

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT⁷

	FY 2013Actual	FY 2014Enacted	FY 2015 Request
Program Level⁸	\$23,139,897	\$23,598,688	\$23,598,688
Orphan Product Grants^{9, 10}	\$12,960,744	\$14,035,060	\$14,035,060
Pediatric Device Consortia Grants¹¹	\$3,000,000	\$3,000,000	\$3,000,000
Program Administration^{12, 13}	\$7,179,153	\$6,563,628	\$6,563,628

Authorizing Legislation: Federal Food, Drug and Cosmetic Act (21 U.S.C. 321-399); Orphan Drug Regulations (21 CFR 316); Humanitarian Use Device and Humanitarian Device Exemption Regulations (21 CFR 814 Subpart H); 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, Section 620

Allocation Method: Direct Federal/Extramural Grants

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

Since its inception in 1982, 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 diagnosis and/or treatment of rare diseases or conditions. An estimated 7,000 rare diseases, with a public health impact affect more than 25 million and many millions more of family members in the United States. Between 85 and 90 percent of these cases are serious or life-threatening.

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' priority to accelerate scientific advances in lifesaving

⁷ 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.

⁸ Assumes 50 percent of non-grant budget from user fees in FY 2015

⁹ Orphan Product Grants are part of the aggregate amount of budget authority contained in the CDER budget line item of the All Purpose Tables.

¹⁰ FY 2013 amount reduced by sequestration and rescissions

¹¹ Pediatric Device Consortia (PDC) Grants are part of the aggregate amount of budget authority contained in the CDRH budget line item of the All Purpose Tables.

¹² Program Administration is part of the aggregate amount of budget authority contained in the Other Activities budget line item of the All Purpose Tables.

¹³ FY 2013 included supplemental increases of \$1,971,718 to support Orphan Product Grants and \$600,000 to support PDC Grants. FY 2014 and FY 2015 include a supplemental increase of \$1,200,000 to support Orphan Product Grants.

cures and quality health outcomes. Further, OOPD activities support FDA's strategic priorities by enhancing the process of developing promising new products into safe, effective, and accessible treatments for patients. Specifically, OOPD programs address FDA Strategic Priority (SP) 2.1, "Advance Regulatory Science and Innovation," and SP 2.4, "Expand Efforts to Meet the Needs of Special Populations." One of FDA's signature initiatives in FDA's Strategic Plan is "Scientific Innovation for Rare Disease Therapies."

Orphan Product Grants Activity

The 1983 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 successfully fostering and encouraging the development of new safe and effective medical products for rare diseases/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.

Of the 650 clinical trials the Orphan Products Grants Program has funded, 54 grants have been used to bring more than 50 orphan products to marketing approval for 48 different serious or life threatening orphan indications. OOPD Grants Program has funded approximately 10 percent of orphan product approvals. In FY 2013, OOPD funded 15 new grants (out of 92 grant applications) and provided funding or continued support for approximately 60 other ongoing clinical study projects.

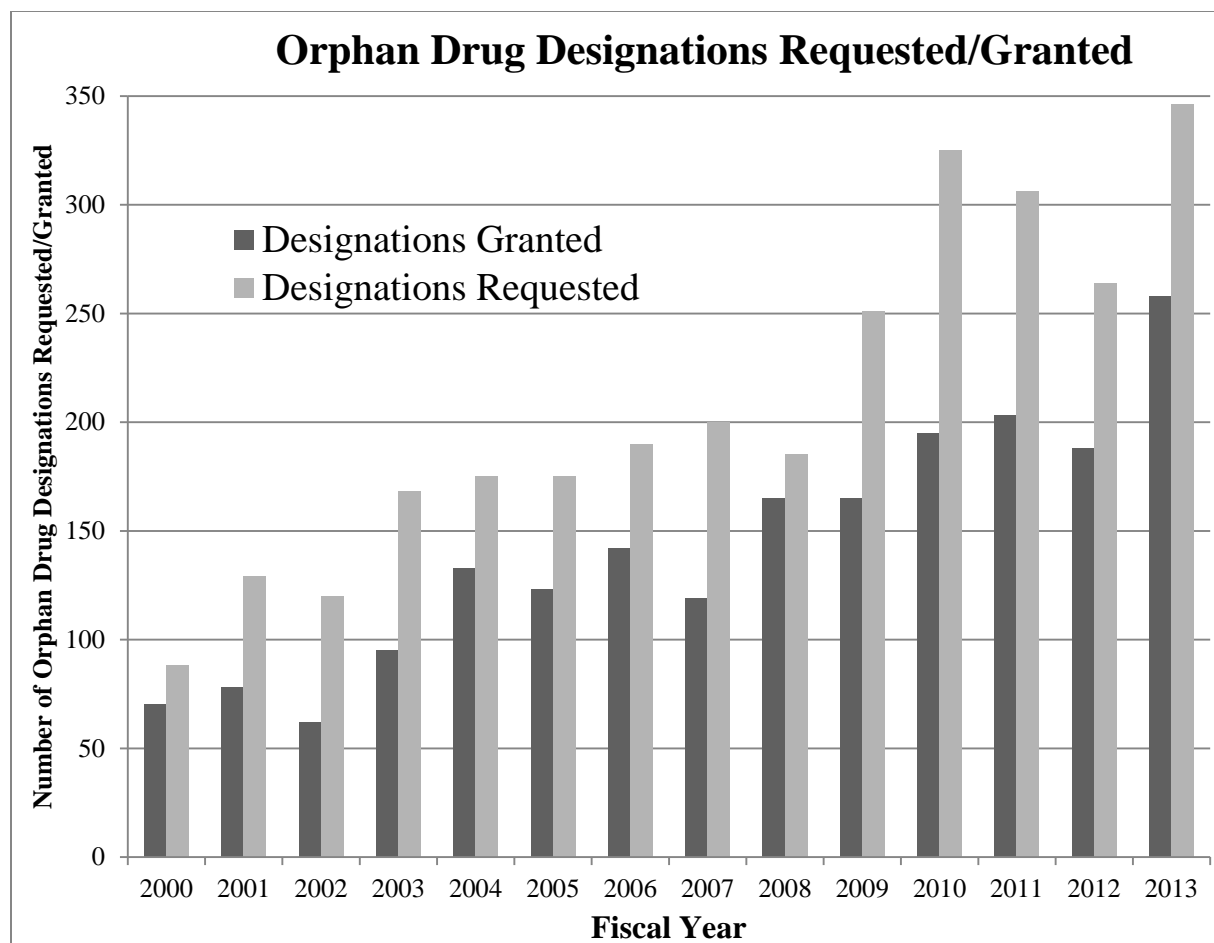
Grants are a very modest investment to better ensure that product development occurs in a timely manner. However, FDA grant funds are covering less and less of the total cost for conducting clinical trials, which continue to increase far faster than the rate of medical inflation. Recent budget cuts and 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 1983 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 seven years of marketing exclusivity upon approval.

