



**U.S. FOOD & DRUG  
ADMINISTRATION**

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



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# 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

myasthenia gravis

Idiopathic pulmonary fibrosis

pulmonary arterial hypertension



pancreatic cancer

graft-versus-host disease

leukemia

# Rare Disease Statistics

cystic fibrosis

glioblastoma

lymphoma

Pompe disease

thalassemia

- ~7,000 known rare diseases<sup>1</sup>

Duchenne muscular dystrophy

Huntington's disease

- Individually rare but collectively affect ~25-30 million Americans of all ages and millions more worldwide<sup>1</sup>

multiple myeloma

malaria

hemophilia

retinitis pigmentosa

tuberculosis

- Chronic, progressive, life-threatening, and/or fatal

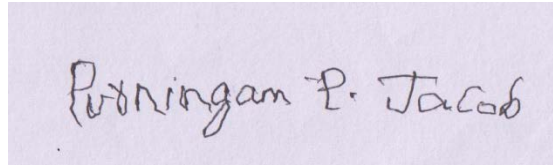
Prader-Willi syndrome

hepatocellular carcinoma

homozygous familial hypercholesterolemia



Lou Gehrig  
(1903-1941)



# Background/History

- Industry reluctant to develop drugs for small populations (“orphan diseases”, “orphan drugs”)

*One of Many  
Rare Disease Heroes*



**Abbey Meyers**

Abbey Meyers pioneered the development and passage of the 1983 Orphan Drug Act, catalyzed by her experience as a parent of a child with Tourette syndrome who lost access to an experimental orphan drug. Through Abbey's efforts, the voices of those with rare diseases were amplified throughout industry and government. Abbey continued to educate and advocate for rare diseases through her work as the founder of the National Organization of Rare Disorders (NORD).





Abbey Meyers formed a coalition of patient advocates; later became the National Organization for Rare Disorders (NORD) ([www.rare diseases.org](http://www.rare diseases.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 to market between 1973 and 1983. Since its passage over 400 products for rare diseases have been approved.

*One of Many Rare Disease Heroes*

**Media/Entertainment Industry**

In the early 1980's Jack Klugman, star of the television series, "Quincy," successfully raised public awareness about rare disease issues by highlighting them in two "Quincy" episodes. He even testified before Congress. Since that time, media has continued to spotlight rare diseases in television, such as "House" and "Mystery Diagnosis," and in films, such as "The Elephant Man" and "Extraordinary Measures."




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  $\geq 200,000$  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)

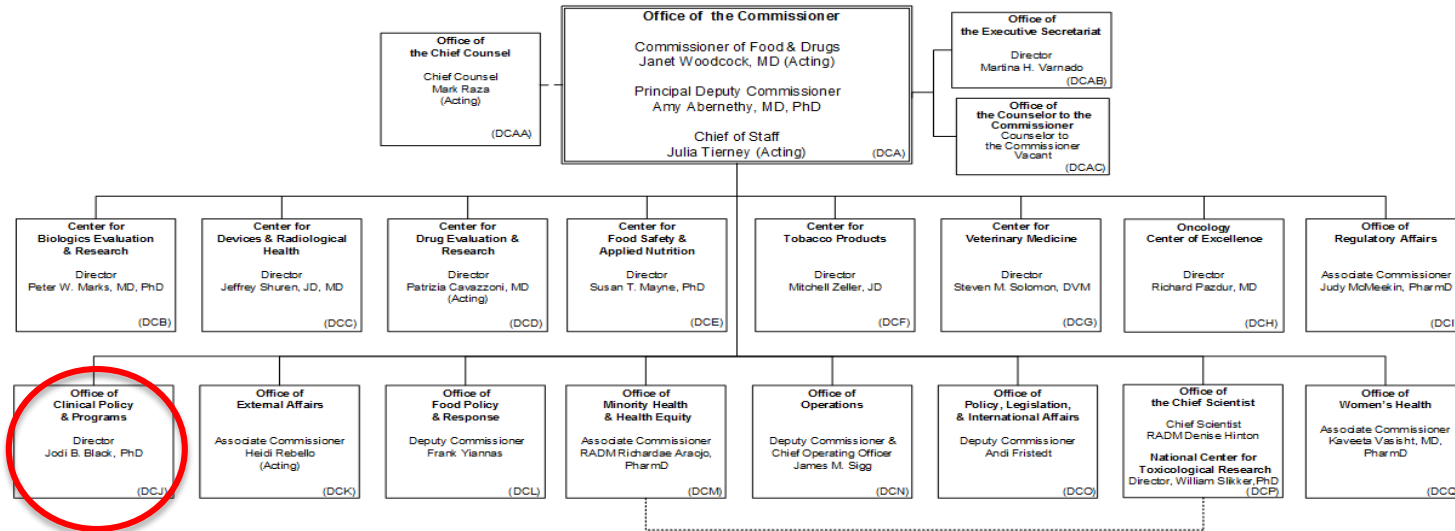
- Mission - to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions
  - Evaluates scientific and clinical data submissions from sponsors to identify and designate products 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?



