Rare Disease Discovery

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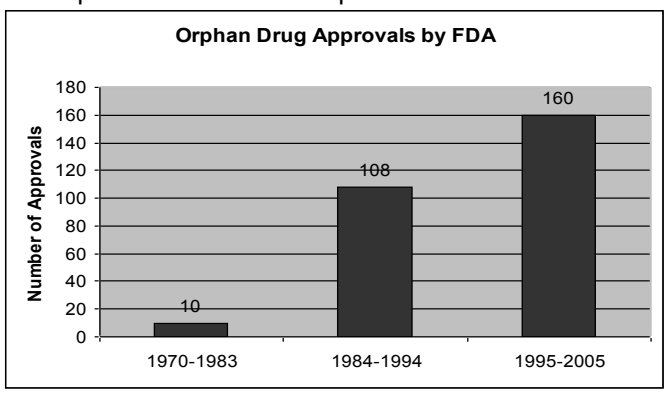
Prepared by: Peter Renevitz

Rare also known as "orphan" diseases are defined as those diseases which afflict 200,000 or less individuals within the United States. There are 6,000 known rare or "orphan" diseases. An estimated 25 million, or 1 in 10, people in the United States are afflicted with a rare disease.[1]

Recent Drug Development

Over the past 10 years (1995-2005), over 160 drugs were approved to treat rare or "orphan" diseases. This compares to 108 in the preceding decade (1984-1994) and fewer than 10 drugs in the 1970s.[2] The growth in this number is directly attributable to the Orphan Drug Act of 1983 which established incentives for drug developers to research therapies for rare diseases.



Federal Incentives and Assistance

Landmark legislation was passed at the federal level in 1983. The federal Orphan Drug Act, and subsequent measures, provide the incentives and assistance from the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) for Orphan Drug Developers:

- Seven-year marketing exclusivity upon FDA approval;
- Tax credit equal to 50% of clinical investigation expenses;
- Exemption of PDUFA application fees;
- Orphan products grant funding;
- Assistance in drug development process; and
- Office of Orphan Products Development assistance.

Prior to 1983, only 38 orphan drugs had been developed to treat orphan diseases. Since the Orphan Drug Act was passed, more than 220 orphan drugs have been approved and marketed in the United States, with more than 800 in the development pipeline.[3]

Federal Legislation

The initial orphan drug incentive legislation was passed in 1983. That measure, the Orphan Drug Act (ODA), provided grant incentives for drug developers who focused upon rare diseases. The success of the ODA led to additional incentives to be passed by Congress and approved by the President. The most recent changes were contained in the Rare Diseases Act of 2002 (PL 107-280 - HR 4013 / S. 1379), which provides the existing National Institutes of Health (NIH) Office of Rare Diseases (ORD) with a statutory authorization to increase the investment in the development of diagnostics and treatments for patients with rare diseases. It extended grants and cooperative agreements for clinical research into, training in, and demonstration of diagnostic, prevention, control and treatment methods. It also increased the authorization of the Food and Drug Administration's (FDA) existing Orphan Products Research Grant program, providing research grants to academic scientists and small companies supporting clinical trials on new orphan drugs, biologics, medical foods, and devices.

The other recent legislation was the Rare Diseases Orphan Product Development Act (PL 107-702, HR 4014). This measure amended the Orphan Drug Act by reauthorizing the Orphan Products Research Grant program contained in the Act at the amounts already-appropriated, and at $25 million per year for the Fiscal Years 2003-2006, providing additional funding for clinical trials of orphan disease therapies.

Current Policy Issues

Part D Formulary Placement. The National Organization of Rare Disorders (NORD) (see Lobbying Organizations) has raised a concern relative to the placement of rare disease medications on Medicare Part D formularies. In letters sent to the Centers for Medicare and Medicaid Services (CMS) regarding this issue, NORD has expressly stated concerns with the provisions surrounding the specialty tiering of drugs. They have stated that: "Unfortunately, the specialty tier – in principle and as drafted – allows plans to practice tier-based discrimination with impunity."[4]

AHRQ comparative effectiveness. The Biotechnology Industry Organization (BIO) is concerned that Agency for Healthcare Research and Quality (AHRQ) comparative effectiveness research will be inappropriately applied to orphan disease treatments. Due to the unique nature of

orphan treatments, many cost effectiveness and cost comparison models will be inapplicable to these products. BIO has urged AHRQ to collaborate with patient groups to ensure that measures do not harm the development pipeline.[5]

