4th Eastern European Conference for Rare Diseases & Orphan Drugs
"Together for Integrative Approach to Rare Diseases"
June 13 - 14, 2009
Plovdiv, Bulgaria

Session 1 – USA Policy on Rare Diseases

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PRESENTATION OUTLINE

- Orphan Drug Act
- Office of Orphan Products Development (OOPD)
- OOPD Programs
  - Designations
  - HUDs
  - Grants
  - Outreach
- Additional Resources

The U.S. Orphan Drug Act Signed in 1983

Established the public policy that the Federal Government could/would assist in the development of products for the diagnosis, prevention or treatment of rare diseases or conditions.

Definition

- An orphan drug is defined in the 1984 amendments of the 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 FDA approval.

“Orphan” Diseases

- Affects <200,000 persons in the US
- Affects >200,000 in US, but no expectation that product development costs will be recovered from sales in the US
- Includes over 6,000 rare diseases
- Collectively affects approximately 25 million Americans
- Frequently serious/life threatening diseases

The Mission of The Office of Orphan Products Development

To assist and encoura
development, and ava
effective products for
diseases/disorders.

How does OOPD serve its Mission?

- Review orphan drug and humanitarian use device designation requests

- Awards and administers grants to support research in rare diseases

How does OOPD serve its Mission?

- Serves as liaison for the public, including medical product companies, FDA review divisions, patient advocacy groups, and other government agencies.

- Provides patients, health care providers and drug sponsors with information regarding the orphan products program and about the FDA review and approval process

What the OOPD Does NOT do

- Pricing
- Access/Insurance
- Intramural research
- Pre-Clinical research

INCENTIVES THROUGH OOPD

DESIGNATION

of ORPHAN STATUS

What Drugs Can Be Designated?

- Eligibility:
  - A previously unapproved drug
  - A new orphan indication for an approved drug
  - The “same drug” as one already approved but with a potential to be “clinically superior”
- Designation request submitted prior to filing a New Drug Application (NDA) for marketing

Incentives
Orphan-Drug Designation

- 7-year marketing exclusivity to the first sponsor obtaining FDA approval of a designated drug – stronger than a patent
- 7.5 year marketing exclusivity for pediatric indications
- Tax credit equal to 50% of clinical investigation expenses
- Exemption/Waiver of application (filing) fees (PDUFA)

Marketing Exclusivity

- Company receives 7 or 7.5 (pediatric indication) years of marketing exclusivity upon FDA approval of a specific orphan drug for a specific indication.

How does this help the company?

- FDA cannot approve the same drug for the same indication during the exclusivity period; this is stronger than a patent

Tax Credits for Orphan Designated Products

- A 50% tax credit for clinical research and testing expenses

How does this help the company?

- The credit can be applied to Federal taxes incurred in the prior year and for up to 20 years against future taxes

Marketing Application Fee for Orphan Designated Products

- In the Orphan Drug Act, Congress exempted designated orphan products from the user fee requirement

How does this help the company?

- In FY 2009, the company would save the user fee of $1,247,200 per application, which would otherwise be paid to FDA whether their product is approved or not

To Obtain Designation

- Sponsor submits designation request to FDA/OOPD
- OOPD Staff review requests
- Criteria:
  - Is population < 200,000 in the U.S. (prevalence)?
  - Is there scientific rationale for the use of the drug in the proposed indication/disease/condition?

Solving the Worldwide "Orphan" Disease Problem - Globally

- Throughout the world, there are many diseases that affect few individuals.
- Rare diseases do not recognize borders.
- Improved communication has made the world a smaller place.
- Development of rare disease therapies should be coordinated globally.

New Joint Template Form for US and EMEA

- Established November 2007
- Can be submitted for orphan designation to US and EMEA
- Form FDA 3671 (http://intranet.fda.gov/omp/forms/internal/FDA-3671_508.pdf)

And then what?

- Once designated, OOPD will work with the sponsor and the FDA Reviewing Division in the development of the product.
- OOPD does not review the product for safety and efficacy.
- OOPD does not approve the product for marketing
- OOPD is the ombudsman for patients and the product to treat them.

The Development of a Drug for a Rare Disease

- The development of a drug product to treat a rare disease – same as for a common disease.
- 2 well-controlled clinical trials
- Must meet the FDA statutory standards for safety and effectiveness.

Successes Since 1983

- **2780** Designation requests submitted
- Approximately **2000** products have received orphan-drug designation.
- **336** orphan-designated products have received FDA approval for marketing.
- Approved orphan-designated products are available to treat patient populations totaling **25 million** in the U.S.

Recent FDA Approvals of Designated Drugs

- Cyanokit (hydroxocobalamine) – Cyanide Poisoning
- Revlimid (lenalidomide) – Multiple Myeloma
- Myozyme (alpha-glucosidase) – Glycogen Storage Disease Type II
- Elaprase (idursulfase) Mucopolysaccharidosis II
- Kuvan (saproterin) – Hyperphenylalanemia
- Treanda (bendamustine HCl) - Chronic Lymphocytic Leukemia
- Xenazine (Tetrabenazine) – Huntington's Disease

Incentives Through OOPD

Humanitarian Use Devices (HUD)

How are Devices Designated?