## Department of Health and Human Services Food and Drug Administration

March 2021



**Legend**  
- - - Direct report to DHHS General Counsel  
..... Direct report to the FDA Commissioner with operational oversight from the Office of the Chief Scientist

# OOPD Core Programs

## DESIGNATION PROGRAMS

<b>1</b>	<b>Orphan Drug Designation &amp; Exclusivity</b>
<b>2</b>	<b>Rare Pediatric Disease (RPD) Designation</b> <ul style="list-style-type: none"> <li><i>Disease or condition must be rare and its serious or life-threatening manifestations must occur in individuals 18 years and younger</i></li> <li><i>Co-administer with Office of Pediatric Therapeutics as of May 15, 2017</i></li> <li><i>Part of the RPD Priority Review Voucher Program</i></li> </ul>
<b>3</b>	<b>Humanitarian Use Device (HUD) Designation</b> <ul style="list-style-type: none"> <li><i>Part of the HUD/HDE pathway</i></li> <li><i>Disease or condition is not more than 8,000 individuals in the US per year</i></li> </ul>

## GRANT PROGRAMS

<b>1</b>	<b>\$15.5M Orphan Products Clinical Trials Grant Program</b> <ul style="list-style-type: none"> <li>Funding and monitoring 75 rare disease clinical trials</li> </ul>
<b>2</b>	<b>\$6M Pediatric Device Consortia Grant Program</b> <ul style="list-style-type: none"> <li>Appropriations increased from \$3M to \$6M in FY2017</li> <li>Funding and monitoring 5 different consortia</li> </ul>
<b>3</b>	<b>\$2M Orphan Products Natural History Grant Program</b>

# Orphan Drug Designation & Exclusivity

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

- 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)



# Orphan Drug Designation & Exclusivity

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

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)

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

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

# Orphan Designations and Approvals



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## Search Orphan Drug Designations and Approvals

● FDA Home ● Developing Products for Rare Diseases & Conditions

This page searches the Orphan Drug Product designation database. Searches may be run by entering the product name, orphan designation, and dates. Results can be displayed as a condensed list, detailed list, or an Excel spreadsheet. [Click for detailed instructions.](#)

### Search Criteria

Due to a system limitation, if your search text for "Product Name" or "Orphan Designation" includes non-English keyboard characters (e.g., ß), the search results will not display. To perform your search, use a wildcard character (% or \*) before the search text or at the end of the search text. For example, to search for "ß-thalassemia," enter "%-thalassemia" or "thalassemia%" in the search box.

Product Name:

Orphan Designation:

Start Date:  End Date:  (default is all dates)

Search results:

Output format:  (Note: The information contained in the downloadable Excel file for the "CF Grid Key" column is for FDA purposes only.)

