Orphan Products Grants Program Overview

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Joint EMA/FDA/MHLW-PMDA orphan medicinal product workshop

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ORPHAN PRODUCTS DEVELOPMENT

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Outline

- OOPD Grants Programs
  - PDC
  - Orphan Clinical Grants Program
- Other Sources of Funding/Opportunities

Grants Programs in OOPD

1. Pediatric Device Consortia Grant Program
2. OPD Clinical Research Grants (R01) for Orphan Diseases

Pediatric Device Consortia Grant Program

Pediatric Device Consortia Grant Program

MEDICAL DEVICES FOR CHILDREN

Food and Drug Administration

PDC Grant Program

- Established from FDAAA 2007 and reauthorized as part of the FDA Safety and Innovation Act of 2012
- Administered by OOPD, but encompasses devices used in all pediatric diseases, not just rare diseases.
- Last Receipt Date for Applications was June 1, 2013

  http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/PediatricDeviceConsortiaGrantsProgram/ucm344551.htm
- **Not a direct research grant**

  funds nonprofit consortia that *support* pediatric device developers

PDC Grant Program

- Over 250 pediatric device projects have been assisted by the pediatric device consortia since October of 2009
- OOPD awarded grants to 7 consortia in FY 2013
- PDC Contact

  Linda Ulrich (Linda.Ulrich@fda.hhs.gov)
- For more information, go to:

  http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/PediatricDeviceConsortiaGrantsProgram/default.htm

Orphan Products Grants Program

Orphan Products Grants Program

- Goal:

  To encourage clinical development of products, including drugs, biologics, medical devices, or medical foods, for use in rare diseases.

- The disease must be rare as defined in the Act (For diseases affecting <200,000 persons in the US).

Unique Program

- Close to the Regulatory aspect
- Have individuals in our office that have come from many backgrounds including the review divisions
- Review Divisions input
- IOM (Institute of Medicine) identified this as a successful attribute of the program (not as easily implemented across other agencies)

Orphan Products Grants Program

- A practical program:
  - Goals are advancing marketing approvals and relevant publications that impact care for rare diseases
- Approximately 100 applications per year
- Competitive grant program – ~15% success
  - Fund about 10-15 new grants per year
- Request for Application (RFA) available at www.fda.gov/orphan
- Application, review, and scoring much like NIH grant application
- Electronic submissions: Grants.gov

Requirements

- Eligibility:
  - Academic and industry sponsored research
  - Domestic or foreign, public or private, for-profit or nonprofit entities
  - Any entity except DHHS Federal agencies

