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

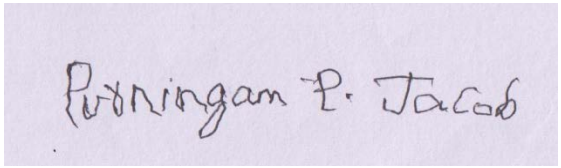
myasthenia gravis
Idiopathic pulmonary fibrosis
pulmonary arterial hypertension
pancreatic cancer
graft-versus-host disease
leukemia
cystic fibrosis
glioblastoma
lymphoma
Pompe disease
thalassemia
Duchenne muscular dystrophy
Huntington's disease
multiple myeloma
malaria
hemophilia
retinitis pigmentosa
tuberculosis
Prader-Willi syndrome
hepatocellular carcinoma
homozygous familial hypercholesterolemia

Rare Disease Statistics

- ~7,000 known rare diseases[1]
- Individually rare but collectively affect ~25-30 million Americans of all ages and millions more worldwide[1]
- Chronic, progressive, life-threatening, and/or fatal

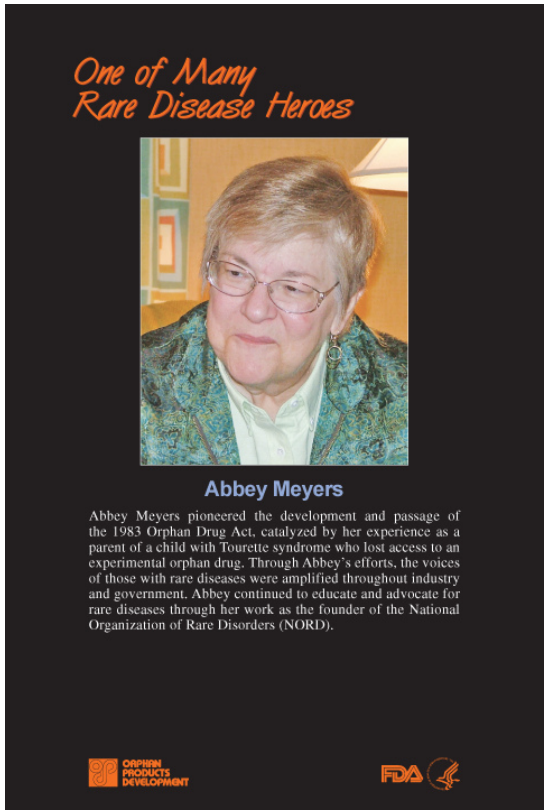
[1] https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases

Lou Gehrig
(1903-1941)

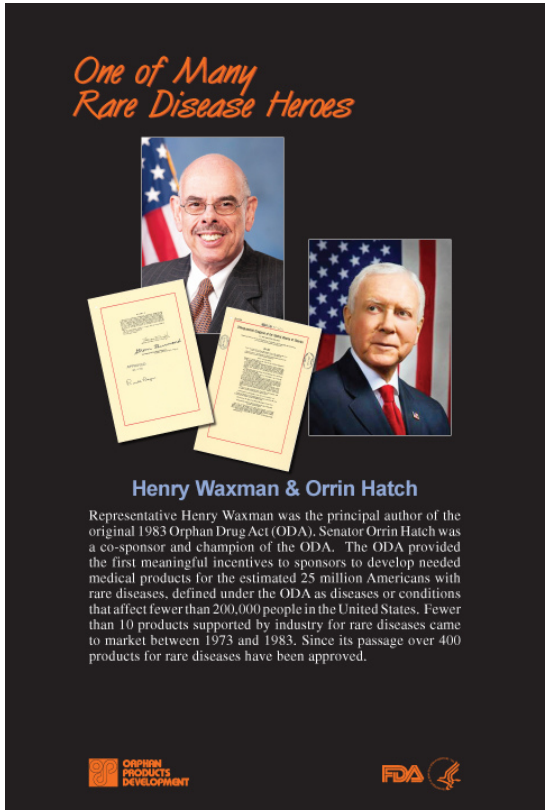


Background/History

- 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)



