



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

Introduction to the Office of Orphan Products Development (OOPD)



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Objectives

- Describe the history of the Office of Orphan Products Development (OOPD)
- Define the Orphan Drug Act
- Identify the core programs within OOPD

myasthenia gravis

Idiopathic pulmonary fibrosis

pulmonary arterial hypertension



pancreatic cancer

graft-versus-host disease

leukemia

cystic fibrosis

Rare Disease Statistics

glioblastoma

lymphoma

Pompe disease

thalassemia

- ~7,000 known rare diseases¹

Duchenne muscular dystrophy

Huntington's disease

- Individually rare but collectively affect ~25-30 million Americans of all ages and millions more worldwide¹

multiple myeloma

malaria

hemophilia

retinitis pigmentosa

tuberculosis

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

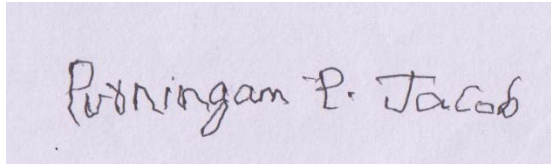
Prader-Willi syndrome

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*



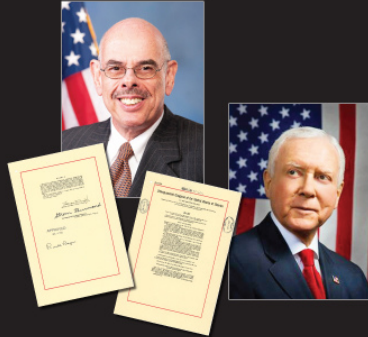
Abbey Meyers

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)

*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: Incentives

- 25% tax credit for qualified clinical trials
- Waiver of PDUFA application fee (currently ~\$2.4 million)
- 7-year market exclusivity
 - [CFR Title 21 Part 316.31](#)
- Grants to support studies of orphan products



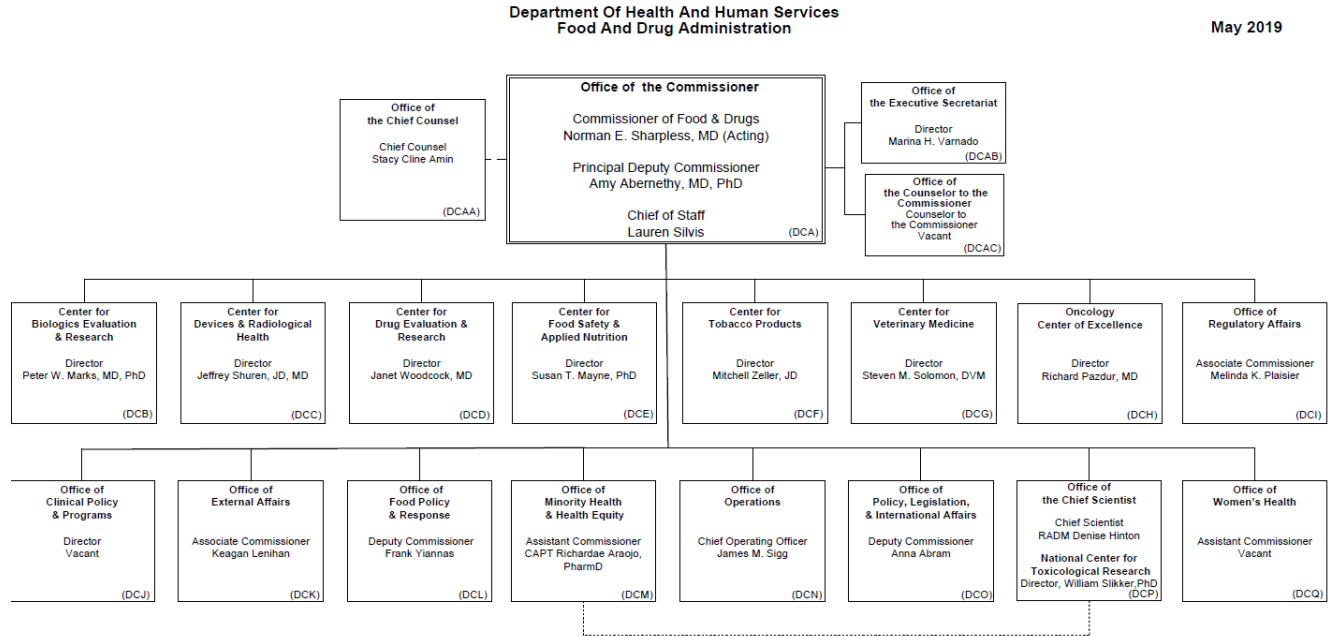
Office of Orphan Products Development (OOPD)

- Established in 1983
- Tasked to administer some provisions of the Orphan Drug Act

Where is OOPD within FDA?