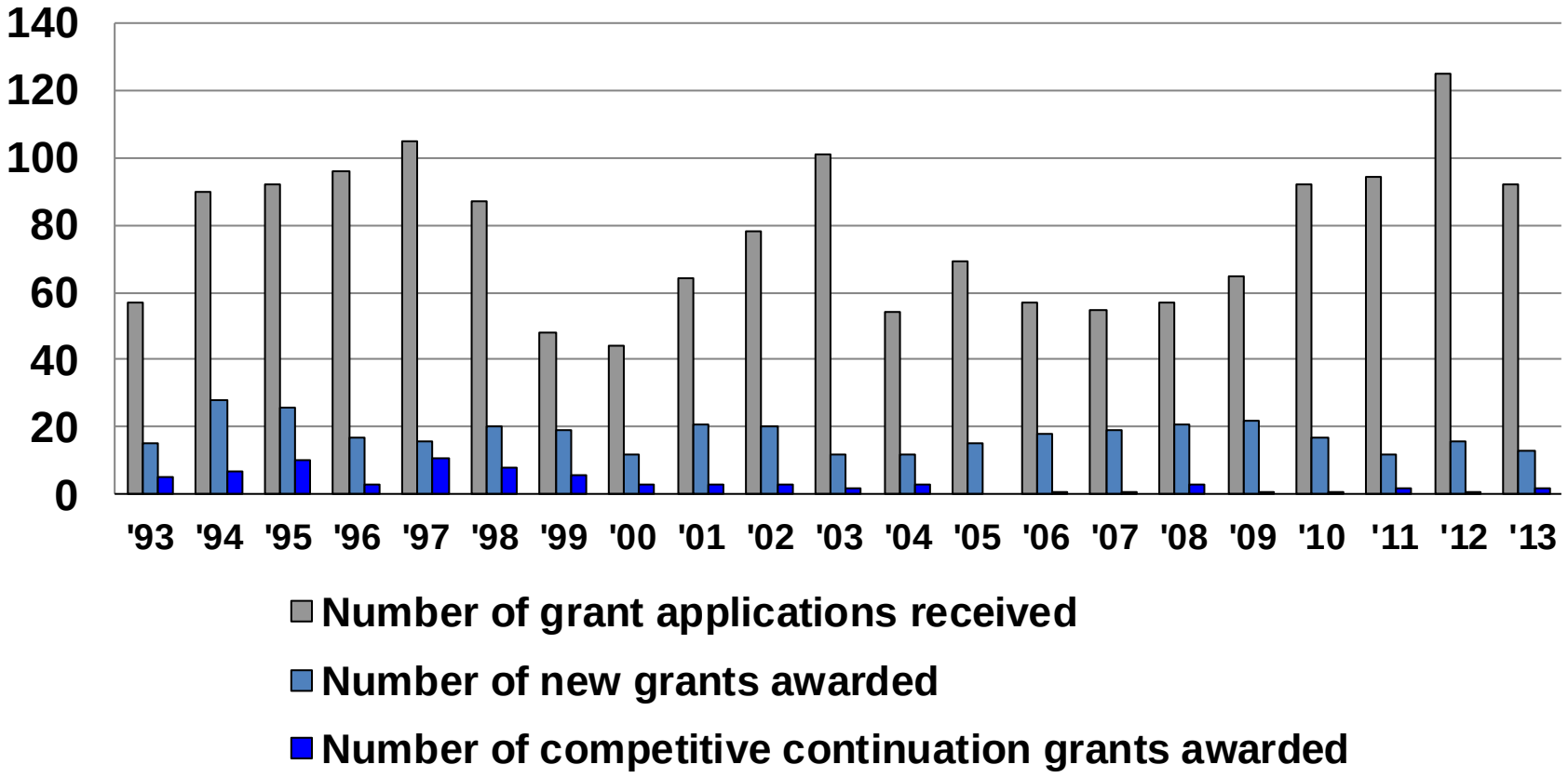
- Requirements:
  - **Clinical study** of an orphan disease or condition
  - A study must advance info towards a market approval
  - Must have active IND/IDE (not on clinical hold)
  - Good Clinical Practices (GCP)
  - Human Subjects Assurance from OHRP (Office of Human Research Protections) "Federal-Wide Assurance or FWA" (www.hhs.gov/ohrp)
  - IRB approval
  - Evidence that drug product is sufficiently available

- Funding dependent on **quality of application** and availability of Federal funds

