

Measuring Progress in Neglected Disease Drug Development

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ABSTRACT

Background: Since the late 1990s, funding for development of neglected disease drugs has increased with an influx of resources from product development partnerships (PDPs). Previous research showed modest gains in drug approvals and products in Phase III of clinical development in the period 2000–2008.

Objective: We assessed the 2009–2013 period in terms of numbers of products in Phase III development and numbers of approvals. Subsequently, we calculated the PDP share in terms of sponsorship of new approvals. We also identified the numbers of 2000–2013 approvals included in the World Health Organization's Essential Drug List (EDL).

Methods: We identified new approvals and Phase III products targeting neglected diseases in the period 2009–2013 by searching ClinicalTrials.gov, IMS R&D Focus, and Investigational Drugs Database, as well as drug regulatory agency websites. Subsequently, we determined which products approved between 2000 and 2013 have been included in the most recent version of the EDL.

Results: We found 20 new approvals targeting neglected diseases in the period 2009–2013. PDPs were the primary sponsor of 57% of new approvals in this time frame. Approvals included 1 new molecular entity, 5 vaccines, 2 new indications, 9 fixed-dose combinations, and 3 new formulations. HIV/AIDS (pediatric indications) and malaria accounted for 60% of approvals in 2009–2013. The average number of new approvals per year for neglected diseases rose from 2.6 in 2000–2008 to 4.9 in 2009–2013. The World Health Organization included 44% of 2000–2013 approved products on the EDL. We found 18 products currently in Phase III of clinical development. Products in Phase III testing included 3 new molecular entities, 6 vaccines, 2 fixed-dose combinations, 5 new indications, and 2 new formulations.

Conclusions: Increased funding through PDPs for neglected disease drug development seems to be producing results. Approvals and products in Phase III testing have shown a steady increase since 2000,

with nearly a doubling of products in 2009–2013, compared with 2000–2008, in terms of the annual average yield. However, only 3 new molecular entities have been approved in 14 years. In addition, malaria and HIV (pediatric indications) seem to have benefited most from increased funding, whereas less success has occurred with other diseases. Inclusion of newly approved products on the EDL has been slow and limited, with only 44% of new approvals added to the list. Uneven progress suggests funding could be better targeted. In addition, PDPs could do more to facilitate access, in particular by working closely with the World Health Organization to assess the clinical effectiveness and cost-effectiveness of new approvals. (*Clin Ther.* 2014;36:1037–1042) © 2014 Elsevier HS Journals, Inc. All rights reserved.

Key word: neglected diseases, essential drug list, product development partnerships, World Health Organisation.

INTRODUCTION

Neglected tropical diseases are a set of ~20 diseases affecting nearly 1 billion people in the world's most impoverished regions: 17 neglected tropical diseases, in addition to the so-called "big 3" (malaria, tuberculosis, and HIV/AIDS).^{1,2} Neglected tropical diseases include, among others, leishmaniasis, Chagas disease, Buruli ulcer, onchocerciasis, and Dengue fever. It is estimated that these diseases cause 35,000 deaths per day worldwide.² Yet until recently, the pharmaceutical industry and global policy-makers paid little attention. Trouiller et al found that only 13 of the >1400 new molecular entities approved worldwide between 1975 and 1999 targeted neglected diseases.^{3,4} After many decades of comparative disregard by policy-makers, governments,

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and the pharmaceutical industry, neglected diseases have caught the world's attention. Beginning in the late 1990s, the Bill and Melinda Gates Foundation has committed significant resources earmarked for neglected disease drug development. Since then, an array of high-profile product development partnerships (PDPs) has been established, such as the Medicines for Malaria Venture, Drugs for Neglected Diseases Initiative, and TB Alliance. Reports suggest significant increases in PDP-sponsored research in neglected disease drug development.^{5,6}

PDPs are nonprofit public-private partnerships created to advance research and development through collaboration among public sector entities such as the World Health Organization, philanthropic organizations, and the pharmaceutical industry. Funding for PDPs derives mostly from philanthropic sources and the public sector. Partnerships also often involve non-monetary donations from pharmaceutical firms, or they entail a firm holding the intellectual property for the product being developed. The specific objectives of individual PDPs vary, but the mission is broadly the same: to develop drugs that address the health needs of vulnerable populations in the developing world.⁷

Public awareness and funding surrounding neglected diseases have increased.⁸ But how productive have the funding and research efforts been? In other words, how many drugs are in the latter stages of the drug development pipeline, and how many products have been approved since 2000? We addressed these questions in the present study. We updated our previous work that examined findings between 2000 and 2008 of approvals targeting neglected diseases and products in the pipeline (Phase III).⁴ Our objectives were to identify numbers of new approvals between 2009 and 2013, Phase III products targeting neglected diseases, the PDP share in terms of sponsorship of new approvals, and listing of new approvals on the World Health Organization's Essential Drug List (EDL).⁹ Increased numbers of approvals are a necessary but insufficient condition to improving patient access to products targeting neglected diseases.¹⁰ Therefore, in addition to identifying new approvals, we examined an access proxy. We selected placement of 2000–2013 approvals on the most recent version of the EDL as an access proxy. The EDL is a benchmark gauge of basic pharmaceutical needs for developing countries. The list, which is updated biennially, includes “those drugs that satisfy the health care needs of the majority of the population; they should therefore be available at all

times in adequate amounts and in appropriate dosage forms, at a price the community can afford.”¹¹

MATERIALS AND METHODS

We identified new approvals and Phase III products targeting neglected diseases in the period 2009–2013 by searching databases of ClinicalTrials.gov, IMS R&D Focus, and Investigational Drugs Database, as well as websites from drug regulatory agencies, including the US Food and Drug Administration and the European Medicines Agency, and the Indian and Brazilian regulatory authorities. We identified 5 categories of newly approved and Phase III products: new molecular entities, new vaccines, new uses of existing drugs, new fixed-dose combinations, and new formulations. We compared numbers of approvals we had previously identified in the 2000–2008 period with those for 2009–2013. We also examined the proportionate share of sponsorship of new neglected disease drug approvals by PDPs and the pharmaceutical

Table I. Number of approvals targeting neglected diseases, 2009–2013.

Disease	No. of Approvals
HIV/AIDS*	8
Malaria	5
Tuberculosis	2
Dengue fever	0
Onchocerciasis/schistosomiasis	0
Leprosy	0
Trachoma	0
Buruli ulcer	0
Rheumatic fever	0
Typhoid and paratyphoid fever	0
Leishmaniasis/chagas disease/ African sleeping sickness	1
Cholera	1
Streptococcus pneumonia	1
Neisseria meningitidis	1
Japanese encephalitis	1
Total approvals	20

*HIV/AIDS is not a neglected disease. However, pediatric indications are included in the Global Funding of Innovation for Neglected Diseases definition of neglected diseases.²

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