OFFICE OF ORPHAN PRODUCTS DEVELOPMENT[28]

(Dollars in Thousands)	FY 2015 Final	FY 2015 Actuals	FY 2016 Enacted	FY 2017 President's Budget	FY 2017 +/- FY 2016
Office of Orphan Products Development (BA Only).....	23,599	23,599	26,099	26,099	---
FTE…….....	27	27	27	27	---

Authorizing Legislation: Federal Food, Drug and Cosmetic Act (21 U.S.C. 321-399); PHS Act (42 U.S.C. 241) Section 301; Safe Medical Device Act of 1990 (as amended) (21 U.S.C. 351-353, 360, 360c-360j, 371-375, 379, 379e, 381); Pediatric Medical Devices Safety and Improvement Act of 2007, Section 305; Food and Drug Administration Safety and Innovation Act of 2013, Sections, 510, 620 and 908.

Allocation Method: Direct Federal/Extramural Grants

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The public health programs of the Office of Orphan Products Development (OOPD) have promoted and advanced the development of innovative products – drugs, biologics, medical devices, and medical foods – that demonstrate promise for the prevention, diagnosis, and/or treatment of rare diseases or conditions. There are an estimated 7,000 rare diseases, with a public health impact that affects more than 25 million Americans and many millions more of family members in the United States. Between 85 and 90 percent of these cases are serious or life-threatening.

Improve and Safeguard Access

OOPD administers major provisions of the 1983 Orphan Drug Act (ODA), relevant sections of the 1990 Safe Medical Devices Act, and other statutes, where Congress sought to provide incentives to promote the development of products for the treatment of rare diseases or conditions. OOPD's program activities directly support the Health and Human Services' strategic goal to advance scientific knowledge and innovation.[29] Further, OOPD activities support FDA's strategic goal to improve access to FDA regulated products that benefit health by enhancing the process of developing promising new products into safe, effective, and accessible treatments for rare disease patients. OOPD programs facilitate product development through collaboration with private, public, and academic entities.

Orphan Product Grants Activity

The Orphan Drug Act created the Orphan Product Grants Program, which is administered by OOPD, to stimulate the development of promising products for rare diseases and conditions. Orphan product grants are a proven method of fostering and encouraging the development of new safe and effective medical products for rare diseases and conditions. These grants support new and continuing extramural research projects that test the safety and efficacy of promising new drugs, biologics, devices, and medical foods through human clinical trials in very vulnerable populations often with life-threatening conditions.

Over 700 clinical trials have been funded by the Orphan Products Grants Program to date. This OOPD Grants Program has supported the marketing approval of more than 55 orphan products

[28] The Office of Orphan Products Development is shown for illustrative purposes and is not contained as a separate line item in the All Purpose Tables.
[29] http://www.hhs.gov/about/strategic-plan/strategic-goal-2/index.html

for serious or life threatening orphan indications. This program has funded approximately 10 percent of all orphan product approvals. In FY 2015, OOPD funded 18 new grant awards – out of 92 grant applications – and provided funding or continued support for approximately 67 other ongoing clinical study projects.

