

**The Office of
Orphan Products Development
Grants Program**

The Food and Drug Administration

Sarah R. Linde-Feucht, M.D.

**Challenges in Drug Development for
Muscle Disease:
A Stakeholders Meeting
August 4-5, 2005
Bethesda, MD**



Objectives

- Explain the mission of the Office of Orphan Products Development (OOPD)
- Describe the major ways in which OOPD contributes to the development of therapies for rare diseases
- Describe the role of OOPD in advancing rare disease research



FDA Mission

Protect Public Health

Assure safety, efficacy, and security of:

- human drugs
- veterinary drugs
- biological products
- medical devices
- food supply
- cosmetics
- products that emit radiation



FDA Mission

Advance Public Health

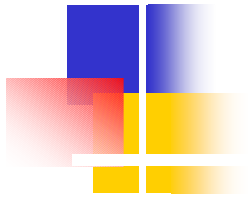
- Help speed innovations to make medicines and foods safer, more effective, and more affordable
- Help public get accurate, science-based information to use medicines and foods to improve their health



Where does OOPD fit in?

FDA Centers and Offices

- Center for Biologics Evaluation and Research (CBER)
- Center for Devices and Radiological Health (CDRH)
- Center for Drug Evaluation and Research (CDER)
- Center for Food Safety and Applied Nutrition (CFSAN)
- Center for Veterinary Medicine (CVM)
- National Center for Toxicological Research (NCTR)
- **Office of the Commissioner (OC)**
- Office of Regulatory Affairs (ORA)



The Mission of the Office of Orphan Products Development

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



What is an Orphan Product?

Drug, biologic, device, or medical food used in the diagnosis and/or treatment of patients with rare diseases



What is a Rare Disease?

- Affects fewer than 200,000 people in the United States
- Affects greater than 200,000 but cost of development exceeds recovery of expenses
- Considered “orphans” because pharma and device industries may have little or no interest in developing therapies for them



Why “orphans” exist

- Economic
 - Poor return on investment
- Regulatory
 - Obstacles in clinical trials



Why is our mission important?

- Between 10 and 20 million Americans suffer from one of the approximately 5,000 identified rare diseases
- In Europe, there may be 25 to 30 million citizens affected by rare diseases
- No effective treatment available
- 85% Serious/Life-Threatening
- 50% Pediatric



Examples of Rare Diseases

- Cystic fibrosis
- Lou Gehrig's disease
- Tourette's syndrome
- Hamburger disease
- Job syndrome
- Acromegaly



How do we achieve our mission?

- **Orphan Drug Designation Program**
- **Humanitarian Use Device Designation Program**
- **Grants Program**
- **Interacting with government agencies, medical and research communities, pharmaceutical and device industries, professional organizations, rare disease groups, and concerned citizens**

The Orphan Drug Act



- Signed January 4, 1983
- Established public policy that Federal Government could/would assist in the development of treatment for rare diseases
- Offers valuable incentives

Gray Days

Prior to Orphan Drug Act

- Fewer than 15 drugs approved for rare diseases
- Patients had limited pharmacotherapeutic options
- Limited clinical data for most drugs
- Drugs that were available prescribed “off-label”





The Orphan Drug Designation Program

- Determines eligibility for incentives of the Orphan Drug Act
- Application for designation submitted to OPD by sponsor
- Two of the criteria applied:
 - Prevalence < 200,000 in U.S.
 - Rationale for use of the drug



Orphan-Drug Designation Incentives

- Primary incentive: seven-year marketing exclusivity to the first sponsor obtaining FDA approval of a designated drug
- Other incentives:
 - Tax credit equal to 50% of clinical investigation expenses
 - Marketing application filing fee waivers
 - Assistance in drug development process
- Orphan products grant funding



Scope of Orphan Designations

- Included:
 - Drugs and biologics
 - Diagnosis, prevention, treatment
 - Not Included:
 - Veterinary Products
 - Medical foods*
 - Medical Devices* handled separately
- *Medical foods and medical devices to treat rare diseases are eligible for orphan grant funding.



Important Note:

- Orphan products must be just as safe and effective as other drugs approved by FDA
- Undergo same review standards as non-orphans
- Devices not included



Market Impact of Orphan Drug Act Incentives

- > 2032 designation requests
- > 1442 designated orphan products
- 267 approved orphan products



Examples of Orphan Drugs

- Tobramycin for Pseudomonas infection in patients with Cystic Fibrosis
- Xyrem (oxybate) in Narcolepsy
- Gleevec (Imatinib) in Chronic myelogenous leukemia
- Topamax (topiramate) in Lennox Gastaut syndrome
- Orfadin (nitisinone) in Tyrosinemia type 1



The Humanitarian Use Device Designation Program

- Manufacturers seeking premarket approval for new medical devices ordinarily must show that products are safe and effective.
- To encourage development of medical devices for rare diseases, FDA will approve such devices if manufacturers demonstrate the safety and probable benefit to patients.



The Humanitarian Use Device Designation Program

- A Humanitarian Device Exemption (HDE) is a provision that exempts sponsors of devices for orphan diseases from the effectiveness requirements of the medical device law, provided the device meets safety conditions and will not expose patients to significant or unreasonable risk.



