5 Research and development funding for infectious diseases of poverty: from landscape to architecture
Chapters 1 to 4 of this report have highlighted the importance of research – at all levels and in different disciplines – in tackling infectious diseases of poverty. There are currently many funders of such research and a wide range of stakeholders involved in the research process. However, resources are limited, so it is critical that funds are distributed and used so that they address the public health needs of disease endemic countries in the most effective way. To do this, we need to improve understanding of the research and development funding landscape, a landscape that has become increasingly complex in recent years. We address this issue in this chapter.
What are the issues at stake?

Deciding how to allocate financial resources for research and development (R&D)\(^1\) relating to health opens up a complex web of competing and sometimes conflicting priorities, in which the needs of the recipients do not always match the interests or the motivations of the donors. With the shadow of the global financial crisis hanging over us, and as we face increasing constraints upon resources, it is not surprising that the funding of R&D for infectious diseases of poverty\(^2\) raises many issues that give cause for concern.

Despite these gloomy times, there does appear to be some good news. Despite a slight decline in 2010, at US$ 3.06 billion, global expenditure on R&D for neglected diseases is nearly 19.5% higher than in 2007 (1, 2). This is a significant rise which, if invested wisely, could produce great dividends. However, we need a better understanding of how research is funded (i.e. of the funding landscape) in order to ensure that funds are directed to where they are needed most.

In this chapter we review the existing knowledge on funding flows and describe the mechanisms through which this funding is channelled and the type of research it supports. We briefly describe the different categories of funders that will be useful for newcomers to the field and for potential recipients of R&D funding; analyse available information on where and how these funders are applying their resources; and outline disease categories plus types of R&D activities targeted by funds aimed at tackling infectious diseases of poverty. We also provide a vignette of findings from an unpublished WHO/TDR commissioned study – the TDR Research and Development Funding for Infectious Diseases of Poverty Landscape Analysis – performed in a partnership involving the Global Forum for Health Research, Policy Cures and Biblioteca Regional de Medicina (BIREME) in Brazil. Building on other studies, this study focuses on infectious diseases of poverty and broadens the scope of R&D to include implementation research and capacity building – areas of research most pertinent for health in disease endemic countries where health systems and research capacity are often weak. The methodology for this WHO/TDR commissioned study is provided later in Box 5.1.

This chapter concludes with recommendations on the ways that the financial architecture governing these flows can be strengthened so that it reflects the key priorities of countries and populations at risk and increases the efficiency with which funds are applied.

The big picture: current funding landscape and some recent trends

A COMPLEX LANDSCAPE

There are three main sources of funds for R&D for infectious diseases of poverty: (i) the public sector (e.g. ministries of science and technology or aid agencies); (ii) the private sector (e.g. multinational pharmaceutical companies or biotechnology companies); and (iii) philanthropic foundations and individuals/private charitable organizations such as The Bill & Melinda Gates Foundation (Gates Foundation) and the Wellcome Trust. One might therefore expect funding flows to be relatively simple – but this is not the case. The funding landscape is confusing for both donors and recipients. Its complexity is characterized by multiple, diverse and overlapping sources of funding; multiple recipients for funding; multiple mechanisms of funding and a multiplicity of

\(^1\) The term “research and development” (R&D) traditionally refers to activities undertaken for the discovery or development of a new product such as a drug or diagnostic tool. In this chapter, and in the WHO/TDR commissioned unpublished study (TDR Research and Development Funding for Infectious Diseases of Poverty Landscape Analysis), we refer to R&D in a broader sense, including areas of research such as implementation research, capacity building and social and environmental drivers of infectious diseases. However, at times we refer to earlier studies (such as those presented in G-FINDER reports) which use a narrower definition of R&D.

\(^2\) The term “infectious diseases of poverty” (as defined in Box 1.1) is used throughout this chapter unless specifically referring to other studies. For instance, the term “neglected diseases” is used when referring to G-FINDER reports (these define “neglected diseases” by means of a three-step filtering algorithm).
roles; absence of overall coordination and prioritization; and a lack of comprehensive data and impact measurement. A full understanding of the financial flows into R&D for infectious diseases of poverty is further complicated by the fact that funders often participate in different mechanisms of support for R&D. Recipients also receive funds from diverse sources; disentangling these is not straightforward. Fig. 5.1 provides an overview of funding flows for R&D which illustrates the complexity. While a multiplicity of funding sources can have advantages, a lack of overall coherence and incomplete data are blunting potential benefits. There is no reliable figure for the proportion of donor funds “wasted” through duplication and un-coordinated initiatives, but it would be expected that better coordination would lead to a release of funds that could be directed to areas of research where they are most needed.

**UNMET TARGETS**

Council on Health Research for Development (COHRED) recommendations dating back to 1990 suggest that low and middle-income countries apply 2% of their total health budget (excluding the portion from external sources) to R&D. This commitment has been regularly reaffirmed at several international conferences such as those held in Mexico, Abuja and Bamako. COHRED also recommended that donor countries spend 5% of their health-related aid on R&D and capacity building but no donor has ever committed to implement this target. Meanwhile, the international community continues to debate the figures and mechanisms to help implement these decisions effectively.

**BALANCING FUNDS AND NEEDS**

Funders can provide funds according to a wide spectrum of criteria. Some diseases need a concerted effort, with all stages of disease-related R&D requiring a large financial investment. For other diseases, a more modest contribution at a specific stage may suffice. In some cases there is a need for basic research, in others there is a need to focus on product development, clinical research or implementation research. The key question is: how can funders best target their support so that they provide the right type of investment, avoid wastage and build capacity? In order to address this question, funders need access to data and knowledge 3 The Ministerial Summit on Health Research, Mexico, 2004; The High Level Ministerial Meeting on Health Research in Africa, Abuja, 2006; and the Global Ministerial Forum on Research for Health, Bamako, 2008.
to inform their funding decisions, and tools to help them “access and compare disease burden, state of the science, and knowledge and product gaps, as the basis for deciding into which disease and product areas they can best invest in” (3).

Some diseases need a concerted effort.... For other diseases, a more modest contribution at a specific stage may suffice. ...The key question is: how can funders best target their support so that they provide the right type of investment, avoid wastage and build capacity?

**CONTRADICTORY TRENDS**

In 2010, a WHO expert working group on research and development coordination and financing recommended that at least US$ 3 billion per year should be allocated for R&D directed at the health priorities of the world’s poor (4). The total figure of US$ 3 billion directed towards R&D for neglected diseases (mentioned earlier) would therefore seem encouraging. Unfortunately, this note of optimism is tempered by trends that seem to go in the opposite direction. Firstly, contributions from philanthropic donors (such the Gates Foundation) and public sector organizations (including the United States of America’s NIH) both fell in 2010, by 12.4% and 5.9%, respectively, compared to the previous year (2). Secondly, funding for basic research related to neglected diseases rose by nearly 15% between 2008 and 2010, much faster than overall allocations to R & D in neglected diseases which rose by 3.6% over the same period. This may have been at the expense of investment in implementation research (which could meet the more immediate need to have impact “on the ground”). For example, in 2010 more than half of the research funding for human African trypanosomiasis (sleeping sickness) went to basic research, despite the fact that control and management would benefit markedly from the development of new, safe, oral drugs that are active against the two stages of this disease (2).

**IMPLEMENTATION RESEARCH FUNDING – THE POOR RELATIVE**

Recent years have seen a shift in funding patterns, with governments and funders from low and middle-income countries playing a large part in R&D for infectious diseases of poverty. Traditionally, funding came from high-income countries. Now low and middle-income countries make greater funding available and there is increased inter-country collaboration between researchers in these countries (“south–south” collaborations). As the research capacity for novel work (basic research or product development) remains limited in low and middle-income countries, the likely priority for these countries is to ensure the delivery of drugs, vaccines and interventions developed elsewhere. Not surprisingly, as much as one third of low and middle-income countries’ government funding for R&D related to infectious diseases of poverty goes to implementation and health systems research (5). However, funding for implementation research remains limited as funders from high-income countries (with the possible exception of philanthropic funders) give this lower priority.