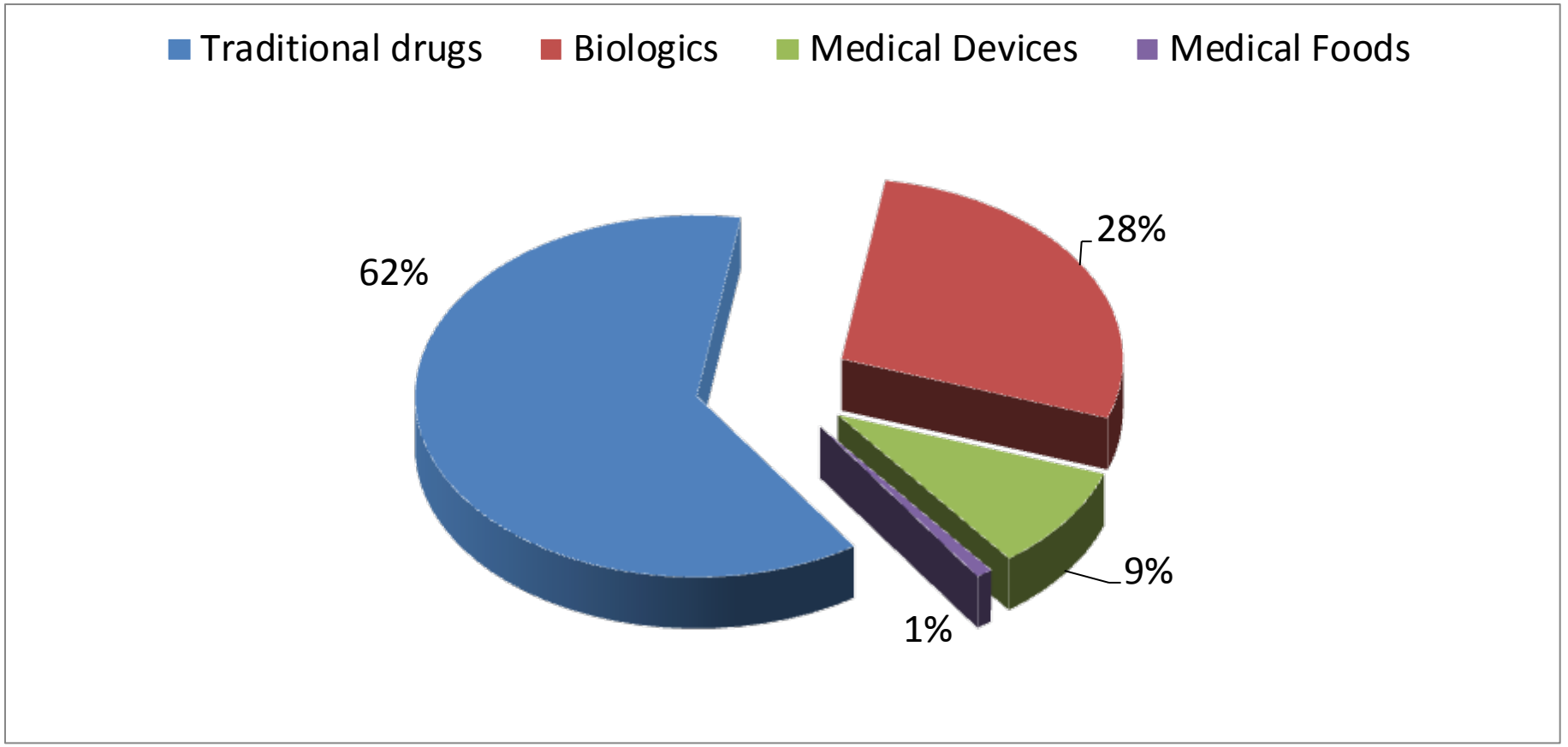
Budget

- The current annual budget for grant funding is approximately $14 million.
  - Clinical trials may be awarded (in total costs = direct and indirect) :
    - 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.

Annual Number of OPD Grant Applications and Grant Awards



Types of Products Currently Supported by Active OPD Grants



Composition of Orphan Grants

- 20% have a Phase 1 component
- 55% have a Phase 2 component
- 25% have a Phase 3 component
- About 20% of funding goes to small companies

Timeline Overview FY 2016

- Next **new** Request for Applications (RFA) receipt date – **February 2015**

  (**October 15, 2014** - next receipt date for resubmissions)

- **IND/IDE must be in effect at time of the grant application submission (IND/IDE must be active/approved and include the protocol for which funding is requested)**
- Protocol submitted to IND/IDE by January 2015
- Application summary statement - ~August 2015
- Earliest start date for award - November 2015
- All FY 2016 funding completed by September 2016

Grant Application Process

- Registrations
  - Request a DUNS number
  - Register with CCR (Central Contractor Registration)
  - Register with Credential Provider
  - Register with Grants.gov
  - Register eRA

Grant Application Process

- Grants.gov
  - Submit electronically through www.grants.gov
  - Follow instructions under "Apply for Grants"
    - Search using RFA information
    - Download copy of application package (SF-424RR) and instructions
      - "Applicant Help" section provides User's Guide, FAQs and other support
    - Complete offline
    - Upload and submit via grants.gov web site
    - Track status of application via grants.gov

Review Process

- Primary Review: Grants scored by independent ad hoc expert panels for technical merit
  - Criteria are in the RFA
    - Funding based on scores (100-500 – lower scores are better)
    - The recent fundable range was 100-140
  - Medical Officer of IND invited to participate in ad hoc panel
  - Summary Statements contain review specifics

Merit Criteria

Ad hoc expert panel reviews application based on the following scientific and technical merit criteria:

- Soundness of study rationale and design
- Appropriateness of statistical powering and plans for results analysis
- Evidence that the proposed number of subjects can be recruited in the requested timeframe
- Qualifications of the investigator and support staff and availability of resources
- Justification for financial support request
- Adequacy of plans for protection of human subjects and study monitoring
- Ability of applicant to complete study within its budget and within the time limits of the grant

Review Process

- Second Level review by a National Council (process approval)

- OPD Project Officer checks prefunding certifications prior to funding (check IRB, foreign sites, etc.)