- A HUD is a medical device intended to treat or diagnose a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year *(incidence).*
- A HUD may undergo further review to determine if it qualifies for a Humanitarian Device Exemption (HDE) through FDA's Center for Devices and Radiological Health. FDA approval of a HDE authorizes marketing of the HUD.

Why Humanitarian Device Exemptions?

- Premarket approval applications for new medical devices *ordinarily* must show that products are safe and **effective**.

- For very rare diseases, FDA will approve such devices if manufacturers demonstrate the safety and **probable benefit** to patients.

- This exemption from the effectiveness standards is the HDE (Humanitarian Device Exemption) provision.

What is a HUD? An HDE?

HUD = Device treating a disease affecting <4,000 in the US per year (incidence)

HDE refers to the exemption for a device to receive approval based on its probable benefit

A few points about HUDs….

- Not for profit (unless pediatric device – see FDAAA 2007)
- Device to be used with facility IRB approval
- No comparable device marketed

What is a HUD? An HDE?

- 209 HUD requests received – 132 granted (63%)
- 49 HDE Humanitarian Device Exemption Marketing Approval via CDRH with probable benefit outweighing the risks

Recent Humanitarian Device Exemption (HDE) Approvals

- Reclaim Deep Brain Stimulation for Obsessive Compulsive Disorder Therapy (Medtronic Neuromodulation)
- IBV Valve System (Spiration, Inc.; used for air leaks of the lung)
- Infuse/Mastergraft Posterolateral Revision Device (Medtronic Sofamor Danek; repair of symptomatic, posterolateral lumbar spine pseudoarthrosis
- Levitronix Centrimag Right Ventricular Assist System (Levitronix LLC; cardiogenic shock due to acute right ventricular failure)

Contacts

- 1. Request for HUD Designation
  - Office of Orphan Products Development: http://www.fda.gov/orphan/HUDS
  - Contact: Debra Lewis, OD, MBA: 301-827-0059 or Debra.Lewis@fda.hhs.gov

- 2. HDE application
  - Center for Devices and Radiological Health/ODE: http://www.fda.gov/cdrh/ode/guidance/1381.pdf
  - Contact: Stephen Rhodes 240-276-4036

INCENTIVES THROUGH OOPD

GRANTS PROGRAM

Orphan Products Grants Program

- **Goal** of the Grants Program: to encourage clinical development of products, including drugs, biologics, medical devices, or medical foods, for use in rare diseases or conditions (affecting <200,000 individuals in the U.S).

Orphan Products Grant Program

- Also, a practical program for advancing marketing approvals and relevant publications that impact on rare diseases

Orphan Products Grants Program

- Request for Application (RFA) available at http://www.fda.gov/orphan
- Application, review, and scoring much like NIH grant application
- Electronic submissions: http://grants.gov

Orphan Products Grants Program

- Approximately 85-95 applications per year
- Competitive grant program – ~30% success
- Fund about 15-20 new grants per year
- Supports academic and industry sponsored research
- Domestic or foreign, public or private, for-profit or nonprofit entities

OPD Grants Program: Requirements

- Clinical studies to be conducted under:
  - **ACTIVE** IND or IDE
  - Good Clinical Practices (GCP)
  - Human Subjects Assurance from OHRP “Federal-Wide Assurance or FWA” (www.hhs.gov/ohrp)
  - IRB approval
  - Rare disease but designation not required.

OPD Grants Program: Budget

- The current annual budget for grant funding is approximately $14 million
  - Clinical trials may be awarded:
    - Up to $200,000 (Phase 1) per year for up to 3 years

    Or

    - Up to $400,000 (Phase 2 and 3) per year for up to 4 years

OPD Grants Program: Review Process

- Primary Review: Grants scored by independent ad hoc expert panels for technical merit
- Second Level review by a National Council (process approval)

Overview Timeline FY 2010 Grant Program

- Next application receipt date – February 3, 2010

- IND/IDE must be in effect at time of the grant application submission (IND must be active and include the protocol for which funding is requested)

Grants Statistics

- To date, since 1983, FDA has provided more than $246 million for more than 500 grants for studies on rare diseases.
- Current annual budget ≈ $14 million
- 43 FDA approved products were at least partially funded through the OOPD Grants Program.

INCENTIVES THROUGH OOPD

OUTREACH

OOPD Outreach

- OOPD assistance in drug development process
  - Liaison with FDA Reviewing Divisions
- Working with the public-interest and advocacy groups to identify concerns and resources.
- Informing academia and industry of the incentives and opportunities for developing products for use in rare diseases or conditions.

Role of Rare Disease Patient Organizations

- Importance cannot be over emphasized! Patient groups are extremely important

- Why?
  - Promote understanding and knowledge of the disease – including natural history
  - Assist in patient recruitment
  - Mutual support and understanding to each other

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) 827-3666

Is the Orphan Drug Act a Success?

- More than 336 drugs and biological products for rare diseases have been brought to the U.S. market since the Act in 1983
- In contrast, less than 10 such products for rare diseases came to market in the decade prior to 1983
- About 43 products Approved through the Grants Program
- More than 25,000,000 patients treated

Questions