This imbalance – whereby most global effort goes into the development of new drugs rather than the development of new ways to deliver products effectively to the poorest populations in an acceptable form and manner – needs to be addressed. The creation of incentives to complete the research
cycle from product development to product implementation is key to controlling infectious diseases of poverty. It is also crucial to advance health systems research, given its broader approach to answering implementation-related questions that affect a range of health problems at the same time.

"The creation of incentives to complete the research cycle from product development to product implementation is key to controlling infectious diseases of poverty."

**THE ROLE OF PRODUCT DEVELOPMENT PARTNERSHIPS: CAN SUCCESS BE MAINTAINED?**

PDPs are intended to bring together for-profit enterprises, academic researchers and others for the purpose of developing a drug, vaccine or intervention that does not have a ready market, a feature characteristic of infectious diseases of poverty. The idea is to facilitate collaboration and provide financial support to promising initiatives involving academics and commercial entities. Over the last decade, the emergence of PDPs that focus on areas such as malaria and diagnostics has helped to maximize the value of contributions from governments, philanthropic funders, academic research centres and private industry by leveraging their individual competencies towards specific goals. Prominent examples of PDPs include the European

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**BOX 5.1. METHODOLOGY AND DATA SOURCES FOR THE WHO/TDR COMMISSIONED STUDY – THE TDR RESEARCH AND DEVELOPMENT FUNDING FOR INFECTIOUS DISEASES OF POVERTY LANDSCAPE ANALYSIS**

As well as other information sources (such as G-FINDER reports) this chapter draws on original research commissioned by WHO/TDR, undertaken in partnership with the Global Forum for Health Research (now part of COHRED), Policy Cures and BIREME, with financial support from the European Commission. This work focuses on infectious diseases of poverty (as defined in Chapter 1) and uses a broad description of R&D that includes implementation research. The research comprised both quantitative and qualitative analyses as outlined below.

**Quantitative study**

The WHO/TDR commissioned study provided an in-depth analysis of R&D spending for infectious diseases of poverty by four major sources – two public sector entities (the United States of America’s NIH and the European Commission) and two private foundations (Gates Foundation in the United States of America, Wellcome Trust in the United Kingdom). These four organizations account for nearly three quarters of global spending on R&D for infectious diseases of poverty (6).

**Qualitative study**

Semi-structured telephone interviews with representatives from 34 public sector funding agencies from 32 countries in the 6 geographical regions defined by WHO were conducted as part of the study. This survey examined the extent to which public sector funders from high-income and disease endemic countries are involved in R&D for infectious diseases of poverty and the priorities that guide their R&D funding activity. Of these interviewees, 16 funders were from high-income countries (6 bilateral aid agencies, 10 national science and technology agencies) and 18 were from low and middle-income countries (7 national health research institutions, 11 national science and technology agencies). Investment data on R&D funding for infectious diseases of poverty between 2007 and 2009 were collected during the interviews and supplemented with data from the 2009 G-FINDER survey (3).
Research output

The study also carried out a bibliometric study of 173,578 articles on infectious diseases of poverty, published between 2000 and 2009, in order to investigate the research outputs produced by low and middle-income country researchers, their research collaboration with other countries and their ownership of research. In this chapter we also use information from literature published post-2009, including the 2010 and 2011 G-FINDER reports (2, 5) that focus primarily on basic and applied (product development) research funding provided by more than 200 institutions, including almost all major high-income country funders and a few of the major low and middle-income country funders such as Brazil, Colombia, India and South Africa.

Some limitations

A combination of the complexity of the financial flows associated with R&D funding for infectious diseases of poverty, the difficulty of obtaining data on funding in relation to certain types of implementation research and the fact that interest in funding of R&D for infectious diseases of poverty is of relatively recent origin means that the information available on the subject is necessarily limited. This is particularly true for implementation research, in-kind support and for funding flows originating in low and middle-income countries. Differences in methods across studies also make comparison of funding flows and their aggregation difficult (6).

Notwithstanding these data collection difficulties, the information on funding flows emanating from the qualitative study referred to in this chapter is a reasonable representation of the characteristics of research spending on infectious diseases of poverty, except for implementation research or on-the-job innovation. This is because the study captured information on organizations with the highest levels of investment in infectious diseases of poverty R&D, and also because all the major categories of agencies known to be involved in R&D funding for infectious diseases of poverty (aid agencies, science and technology agencies and private foundations) were included in the study.

and Developing Countries Clinical Trials Partnership (EDCTP), International AIDS Vaccine Initiative (IAVI), Program for Appropriate Technology in Health (PATH), Aeras Global TB Vaccine Foundation (Aeras), Medicines for Malaria Venture (MMV) and the Drugs for Neglected Diseases initiative (DNDi). Since their inception, PDPs have benefited greatly from non-financial contributions: for instance, the pharmaceutical industry has donated drugs and made molecule databases and technical expertise available at little or no cost4. Such collaborative efforts have allowed PDPs to deliver nine new drugs, diagnostics and vaccines for malaria, tuberculosis (TB), meningitis and visceral leishmaniasis.

PDPs have also developed the largest pipeline of products for neglected diseases ever assembled: over 140 projects are currently in development (3). Yet, despite this success, in 2010 PDPs received US$ 97 million less funding than in 2008 (2). It is too early to say whether this indicates that PDPs are losing their place as “flavour of the day” for large donors, but it is certainly a cause for concern at a time when several PDP products are reaching the Phase III human clinical trial stage.

4 In 2012, for example, a number of pharmaceutical companies and global health organizations formed a new partnership to combat neglected tropical diseases through drug donation, sharing of expertise and knowledge, and support for R&D. (http:// www.unitingtocombatntds.org, accessed 29 February 2012).
A more detailed picture of funding of R&D for infectious diseases of poverty

WHAT IS THE TREND FOR R&D FUNDING?

Detailed long-running data on funding of R&D for infectious diseases of poverty are unavailable. With the exception of HIV-related R&D funding, little is known about funding of R&D for infectious diseases of poverty prior to 2007. What is known is that expenditure on total health R&D increased by more than four times in nominal terms during the period from 1986 to 2005 (7, 8) – an increase beyond inflation. It is likely that the last decade also experienced much faster growth in funding of R&D for infectious diseases of poverty compared to the 1980s and 1990s, in line with overall health R&D. This is particularly true due to increased support from the Gates Foundation; increased funds from private companies, philanthropists and governments for a number of PDPs; and new funding vehicles such as GAVI Alliance and the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). Compared to preceding decades, public–private partnerships (PPPs) led to significantly expanded efforts towards new drug development in the period from 2000 to 2005 (7, 9). Countries such as Argentina, Brazil, China, India and South Africa also account for a small but rising share of funding for R&D in the first decade of the millennium (2, 8). For instance, Brazilian funding of R&D for health grew by nearly 29% in real terms between 2000 and 2005 (10).

G-FINDER reports are currently the only source providing aggregated data covering major public, private and philanthropic contributions to funding directed towards R&D for neglected diseases for the period from 2007 to 2010. These G-FINDER reports do not include estimates on R&D funds related to implementation research, capacity building or “knowledge translation”. This means, for example, that data on funding via bilateral agencies that focus on health service financing or delivery issues are excluded; nor do they include information on funding for research on social and environmental drivers of health.

As mentioned earlier, funding of R&D for neglected diseases increased by nearly 20% between 2007 and 2010, with total funding of just over US$ 3 billion in 2010 (2). Although comparable estimates for earlier years are unavailable, estimates for R&D on all health were in the region of US$ 105 million at the beginning of the millennium (7). This gives some perspective on the tremendous growth in R&D for infectious diseases of poverty that has occurred over the last decade.

Figure 5.2 shows the total funding for R&D during 2007–2010, and indicates how funding levels have increased since 2007 (funding for 2010 was lower than for 2009, possibly reflecting the global financial crisis’ delayed effect on public and philanthropy funds).

![FIG. 5.2. Total R&D funding of neglected diseases (2007–2010, US$, millions). Source: Based on Table 2 in reference (2)](image-url)
WHO IS FUNDING R&D?