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

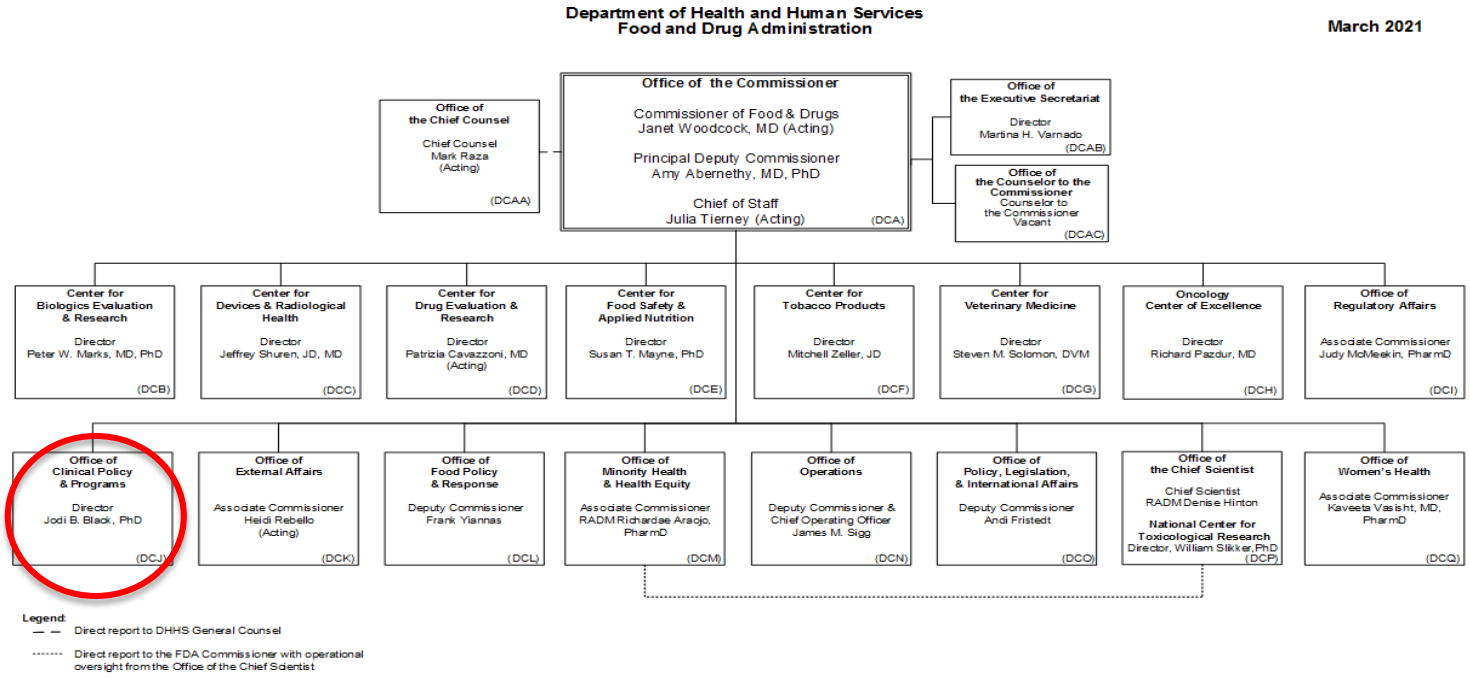
Office of Orphan Products Development (OOPD)

- 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	
1	**Orphan Drug Designation & Exclusivity**
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	
1	$15.5M Orphan Products Clinical Trials Grant Program • Funding and monitoring 75 rare disease clinical trials
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

