

NEGLECTED DISEASE RESEARCH & DEVELOPMENT: HOW MUCH ARE WE REALLY SPENDING?



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ACRONYMS	
Aeras	Aeras Global TB Vaccine Foundation
ARV	Anti-Retroviral Drug
DALY	Disability-Adjusted Life Year
DCs	Developing Countries
DNDi	Drugs for Neglected Diseases initiative
EAggEC	Enteraggregative E. coli
EDCTP	European and Developing Countries Clinical Trials Partnership
ETEC	Enterotoxigenic E. coli
EU	European Union
FDC	Fixed-Dose Combination
FTE	Full-Time Equivalent
GDP	Gross Domestic Product
GERD	Gross Expenditure on R&D
G-FINDER	Global Funding of Innovation for Neglected Diseases
G7	Group of 7
HICs	High Income Countries
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IAVI	International AIDS Vaccine Initiative
IDCs	Innovative Developing Countries
iOWH	Institute for One World Health
IPM	International Partnership for Microbicides
LMICs	Low- and Middle-Income Countries
MICs	Middle Income Countries
MIDRP	Military Infectious Disease Research Program
MMV	Medicines for Malaria Venture
MNC	Multinational Pharmaceutical Company
MVI	PATH Malaria Vaccine Initiative
MVP	PATH Meningitis Vaccine Project
MRC	UK Medical Research Council
MSF	Médecins Sans Frontières
NCE	New Chemical Entity
NIH	National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
PATH	Program for Appropriate Technology in Health
PDP	Product Development Partnership
R&D	Research and Development
RoI	Return on Investment
RTWG	HIV Vaccines and Microbicides Resource Tracking Working Group
SME	Small to Medium Enterprise
S&T	Science and Technology
TAG	Treatment Action Group
TB	Tuberculosis
TB Alliance	Global Alliance for TB Drug Development
TDR	WHO-based Special Programme for Research and Training in Tropical Diseases
UK	United Kingdom
US	United States of America
USD	United States dollar
WHO	World Health Organization

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EXECUTIVE SUMMARY

The survey

G-FINDER is a survey of global investment into Research and Development (R&D) of new products for neglected diseases. In its inaugural year, G-FINDER surveyed 134 funders in 43 countries for their 2007 R&D investment into:

- ▶ 30 neglected diseases
- ▶ 127 product areas for these diseases, including drugs, vaccines, diagnostics, microbicides, vector control products and platform technologies
- ▶ All types of product-related R&D, including basic research, discovery and preclinical, clinical development, Phase IV and pharmacovigilance studies, and baseline epidemiological studies

Findings

DISEASE FUNDING

Just over \$2.5 billion was spent on neglected disease R&D in 2007. Of this amount, almost 80% went to three diseases: HIV/AIDS (\$1.1 billion or 42.3%), malaria (\$468.4 million; 18.3%) and tuberculosis (\$410.4 million; 16.0%). The remaining neglected diseases and disease groupings each received less than 5% of global funding, including diarrhoeal illnesses (\$113.9 million; 4.5%), the helminth infections (\$51.6 million; 2.0%) and bacterial pneumonia and meningitis (\$32.5 million; 1.3%). Five diseases - leprosy, Buruli ulcer, trachoma, rheumatic fever, and typhoid and paratyphoid fever - received less than \$10 million or 0.4% of total global investment each.

Over \$2.5 billion was spent on neglected disease R&D in 2007. Of this amount, almost 80% went to three diseases: HIV/AIDS, malaria and TB.

FUNDERS

Public and philanthropic funders provided around 90% of global R&D funding for neglected diseases, with the public sector providing \$1.8 billion (69.4%) and philanthropists providing \$538.3 million (21.0%).

The US Government represented nearly three-quarters of global public spend (\$1.25 billion or 70.4%), while European governments and the European Commission collectively provided \$384.9 million (21.7%). Two funders made up 95% of total philanthropic spend, these being the Bill & Melinda Gates Foundation (\$452.1 million or 84.0%) and the Wellcome Trust (\$60 million or 11.1%).

There was a marked concentration of funders, with two organisations – the US National Institutes of Health (NIH) and the Bill & Melinda Gates Foundation – together providing 59.3% of the global total. Over 80% of total global funding was provided by only 12 organisations.

Pharmaceutical industry funding was aggregated for confidentiality reasons. Collectively, the private sector contributed 9.1% (\$231.9 million) of global funding, making this group the third largest source of investment after the NIH and the Bill & Melinda Gates Foundation. This contribution refers only to industry's own investments, excluding funding provided by Product Development Partnerships (PDPs) or others to industry programmes.

FUNDING FLOWS

Around 20% of global funding was invested by public institutions and private companies into internal programmes. The remaining 80% was granted by funders to external organisations either directly or via intermediary organisations and PDPs.

Overall, intermediary organisations and PDPs managed nearly one-quarter of global neglected disease product investments in 2007, with a high proportion (nearly one-third) of funder grants being routed through them.

Discussion

Intuitively, there is a sense that the highest ‘health return on investment’ would result from investing in the highest burden diseases, as measured by DALYs (Disability Adjusted Life Years). In practice, the reality is far more complex. The likely health return on a given neglected disease R&D investment depends on the potential health impact of that investment against the cost of the investment, discounted for risk.

The potential health impact in turn depends on the severity of R&D need (of which DALYs and severity of product shortfall are the two main components) and the severity of underfunding in the selected area. Cost will depend on the type of products needed and the degree of advancement of the global research portfolio. This cost/benefit ratio must then be discounted for risk, which will chiefly depend on the state of science and technology in the area of investment under consideration, as well as the intrinsic risks of pharmaceutical product development.

DALYs act as a *multiplier* of the likely health impact of a new product in a given area. However, they cannot indicate how much investment is needed to create that new product. This is because cost and risk relate to the state of science and the type of R&D needed rather than to the disease or the number of people affected.

Funders will weigh up these factors based on their own agendas, preferences, risk appetite, budgetary constraints and political time horizons. However, the G-FINDER data can support funders by identifying where investment is lacking and where additional funding can potentially have a high impact.

An overview of the G-FINDER data confirmed that there were marked gaps not only in terms of funders and diseases (as noted above) but also in terms of products. The lion’s share of global investment went to R&D for drugs and vaccines, with very little dedicated to diagnostics. Meanwhile, platform technologies (e.g. adjuvants, diagnostic platforms and delivery devices, which are not disease-specific) received only 0.4% of global funding. These marked variations suggest that factors beyond science, technology and opportunity were playing a role.

The G-FINDER data can support funders by identifying where investment is lacking and where additional funding can potentially have a high impact.

Conclusion

The participation of many organisations and countries in the development of new neglected disease products is a remarkable and welcome change from past decades of inertia and neglect. However, a broadening of funding efforts so that all who are able to contribute do so, and all diseases receive the attention they deserve, would lead to a dramatically positive impact on the health of developing country patients afflicted with these diseases. This is more important than ever in tough economic times if we are to ensure that those most in need do not end up paying the highest price.

INTRODUCTION

Background to the G-FINDER survey

The creation of a vaccine for HIV/AIDS, more effective diagnostics for tuberculosis (TB), and better treatments for leishmaniasis and sleeping sickness would greatly improve health in the developing world in line with the United Nations Millennium Development Goals. The need for new pharmaceutical tools to prevent and treat neglected diseases is widely accepted¹. However, funders wishing to invest in this vitally important area must currently make their funding decisions in the face of conflicting or absent information.

Definitions of what constitutes a neglected disease vary² and, even when there is consensus, there are sometimes conflicting views on what new products are required. There is also little or no information on how much is currently invested into developing new products for neglected diseases. Some figures on general health research funding have been published by the Council on Health Research for Development³ and the Global Forum for Health Research⁴, but these do not disaggregate product-related Research and Development (R&D) or investment into neglected diseases. Since 2000, R&D funding data has been published for some diseases – including annual surveys for HIV/AIDS biomedical prevention since 2000⁵ and for TB R&D since 2005⁶, and a survey of 2004 malaria R&D funding⁷ – but the findings cannot be easily compared since each survey uses different methodologies and covers different diseases, products, funders and countries. For most neglected diseases, there is simply no information on global R&D spend.

In order to address these information deficits, the Bill & Melinda Gates Foundation commissioned the George Institute for International Health to conduct five sequential annual surveys to provide consistent, comparable, comprehensive data over time on investment into R&D of new pharmaceutical products to prevent, manage or cure neglected diseases of the developing world. This report sets out the results of the first survey of Global Funding of Innovation for Neglected Diseases – the G-FINDER survey – which captures 2007 investment data.

The survey

WHICH DISEASES AND PRODUCTS ARE INCLUDED?

We aimed to make the G-FINDER survey as comprehensive as possible, since it is likely to be of greatest use if it allows an ‘apples to apples’ comparison across all neglected disease areas.

G-FINDER therefore includes both classical Type III neglected diseases, defined as diseases that are ‘overwhelmingly or exclusively incident in the developing countries’; as well as developing-country presentations of Type II diseases that are ‘incident in both rich and poor countries, but with a substantial proportion of the cases in the poor countries’ and where R&D is ‘not in proportion to global need or addressed to the specific disease conditions of poor countries’⁸. It does not include Type I diseases such as hypertension or diabetes that occur commonly in both rich and poor countries since, for these diseases, ‘the incentives for R&D exist in the rich country markets (and therefore) ... products get developed’.

It also covers all relevant pharmaceutical products for these diseases, including:

- ▶ Drugs
- ▶ Vaccines (preventive and therapeutic)
- ▶ Diagnostics
- ▶ Microbicides
- ▶ Vector control products (pesticides, biological control agents and vaccines targeting animal reservoirs)
- ▶ Platform technologies (adjuvants, diagnostic platforms and delivery devices). These are technologies that can potentially be applied to a range of diseases and products, neglected and commercial, but which have not yet been attached to a specific product for a specific disease

Within these parameters, the final scope of G-FINDER was reached using a rigorous methodology. We compiled a long-list of Type II and III developing world diseases and products that had been identified as neglected by a major health organisation or publication, including the World Health Organization (WHO), the WHO-based Special Programme for Research and Training in Tropical Diseases (TDR), Commission on Macroeconomics and Health, Global Network for Neglected Tropical Diseases and a range of academic authors.^{9 10 11 12}

These disease and product lists were submitted to an international Advisory Committee composed of experts in neglected diseases and neglected disease product development (see Annexe 2). They were asked to filter the lists based on the three criteria outlined in Figure 1. When the Advisory Committee could not reach a decision on a specific disease or product, additional experts were called in to provide specialist advice.

This process resulted in a final list of 30 diseases and 127 product areas that were considered neglected. Although many were commonly acknowledged neglected diseases such as malaria, TB and helminth infections, the final list also included developing world diseases that often receive less attention, such as pneumonia, diarrhoeal illnesses, trachoma and rheumatic fever.

Three platform technology areas were also nominated as needing further investment:

- ▶ Adjuvants and immunomodulators. These are products or components that boost the human immune response to a range of different drugs or vaccines
- ▶ Diagnostic platforms. For example, technologies to allow breath tests rather than blood tests could theoretically be adapted for several diseases (such as its use in alcohol testing for drivers)
- ▶ Delivery technologies and devices. For example, intra-nasal delivery of a range of vaccines; or slow release technologies to allow less frequent dosing of a wide range of drugs

As noted, G-FINDER's brief was to measure global investment into R&D of products for neglected diseases of the developing world. The Advisory Committee and additional specialists therefore nominated several disease-product categories as 'restricted'. This was important to prevent neglected disease data being swamped by funding for activities not directly related to product development (e.g. advocacy, behavioural research); or by 'white noise' from overlapping commercial R&D investments (e.g. HIV/AIDS drugs or pneumonia vaccines targeting Western markets); and investments in platform technologies with shared Western applications.

For the latter categories, where commercial overlap was significant, only investment specifically targeted at developing-country needs was eligible for inclusion in G-FINDER. As an example, eligible pneumonia vaccine investments were defined by strain, vaccine type and target age group; while eligible HIV/AIDS drug investments were restricted to developing-country relevant products such as fixed-dose combinations (FDCs) and paediatric formulations. Eligibility for inclusion was also tightly defined for platform technologies to ensure that only funding for platforms for developing world use were included, as opposed to investment into platforms developed for commercial applications. Private sector investment into platform technologies was therefore excluded. (See Annexe 5 for outline of R&D funding categories, setting out inclusions and exclusions.)

The final agreed scope of G-FINDER diseases, products and technologies is shown in Table 1.

Figure 1. 3-step FILTER to determine scope of neglected diseases covered by G-FINDER

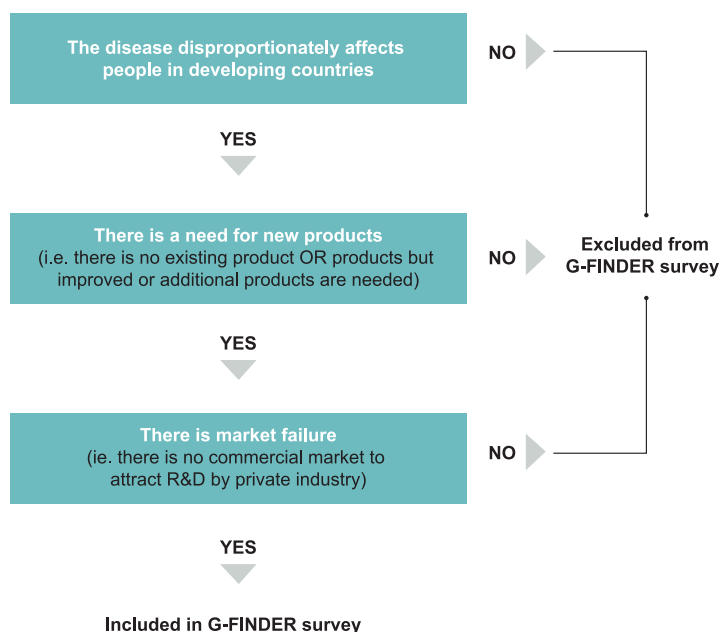


Table 1. G-FINDER diseases, products and technologies

	Restricted	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Microbicides	Vaccines (Therapeutic)	Vector Control Products
HIV/AIDS	Restricted	Restricted	Y	Y	Y			
Malaria								
<i>P. falciparum</i>	Y	Y	Y	Y				Y
<i>P. vivax</i>	Y	Y	Y	Y				Y
Other and/or unspecified malaria strains	Y	Y	Y	Y				Y
TB	Y	Y	Y	Y		Y		
Kinetoplastids								
Chagas' disease	Y	Y	Y	Y		Y		Y
Leishmaniasis	Y	Y	Y	Y		Y		
Sleeping Sickness	Y	Y	Y	Y				Y
Multiple diseases	Y	Y	Y	Y		Y		Y
Diarrhoeal diseases								
Rotavirus			Restricted					
Enterotoxigenic E. coli (ETEC)			Y	Y				
Cholera	Y	Restricted	Y	Y				
Shigella	Y	Restricted	Y	Y				
Cryptosporidium	Y	Restricted	Y	Y				
Enteraggregative E.coli (EAggEC)			Y	Y				
Giardia				Y				
Multiple diseases	Y	Y	Y	Y				
Dengue	Y	Y	Y	Y		Y		Y
Helminths								
Roundworm (Ascariasis)	Y	Y						
Hookworm (Ancylostomiasis & Necatoriasis)	Y	Y	Y					
Whipworm (Trichuriasis)	Y	Y						
Strongyloidiasis & other intestinal roundworms	Y	Y	Y	Y				
Lymphatic Filariasis (Elephantiasis)	Y	Y						Y
Onchocerciasis (River Blindness)	Y	Y	Y	Y				Y
Schistosomiasis (Bilharziasis)	Y	Y	Y	Y				Y
Tapeworm (Cysticercosis/Taeniasis)	Y	Y						Y
Multiple diseases	Y	Y	Y	Y				Y
Bacterial Pneumonia & Meningitis								
<i>Streptococcus pneumoniae</i>			Restricted	Y				
<i>Neisseria meningitidis</i>			Restricted	Y				
Both bacteria				Y				
Typhoid and Paratyphoid Fever	Y	Y		Y				
Leprosy	Y	Y		Y				
Buruli Ulcer	Y	Y	Y	Y				
Trachoma			Y	Y				
Rheumatic Fever			Y					
		Adjuvants and immunomodulators		Delivery technologies and devices		Diagnostic platforms		
Platform technologies (non-disease specific)		Restricted		Restricted		Restricted		

Restricted denotes a category where only some investments are eligible, as defined in the outline of the R&D funding categories (see Annexe 5)

Y (Yes) denotes a category where a disease or product was included in the survey

WHAT TYPES OF INVESTMENTS ARE INCLUDED?

G-FINDER's objective was to quantify only those investments specifically targeted at creating new pharmaceutical products for neglected diseases. These are:

- ▶ Basic research
- ▶ Product discovery and preclinical development
- ▶ Product clinical development
- ▶ Phase IV/ pharmacovigilance studies of new products
- ▶ Baseline epidemiology in preparation for product trials

Although we recognise the vital importance of activities such as advocacy, implementation research, community education and general capacity building, these were outside the scope of G-FINDER. We also excluded investment into non-pharmaceutical tools such as bednets or circumcision and general therapies such as painkillers or nutritional supplements, as these could not be ringfenced to neglected disease treatment only.

A detailed list of R&D inclusions and exclusions tailored to each product area was prepared based on previous categorisations developed by the US National Institutes of Health (NIH)¹³ and the Wellcome Trust. This was particularly important for diagnostics, vector-control products and platform technologies, where development pathways for commercial and public health markets can differ. This list was also submitted to the Advisory Committee for advice, input and clearance, leading to a final prescriptive list of included and excluded R&D activities for each research category (See Annexe 5).

HOW WAS DATA COLLECTED?

Two key principles guided the design of the G-FINDER survey. The data should be as consistent and comparable as possible across all funders and diseases and as close to 'real' investment figures as we could get.

G-FINDER was therefore designed as an online survey into which all organisations entered their data in the same way according to the same definitions, the same categories, and with the same inclusions and exclusions. We only accepted primary grant data¹. Survey respondents were asked to enter every neglected disease grant they had disbursed or received in 2007 into a password-protected online database. They were asked to only include disbursements as opposed to commitments made but not yet disbursed. If accurate data was not available, we did not substitute secondary data or estimates.

Multinational pharmaceutical companies (MNCs) also agreed to provide full accurate data on their neglected disease investments. However, as firms do not operate on a grant basis, the reporting tool was varied somewhat. Instead of grants, companies agreed to enter the number of staff working on neglected disease programmes, their salaries, and direct project costs related to these programmes. All investments were allocated by disease, product and research type according to the same guidelines used for online survey recipients. As with other respondents, companies were asked to include only disbursements rather than commitments. They were also asked to exclude 'soft figures' such as in-kind contributions and costs of capital.

The survey was open for a 10-week period from July to September 2008 during which intensive follow-up and support were provided to key recipients, leading to a final total of 5,116 grants or investments recorded in the database.

With the exception of NIH grants, all entries over \$0.5 million (i.e. any grant over 0.02% of total funding) were then verified against the inclusion criteria and cross-checked for accuracy. Cross-checking was conducted through automated reconciliation reports that matched grants reported disbursed by funders with grants reported received by intermediaries and product developers. Any discrepancies were resolved by contacting both groups to identify the correct figure. Industry data was aggregated to the level of multinational and small companies in order to protect the confidentiality of the companies involved.