As mentioned at the start of this chapter, funding flows for R&D related to infectious diseases of poverty are complicated. They involve a mix of sources of funds such as the Gates Foundation, NIH and the United States Agency for International Development (USAID) and sometimes (multiple) intermediaries, such as the Global Fund, GAVI Alliance and various PDPs that bring together funds from multiple sources before transferring them directly to recipients (5, 11). Bilateral agencies such as USAID or Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) can provide funds directly to the final recipient. Estimating the full magnitude of funding for R&D without double counting requires a separation between ultimate sources of funds and intermediaries, just as under the national health accounts framework commonly used for studying flows of funds for financing health care (12).

Data from the G-FINDER report for 2010 are summarized in Fig. 5.3 (2). This shows that high-income country governments are the major sources of R&D funds for neglected diseases, followed by philanthropies and private enterprises (two of the largest being the Gates Foundation and the Wellcome Trust, both based in high-income countries). Government funding from low and middle-income countries (such as India and South Africa) accounted for only about 2.1% of R&D funding. Although not displayed in Fig. 5.3, private pharmaceutical companies located in low and middle-income countries also fund R&D related to infectious diseases of poverty. Taken as a share of overall R&D allocations by private companies in both high-income and low and middle-income countries, however, their spending is rather small (2, 13). In summary, the picture that emerges is that the bulk of funding towards R&D for neglected diseases originates in high-income countries.

**Public sector funding:** in high-income countries, governmental funding of R&D for neglected diseases is channelled mainly via science and technology agencies such as the NIH in the United States of America and the MRC in the United Kingdom. Counterpart agencies in low and middle-income countries include the Indian Council of Medical Research (ICMR) and the National Council for Scientific and Technical Research (Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET) in Chile. However, the picture is more complicated than it first appears, with funds ultimately coming from a number of different sources in various ministries. In Brazil, for instance, sources of funding include the Ministry of Health, the Ministry of Science and Technology, and the Ministry of Education (10). Public funds can also be directed via bilateral aid agencies such as USAID (United States of America), the Department for International Development (DFID) (United Kingdom) and the Swedish International Development Cooperation (SIDA) (Sweden) and sometimes in the form of government contributions to multilateral institutions/international organizations such as The World Bank and WHO.
Among public sector funders, the United States of America was the single largest provider of contributions for neglected diseases R&D, giving approximately US$ 1.39 billion in 2010—nearly ten times as much as the United Kingdom, the next highest government funder (2). Most of these funds were provided via the NIH. The United Kingdom and the European Commission together provided a total of US$ 256 million. Other individual European countries such as France and Germany also made significant funding contributions, and Europe as a whole accounted for more than one fifth of all public funding of neglected diseases R&D.

Neither the Russian Federation nor China contributed data from a significant number of funders for either of the G-FINDER series of reports, so the contribution to R&D for neglected diseases from these countries is poorly represented. In other emerging world economies for which data are available, India and South Africa made major investments, with India featuring in the top 12 public funders of R&D for neglected diseases worldwide (2).

**Private sector funding:** the private sector provides a significant chunk of R&D funding for neglected diseases. Private sector funding was dominated by large multinational pharmaceutical companies that invested a total of US$ 442 million (87.9% of private contributions) in 2010. An additional US$ 61 million (12.1%) was contributed by smaller pharmaceutical and biotechnical companies (2).

Pharmaceutical companies also contribute (in cash or kind) to the development of vaccines and diagnostics — either directly or as participants in PDPs. For example, DNDi (see Box 5.2) obtained approximately US$ 2.8 million of its financing in 2010 (about 8% of its annual expenditures) from multiple sources that included GlaxoSmithKline, Sanofi-Aventis and Epichem Pty Ltd, along with

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**BOX 5.2. THE DRUGS FOR NEGLECTED DISEASES INITIATIVE**

The Drugs for Neglected Diseases initiative (DNDi) was launched in 2003 as a collaborative partnership between multiple institutions: the Oswaldo Cruz Foundation in Brazil, Indian Council of Medical Research, Kenya Medical Research Institute, the Ministry of Health in Malaysia, the Institut Pasteur in France, Médecins Sans Frontières (MSF) and WHO/TDR. It operates on a not-for-profit model which is directed and driven by the public sector.

DNDi’s primary goal is to support the development of new drugs for key neglected diseases such as human African trypanosomiasis, visceral leishmaniasis and Chagas disease. For this purpose it seeks to address key gaps in the R&D pipeline through three types of work: (i) long-term projects — relating to the identification of new compounds in basic research, (ii) medium-term projects — validating compounds that have not reached the stage of clinical development, and (iii) short-term projects — on new formulations of products that are already available.

To meet its goal DNDi has collaborative arrangements with both industry and academia. In 2010, most of DNDi’s funding came from government sources (aid agencies) and private foundations. Some in-kind contributions came from private entities and universities. In 2010, DNDi spent a total of €24.9 million, 75% of which was devoted to R&D activities for neglected diseases.

Recent successes from this collaborative effort include the registration of two artemisinin-based combination therapies (ACTs) for the treatment of malaria as well as drugs for sleeping sickness and visceral leishmaniasis.

Source: Reference (14).

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5 This is almost certainly a conservative estimate of contributions from the United States of America, since funding via USAID directed to health systems strengthening interventions was excluded (2).
completion of regulatory requirements related to the registration and approval of drugs. No monetary estimates of these in-kind contributions were available.

Funding from private charitable organizations/philanthropic foundations and individuals: this category is dominated by the Gates Foundation and the Wellcome Trust. In 2010, the Gates Foundation contributed around US$ 456 million and the Wellcome Trust provided US$ 80 million to neglected diseases R&D. Together, the two organizations accounted for over 94% of all philanthropic spending (2).

HOW ARE FUNDS BEING CHANNELLED?

The main flow of resources from funder to recipient is shown earlier in this chapter (Fig. 5.1). These are intramural or self-funding (direct funding for internal researchers) or extramural funding (either direct funding for external researchers or allocated via PDPs and other intermediaries).

Intramural or self-funding (direct funding for internal researchers): funding of internal research is common among both science and technology agencies and private sector entities. Providing for institutional, salary and research support, this type of funding is usually restricted to large organizations such as pharmaceutical companies, the NIH, MRC, ICMR and the Institut Pasteur. In 2010, the total amount of self-funded R&D for neglected diseases reported by G-FINDER respondents was almost US$ 872 million. Intramural funding from major government science and technology agencies (including the NIH and MRC) equalled approximately one fifth of their expenditures in 2010, even though there was considerable variation across agencies (13% for NIH, more than 69% for MRC) (2). Data about NIH funding suggest a relatively stable share of intramural funding in recent years (see Fig. 5.5).

Almost all (99%) of R&D funding from private corporations was intramural. In sharp contrast, all of the R&D funds from major philanthropic organizations such as the Gates Foundation and the Wellcome Trust were extramural in nature (2). The same is true for government funding channelled via bilateral agencies such as DFID, SIDA and USAID. Respondents from science and technology agencies in 15 low and middle-income countries also reported that nearly one quarter of their R&D allocations were intramural (WHO/TDR commissioned study).

Funding from public and philanthropic sources also supports academic–industry partnerships and small business R&D ventures (often known as PDPs – such as MMV, see Box 5.3), or PPPs (15, 16).

**FIG. 5.4.** Summarizes the G-FINDER 2011 survey findings on the respective shares of the different channels of funding (2). Intramural funding accounts for around one quarter of all R&D whereas extramural funding goes mainly to researchers and on contributions to PDPs.

Source: Based on Figure 27 in reference (2).
The Gates Foundation, DFID, USAID and European bilateral aid agencies have been a major source of funding for PDPs (see Table 5.1). PDP contributions often account for the entire R&D contribution of many bilateral agencies (2). This is in contrast to funding by science and technology (government) agencies (such as the NIH) which are not listed among major funders of PDPs in the G-finder 2011 report (2) and accounted for only about 1.4% of PDP funding in 2009 (5).

**FIG. 5.5.** Recent trends in shares of intramural funding in National Institutes of Health and the Medical Research Council, 2007 to 2010 (%). Source: Tables 30 and 31 in reference (2).