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

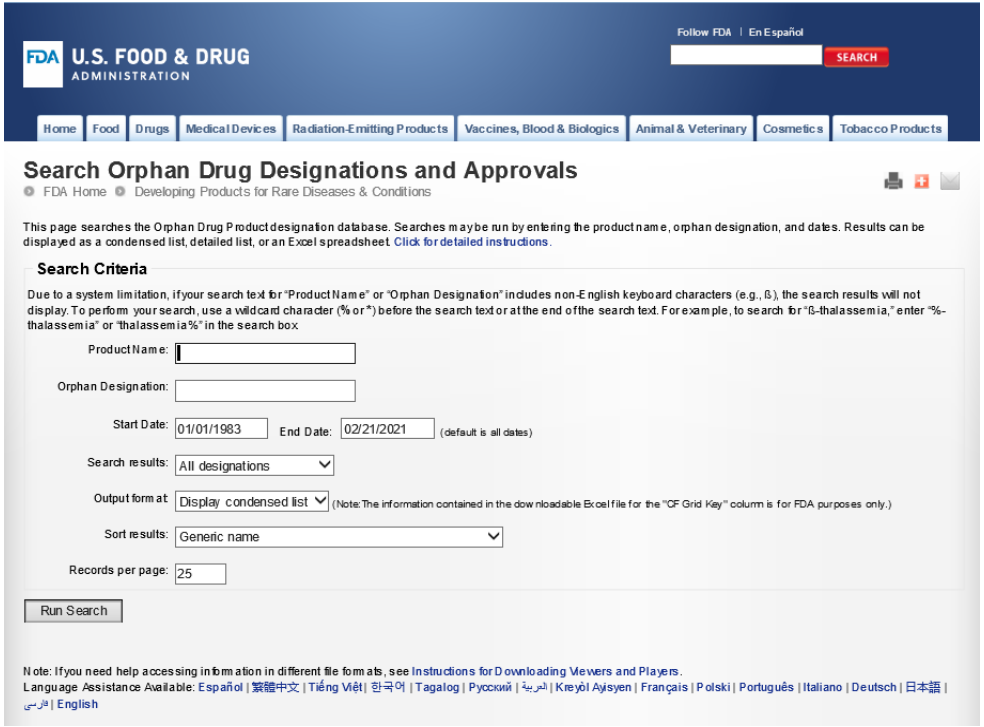
- Distinct from other exclusivities
- Determined by OOPD upon marketing approval
- OOPD sends letter to recognize exclusive approval per 21 CFR 316.34(a), then identified in Orange Book
- Exclusivity can be “broken” in cases of:
  - Drug shortage
  - Another drug is clinically superior to the approved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