¹ An exception was made for some NIH data, where a proportion of grants could not be collected in this way due to changes in their data management system (see below on how exceptions were handled).

WHO WAS SURVEYED?

G-FINDER is primarily a survey of funders. In its first year, the survey was sent to 134 funders in 43 countries around the world. These were:

- ▶ Public, private and philanthropic funders in:
 - High- and Middle-Income Countries (HICs and MICs) that were part of the Organisation for Economic Co-operation and Development (OECD)
 - European Union (EU) Member States and the European Commission
 - HICs and MICs outside the OECD with a significant research base (Singapore, Israel and the Russian Federation)
- ▶ Public funders in selected Innovative Developing Countries (IDCs) (South Africa, Brazil)

In subsequent years, the survey will expand to include private sector funding in these two IDCs, public and ideally private sector funding in additional IDCs (India, China, Cuba), and public funding in other Low- and Middle-Income Countries (LMICs).

In addition to funders, G-FINDER also surveyed a wide range of funding intermediaries and Product Development Partnerships (PDPs), as well as researchers and developers who received funding. Data from these groups was used to track funding flows through the system, prevent double-counting, verify reported data, and better understand how and where R&D investments were made.

The survey was sent to 551 organisations identified as being involved in neglected disease product development. These were prioritised into three groups based on their R&D role (funder, intermediary/PDP or developer), level of funding, and area of disease and product activity:

- ▶ The maximum priority group included 25 organisations known from previous surveys to be major funders (over \$10 million per year) or major private sector developers investing internally into one of the 30 target neglected diseases
- ▶ A high priority group of 85 organisations included known significant funders (\$5-10 million per year); potential research funders in high-Gross Expenditure on R&D (GERD) countriesⁱⁱ; and a range of academic research institutes, PDPs, government research institutes, multinational pharmaceutical firms and small companies, who collectively provided good coverage of R&D in all disease areas
- ▶ The remaining survey recipients were known small funders (less than \$5 million per year) and other known grant recipients, including many academic groups and public research institutions

The G-FINDER process focused on the 110 organisations in the maximum and high priority groups, who likely represented the majority of global neglected disease R&D funding and activity.

We received complete financial information from 150 organisations. In the maximum priority group, 23 of 25 recipients (92%) provided funding information for 2007. In the high priority group, 77 organisations (91%) provided full funding information for 2007. Two private sector maximum priority organisations, Wyeth and Merck & Co (both MNCs) did not provide data; and one multinational company, sanofi-aventis, provided drug but not vaccine data. (See Annexe 4 for a list of survey participants.)

ⁱⁱ Gross Expenditure on R&D as a percentage of Gross Domestic Product (GDP)

Reading the findings

In reading the results of the G-FINDER survey, it is helpful to note that all reported funding is 2007 funding and that all figures are in 2007 US\$.

Unless noted otherwise, all DALY (Disability Adjusted Life Year) figures in the report are 2004 DALYs for LMICs, as reported by the WHO in the 2004 update of the Global Burden of Disease¹⁵, which represented the most comprehensive and recent figures available. In some cases, WHO estimates may be lower than those derived using other methods or published by other groups, however they allowed the most consistent approach across diseases.

For brevity, we use the term 'Developing Countries' (DCs) to denote low and middle income countries; and 'OECD-plus' to collectively denote countries that are members of the OECD, EU Member States, the European Commission, and HICs and MICs outside the OECD but with a significant research base (Singapore, Israel and the Russian Federation).

Around \$50 million (2.0%) of overall funding was reported to the survey as 'unspecified', usually for multi-disease programmes for which apportioning by disease could not easily be done. A proportion of funding for some diseases was also 'unspecified', for instance, when funders reported a grant for research into TB basic research and drugs without apportioning funding to each product category. This means that reported funding for specific diseases and products will be slightly lower than actual funding, with the difference being included as 'unspecified' funding. This is likely to particularly affect NIH figures for individual diseases, as the NIH had a higher number of unspecified grants than other donors.

Finally, readers should be aware that, as with all surveys, there are limitations to the data presented. Survey non-completion by funders will have an impact, as will methodology (See Annexe 1 for further details).

FINDINGS

Funding by disease

Just over \$2.5 billion was invested into R&D of new neglected disease products in 2007, with HIV/AIDS, TB and malaria receiving nearly 80% of this amount. Funding for each disease area is discussed in separate sections below.

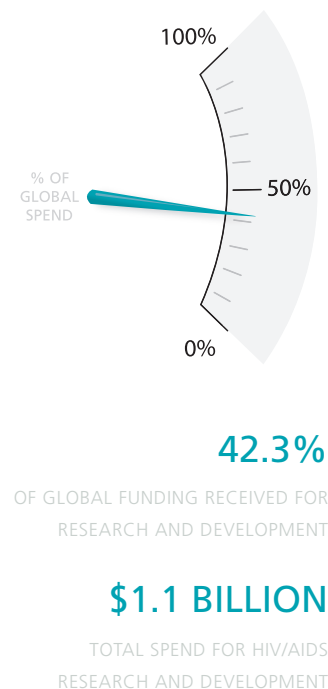
When reading the funding tables, it is important to note that some of the ‘diseases’ listed below are actually groups of diseases, such as diarrhoeal illnesses or helminth infections. This grouping reflects common practice; for instance, burden of disease DALYs are generally reported according to these categories. It also reflects the shared nature of research investments in some areas. For example, research into kinetoplastids often pertains to more than one kinetoplastid disease, while *Streptococcus pneumoniae* R&D is often targeted at both pneumonia and meningitis. Where possible, however, information is broken down to disease level.

We also remind readers that the investments below are for neglected diseases and exclude investments into commercial products for related Western markets.

Table 2. Total R&D funding by disease in 2007

DISEASE	AMOUNT (US\$)	%
HIV/AIDS	1,083,018,193	42.3
Malaria	468,449,438	18.3
Tuberculosis	410,428,698	16.0
Kinetoplastids	125,122,839	4.9
Diarrhoeal diseases	113,889,118	4.4
Dengue	82,013,895	3.2
Helminths (Worms & Flukes)	51,591,838	2.0
Bacterial Pneumonia & Meningitis	32,517,311	1.3
Typhoid and Paratyphoid Fever	9,117,212	0.4
Leprosy	5,619,475	0.2
Buruli Ulcer	2,412,950	0.1
Trachoma	1,679,711	0.1
Rheumatic Fever	1,670,089	0.1
Core funding of a multi-disease R&D organisation	110,921,673	4.3
Platform technologies	9,997,189	0.4
Unspecified disease	51,619,120	2.0
Grand Total	2,560,068,749	100.0

HIV/AIDS



The Acquired Immune Deficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV). This virus infects cells of the human immune system, destroying or impairing their function. As the immune system becomes progressively weaker, the person becomes more susceptible to other diseases, often dying from TB or fungal infections.

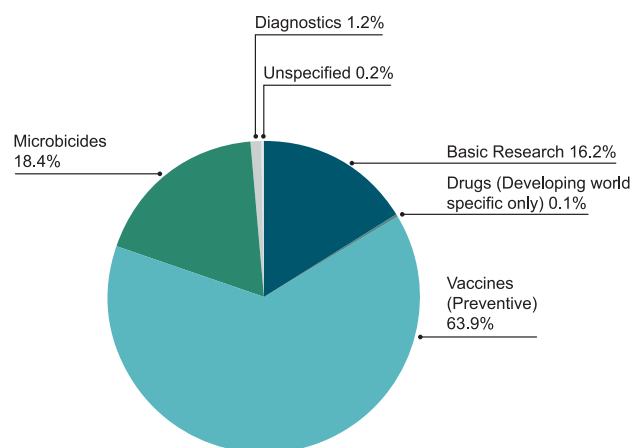
HIV/AIDS was responsible for 57.8 million DALYs and 2 million deaths in 2004, when it was the third highest cause of morbidity and mortality from neglected diseases in the developing world.

R&D needed for HIV/AIDS in developing countries (DCs) includes:

- ▶ Basic research
- ▶ Drugs specific to DC needs
- ▶ Preventive vaccines
- ▶ Diagnostics
- ▶ Microbicides

HIV/AIDS received \$1.1 billion in R&D funding in 2007ⁱⁱⁱ. Of this, \$691.5 million (63.9%) was directed to vaccines, \$199.5 million (18.4%) to microbicides and \$176.3 million (16.2%) to basic research. Less than \$1 million (0.1%) was invested in development of HIV/AIDS drugs targeted at developing world needs, such as paediatric formulations and fixed-dose anti-retroviral (ARV) combinations (Fig 2). New diagnostics aimed at developing world use received a relatively modest \$12.4 million (1.2%).

Figure 2: HIV/AIDS R&D funding by product type in 2007



Twelve organisations provided 92.4% of global HIV/AIDS funding, of whom eleven were public funders who collectively represented 83.9% of HIV/AIDS R&D funding.

ⁱⁱⁱ The breakdown of investment by product differs from the HIV Vaccines and Microbicides Resource Tracking Working Group (RTWG) survey, which includes basic research funding within its vaccine and microbicide investment figures, while G-FINDER reports basic research separately from vaccine and microbicide investment figures. Overall HIV/AIDS investment figures differ very little (~9%) between RTWG and G-FINDER, with this difference primarily reflecting 1) the RTWG's inclusion of policy and advocacy, both excluded from G-FINDER and 2) the exclusive use of primary data by G-FINDER, while the RTWG survey included estimated figures.

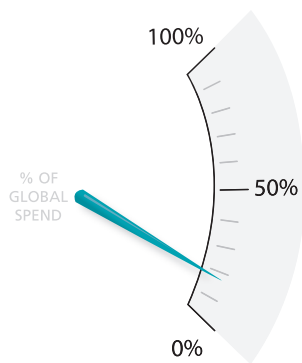
Table 3. Top 12 HIV/AIDS funders

FUNDER	AMOUNT (US\$)	%
US National Institutes of Health	678,816,000	62.7
Bill & Melinda Gates Foundation	91,975,642	8.5
United States Agency for International Development	67,457,000	6.2
UK Department for International Development	31,151,182	2.9
US Department of Defense ^{iv}	27,800,000	2.6
European Commission	24,794,890	2.3
Russia Ministry for Health and Social Development	16,666,666	1.5
Irish Aid	13,704,784	1.3
Dutch Ministry of Foreign Affairs	13,188,114	1.2
UK Medical Research Council	13,101,548	1.2
Canadian International Development Agency	11,796,354	1.1
French National Agency for AIDS Research	10,511,570	1.0
Subtotal top 12 funders	1,000,963,749	92.4
Disease Total	1,083,018,193	100.0

^{iv} The Department of Defense funding included in all G-FINDER figures represents only funding from the Military Infectious Diseases Research Program (MIDRP)

An analysis of the breakdown between public and private sector funding was not conducted as non-participation or partial participation in the survey by some private sector firms. In particular, non-participation by three multinational companies, meant that private sector investments were almost certainly underreported in the vaccine category, but also to a degree in the diagnostics category.

MALARIA



18.3%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$468.4 MILLION

TOTAL SPEND FOR MALARIA
RESEARCH AND DEVELOPMENT

Malaria is transmitted through the bite of an infected mosquito. The two most common types of malaria are caused by *P.falciparum* and *P.vivax*. Once infected, the patient experiences fever, headache and vomiting, and may become severely anaemic as the parasite infects their red blood cells. Left untreated, malaria can cause severe illness, and *P.falciparum* malaria is often fatal especially in children under 5 years of age and pregnant women. In many parts of the world, the parasites have developed resistance to a wide range of anti-malarial drugs.

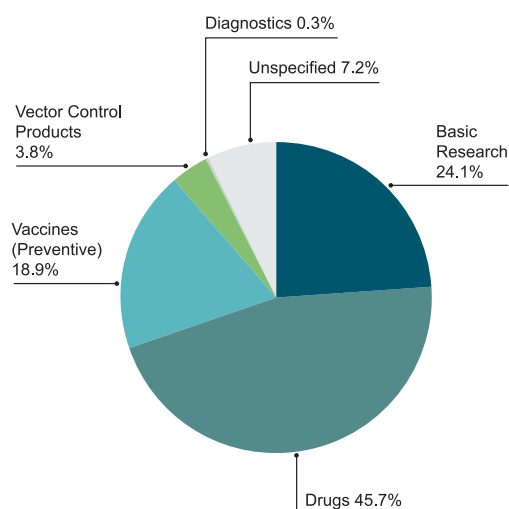
Malaria caused 33.9 million DALYs and at least 890,000 deaths in the developing world in 2004, making it the fifth highest cause of morbidity and mortality from neglected diseases. Although less fatal than *P.falciparum* malaria, *P.vivax* is estimated to account for 25–40% of the global malaria burden¹⁶.

Malaria R&D is needed in many areas including:

- ▶ Basic research
- ▶ Drugs
- ▶ Preventive vaccines
- ▶ Diagnostics
- ▶ Vector control products

Global funding for malaria R&D was \$468.4 million, with drug development receiving nearly half this amount (\$214.1 million or 45.7%). Basic research was the next highest funded category at \$112.9 million (24.1%), while vaccines received \$88.4 million (18.9%). Vector control products, such as insecticides and biological control measures, received \$17.7 million (3.8%). Malaria diagnostics received limited funding of \$1.6 million (0.3% of the total) (Fig 3).

Figure 3: Malaria R&D funding by product type in 2007



The bulk of funding was reported as funding either for malaria generally (\$337.9 million or 72.1%) or specifically for *P.falciparum* (\$126.2 million or 26.9%), with only 0.9% of the total (\$4.4 million) recorded as funding specifically for *P.vivax*. However, these figures should be interpreted with caution, as many funders were simply unable to break data down to this level.

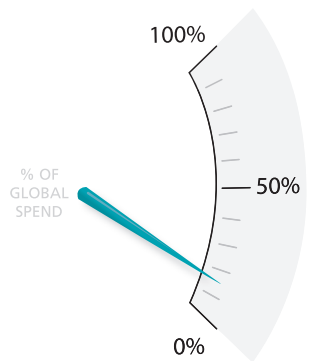
Public and philanthropic funders provided \$375.3 million (80% of total funding for malaria R&D), with twelve organisations providing the majority of this amount (75.9%) (See Table 4). Industry funding was also substantial at \$90.8 million or 19.4%.

Table 4. Top 12 malaria funders

FUNDER	AMOUNT (US\$)	%
Bill & Melinda Gates Foundation	124,464,185	26.6
US National Institutes of Health	84,422,644	18.0
US Department of Defense	33,126,578	7.1
Wellcome Trust	28,255,207	6.0
European Commission	21,673,026	4.6
UK Medical Research Council	18,594,597	4.0
Institut Pasteur*	13,142,888	2.8
United States Agency for International Development	9,249,900	2.0
Australian National Health and Medical Research Council	7,692,288	1.6
Dutch Ministry of Foreign Affairs	5,493,975	1.2
Irish Aid	5,481,914	1.2
UK Department for International Development	4,003,611	0.9
Subtotal top 12 funders	355,600,814	75.9
Disease Total	468,449,438	100.0

* Institut Pasteur was only able to provide partial investment data for 2007. So this figure, while broadly representative, may not reflect their total investments into G-FINDER diseases.

TUBERCULOSIS



16.0%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$401.4 MILLION

TOTAL SPEND FOR TB RESEARCH
AND DEVELOPMENT

TB is a bacterial disease that usually affects the lungs, and is spread by droplets from the throat and lungs of infected people. After infection, TB may remain latent with no symptoms. However, if it progresses to active disease, it causes coughing (sometimes with blood), night sweats, fever and weight loss. TB was called 'consumption' in the past because it seemed to consume people from within. TB is a leading cause of death among people with AIDS.

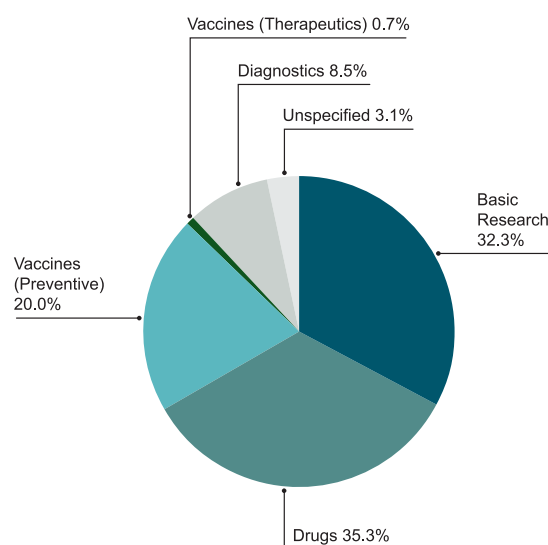
TB was responsible for 34 million DALYs and 1.4 million deaths in 2004. It was the fourth highest cause of morbidity and mortality from neglected diseases.

R&D needs for TB include:

- ▶ Basic research
- ▶ Drugs
- ▶ Diagnostics
- ▶ Preventive vaccines
- ▶ Therapeutic vaccines

TB funding for 2007 totalled \$410.4 million. Around one-third of this amount went to drug R&D (\$145.1 million or 35.3%), closely followed by basic research at \$132.4 million (32.3%). TB vaccines were funded at similar levels to malaria vaccines in both actual and relative terms, receiving \$82.3 million (20.0%) of total TB funding. However, TB diagnostics fared dramatically better than malaria diagnostics, receiving 8.5% of global TB investment (\$35.0 million) (Fig 4). This was the case despite likely under-reporting of TB diagnostic activity by small companies who did not participate in the G-FINDER survey.

Figure 4: TB R&D funding by product type in 2007



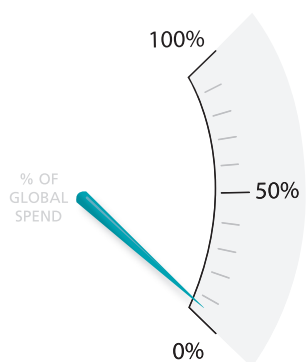
As with malaria funding, TB funding also showed an approximately 80/20 split between public and philanthropic funding (\$342.9 million or 83.5%), and industry funding (\$66 million or 16.1%).

Table 5. Top 12 TB funders

FUNDER	AMOUNT (US\$)	%
US National Institutes of Health	121,741,199	29.7
Bill & Melinda Gates Foundation	115,864,538	28.2
European Commission	21,455,029	5.2
UK Medical Research Council	12,710,433	3.1
Dutch Ministry of Foreign Affairs	12,187,935	3.0
US Centers for Disease Control	11,617,000	2.8
Institut Pasteur	7,996,742	1.9
German Federal Ministry of Education and Research*	4,391,435	1.1
Irish Aid	4,111,435	1.0
UK Health Protection Agency	3,903,521	1.0
United States Agency for International Development	3,893,436	0.9
Statens Serum Institute	3,672,882	0.9
Subtotal	323,545,584	78.8
Disease Total	410,428,697	100.0

* The German Federal Ministry of Education and Research did not participate in the survey. Their contribution was compiled from grant information provided by funding recipients and may be an underestimate of their true investment

KINETOPLASTID DISEASES



4.9%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$125.1 MILLION

TOTAL SPEND FOR KINETOPLASTID
DISEASES RESEARCH AND
DEVELOPMENT

Kinetoplastid infections are caused by related parasites and include three diseases: sleeping sickness, Chagas disease and leishmaniasis. Human African trypanosomiasis, also known as African sleeping sickness, initially presents with similar symptoms to a viral illness but eventually infects the brain where it leads to confusion, coma and death. Chagas disease also has two stages, with late stage Chagas leading to heart failure and death. Leishmaniasis can cause skin lesions or, in its more severe form, can infect and damage internal organs (spleen, liver and bone marrow). Kinetoplastid diseases are often fatal if left untreated.