**TABLE 5.1. MAJOR FUNDERS OF PRODUCT DEVELOPMENT PARTNERSHIPS (PDPs), 2007–2010**

<table>
<thead>
<tr>
<th>Funder</th>
<th>To PDPs 2007 (US$)</th>
<th>To PDPs 2008 (US$)^</th>
<th>To PDPs 2009 (US$)^</th>
<th>To PDPs 2010 (US$)^</th>
<th>% of org’s funds given to PDPs 2010</th>
<th>Share of total PDP funding 2010 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gates Foundation</td>
<td>231,183,854</td>
<td>351,426,826</td>
<td>288,742,058</td>
<td>253,755,901</td>
<td>55.7</td>
<td>52.5</td>
</tr>
<tr>
<td>UK DFID</td>
<td>33,430,151</td>
<td>28,094,083</td>
<td>77,492,166</td>
<td>97,229,720</td>
<td>100.0</td>
<td>20.1</td>
</tr>
<tr>
<td>USAID</td>
<td>40,776,000</td>
<td>40,052,987</td>
<td>37,730,743</td>
<td>40,243,034</td>
<td>46.8</td>
<td>8.3</td>
</tr>
<tr>
<td>Dutch DGIS</td>
<td>32,170,024</td>
<td>19,807,172</td>
<td>19,454,348</td>
<td>15,833,146</td>
<td>92.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Norwegian NORAD</td>
<td>13,271,949</td>
<td>12,389,471</td>
<td>11,667,625</td>
<td>9,047,299</td>
<td>100.0</td>
<td>1.9</td>
</tr>
<tr>
<td>European Commission</td>
<td>4,034,158</td>
<td>--</td>
<td>1,466,939</td>
<td>7,914,688</td>
<td>8.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Spanish MAEC</td>
<td>3,426,196</td>
<td>13,116,474</td>
<td>14,323,053</td>
<td>7,159,668</td>
<td>100.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Irish Aid</td>
<td>23,586,318</td>
<td>6,820,567</td>
<td>5,227,392</td>
<td>6,508,789</td>
<td>99.7</td>
<td>1.3</td>
</tr>
<tr>
<td>MSF</td>
<td>7,187,885</td>
<td>7,275,268</td>
<td>4,563,905</td>
<td>4,725,479</td>
<td>100.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Swedish SIDA</td>
<td>10,505,557</td>
<td>11,188,482</td>
<td>7,952,989</td>
<td>4,231,695</td>
<td>31.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Swiss SDC</td>
<td>1,861,163</td>
<td>1,870,609</td>
<td>2,009,185</td>
<td>3,764,103</td>
<td>86.2</td>
<td>0.8</td>
</tr>
<tr>
<td>World Bank</td>
<td>3,610,000</td>
<td>3,477,842</td>
<td>2,802,745</td>
<td>2,757,154</td>
<td>100.0</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Subtotal top 12 PDP funders</strong></td>
<td><strong>426,662,580</strong></td>
<td><strong>528,101,928</strong></td>
<td><strong>485,636,091</strong></td>
<td><strong>453,170,675</strong></td>
<td><strong>56.9</strong></td>
<td><strong>93.8</strong></td>
</tr>
<tr>
<td><strong>Total PDP funding</strong></td>
<td><strong>469,392,952</strong></td>
<td><strong>580,084,383</strong></td>
<td><strong>530,049,041</strong></td>
<td><strong>483,166,820</strong></td>
<td><strong>90.9%</strong></td>
<td><strong>91.0%</strong></td>
</tr>
<tr>
<td>% of total PDP funding (top 12)</td>
<td><strong>90.9%</strong></td>
<td><strong>91.0%</strong></td>
<td><strong>91.6%</strong></td>
<td><strong>93.8%</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^ Figures are adjusted for inflation and reported in 2007 US dollars
* Subtotals for 2007, 2008 and 2009 top 12 reflect the top funders for those years, not the top 12 for 2010
- No reported funding in category
Source: G-FINDER report
Box 5.3. The Medicines for Malaria Venture

The Medicines for Malaria Venture (MMV) was launched in 1999 with initial seed money from the governments of Switzerland, the Netherlands and the United Kingdom (DFID), as well as the World Bank and the Rockefeller Foundation. This not-for-profit PDP has the stated aim of “discovering, developing and facilitating delivery of new, effective and affordable antimalarial drugs”.

Funding and support for MMV is now received from government/public sources, the private sector, private foundations, philanthropies and multilateral and bilateral agencies. MMV is focused on delivering products which are safe and effective against resistant malaria strains for treatment and for prophylactic use by children and during pregnancy. Activities include supporting discovery research on antimalarials as well as clinical trials bringing together academia and industry. In 2010, 77% of MMV’s budget was spent on R&D, and another 9% on activities to enhance the delivery of antimalarials to populations in low and middle-income countries. In 2008, MMV successfully registered Coartem® Dispersible, a paediatric antimalarial treatment. The majority (63.9%) of the US$ 553 million funds spent in 2010 came from the Gates Foundation. Other significant funders included DFID (15%), the Netherlands Ministry of Foreign Affairs, (3.4%), the Wellcome Trust (4.1%), USAID (2.5%), Irish Aid (2.3%) and the Spanish Agency for International Cooperation (2.1%).

MMV’s dependence on resources from philanthropic organizations has belied the initial expectations of major funding from the public sector. Contributions originating from industry consisted primarily of expertise and resources. MMV insists on exclusivity with respect to licensing of programme-specific intellectual property. To enable the development and launch of drugs for the benefit of target populations, licenses are preferably royalty free and transferable.

Source: Reference (17).

Extramural funding (direct funding for external researchers or allocated via PDPs and other intermediaries): this is the main mechanism by which many funders support R&D, accounting for nearly 53% of all allocations in 2010 (2). Science and technology agencies rely overwhelmingly on this channel to transfer resources for R&D. Estimates based on a survey of 10 major science and technology agencies in high-income countries suggest that nearly 74% of their funding for infectious disease of poverty in 2009 was channelled as direct external research funding (WHO/TDR commissioned study). As one illustrative example, in 2009, NIH allocations to PDPs, other intermediaries and intramural research amounted to about 16% of its aggregate allocations, so that more than 80% of its funds directly supported external R&D (5).

A similar proportion of R&D funds provided by 14 of the agencies contacted in low and middle-income countries supported external research. The breakdown by shares of R&D allocated in the two sets of countries is reported in Fig. 5.6.

Figure 5.6. Science & technology agency allocations (%) of R&D for infectious diseases of poverty: comparison between high-income and low and middle-income countries, 2009.

Source: WHO/TDR commissioned study
In contrast to science and technology agencies, the funding pattern of aid agencies was characterized by a heavy emphasis on PDPs, other intermediaries and nongovernmental organizations (NGOs). The data indicate that 75% of development agencies’ funding of R&D for neglected diseases was channelled via PDPs (2, 5).

**How are R&D funds allocated?**

There are three main ways to look at the data related to funding of R&D for infectious diseases of poverty.

1. **Which diseases is funding focused on?**
2. **What type of research is funded?**
3. **Who is being funded?**

**WHICH DISEASES IS FUNDING FOCUSED ON?**

The allocation of funds for neglected diseases in 2010 is shown by disease category in Fig. 5.7.

The data highlight the dominant place of the so-called “big three” diseases (HIV, TB and malaria) in the allocation of research funds. Funds for these three diseases together account for more than 70% of total R&D for neglected diseases allocations. Other significant, but much smaller, allocations went towards R&D for diarrhoeal diseases, dengue and diseases caused by kinetoplastids such as human African trypanosomiasis.