Statistics and Recent Approvals

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

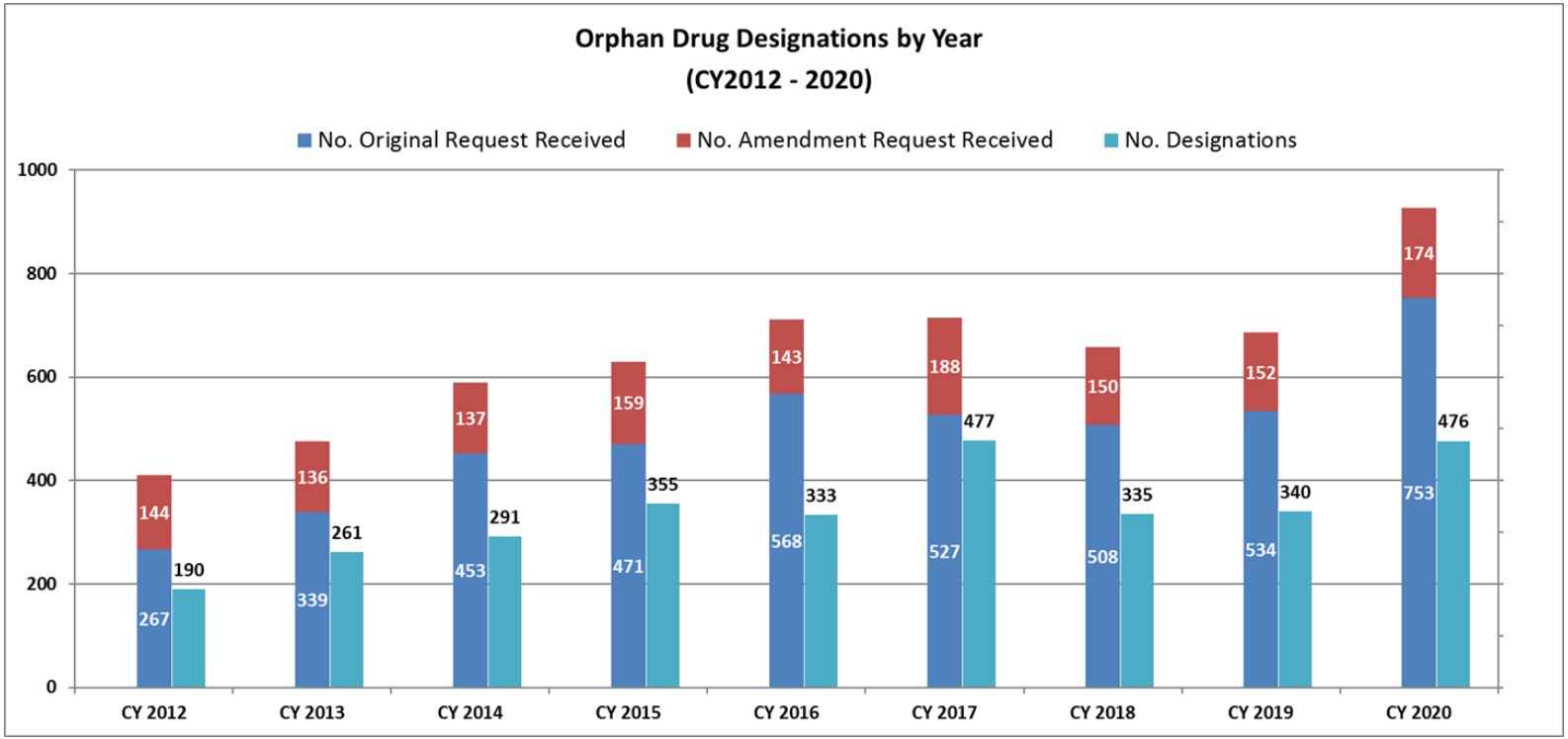
- Since inception (1983)
  - Designations: >5,800
  - Approvals: >950 product indications (for >250 rare diseases)
- Recent approvals
  - Zokinvy (lonafarnib) – Hutchinson-Gilford progeria syndrome and progeroid laminopathies
  - Orladeyo (berotralstat) – hereditary angioedema
  - Tecartus (brexucabtagene autoleucel) – mantle cell lymphoma
  - Sevenfact (coagulation factor VIIa (recombinant)-jncw) – hemophilia A or B with inhibitors

Orphan Designations and Approvals



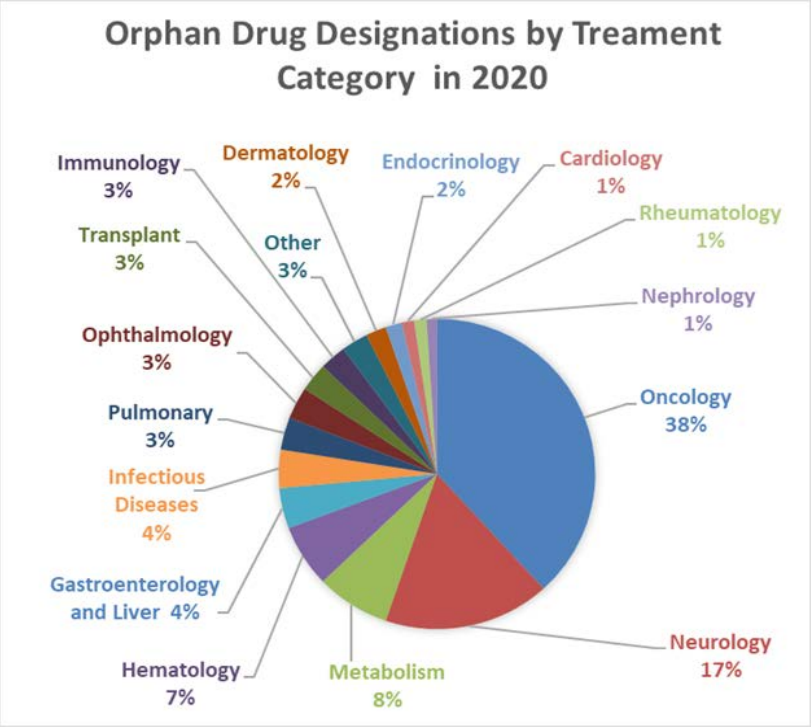
https://www.accessdata.fda.gov/scripts/opdlisting/oopd/