Federal Entities

National Institutes of Health Office of Rare Diseases (ORD). The office was established in 1983 within the Office of the Director of the National Institutes of Health (NIH), and established in statute in 2002 (PL 107-280). The stated goals of ORD are to stimulate and coordinate research on rare diseases and to support research to respond to the needs of patients who have any rare disease. In May 2006, the NIH announced $71 million in funding, over five years, to launch the first clinical studies of its Rare Diseases Clinical Research Network (RDCRN).[6]

The Food and Drug Administration Office of Orphan Products Development (OOPD) has, since 1982, been engaged in promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. They interact with medical and research communities, professional organizations, academia, and the pharmaceutical industry, as well as rare disease groups. The OOPD administers the program to provide incentives for sponsors to develop products for rare diseases, including the Orphan Products Grants Program.

Lobbying and Advocacy Organizations

The National Organization for Rare Disorders (NORD), a 501(c)3 organization established in 1983, is a federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. It is focused upon the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service. NORD provides information about diseases, referrals to patient organizations, research grants and fellowships, advocacy for the rare-disease community, and Medication Assistance Programs.

The Genetic Alliance links patient advocacy, community organizations, government, industry, and private entities. They attempt to foster a climate that will lead to the development of technologies and therapies; develop cohorts for clinical trials; and increase the availability of linked, annotated biological resources.

Conclusion

The Orphan Drug Act has proven to be a success in delivering: 1619 active designated orphan products, 294 approved orphan products (227 drugs, 67 biologics) with the potential to treat 15 million patients.[7] In addition, there were some unintended beneficial results from the Orphan Drug Act, including improving the economic benefit of developing products, encouraging the growth of biotechnology, developing jobs in the biotechnology

Recent Rare Disease Compound Development

Disease	Compound	Manufacturer	Year
myelodysplastic syndromes (MDS)	decitabine	SuperGen	2006
T-Cell acute lymphoblastic leukemia	Nelarbine	GlaxoSmithKline	2005
Chronic iron overload	Deferasirox	Novartis	2005
Advanced renal cell carcinoma	Sorafenib tosylate	Bayer and Onyx	2005
Myelodysplastic disorder	Lenalidomide	Celgene	2005
Mucopolysaccharidosis VI	Galsufase	BioMarin	2005
Severe primary IGF-I deficiency	Mecasermin	Tercica	2005
Glioblastoma	Temozolomide	Schering	2005
Secondary hyperparathyroidism	Cinacalet	Amgen	2004
Malignant pleural mesolthelioma	Pemetrexed	Eli Lilly & Co	2004
Acute lymphoblastic leukemia	Clofarabine	Bioenvision, Inc.	2004
Pulmonary arterial hypertension	Iloprost	CoTherix	2004

Source: A Decade of Innovation: Advances in *the Treatment of Rare Diseases, Pharmaceutical Research and Manufacturers Association, 2006.*

and pharmaceutical industries, and developing of cutting-edge technology.[8] The advancement of health care technology dramatically benefiting patient health points to the clear success of the Orphan Drug Act and its successors. It is clear that further work remains to be conducted in this area and that the incentives and assistance provided by the NIH and the FDA should be maintained.

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[1] Rare Disease Act, geneticalliance.org\public policy\federal legislation, 10/31/06

[2] More rare disease money, L. Bonetta, Nature Medicine Vol. 8, pp 1190- 1191 (2002)

[3] Food and Drug Administration, Office of Orphan Products Development, "List of All Approved Orphan Products Through the Year 2005," May 13, 2005.

[4] NORD Letter dated March 6, 2006 to CMS Administrator, re: Draft Transition Process Requirements for Part D Sponsors.

[5] BIO letter dated March 1, 2006 to AHRQ Effective Health Care Program, re: Medicare Prescription Drug, Improvement, and Modernization Act of 2003; Section 1013: Identification of Priority Topics for Effective Health Care Research; 71 Fed. Reg. 600, (January 5, 2006).

[6] Rare Disease Research Gets a Boost, Hampton, JAMA, June 28, 2006 (v. 295, n. 24), pg. 2837

[7] How do We Get to Treatments: The Orphan Drug Act Incentives to Drug Development, Haffner, Food and Drug Administration Office of Orphan Products Development, July 28, 2006.

[8] Ibid