Fig. 5.8 attempts to capture variations in R&D allocations across different categories of funders by examining the distribution of funds across four types of funding agencies – (i) government sources in high-income countries; (ii) government sources in low and middle-income countries; (iii) philanthropic organizations; and (iv) the private sector. Fig. 5.8 clearly shows the dominance of the “big three” diseases in the funding of R&D for neglected diseases, irrespective of the ultimate source of funding. The combined share of funding for these three diseases accounts for approximately 52% of funding from low and middle-income country governments and more than 76% from high-income country governments. However, low and middle-income country government funders allocated relatively greater shares of their R&D spending towards other conditions – for example, over 10% of their spending was directed towards dengue R&D; another 26% went to diarrhoeal diseases, kinetoplastid infections and helminth infections. Even within low and middle-income countries there were significant variations in government R&D funding by disease (not shown). For example, South Africa heavily emphasized HIV/AIDS, TB and malaria over other conditions in its R&D funding for neglected diseases. This is not surprising given the significant challenges posed by these three conditions in that country. More than 90% of South Africa’s public funding on R&D for neglected diseases is allocated to this disease cluster. The distribution of R&D funding by Colombia, with its heavy emphasis on kinetoplastid infection, dengue and malaria, similarly reflects local disease priorities (5).
A second observation from Fig. 5.8 is the considerable variation in the relative share of funding towards R&D for HIV, TB and malaria across types of funders. The public sector in high-income countries allocated the largest proportion of its R&D spend towards HIV/AIDS but that was not the case for any of the other funders in 2010. Conversely, both low and middle-income country governments and philanthropic organizations placed emphasis on malaria. For private entities, TB and malaria appear to have greater priority.

The different patterns in R&D spending by high-income (compared with low and middle-income) country government (public) funders leaves open the question: is the variation in allocations to different health conditions a reflection of a real difference in priorities of the different sets of funding organizations that ought to concern policymakers, or does it reflect a degree of tacit collusion to avoid duplication in resource use? There is a need for clarity on the ways in which the different institutions prioritize their funding of R&D – an issue that is addressed later in this chapter.

Data on trends in allocations of R&D funding to different health conditions are not easily obtained from the G-FINDER dataset. This is due to the differences in respondent participation in the three years for which the data were collected, especially among private sector enterprises and low and middle-income country governments. For this reason Fig. 5.9 reports the changing shares of HIV, TB and malaria versus other diseases in the funding allocations of high-income country governments and philanthropic organizations only, given that data from these sources were collected on a reasonably consistent basis from 2007 to 2010 (2).

Fig. 5.9 shows that the share of high-income country spending on R&D for neglected diseases that went to HIV, TB and malaria has declined slightly in recent years – from 79.2% in 2007 to 76.1% in 2010. The declining share of public sector spending on HIV/AIDS R&D accounts for much of this reduction – in fact the reduction in the share of R&D spending that went towards HIV/AIDS exceeds the overall decline in the share of the “big three” diseases. The resulting “space”
has been filled to some extent by a rising proportion of spending towards TB and malaria, as well as an increased proportion of spending towards diarrhoeal diseases and diseases caused by kinetoplastids. The share of spending on the “big three” diseases has declined among philanthropic organizations too, from around 70% in 2007 to 67% in 2010. The share of philanthropies’ contributions towards TB R&D has remained stable over this period but there was a decline in the share for malaria in 2010. However, the share of “other conditions” seems to be increasing, mainly for dengue and helminths.

In contrast to the huge allocations made to HIV, TB and malaria – and, in recent years, the rising allocations to dengue, diarrhoeal diseases and diseases caused by helminths and by kinetoplastids – some other categories of infectious diseases of poverty receive relatively very small amounts of financing. Thus, in 2010, R&D funding for HIV/AIDS, TB and malaria was approximately US$ 1.12 billion, US$ 0.60 billion and US$ 0.55 billion, respectively (2). This contrasts markedly with funding dispersed towards R&D for Buruli ulcer (US$ 0.006 billion), trachoma (US$ 0.005 billion) and rheumatic fever (US$ 0.002 billion) (2). It is also noteworthy that R&D funding for bacterial infections causing rheumatic fever and trachoma has not been increasing, at least if the trends in the four years for which there are data (2007, 2008, 2009 and 2010) are any guide.

WHAT TYPE OF RESEARCH IS FUNDED?

Funding for infectious disease-related R&D can potentially support three major categories.

1. Basic research encompasses studies into the etiology of a disease or studies that increase scientific knowledge and understanding of a disease, disease processes or the pathogen or vector. They are not yet directed towards a specific intervention, product or health technology.

2. Product development constitutes a second category of research and is characterized by the discovery and development of new products and interventions (including drugs, vaccines, diagnostics and vector control...
tools. This includes research activities and processes necessary to develop and improve new compounds or devices specifically designed to prevent, diagnose, treat or cure infectious diseases of poverty. This category includes clinical trials.

3. Implementation research includes the development of delivery mechanisms for existing and new products, including interventions aimed at the broader health system to decrease the burden of infectious diseases of poverty. This category also includes behaviour-linked research that has implications for the prevention of infectious diseases of poverty (e.g. community willingness to use a product).

Although not readily classifiable under the above categories, implications for the sustainability of research programmes dictate that resource flows to build research capacity should also be included as an area of R&D that receives support. For greater precision though, only those elements of capacity building directly associated with research on infectious diseases of poverty ought to be included as a funding priority.

Detailed data on R&D allocations for infectious diseases of poverty are not readily available for all of these categorizations. The G-FINDER survey essentially collected data on the first two categories of research for neglected diseases – basic research and product development. Fig. 5.10 shows this information for 2010, with the product development category further broken down into prevention, therapeutics and diagnostics.

Overall, 24% of R&D for neglected diseases (US$ 721 million at 2007 prices) was allocated to basic research, and about 69% to product development, of which funds for prevention (vaccines) were a major component (2). R&D funding for preventive vaccines for five health conditions – HIV, TB, malaria, dengue and diarrhoeal diseases – amounted to just over US$ 1 billion in 2010, more than one third of the R&D allocations reported in the survey for that year (2).

Underlying this aggregate picture are differences in practices across the different categories of ultimate funders. For example, about 36% of all R&D spending by science and technology agencies from high-income countries went towards basic research: 13% of bilateral aid agency/multilateral institution R&D spending went on basic research (WHO/TDR commissioned study).

No data were available on the amounts of funding allocated for capacity building and/or implementation research, but the research teams’ interviews with aid agency representatives suggest that capacity building was a priority concern (WHO/TDR commissioned study). In contrast, only a few of the science and technology agency representatives (3 of the 10 high-income countries covered by the study) cited capacity building as an important priority. However, in practice, the distinctions between the science and technology agencies and aid agencies with regard to capacity building goals may not be as sharp. There are multiple examples of other ways in which science and technology agencies help build capacity for R&D in low and middle-income countries, such as via funding of research collaborations between groups from such countries.

**FIG. 5.10. Allocation of R&D funds for neglected diseases by type, 2010.**
Source: Based on Table 20 in reference (2).
countries and higher-income countries such as Canada, Japan, the United Kingdom and the United States of America (WHO/TDR commissioned study, (18). The WHO/TDR commissioned study also highlighted that the Canadian Global Health Research Initiative (which develops capacity for clinical trials research among researchers) works in the field of capacity building and that the MRC supports capacity building by co-funding activities in collaboration with DFID (WHO/TDR commissioned study).

Fig. 5.11 shows the allocation of funding from high-income country science and technology and aid agencies according to different types of research activity. Vaccine development accounts for the largest share of R&D spending on infectious diseases of poverty by both types of organization. The other noteworthy observation from Fig. 5.11 is the significant share of spending by aid agencies that support drug development R&D – primarily via PDPs.

There is limited published information available on the support that low and middle-income country agencies provide for R&D on infectious diseases of poverty. Interviews and quantitative data suggest that implementation research accounts for a substantial proportion of their allocations, perhaps as much 35% of all allocations for infectious diseases of poverty-related activities (WHO/TDR commissioned study). Estimates suggest that, of the funds allocated for R&D, one third was allocated to basic research, product development and implementation research, respectively. The lack of data on implementation research funding for infectious diseases of poverty by agencies in high-income countries means that a direct comparison is not possible. However, it should be noted that at least some of the implementation research in low and middle-income countries was funded from grants made available by organizations such as the Global Fund which, in turn, are funded by high-income country governments, philan-
thropies and multilateral institutions (WHO/TDR commissioned study).