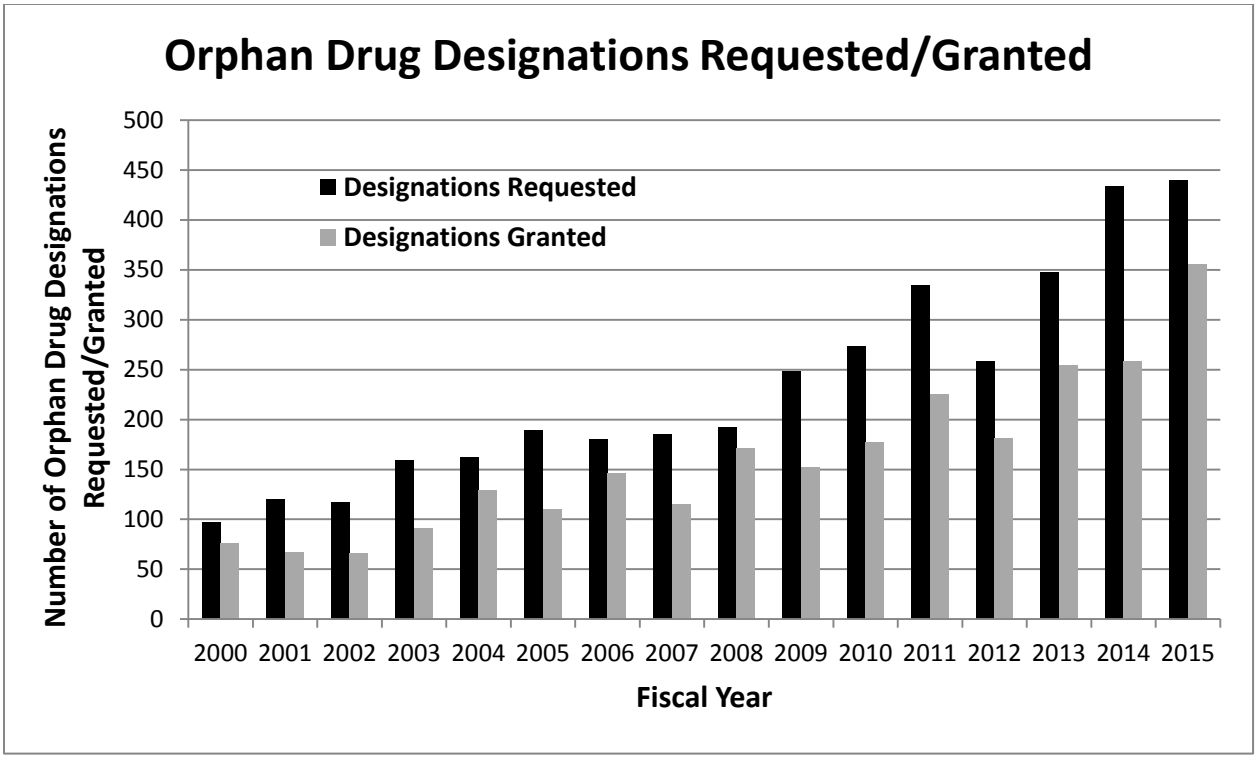
Grants are a modest investment to better ensure that product development occurs in a timely manner. However, FDA grant funds are covering less and less of the total cost for conducting clinical trials, which continue to increase far faster than the rate of medical inflation. Increases in the costs of clinical trials have reduced the capacity of the program to provide the needed monetary support to researchers actively conducting clinical trials that increase the number of new, safe and effective diagnostic and therapeutic options for patients with rare diseases.

Orphan Drug Designation Activity

The Orphan Drug Act also created the orphan drug designation program which provides financial incentives to sponsors for developing drugs and biologics for rare diseases and conditions, which is generally defined as one affecting fewer than 200,000 persons in the United States. OOPD evaluates applications from sponsors who are developing drugs to treat rare diseases to determine eligibility for orphan drug designation. Sponsors whose drugs are designated as orphan are eligible for significant tax credits for clinical trial costs, user fee waiver of marketing applications, and upon approval, consideration for seven years of marketing exclusivity.

Of the 3,500 orphan drug designations OOPD issued since 1983, over 500 have resulted in marketing approval, the vast majority with orphan exclusivity. In contrast, the decade prior to 1983 saw fewer than ten such products developed by industry make it into the market. During FY 2015, OOPD received a record 440 new applications for orphan drug designation. These included potential treatments for many kinds of rare cancers, sickle cell disease, and Ebola. OOPD designated a record 355 orphan drugs in FY 2015. FDA approved 40 orphan designated drugs for marketing in FY 2015.

The number of requests for orphan designation has quadrupled since FY 2000. Not only are the requests rapidly increasing, but the complexity of the science associated with these orphan drugs is increasing due, in part, to advances in pharmacogenomics and precision medicine. In FY 2015, approximately 33 percent of all the new molecular entities that FDA approved were orphan designated drugs and biologics.



