentersOffices/OrganizationCharts/UCM288864.pdf

The U.S. Orphan Drug Act Signed in 1983

Established the public policy that the Federal Government could/would assist in the development of treatment for rare diseases

What is an Orphan Drug? U.S. Definition

An orphan drug is defined in the 1984 amendments of the U.S. Orphan Drug Act as a drug intended to treat a condition affecting fewer than 200,000 persons in the United States, or which will not be profitable within 7 years following approval by the U.S. Food & Drug Administration.

Orphan Diseases

- 'Rare' defined as prevalence of <200,000 in the U.S.
- Includes over 6,000 rare diseases
- Collectively affects approximately 25 million Americans
- Frequently serious/life threatening

The Mission of The Office of Orphan Products Development

To assist and encourage the identification, development, and availability of safe and effective products for people with rare diseases/disorders.

OOPD Programs

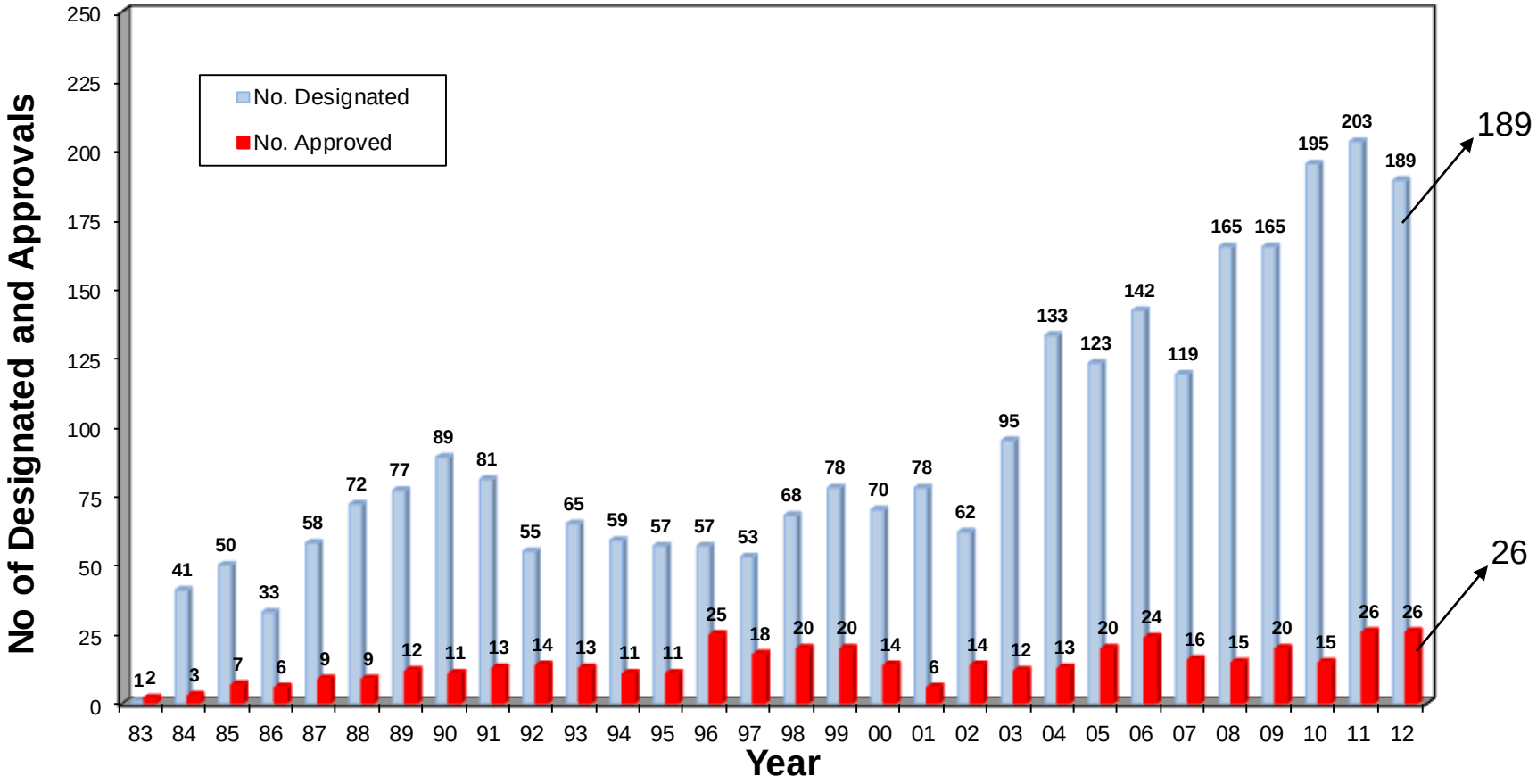
- Orphan Drug Designation Program
- Humanitarian Use Device Designation Program
- Pediatric Devices Consortia Grants Program
- Orphan Products Grants Program