Proposed future state OC organization chart



- Legend:**
- Direct report to DHHS General Counsel
 - Formally reports to The Commissioner but day-to-day oversight is from Office of The Chief Scientist

OOPD Core Programs

DESIGNATION PROGRAMS	
1	Orphan Drug Designation & Exclusivity
2	Rare Pediatric Disease (RPD) Designation <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> • Part of the HUD/HDE pathway • Disease or condition is not more than 8,000 individuals in the US per year

GRANT PROGRAMS	
1	\$15M Orphan Products Clinical Trials Grant Program <ul style="list-style-type: none"> • Funding and monitoring 85 rare disease clinical trials
2	\$6M Pediatric Device Consortia Grant Program <ul style="list-style-type: none"> • Appropriations increased from \$3M to \$6M in FY2017 • Funding and monitoring 5 different consortia
3	\$2M Orphan Products Natural History Grant Program <ul style="list-style-type: none"> • NIH providing additional \$3.5M to fund total of 6 studies

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, waiver of user fee, 7-year exclusivity)

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

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

- Since inception (1983)
 - Designations: >4,975
 - Approvals: >780 products (for >250 rare diseases)
- Recent approvals
 - Keytruda[®] (pembrolizumab) – Malignant melanoma
 - Tecentriq[®] (atezolizumab) – Small cell lung cancer
 - Egaten[™] (triclabendazole) - Fascioliasis
 - Lonsurf[®] (trifluridine/tipiracil) – Gastric cancer

Orphan Designations and Approvals

U.S. Department of Health & Human Services

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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

Product Name: (single search term without quote marks)

Orphan Designation: (or wildcard characters)

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

Search results:

Output format:

Sort results:

Records per page:

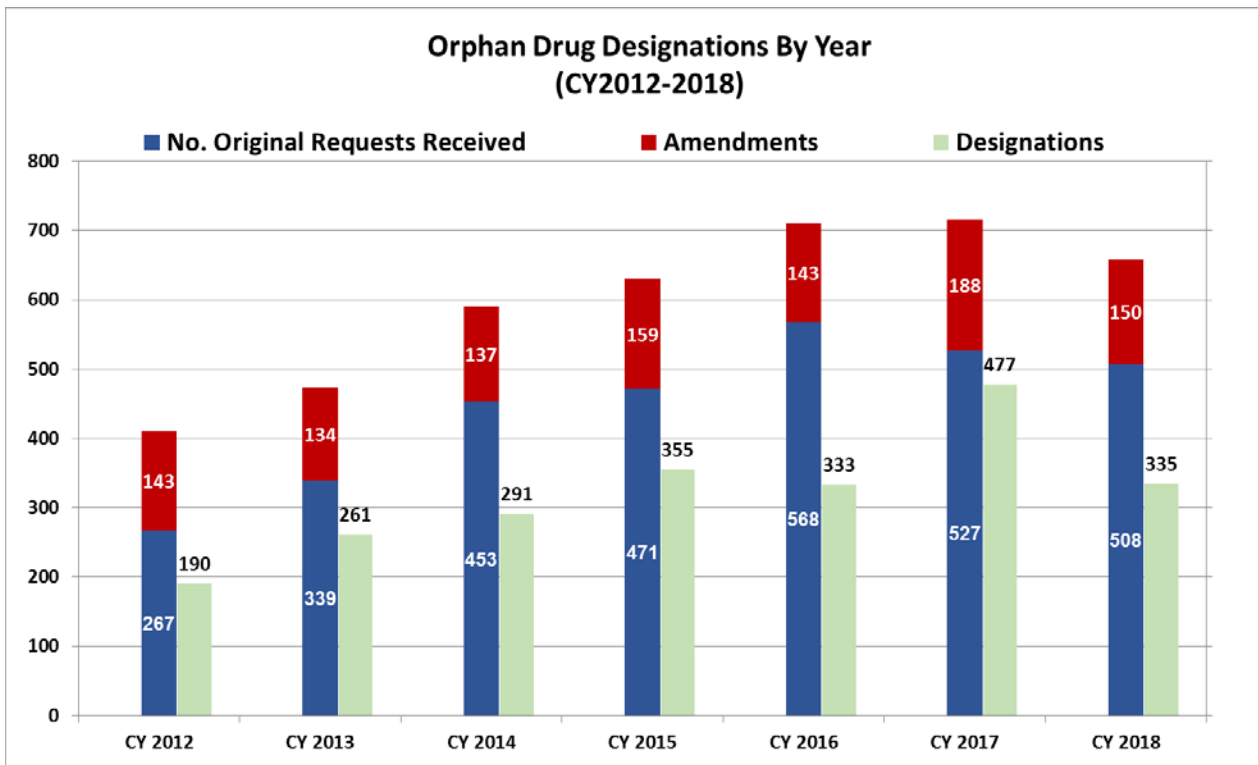
Run Search

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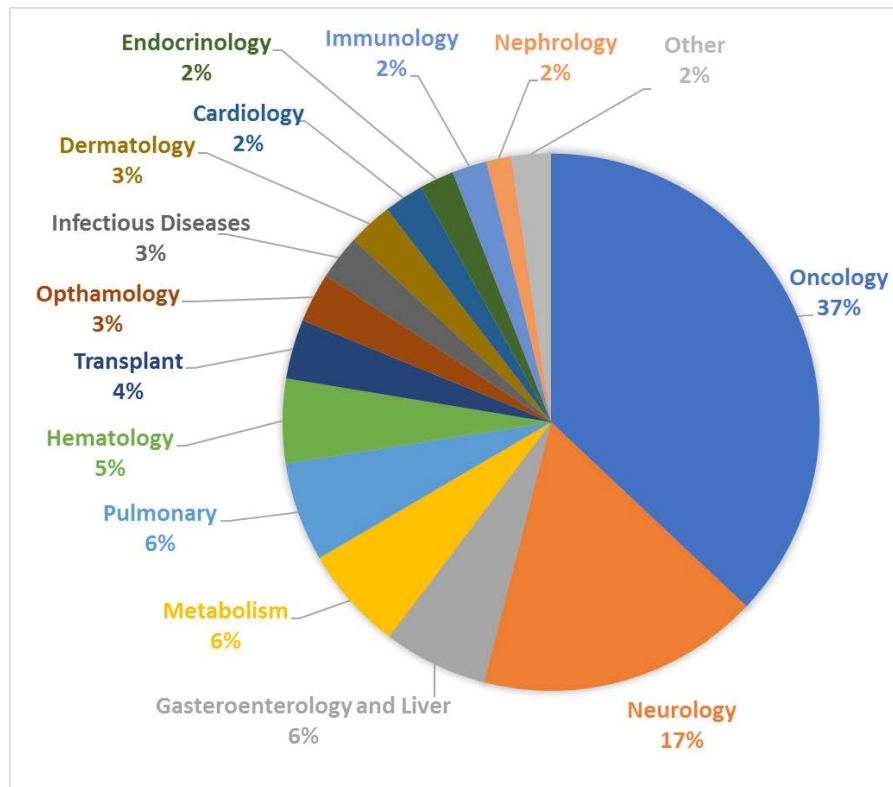
<https://www.accessdata.fda.gov/scripts/opdlisting/oopd/>