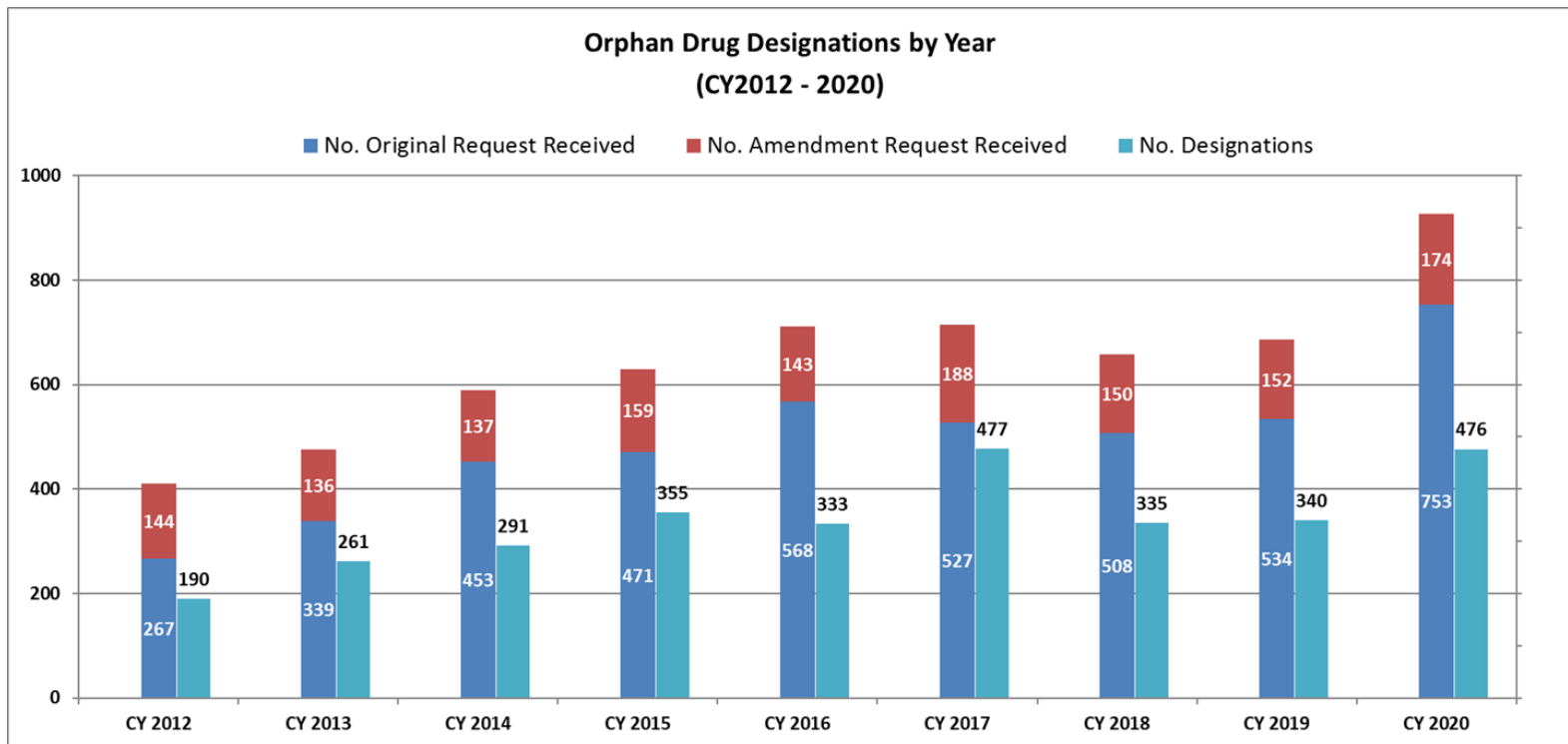
Sort results:

Records per page:

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<https://www.accessdata.fda.gov/scripts/opdlisting/oopd/>

# Orphan Drug Designation Trends

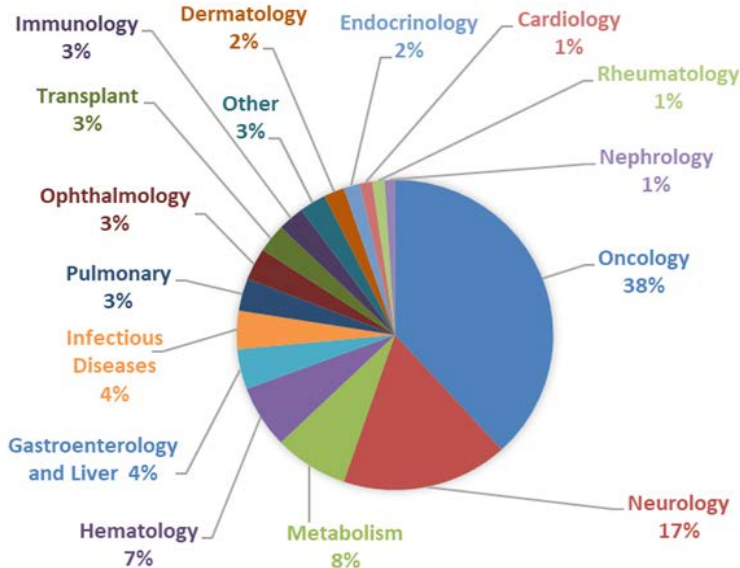


Note: Designations granted in a given year may include requests received from that year as well as previous years.

