MARKET-DRIVEN RESEARCH AND DEVELOPMENT HAS OFFERED a few new treatments for patients with rare illnesses. In the United States, rare or “orphan” diseases are defined as illnesses with a prevalence of fewer than 200,000 individuals at any given time; examples include Creutzfeldt-Jakob disease, Wilson disease, and Landau-Kleffner syndrome. Similarly, “orphan” drugs are those that are likely to be unprofitable either because the patient population is too small or because the disease is prevalent only in developing nations. Thus, even drugs targeting Chagas disease, which threatens a quarter of the population of Latin America, or African trypanosomiasis, which affects nearly 300,000 individuals per year, are considered orphan because of their low profitability. The Global Forum for Health Research has estimated that about 90% of total biomedical research funding is spent on only 10% of the world’s health burden.

Orphan drug development is limited, in part, by a general lack of knowledge about the pathophysiology of these diseases and the relative unavailability of subjects for clinical trials. The major hurdle, however, is the cost of investing in a pharmaceutical agent with poor market potential. Given the small number of patients who would benefit from an orphan drug, or, in the case of developing nations, the small number of patients who could pay for the medication, there is little motivation for industry to invest in these drugs.

Some proponents of orphan drug development have argued for more public funding and legislation to increase market-driven research on orphan drugs. For orphan drug investigation in the United States, these options appear to have been partly successful. The US Orphan Drug Act, signed into law in 1983, provides incentives to the pharmaceutical industry for rare disease drug development such as market exclusivity for orphan drugs designated by the US Food and Drug Administration (FDA), research tax credits for clinical studies of orphan diseases, and the establishment of federal Orphan Product Development grants. Before 1983, only 7 drugs were available to treat orphan diseases. Since then, however, more than 900 orphan drugs have been developed, and more than 200 have received marketing approval by the FDA. In addition, on November 7, 2002, the Rare Diseases Act and Rare Disease Orphan Product Development Act were signed into law. These acts established an Office of Rare Diseases within the National Institutes of Health and authorized appropriations for Rare Disease Regional Centers of Excellence. Japan, Australia, and the European Union have spurred development of drugs for rare diseases in similar ways. These approaches are not nearly as applicable, however, to rare or prevalent diseases of developing nations, which are unable to offer the same market incentives as developed countries.

One way to increase funding for orphan drugs in developing nations is through public-private partnerships, whereby the private sector (including for-profit pharmaceutical agencies and not-for-profit philanthropic foundations) joins the public sector (government and universities) to coordinate and fund research projects that address orphan diseases in developing nations. Such partnerships are unique in that they foster competitive drug development but are managed as not-for-profit “social ventures.” Recently established partnerships include the Medicines for Malaria Venture and the Hookworm Vaccine Initiative.

While public-private partnerships represent a new mechanism for drug development in developing nations, they do not provide the solution for all orphan illnesses. Diseases that are both rare and endemic to impoverished nations will require largely need-driven, nonprofit approaches. One such initiative, the Drugs for Neglected Diseases initiative (DNDi), was established in 1999 by the nonprofit organization Doctors Without Borders. Although DNDi relies on pharmaceutical companies for scientific expertise and catalogs of active compounds, it operates from the premise that drugs for neglected diseases are public goods. The initiative aims to secure long-term funding from governments, international organizations, foundations, and individual charitable contributions. By forming research initiatives using collaborations between international scientists, health care workers, and nonprofit organizations and by using funds largely from the public sector, DNDi may represent another strategy to address orphan illnesses with low prevalence in developing nations.

REFERENCES