Despite the difficulty in making comparisons across high-income and low and middle-income country funders, there are good reasons to believe that the share of research funds allocated to implementation research for infectious diseases of poverty by low and middle-income country institutions is larger than their high-income country counterparts. Local funders in low and middle-income countries reported that their limited research capacity for novel work in the areas of basic research and product development caused them to turn their attention to the delivery of drugs, vaccines and interventions developed elsewhere. For the same reason, their funding programmes tended to have a greater focus on capacity building; this was highlighted in interviews with funder representatives of Brazil, Colombia, India, South Africa and the United Republic of Tanzania (WHO/TDR commissioned study). Interviews conducted with multiple public sector funders from high-income countries confirmed this observation of differences between low and high-income countries: high-income country funders give lower priority to implementation research relative to low and middle-income country funders. The study also highlighted the fact that existing legislation in South Africa requires a minimum of 30% of R&D funding to be allocated to capacity building; Brazil, Colombia, India and The United Republic of Tanzania all reported implementing specific strategies aimed at developing capacity for research and industry development.

WHO IS BEING FUNDED?

About one quarter of all R&D funding (excluding implementation research) is intramural funding from large private enterprises and science and technology agencies of high-income country governments. The private enterprise component of R&D funding is almost all intramural and, as these firms are based primarily in high-income countries, the majority of funds are automatically directed towards high-income country researchers. The share of intramural allocations in total R&D funds of high-income country science and technology agencies are relatively smaller, but the basic claim – that most intramural funds go to high-income country researchers – remains valid.

Extramural funds from agencies and philanthropies account for about 54% of all R&D spending. Funding may be provided as project grants, career development awards or fellowships. Sometimes the grant requires a co-contribution by research partners or other sponsors. The funds are usually awarded competitively after a scientific peer review of proposed research and, as in the case of intramural allocations, go mostly to domestic (high-income country) researchers. Direct external grants among science and technology agencies in high-income countries were geared predominantly towards domestic (high-income country) researchers. Six of the ten science and technology agencies interviewed stated that all, or almost all, of their direct external spending on infectious diseases of poverty went to local/domestic researchers (WHO/TDR commissioned study).

When the agencies supported overseas research, this was mostly in the context of collaborative projects between high-income and low and middle-income countries. Some high-income country agencies also collaborated with each other in formulating joint invitations for grant proposals, again mostly for proposals directed at local (high-income) researchers. One exception is the Canadian Global Health Research Initiative that funds overseas researchers even in the absence of Canadian collaborators (WHO/TDR commissioned study).

As noted earlier, funding by high-income country aid agencies tends to be directed towards PDPs which focus on product development. Most recipients of R&D funds via the PDP vehicle (which usually serves as an intermediary) tend to be researchers and firms in high-income countries. In 2007, more than 70% of disbursements through PDPs went to private companies, academic and public research institutions in wealthy donor countries, while less than 13% of the available funds was directed to research organizations and companies in low and
middle-income countries. Although some organizations such as DFID and USAID have allocated grants towards R&D for infectious diseases of poverty through a competitive process (usually in the context of health systems strengthening), in most cases aid agencies allocated funds on the basis of their past experience with specific recipients and their own strategic priorities. Development agencies also sometimes team with philanthropic organizations and/or science and technology agencies for specific grant-making activities related to capacity building. Examples include DFID’s collaboration with the MRC and the Wellcome Trust to support clinical trials and research capacity building in Africa (WHO/TDR commissioned study). Much the same pattern of funding is observed in low and middle-income countries.

**Funding of R&D for infectious diseases of poverty: implications of a bibliometric analysis**

Research outputs of low and middle-income country researchers can help improve our understanding of R&D funding flows for infectious diseases of poverty directed towards them. For example, assessing patterns in research output from low and middle-income country research institutions can shed light on funding directed towards capacity building and implementation. Moreover, in cases where the research has been funded locally, research outputs can also help us better understand the priorities of low and middle-income country funders. If greater research productivity translates into increased likelihood of receiving research income in the future, trends in research output can perhaps also serve as indicators for the direction of future funding flows.

A bibliometric study of research into infectious diseases of poverty (part of the WHO/TDR commissioned study), provides some information in this regard. The study reviewed about 173,500 articles and reviews published on infectious diseases of poverty between 2000 and 2009 and was able to identify the country of affiliation of the first author in almost 150,000 cases. Of this total, 69.4% had first authors affiliated to high-income countries, 27.7% to middle-income countries and the remainder (2.9%) to low-income countries. Table 5.2 lists the top three countries with institutions to which the largest percentages of first authors were affiliated, categorized according to low, middle and high-income country. Not surprisingly, the United States of America and the United Kingdom emerge at the top in terms of publications. Among first authors

### Table 5.2. Proportion of publications on infectious diseases of poverty with a first author by country, categorized according to World Bank income categories, 2000–2009.

<table>
<thead>
<tr>
<th>Country</th>
<th>High-income</th>
<th>Number of articles (share)</th>
<th>Middle-income</th>
<th>Number of articles (share)</th>
<th>Low-income</th>
<th>Number of articles (share)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>37,693</td>
<td>(25.9%)</td>
<td>Brazil</td>
<td>8,447</td>
<td>(5.8%)</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>10,911</td>
<td>(7.5%)</td>
<td>China</td>
<td>8,191</td>
<td>(5.6%)</td>
<td>Kenya</td>
</tr>
<tr>
<td>France</td>
<td>7,241</td>
<td>(5.0%)</td>
<td>India</td>
<td>3,576</td>
<td>(2.5%)</td>
<td>United Republic of Tanzania</td>
</tr>
<tr>
<td>All countries</td>
<td>100,852</td>
<td>(69.4%)</td>
<td>All countries</td>
<td>40,296</td>
<td>(27.7%)</td>
<td>All countries</td>
</tr>
</tbody>
</table>

Source: WHO/TDR commissioned study.
from middle-income countries, the largest group, comprising almost 5.8% of publications, was from Brazil, followed by India and China. Researchers from Kenya dominated the list of first authors from low-income countries, followed by researchers in Ethiopia and the United Republic of Tanzania.

PROMISING TRENDS

Although only about 30% of all the research papers on infectious diseases of poverty published during the period from 2000 to 2009 identified by the study had a first author affiliated to a low or middle-income country institution, the actual level of engagement in research (as indicated by the publication of articles with first authors affiliated to low and middle-income countries) overall has been increasing steadily over the past decade. When articles are analysed by year, the proportion of published articles on infectious diseases of poverty with first authors from low and middle-income countries increases from 5% in 2000 to 13% in 2009.

There are also positive features in the composition of the research being undertaken in low and middle-income countries. One recent study found that malaria featured in nearly 48% of the papers that had an investigator affiliated to a sub-Saharan African institute as the first-author, compared to global figures showing that 17% of the papers were on malaria\textsuperscript{6}. The proportion of articles on HIV/TB co-infection, human trypanosomiasis and Buruli ulcer co-authored by researchers from sub-Saharan Africa was three times the global proportion of research articles published on these diseases. The proportion of articles on helminths and on TB matched global patterns but research articles addressing bacterial and protozoan infections, as well as dengue, had few sub-Saharan researchers as first authors. Overall, these trends suggest a growing research capacity and the emergence of a distinct research agenda in the region.


Drivers of Research Funding Flows for Infectious Diseases of Poverty: What Do the Funders Say?

Financial flows for R&D for infectious diseases of poverty are a function of the resource constraints faced by funders as well as their strategic priorities. In an attempt to understand what these priorities might be the WHO/TDR commissioned study conducted semi-structured interviews with representatives of 34 funders in 32 countries from different parts of the world in order to assess the criteria upon which public sector donors selected their funding priorities (WHO/TDR commissioned study). Table 5.3 summarizes their responses.

Most public sector R&D funding agencies follow some guidelines that drive their funding strategy. Science and technology agencies and/or health research institutions tend to focus on national research agendas, although these may range from general science and technology frameworks (independent of health priorities) – as in the case of Japan’s Ministry of Education, Culture, Sports, Science and Technology (MEXT) – to Australia’s National Health and Medical Research Council (NHMRC) that has well-defined health research priorities. In addition, the guidelines are loose enough to allow local researchers to have key influence. For most funders, especially in high-income countries, the scientific quality of proposals is usually of primary importance when funds are awarded. As indicated by interview responses, low and middle-income country agencies seem to have less flexibility (relative to their high-income counterparts) in the selection of their R&D funding strategy. This may be because low and middle-income country agencies are more likely to face greater constraints on funds and so have greater reliance on donor groups that may have a separate set of priorities (although no quantitative assessment is available to substantiate this). However, in a recent report (10), the Global Forum for Health Research analysed the funding patterns of science and technology agencies in a number of Latin American countries – Argentina, Brazil, Chile, Cuba,
Paraguay and Uruguay. This found that there is little evidence of compromised priorities in allocations among science and technology agencies from better off (middle-income) nations. Moreover, the relatively high allocations to communicable diseases among their poorer counterparts (such as Bolivia and Paraguay) also suggests that local funding is not too misaligned with the disease burden.