Of the over 2,900 orphan drug designations OOPD issued since 1983, over 450 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 come to market. During FY 2013, OOPD received 3 new applications for orphan drug designation. These included potential treatments for many kinds of rare cancers and sickle cell disease. OOPD designated 235 orphan drugs in FY 2013. FDA approved 36 orphan designated drugs for marketing in FY 2013.

The number of requests for orphan designation has more than doubled since 2000. Not only are the requests increasing, but the complexity of the science associated with these orphan drugs is increasing due to advances in pharmacogenomics and personalized medicine. In FY 2013, 45 percent of all the new molecular entities (NME) FDA approved were orphan designated drugs and biologics.



Humanitarian Use Device Designation Activity

The purpose of the Humanitarian Use Device (HUD) program is to encourage the discovery, development, and use of medical devices intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. The HUD program was authorized by the Safe Medical Devices Act and 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 Federal Food, Drug, and Cosmetic Act. Since 1990, 58 HUD devices have been approved for marketing through the HDE pathway.

Except in certain circumstances, HUDs 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 Food and Drug Administration Safety and Innovation Act, a HUD is eligible to be sold for profit after receiving HDE approval if the device meets certain criteria. Currently, eight 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 2013, OOPD received 25 new HUD applications and designated twelve devices. An additional four devices were designated based on HUD applications originally submitted in prior years for a total of 16 HUD devices designated in FY 2013. In FY 2013, one device received an HDE approval from CDRH and five manufacturers received approval 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. The 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. The program was re-authorized in FY 2013 in the Food and Drug Administration Safety and Improvement Act (FDASIA). In FY 2014, nine consortia are included in this program – seven were awarded grants in FY 2013 as part of a five year cycle, two others continue from the previous grant award cycle. The consortia are based out of Boston, Philadelphia, District of Columbia, Atlanta, Ann Arbor, Los Angeles, San Francisco, and Palo Alto.

Since the Program's inception in 2009, a total of \$14.6 million have been awarded to the consortia in five years. Collectively, the consortia have supported the development of more than 240 potential pediatric devices, many of which are in the early stages of development. The success of the consortia has also garnered more than \$14 million additional non-federal research dollars to support pediatric device development research.

Outreach Activity

OOPD participates in significant 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 Orphan Products Grants Program, and the science of developing therapeutic products for rare diseases/conditions
- assisting patients and advocacy groups on issues of concern related to rare diseases and orphan products, such as drug shortages.

In FY 2013, OOPD received more than 51 invitations to speak and participate at orphan drug stakeholder meetings and including conferences. OOPD made presentations and participated in 36 of these meetings, 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 2013 include conducting training courses for researchers and reviewers, workshops for drug and device sponsors, and presentations to national and international rare disease patient groups. In FY 2014 through FY 2016, 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 2011 Actual	\$22,785,290	\$22,785,290	\$0
FY 2012 Actual	\$23,636,200	\$23,636,200	\$0
FY 2013 Actual	\$23,139,897	\$23,139,897	\$0
FY 2014 Enacted	\$23,598,688	\$23,598,688	\$0
FY 2015 Budget Request	\$23,598,688	\$23,598,688	\$0

BUDGET REQUEST

The FY 2015 Budget for the Office of Orphan Products Development is \$23,598,688 in budget authority, which is the same as the FY 2014 Enacted level. It will support eight Orphan Product Grants and seven Pediatric Consortia Grants (new and continuations).

PERFORMANCE

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 +/- FY 2014
<u>293207</u> : Percentage of reviews of first-time and amended orphan drug designation applications completed in 90 days or less. (<i>Output</i>)	FY 2013: 91% (Historical Actual)	75%	75%	maintain
<u>293208</u> : Percentage of Humanitarian Use Device designation reviews completed in 45 days or less. (<i>Output</i>)	FY 2013: 100% (Historical Actual)	95%	95%	maintain

PROGRAM ACTIVITY DATA

PROGRAM WORKLOAD AND OUTPUTS	FY 2013 Actual	FY 2014 Estimate	FY 2015 Estimate
Grants Programs			
New Orphan Product Grants Awarded	5	8	8
Total Pediatric Consortia Grants (New and Continuations)	7	7	7
Orphan Drug Requests, Designations, and Market Approvals			
New Designation Requests	330	270	270
Designations	235	189	189
FDA Marketing Approvals	36	20	20
HUD Requests and Designations			
New Designation Requests	25	25	25
Designations	14	14	14