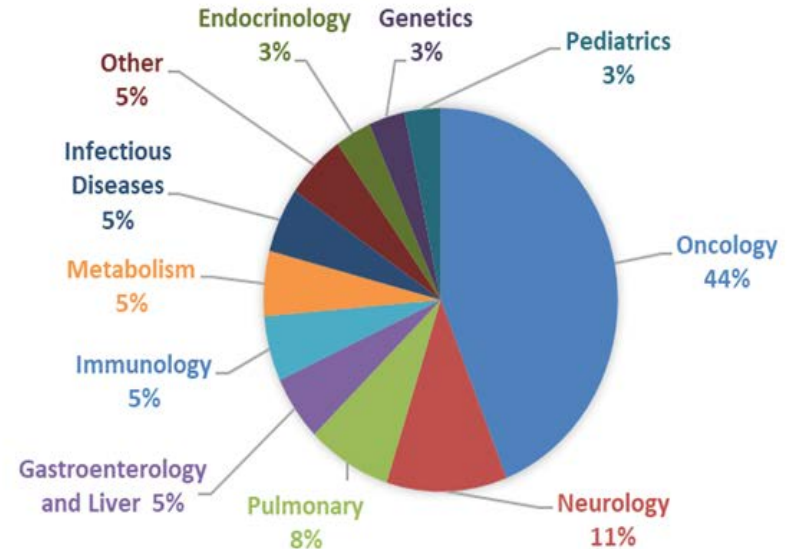
# Orphan Drug Designations and Approvals by Treatment Category in 2020



Orphan Drug Designations by Treatment Category in 2020



Orphan Approvals by Treatment Category in 2020



# Rare Pediatric Disease (RPD) Designation

DESIGNATION PROGRAMS	
1	Orphan Drug Designation & Exclusivity
2	Rare Pediatric Disease (RPD) Designation
3	Humanitarian Use Device (HUD) 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  $\leq 18$  yo)
- Designated products may qualify for RPD Priority Review Voucher Program