Development aid agencies differ from science and technology agencies in that broader development issues, rather than scientific and technical considerations, may be driving their funding strategies and influencing their

TABLE 5.3. PRIORITY SETTING IN R&D FOR INFECTIOUS DISEASES OF POVERTY: RESULTS FROM INTERVIEWS WITH 32 FUNDING AGENCIES, 2009.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Number of agencies surveyed</th>
<th>High-income country science and technology agencies</th>
<th>High-income country aid agencies</th>
<th>Low-income country</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td><strong>Is there a national research agenda that serves as a guide?</strong></td>
<td></td>
<td>Yes, general national research framework and/or health-specific</td>
<td>Follow government department agendas. Some agencies have specific global health research frameworks</td>
<td>Yes, majority have national health research agendas These may not always be followed, especially in low-income countries</td>
</tr>
<tr>
<td><strong>Influenced by funding patterns of other agencies</strong></td>
<td></td>
<td>No</td>
<td>Yes</td>
<td>Yes: low-income countries No: middle-income countries</td>
</tr>
<tr>
<td><strong>Use of external priority-setting framework</strong></td>
<td></td>
<td>No</td>
<td>No</td>
<td>Yes, but only as an aid to priority setting, therefore often adapted to local context</td>
</tr>
</tbody>
</table>

**Relevance of priority setting factors**

<table>
<thead>
<tr>
<th>Scientific and technical factors</th>
<th>High</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigator driven agendas</td>
<td>Yes</td>
<td>No</td>
<td>Seldom</td>
</tr>
<tr>
<td>International agendas</td>
<td>Occasionally</td>
<td>Frequently</td>
<td>Frequently</td>
</tr>
<tr>
<td>Disease burden</td>
<td>Yes (mostly national)</td>
<td>Yes (global)</td>
<td>Yes (only national)</td>
</tr>
<tr>
<td>Political agenda</td>
<td>Low to medium</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Results driven agenda</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Economic</td>
<td>Occasionally</td>
<td>High</td>
<td>Frequently</td>
</tr>
</tbody>
</table>

Source: WHO/TDR commissioned study
funding allocations. In addition, their focus tends to be global and so includes global disease priorities. This means, for instance, that the Millennium Development Goals (MDGs) are incorporated in their R&D funding strategy. In turn, this also implies that the funding strategies of agencies of a similar nature are likely to influence each other’s priorities, as reflected in the survey responses from their representatives (see Table 5.3).

**Future trends in the funding landscape**

These can be considered from the standpoint of short-run concerns and longer-run demand and supply pressures. In the short run, the ongoing global financial crisis is likely to impose serious constraints on the growth of funding for R&D for infectious diseases of poverty. In fact, there already appears to be a slowdown and even a decline in allocations (2). Even the NIH, which increased fund allocations between 2008 and 2009, was able to achieve this increase only on the basis of the stimulus spending introduced by the American government in 2009. Once the stimulus funding ended, the NIH experienced a decline in its funding in 2010 (2). The Gates Foundation contributed a smaller amount of funds to infectious diseases of poverty in 2009 than in 2008. In contrast to high-income countries, however, many middle-income economies (such as Brazil, China, Colombia, India and South Africa) are experiencing rapid economic growth and can be expected to fund increasing levels of R&D for infectious diseases of poverty. For instance, both Colombia and South Africa have already set ambitious agendas for research R&D on infectious diseases of poverty (2). Clearly, as a consequence of the global finance crisis, the poorest and donor-dependent countries will face resource constraints given that they are likely to be much more dependent on R&D funds from high-income countries rather than from middle-income nations experiencing rapid growth.

Longer-run trends may also be relevant in influencing R&D fund availability for infectious diseases of poverty. Interviews with representatives from high-income country science and technology agencies showed that a significant majority expected their funding of R&D for infectious diseases of poverty to either remain the same or decline in future years (WHO/TDR commissioned study), due to a combination of overall resource restrictions as well as diversion of funds to address the rising incidence of noncommunicable diseases in low and middle-income countries (19). A similar sentiment was expressed by all aid agency representatives that took part in the study. As well as budgetary constraints, these agencies also expressed dissatisfaction with current funding mechanisms that they felt were inefficient and failed to contribute sufficiently to research capacity building in low and middle-income countries. In contrast, funding agencies in middle-income countries covered by the study were optimistic about rising allocations to R&D for infectious diseases of poverty in the future. Some of these agencies expressed a need for a greater indigenization of research capacity and agendas and were moving in that direction by promoting local research capacity on a priority basis.

In addition to the trends outlined above, other issues will likely put pressure on R&D funding for infectious diseases of poverty. As outlined in Chapter 2, climate change may increase the risks of infectious disease in the tropical regions where many of the poor live. This will probably lead to further pressures on available resources for R&D, even within the infectious diseases of poverty group (20). With increasing demands from multiple directions for R&D funds (e.g. for noncommunicable diseases and for new forms of infectious conditions), it is not surprising that pressures on existing resources will increase and that donors are increasingly concerned about “value for money”, looking for increased effectiveness in the funding of R&D for infectious diseases of poverty (WHO/TDR commissioned study).
Key challenges in funding R&D

A major challenge for funding of R&D is to ensure that available resources are well-spent. This effectiveness criterion can be used to assess the existing pattern of financial flows and the associated institutions that form the “financing architecture”.

At least four elements influence effectiveness:

1. making the right type of R&D investments (allocative efficiency)
2. avoiding wastage (technical efficiency)
3. capacity building leading to a sustainable agenda
4. strengthening the data reservoir to help decision-making on funding flows.

The first two elements should ensure that existing funds are spent so as to achieve the desired outcomes (i.e. gains in health via R&D) at the lowest cost possible. However, given that the health policy concerns to be addressed by R&D are not a one-shot problem, there is also the challenge of ensuring that priority setting responds to changing circumstances and that information is available for this purpose.

MAKING THE “RIGHT TYPE” OF R&D INVESTMENTS

When funding is limited, at least three criteria are likely to be important to determine the “right” activities to support: (i) the health condition of the population should warrant investment; (ii) the investment is aligned with the priorities of the target population; (iii) the investment has a high probability of success.

It is generally accepted that a high burden of infectious diseases of poverty is closely linked to low socioeconomic status. The likelihood of success for R&D investment will depend on whether tools and technologies (such as drugs, vaccines and diagnostics) that can be readily developed into products already exist. Often, such tools do exist and therefore the mechanism of implementation becomes the central priority (21). However, translational research and social innovation (for the production, delivery and uptake of products directed towards low and middle-income countries) tend to receive much less funding relative to other areas and needs – particularly for diseases other than HIV/AIDS, TB and malaria. Indeed, as we have already discussed, implementation and health systems research are primarily of local interest and much less attractive to external funders. There also needs to be a general shift away from drug development investments towards more investment in implementation research (for all infectious diseases of poverty, not just the “big three”).

A focus on implementation in relation to existing tools and technologies is apparent when analysing the R&D funding patterns of low and middle-income country science and technology agencies (WHO/TDR commissioned study). However, priorities differ even within low and middle-income countries. For instance, in South Africa, the Department of Science and Technology places a high priority on research funding for addressing HIV/AIDS, TB and malaria; in India, the ICMR emphasizes diarrhoeal diseases; and, in Brazil, the Department of Science and Technology provides considerable funding towards research on dengue and kinetoplastids in addition to the “big three”. As most existing funding for R&D for infectious diseases of poverty comes from high-income countries, it is important that funding is not skewed by their priorities but is congruent with low and middle-income country priorities, at least until R&D funds from low and middle-income countries begin to catch up. Local priorities may also change over time, so there is a need for much greater input from low and middle-income countries in setting research priorities. Currently, this does not appear to be very common. At the very least there is a need for strong low and middle-income country research partners in collaborative arrangements with researchers within high-income countries, so that the former can influence research questions. Un-
fortunately this is not observed in practice – for example, African biomedical collaborations follow the classical partnership pattern i.e. partnerships are built with institutions in Europe and the United States of America but levels of local funding of R&D are low. The net outcome is a lack of local ownership of the research undertaken (22).

