FDA Drug Topics: FDA’s Office of Orphan Products Development (OOPD) – An Overview and Update

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CAPT Nicole Wolanski
Objectives

• Describe the mission of Office of Orphan Products Development (OOPD)

• Define rare disease in accordance with the Orphan Drug Act

• Identify the incentives associated with orphan drug designation
Rare Disease Statistics

- ~7,000 known rare diseases
- Individually rare but collectively affect ~25-30 million Americans of all ages and millions more worldwide
- Chronic, progressive, life-threatening, and/or fatal

www.fda.gov

Lou Gehrig (1903-1941)
Background/History

- Industry reluctant to develop drugs for small populations ("orphan diseases", "orphan drugs")
Abbey Meyers formed a coalition of patient advocates; later became the National Organization for Rare Disorders (NORD) (www.rarediseases.org)
One of Many Rare Disease Heroes

Henry Waxman & Orrin Hatch

Representative Henry Waxman was the principal author of the original 1983 Orphan Drug Act (ODA). Senator Orrin Hatch was a co-sponsor and champion of the ODA. The ODA provided the first meaningful incentives to sponsors to develop needed medical products for the estimated 25 million Americans with rare diseases, defined under the ODA as diseases or conditions that affect fewer than 200,000 people in the United States. Fewer than 10 products supported by industry for rare diseases came in market between 1973 and 1983. Since its passage over 400 products for rare diseases have been approved.

One of Many Rare Disease Heroes

Medical drama “Quincy, M.E.”
(1976-1983)
Orphan Drug Act

• President Ronald Reagan signed into law January 4, 1983

• Main provisions
  – Establishes definition of a rare disease/condition
  – Provides financial incentives for developing orphan products
Orphan Drug Act: Definition of a rare disease

- Affects <200,000 persons in the U.S., or
- Affects >200,000 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug
Orphan Drug Act: Designation Incentives

- 25% tax credit for qualified clinical trials
- Exempt from PDUFA application fee (currently ~$2.9 million)
- 7-year market exclusivity
  - CFR Title 21 Part 316.31
Orphan Drug Act: Grants for Orphan Products

- Orphan Product Grant programs support research of promising therapies for rare disease patients
Office of Orphan Products Development (OOPD)

- Established in 1982
- Tasked to administer some provisions of the Orphan Drug Act
- **Vision**: The availability of safe and effective products for patients who live with rare diseases
Office of Orphan Products Development (OOPD)

• Mission - to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions
  – Evaluates scientific and clinical data submissions from sponsors to identify and designate products as promising for rare diseases and to further advance scientific development of such promising medical products
  – Works on rare disease issues with the medical and research communities, professional organizations, academia, governmental agencies, industry, and rare disease patient groups
Where is OOPD within FDA?
# OOPD Core Programs

## DESIGNATION PROGRAMS

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<th>Program Name</th>
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<td>1</td>
<td>Orphan Drug Designation &amp; Exclusivity</td>
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</table>
| 2 | Rare Pediatric Disease (RPD) Designation          | * Disease or condition must be rare and its serious or life-threatening manifestations must occur in individuals 18 years and younger*  
     |                                                 | * Co-administer with Office of Pediatric Therapeutics as of May 15, 2017*  
     |                                                 | * Part of the RPD Priority Review Voucher Program*                                                                                         |
| 3 | Humanitarian Use Device (HUD) Designation         | * Part of the HUD/HDE pathway*  
     |                                                 | * Disease or condition is not more than 8,000 individuals in the US per year*                                                             |

## GRANT PROGRAMS

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<tr>
<td>1</td>
<td>$15.5M Orphan Products Clinical Trials Grant Program</td>
<td>* Funding and monitoring 75 rare disease clinical trials*</td>
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</table>
| 2 | $6M Pediatric Device Consortia Grant Program      | * Appropriations increased from $3M to $6M in FY2017*  
     |                                                 | * Funding and monitoring 5 different consortia*                                                                                             |
| 3 | $2M Orphan Products Natural History Grant Program |                                                                                                                                                                                                       |
Orphan Drug Designation & Exclusivity

- Goal: Stimulate development of drugs/biologics for rare diseases
- OOPD roles/responsibilities:
  - Review applications/requests for orphan designation
  - Grant special status (“orphan designation”) to products that meet eligibility criteria (prevalence <200,000, sufficient scientific rationale)
- Designated products may qualify for special financial incentives (tax credit, exemption from user fee, 7-year exclusivity)

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# Orphan Drug Designation & Exclusivity