Responsibilities of Applicants

- Response to Summary Statement Critiques & Complete OOPD Pre-Certification Form
- Maintain Regulatory requirements (IRB, FWA, IND, Clinicaltrials.gov, GCP)
- Verify an adequate supply of study product is available
- Set enrollment goals
- Quarterly progress reports to the grant
- Publication of study results encouraged
- Submit Type V Applications for following years with Progress report

How OOPD interacts with Grantees

- PO is assigned grant, introduces to grantee and review division RPM
- Establishes enrollment goals with grantee
- Ensures regulatory requirements maintained (IND ARs, IRB approvals, FWA, etc)
- Evaluates progress and makes recommendations for continued funding
- If issues with enrollment/study progress, PO will work with grantee. Always defer to Review Division for any study changes suggested (inclusion criteria/exclusion criteria/age/patient numbers, etc)

Future Years Support

- Future years of noncompetitive continuation of support depends on:
  - Performance during the preceding year
  - Compliance with regulatory requirements of IND/IDE
  - Availability of Federal funds

Grants Statistics

- To date, since 1983, FDA has provided more than $320 million for more than 530 grants for studies on rare diseases.
- Current annual budget ≈ $14-15 million
- >50 FDA approved products were at least partially funded through the OOPD Grants Program.

Approved Products Supported by Orphan Grants

- Examples of products partially funded by OOPD grants approved for marketing:
  - Kalydeco (ivacaftor): Cystic fibrosis
  - Berlin Heart EXCOR Pediatric Ventricular Assist Device: Bridge to cardiac transplantation for pediatric patients.
  - Xiaflex (collagenase): Dupuytren's disease
  - Folotyn (pralatrexate): Relapsed T-Cell non-Hodgkin's lymphoma
  - Anascorp (Centruroides (Scorpion) Immune F(ab')2 (Equine) Injection): Envenomation by poisonous scorpions in the US
  - Valchlor (mechlorethamine): Mycosis fungoides
  - Elaprase (idursulfase): Enzyme replacement therapy for patients with MPS II (Hunter Syndrome).

Funded Studies

- Search OOPD funded studies at:
  http://www.accessdata.fda.gov/scripts/opdlisting/oopdgrants/

- Clinicaltrials.gov

10 FDA Hints – Useful Homework

1. Start early, plan carefully, write clearly and objectively
2. Establish good relations w/ FDA review divisions via IND process. OPD invites FDA review divisions to the review as a resource (***FDA does not score the application***)
3. Read the RFA and instructions carefully not just for deadlines
4. Use the Grant Writing Tips from NIH Extramural Programs: http://grants.nih.gov/grants/grant_tips.htm
5. Contact OPD for program clarifications – see OPD contact information below

10 FDA Hints – Useful Homework

6. Contact FDA Grants Management for budget help: Vieda Hubbard (Vieda.Hubbard@fda.hhs.gov)
7. If you do not have expertise for issues, provide letters of collaboration for the needed expertise
8. Panel Reviewers are busy, so say it in fewer words if possible
9. Use outside readers improve the quality of the proposal
10. Don't be discouraged – read summary statements and address all critiques

Other Grant Opportunities

- **Other Federally funded grants**
  - Grants.gov- search under "find grant opportunities"
  - Small business funding opportunities:
    - Small Business Innovation Research (SBIR) program
    - Small Business Technology Transfer (STTR) Program
- **Patient Advocacy Groups**
  - NORD's Research Grant Program
    - Small grants to academic scientists studying new treatments or diagnostics for rare diseases. (www.rarediseases.org)
  - Disease Specific/Patient Advocacy Groups
- **International Opportunities**
  - International Rare Disease Research Consortium (IRDiRC)
    - Global effort to deliver 200 new therapies for patients with rare diseases by 2020

Other US Opportunities
(not necessarily grants)

NIH National Center for Advancing Translational Sciences (NCATS)

http://www.ncats.nih.gov/

Therapeutics for Rare and Neglected Diseases (TRND)

- provides drug development operational support such as medicinal chemistry, animal pharmacology, or IND enabling studies to advance the drug program
- Access to specialized expertise and resources to develop and execute a milestone-driven drug development program

BrIDGs (Bridging Interventional Development Gaps (Formerly called Rapid Access to Interventional Development (RAID))

- Support preclinical studies to enable submission of IND applications
- Not Grant Support but Services such as: production/bulk supply, GMP manufacturing, formulation, PK testing, animal tox, manufacture of clinical trial supplies

Office of Rare Diseases Research (ORDR)

- Scientific Conferences, Rare Diseases Clinical Research Network, Bench to Bedside (intra and extra-mural research)

Orphan Products Grants Program

- Contact:
  - Katherine Needleman, PhD
    Director of Orphan Products Grants Program
    (Katherine.Needleman@fda.hhs.gov)

*For more information, go to OOPD's website

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/WhomtoContactaboutOrphanProductDevelopment/default.htm