The problem of control and moral hazard: The flip side of low and middle-income countries having a greater say in the direction of funds from high-income countries is the creation of incentive problems. Funders would likely be unhappy to lose control over their funding and want to see results from their contributions. Conversely, easier access to large amounts of funds to meet local priorities might generate moral hazard problems as low and middle-income country counterparts come up with proposed activities for funding that will not be cost effective, and that will yield outcomes that are not easy to measure. Local contributions to create an incentive for such funding arrangements between high-income and low and middle-income countries are a useful option but will not really solve the problem, given the disproportionate size of their relative contributions. For this reason, collaborative arrangements involving strong links between various low and middle-income countries, and characterized by strong leadership from such countries, are likely to be much more effective in addressing low and middle-income country priorities. Another example of a south-led initiative for R&D funding related to infectious diseases of poverty is the African Network for Drugs and Diagnostics Innovation (ANDI) which focuses on the discovery, development and delivery of tools to address Africa’s health needs (22). ANDI aims to establish “the African innovation fund”, a US$ 600 million endowment to support a portfolio of collaborative projects and partnerships that (a) generate health product innovation at all stages of the value chain; and (b) build capacity and support for the infrastructural development of African institutions.

To strengthen their ownership of their research agenda, low and middle-income countries can credibly commit to a particular set of priorities related to R&D funding requirements for infectious diseases of poverty through various policies. Ideally, such policies should be backed by legislation and used to develop plans to guide appropriate donor investments and efforts to strengthen health systems. A prerequisite for establishing such research agendas is the existence of appropriate legal frameworks that support national policies for health research and that may also enable low and middle-income countries to achieve greater control over research performed within their borders and on their behalf. Such a system could oblige funders to align their policies and practices with nationally defined R&D agendas.

AVOIDING WASTAGE

Efficiency in funding of R&D for infectious diseases of poverty can be enhanced in the following three ways.

1. **Reduce duplication and improve coordination of R&D funding for priority conditions.**

   Duplication is most obvious in the case of PDPs. For example, development of anti-malarials is on the agenda of both MMV and DNDi. Several PDPs also focus on the enhanced delivery of services to get their products to poor populations in need. The GAVI Alliance states one of its missions to be: “saving people’s lives and protecting people’s health by increasing access to immunisation in poor countries”. In this endeavour GAVI Alliance funds not only the provision of vaccines to needy populations, but also activities that help enhance health care delivery mechanisms. MMV includes similar activities in its portfolio, including supporting health care services and improving the supply chain. Enhancing access to health services is also a key goal of DNDi. Instead of separate funded programmes focussed on improving health care services – a tradition with vertical programmes – an integration of health care delivery interventions at the country level is likely to be more efficient.
2. Reduce competition for funds as this is a source of wastage. For example, different PDPs compete for funds from the same group of donors (usually bilateral donors and private foundations). Advocacy activity by one PDP entity potentially impacts the ability of others to benefit from the same “pot”. Consequently, these other groups then need to invest more in advocacy relating to their activities. Overall advocacy-related expenditures are increased as a result. This inefficiency is likely to be greater as resource constraints related to R&D for infectious diseases of poverty increase. This argument can also be carried beyond competition for funds between PDPs; competition for funding is likely to increase as NCDs place an increasingly greater burden on low and middle-income countries. An appropriate course of action would be to better integrate funding decisions for R&D across diseases and rely more on competitive awards.

3. Improve the coordination of priorities for action. This should lead to a harmonized approach to funding of R&D. This could be similar to that proposed by the WHO Expert Working Group on Research and Development Financing (4). The proposal envisages (a) the establishment of working groups and a supervisory group to draw up research agendas and set priorities on the basis of information from a range of sources, including a new global health research observatory; (b) working and supervisory group recommendations on the distribution of the elements of the required R&D among researchers working in different settings, including basic research laboratories, development or scale up plants, clinics, health services and communities, in both public and private environments in different countries; (c) creation of a mechanism for the funding and coordination of global health research and innovation to facilitate and support, involving targeted R&D into new drugs, vaccines, diagnostics and intervention strategies for health conditions of the poor for which adequate interventions are not presently available; and (d) support for research disciplines (primarily conducted in low and middle-income countries) that includes health policy and systems research, social science and behavioural research, implementation/operations research and research on the determinants of health.

CAPACITY BUILDING

Research capacity building is needed for the purposes outlined above, especially as the local capacity for research is limited. It would also help create local expertise in low and middle-income countries to help define health priorities that can be used to influence the funding priorities of high-income country agencies. Local capacity for health research would help focus on topics related to operational and implementation research in low and middle-income country settings that have not yet attracted much funding from high-income country agencies. Finally, improvement of local research capacity will help strengthen existing research and training institutions in these countries and therefore contribute to the future generation of scholars.

STRENGTHENING THE DATA RESERVOIR TO HELP DECISION-MAKING ON FUNDING FLOWS

There is much that we still do not know about funding flows related to R&D for infectious diseases of poverty. Data are lacking in a number of key areas, including implementation research; support for capacity building; and a broader class of research activities that explore aspects of behaviour, economics, politics, trade and the environment as they apply to infectious diseases of poverty. There is also a need for information on a larger set of countries, mainly low and middle-income countries, and to develop a classification system to organize data on R&D for health. Apart from deciding what to include or exclude under the definition of “R&D for infectious diseases of poverty”, there is also a need to address the issue of separating ultimate funders from recipients of funds and from intermediaries (such as PDPs). A good model for this is the work on National Health
Accounts for which an updated classification system was recently developed (through a collaborative arrangement by the Organisation for Economic Co-operation and Development [OECD], the WHO and the European Commission). The project involved a number of researchers from around the world with expertise in health financing (12). Information systems to help capture data on funding flows for R&D on health would certainly be needed to support this work.

What would the future funding architecture look like?

The funding landscape for infectious diseases of poverty is full of promise and it would be irresponsible to leave the reader of this chapter with the impression that infectious diseases of poverty have not benefited greatly from investments already made into R&D for these diseases. Yet, much remains to be done to ensure that R&D funding for infectious diseases of poverty is able to address health policy priorities effectively.

We therefore conclude with three key challenges that constitute the cornerstones for the future funding architecture, as we would like to see it.

Firstly, funding must be relevant to the needs on the ground. This has to face the reality of imbalances between high and low and middle-income countries, associated political pressures and differences in priorities in what is a very competitive environment. We have seen that basic research is well catered for but implementation research – which can make a practical difference for affected populations – remains the “poor relative”. Mechanisms to ensure that there is a better balance between funds for various kinds of R&D therefore need to be established.

Secondly, there needs to be a drastic reduction in the many forms of wastage that presently plague the funding landscape. Competing and overlapping research agendas between PDPs; duplication of efforts to secure funds; and too much funding in small amounts going towards research efforts that are unlikely to make a real impact are all part of the wastage that needs to be tackled.

Thirdly, in the long term the research effort for mitigating the negative impact of infectious diseases of poverty cannot be sustained by funds from high-income countries alone. Regions and countries most directly concerned by infectious diseases of poverty have a wealth of research potential, and there is likely to be considerable new funding capacity for supporting R&D in emerging economies such as Brazil, China and India. Moreover, the research agenda is still too often influenced by factors and considerations that do not integrate capacity building right from the start. This must change, so that capacity building is considered integral to funding activities.

The funding architecture for R&D into infectious diseases of poverty will begin to take shape once we have found ways of starting to address these challenges – a task that must be shared by all parties concerned.

The three cornerstones of the future funding architecture:
1. The funding must be relevant to the needs on the ground.
2. Wastage must be drastically reduced.
3. Capacity building must be integral to all funding activities.
References – Chapter five