## DESIGNATION PROGRAMS

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<td>Orphan Drug designation</td>
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<td>Orphan drug exclusivity</td>
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**1. Orphan Drug Designation & Exclusivity**

- Orphan drug designation: a specific disease or condition
- Orphan drug exclusivity: a specific approved indication or use
7-year Orphan Exclusivity

• Seven years of market exclusivity: FDA cannot approve same drug for same indication
  ➢ if the drug is approved for an indication within scope of the orphan designation; and
  ➢ the same drug has not been previously approved for the same indication
• Only to the first sponsor to receive approval for that drug for the orphan designated indication
7-year Orphan Exclusivity

- Distinct from other exclusivities
- Determined by OOPD upon marketing approval
- OOPD sends letter to recognize exclusive approval per 21 CFR 316.34(a), then identified in Orange Book
- Exclusivity can be “broken” in cases of:
  - Drug shortage
  - Another drug is clinically superior to the approved drug
Statistics and Recent Approvals

• Since inception (1983)
  – Designations: >5,800
  – Approvals: >950 product indications (for >250 rare diseases)

• Recent approvals
  – Zokinvy (lonafarnib) – Hutchinson-Gilford progeria syndrome and progeroid laminopathies
  – Orladeyo (berotralstat) – hereditary angioedema
  – Tecartus (brexucabtagene autoleucel) – mantle cell lymphoma
  – Sevenfact (coagulation factor VIIIa (recombinant)-jncw) – hemophilia A or B with inhibitors
Orphan Designations and Approvals

https://www.accessdata.fda.gov/scripts/opdlisting/oopd/
Orphan Drug Designation Trends

Note: Designations granted in a given year may include requests received from that year as well as previous years.
Rare Pediatric Disease (RPD) Designation

- **Goal:** Stimulate development of products for rare diseases in pediatric patients

- **OODP roles/responsibilities:**
  - Co-administered with Office of Pediatric Therapeutics (OPT)
  - Grant special status ("RPD designation") to products that meet eligibility criteria (prevalence <200,000; serious/life-threatening manifestations primarily affect those ≤18 yo)

- Designated products may qualify for RPD Priority Review Voucher Program
Statistics and RPD Vouchers

• Since inception (2012)
  – RPD designations: >560
  – RPD vouchers: 28

• RPD vouchers
  – May be redeemed to receive a priority review of a subsequent marketing application for a different product
  – May be transferred (including by sale)
  – 14 vouchers have been sold ($67.5-350 million)
RPD Designation Trends

Rare Pediatric Drug Designations by Year (CY2013-2020)

- No. Original Request Received
- No. Amendment Request Received
- No. Designations

<table>
<thead>
<tr>
<th>Year</th>
<th>Original Requests</th>
<th>Amendments</th>
<th>Designations</th>
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<tr>
<td>CY 2013</td>
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<td>14</td>
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<td>CY 2015</td>
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<td>CY 2019</td>
<td>2</td>
<td>66</td>
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<tr>
<td>CY 2020</td>
<td>25</td>
<td>284</td>
<td>241</td>
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Humanitarian Use Device (HUD) Designation Program

- Goal: Stimulate development of medical devices for rare diseases

- OOPD roles/responsibilities:
  - Review applications/requests for HUD designation
  - Grant special status (“HUD designation”) to products that meet eligibility criteria (incidence <8,000/year, sufficient scientific rationale)

- HUD-designated products may qualify for Humanitarian Device Exemption (HDE) pathway (safety + “probable benefit”)

DESIGNATION PROGRAMS

1. Orphan Drug Designation & Exclusivity
2. Rare Pediatric Disease (RPD) Designation
3. Humanitarian Use Device (HUD) Designation
Statistics

• Since inception (1990)
  – Requests received: >460
  – Designated HUDs: >280
  – HDE approvals: 78
HUD Designation Trends

Humanitarian Use Device Designations by Year
(CY2012 - 2020)
Orphan Products Grants Video
Clinical Trials Grant Program

- Provide funding for clinical studies that contribute to market approval of orphan products
- Budget: ~ $15.5 million/year
  - Phase 1: Up to $250,000/year x 3 years
  - Phases 2 & 3: Up to $500,000/year x 4 years
  - Fund ~75 studies/year (~$5.5 million for new grants, ~$10 million for non-competing continuation grants)
OOPD Roles and Responsibilities

- **Review grant applications**
  - Primary review (active IND, prevalence <200,000)
  - Ad hoc review panel (medical need, scientific merit, qualifications of investigators, potential for marketing approval, budget)
  - Best cored applications funded