Product Designations

Below are examples of Orphan Product designations that occurred in 2015.[30]

Date	Product	Purpose or Benefit
June 2015	Recombinant virus serotype (rh74) expressing the human GALGT2 gene	A gene therapy for the treatment of Duchenne muscular dystrophy – a life-threatening, progressive rare disease with no curative therapy
March 2015	Adeno-associated viral vector type 2 expressing human recombinant retinal pigment epithelial 65KDa protein gene	A gene therapy to treat retinitis pigmentosa, a rare genetic defect causing blindness
March 2015	Sevuparin	To treat sickle cell disease – a rare, life-threatening, inherited blood disorder, with no approved treatment for children
March 2015	Sonidegib	To treat the rare, life-threatening pediatric brain cancer, medulloblastoma

30 For more information on product approvals and designations visit http://www.fda.gov/NewsEvents/ProductsApprovals/

Rare Pediatric Disease Priority Review Voucher Designation
Food and Drug Administration Safety and Innovation Act (FDASIA) added Section 529 to the FD&C Act to encourage development of new drug and biological products ("drugs") for the prevention and treatment of qualifying rare pediatric diseases. This legislation created the Rare Pediatric Disease Priority Review Voucher (PRV) program wherein the sponsor of an approved drug to prevent or treat a rare pediatric disease may receive a voucher for a priority review of a subsequent drug.

Sponsors who are interested in receiving a rare pediatric disease priority review voucher may first request a "rare pediatric disease" designation through OOPD. While such designation is not required to receive a voucher, requesting designation in advance may expedite a sponsor's future request for a priority review voucher. In FY 2015, OOPD received 31 rare pediatric disease designation requests plus 2 consults from submitted marketing applications needing rare pediatric disease determinations. Of these, OOPD determined that 21 met the definition of a "rare pediatric disease." As of December 2015, six rare pediatric disease priority review vouchers were issued.

The program is due to sunset on September 30, 2016.

Humanitarian Use Device (HUD) Designation Activity
The HUD program, created from provisions of the Safe Medical Devices Act, encourages the development of devices for rare diseases and is administered by OOPD.

OOPD reviews applications from sponsors requesting HUD designation. A device that has received HUD designation is eligible for Humanitarian Device Exemption (HDE) approval if, among other criteria, the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of available devices or alternative forms of treatment. FDA approval of an HDE application authorizes the applicant to market the device. This marketing approval is subject to certain profit and use restrictions set forth in Section 520(m) of the FD&C Act. Since 1990, 66 HUD devices have been approved for marketing through the HDE pathway.

Except in certain circumstances, a HUD approved under an HDE cannot be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (for profit). Under Section 520(m)(6)(A)(i) of the FD&C Act, as amended by FDASIA, a HUD is eligible to be sold for profit after receiving HDE approval if the device meets certain criteria. Currently, eleven manufacturers have received approval to market their devices for profit and other sponsors have submitted requests to qualify for the exemption from profit prohibition.

In FY 2015, OOPD received 21 new HUD applications and designated six devices. An additional four devices were designated based on HUD applications originally submitted in prior years for a total of 10 HUD devices designated in FY 2015. In FY 2015, four devices received an HDE approval from CDRH and of these, one manufacturer was authorized to market their device for profit. Also, in FY2015, two manufacturers who previously had HDE approval were authorized to market their devices for profit.

Pediatric Device Consortia Grants Activity
There is a significant public health need for medical devices designed specifically for children. This need is due in part to the lack of commercial incentives and market forces to drive pediatric

medical device development, as well as the challenges of pediatric device development including differences in size, growth, development, and body chemistry that impact pediatric device requirements. Section 305 of the Pediatric Medical Device Safety and Improvement Act of 2007 (part of the 2007 FDAAA legislation) mandates demonstration grants for improving pediatric device availability through pediatric device consortia.

The FDA Pediatric Device Consortia Grant Program, administered in OOPD, supports nonprofit consortia that promote the development of pediatric medical devices. In FY 2015, the consortia funded in this program are based out of Ann Arbor, MI; Atlanta, GA; Boston, MA; Washington, DC; Lebanon, NH; Los Angeles, CA; Philadelphia, PA; and San Francisco, CA.