Orphan Drug Designation Trends

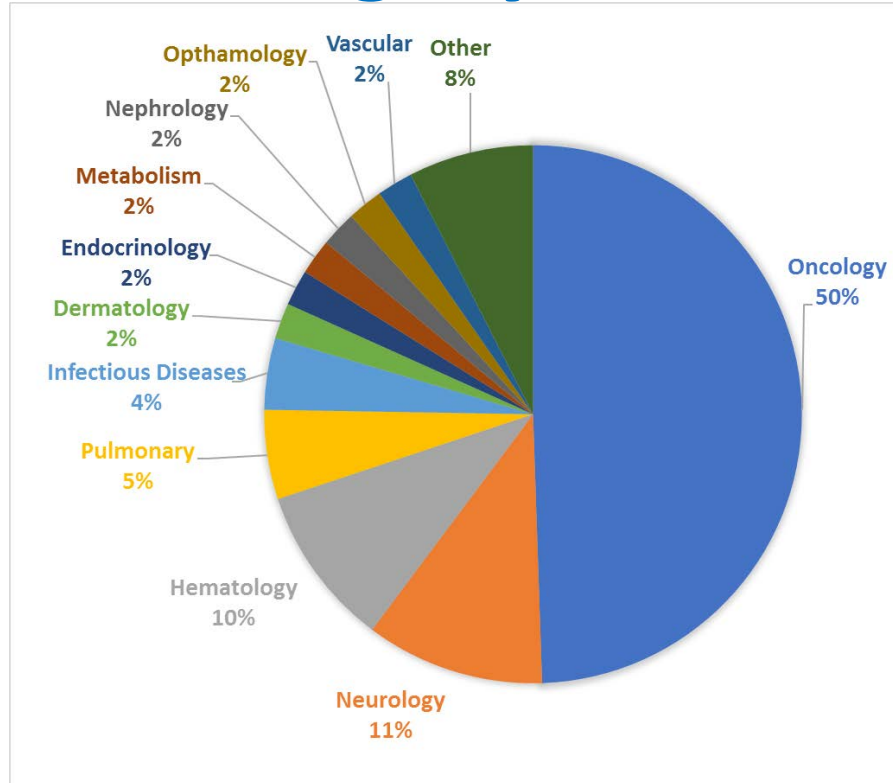


Note: Designations granted in a given year may include requests received from that year as well as previous years.