In 2004, the three kinetoplastid diseases were responsible for 4.1 million DALYs and 110,000 recorded deaths in the developing world. They ranked as the 8th highest cause of mortality and 9th highest cause of morbidity from neglected diseases.

R&D is needed in every area, including:

- ▶ Basic research for all 3 diseases
- ▶ Drugs for all 3 diseases
- ▶ Preventive vaccines for all 3 diseases
- ▶ Diagnostics for all 3 diseases
- ▶ Vector control products for sleeping sickness and Chagas disease
- ▶ Therapeutic vaccines for leishmaniasis

Collectively, kinetoplastids R&D received \$125.1 million in 2007. This included just over 50% of funding (\$62.6 million) to drug development; 34.1% to basic research (\$42.7 million); 9.1% (\$11.3 million) to vaccines, both preventive and therapeutic; and just under 6% (\$7.3 million) to development of new diagnostics. Funding for vector control products was under \$0.5 million (0.3% of the total).

It is also helpful to breakdown funding within each disease in order to identify how specific product categories compared. We note that the higher level of funding targeting drug development for leishmaniasis and sleeping sickness likely reflects the presence of a PDP working in these diseases.

Table 6. Funding for kinetoplastids product R&D in 2007 (US\$)

		Basic Research		Drugs	Vaccines (Preventive)		Vaccines (Therapeutic)	Diagnostics	Vector control products		Unspecified	Total	%
Leishmaniasis	16,961,019	21,890,911	2,560,030	6,222,783	3,581,215				54,664	51,270,622		41.0	
Sleeping Sickness	16,710,088	20,535,164	1,255,000		2,811,906	56,543	-		41,368,700		33.1		
Chagas disease	5,875,634	972,031	1,301,235	-	922,522	377,918	649,983		10,099,322		8.1		
Multiple kinetoplastids	3,165,251	19,218,944	-	-	-	-	-	-	22,384,194		17.9		
Total	42,711,992	62,617,049	5,116,265	6,222,783	7,315,643	434,460	704,647	125,122,839	100.0				

- No reported funding in this category
Category not included in G-FINDER

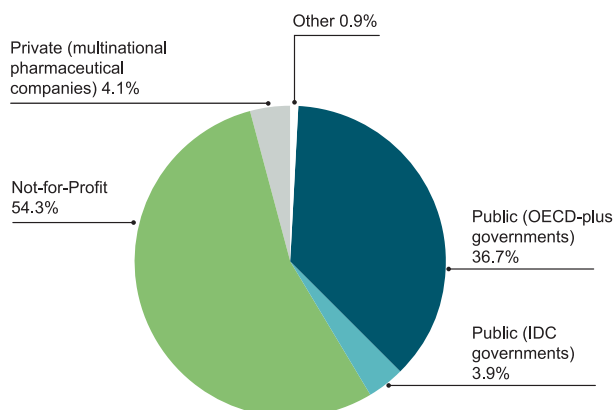
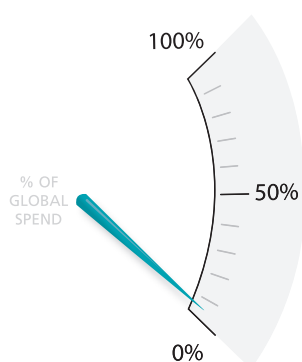


Figure 5. Kinetoplastids R&D funding by funder type in 2007

Funding for kinetoplastids R&D was predominantly from philanthropic organisations (\$67.9 million or 54.3%), and public funders in the West and IDCs (40.6% of funding or \$50.9 million), making up 94.9% of total global funding.

DIARRHOEAL DISEASES



4.4%

% OF GLOBAL FUNDING RECEIVED FOR RESEARCH AND DEVELOPMENT

\$113.9 MILLION

TOTAL SPEND FOR DIARRHOEAL DISEASES RESEARCH AND DEVELOPMENT

Diarrhoeal diseases are a group of illnesses caused by viruses, bacteria or protozoa, and presenting with fever and diarrhoea (sometimes bloody). They range from rotavirus and *E.coli*, which occur relatively commonly in the West; to cholera and shigella, which are mostly found in developing world settings. Diarrhoeal diseases mainly affect children under 5 years of age and are often transmitted by contaminated food or water. Although they rarely cause death in Western settings (due primarily to higher levels of available health care) their impact in the developing world is severe.

Diarrhoeal illnesses were collectively responsible for 72.3 million DALYs and just over 2 million deaths in the developing world in 2004, making them the second highest cause of neglected disease mortality and morbidity. In 2004, diarrhoeal illnesses were responsible for one in every six deaths of children under 5 years of age.

A wide range of R&D is needed for the diarrhoeal illnesses including:

- ▶ Basic research for cholera, shigella and cryptosporidium
- ▶ Drugs for cholera, shigella and cryptosporidium
- ▶ Vaccines for rotavirus, *E.coli*, cholera, shigella and cryptosporidium
- ▶ Diagnostics for all the diarrhoeal diseases with the exception of rotavirus

Diarrhoeal diseases received \$113.9 million in 2007 with rotavirus, cholera and shigella receiving nearly half of total funding.

Table 7. Funding for diarrhoeal diseases product R&D in 2007 (US\$)

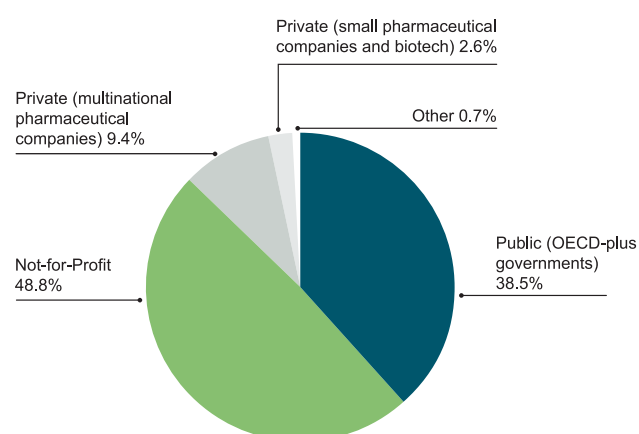
	Basic Research		Drugs	Vaccines (Preventive)		Diagnostics	Unspecified	Total	%
Rotavirus			22,844,338			-	22,844,338	20.1	
Cholera	11,321,988	111,427	6,100,744	-	380,250	17,914,409	15.7		
Shigella	1,707,731	-	9,371,682	-	3,426,196	14,505,609	12.7		
Enterotoxigenic E.coli			11,945,246	165,000	179,290	12,289,536	10.8		
Cryptosporidium	5,329,011	2,609,239	-	-	-	7,938,250	7.0		
Enterocaggregative E.coli (EAggEC)			-	-	-	-	0.0		
Giardia			-	-	-	-	0.0		
Multiple diarrhoeal diseases	-	10,384,636	16,300,222	7,055,146	4,656,972	38,396,975	33.7		
Total							113,889,118	100.0	

- No reported funding in this category
 Category not included in G-FINDER

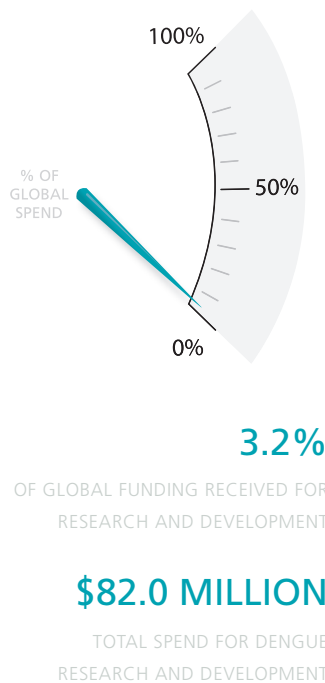
Strict definitions were imposed on eligible drug and vaccine investments for most diseases in Table 7 to avoid inclusion of overlapping commercial activity. These restrictions mean that totals for different product categories cannot reasonably be compared.

Investment was primarily from philanthropic funders (48.8% or \$55.6 million) and public funders (38.5% or \$43.8 million), although products for diarrhoeal diseases also drew private sector investment of \$13.7 million (12% of the total).

Figure 6. Diarrhoeal diseases R&D funding by funder type in 2007



DENGUE



Dengue is transmitted by mosquitoes. It causes a severe flu-like illness. Its most severe form, dengue haemorrhagic fever, is a leading cause of serious illness and death among children in some Asian countries.

Dengue differs from many tropical diseases by virtue of having a somewhat larger commercial market due to travellers, military and to its prevalence in relatively higher income developing countries in South East Asia.

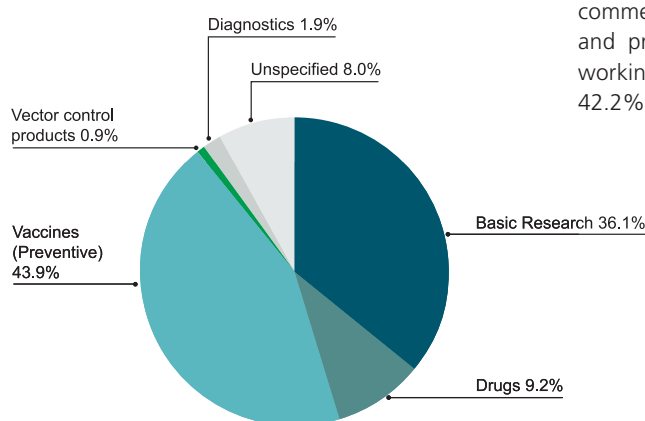
Dengue was responsible for 663,000 DALYs and 18,000 deaths in 2004. It ranked as the 11th highest cause of morbidity and 10th highest cause of mortality from neglected diseases.

R&D needed for dengue includes:

- ▶ Basic research
- ▶ Drugs
- ▶ Preventive vaccines
- ▶ Diagnostics
- ▶ Vector control products

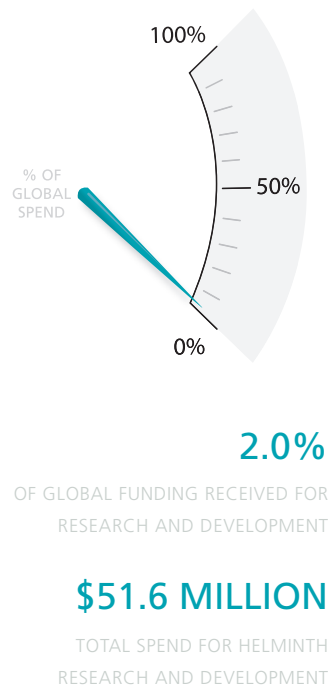
Global funding for dengue R&D totalled \$82.0 million in 2007, of which nearly half was devoted to vaccine development and just over one-third to basic research.

Figure 7: Dengue R&D funding by product type in 2007



Just over 40% of funding (\$33.8 million) came from private companies and the US Department of Defense, which may reflect the interest of these groups in commercial dengue vaccine markets and protection of military personnel working in endemic areas. A further 42.2% came from the NIH.

HELMINTH INFECTIONS



Helminths are parasitic worms and flukes that can infect humans. They include hookworms, roundworms, whipworms and tapeworms; as well as elephantiasis (lymphatic filariasis), river blindness (onchocerciasis) and schistosomiasis.

Adult worms live in the intestines and other organs, and the infection is transmitted through food, water, soil or other objects.

Helminths can cause malnutrition and impaired mental development (e.g. hookworms) or progressive damage to the bladder, ureters and kidneys (schistosomiasis). Onchocerciasis is a major cause of blindness in many African and some Latin America countries, while elephantiasis causes painful, disfiguring swelling of the legs and genitals.

Helminth infections are the 6th highest cause of morbidity and the 9th highest cause of mortality, with 12 million DALYs in 2004 (around one-third that of malaria). However, some estimates suggest that 49 million DALYs or more are lost to helminth infections annually¹⁷. Furthermore, although some estimates indicate that helminth infections are rarely fatal, causing only 47,000 deaths compared to nearly one million recorded for malaria in the same period, other estimates indicate that these infections are responsible for 415,000 annual deaths¹⁷.

Helminth infections require a range of R&D including:

- ▶ Basic research for all the listed infections
- ▶ Drugs for all the listed infections
- ▶ Vaccines for strongyloides, onchocerciasis, schistosomiasis and hookworm
- ▶ Diagnostics for strongyloides, onchocerciasis and schistosomiasis
- ▶ Vector control products for lymphatic filariasis, onchocerciasis, schistosomiasis and tapeworm

The helminth infections received \$51.6 million in R&D funding in 2007, with schistosomiasis receiving just under half, perhaps as a reflection of its higher mortality rates.

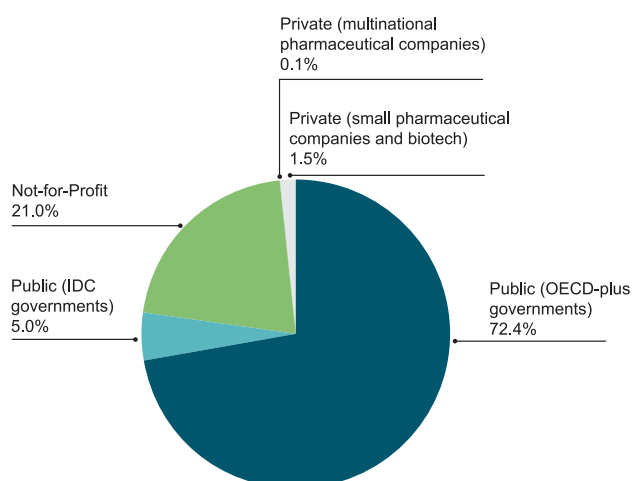
Table 8. Funding for helminth diseases product R&D in 2007 (US\$)

		Basic Research		Drugs	Vaccines (Preventive)		Vaccines (Therapeutic)	Diagnostics	Vector control products		Unspecified	Total	%
Schistosomiasis (Bilharziasis)	13,705,190	870,254	8,019,820	-	39,980	329,847	557,511	23,522,601	45.6				
Hookworm (Ancylostomiasis & Nectoriasis)	1,479,348	-	7,156,689				-	8,636,037	16.7				
Lymphatic Filariasis (Elephantiasis)	4,476,370	-				-	949,554	5,425,924	10.5				
Onchocerciasis (River Blindness)	197,945	651,000	-		-	-	959,335	1,808,280	3.5				
Roundworm (Ascariasis)	1,404,964	-					-	1,404,964	2.7				
Tapeworm (Cysticercosis/Taeniasis)	984,610	-				74,644	-	1,059,254	2.1				
Strongyloidiasis & other intestinal roundworms	433,331	-	-		58,845		-	492,176	1.0				
Whipworm (Trichuriasis)	133,272	-					-	133,272	0.3				
Multiple helminths	7,086,183	516,954	-		-	-	1,506,193	9,109,330	17.7				
Total	29,901,213	2,038,207	15,176,509	-	98,824	404,491	3,972,592	51,591,838	100.0				

- No reported funding in this category
 Category not included in G-FINDER

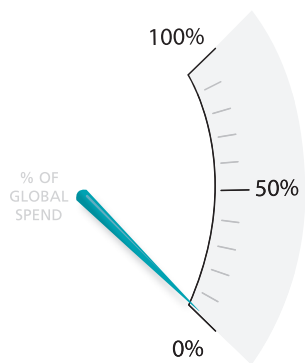
Overall, funding was highly concentrated with over half going to basic research (\$29.9 million). Investment into applied product research (\$21.8 million in total) was almost entirely directed towards preventive vaccines, while drugs, diagnostics and vector control products for the helminth infections collectively received only \$2.5 million.

Figure 8. Helminth diseases R&D funding by funder type in 2007



R&D targeted at the helminth infections was predominantly funded by the public sector (\$40 million or 77.4%). Virtually all the remainder came from philanthropic funders (\$10.8 million or 21.0%), with these two sectors representing 98% of global funding. We note, however, that one of the two multinational companies that did not participate in the G-FINDER survey is known to be developing an anti-helminth drug in conjunction with TDR.

BACTERIAL PNEUMONIA & MENINGITIS



1.3%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$32.5 MILLION

TOTAL SPEND FOR BACTERIAL
PNEUMONIA & MENINGITIS
RESEARCH AND DEVELOPMENT

Pneumonia is a lung infection transmitted by the cough or sneeze of infected patients. It presents with cough, fever, chest pain and shortness of breath, and can be fatal especially in young children and elderly patients. Although caused by a range of bacteria and viruses, *Streptococcus pneumoniae* (which also causes meningitis) is by far the most common cause of pneumonia in the developing world.

Bacterial meningitis is an infection of the fluid that surrounds the brain and the spinal cord and is mostly caused by *S.pneumoniae* and *Neisseria meningitidis*. Meningitis is transmitted from person to person through droplets of respiratory or throat secretions. Symptoms include severe headache, fever, chills, stiff neck, nausea and vomiting, sensitivity to light and altered mental state. Even with early diagnosis and treatment, 5 to 10 percent of patients die within 24-48 hours of onset of symptoms. Meningitis epidemics occur commonly in the sub-Saharan African meningitis belt.

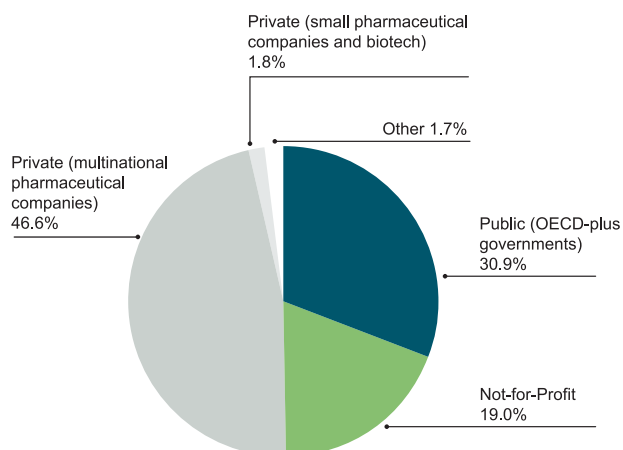
Although both diseases also cause significant morbidity and mortality in the West, the absence of preventive vaccines suited to developing world strains makes their health impact far more severe in poor countries.

Lower respiratory infections, mostly pneumonia, were responsible for 93.3 million DALYs and 3.9 million deaths in the developing world in 2004. Pneumonia ranked as the number one cause of morbidity and mortality of any neglected disease and was responsible for nearly one in five deaths in children under 5 years of age. Meningitis ranked as the 7th highest cause of morbidity, the 6th highest cause of mortality and was responsible for 11.3 million DALYs and 340,000 deaths in 2004.