Orphan Product Designation

Orphan Drug Designation Program

- Intended to promote the development of drugs and biologics for rare diseases
- Drug/biologic may be “designated” as an “orphan drug” if it is to prevent, treat, or diagnose a disease/condition that occurs in <200,000 patients in U.S.
- Incentives associated with designation:
  - Tax Credits – 50% tax credit for clinical research and testing expenses
  - Waiver of User Fees – In FY 2013 ~$1.9 M per application, which would otherwise be paid to FDA whether their product is approved or not
  - 7 years of marketing exclusivity upon FDA approval of a specific orphan drug for a specific indication

Orphan Drug Designations/Approvals



Approx Total # Designation requests submitted through 2012 = > 3900

Approx Total # of Designations through 2012 = > 2700

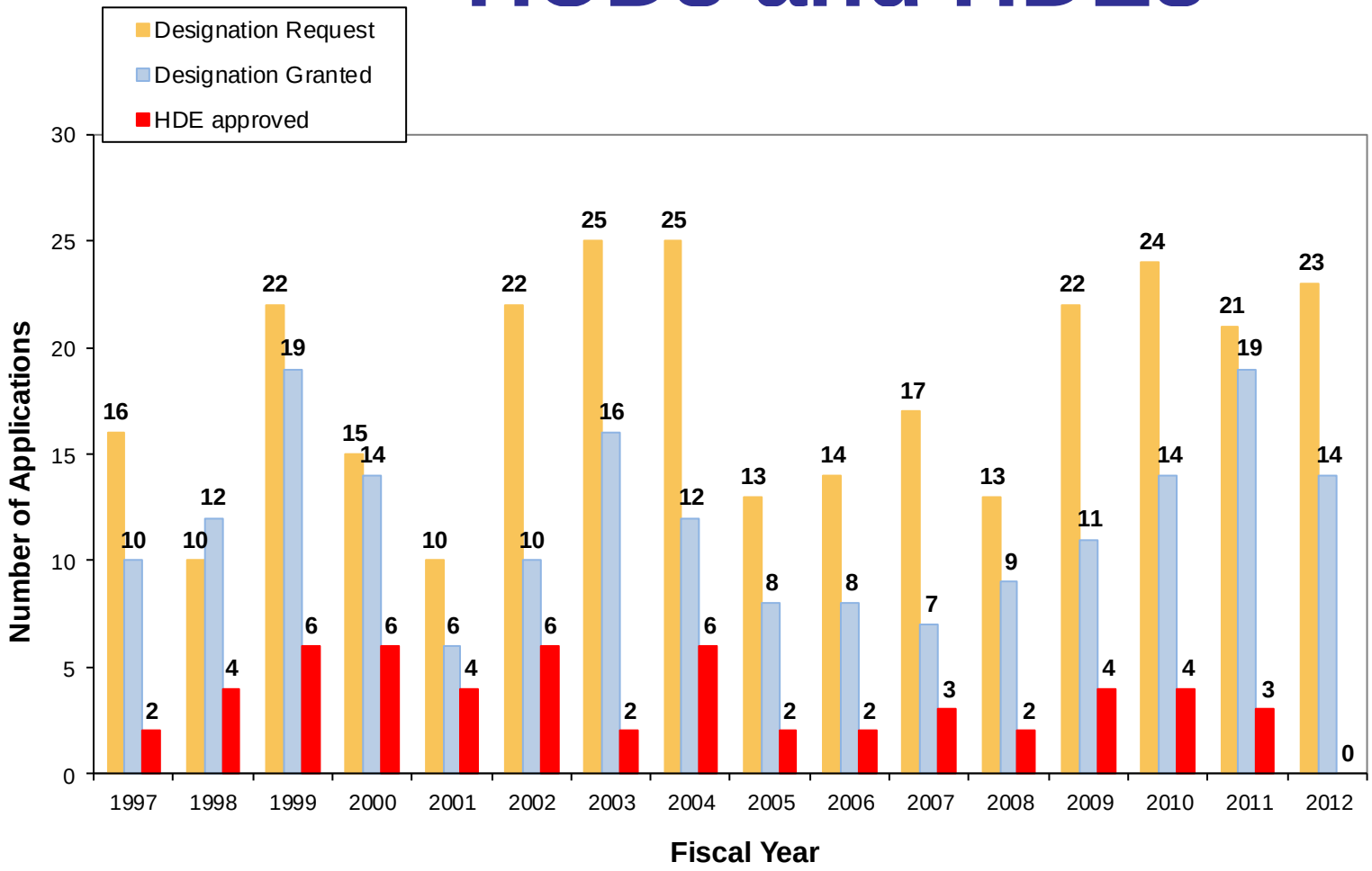
Approx Total # of approvals of orphan designated products through 2012 = >420