Orphan Drug Designations by Treatment Category in 2018



Orphan Approvals by Treatment Category in 2018



Rare Pediatric Disease (RPD) Designation

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

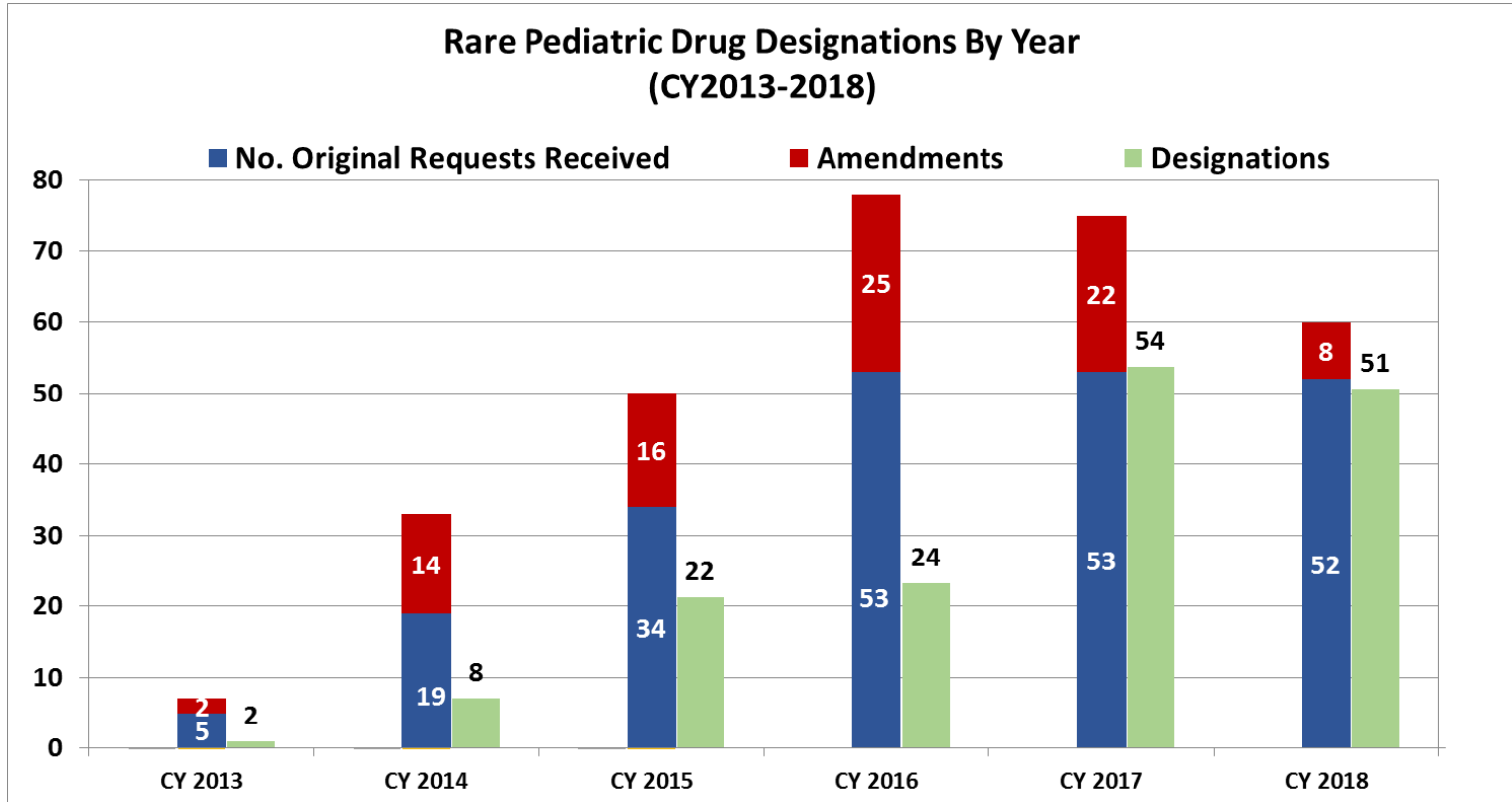
- Goal: Stimulate development of products for rare diseases in pediatric patients
- OODP roles/responsibilities:
 - Co-administered with Office of Pediatric Therapeutics
 - Grant special status (“RPD designation”) to products that meet eligibility criteria (prevalence <200,000; serious/life-threatening manifestations primarily affect those ≤ 18 yo)
- Designated products may qualify for RPD Priority Review Voucher Program

Statistics and RPD Vouchers

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

- Since inception (2012)
 - RPD designations: >175
 - RPD vouchers: 18
- 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)
 - 11 vouchers have been sold (\$67-350 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