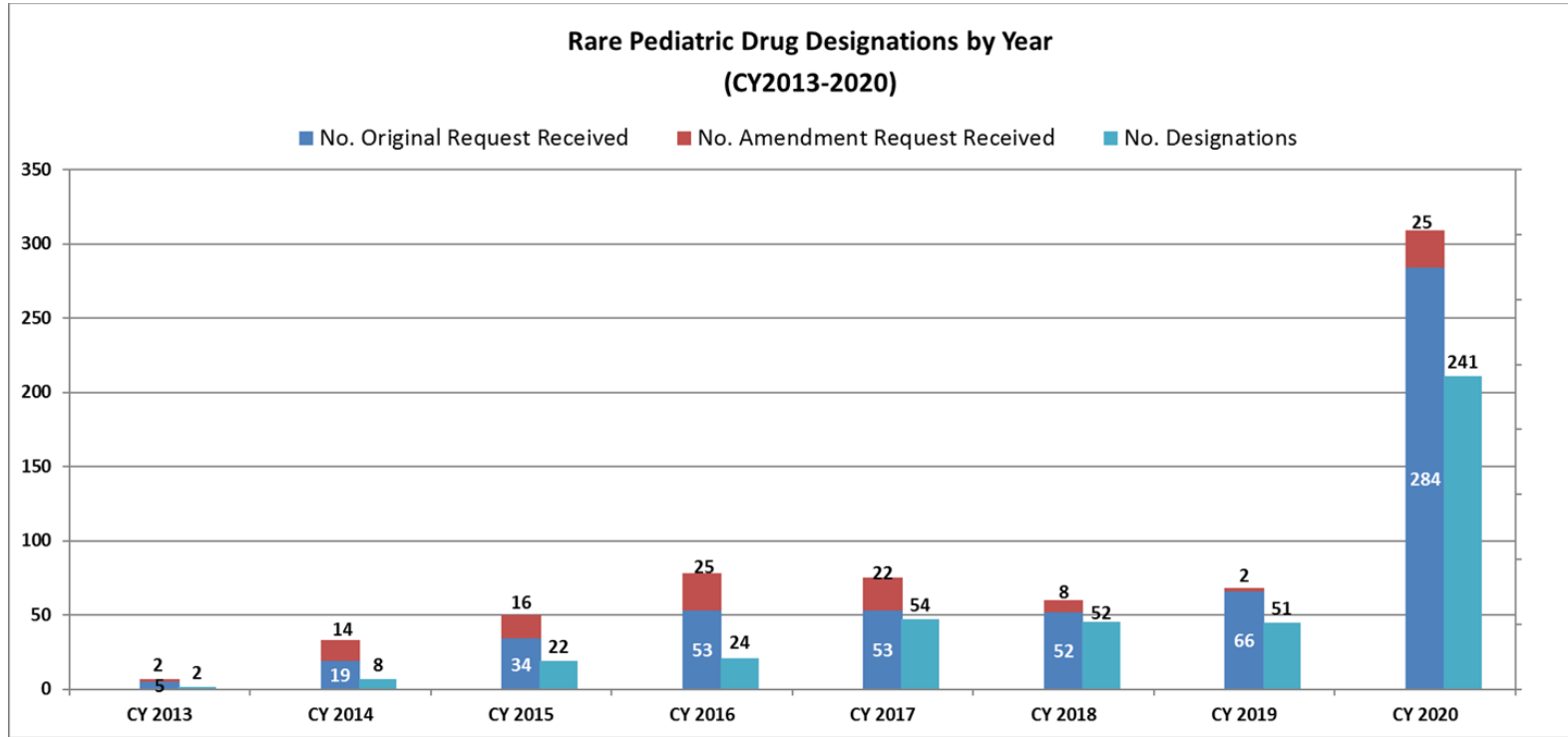


# Statistics and RPD Vouchers

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

- 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



# Humanitarian Use Device (HUD) Designation Program



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

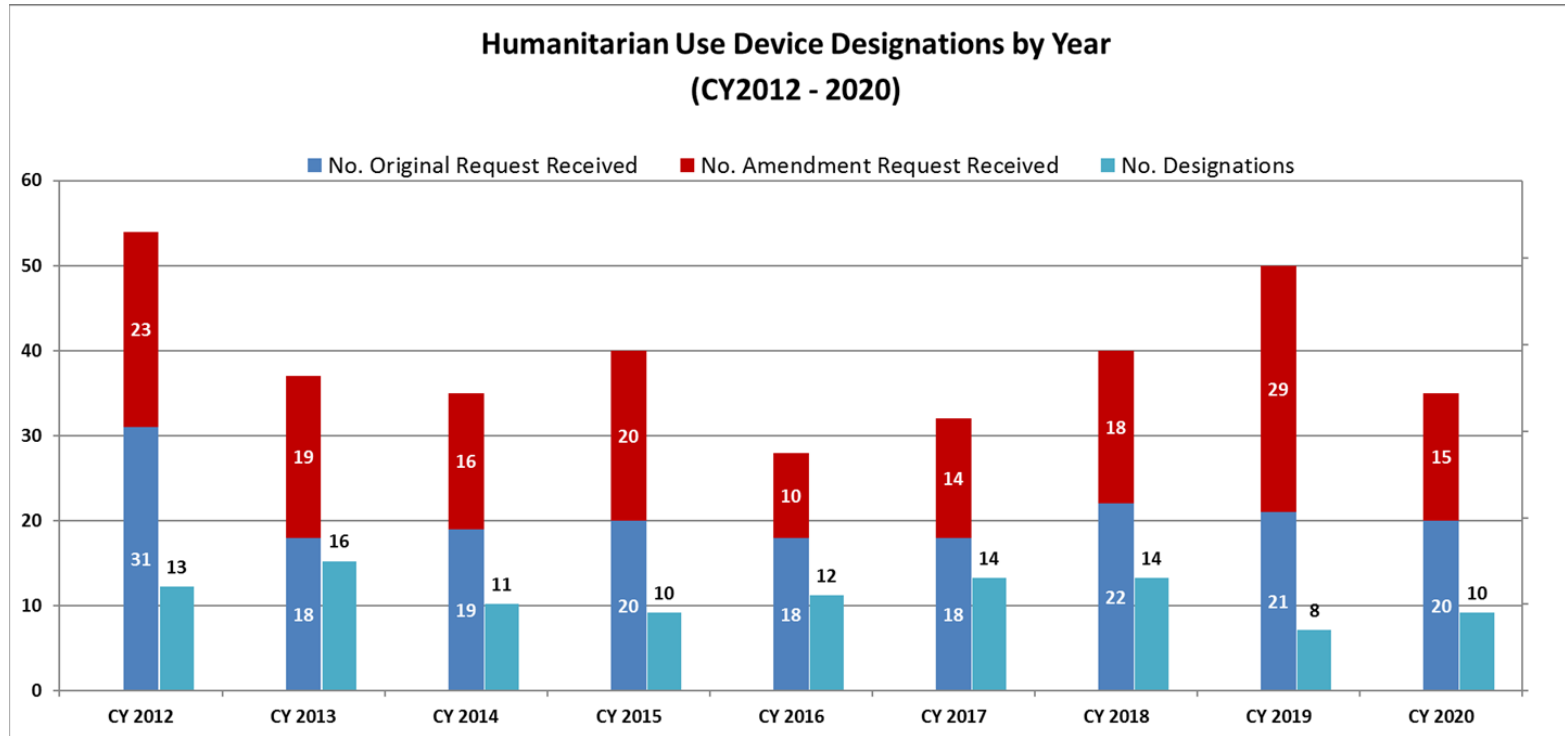
- Goal: Stimulate development of medical devices for rare diseases
- OOPD roles/responsibilities:
  - Review applications/requests for HUD designation
  - Grant special status (“HUD designation”) to products that meet eligibility criteria (incidence <8,000/year, sufficient scientific rationale)
- HUD-designated products may qualify for Humanitarian Device Exemption (HDE) pathway (safety + “probable benefit”)