New products needed for pneumonia and meningitis are:

- ▶ Vaccines that include developing world strains
- ▶ Diagnostics

Figure 9. Bacterial pneumonia and meningitis R&D funding by funder type in 2007

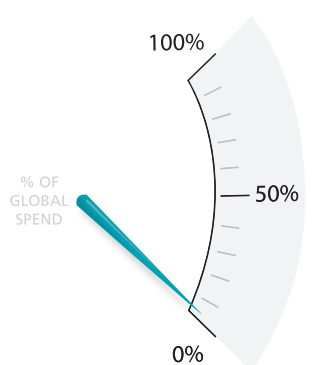


Funding for bacterial pneumonia and meningitis specific to developing world settings was \$32.5 million in 2007. Vaccine R&D received the bulk of funding (\$27.2 million or 83.7%), with diagnostics receiving \$2.5 million (7.6%). The remainder consisted of \$2.8 million in unspecified funding.

Public funders provided 30.9% (US\$ 10.1 million) of total funding, while the private sector provided 48.4% (\$15.8 million). Around \$380,000 was also donated by the general public to develop new products for pneumonia and meningitis of the developing world.

Pneumonia and meningitis stood out from other diseases by virtue of their notably higher level of private sector funding. This is likely to reflect overlap with commercial vaccine interests, as several vaccines for both diseases are already marketed in the West. Private sector investment may be even higher than recorded here, since two multinational companies that did not provide vaccine data to G-FINDER have, or have had, commercial programmes for broad-spectrum pneumococcal vaccines. At least one of these vaccines is virtually completed (registration for paediatric use in Europe is expected in 2009¹⁸), although it is unclear if its development programme included any developing country trial component.^{iv}

TYPHOID & PARATYPHOID FEVER



3.2%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$82 MILLION

TOTAL SPEND FOR TYPHOID &
PARATYPHOID FEVER RESEARCH
AND DEVELOPMENT

Typhoid and paratyphoid fever are bacterial diseases transmitted by contaminated food or drink. Symptoms include high fever, malaise, headache, constipation or diarrhoea, rose-coloured spots on the chest, and enlarged spleen and liver.

There are no reliable burden of disease figures for typhoid and paratyphoid fever. A widely accepted figure is the WHO estimate that typhoid and paratyphoid accounted for around 16 million cases and 160,000 deaths in 2000¹⁹.

R&D needed for typhoid and paratyphoid fever includes:

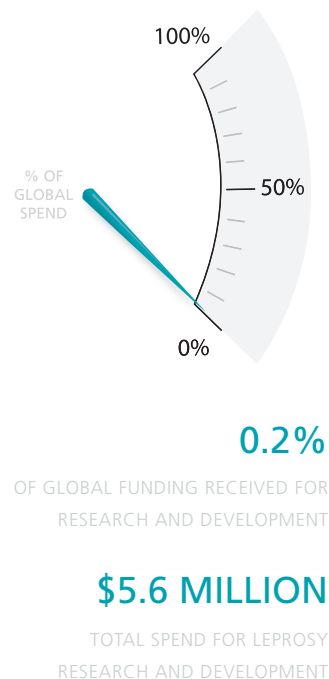
- ▶ Basic research
- ▶ Drugs
- ▶ Diagnostics

Typhoid and paratyphoid fever received \$9.1 million in R&D funding in 2007. Only three groups reported funding in this area - the NIH, which provided close to 90% of funding (\$8.1 million); the UK Medical Research Council (MRC); and the UBS Optimus Foundation. No private sector investment was reported.

The entirety of this funding was spent on basic research. There was no reported investment into development of drugs or diagnostics for typhoid and paratyphoid fever.

^{iv} Publicly available trial databases show no developing country trials

LEPROSY



Leprosy is caused by the family of bacteria responsible for TB, and is also transmitted via droplets from the nose and mouth of untreated patients, but it is far less infectious than TB. Leprosy mainly affects the skin and nerves and, if left untreated, causes nerve damage that leads to muscle weakness and wasting, and permanent disabilities and deformities.

Leprosy was responsible for 194,000 DALYs and 5,000 deaths in 2004. A successful eradication programme means incidence is decreasing. Nevertheless, around a quarter of a million new cases of leprosy are recorded each year. Leprosy ranked as the 11th highest cause of mortality and 12th highest cause of morbidity from neglected diseases.

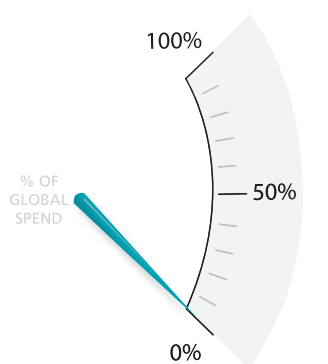
R&D needed for leprosy includes:

- ▶ Basic research
- ▶ Drugs
- ▶ Diagnostics

Leprosy R&D received \$5.6 million in 2007. Over three-quarters of funding was dedicated to basic research (\$4.3 million or 76.8%) and a further 10.7% (\$0.6 million) to new leprosy diagnostics. Development of new drugs to replace current treatment regimens, which require 6-12 months of multiple drug therapy, received only \$20,000 in global investment.

The entirety of leprosy R&D funding came from public and philanthropic investors, with Brazil's contribution of just over one-quarter of the total, likely reflecting domestic priorities (Brazil has the second highest leprosy incidence after India²⁰).

BURULI ULCER



0.1%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$2.4 MILLION

TOTAL SPEND FOR BURULI ULCER
RESEARCH AND DEVELOPMENT

Buruli ulcer starts as a painless lump that becomes an invasive ulcerating lesion, leading to disfiguration and functional impairment. It typically affects the rural poor with the greatest number of cases in children under 15 years of age. Little research has been done on Buruli ulcer, with the result that the method of transmission remains unknown, and surgical removal or amputation remains the mainstay of treatment.

Buruli ulcer occurs in 30 countries, but predominantly in Western Africa especially in Benin, Côte d'Ivoire and Ghana. No DALY figures are available, although WHO estimates that Buruli ulcer affects more than 7000 people per annum²¹.

Buruli ulcer needs a wide range of R&D including:

- ▶ Basic research
- ▶ Drugs
- ▶ Vaccines
- ▶ Diagnostics

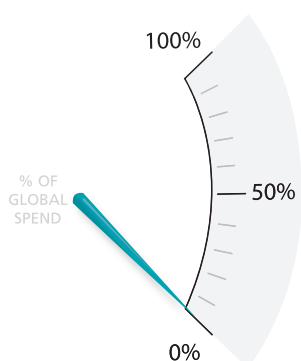
Buruli ulcer received \$2.4 million in R&D funding in 2007. Allocation of the majority of this funding (62.5%) was unspecified, therefore we are unable to comment on distribution between product categories.

European funders took the lead on Buruli ulcer R&D, providing over half of the total. However, in general there were few funders and no large funders.

Table 9. Buruli ulcer R&D funders in 2007

FUNDER	AMOUNT (US\$)	%
European Commission	726,354	30.1
US National Institutes of Health	656,291	27.2
Institut Pasteur	645,769	26.8
Australian National Health and Medical Research Council	220,584	9.1
Unspecified funders and industry	163,952	6.8
Disease Total	2,412,950	100.0

TRACHOMA



0.1%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$1.7 MILLION

TOTAL SPEND FOR TRACHOMA
RESEARCH AND DEVELOPMENT

Trachoma is an eye infection spread by contact with an infected person and by eye-seeking flies. If untreated, it leads to blindness.

Trachoma was responsible for 1.3 million DALYs, making it the 10th highest cause of morbidity from neglected diseases. However, although debilitating, mortality was zero as trachoma is not a fatal disease.

New products needed for trachoma include:

- ▶ Vaccines
- ▶ Diagnostics

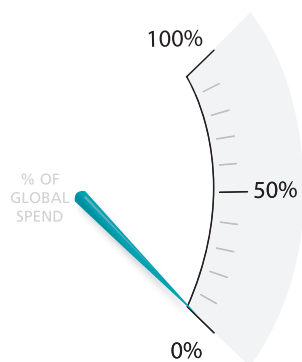
A total of \$1.7 million was invested in trachoma R&D in 2007. However, much of this funding (41.2%) was recorded as 'unspecified', therefore we are unable to comment on its distribution between product categories. Trachoma diagnostics received at least \$0.9 million of this funding.

Most funding for trachoma was provided by a philanthropic group, although, as with Buruli ulcer, there was also some industry funding.

Table 10. Trachoma R&D funders in 2007

FUNDER	AMOUNT (US\$)	%
Wellcome Trust	1,461,110	87.0
Johns Hopkins University	29,198	1.7
Unspecified funders and industry	189,403	11.3
Disease Total	1,679,711	100.0

RHEUMATIC FEVER



0.1%

OF GLOBAL FUNDING RECEIVED FOR
RESEARCH AND DEVELOPMENT

\$1.7 MILLION

TOTAL SPEND FOR RHEUMATIC
FEVER RESEARCH AND
DEVELOPMENT

Rheumatic fever is a bacterial infection that most commonly affects children 5-14 years of age. It usually follows an untreated bacterial throat infection and can lead to rheumatic heart disease, in which the heart valves are permanently damaged. It may progress to heart failure and stroke.

Rheumatic fever was responsible for 5.1 million DALYs and 280,000 deaths in 2004. It was the 7th highest cause of mortality and 8th highest cause of morbidity from neglected diseases.

Products needed for rheumatic fever are:

- Vaccines

R&D for rheumatic fever vaccines targeted at the developing world received \$1.7 million in 2007.

Table 11. Rheumatic fever R&D funders in 2007

FUNDER	AMOUNT (US\$)	%
US National Institutes of Health	1,284,919	76.9
Australian National Health and Medical Research Council	385,170	23.1
Disease Total	1,670,089	100.0

Table 12. Summary table of overall neglected disease and product funding (US\$ million)

	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Microbicides	Vaccines (Therapeutic)	Vector Control Products	Unspecified products	Total
HIV/AIDS	176.3	0.8	691.5	12.4	199.5		2.5		1,083.0
Malaria									
<i>P. falciparum</i>	39.0	34.3	52.0	0.6		0.3	-		126.2
<i>P. vivax</i>	2.0	0.1	1.8	0.2		-	0.3		4.4
Other and/or unspecified malaria strains	71.9	179.7	34.6	0.8		17.4	33.4		337.9
Malaria Total									468.4
TB	132.4	145.1	82.3	35.0		3.0	12.7		410.4
Kinetoplastids									
Chagas' Disease	5.9	1.0	1.3	0.9		-	0.4	0.6	10.1
Leishmaniasis	17.0	21.9	2.6	3.6		6.2	0.1		51.3
Sleeping Sickness	16.7	20.5	1.3	2.8		0.1	-		41.4
Multiple diseases	3.2	19.2	-	-		-	-		22.4
Kinetoplastids Total									125.1
Diarrhoeal diseases									
Rotavirus			22.8				-		22.8
Enterotoxigenic E.coli (ETEC)			11.9	0.2			0.2		12.3
Cholera	11.3	0.1	6.1	-			0.4		17.9
Shigella	1.7	-	9.4	-			3.4		14.5
Cryptosporidium	5.3	2.6	-	-			-		7.9
Enteropathogenic E.coli (EPEC)			-	-			-		-
Giardia				-			-		-
Multiple diseases	-	10.4	16.3	7.1			4.7		38.4
Diarrhoeal diseases Total									113.9
Dengue	29.6	7.5	36.0	1.6		-	0.8	6.5	82.0
Helminths									
Roundworm (Ascariasis)	1.4	-					-		1.4
Hookworm (Ancylostomiasis & Necatoriasis)	1.5	-	7.2				-		8.6
Whipworm (Trichuriasis)	0.1	-					-		0.1
Strongyloidiasis & other intestinal roundworms	0.4	-	-	0.1			-		0.5
Lymphatic Filariasis (Elephantiasis)	4.5	-				-	0.9		5.4
Onchocerciasis	0.2	0.7	-	-		-	1.0		1.8
Schistosomiasis (Bilharziasis)	13.7	0.9	8.0	0.04		0.3	0.6		23.5
Tapeworm (Cysticercosis/Taeniasis)	1.0	-				0.1	-		1.1
Multiple diseases	7.1	0.5	-	-		-	1.5		9.1
Helminths Total									51.6
Bacterial Pneumonia & Meningitis									
<i>Streptococcus pneumoniae</i>			16.8	1.6			2.1		20.5
<i>Neisseria meningitidis</i>			10.4	0.1			0.7		11.2
Both bacteria				0.8			-		0.8
Bacterial Pneumonia & Meningitis Total									32.5

	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Microbicides	Vaccines (Therapeutic)	Vector Control Products	Unspecified products	Total
Typhoid & Paratyphoid Fever	9.1	-	-	-	-	-	-	-	9.1
Leprosy	4.3	0.02	-	0.6	-	-	-	0.7	5.6
Buruli Ulcer	0.9	-	-	0.02	-	-	-	1.5	2.4
Trachoma	-	-	-	0.9	-	-	-	0.7	1.7
Rheumatic Fever	-	-	1.4	-	-	-	-	0.2	1.7
Core funding of a multi-disease R&D organisation	-	-	-	-	-	-	-	-	110.9
Unspecified disease	-	-	-	-	-	-	-	-	51.6
			Adjuvants and immunomodulators		Delivery technologies and devices		General diagnostic platforms		
Platform technologies	-	-	2.7	-	2.5	-	4.8	-	10.0
Total R&D funding	-	-	-	-	-	-	-	-	2,560.1

- No reported funding in this category
 Category not included in G-FINDER

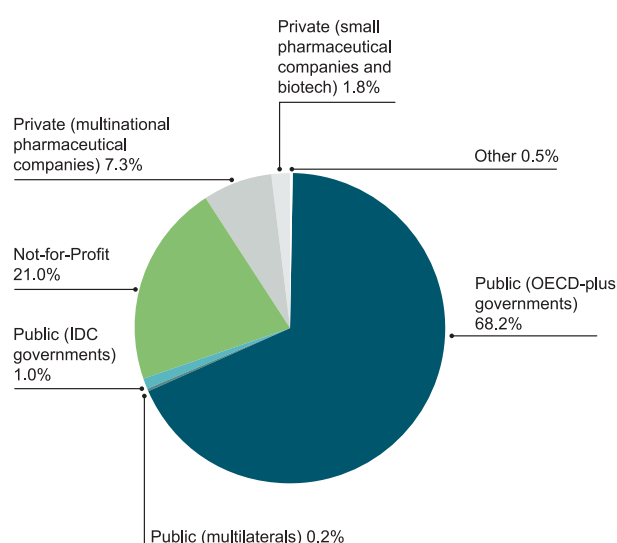
NEGLECTED DISEASE FUNDERS

Funders overall

Neglected disease funding remains primarily the realm of public and philanthropic donors, who collectively invested \$2.3 billion or 90.5% of the funding total in 2007 (Fig 10). Public donors, including government and multilateral groups, provided \$1.8 billion (69.4%) while philanthropic and not-for-profit funders invested \$538.3 million (21.0%). The two IDCs included in year one of the survey together represented 1.0% of global spend.

The private pharmaceutical industry provided 9.1% of the global total, with an aggregate investment of \$231.8 million. This contribution refers only to the industry's own investments, excluding funding provided by PDPs or others to industry programmes. This collectively made the pharmaceutical industry the third largest global investor in neglected disease R&D behind the NIH and the Bill & Melinda Gates Foundation. Small pharmaceutical companies and biotechs (SMEs) represented around 20% of reported industry investment (\$46.2 million), with multi-national firms contributing \$185.7 million (80%).

Figure 10. Total R&D funding by funder type in 2007



Public funders

The US Government represented nearly three quarters of global public spending with an investment of \$1.3 billion (70.4%) through its various institutes and agencies (see Table 13). European Governments and the European Commission collectively provided \$384.9 million (22.4%), with the UK, Netherlands, Ireland and Sweden dominating the field. The increasing role played by IDCs and non traditional funders was notable, with Brazil ranking as the 6th largest government funder and Russia as the 10th despite their significantly lower per capita GDPs^v.

Table 13. Top 12 government/public funders

RANK	COUNTRY	AMOUNT (US\$)	%
1	United States of America	1,250,935,091	70.4
2	European Commission	121,366,882	6.8
3	United Kingdom	100,781,214	5.7
4	Netherlands	34,088,694	1.9
5	Ireland	24,271,557	1.4
6	Brazil	21,970,169	1.2
7	Sweden	21,566,527	1.2
8	Canada	19,134,610	1.1
9	Australia	18,166,780	1.0
10	Russia	16,666,666	0.9
11	Belgium	15,851,130	0.9
12	France	13,892,238	0.8
Top 12 government/public funders subtotal		1,658,691,558	93.3
Total Public Funding		1,777,173,493	100.0

^v Per capita GDP of Brazil is \$6,938 and of Russia is \$9,075, while all remaining funders have per capita GDPs over \$42,000 ²²

PUBLIC FUNDING PATTERNS

Public funding by governments in the OECD-plus countries and multilaterals, showed a strong overall tendency to focus on only a few neglected diseases and to fund traditional products rather than new platforms.

Almost 80% of public funding was allocated to HIV/AIDS, TB and malaria. High-burden, high mortality diseases such as pneumonia/ meningitis, diarrhoeal illnesses and the helminth infections together received only 5.2% of global public funding, with kinetoplastid diseases receiving around half this amount.

In general, funding by these governments and multilaterals focused heavily on drugs, vaccines and diagnostics, with very limited funding for platform technologies such as adjuvants to improve vaccine efficacy, new delivery devices such as nasal vaccine technologies, or new diagnostic platforms such as patch tests to replace blood tests in resource-poor settings. Collectively, only \$3.6 million (0.2% of their total funding) was invested into new technology platforms for neglected diseases. We note, though, that as with other very neglected areas, a component of this reported underfunding may be due to funder inability to identify these specific investments.

Table 14. Public funding (OECD-plus governments and multilaterals) by disease

DISEASE OR R&D AREA	AMOUNT (US\$)	%
HIV/AIDS	950,883,566	54.4
Tuberculosis	220,574,931	12.6
Malaria	216,816,736	12.4
Dengue	58,179,305	3.3
Kinetoplastids	45,974,572	2.6
Diarrhoeal diseases	43,811,832	2.5
Helminths (Worms & Flukes)	37,365,084	2.1
Bacterial Pneumonia & Meningitis	10,045,739	0.6
Typhoid and Paratyphoid Fever	9,063,018	0.5
Leprosy	3,476,655	0.2
Buruli Ulcer	2,248,998	0.1
Rheumatic Fever	1,670,089	0.1
Trachoma	29,198	0.0
Platform technologies	3,589,301	0.2
<i>Delivery technologies and devices</i>	<i>2,520,889</i>	<i>0.1</i>
<i>General diagnostic platforms</i>	<i>1,045,152</i>	<i>0.1</i>
<i>Adjuvants and immunomodulators</i>	<i>23,260</i>	<i>0.0</i>
Core funding of a multi-disease R&D organisation	96,943,896	5.5
Unspecified disease	47,663,432	2.7
Total public funding (OECD-plus governments and multilaterals)	1,748,336,354	100.0

By contrast, the two IDC governments included in the survey (South Africa and Brazil) spent over a quarter of their funding (27.9%) on the kinetoplastids and helminth diseases, compared to 40.2% on HIV/AIDS, TB and malaria. They also invested more into new platform technologies for developing world diseases than all OECD-plus governments combined. Although there are a number of possible explanations for these funding patterns, this may reflect high domestic incidence of these diseases (e.g. visceral leishmaniasis in Brazil); crowding out due to funding activity in HIV/AIDS, TB and malaria by the OECD-plus governments; or its inverse (i.e. a need to self-fund product research that is relatively neglected by others).