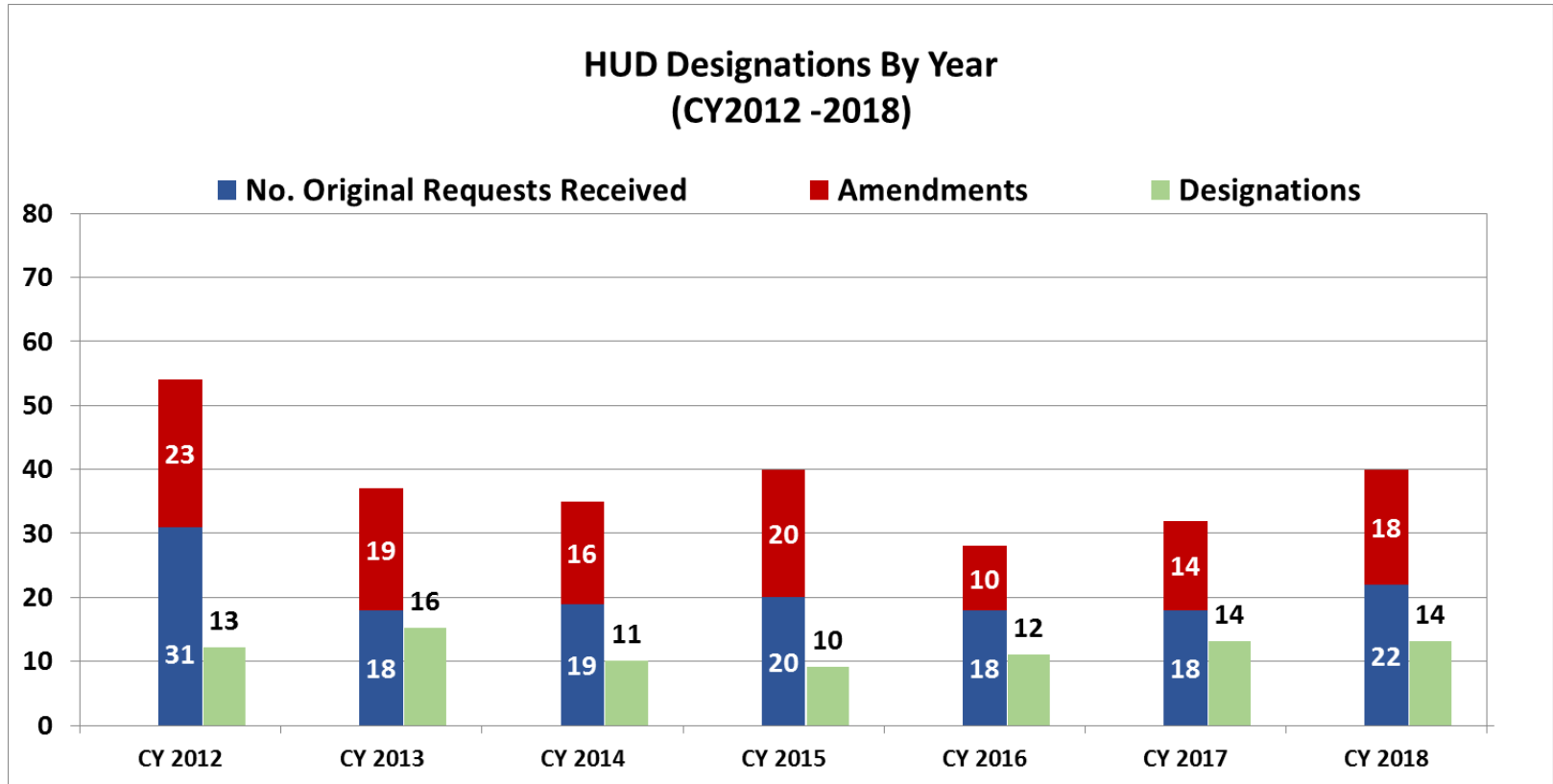
- Goal: Stimulate development of medical devices for rare diseases
- OOPD roles/responsibilities:
 - Review applications/requests for HUD designation
 - Grant special status (“HUD designation”) to products that meet eligibility criteria (incidence <8,000/year, sufficient scientific rationale)
- HUD-designated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

Statistics

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

- Since inception (1990)
 - Requests received: 423
 - Designated HUDs: 272
 - HDE approvals: 75

HUD Designation Trends



Orphan Products Grants Video

- <https://www.youtube.com/watch?v=QqJjknKoldU>

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 ~85 studies/year (~\$5.5 million for 12-18 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

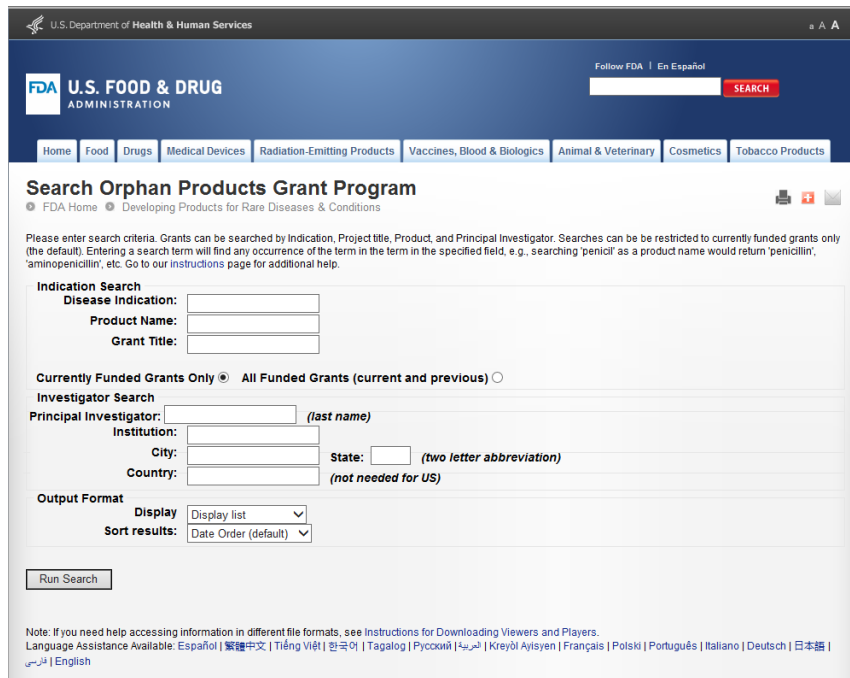
- Review grant applications
 - Primary review (active IND, prevalence <200,000)
 - Ad hoc review panel (medical need, scientific merit, qualifications of investigators, potential for marketing approval, budget)
 - Best cored applications funded (12-18/year)
- Oversee funded grants
 - Enrollment goal
 - Review quarterly updates
 - Review annual progress updates
 - Conduct teleconference grant evaluations/site visits