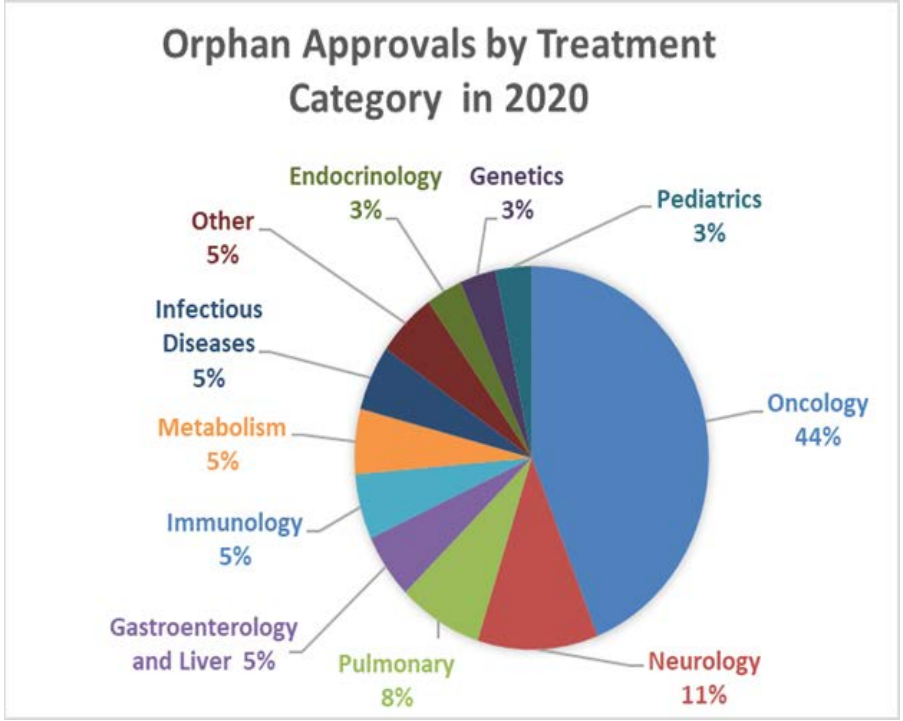
Orphan Drug Designation Trends



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

Orphan Drug Designations and 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