- **Oversee funded grants**
  - Enrollment goal
  - Review quarterly updates
  - Review annual progress updates
  - Conduct teleconference grant evaluations/site visits

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<td>Orphan Products Natural History Grant Program</td>
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Statistics & Studies Funded

• Since inception (1983):
  – Applications received: >2,800 (100/year)
  – Studies funded: >750
  – Approved products supported by OOPD grants: ~75

GRANT PROGRAMS

1. Clinical Trials Grant Program
2. Pediatric Device Consortia Grant Program
3. Orphan Products Natural History Grant Program
Examples of Approved Products Supported by Orphan Grants

- Triheptanoin (Dojolvitm) for long-chain fatty acid oxidation disorders (LC-FAOD)
- Teprotumumab (Tepezza) for Thyroid Eye Disease
- Cysteamine bitartrate (Procysbi) for Nephropathic Cystinosis
- Deferiprone (Ferriprox) for Iron overload in hematologic disorders requiring chronic transfusion therapy
- Ivacaftor (Kalydeco) for Cystic Fibrosis Subjects with G551D
- Dinutuximab (Unituxin) for Neuroblastoma
- Mepolizumab (Nucala) for Hypereosinophilia
- Sirolimus (Rapamune) for Lymphangioleiomyomatosis
- Berlin Heart EXCOR® Pediatric Ventricular Assist Device (VAD) for Bridge to heart transplantation in children

www.fda.gov
Orphan Products Grants

https://www.accessdata.fda.gov/scripts/opdlisting/oopdgrants/
Pediatric Device Consortia (PDC) Program

- Goal: Stimulate development of devices for pediatric patients
- Funds consortia (networks); not a direct research grant
  - Consortia support pediatric device developers
- Budget: $6 million
  - $1—$1.35 million/year up to 5 years
  - Currently funds 5 PDCs
Statistics & Approved Products

- Pediatric device projects assisted: >2,000
- Legally marketed devices supported by PDC
  - AtriCure Inc. Cryo2 cryoICE cryo-ablation probe
  - The 410 Medical Inc. LifeFlow® Blood System
Natural History Grant Program

- Provide funding for studies that characterize the natural history of rare diseases
- **Budget: ~ $2 million**
  - Retrospective: Up to $150,000/year x 2 years
  - Prospective: Up to $400,000/year x 5 years
  - Funds 2-5 studies/year

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OOPD Roles and Responsibilities

- Review process similar to Clinical Trials Grant Program
  - First review (for responsiveness)
  - Second review (external ad hoc panel of experts)
  - Final awards determined by rank ordered priority scores

- Management of funded grants similar to Clinical Trials Grant Program
  - Project officer monitors progress of study
Rare Disease Day 2021

https://www.fda.gov/industry/orphan-products-development-events/fda-rare-disease-day-2021
Summary

• Orphan Drug Act (ODA) stimulates orphan product development
  – 1983-present: >950 approved indications for >250 rare diseases

• ODA inspired implementation of orphan legislation worldwide

• Still a great need for patients with rare disease
  – ~7,000 rare diseases still need safe and effective treatment
Additional Resources

• [www.fda.gov/orphan](http://www.fda.gov/orphan)
Challenge Question #1

The mission of OOPD is to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

A. True
B. False
Challenge Question #2

Per the Orphan Drug Act, a definition of a rare disease is that it affects:

A. <200,000 persons in the U.S.
B. <300,000 persons in the U.S.
C. <200,000 persons worldwide
Challenge Question #3

Orphan drug designation provides which of the following incentives:

A. 25% tax credit for qualified clinical trials
B. Exemption from PDUFA application fee for NDA
C. Potential eligibility for 7-year market exclusivity
D. All of the above
Challenge Question #4

OOPD programs include 3 designation programs and 3 grants programs.

A. True
B. False
References

• Developing Products for Rare Diseases & Conditions: https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/default.htm.
• Designating an Orphan Product: Drugs and Biological Products https://www.fda.gov/industry/developing-products-rare-diseases-conditions/designating-orphan-product-drugs-and-biological-products
• Rare Pediatric Disease Designation Program: https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDisease PriorityVoucherProgram/default.htm.
• About Orphan Products Grants https://www.fda.gov/industry/developing-products-rare-diseases-conditions/about-orphan-products-grants
• Pediatric Device Consortia Grants Program https://www.fda.gov/industry/developing-products-rare-diseases-conditions/pediatric-device-consortia-grants-program