The Humanitarian Use Device Designation Program

- A Humanitarian Use Device (HUD) is a medical device intended to benefit patients in the diagnosis and/or treatment of a disease or condition that affects or is manifested in fewer than 4,000 patients per year in the United States.



The Humanitarian Use Device Designation Program

Two-step process:

- HUD designation request submitted to OOPD.
- After HUD designation, an HDE application may be submitted to the Center for Devices and Radiological Health Office of Device Evaluation.



How does an HDE compare to a Premarket Approval (PMA)?

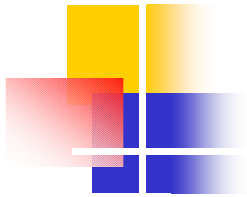
- Both are marketing approvals
- Approval thresholds differ:
 - PMA – safety and effectiveness
 - HDE – safety and probable benefit
- Institutional Review Board approval required for HDE
- Profit not allowed for HDE



Statistics

Since October 1996

- 155 HUD Requests received
- 104 Devices designated as HUDs by OOPD
- 38 Devices approved as HDEs by CDRH



Orphan Products Development Grants Program

- To encourage clinical development of products which demonstrate promise for rare diseases/disorders
- Funds clinical (not basic) research in rare diseases
- Since 1983, more than \$150 million awarded



Orphan Products Development Grants Program Overview

- Total budget: \$14.3 million FY 2006
- Award 10-15 new grants per year
- Manage 60-70 active grants
- Up to three years
 - \$200,000 Phase I
 - \$350,000 Phase II & III
- 39 approved products funded by OPD grants



Distribution of OOPD Grants

- Drugs approx. 80%
- Biologics approx. 14%
- Devices approx. 5%
- Medical Foods less than 1%



Examples of OOPD Grants

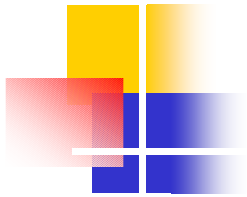
- Auditory Brainstem Implant for Neurofibromatosis
- Enzyme-Reactors for Management of Phenylketonuria
- Alendronate in Pediatric Gaucher Disease



Looking back 20 years....

- 1983
 - 8 awards/active grants
 - Budget: \$500,000

- 2003
 - 15 new awards
 - Portfolio of 70+ grants
 - Budget: \$13.3 million



Application Process

- Issue Request for Applications (RFA) annually in *Federal Register*
- Perform administrative review
- Convene ad hoc panel of outside experts for scientific review
- Prepare summary statements
- Present to Advisory Council
- Advise - Fund - Monitor



Application Process – Federal Register Notice

- Request for Applications (RFA)
 - Description of Funding Opportunity
 - Program Research Goals
 - Award Information
 - Grant
 - Amount
 - Length of support
 - Funding restrictions – Human Research Subjects Protection



Application Process – Federal Register Notice

- Request for Applications (RFA)
 - Application information
 - Dun and Bradstreet Number
 - Central Contractor Registration
 - Address to send application
 - Receipt Date(s)



Application Process – Federal Register Notice

- Request for Applications (RFA)
 - Eligibility
 - Foreign or domestic
 - Public or Private
 - For-profit or Non-profit
 - Local, State, and Non-HHS Federal Agencies



Application Process - Administrative Review

- **Study is a clinical trial**
- **Relevance to OOPD Grants Program goals**
- **Prevalence is fewer than 200,000 U.S. patients**
- **Study must be performed under an active IND/IDE (except medical foods)**
- **Budget is within limits**
- **Availability of sufficient product**
- **Protocol should be included in application**



Application Process - Scientific and Technical Review

- Soundness of the rationale
- Appropriateness of study design
- Statistical justification for proposed enrollment - POWER
- Potential for patient accrual
- Qualifications of investigator & support staff



Application Process - Scientific Review

- Adequacy of resources and environment
- Budget Justification
- Informed consent documents and IRB approval
- Potential for completion of study within stated time and budget



Application Process

- Scoring based on scientific and technical review
- Prepare summary statements
- Present to Advisory Council
- Advise - Fund - Monitor



Management of Funded Grants

- Assignment to Project Officer
 - Liaison between grantee and FDA review division
 - Enrollment goals/achievement
 - Quarterly progress updates
 - Site visits to assure grant compliance
 - Sponsor acquisition
- Continuation funding dependent on progress



Grants Program Accomplishments

- **39** Orphan products received FDA approval as a result of orphan grant funding
- Hundreds of publications, abstracts, and presentations have been produced as a result of orphan product grant studies



Summary

The mission of the Office of Orphan Products Development (OOPD) is to facilitate the development of products for rare diseases.



Summary

Four major ways in which OOPD contributes to this development:

- Orphan Drug Designation Program
- Humanitarian Use Device Designation Program
- Interacting with Government, Academia, Industry, and Community
- **Grants Program**



Resources

- Food and Drug Administration
 - Office of Orphan Products Development
 - 301-827-3666
 - 800-300-7469
 - www.fda.gov/orphan
- National Institutes of Health
 - Office of Rare Diseases
 - 301-402-4336
 - Rarediseases.info.nih.gov
- National Organization for Rare Disorders
 - 800-999-6673
 - www.rarediseases.org