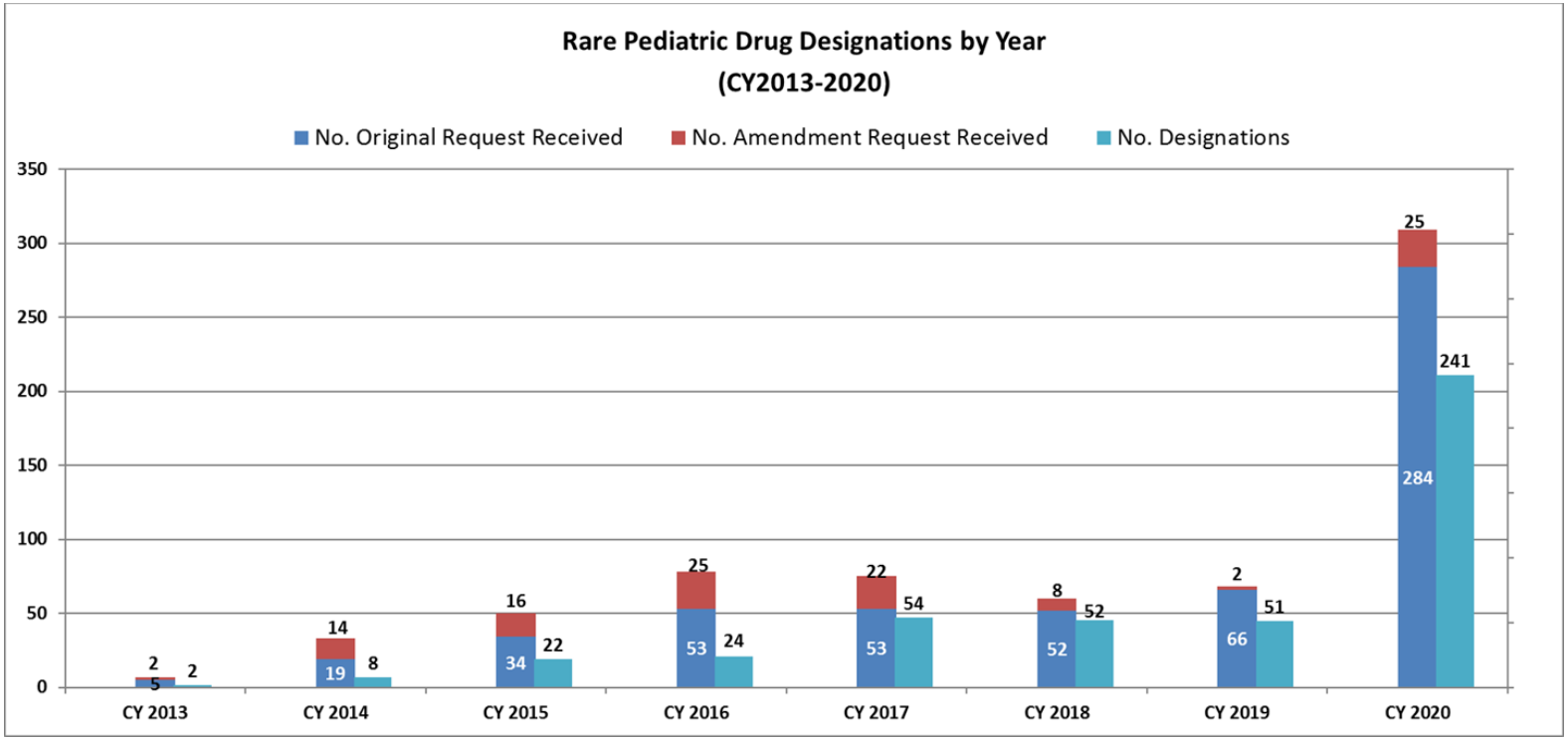
- Goal: Stimulate development of products for rare diseases in pediatric patients
- OODP roles/responsibilities:
  - Co-administered with Office of Pediatric Therapeutics (OPT)
  - Grant special status ("RPD designation") to products that meet eligibility criteria (prevalence <200,000; serious/life-threatening manifestations primarily affect those ≤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