Table 15. Public funding by IDCs (Brazil and South Africa) by disease

DISEASE OR R&D AREA	AMOUNT (US\$)	%
Kinetoplastids	4,906,145	18.3
HIV/AIDS	4,181,862	15.6
Tuberculosis	3,643,016	13.6
Malaria	2,938,682	11.0
Helminths (Worms & Flukes)	2,580,219	9.6
Dengue	1,623,000	6.1
Leprosy	1,455,070	5.4
Platform technologies	4,387,764	16.5
<i>General diagnostic platforms</i>	1,725,875	6.5
<i>Adjuvants and immunomodulators</i>	2,661,889	10.0
Core funding of a multi-disease R&D organisation	950,930	3.6
Unspecified disease	76,787	0.3
Total public funding by IDCs	26,743,475	100.0

If NIH funding was excluded, public funders overall provided 53.3% of their investments through PDPs (\$307.7 million), and 17.2% directly to product researchers and developers (\$99 million).

However, inclusion of NIH funding led to a reverse in this pattern with over 82% of overall public funding granted either directly to external research organisations (\$1.2 billion or 65.6%) or used for internal programmes (\$298.7 million or 16.8%), while only 17.4% (\$307.7 million) was disbursed via PDPs. This reflects the predominance of the NIH as a public funder, and therefore their influence on the overall funding picture.

Philanthropic funders

Philanthropic funding was highly concentrated, with two organisations – the Bill & Melinda Gates Foundation and the Wellcome Trust – providing 95.1% of the global total. Médecins Sans Frontières (MSF) was the only other philanthropic organisation to provide more than 0.5% of total funding. This meant that collectively the general public represented the fourth largest source of philanthropic funding for neglected disease R&D.

Table 16. Top philanthropic funders

FUNDER	AMOUNT (US\$)	%
Bill & Melinda Gates Foundation	452,102,715	84.0
Wellcome Trust	59,985,371	11.1
Médecins Sans Frontières	7,187,885	1.3
All other philanthropic organisations	16,970,326	3.2
Funds raised from the general public	2,064,283	0.4
Total philanthropic funding	538,310,580	100.0

PHILANTHROPIC FUNDING PATTERNS

Philanthropic funding showed a more diverse pattern than public sector funding, with around one-quarter (26.1%) of total philanthropic investment devoted to kinetoplastid diseases (12.6%) and high burden diseases such as pneumonia/meningitis, diarrhoeal illnesses and helminth infections (13.5% collectively). The relatively high funding for kinetoplastids may reflect the presence in this field of a PDP that is supported by a range of philanthropic donors.

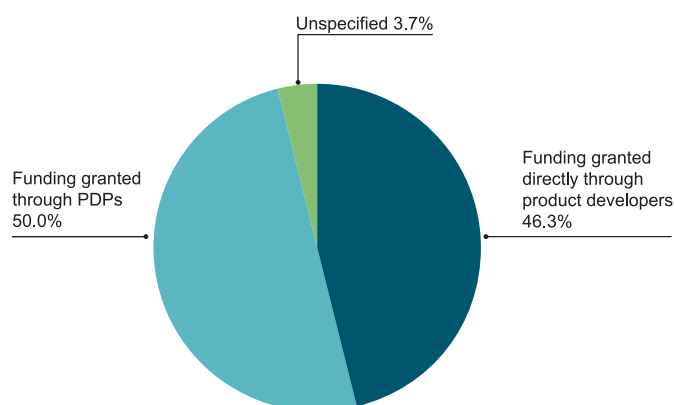
Less than 0.2% of funds were collectively allocated to leprosy and typhoid and paratyphoid fever, and there was no reported philanthropic funding for Buruli ulcer or rheumatic fever. Platform technologies also received limited philanthropic funding in 2007, at around 0.4% of their total investment.

Table 17. Philanthropic funding by disease

DISEASE OR R&D AREA	AMOUNT (US\$)	%
Malaria	155,550,721	28.9
Tuberculosis	118,664,226	22.0
HIV/AIDS	100,983,453	18.8
Kinetoplastids	67,927,698	12.6
Diarrhoeal diseases	55,568,392	10.3
Helminths (Worms & Flukes)	10,831,571	2.0
Bacterial Pneumonia & Meningitis	6,168,184	1.1
Dengue	2,113,145	0.4
Trachoma	1,461,110	0.3
Leprosy	658,000	0.1
Typhoid and Paratyphoid Fever	54,194	0.0
Platform technologies	2,020,125	0.4
General diagnostic platforms	2,020,125	0.4
Core funding of a multi-disease R&D organisation	13,026,847	2.4
Unspecified disease	3,282,916	0.6
Total philanthropic funding	538,310,580	100.0

Philanthropic funders also provided a high proportion (50%) of funds through PDPs rather than as direct grants to researchers and developers.

Figure 11. Philanthropic R&D funding patterns



Philanthropic funding was predominantly invested into applied R&D aimed at translating basic research into new products for neglected diseases (\$440 million dollars or 82% of their total investment), rather than basic research. However, this is likely to reflect the practices of the predominant funder, the Bill & Melinda Gates Foundation, rather than indicating philanthropic funding practices more generally.

Private sector funders

For confidentiality reasons, industry investments were aggregated. However, we note that, had this not been the case, some pharmaceutical companies would have appeared in the list of Top Twelve funders based on the size of their internal investments.^{vi} It is remarkable that investment by some private firms is now rivalling or exceeding spending by many public organisations, and indeed many Group of 7 (G7) and OECD countries.

As would be expected, private companies chiefly invested their own funds into internal neglected disease R&D programmes, or received grant funding for these programmes from external partners such as PDPs. However, it is worth noting that companies also provided around \$1.9 million in grants to neglected disease programmes being conducted by external groups.

FUNDING PATTERNS OF MULTINATIONAL PHARMACEUTICAL COMPANIES

The majority (74.6%) of private sector investment by MNCs went into HIV/AIDS, TB and malaria, with over \$130.7 million (70.4%) invested into TB and malaria alone.

Perhaps not unexpectedly, firms also made significant investments into dengue, pneumonia, meningitis and the diarrhoeal illnesses, where neglected disease activity can be piggybacked onto activity targeting commercial markets for these diseases. These more 'commercial' neglected diseases represented \$41.8 million (22.5%) of the total MNC investment.

Table 18. Multinational pharmaceutical company (MNC) funding by disease

DISEASE OR R&D AREA	INVESTMENT (US\$)	%
Malaria	80,171,520	43.2
Tuberculosis	50,559,935	27.2
Dengue	15,982,205	8.6
Bacterial Pneumonia & Meningitis	15,164,876	8.2
Diarrhoeal diseases	10,696,100	5.8
HIV/AIDS	7,835,409	4.2
Kinetoplastids	5,133,194	2.8
Trachoma	104,000	0.1
Helminths (Worms & Flukes)	61,200	0.0
Total funding by MNCs	185,708,440	100.0

Investment by MNCs in low-or-no commercial disease areas such as the kinetoplastid diseases was less than 3%, and less than 1% for trachoma and helminth infections. The latter may, however, be underreported as Wyeth (which did not participate in the G-FINDER survey) is collaborating with TDR in the development of moxidectin for onchocerciasis, for which phase II trials were in progress through 2007. There was no reported investment by multinational firms in leprosy, Buruli ulcer, rheumatic fever, or typhoid and paratyphoid fever.

Non-participation in G-FINDER of firms active in selected disease categories means that percentages across the board are too skewed to justify an analysis of industry funding patterns. However, given our knowledge of the R&D programmes of non-participating firms, we note that HIV/AIDS, TB and malaria would likely represent an even greater percentage of total private sector investment if full MNC survey participation had taken place.

^{vi} Internal investment refers to investments made by firms from their internal funds. It does not include funding from external sources such as PDPs, which is reported against the original funding source (generally public or philanthropic)

FUNDING PATTERNS OF SMALLER PHARMACEUTICAL AND BIOTECHNOLOGY FIRMS

Small pharmaceutical company participation in the survey was relatively low at just under 20% of companies who received the survey (29 out of 149 firms) (see Annexe 4 for survey respondent list) therefore reported funding in this sub-sector is likely to be an underestimate. Areas where small companies are known, or thought, to have unreported activity include pneumonia, meningitis and diagnostics, particularly HIV/AIDS, TB and malaria diagnostics.

As with other groups, small company investment was predominantly in the field of HIV/AIDS, TB and malaria, representing nearly \$37.8 million (81.9% of total investment). There was modest SME expenditure on more 'commercial' neglected diseases such as dengue and the diarrhoeal illnesses, but virtually nothing on the remaining neglected diseases, including helminths, kinetoplastids, Buruli ulcer, leprosy, rheumatic fever, or typhoid and paratyphoid fever.

Table 19. Smaller pharmaceutical company (SME) funding by disease

DISEASE OR R&D AREA	INVESTMENT US\$	%
Tuberculosis	15,394,780	33.3
HIV/AIDS	11,800,216	25.6
Malaria	10,622,063	23.0
Dengue	3,412,551	7.4
Diarrhoeal diseases	2,980,328	6.5
Helminths (Worms & Flukes)	753,763	1.6
Bacterial Pneumonia & Meningitis	582,161	1.3
Kinetoplastids	16,323	0.0
Buruli Ulcer	15,200	0.0
Unspecified disease	595,986	1.3
Total funding by SMEs	46,173,372	100.0

IN-KIND CONTRIBUTIONS

As noted above, in addition to their direct spend, companies conducting neglected disease R&D also incur a range of other costs, for instance infrastructure costs and costs of capital. These costs have not been included in G-FINDER due to the difficulty of quantifying or allocating them accurately to neglected disease programmes. Companies also provide in-kind contributions that are specifically targeted to neglected disease R&D but which cannot easily be captured in dollar terms, as seen in Table 20. We note that while some companies have nominated areas where they provide such contributions; others wished to remain anonymous. Although difficult to quantify, these inputs nevertheless represent a substantial value to their recipients and a significant cost to companies.

Table 20. Typical industry in-kind contributions to neglected disease R&D

IN-KIND CONTRIBUTION	EXAMPLES	SOME COMPANY DONORS
Transfer of technology & technical expertise to develop, manufacture, register and distribute neglected disease products	<ul style="list-style-type: none"> ▶ Identifying scientific obstacles ▶ Sharing best practices and developing systems for clinical, technical and regulatory support ▶ Developing capacity for pharmacovigilance ▶ Donating equipment 	<p>AstraZeneca Eli Lilly GSK Pfizer sanofi-aventis</p>
Provision of expertise	<ul style="list-style-type: none"> ▶ Supporting clinical trials ▶ Collaboration of scientists, sharing trial results and facilitating parallel, concurrent testing ▶ Providing expertise in toxicology/ADME and medicine ▶ Providing expertise in legal issues and business development ▶ Evaluating new compounds proposed by external partners ▶ Allowing senior staff to take sabbaticals working with Neglected Disease groups 	<p>AstraZeneca Eli Lilly GSK Novartis Pfizer sanofi-aventis</p>
Teaching and training	<ul style="list-style-type: none"> ▶ In-house attachments offered to Developing Country (DC) trainees in medicinal chemistry, clinical trial training etc ▶ Providing training courses for DC researchers at academic institutions globally ▶ Organising conferences and symposia on Neglected Disease-specific topics 	<p>GSK Novartis sanofi-aventis</p>
Intellectual Property	<ul style="list-style-type: none"> ▶ Access to proprietary research tools and databases ▶ Sharing compound libraries with WHO or with researchers, who can test and screen them for possible treatments ▶ Providing public and not-for-profit groups with information on proprietary compounds they are seeking to develop for a neglected disease indication ▶ Forgoing license or providing royalty-free license on co-developed products 	<p>Eli Lilly GSK Novartis Pfizer sanofi-aventis</p>
Regulatory assistance	<ul style="list-style-type: none"> ▶ Making right of reference to confidential dossiers and product registration files to facilitate approval of generic combination products ▶ Covering the cost of regulatory filings 	<p>Eli Lilly GSK</p>

Funding by organisation

Examination of funding from the perspective of individual organisations proved illuminating. This showed that global investment into creating new neglected disease products is heavily reliant on a mere handful of donors. Twelve organisations provided just over 81 % of global funding, with the US National Institutes of Health and the Bill & Melinda Gates Foundation collectively investing \$1.5 billion or 59.3% of the total (Table 21). In 2007, each of these 12 organisations invested over \$20 million into neglected disease R&D.

Table 21. Top 12 neglected disease funders by organisation

RANK	FUNDER	AMOUNT (US\$)	%
1	US National Institutes of Health	1,064,859,791	41.6
2	Bill & Melinda Gates Foundation	452,102,715	17.7
3	European Commission	121,366,882	4.7
4	US Department of Defense	86,914,578	3.4
5	United States Agency for International Development	80,600,336	3.1
6	Wellcome Trust	59,985,371	2.3
7	UK Medical Research Council	51,716,968	2.0
8	UK Department for International Development	47,565,987	1.9
9	Dutch Ministry of Foreign Affairs	33,951,646	1.3
10	Institut Pasteur	31,617,540	1.2
11	Irish Aid	24,271,557	0.9
12	Swedish International Development Agency	21,529,014	0.8
Subtotal top 12 funders		2,076,482,385	81.1
TOTAL R&D FUNDING		2,560,068,749	100.0

Funding flows

Organisations who fund neglected diseases are highly diverse. Some are pure funders, that is they conduct no research themselves but instead provide grants to others who conduct R&D: the Bill & Melinda Gates Foundation is a typical 'pure funder'. Other organisations have a self-funded model, using their own general budget to support and progress internal research programmes: large pharmaceutical firms typify the 'self-funder' model. Yet other groups, such as the NIH, operate on a mixed model, providing funding to external groups but also using a proportion of funds on their own internal research programmes.

Overall, there was an approximately 80/20 split between external and internal allocation of global funding. That is, around 20% of global funding for neglected disease R&D was spent internally by groups such as NIH or drug companies on their own programmes, while around 80% was allocated by funders to external organisations working on neglected disease R&D.

Figure 12. Overall R&D funding patterns

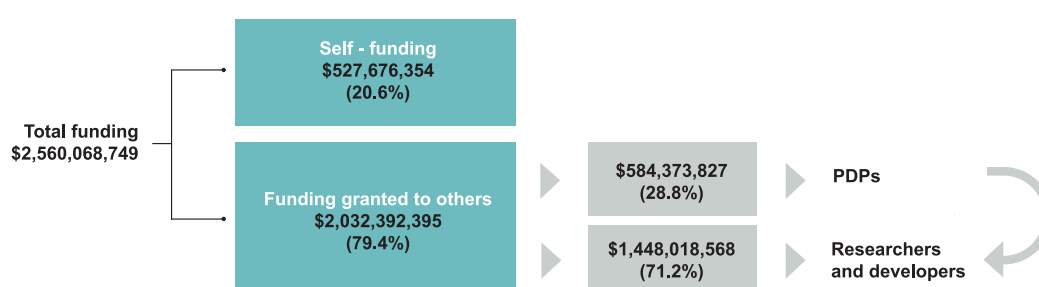


Table 22 sets out the 10 organisations reporting the highest level of internal funds dedicated to neglected disease R&D. Although most of these are, as expected, government agencies and private firms, a number of public institutes such as the Institut Pasteur invested substantial amounts into their own neglected disease programmes using funds raised predominantly from private donations, government support, and income from their intellectual property and investments.

Table 22. Self-funders: The Top 10 groups

RANK	ORGANISATION	AMOUNT (US\$)	%
1	Aggregate Pharmaceutical and Biotechnology Company Respondents	228,957,902	8.9
2	US National Institutes of Health *	133,097,100	5.2
3	US Department of Defense *^	70,340,000	2.7
4	UK Medical Research Council *	35,989,099	1.4
5	Institut Pasteur *	31,617,540	1.2
6	French National Agency for AIDS Research	10,278,588	0.4
7	US Centers for Disease Control	5,703,200	0.2
8	UK Health Protection Agency	3,903,521	0.2
9	Statens Serum Institute	3,672,882	0.1
10	Inserm - Institute of Infectious Diseases	1,774,770	0.1
Subtotal self-funded R&D		525,334,601	20.5
Total R&D funding		2,560,068,749	100.0

* These groups are also Top 10 overall funders (including self-funding plus external funding)

^ The Department of Defense figure is likely under-estimated as it includes civilian and contract salaries but excludes salaries of military researchers within Army and Navy laboratories

INTERMEDIARY ORGANISATIONS AND PRODUCT DEVELOPMENT PARTNERSHIPS

Intermediary groups such as TDR and PDPs^{vii} operate by raising funds directly and in-kind from the public, private and philanthropic sectors. They conduct product development directly or virtually, in conjunction with public research institutes, academic organisations, contract research organisations and industry partners, to whom they disburse the funds they have raised. (The amount passed on varies as some PDPs also conduct in-house research, using a proportion of donor funds to support this.) PDPs play a central role in developing and managing a product portfolio in a given disease area, allocating donor funding between projects, and reviewing and auditing the progress of projects individually and against others in the portfolio and externally. PDPs also play a role in leveraging industry funding and activity (both internal and in-kind). That is, the presence of a PDP partner makes it possible for a private company to invest internal funds on a neglected disease programme in a cost-effective way

The top 10 intermediaries and PDPs in terms of funding received in 2007 are shown below. This funding was almost equally derived from public (\$307.7 million or 52.7%) and philanthropic sources (\$269.2 million or 46.1%).