Humanitarian Use Devices (HUD)

Humanitarian Use Devices (HUDs)

- Intended to promote the development of devices for rare diseases
- Definition of “HUD”
  - Device used to prevent, treat, or diagnose a disease or condition affecting <4,000 individuals in US per year
- If designated as a “HUD,” can qualify to enter the market through the “HDE” pathway
  - “HDE” = Humanitarian Device Exemption Pathway
  - Safety and Probable Benefit
  - Exemption from the effectiveness standard
    - Restriction on profit (FDAAA 2007/FDASIA 2012)
    - Device to be used with facility IRB approval
    - No comparable device marketed

HUDs and HDEs



Total # HUD requests received = 292
Total # HUDs granted = 189
Total # HDEs approved =56

Pediatric Devices Consortia Grants Program

Pediatric Device Consortia Grant Program

Pediatric Devices Consortia Grants Program

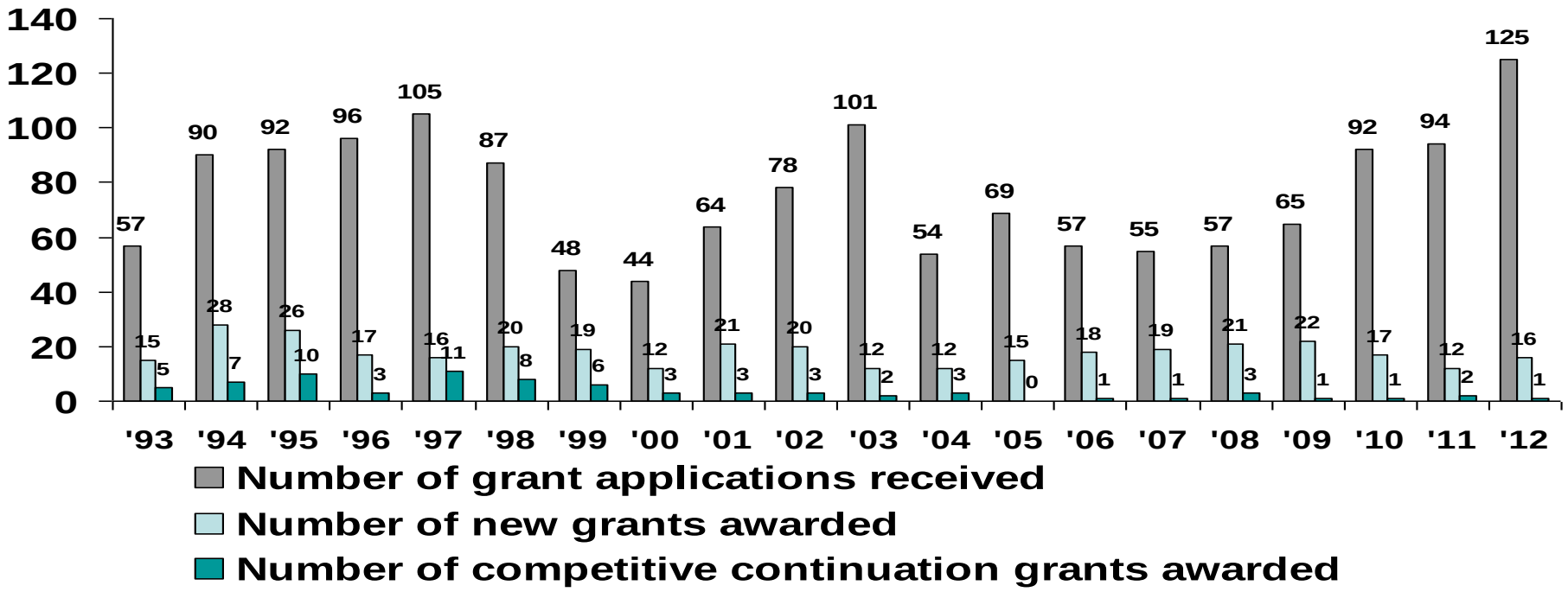
- Support development of consortia to promote pediatric device development
- Consortia currently funded:
  - University of Michigan MPED & PMDI Pediatric Medical Device Consortium
  - University of California, San Francisco Pediatric Device Consortium
  - Atlanta Pediatric Device Consortium
- Re-authorized for $5.25 million/year for next 5 years
  - Funded over $11 million since 2009
- New RFA was issued; Receipt date in June 2013