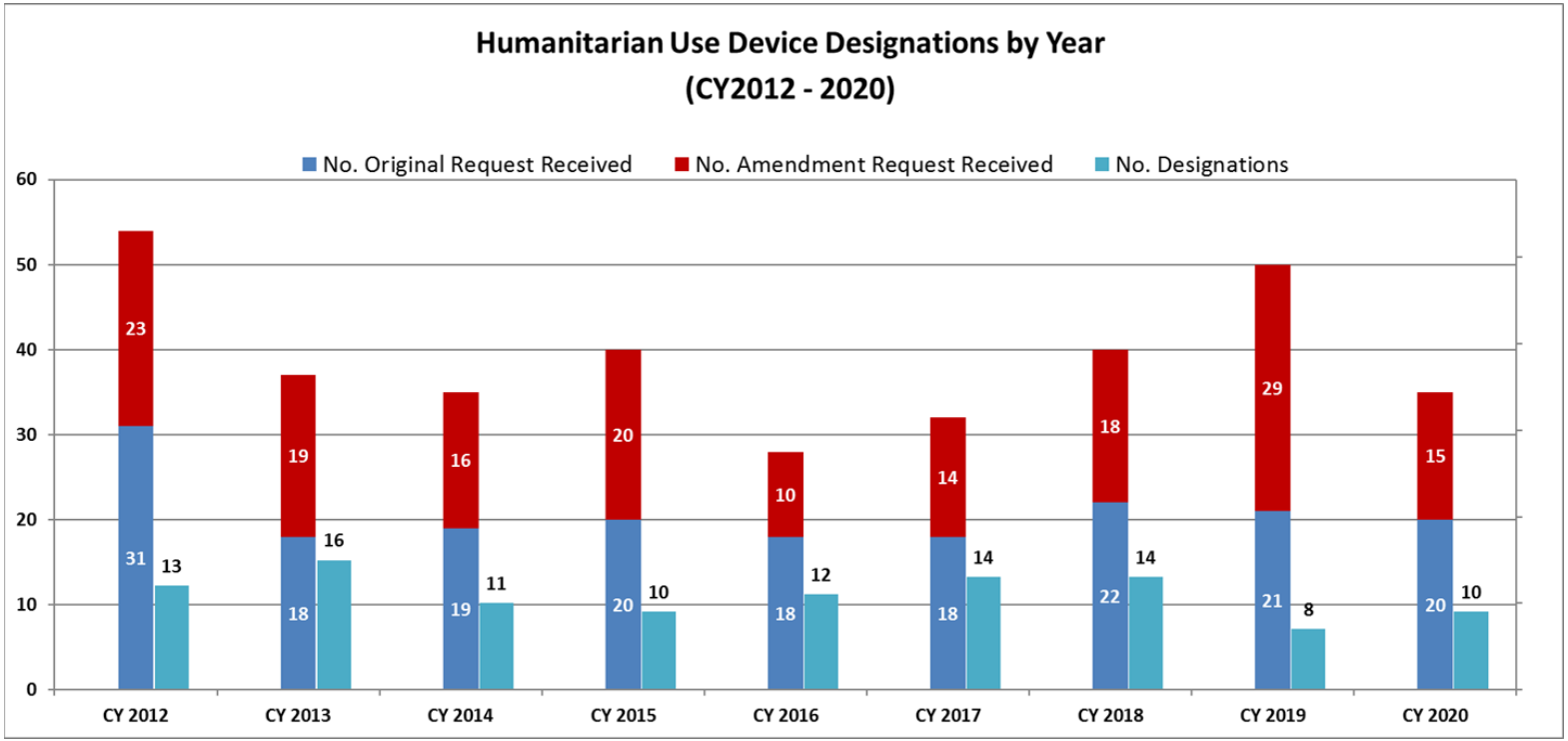
- Goal: Stimulate development of medical devices for rare diseases
- OOPD roles/responsibilities:
  - Review applications/requests for HUD designation
  - Grant special status ("HUD designation") to products that meet eligibility criteria (incidence <8,000/year, sufficient scientific rationale)
- HUD-designated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

Statistics

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

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

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

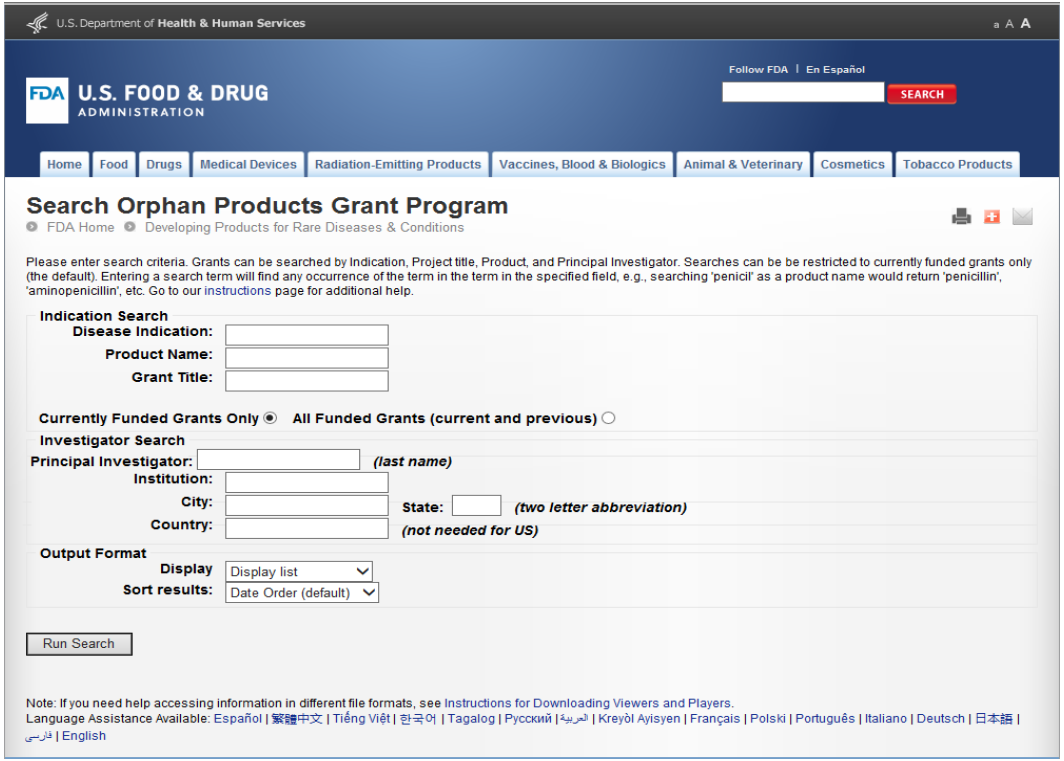
GRANT PROGRAMS	
1	Clinical Trials Grant Program
2	Pediatric Device Consortia Grant Program
3	Orphan Products Natural History Grant Program