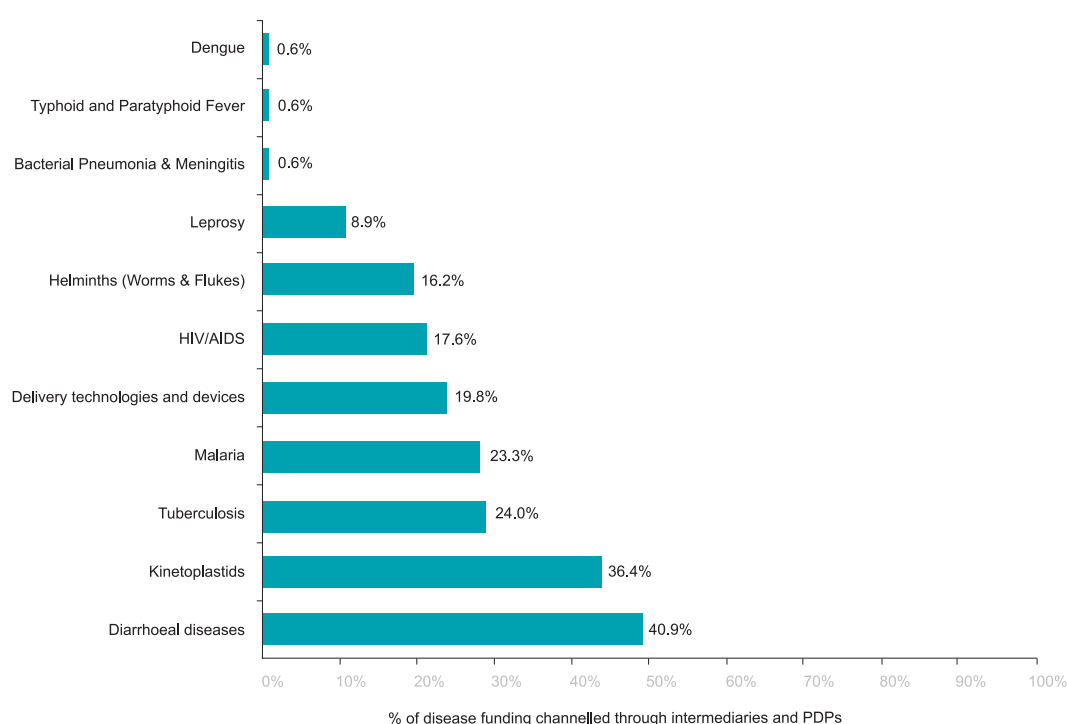
^{vii} This report defines PDPs as public health driven, not-for-profit organisations that drive product development in conjunction with external partners

Table 23. Funds received by intermediaries and PDPs in 2007

INTERMEDIARY ORGANISATIONS AND PDPs	AMOUNT US\$
International AIDS Vaccine Initiative	81,297,482
Medicines for Malaria Venture	75,982,931
European and Developing Countries Clinical Trials Partnership	50,803,467
International Partnership for Microbicides	46,311,916
Aeras Global TB Vaccine Foundation	40,121,983
Global Alliance for TB Drug Development	39,587,358
PATH	38,024,679
Special Programme for Research and Training in Tropical Diseases (TDR)	32,675,307
Drugs for Neglected Diseases initiative	28,520,251
Institute for One World Health	27,377,321
Other intermediaries and PDPs	123,671,134
TOTAL funding to intermediaries and PDPs	584,373,827

G-FINDER shows that in 2007, nearly 30% of external funding (\$584.4 million) was given via intermediaries and PDPs rather than being granted directly to researchers and developers. As a result, intermediaries and PDPs managed nearly one-quarter of global neglected disease product investment in 2007 (22.8%).

The predominance of intermediaries and PDPs varied greatly between diseases, with 40.9% of global funding for R&D in diarrhoeal diseases going to intermediaries (chiefly PDPs), but only 8.9% of global leprosy funding (see Figure 13) going to intermediaries. This variability may reflect a range of factors. These may include an R&D focus on basic research for diseases such as HIV/AIDS (most intermediary organisations and PDPs focus on applied research). Funders may also preferentially fund through PDPs in disease areas that have PDPs with a proven track record, established product portfolio and active advocacy programmes. Where such PDPs do not exist, funders will need to (or may choose to) allocate funding directly. There is no active intermediary/ PDP, in Buruli ulcer, trachoma and rheumatic fever.

Figure 13. Percentage of disease R&D funding given via intermediaries and PDPs*

* No intermediary or PDP organisation exists for Buruli ulcer, Trachoma or Rheumatic fever

DISCUSSION

Allocation of R&D funding

Intuitively, there is a sense that most neglected disease R&D funding should go to diseases that cause the most widespread suffering in the developing world, as traditionally measured by DALYs. Or, to put it differently, the highest 'health return on investment' would result from investing in the highest burden diseases. For instance, pneumonia and the diarrhoeal illnesses collectively accounted for 165 million DALYs in low and middle income countries in 2004 – around one-third higher than HIV/AIDS, TB and malaria, which collectively accounted for 125 million DALYs in these countries in the same year. Based on a simple DALY-investment equation, R&D funders would therefore preferentially invest in pneumonia and the diarrhoeal illnesses.

In practice, the reality is more complex, since the likely health return on a neglected disease R&D investment (the RoI) will depend on the potential health impact against the cost of the investment, discounted for risk.

Figure 14. Health return on investment

$$\frac{\text{POTENTIAL HEALTH IMPACT}}{\text{COST}} \times \text{RISK} = \text{HEALTH RETURN ON INVESTMENT}$$

(Severity of need X Severity of underfund)

The potential health impact of an investment in turn depends on the severity of R&D need (of which DALYs and severity of product shortfall are the two main components) and the severity of underfunding in a given area. The cost and risk of that investment will depend on the state of science and type of R&D, but are largely unrelated to the disease or to the number of people affected. Thus, development of a new FDC will cost roughly the same and incur roughly the same risk, irrespective of whether it is for a high-burden disease such as HIV/AIDS or a lower-burden disease like leprosy. These are discussed in more detail below.

SEVERITY OF NEED

Severity of need depends on a range of factors:

- ▶ Burden of disease (commonly measured by DALYs)
 - Morbidity
 - Mortality
- ▶ Disease trend (commonly measured by DALYs)
 - Emerging
 - Established but increasing
 - On course for eradication
- ▶ Severity of product shortfall
 - No products
 - Poor products (low efficacy, low safety, unsuitable or too expensive)
 - Good product/s but back-ups needed e.g. due to risk of resistance

DALYs play a crucial role in determining severity of need, and therefore potential health impact. For all their flaws, DALYs nevertheless provide a roughly comparable measure of burden of morbidity and mortality across diseases. Thus they help track the impact of eradication measures for diseases such as polio and leprosy; the emergence of new diseases; and the increasing burden of many high mortality/ high morbidity diseases, including HIV/AIDS, TB and malaria.

Importantly, DALYs are a *multiplier* of the likely health impact of a new product in a given area. Thus a new product for a disease with low DALYs will have a lesser impact than a new product for a disease with a very high DALY burden. However, DALYs cannot indicate how much investment is needed to create that new product, since this relates to the science and type of R&D, not to the disease or number of patients, as discussed below.

A second key component in determining severity of need is the state of existing products. A new vaccine where none existed before will have a very significant impact, particularly for a disease with a high DALY multiplier – for example, pneumonia or HIV. Improving an existing treatment – for instance, through shorter treatment courses or higher efficacy – will reduce DALY burden to a lesser extent, although it may greatly improve the suitability of treatments for patients, or may benefit health systems by reducing resource usage.

SEVERITY OF UNDERFUNDING

The second determinant of potential health impact relates to the level of funding. Severity of underfunding can be estimated by using G-FINDER data to review the level of global funding in the R&D area under consideration, in particular to identify if funding is clearly *below* what would be needed to deliver a successful product. Table 12 is helpful in this respect. Increased funder investment in an under-funded area will greatly increase the likelihood that a new product will be developed, and thus will increase the potential health impact.

Whether funding in a given area is *enough* is a harder question to answer. In established disease and product categories, for instance malaria drugs or bacterial vaccines, published cost estimates and portfolio information are a helpful guide to the likely investment needed; particularly when set against the G-FINDER information. However, in new research areas and where basic science is lacking, there is no easy answer to this question. (See the discussion on cost and risk below).

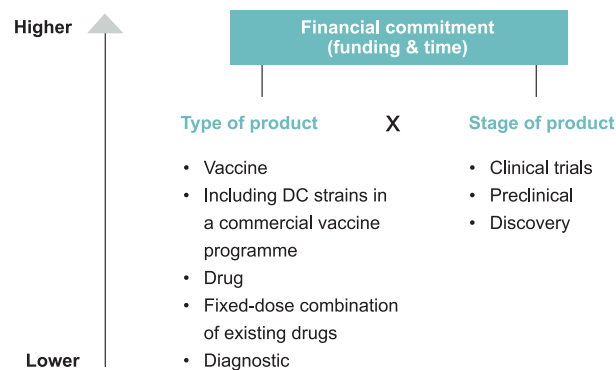
COST

The RoI decision also requires an assessment of the likely cost of R&D in a given disease and product area. How much funding will be needed, and over what time? The answer to this question is chiefly driven by the type of R&D needed, since costs vary dramatically depending on the kind of product being developed and how far down the development pathway it is. In general, diagnostics are far cheaper to develop than drugs; with development costs in the low tens of million; and drugs are far cheaper to develop than vaccines. As an example, we note that total discovery and development costs for a novel TB drug have been estimated at \$115 million to \$240 million, including cost of failure²⁴; but that vaccine development from research and discovery through to product registration is estimated at \$200 million to \$500 million, including cost of failure²⁶. (Cost of failure is the cost of the failed projects along the development path that eventually leads to a successful product.) Similarly, out-of-pocket costs for clinical development of an anti-malarial drug are \$30 million; while typical out-of-pocket costs for clinical development of a malaria vaccine are just over \$100 million²³. As reference, we note that Tufts University estimated the cost of developing a drug for Western markets at \$403 million (in 2000 US\$), including cost of failure.²⁵

The cost of developing a neglected disease product is also generally significantly lower if that product is based on existing products (e.g. a FDC of existing anti-malarial drugs), or if the neglected disease programme can be 'piggybacked' onto a commercial development programme (e.g. inclusion of developing country strains into a commercial pneumonia or meningitis vaccine). For all products, clinical development is more expensive than pre-clinical or discovery research by at least a factor of ten, and sometimes closer to one hundred. Taken in combination, this means that clinical vaccine development is markedly more expensive than preclinical drug discovery.

Combining G-FINDER information with the funder's assessment of severity of need, allows an assessment of the potential health RoI under consideration. Investment into an area with high severity of need which has a large funding gap, will offer a potentially very high health return on a given investment.

Figure 15. Factors influencing R&D cost



RISK DISCOUNT

The potential health return must now be discounted for risk. In the case of pharmaceutical R&D, risk is mostly associated with:

- ▶ The state of science and technology in a given area
- ▶ The type of product
- ▶ The point in the product cycle where the investment will be made

The lowest scientific risk exists for diseases and products where the science and technology are well understood, for instance meningitis vaccine research. The highest scientific risk will attach to areas where basic science and technology challenges are still being worked out, and where there is no proof of concept in humans, for instance research into HIV immunity or Buruli ulcer transmission. When the science and technology are lacking, it is simply impossible to know if a given level of funding will deliver success or not. It may be that \$100,000 given to the right researcher will solve a key scientific challenge in a very short time; or that the funder will spend one billion dollars over 10 years without seeing a solution.

Some types of products are also inherently less 'risky' than others, for instance, diagnostics present less challenging regulatory and community hurdles for product developers than vaccines (which will be given to many thousands of healthy babies).

Pharmaceutical R&D also has intrinsically high levels of risk, with failure rates (attrition rates) being highest in the early discovery stages, reducing as the product moves along the development pathway to late-stage clinical trials, where failure rates are lowest. Risk is particularly low if R&D is based on products that already exist, for example, addition of new strains to existing vaccines, combination of existing drugs into new fixed-dose combinations, or development of new formulations of existing products; even in these cases, however, failures can still occur. If the global portfolio in a given product area is relatively large and relatively advanced, overall risk will be lower, especially if funders use a portfolio investment approach rather than providing grants to single projects. If there are few or no products in development, investment risk may be higher.

THE SUBJECTIVITY FACTOR

Funder beliefs and preferences also play a role in making investment decisions. For instance, some funders may prefer to focus on diseases where no safe effective treatments exist (e.g. late-stage Chagas disease) even though these diseases do not have the highest morbidity and mortality. Others may prioritise diseases with a higher relative or absolute mortality, such as dengue or meningitis, over diseases with lower relative mortality but a higher DALY burden such as the helminth infections. Yet others may give greatest weight to disease trends, focussing their efforts on eradicable diseases

(where a DALY averted has a premium); or, by contrast, believing that the best path is to invest preemptively in emerging disease areas, or in developing back-up therapies against future development of resistance, for instance by supporting development of new anti-helminthic drugs.

As with their assessment of health impact, funders will also have different approaches to cost and risk. Funders with a high tolerance for scientific risk but limited budgets may choose to invest in areas where science is lacking, believing their best contribution will be funding the science base needed to unlock the path to new products, as occurred with the first polio vaccines. Such funders might, for example, focus on funding basic immunological research for HIV/AIDS or TB, or diagnostic discovery for little understood diseases like Buruli ulcer. Conversely, funders with a low appetite for risk but larger budgets may prefer to invest in clinical development of pneumonia and meningitis vaccines, where costs will be higher but where the science and technology are well established. Yet other funders may find that investing relatively modest sums to develop low-risk new fixed-dose drug combinations for malaria or HIV/AIDS will best suit their situation.

EXAMPLE: RHEUMATIC FEVER

High severity of need

Rheumatic fever ranks as the 7th highest cause of mortality and 8th highest cause of morbidity from neglected disease in the developing world. Disease levels remain steady. Treatment of cardiac complications of rheumatic fever requires tertiary care facilities, which are unavailable to poor and rural populations in much of the developing world, therefore a preventive vaccine is vital in these settings. However, there is currently no such vaccine.

High level of underfunding

G-FINDER shows that global investment in R&D of a rheumatic fever vaccine was only \$1.4 million in 2007, however the 'out-of-pocket' cost of developing an anti-bacterial vaccine is known to be in the hundreds of millions of dollars. Thus, the level of underfunding is very high.

Modest short-term cost

The cost of investing in this area is likely to be low since, although this is vaccine research, projects are in preclinical development or earlier. Modest investments over a few years would therefore be expected to have a significant impact on advancing the field.

Moderate scientific risk

This very high potential return now needs to be discounted for risk. In the case of rheumatic fever, the disease and its transmission are well understood, as are the science and technology of anti-bacterial vaccine development and production. However, there is no global portfolio, the research community is relatively small and individual projects are in the earlier stages of development.

Based on the high need and large funding gap, investment into rheumatic fever vaccine would therefore offer a very high potential health return. This, compounded with a moderate cost and risk should make any investment into this product attractive. Funders will also factor their own values and preferences into this assessment. Some may prefer to focus on a higher-profile disease than rheumatic fever; or on an area where risk is mitigated by the presence of a PDP with a large project portfolio. Others may preferentially fund rheumatic fever in view of its high impact on children or because, as a small funder, they want to work in an under-funded area where their dollars have a higher potential impact.

Funding gaps and drivers

DISEASES

Three diseases – HIV/AIDS, TB and malaria – received close to 80% of overall R&D funding. The remaining neglected diseases and disease categories surveyed each received less than 5% of global funding. For example, the three kinetoplastid diseases collectively received 4.9% of total global funding; the seven diarrhoeal illnesses collectively received 4.4% of global funding; the eight helminth infections collectively received 2.0%; and the two types of bacterial pneumonia and meningitis collectively received 1.3%. Five diseases – leprosy, Buruli ulcer, trachoma, rheumatic fever, and typhoid and paratyphoid fever – each received less than \$10 million or 0.4% of total global investment. In many disease areas, funding was well below what is feasibly needed to create even one new product.

As discussed above, many factors influence R&D funding decisions, including burden of disease, state of science and technology, presence of existing therapies, size and degree of advancement of the global research portfolio, and type of products needed. Nevertheless, the predominance of funding for HIV/AIDS, TB and malaria suggests funders may also be influenced by other factors.

These may include the presence of civil society groups or PDPs with active advocacy and fundraising activities; the existence of trusted research and development groups; funder perceptions and preferences; or the presence of policy frameworks and funding mechanisms that prioritise specific diseases. Private company funding patterns also suggest that firms are responding not only to commercial signals, but possibly also to public policy settings that prioritise certain diseases, or to the presence in selected disease areas of development partners and PDPs they can work with.

PRODUCTS

With the exception of the IDCs, there was a very marked tendency among public and philanthropic funders to focus on drug and vaccine R&D. Diagnostics were largely neglected, and platform technologies even more so. Global investment into vaccine adjuvants, diagnostic platforms and new delivery devices was less than 0.4% of total funding; well below the levels needed for success. We note, though, that as with other very neglected areas, a component of this reported underfunding may be due to funder inability to identify these investments.

Low funding for diagnostics and platform technologies is of particular concern as these can deliver a high health impact for a relatively modest investment of resources. Diagnostics can rationalise treatment use, circumvent progression to resistant or untreatable presentations of diseases such as leprosy and Chagas disease, and improve burden of disease estimates. Advances in platform technologies offer an even higher impact, since they are by their nature applicable across many neglected diseases.

FUNDERS

A striking feature of the G-FINDER results was the recognition that two organisations were responsible for nearly two-thirds of global R&D funding for neglected diseases in 2007; and that over 80% of the global total came from only 12 organisations. This high concentration of funding means that the preferences of only a few organisations play a very substantial role in determining global disease focus and funding patterns for neglected disease R&D. For instance, the NIH predominantly funds through direct grants rather than via intermediary organisations and PDPs; while the Bill & Melinda Gates Foundation predominantly funds applied rather than basic research. The heavy reliance on so few funding sources is also of concern at a time when economic uncertainty, tight public budgets and falling returns on endowments may greatly reduce the interest and capacity of individual organisations to continue investing in neglected disease R&D at the same levels.

Conclusion

The participation of so many organisations and countries in the development of new neglected disease products is a remarkable and welcome change from past decades of inertia and neglect²⁷. It is clear, however, that these efforts were not evenly distributed, with some of the world's wealthiest countries missing in action from the top 10, top 20 or even top 50 funders. It is also remarkable that investment by some philanthropic organisations and private firms is now rivalling or exceeding spending by many public organisations, and indeed many G7 and OECD countries. While commending these companies and philanthropists, we note that their efforts are meant to support, not replace, those of wealthy governments around the world.

The predominance of research into new products for HIV/AIDS, malaria and TB is understandable – and the generosity of funding is both necessary and a credit to funders – however all neglected diseases, including these three, should receive the attention and funding needed to achieve discovery, development and registration of new products.

A broadening of funding efforts so that all who are able to contribute do so, and that all diseases receive the attention they deserve, would lead to a dramatic positive impact on the health of developing country patients afflicted with these diseases.

We hope the information presented in the G-FINDER report will assist funders, even those with modest budgets, to see where they can make a substantial and valuable impact by supporting development of new tools for neglected diseases that affect millions. In tough economic times, it will be more important than ever for all funders – large and small; public, philanthropic and private; Western and developing countries – to contribute what they can to ensure that the poorest of the poor do not end up paying the highest price.

ANNEXE 1

ADDITIONAL METHODOLOGICAL CONSIDERATIONS

IDENTIFICATION OF SURVEY RECIPIENTS

Survey recipients were identified through a number of avenues:

- ▶ Health Policy Division contacts database. The HPD has been working in the neglected disease field since 2004, during which time it has developed a large internal database of neglected disease funders, intermediaries, and product developers
- ▶ Previous neglected disease surveys in HIV/AIDS, TB, and malaria. We liaised closely with these survey groups to exchange information on known organisations in the field
- ▶ The 43 participating countries were ranked according to their Gross Expenditure on R&D (GERD) as a percentage of their gross domestic product (GDP), as reported by the OECD²⁸. R&D funding organisations within countries with high R&D expenditure were added to our recipient list.

The above was supplemented with an active search for known or suspected funders, Product Development Partnerships (PDPs), developers and researchers for all other 27 neglected diseases, so as to ensure our recipient list did not overlook non-malaria, non-TB or non-HIV/AIDS stakeholders. This included input by members of our Advisory Committee, who were asked to review and complete our recipient list for their respective areas of expertise.

Collation of this information resulted in a list of 551 organisations in the 43 target countries, who had previously recorded involvement in neglected disease product development. Of these, 134 were funders (the target group for the survey).