Since the program's inception in 2009, a total of $21.4 million has been awarded to the consortia. Collectively, the consortia have supported the development of more than 570 potential pediatric devices, many of which are in the early stages of development. Eight new devices are now available for use in pediatric patients as a result of advisory assistance received from the consortia, including the "Buzzy" device for relief of pain associated with needlesticks; the Rhinoguard to assist in nasotracheal intubation; and an external compressor brace for pectus carinitum. The consortia collectively have also raised more than $65 million of additional non-FDA funds to support pediatric device development research.

Promote Informed Decisions

OOPD participates in significant communication and outreach activities by:

- providing information on incentives available to develop products for rare diseases to external stakeholders including industry, the patient community, advocacy groups, and international regulatory agencies
- speaking at meetings and conferences on the FDA designation and approval processes, the OOPD grant programs, and the science of developing therapeutic products for rare diseases and conditions
- assisting patients and advocacy groups on issues of concern related to rare diseases and orphan products, such as pediatric device needs and orphan drug shortages
- providing web-based rare disease and orphan product resources and information to various stakeholders such as industry, the patient community, advocacy groups, and international regulatory agencies

In FY 2015**,** OOPD participated in 68 individual industry outreach meetings. In addition, OOPD received more than 38 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 26 of these meetings both nationally and internationally, often to explain how orphan drugs and humanitarian devices could be developed with ODA incentives and HDE provisions, as well as FDASIA requirements for rare diseases.

At these meetings, the missions of OOPD and FDA were explained, and questions and concerns from stakeholders were addressed. Examples of public health related OOPD outreach activities in FY 2015 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. In FY 2016 through FY 2017, OOPD will continue the outreach efforts to enhance all stages of the development and approval process for products to treat rare disease patients.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2013 Actual	$23,140,000	$23,140,000	$0
FY 2014 Actual	$24,745,000	$24,745,000	$0
FY 2015 Actual	$23,599,000	$23,599,000	$0
FY 2016 Enacted	$26,099,000	$26,099,000	$0
FY 2017 President's Budget	$26,099,000	$26,099,000	$0

BUDGET REQUEST

The FY 2017 Budget Request is $26,099,000 in budget authority. With this funding level, OOPD will fund a total of 15 to 20 new grant awards and provide funding or continued support for approximately 75 other ongoing clinical study projects.

In addition, in FY 2017, OOPD plans to initiate a new, much needed, Grants Program to fund targeted rare disease natural history studies that provide the critical foundation for a drug or device's clinical development program. These natural history studies will assist in drug development and identification of treatment options in many ways like formulating sensitive clinical outcome measures, identifying appropriate subpopulations or developing biomarkers. Despite their importance, funding to conduct such studies is sorely lacking. In FY 2017, OOPD plans to award 2-4 grants for targeted natural history studies to expedite development of products for these vulnerable populations.

PERFORMANCE

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2016 Target	FY 2017 Target	FY 2017 +/- FY 2016
293207: Percentage of reviews of first-time and amended orphan drug designation applications completed in 90 days or less. *(Output)*	FY 2015: 90% (Historical Actual)	75%	75%	Maintain
293208: Percentage of Humanitarian Use Device designation reviews completed in 45 days or less. *(Output)*	FY 2015: 100% (Historical Actual)	95%	95%	Maintain

PROGRAM ACTIVITY DATA

Office of Orphan Products Development				
Program Workload and Outputs	**FY 2014 Actuals**	**FY 2015 Actuals**	**FY 2016 Estimate**	**FY 2017 Estimate**
Grant Programs				
Total Orphan Product Grant (New and Continuations)	80	85	90	90
Total Pediatric Consortia Grants (New and Continuations)	8	8	8	8
Orphan Drug Designation Requests/Designations Granted/Orphan Drug Approvals				
New Orphan Drug Designation Requests	434	440	440	440
Drug Designations Granted	285	335	335	335
FDA Orphan Drug Marketing Approvals	45	40	40	40
HUD Requests and Designations				
New HUD Designation Requests	17	21	25	25
HUD Designations	12	10	14	14
Rare Pediatric Disease Priority Review Voucher Designation/Consultation Requests	**15**	**31**	**40**	**0**

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