Orphan Products Grants Program

Orphan Products Grants Program

- ~ $14 million annual budget to fund clinical development of products for rare diseases
  - For Phase 1 Studies:
    - Up to $200,000 per year for up to 3 years
  - For Phase 2 and 3 Studies:
    - Up to $400,000 per year for up to 4 years
- Success of the program:
  - > 40 products partially funded by OOPD grants approved for marketing
  - 2 out of the 26 approved orphan drugs from 2012 received OPD funds
    - Kalydeco (ivacaftor) for cystic fibrosis
    - Juxtapid (lomitapide) for homozygous familial hypercholesterolemia
- Next New Application receipt date: February 5, 2014

Annual # of Grant Applications



Generally, receive ~100 applications/year and fund 10-15 new grants/year (~15% success)

For a list of past and currently funded grants:

http://www.accessdata.fda.gov/scripts/opdlisting/oopdgrants/

Collaborations

FDA-Wide Collaborations

- Rare Disease Council
  - Communicate, coordinate and collaborate rare diseases issues
  - Consists of OOPD,CDER, CBER, CDRH, CFSAN, OHCA
- Patient Communications
  - Responding to individual patient-level questions to planning large-scale educational programs
- Drug Shortage Issues
- FDASIA Implementation
- Outreach
  - Produced a number of workshops (Science of Small Clinical Trials, Pediatric Device Workshop, Orphan Products Designations and Grants)

Inter-Agency and International Collaborations

- Inter-agency Collaborations
  - CMS (Center for Medicare & Medicaid Services)
  - NIH (National Institutes of Health)
- International Collaborations
  - EMA
  - Health Canada
  - IRDiRC

Where are we going?
PDUFA

PDUFA – Prescription Drug User Fee Act

- PDUFA enacted in 1992
- PDUFA IV/Food and Drug Administration Amendments Act (FDAAA) (2007) focused largely on safety
- **PDUFA V/FDA Safety and Innovation Act (FDASIA):**
  - Authorized in 2012
  - law ensures that FDA will continue to receive a source of stable and consistent funding during fiscal years 2013-2017 that will allow the agency to fulfill its mission to protect and promote public health by helping to bring to market critical new medicines for patients.
  - patient centered
    - factor in risk tolerance of patients with unmet medical needs
    - explore endpoints most important to patients

PDUFA V: 1st legislation since ODA to *specifically* address rare diseases

- *Enhancing Regulatory Science & Expediting Drug Development*
  - Initiatives to enhance FDA-Sponsor communication
  - Approaches and methods for the conduct of meta-analysis
  - Advancing the use of biomarkers and pharmacogenomics
  - Advancing the development of patient reported outcomes and other endpoint assessment tools
  - Initiative to advance the development of drugs for rare diseases
    - Funding and programmatic direction for CDER's Rare Disease Program