RESTRICTIONS ON SPECIFIC DISEASE-PRODUCT AREAS: METHODOLOGY AND EXAMPLES

In R&D areas where commercial overlap was significant, only investment specifically targeted at developing country needs was eligible for inclusion in G-FINDER. The definition of what constituted a 'developing-country-specific' investment for each restricted disease and product category was reached through an intensive consultation process with the Advisory Committee. In some cases, views of additional disease experts were sought before consensus could be reached. This resulted in a tailored set of criteria for each restricted disease-product category, reflecting differences in disease and product profiles, research approaches, and products already available (see example below).

Example - Disease-product restrictions for bacterial pneumonia and meningitis vaccines

The Advisory Committee consensus was that vaccines for only some strains of bacterial pneumonia and meningitis (*Streptococcus pneumoniae* and *Neisseria meningitidis*) should be eligible for inclusion in G-FINDER. The Committee then defined 'developing-country-specific' products, for which investments could be included, as those that met the following criteria. For *S. pneumoniae*, the vaccine should be, at a minimum, designed for use in infants less than two years of age and provide coverage against *S. pneumoniae* serotypes 1, 5, and 14. For *N. meningitidis*, the vaccine should provide coverage against *N. meningitidis* serotype A, be a conjugate rather than a polysaccharide vaccine, be designed for use in infants less than two years of age, and be designed to cost less than a dollar per dose. For multi-valent pneumonia vaccines covering Western and developing country strains, only developing-country-specific costs were eligible, defined as trials, registration, and Phase IV/pharmacovigilance studies carried out in the target developing countries for the vaccine. (See Table 1 in main report: G-FINDER disease, products and technologies for full inclusions for G-FINDER)

HANDLING OF FINANCIAL DATA

The process for handling and aggregating grant data was developed with the help of other survey groups, who kindly shared their experience with us at a start-up workshop, input from the Stakeholders Network, and support from the financial consultant who had taken part in designing the Malaria R&D survey. All provided input on issues to be managed in the design process, such as national and organisational variations in record-keeping and classification systems, multi-year disbursements, allocation of platform research and core funding between different diseases, overheads, double-counting of donor funding by intermediary or recipient bodies, and variations in financial years and currencies.

The following key financial data collection principles were used:

- ▶ Survey recipients were asked to enter grant-by-grant expenditures incurred during their financial year (as opposed to the 2007 calendar year) that had the largest overlap with 2007
- ▶ All survey recipients entered data in their local currency. At the end of the survey period, foreign currencies were then converted to US dollars based on the 2007 average annual exchange rate as reported by the International Monetary Fund²⁹

SURVEY TOOL AND PROCESS

In order to be as consistent and comprehensive as possible across the range of neglected diseases surveyed, we followed two core principles:

1. Only primary data reported by the funders, PDPs, and product developers themselves were included in the survey. If these data were not available, they were not supplemented with secondary data or estimates
2. All primary grant data were collected using the same online/offline reporting tool and inclusion/exclusion framework for all survey recipients

The only exception to the second principle above was the NIH, where a proportion of grants could not be collected in this way due to NIH data management system changes (see below on how exceptions were handled). Because of this, only the Office of AIDS Research and the intramural arm of the National Institute of Allergy and Infectious Diseases were able to provide primary grant data. Taken together, these represented 68% of NIH 2007 expenditures on neglected disease R&D accounted for in the survey. On the advice of the NIH, the remaining 32% were obtained and filtered from official public databases.

Survey tool

Survey participants were asked to enter every neglected disease grant they had disbursed or received in 2007 into a password-protected online database, including the grant amount, grant identification number, a brief description of the grant, and the name of the funder or recipient of the grant. They were also asked to confirm their organisation details such as role in funding (e.g. funder, fund manager, product developer), financial year, currency used, type of organisation (e.g. private sector firm, academic institution, PDP, multilateral organisation), and country where they were located. Each grant was entered using a three-step process where the survey recipient had to choose (1) a specific disease or sub-disease; (2) a product type (e.g. drugs, vaccines, microbicides); and (3) a research type within the product (e.g. discovery and preclinical, clinical development); according to pre-determined categories as described below (see Annexe 6 for screenshots). Where survey recipients could not provide data to this level of detail, they were asked to provide the finest level of granularity they could. If survey recipients were not able to allocate the grant to a single disease in step 1, three options were available:

- ▶ 'Core funding of a multi-disease organisation' (e.g. funding to an organisation working in multiple diseases, where the expenditure per disease was not known to the funder)
- ▶ 'Platform technologies', further allocated as investment into diagnostic platforms; adjuvants, and immunomodulators; or delivery device platforms
- ▶ 'Unspecified R&D' for any grants that still could not be allocated

Data sharing with other surveys

Primary grant data for selected diseases were also shared with and between other survey groups (Families USA, Treatment Action Group, and the HIV Vaccines and Microbicides Resource Tracking Working Group) to avoid re-surveying funders when possible. Any primary grant data received by other groups were reviewed and reclassified according to G-FINDER guidelines prior to entry into the database.

DATA CLEANING

Survey closure was followed by a three-month period of intensive cleaning, cross-checking, and organising of the complex dataset collected.

All grants over \$0.5 million (i.e., any grant over 0.02% of total funding), except for the portion of NIH grants obtained through their databases, were then verified through a three-step process:

1. Each grant was reviewed against our inclusion criteria. Over 3,000 grants were manually checked for correct allocation
2. Automated reconciliation reports were used to cross-check 'disbursed' funding reported by funders against 'received' funding reported by the recipients
3. Uncovered discrepancies were solved through direct contact with the funder and recipient to identify the correct figure

Industry figures were reviewed against industry portfolio information held by the George Institute and against Full-Time Equivalent (FTE) and direct costs provided by other companies. Costs that fell outside the expected range, for example, above average FTE costs for clinical staff, were queried and corrected with the company.

LIMITATIONS TO INTERPRETATION

Potential limitations with any survey, including G-FINDER, are:

Survey non-completion

While data from public maximum priority funders is close to 100% complete, private sector investments are under-reported due to the absence of full data from several maximum priority multinational companies. For instance, at least one of the non-participating companies has a late-stage pneumonia vaccine programme for commercial markets, but this may have included some investment in developing country studies that will have been missed. One of the non-participating firms also had a late-stage HIV/AIDS vaccine in development, which will have led to significant underreporting of HIV/AIDS vaccine investments.

In two specific areas, lack of small company data is likely to have an impact:

- ▶ Diagnostics, particularly for HIV/AIDS and TB and malaria. A total of 150 small firms were identified as having neglected disease R&D activity, many of them working in the HIV/AIDS and TB diagnostics field; however only 28 of these provided data for the survey
- ▶ The omission of developing country firms in the first year of the survey means likely under-reporting in diseases where these firms are active and where they self-fund this activity. Where this work is funded by PDPs, TDR or OECD-plus funders it will have been captured

Response rate

Differing levels of responsiveness between organisations and countries may also skew the findings. For instance, the Australian location of the G-FINDER group may have encouraged higher levels of responsiveness from Australian funders, while funders in non-English speaking settings may have been less enthusiastic in their levels of response. This is not known to have occurred.

Missing data

Finally, G-FINDER can only report the data that was given to us. Although strenuous efforts were made to check the classification, accuracy and completeness of grants, in a survey this size it is likely some data will still have been incorrectly entered or that funders may have accidentally omitted some grants. The requirement to use public official databases for some NIH data, as opposed to raw grant

data, also means these figures may contain inaccuracies or omissions that we were unable to detect. We believe, however, that the checks and balances built into the G-FINDER process mean that such mistakes, if present, will have a minor overall impact.

VARIATION BETWEEN SURVEYS

Annual surveys of global R&D investment into some neglected diseases such as HIV/AIDS and TB in 2007 have also been published. Although G-FINDER worked in close collaboration with these groups, both to ease survey fatigue on the part of funders and to clarify any major variance in our findings, each survey nevertheless has slightly different figures. This is chiefly due to differences in scope, in particular inclusion in other surveys of funding for advocacy, capacity-building and operational studies – all excluded from G-FINDER. Methodological differences have also led to variations, for instance, differing methodologies of collecting private sector data; and differing classifications of some R&D activities. As mentioned in the main report, classification of some funding as ‘unspecified’ by G-FINDER (e.g. multi-disease programmes) may lead in some cases to different figures than disease-specific surveys. Finally, some funders responded to one survey but not to others, leading to different datasets.

These variations are expected to diminish over the coming years as collaboration and data-sharing between surveys improve even further.

ANNEXE 2

ADVISORY COMMITTEE MEMBERS & ADDITIONAL EXPERTS

ADVISORY COMMITTEE MEMBER	ORGANISATION	TITLE
Ripley Ballou	Bill & Melinda Gates Foundation	Deputy Director for Vaccines, Infectious Diseases Development, Global Health Program
Lewellys F. Barker	Aeras Global TB Vaccine Foundation	Senior Medical Advisor, Regulatory Affairs & Quality Assurance
Ted Bianco	Wellcome Trust	Director of Technology Transfer
Simon Croft	London School of Hygiene & Tropical Medicine	Professor of Parasitology
Michael J. Free	PATH	Vice President and Senior Advisor for Technologies Global Program Leader, Technology Solutions
Nirmal K. Ganguly	Centre for Health Technology, National Institute for Immunology, India	Distinguished Biotechnology Fellow
Carole Heilman	National Institute of Allergy and Infectious Diseases (NIAID), United States	Director of Division of Microbiology and Infectious Diseases
Janet Hemingway	Innovative Vector Control Consortium (IVCC)	Chief Executive Officer
Peter Hotez	George Washington University and Sabin Vaccine Institute	President, Sabin Vaccine Institute Distinguished Research Professor Walter G. Ross Professor and Chair of the Department of Microbiology, Immunology and Tropical Medicine
Marie-Paule Kieny	WHO - Initiative for Vaccine Research (IVR)	Director
	International AIDS Vaccine Initiative (IAVI)	Senior Vice President of Research & Development
Wayne Koff	Bill & Melinda Gates Foundation	Director of Infectious Diseases Development, Global Health Program
Regina Rabinovich	World Health Organization:WHO-based Special Programme for Research and Training in Tropical Diseases (TDR)	Director
Robert Ridley		
Joseph Romano	International Partnership for Microbicides (IPM)	Chief of Product Development
Giorgio Roscigno	Foundation for Innovative New Diagnostics (FIND)	Chief Executive Officer
Melvin K. Spigelman	The Global Alliance for TB Drug Development	President and Chief Executive Officer
Timothy Wells	Medicines for Malaria Venture (MMV)	Chief Scientific Officer

ADDITIONAL EXPERT	ORGANISATION	TITLE
Mark Alderson	PATH	Director, Pneumococcal Vaccine Project
Carol Dahl	Bill & Melinda Gates Foundation	Director, Global Health Discovery, Global Health Program
Martin Friede	WHO – Initiative for Vaccine Research (IVR)	Technical Officer
Richard L. Guerrant	University of Virginia School of Medicine	Director, Center for Global Health, and Thomas H. Hunter Professor of International Medicine in the Division of Infectious Diseases and International Health
Marc LaForce	PATH	Global Program Leader, Meningitis Vaccine Project

ANNEXE 3

STAKEHOLDER NETWORK MEMBERS

ORGANISATION	COUNTRY
AstraZeneca	UK
Bill & Melinda Gates Foundation	USA
Brazilian Ministry of Health, Department of Science and Technology	Brazil
Crucell	The Netherlands
UK Department for International Development	UK
Eli Lilly and Company	USA
European Commission	Belgium
GlaxoSmithKline	UK
Irish Aid	Ireland
Merck and Co Inc	USA
Dutch Ministry of Foreign Affairs	The Netherlands
Novartis International AG	Switzerland
Otsuka	Japan
Pfizer	USA
Public Health Agency of Canada	Canada
sanofi-aventis	France
South African Department of Science and Technology	South Africa
Swiss Agency for Development and Cooperation	Switzerland
UK Medical Research Council	UK
United States Agency for International Development	USA
US Centers for Disease Control	USA
US Department of Defense	USA
US National Institutes of Health	USA
Wellcome Trust	UK
Wyeth	USA

ANNEXE 4

SURVEY RESPONDENT LIST

ORGANISATION NAME*

- Academy of Finland
- Ace Biosciences
- Aeras Global TB Vaccine Foundation (Aeras)
- African Malaria Network Trust (AMANET)
- American Leprosy Missions
- AstraZeneca
- Atom Sciences, Inc.
- Australian Army Malaria Institute
- Australian National Health and Medical Research Council (NHMRC)
- Australian Queensland Department of Tourism, Regional Development and Industry
- Bavarian Nordic
- Becton, Dickinson and Company (BD)
- Belgian Development Cooperation (DGDC)
- Bernhard Nocht Institute for Tropical Medicine (BNI)
- Bill & Melinda Gates Foundation
- Bio Manguinhos
- Bioption AB
- Brazilian Ministry of Health, Department of Science and Technology
- Bristol University
- Cambridge University
- Canadian Institutes of Health Research (CIHR)
- Canadian International Development Agency (CIDA)
- Carlos III Health Institute
- Cepheid
- Consortium to Respond Effectively to the TB/HIV Epidemic (CREATE)
- Crucell
- Crusaïd
- Dafra Pharma International Ltd
- Danish International Development Agency (DANIDA)
- Drugs for Neglected Diseases initiative (DNDi)
- Dutch Ministry of Foreign Affairs
- Eli Lilly
- Emergent Biosolutions (including Microscience and Antex biologicals Inc)
- EpiVax
- European and Developing Countries Clinical Trials Partnership (EDCTP)
- European Commission
- European Malaria Vaccine Initiative (EMVI)
- Federal University of Bahia
- Fondazione Centro San Raffaele del Monte Tabor
- Foundation for Innovative New Diagnostics (FIND)
- Fundació Clínic per la Recerca Biomèdica
- George Washington University
- GeoVax Labs, Inc.
- German Federal Ministry for Economic Cooperation and Development (BMZ)
- German Research Foundation (DFG)
- GlaxoSmithKline (GSK)
- Global Alliance for TB Drug Development (TB Alliance)
- Global Vaccines, Inc.
- Globelmmune, Inc.
- Hawaii Biotech, Inc.
- Health Research Council of New Zealand (HRC)
- Infectious Disease Research Institute (IDRI)
- Innovative Vector Control Consortium (IVCC)
- Inserm - Institute of Infectious Diseases
- Institut Pasteur
- Institute for One World Health (IOWH)
- International AIDS Vaccine Initiative (IAVI)
- International Partnership for Microbicides (IPM)
- International Vaccine Institute (IVI)
- Inviragen, Inc.
- Irish Aid
- Israeli Ministry of Health
- Italian National Institute of Health, Istituto Superiore di Sanità (ISS)
- Jacobus Pharmaceuticals
- Japanese National Institute of Infectious Diseases (NIID)
- Johns Hopkins University
- KNCV Tuberculosis Foundation
- Korean Institute of Tuberculosis
- Liverpool School of Tropical Medicine (LSTM)
- London School of Hygiene and Tropical Medicine (LSHTM)
- Malaria Consortium
- Max Planck Society - Max Planck Institute for Infection Biology (MPIIB)
- Medicines for Malaria Venture (MMV)
- Mexican National Institute of Public Health (INSP)
- Microbial Novoteqs, Inc.
- Microbicides Development Programme (MDP)

ORGANISATION NAME*

- Multilateral Initiative on Malaria (MIM)
- National Agency for AIDS Research (ANRS)
- Novartis
- Otsuka
- Palumed S.A.
- Pediatric Dengue Vaccine Initiative (PDVI)
- Pepscan Systems
- Pfizer
- Premier Medical Corporation Ltd.
- PATH (including Malaria Vaccine Initiative, Meningitis Vaccine Project, Rotavirus Vaccine Program, Pneumococcal Vaccine Project, and other programs)
- Proteome Systems
- Public Health Agency of Canada (PHAC)
- Queensland Institute of Medical Research (QIMR)
- Rosalind Franklin University of Medicine and Science
- Royal Tropical Institute (KIT)
- Rush University Medical Center
- Sabin Vaccine Institute
- Salubris Group
- sanofi-aventis
- Sequella
- Shin Poong Pharma
- Sigma Tau
- South African Department of Science and Technology (DST)
- South African Medical Research Council
- South African National Research Foundation
- Spanish Agency of International Cooperation for Development (AECID)
- Statens Serum Institute (SSI)
- Swedish International Development Agency (SIDA)
- Swiss Agency for Development and Cooperation (SDC)
- Swiss State Secretariat for Education and Research (SER)
- Targeted Genetics
- The Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA)
- Topo Target
- UK Department for International Development (DFID)
- UK Health Protection Agency
- UK Medical Research Council (MRC)
- United States Agency for International Development (USAID)
- US Centers for Disease Control (CDC)
- US Department of Defense (DOD)
- US National Institutes of Health (NIH)
- US Veterans Affairs
- Universidad Autonoma de Madrid
- University of Auckland
- University of Bergen
- University of Dundee
- University of Durham
- University of Liverpool
- University of Melbourne
- University of Mississippi
- University of Nebraska Medical Center
- University of North Carolina
- Vakzine Projekt Management GmbH
- Walter and Eliza Hall Institute of Medical Research
- Walter Reed Army Institute of Research (WRAIR)
- Wave 80 Biosciences
- Wellcome Trust
- WHO-based Special Programme for Research and Training in Tropical Diseases (TDR)
- World Bank
- World Health Organization: Initiative for Vaccine Research (WHO/IVR)

* Does not include all recipients as some organisations preferred to remain anonymous

ANNEXE 5

SUMMARY OF RESEARCH & DEVELOPMENT REFERENCE DOCUMENT

The full R&D reference document is lengthy (21 pages) and detailed, therefore only a summary is presented here. Please see (<https://studies.thegeorgeinstitute.org/gfinder/registered/docs/help.jsp>) for the full document.