Statistics & Studies Funded

- Since inception (1983):
 - Applications received: >2,500 (100/year)
 - Studies funded: >700
 - Approved products supported by OOPD grants: ~60

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

Orphan Products Grants



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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 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)

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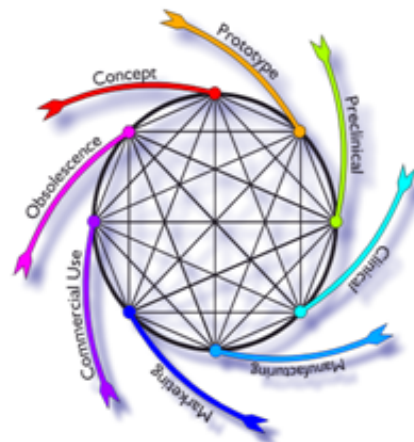
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Pediatric Device Consortia (PDC) Program

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

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

- Since 2009
 - Pediatric device projects assisted: >1,040
 - Advanced prototypes developed: 44
 - Device projects given regulatory advice: 549
- Legally marketed devices supported by PDC
 - Buzzy—cold and vibration for relief of pain with needle sticks
 - External compression brace for pectus carinatum – improves protrusion of sternum and ribs



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

Summary

- Orphan Drug Act (ODA) stimulates orphan product development
 - 1973-1983: 10 approvals
 - 1983-present: >730 approvals 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 diseases
 - ~7,000 rare diseases still need safe and effective treatment

Additional Resources

- www.fda.gov/orphan



The screenshot shows the FDA website page for 'Developing Products for Rare Diseases & Conditions'. The header includes the FDA logo and 'U.S. FOOD & DRUG ADMINISTRATION'. A search bar and a menu icon are visible in the top right. The main heading is 'Developing Products for Rare Diseases & Conditions'. Below the heading are social media sharing options for Facebook, Twitter, LinkedIn, Email, and Print. The main content area contains a paragraph about the FDA Office of Orphan Products Development (OOPD) mission. On the left side, there are two sidebar links: 'Developing Products for Rare Diseases & Conditions' and 'Designating an Orphan Product: Drugs and...'. On the right side, there is a 'Content current as of: 12/20/2018' 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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The FDA Office of Orphan Products Development (OOPD) mission is 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. In fulfilling that task, OOPD 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. The office also works on rare disease issues with the medical and research communities, professional organizations, academia, governmental agencies, industry, and rare disease patient groups.

Developing Products for Rare Diseases & Conditions

Education and Media Resources

Designating an Orphan Product: Drugs and

Content current as of: 12/20/2018

Regulated Product(s)
Drugs
Prescription Drugs

Challenge Question #1

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

- A) Affects <200,000 persons in the U.S.
- B) Affects <300,000 persons in the U.S.
- C) Affects <200,000 persons worldwide

Challenge Question #2

The Orphan Drug Act:

- A) Establishes definition of a rare disease/condition
- B) Provides financial incentives for developing orphan products
- C) Both

Challenge Question #3

OOPD programs provide incentives to develop medical products to treat, diagnose or prevent rare diseases and conditions.

- A) True
- B) False

Challenge Question #4

OOPD programs include 3 designation programs and 3 grants programs.

- A) True
- B) False



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