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

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

Orphan Products Grants

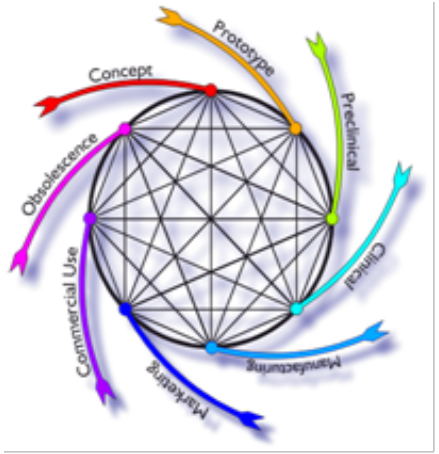


https://www.accessdata.fda.gov/scripts/opdlisting/oopdgrants/

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

- 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

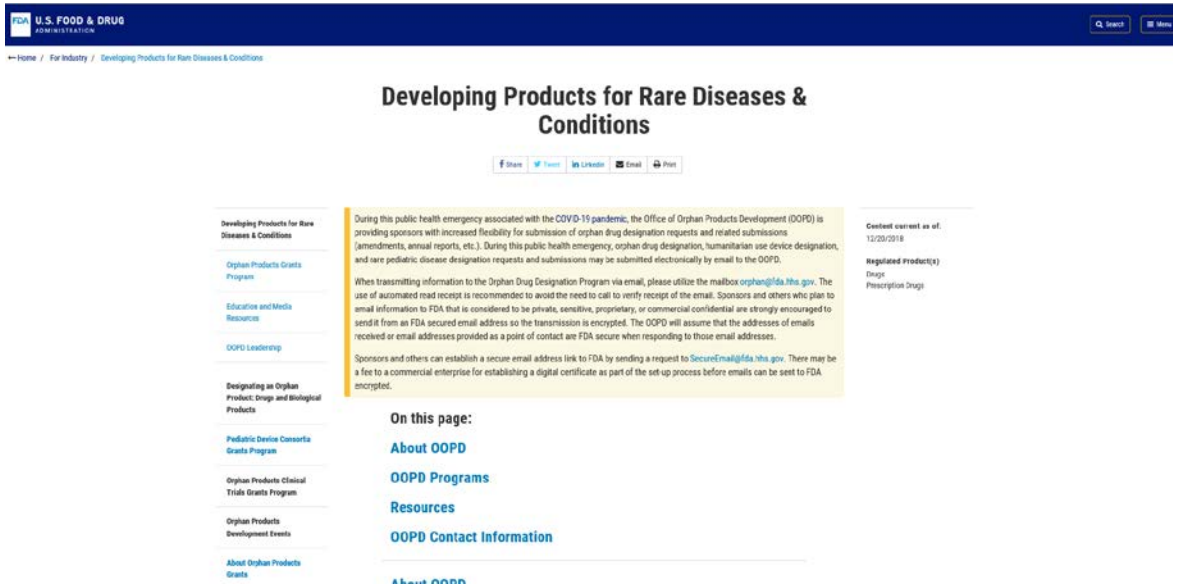
https://www.fda.gov/industry/orphan-products-development-events/fda-rare-disease-day-2021

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



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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