# Statistics

- Since inception (1990)
  - Requests received: >460
  - Designated HUDs: >280
  - HDE approvals: 78

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

# HUD Designation Trends



# Orphan Products Grants Video



# Clinical Trials Grant Program

GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History 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

GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History Grant Program

- 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



# 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 (Dojolvim) 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 Lymphangiomyomatosis
- Berlin Heart EXCOR<sup>®</sup> Pediatric Ventricular Assist Device (VAD) for Bridge to heart transplantation in children



# Orphan Products Grants

U.S. Department of Health & Human Services

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## Search Orphan Products Grant Program

FDA Home | Developing Products for Rare Diseases & Conditions

Please enter search criteria. Grants can be searched by Indication, Project title, Product, and Principal Investigator. Searches can be restricted to currently funded grants only (the default). Entering a search term will find any occurrence of the term in the specified field, e.g., searching 'penicil' as a product name would return 'penicillin', 'aminopenicillin', etc. Go to our [instructions](#) page for additional help.

**Indication Search**

Disease Indication:

Product Name:

Grant Title:

Currently Funded Grants Only  All Funded Grants (current and previous)

**Investigator Search**

Principal Investigator:  (last name)

Institution:

City:  State:  (two letter abbreviation)

Country:  (not needed for US)

**Output Format**

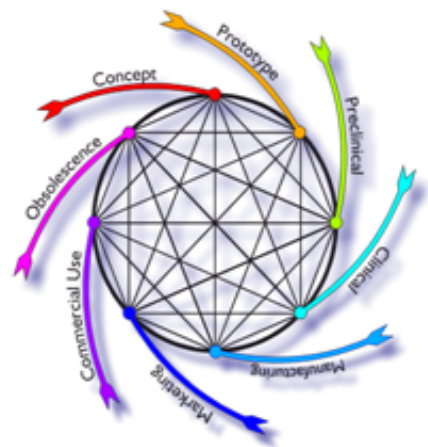
Display:

Sort results:

Note: If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).  
 Language Assistance Available: Español | 繁體中文 | Tiếng Việt | 한국어 | Tagalog | Русский | العربية | Kreyòl Ayisyen | Français | Polski | Português | Italiano | Deutsch | 日本語 | العربية | English

# 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



GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History Grant Program

# Statistics & Approved Products

GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History Grant Program

- 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

GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products 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

