Developing Orphan Products: FDA and Rare Disease Day

Photodisc

Organizations around the world are observing February 28, 2009, as the 2nd annual World Rare Disease Day—an important time for bringing attention to the needs of people with rare diseases.

The Food and Drug Administration (FDA) is committed to advancing rare disease therapies through the development of orphan products. When former President Ronald Reagan signed the Orphan Drug Act (ODA) of 1983 into law, no one could have imagined then that it would become one of the most important pieces of health care legislation today.

The ODA means hope for more than 25 million Americans who currently have one of 7,000 rare diseases, which includes rare disorders or conditions. More than 300 orphan

New treatments bring hope to people with rare diseases. About 80% of the 7,000 rare diseases in the United States are genetic in origin, and about 75% affect children.

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products for treatment of rare diseases have been approved by FDA since this groundbreaking legislation went into effect. In the decade before the ODA was passed, only 10 treatments had been developed for rare diseases.

What Is an Orphan Drug?

The term "orphan drug" refers to a drug or biologic (such as a vaccine or blood product) that treats a rare disease or condition. The ODA defines a disease as rare if fewer than 200,000 people in the United States have it.

An orphan drug may be a completely new product or an approved drug that's being used in the new context of a rare disease. A drug or biologic must be designated an "orphan drug" through an FDA approval process. To date, more than 1,700 drugs and biologics have been designated as orphan drugs, with more than 300 achieving marketing approval.

What Is a Humanitarian Use Device?

Although medical devices are not eligible for orphan designation, FDA has made it easier and less costly for manufacturers to bring devices for rare diseases to the market through a two-step process.

The first step is FDA approval of the device as a Humanitarian Use Device. The second step is FDA approval to market the device under the Humanitarian Device Exemption (HDE) provisions of the Safe Medical Devices Act of 1990.

This Act allows a medical device to be approved under certain conditions if manufacturers show that the probable benefit outweighs the risks for patients with an extremely rare condition that affects fewer than 4,000 persons in the United States per year. The provision requires only evidence that the probable health benefit of the device is greater than the risk of use—a standard that is less costly to achieve than the level of safety and effectiveness required for other marketing approvals.

To date, FDA's Office of Orphan Products Development (OOPD) has designated 133 humanitarian use devices, and 44 of those were approved as HDEs. Two such devices include a stent to treat urinary tract obstruction in unborn babies, and a titanium rib for children born unable to survive without an adequate ribcage. Neither of these devices would have been available outside this program.

How the Orphan Drug Act Has Helped

Developing a new drug or device can be expensive. Because rare diseases affect a relatively small number of people, drug companies generally demonstrate little interest in performing research or development of new products to treat such diseases. Developers face a further difficulty in testing potential treatments because it is difficult to recruit a sufficient number of people to study safety and effectiveness.

The ODA offers a drug developer financial benefits and incentives in exchange for performing research and development, and fulfilling the requirements to get a drug approved for a rare disease or condition.

These financial benefits and incentives include:

- Annual grant funding to defray the cost of clinical testing
- Tax credits for the costs of clinical research
- Assistance in clinical research study designs
- Seven-year period of exclusive marketing after an orphan drug is approved
- Waiver of Prescription Drug User Fee Act (PDUFA) filing fees (over $1,000,000 per application for FY 2009)

These benefits help manufacturers recover the costs of developing a drug for small numbers of people. Since being signed in 1983, the Act has been amended by Congress several times—1984, 1985, 1988, 2007—to provide further incentives for treatment development.

In separate legislation in 2007, a newly authorized "priority review voucher" (PRV) for tropical disease treatments may potentially provide additional revenue to support research and development for diseases that are rare in the United States.

FDA's Office of Orphan Products Development

In 1982, FDA established the Office of Orphan Products Development (OOPD) to identify potential orphan products and to promote the development of those that demonstrate promise for diagnosing or treating rare diseases.

The office's director, Timothy Coté,

The ODA promises to identify and address even more challenging opportunities that might ultimately translate into hope for people with rare diseases or conditions.

M.D., MPH, encourages OOPD to foster the development of safe and effective treatments for rare diseases by collaborating with:

- medical and research communities
- professional organizations
- academia
- pharmaceutical industry
- patient organizations

OOPD's accomplishments during the 2008 calendar year include:

- OOPD granted 165 new orphan drug designations to promising drugs and biologic agents, and 8 new humanitarian use device designations.

- OOPD continued its highly successful grant program to support new and continuing extramural research projects that test the safety and efficacy of promising new drugs, biologics, medical devices, and medical foods for rare diseases and conditions through human clinical trials. Since 1983, OOPD has awarded more than $246 million in support of more than 480 grants, which in turn have contributed to the development of at least 43 FDA-approved products. The total 2009 budget for grants is approximately $14 million. Typically, there are about 80 active grant-funded projects at any one time and approximately 15-20 new grants are funded each year.

- OOPD co-organized a conference with the National Institutes of Health (NIH) and FDA's Center for Biologic Evaluation and Research to highlight the need for a new Coral Snake Antivenom, existing supplies for which will run out in 18 months.

- OOPD inaugurated a new month-long course in collaboration with NIH's Office of Rare Diseases. In January 2009, 230 attendees participated in "The Science of Small Clinical Trials." The course was designed to increase awareness about the special requirements of performing drug research and evaluation in small populations.

- OOPD initiated efforts to find potentially promising drugs mentioned in FDA's records which have been abandoned by their developers for reasons other than their clinical safety and effectiveness (for example, due to a business decision or merger).

Toward a More Promising Future

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According to Dr. Coté , that means continuing and expanding one of the federal government's most successful grant programs and increasing the number of promising compounds receiving orphan status designation for rare diseases.

"The good news," Dr. Coté says, "is that dramatic scientific innovations are offering new hope for the formerly incurable; we are truly on the cusp of a radical transformation in treatments for rare diseases." FDA

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Rare Disease Day 2009
www.rarediseaseday.org/

FDA Office of Orphan Products Development (OOPD)
www.fda.gov/orphan/

NIH Office of Rare Diseases (ORD)
http://rarediseases.info.nih.gov

The Genetic and Rare Diseases Information Center
http://rarediseases.info.nih.gov/

National Organization for Rare Diseases (NORD)
www.rarediseases.org/