Book Reviews

Issues of Drug Development

Orphan Drugs. Medical versus Market Value. CAROLYN H. ASBURY. Lexington (Heath), Lexington, Mass., 1985. xviii, 221 pp. $27.

The Orphan Drug Act was passed in the last days of the 97th Congress and became law in January 1983. The law is designed to provide incentives for the development and marketing of medically useful therapies that have become "orphans" in our market-oriented system. Though this system has produced major therapeutic advances in areas such as infectious diseases, contraception, and mental illness, relatively rare conditions like multiple sclerosis, Huntington's disease, or myoclonus have not fared as well. The problem is that to develop and obtain approval to market medicines for such conditions can be enormously expensive—costing tens of millions of dollars. High development costs coupled with small markets, lack of patent protection, and potentially high liability risks all contribute to the problem of orphanization. Though the pharmaceutical industry has made some drugs for rare diseases available as a form of corporate good will, many potentially useful therapies remain on the shelf as orphans.

Though this problem has long been recognized by many academic researchers and the relevant patient groups, orphan drugs were a relatively low-priority issue in Congress until an episode of the television program "Quincy" dramatized the problem in 1981. This was the catalyst for expanded media attention and public hearings. An alliance of patient groups, the National Organization for Rare Diseases, came together in this new environment to become an effective lobby for congressional action. After a series of political maneuvers and delicate compromises, the Orphan Drug Act was enacted and signed by President Reagan.

These events are vividly described in this book by Carolyn Asbury. She provides an expert, insider's view of the problem. In addition to her Ph.D. thesis work on orphan drugs, she collaborated with Congressman Waxman's House Subcommittee on Health and the Environment to prepare and analyze a survey of 196 orphan drug candidates as part of the hearings process. This provided valuable information on the scope and causes of the problem, which had previously been analyzed only piecemeal.

Asbury's book provides an extensive analysis of the orphan drug problem and its relations to other developments in pharmaceuticals. She has pulled together and synthesized a great deal of useful material that has previously been accessible only in academic conference volumes and journals. Though the book will sometimes be tedious reading for the general reader, it will reward those who are persistent. It is quite comprehensive and includes among other things a fascinating discussion of the organizational changes now occurring in molecular biology and what these portend for the orphan drug problem.

A key policy question, of course, is how effective the Orphan Drug Act will be in stimulating the development of drugs for rare illnesses. The last few chapters of Asbury's book analyze the legislation and discuss what has occurred since it was passed two years ago. Under the act, the Food and Drug Administration is empowered to assign orphan drug status to any drug for which there is no reasonable expectation that development and distribution costs would be covered by U.S. sales. FDA guidelines have designated as orphan diseases those with patient populations of less than 200,000. The act provides for a 50-percent tax credit on the costs of clinical development for a drug for an orphan disease and a seven-year marketing exclusivity period. It also requires the FDA to provide recommendations to sponsors who wish to know, in advance of testing, what will be required to obtain marketing approval. Some modest public funds for orphan drug R&D are also authorized by the legislation.

Though it is too soon to assess the effectiveness of the law, there have been both encouraging and discouraging developments. On the plus side, great strides have been made in expanding the sources of information on orphan drugs. As Asbury indicates, a strong network of cooperating institutions representing industry, government, universities, and voluntary health groups has evolved in the orphan drug area. As a result, many of the compounds that were identified as orphans now have corporate parents. Six orphan products were approved by the FDA in 1983 and five in 1984. In addition, 37 products under development were given orphan drug status by the FDA in 1984. This is a dramatic increase in orphan drug development.

Whether this momentum will carry beyond the exploration of known orphan drug compounds into new areas of R&D is much more conjectural. The key economic incentives provided by the act, tax credits, have been little utilized by the pharmaceutical industry. Pharmaceutical firms have argued that the economic stimulus for long-term R&D on orphan drugs provided in the act is too small and too limited in character. Many of the R&D expenditures that are necessary for regulatory approval (for example, those for preclinical testing and animal toxicology tests) do not carry tax credits. In addition, the act provides inadequate incentives for products for which liability risks are large, such as vaccines, in the case of which firms have continued to withdraw from the market and R&D activity.

The orphan drug problem is obviously a complex one that gives rise to difficult policy trade-offs and dilemmas. It will require continued societal attention in the years ahead. This book by Asbury is a valuable contribution to our understanding of the problem.

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Pan paniscus

The Pygmy Chimpanzee. Evolutionary Biology and Behavior. RANDALL L. SUSMAN, Ed. Plenum, New York, 1984. xxviii, 435 pp., illus. $59.50. From a symposium, Atlanta, Ga., Aug. 1982.

Based on contributions to a widely attended symposium held in conjunction with the ninth congress of the International Primatological Society, this volume focuses on the systematics, molecular biology, morphology, behavior, and ecology of a single primate species: *Pan paniscus*, the pygmy chimpanzee, the least known of the great apes. A number of evolutionary questions arise with respect to the pygmy chimpanzee. First, what exactly are its phyletic affinities with the other African hominoids, in particular the common chimpanzee? Second, does it represent, as its common name implies, a phyletic dwarf—as the talapoin monkey does among Old World