# OOPD Roles and Responsibilities

GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History Grant Program

- 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>

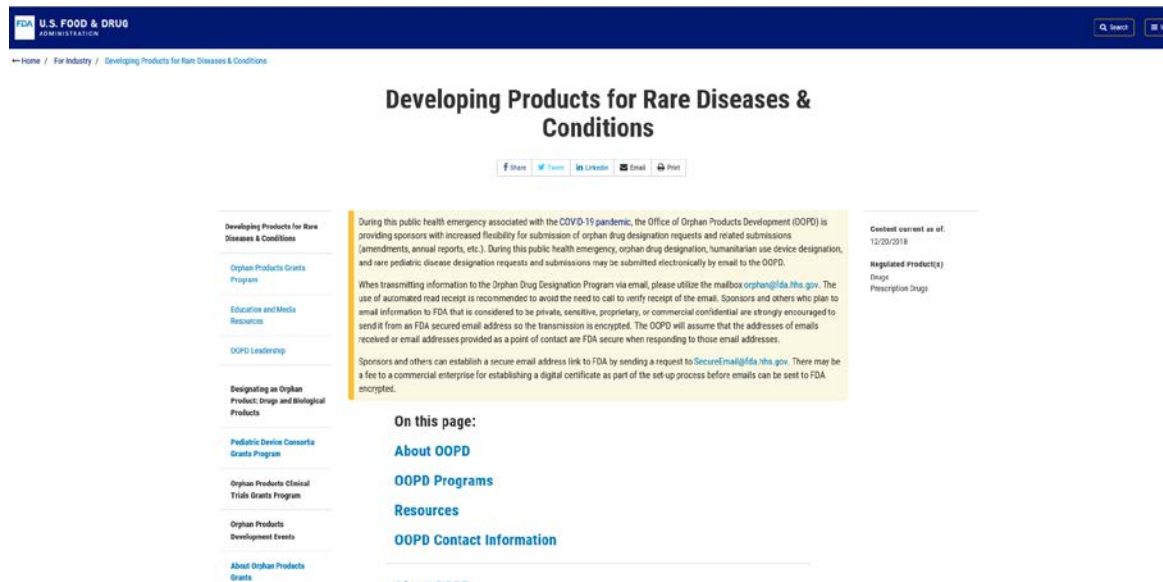


# Summary

- Orphan Drug Act (ODA) stimulates orphan product development
  - 1983-present: >950 approved indications for >250 rare diseases
- ODA inspired implementation of orphan legislation worldwide
  - Japan (1993), Australia (1998), European Union (1999)
- 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)



The screenshot shows the FDA website page for "Developing Products for Rare Diseases & Conditions". The page features a dark blue header with the FDA logo and navigation links. The main content area is white with a blue sidebar on the left. The sidebar contains links to various programs and resources. The main content area has a title "Developing Products for Rare Diseases & Conditions" and a sub-header "On this page:" followed by a list of links: "About OOPD", "OOPD Programs", "Resources", and "OOPD Contact Information". The main content area also contains a large yellow box with text about the COVID-19 pandemic and the OOPD program, and a "Regulated Product(s)" section listing "Drugs" and "Prescription Drugs".

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## Developing Products for Rare Diseases & Conditions

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**Developing Products for Rare Diseases & Conditions**

- Orphan Products Grants Program
- Education and Media Resources
- OOPD Leadership
- Designating an Orphan Product: Drugs and Biological Products
- Pediatric Device Consortia Grants Program
- Orphan Products Clinical Trials Grants Program
- Orphan Products Development Events
- About Orphan Products Grants

During this public health emergency associated with the COVID-19 pandemic, the Office of Orphan Products Development (OOPD) is providing sponsors with increased flexibility for submission of orphan drug designation requests and related submissions (amendments, annual reports, etc.). During this public health emergency, orphan drug designation, humanitarian use device designation, and rare pediatric disease designation requests and submissions may be submitted electronically by email to the OOPD.

When transmitting information to the Orphan Drug Designation Program via email, please utilize the mailbox [orphan@fda.hhs.gov](mailto:orphan@fda.hhs.gov). The use of automated read receipt is recommended to avoid the need to call to verify receipt of the email. Sponsors and others who plan to email information to FDA that is considered to be private, sensitive, proprietary, or commercial confidential are strongly encouraged to send it from an FDA secured email address so the transmission is encrypted. The OOPD will assume that the addresses of emails received or email addresses provided as a point of contact are FDA secure when responding to those email addresses.

Sponsors and others can establish a secure email address link to FDA by sending a request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). There may be a fee to a commercial enterprise for establishing a digital certificate as part of the set-up process before emails can be sent to FDA encrypted.

On this page:

- [About OOPD](#)
- [OOPD Programs](#)
- [Resources](#)
- [OOPD Contact Information](#)

Regulated Product(s)

- Drugs
- Prescription Drugs

Content current as of: 12/20/2018

# 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/RarePediatricDiseasePriorityVoucherProgram/default.htm>.
- Humanitarian Use Device (HUD) Designation program:  
<https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/DesignatingHumanitarianUseDevicesHUDS/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>



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