U.S. orphan product designations more than doubled from 2000-02 to 2006-08

Designations increased from a total of 208 in 2000-02 to 425 in 2006-08

- During the 2000s, orphan products comprised 22% of all new molecular entities (NMEs) and 31% of all significant biologics (SBs) receiving U.S. marketing approval.

- Orphan products receiving priority review status rose from 35% of all orphan NMEs in 2000-02 to 50% in 2006-08; during the same time the share of orphan SBs receiving priority review status rose from 17% to 67%.

- From 2000-02 to 2006-08, average total development time for orphan products dropped by 2.3 months for NMEs and 37.5 months for SBs.

- Big biopharma’s share of orphan product approvals in the U.S. grew from 35% in 2000-02 to 56% in 2006-08.

- While biotech firms during the 2000s have garnered, on average, about one-third of all orphan drug approvals, they received just over 50% of orphan drug designations.

- Sponsors engaged in clinical development funded through orphan grants reported that 22% of their programs led to approvals, which compares with a clinical approval success rate of 16% among mainstream drug developers.

Since the Orphan Drug Act of 1983 was signed into law, it has resulted in more than 2,000 designations and 350 market approvals of drugs and biologicals for rare diseases considered “orphans,” that is, diseases affecting 200,000 or fewer patients in the U.S. Currently, approximately 6,000 orphan diseases affect more than 25 million people in the U.S.

Pharmaceutical and biotech firms have responded to the need to develop new medicinal products to treat orphan diseases. The Food and Drug Administration (FDA), in turn, has more than doubled the number of investigational compounds awarded orphan designation in the last five years alone. Reflecting the urgency in developing new drugs to treat orphan diseases, the FDA has increased the number of products getting priority review status during the past decade. These trends are summarized in this Tufts CSDD Impact Report, updating an earlier review reported in Tufts CSDD Impact Report 2002 May/Jun;4(3).
The number of orphan product designations more than doubled from 2000-02 to 2006-08

During the 2000s, orphan products comprised 22% of all NMEs and 31% of all SBs receiving U.S. marketing approval.

The number of orphan product designations increased from 208 in 2000-02 to 425 in 2006-08.

Therapeutic categories common to orphan and mainstream markets, such as antineoplastics, cardiovascular, and endocrine products, now comprise about 70% of orphan approvals. This contrasts with the 1990s, when the dominant therapeutic categories for orphan approvals differed from mainstream product approvals.

The share of orphan products accorded priority review status increased during the 2000s

Orphan products receiving priority review status rose from 35% of all orphan NMEs in 2000-02 to 50% in 2006-08.

During the same time, orphan SBs given priority review status increased from 17% to 67% of all orphan SBs.

Compared to non-orphan product approvals, for which 30% on average had priority review status, orphan product approvals were more likely to be considered advances over currently available therapeutic options on the market.

Average total development time for orphan products declined during the 2000s

From 2000-02 to 2006-08, average total development time (from investigational new drug application [IND] filing to NDA approval) for orphan NMEs dropped by 2.3 months.

During the same time, average total development time for orphan SBs declined by 37.5 months. Note that SB cohorts were relatively small, e.g., 5 products per cohort.

Although total development times for most orphan and mainstream NMEs and SBs were similar during the first half of the 2000s, in 2006-08 orphan times were faster.
Big biopharma garnered a growing share of orphan product approvals during the 2000s

The share of orphan product approvals by large pharma (companies with more than $1B in annual revenue) and large biotechs (more than 500 employees) in the U.S. grew from 35% in 2000-02 to 56% in 2006-08.

During the same time, small companies (biotechs with 100 or fewer employees, phamas with $100 million or less in annual revenue) saw their share of orphan product approvals decline from 44% to 33% of all such approvals.

The number of “orphan blockbusters” increased from a decade ago when 4 orphans made the Top 200 list for U.S. drug sales in 1999-01. In 2006-08, 16 orphan products made the list, with annual sales ranging from $200 million to nearly $2 billion.

Pharmaceutical companies outflank biotech firms in winning approval for orphan drugs

In 2006-08, biotech companies won 28% of all orphan drug approvals, a drop from its 39% share of 2000-02.

While biotech firms have received, on average, about one-third of all orphan drug approvals during the 2000s, they garnered just over 50% of orphan drug designations.

Most recently, an increasing number of nonprofit research institutes, academic medical centers, and other non-traditional sponsors have been winning orphan drug approvals.

Orphan grant-funded R&D has led to more product approvals, compared to mainstream R&D

According to a Tufts CSDD survey of 72 orphan product development grantees, 87% were affiliated with academic institutions and 6% with a nonprofit research center. Only 7% identified themselves as a corporate entity.

Sponsors engaged in orphan grant-funded development reported that 22% of their clinical programs led to approvals, which compares with a clinical approval success rate of 16% among mainstream drug developers.

For FY 2010, more than $14 million in orphan grants has been budgeted by the FDA, which is expected to support 60-85 drug, biologic, medical device, and medical food projects.
About this study
The findings summarized in this report are derived primarily from two sources: Tufts CSDD databases and surveys of orphan grant recipients conducted by Tufts CSDD in the mid-2000s. In its analyses, Tufts CSDD utilizes data collected from sponsors of newly marketed drugs as well as from publicly available sources, such as FDA websites. The orphan grantee survey was conducted on a sample universe comprised of all 117 recipients of FDA orphan product grants from 1991-98, who responded to questionnaires in 2002 and 2005. This allowed for a minimum follow-up period of eight years to a maximum of 15 years. The response rate was 62% for the first survey, with six respondents subsequently lost to follow-up by the second survey.

The review was conducted by Christopher-Paul Milne, DVM, MPH, JD, Associate Director, and, Lanna Feldman, BA, Research Analyst, both of the Tufts Center for the Study of Drug Development, and Danielle Delosh, BA, Research Intern.

Definition of terms
Clinical approval success rate — Percentage of investigational new compounds entering clinical testing that eventually obtain FDA marketing approval for a new drug application (NDA) or biologics license application (BLA).

NME — New molecular entity. Refers to a newly developed compound, whose active ingredient has not been previously approved in the U.S. The term was coined by the FDA for use in its published statistical reports.

Orphan drug — Drug developed for a rare disease or condition, which, in the U.S., affects fewer than 200,000 people, or, in the European Union, affects 5 per 10,000 people or fewer. Because sales of orphan drugs are likely to be small compared to their development costs, sponsors are awarded exclusive rights to market these medicines for a period of time as an incentive to develop them, in addition to access to tax credits, R&D grants, fee waivers, and FDA technical and scientific advice.

Priority drug — A new drug considered by the FDA to offer high therapeutic value and earmarked for priority review. The FDA’s Center for Biologics Evaluation and Research (CBER) also grants priority review status, but the criteria are somewhat different than the FDA’s Center for Drug Evaluation and Research (CDER) – the product must also be for serious or life-threatening illness.

Significant biologic — A new biologics license application (BLA)—that is, an application to FDA for a license to market a new biological product—which the FDA considers to be especially important.

About the Tufts Center for the Study of Drug Development
The Tufts Center for the Study of Drug Development at Tufts University provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Tufts CSDD conducts a wide range of in-depth analyses on pharmaceutical issues and hosts symposia, workshops, and public forums.

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