FDASIA and PDUFA Performance Goals: Provisions Related to Rare Diseases

- Expedited Approval for Serious or Life-Threatening Diseases/ Conditions
  - Accelerated Approval
  - Breakthrough Therapies
- Rare Pediatric Disease Voucher Program
- Patient-Focused Drug Development
- External Experts
- Humanitarian Device Exemptions

Reauthorization of Grants:

1. ***Orphan Products Grant Program - $30M/year***
2. ***Pediatric Devices Consortia Grant Program - $5.2M/year***

Expedited Approval for Serious or Life-Threatening Diseases/ Conditions:

Accelerated Approval

- Expands the scope of products that qualify for expedited development and review and the range of endpoints that may be used to gain approval
- FDA may approve an NDA/BLA for a product for a serious or life-threatening condition: including FT product based on a determination that the product has an effect on a:
  - Surrogate endpoint that is reasonably likely to predict clinical benefit

  OR
  - Clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict effect on irreversible morbidity or mortality or other clinical benefit
- Takes into account severity, rarity, or prevalence, as well as lack of alternative treatments

Expedited Approval for Serious or Life-Threatening Diseases/ Conditions:

Breakthrough Therapy

- Designate drug as a breakthrough therapy if:
  - Intended to treat a serious or life-threatening disease/condition AND
  - Preliminary clinical evidence indicates that drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints
- Submit request for designation with or as an amendment to an IND; 60 day review
- If designated:
  - Eligible for everything Fast Track receives
  - Also get more interactive involvement with review division to help guide efficient yet scientifically appropriate trial design
    - Meetings/development advice

Rare Pediatric Disease Priority Review Vouchers

- Similar to and inspired by the Tropical Disease Priority Review Voucher Program
- Uses priority review vouchers as an incentive to develop drugs and biologics for “rare pediatric diseases” (primarily for individuals aged birth to 18 years)
- Designation provisions to determine if a product qualifies as one for a rare pediatric disease and whether an application qualifies as a rare pediatric disease product application
- On approval, provides a voucher entitling subsequent drug or biologic application to priority review
    - Sponsor may transfer entitlement to voucher
    - Must notify FDA 90 days prior to submission that will use PRV
    - Subject to priority review user fee

Patient-Focused Drug Development

- FDA to conduct 20 meetings on different disease areas to obtain patient perspective on disease severity or unmet medical need
  - Sept. 24, 2012 – Published a preliminary list of nominated disease areas and the criteria used for nomination
    - Included rare diseases (e.g., sickle cell disease, amyloidosis, hereditary angioedema)
  - April 11, 2013 – FR published initial 12 diseases to be addressed in FY 2013-2015
    - Includes: Alpha-1 antitrypsin deficiency, idiopathic pulmonary fibrosis, neurological manifestations of inborn errors of metabolism, Huntington's disease, pulmonary arterial hypertension, sickle cell disease
  - April 25 & 26, 2013 – Bethesda, MD – 1st of 20 meetings on Chronic Fatigue Syndrome and myalgic encephalomyelitis (non-rare)

External Experts

- Use experts for consultation in pre-approval period
  - Example topics may include:
    - Severity of rare diseases
    - Unmet medical need associated with rare diseases
    - Willingness and ability of individuals with a rare disease to participate in clinical trials
    - Assessment of benefits and risks of therapies to treat rare diseases
- FDA to develop and maintain a list of external experts used for consultation

Humanitarian Device Exemption

- **Expands** profit-making ability of HDE Devices to include:
  - Disease Does Not occur in pediatrics (ONLY occurs in adults)

  OR

  - Disease occurs in pediatric patients in such numbers that the development of the device for such patients is impossible, highly impracticable, or unsafe (Majority Adults)

- Amended provision does not cap the number of devices for which the manufacturer may obtain a profit per year at 4000 devices

Summary

- > 6000 Rare Diseases; 25 million Americans
- > 2700 Designations through 2012; 189 HUDs
- > 420 approvals of orphan designated products through 2012; 56 HDEs
- Only ~ 250 diseases with treatments
- Lots More To Do!

OOPD Website

- http://www.fda.gov/orphan

Your Link to:

  - Overview of FDA Office of Orphan Products Development
  - Guidelines for designation application
  - List of designated and approved orphan products
  - Grant application information
  - List of ongoing orphan grant studies
  - Contact information for OOPD staff
- Main Telephone # is (301) 796-8660

Thank You!