1 BASIC RESEARCH

Studies that increase scientific knowledge and understanding about the disease, disease processes, pathogen or vector, but which are not yet directed towards a specific product

- Natural history and epidemiology
- Immunology of disease
- Biology of disease
- Biochemistry of the pathogen
- Genetics of the pathogen
- Bioinformatics and proteomics
- Pathophysiology and disease symptoms
- Vector biology, biochemistry and genetics

2 DRUGS

Research activities and processes necessary to develop and improve new compounds specifically designed to cure or treat neglected diseases; including drug discovery or design, preclinical and clinical development and other activities essential for successful drug development and uptake

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies associated with newly approved drugs only
- Baseline epidemiology directly linked to trials of products in development

3 PREVENTIVE VACCINES

*Research activities and processes necessary to develop and improve investigational vaccines specifically intended to **prevent** infection; including vaccine design, preclinical and clinical development and other activities essential for successful vaccine development and uptake*

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies associated with newly approved vaccines only
- Baseline epidemiology directly linked to trials of products in development

4 DIAGNOSTICS

Research activities and processes necessary to develop, optimise, and validate diagnostic tests for use in resource-limited settings (cheaper, faster, more reliable, ease of use in the field); including discovery and design, preclinical and clinical evaluation, and other activities essential for successful deployment for public health use

- Discovery and preclinical
- Clinical evaluation
- Operational research necessary to support WHO recommendation for global public health use

5 MICROBICIDES

Research activities and processes necessary to develop and improve topical microbicides specifically intended to prevent HIV transmission; including microbicide discovery or design, preclinical and clinical development, and other activities essential for successful microbicide development and uptake

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies associated with newly approved microbicides only
- Baseline epidemiology directly linked to trials of products in development

6 THERAPEUTIC VACCINES

*Research activities and processes necessary to develop and improve investigational vaccines specifically intended to **treat** infection; including vaccine design, preclinical and clinical development, and other activities essential for successful vaccine development and uptake*

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies associated with newly approved vaccines only
- Baseline epidemiology directly linked to trials of products in development

7 VECTOR CONTROL PRODUCTS

A) PESTICIDES

ONLY includes chemical pesticides intended for global public health use and which specifically aim to inhibit and kill vectors associated with transmitting poverty-related diseases, including:

- Primary screening and optimisation
- Secondary screening and optimisation
- Development
- WHO Pesticide Evaluation Scheme (WHOPES)

B) BIOLOGICAL CONTROL PRODUCTS

ONLY includes research and development of innovative biological control interventions that specifically aim to kill or control vectors associated with transmitting poverty-related diseases, including:

- Microbial/ bacteriological larvicides
- Sterilisation techniques
- Genetic modification measures

C) VACCINES TARGETING ANIMAL RESERVOIRS

ONLY includes research and development of veterinary vaccines specifically designed to prevent animal to human transmission of neglected diseases

8 CANNOT BE ALLOCATED TO ONE DISEASE

A) CORE FUNDING OF A MULTI-DISEASE R&D ORGANISATION

B) PLATFORM TECHNOLOGIES

- Adjuvants and immunomodulators
- Delivery technologies and devices
- General diagnostic platforms

*This category has **strict limitations**. It ONLY includes funding for R&D for the above, which also meets the following conditions:*

- It is conducted by **public, philanthropic or not-for-profit entities**

- It is **basic research** i.e. it is not yet directed towards a specific disease or product area
- It is aimed at developing safer, cheaper, more effective products suitable for use in developing countries
- The resulting research findings or leads **MUST** be accessible to organisations developing pharmaceutical or biological products for neglected diseases

c) UNSPECIFIED R&D

Funding that cannot be apportioned to any specific disease categories

9 OUT OF SCOPE (EXCLUDED FROM THE SURVEY)

A) GENERAL EXCLUSIONS

- Non-pharmaceutical tools including; adult male circumcision, cervical barriers, HSV-2 prevention, bednets, traps, water sanitation tools
- General supportive, nutritional and symptomatic therapies, including: Oral rehydration therapy, micronutrient supplementation, vitamins and anti-pyretics, painkillers
- Products developed and used for veterinary purposes
- In-kind contributions
- Additional exclusions for private sector investment include industry overhead costs, capital costs and opportunity costs due to the difficulty of quantifying these and allocating them to the neglected disease investment

B) NON-PRODUCT R&D

*Our intention is to capture investments into **neglected disease product development** as accurately as possible. Therefore, the following R&D activities are excluded from the survey*

- Clinical studies that are not linked to development of a NEW product
- Health services and access research
- GENERAL capacity building (human & infrastructure)

Capacity building activities are excluded except those that are **DIRECTLY** linked to development of a new neglected disease product

C) SELECTED DISEASE AND PRODUCT RESTRICTIONS

*Commercial diseases where incentives for R&D already exist; or product R&D already occurs in response to the existing Western markets, are **EXCLUDED** from this survey*

Basic research

*Basic research is **LIMITED** for the following diseases:*

- HIV/AIDS: **ONLY** includes basic research related to preventative vaccines and microbicides (e.g. immunological responses to potential antigens, mechanism of mucosal transmission)
- Multiple Diarrhoeal diseases

Drugs

*R&D for drugs is **LIMITED** for the following diseases:*

- HIV/AIDS: **ONLY** includes label extensions and reformulations for developing country use (e.g. paediatric or slow-release formulations; fixed dose combinations).
- diarrhoea caused by cholera, shigella, cryptosporidium: **ONLY** includes pharmacological interventions that target the pathogen, not supportive therapies.

Preventive Vaccines

*R&D for preventive vaccines is **LIMITED** for the following diseases:*

- *Bacterial pneumonia caused by S. pneumoniae*

ONLY includes R&D on vaccines specifically for developing-country registration. Such a vaccine must at a minimum: a) be designed for use in infants less than two years of age; and b) provide coverage against *S. pneumoniae* serotypes 1, 5, and 14.

For multi-valent vaccines covering Western and developing country strains, only developing country-specific costs should be entered; including for trials, registration and Phase IV/pharmacovigilance studies.

- *Bacterial pneumonia or meningitis caused by N. meningitidis*

ONLY includes R&D on vaccines specifically for developing-country registration. Such a vaccine must, at a minimum: a) provide coverage against *N. meningitidis* serotype A; b) be a conjugate vaccine; c) be designed for use in infants less than two years of age; and d) be designed to cost less than a dollar per dose.

For multi-valent vaccines covering Western and developing country strains, only developing country-specific costs should be entered; for example, for trials, registration and Phase IV/pharmacovigilance studies in the target developing countries.

- *Diarrhoea caused by rotavirus*

ONLY includes developing country-specific R&D, including clinical trials, registration and Phase IV/pharmacovigilance studies in the target developing countries.

Diagnostics

See above

Vaccines (Therapeutic)

See above

Microbicides

Applications that may have Western markets or be useful for other STDs (e.g. mucosal delivery technology, adjuvants) are EXCLUDED

Vector Control Products

Baits, traps, predation measures, biological larvicides, habitat control and infrastructure measures are excluded from this product category. Vaccines developed and used solely for veterinary purposes are excluded from this product category

Cannot be allocated to one disease

- Adjuvants and immunomodulators
- General diagnostic platforms
- Delivery devices and technologies

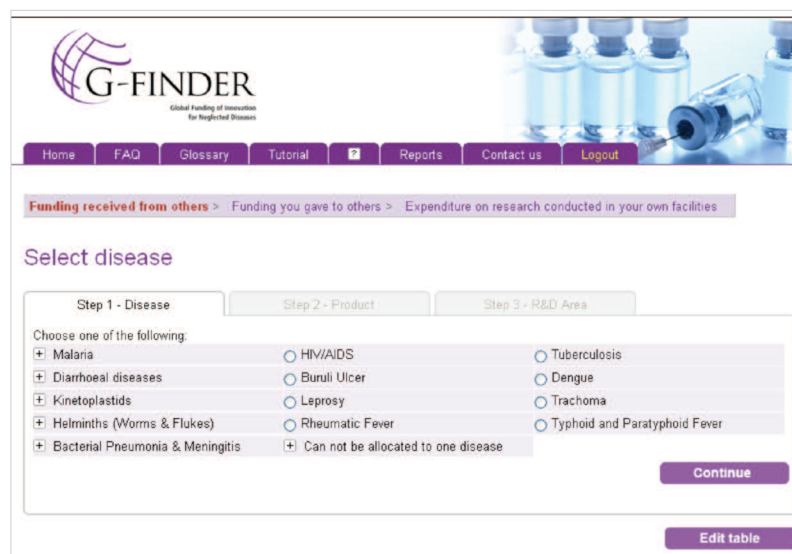
This category has strict limitations (see above)

ANNEXE 6

Snapshots of the G-FINDER survey

3 Step Process:

STEP 1 SELECT DISEASE



G-FINDER
Global Funding of Innovation
for Neglected Diseases

Home FAQ Glossary Tutorial ? Reports Contact us Logout

Funding received from others > Funding you gave to others > Expenditure on research conducted in your own facilities

Select disease

Step 1 - Disease Step 2 - Product Step 3 - R&D Area

Choose one of the following:

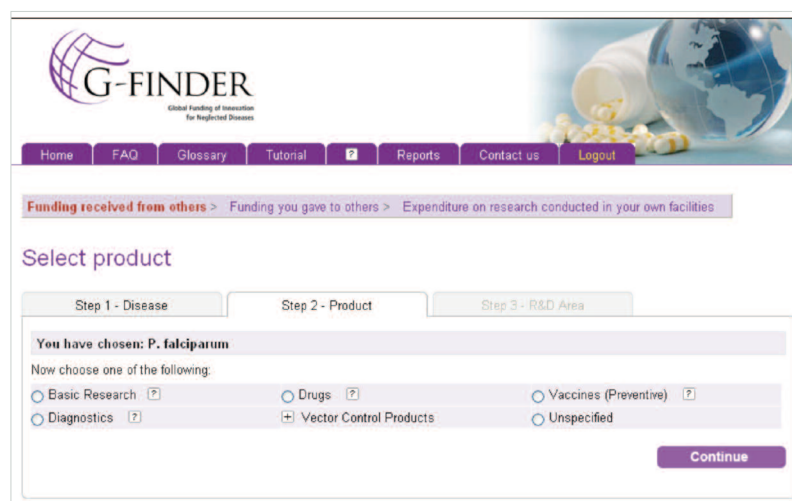
<input checked="" type="checkbox"/> Malaria	<input type="checkbox"/> HIV/AIDS	<input type="checkbox"/> Tuberculosis
<input checked="" type="checkbox"/> Diarrhoeal diseases	<input type="checkbox"/> Buruli Ulcer	<input type="checkbox"/> Dengue
<input checked="" type="checkbox"/> Kinetoplastids	<input type="checkbox"/> Leprosy	<input type="checkbox"/> Trachoma
<input checked="" type="checkbox"/> Helminths (Worms & Flukes)	<input type="checkbox"/> Rheumatic Fever	<input type="checkbox"/> Typhoid and Paratyphoid Fever
<input checked="" type="checkbox"/> Bacterial Pneumonia & Meningitis	<input checked="" type="checkbox"/> Can not be allocated to one disease	

Continue

Edit table

3 Step Process:

STEP 2 SELECT PRODUCT



G-FINDER
Global Funding of Innovation
for Neglected Diseases

Home FAQ Glossary Tutorial ? Reports Contact us Logout

Funding received from others > Funding you gave to others > Expenditure on research conducted in your own facilities

Select product

Step 1 - Disease Step 2 - Product Step 3 - R&D Area

You have chosen: P. falciparum

Now choose one of the following:

<input type="checkbox"/> Basic Research ?	<input type="checkbox"/> Drugs ?	<input type="checkbox"/> Vaccines (Preventive) ?
<input type="checkbox"/> Diagnostics ?	<input checked="" type="checkbox"/> Vector Control Products	<input type="checkbox"/> Unspecified

Continue

3 Step Process:

STEP 3 SELECT R&D AREA

G-FINDER
Global Funding of Innovation for Neglected Diseases

Home | FAQ | Glossary | Tutorial | ? | Reports | Contact us | Logout

Funding received from others > Funding you gave to others > Expenditure on research conducted in your own facilities

Select R&D area

Step 1 - Disease | Step 2 - Product | Step 3 - R&D Area

You have chosen: P. falciparum > Vaccines (Preventive)

Now choose one of the following:

☐ Discovery and preclinical ?
 ☐ Clinical development ?
 ☐ Phase IV/Pharmacovigilance ?
 ☐ Baseline epidemiology ?
 ☐ Unspecified

Continue

TABLE ENTERING DATA

G-FINDER
Global Funding of Innovation for Neglected Diseases

Home | FAQ | Glossary | Tutorial | ? | Reports | Contact us | Logout

Funding received from others > Funding you gave to others > Expenditure on research conducted in your own facilities

Select your R&D area

Step 1 - Disease | Step 2 - Product | Step 3 - R&D Area

You have chosen: P. falciparum > Vaccines (Preventive) > Clinical development

Now choose one of the following:

☐ Discovery and preclinical ?
 ☐ Clinical development ?
 ☐ Phase IV/Pharmacovigilance ?
 ☐ Baseline epidemiology ?
 ☐ Unspecified

Table: Funding received from others

Description	Name of Funding Organisation*	Grant Name and/or Brief Description*	Currency	Amount*	Action
1 P. falciparum > Vaccines (Preventive) > Clinical development			USD		Save

* Required fields

New entry

Continue to next table

Change disease | Change product | Change R&D area

Exit and return to survey later

Grants that cannot be allocated to one disease:

FIRST STEP DROP-DOWN SELECTIONS

Grants that cannot be allocated to one disease:

SECOND STEP R&D REFERENCE DOCUMENT POP UP TO GUIDE CORRECT ALLOCATION

AUTHORS



Dr Mary Moran

DIRECTOR, HEALTH POLICY DIVISION

MBBS (Bachelor of Medicine, Bachelor of Surgery, Hons); Grad Dip FAT (Foreign Affairs and Trade); FRSM

Dr Mary Moran trained as a medical doctor, working for 13 years in Emergency Medicine in Australia. A post-graduate degree in international relations and politics at University of NSW and Monash University (1995) led her into a diplomatic career with the Australian Department of Foreign Affairs & Trade, including a posting to London where she specialised in environmental issues and international trade. Mary subsequently worked with Medecins Sans Frontieres, initially as Director of the Access to Essential Medicines Campaign in Australia and later as a Europe-based advocate on issues relating to access to medicines for neglected patients. In 2004, she founded the Pharmaceutical R&D Policy Project (PRPP) at the London School of Economics & Political Science and supervised its relocation in 2006 to The George Institute for International Health, Sydney, in 2006 where it was consolidated as the Health Policy Division. Mary is an Honorary Senior Lecturer at the London School of Hygiene and Tropical Medicine, and has acted as an Expert Adviser to a range of organisations including the World Health Organisation, European Commission, EDCTP and Wellcome Trust.



Dr Javier Guzman

DIRECTOR OF RESEARCH

MBBS (Bachelor of Medicine, Bachelor of Surgery, Hons); MSc in Health Policy, Planning and Financing (LSHTM - LSE)

Dr Javier Guzman trained as a medical doctor and worked in planning and implementation of primary health care projects in the Colombian countryside for several years. He mainly worked in early detection and treatment programmes of endemic infectious diseases such as malaria, tuberculosis and Chagas disease. Javier moved to the UK in 2002, where he worked as a Post Graduate Clinical Fellow in Paediatrics at the Royal London Hospital. In 2004, he obtained his MSc in Health Policy, Planning and Financing from the London School of Economics and the London School of Hygiene and Tropical Medicine. In August 2004, he joined the PRPP at the London School of Economics where he worked mainly on the performance of different R&D models and pipelines. Javier moved to Australia in April 2006 and now heads the HPD's research team. He is currently doing his MBA-Executive at the Australian Graduate School of Management, Sydney.



Anne-Laure Ropars

SENIOR POLICY ANALYST

BSc (Mech Eng, Hons); MSc (Mech Eng, Hons); MA in Political Economy and International Relations (Hons)

Anne-Laure Ropars originally trained and worked as a mechanical engineer. After completing a Masters degree in political economy and international relations at the University of Chicago, she worked for a number of years as a consultant specialising in European and developing country health systems and policies. Her clients have included the EU-based pharmaceutical industry, philanthropic organisations (Rockefeller Foundation, Bill & Melinda Gates Foundation), and government bodies (DFID, USAID). Anne-Laure's project experience spans drug procurement policy in Sub-Saharan Africa, market-based mechanisms to reduce the price of essential drugs in Ghana, to drug reimbursement policies in European countries. She joined the PRPP at its creation in 2004, and headed the London office of the Health Policy Division (HPD) from 2006 to 2008 before moving to a consultancy role with HPD. She is an Honorary Lecturer at the London School of Hygiene and Tropical Medicine.



Alina McDonald

POLICY ANALYST

BSc (Bachelor of Science); LLB (Bachelor of Law, Hons)

Alina McDonald undertook training in science and law at the University of Sydney. She majored in medical sciences, health law and international law. She completed her study of international law at the University of Utrecht in the Netherlands. After contributing towards an EU-funded bioethics research project based in Berlin, she joined The George Institute for International Health in January 2005 to work on a series of health policy Roundtables with the Chinese Ministry of Health. Alina contributed to two Roundtables, held in Beijing, on issues including patient safety and access to basic health care where she conducted background research, managed international stakeholders and prepared policy reports for the Ministry of Health. In early 2006, she had a short-term secondment to the World Health Organization in Geneva to work with the secretariat for the Framework Convention on Tobacco Control. Alina joined the Health Policy Division in Sydney in June 2006 and conducts qualitative and quantitative analysis including for the projects "Malaria product pipeline: planning for the future" and G-FINDER – Global Funding of Innovation for Neglected Diseases. She is currently undertaking postgraduate study in international intellectual property issues and regulation at the University of Technology, Sydney.



Tanja Sturm

POLICY ANALYST

BA (Bachelor of Arts); MA (Master of Arts); MSc in Health Policy, Planning and Financing (LSHTM - LSE)

Tanja Sturm joined the London-based HPD in November 2007 as a Policy Analyst. Prior to joining The George Institute, Tanja worked as a consultant for the World Health Organization (WHO) in Geneva where she was involved in several projects relating to medicines pricing and affordability in Africa. In 2006, Tanja obtained her MSc in Health Policy, Planning and Financing (HPPF) from the London School of Economics and the London School of Hygiene and Tropical Medicine. Prior to this, Tanja worked as a Latin America editor at the Economist Intelligence Unit (EIU). At the EIU Tanja was the lead analyst for a number of Latin

American countries and was responsible for conducting two-year macro-economic forecasts and quarterly risk ratings. Before joining the EIU, Tanja worked as a healthcare research analyst at Global Insight. Here she provided blue-chip companies with in-depth research relating to political and pharmaceutical market trends in Latin America, pharmaceutical regulation, pricing and reimbursement affairs, and US pharmaceutical company competitor intelligence. Tanja's previous academic training includes a BA in History and Spanish and an MA in Latin American Studies.



Nicole Jameson

RESEARCH ASSOCIATE

BA (Bachelor of Arts); MIPH (Master of International Public Health)

Nicole Jameson completed her Bachelor of Arts at the University of Sydney, majoring in Thai language. While completing her Masters degree in International Public Health she worked as a project coordinator with the Research Institute for Asia and the Pacific (RIAP) at the University of Sydney, where she managed short-term training programs for senior public and private sector delegations from the People's Republic of China. Nicole joined The George Institute for International Health as Student & Visiting Fellow Coordinator in January 2007, where she was responsible for establishing, coordinating and maintaining systems to support the induction, development and departure of visiting scholars and postgraduate students within the Institute. Nicole joined the Sydney-based HPD team as a research assistant in November 2007.



Sam Ryan

RESEARCH ASSOCIATE

BEcon (Bachelor of Economics, Hons); LLB (Bachelor of Law)

On completion of his Bachelor of Economics with Honours in Political Science Sam Ryan worked for several years as a researcher with Medecins Sans Frontieres on the Access to Essential Medicines Campaign. Subsequently, he completed a law degree focusing on international trade, medical and intellectual property law while working as a senior logistician with International SOS, the world's largest emergency medical assistance company. Sam initiated, established and participated in the first university exchange program between Australia and India, studying at the National Law School of India University in Bangalore. While studying in India Sam worked as a paralegal with Dua Associates, a local Indian law firm, and as a trade associate for the ASEAN Focus Group, a regional trade and investment consultancy, for whom he developed strategies for innovative legal service outsourcing. In 2005 Sam began work with Australian Department of Health and Ageing as a legal and policy advisor on issues including the implementation of pharmaceutical aspects of the Australia-US Free Trade Agreement and reform of the Australian Pharmaceutical Benefits Scheme. He joined the HPD in November 2007.



Lindsey Wu

RESEARCH ASSOCIATE

BAS Biotechnology, BA Economics, MSc Biomedicine, Bioscience and Society (LSE)

Lindsey joined the London-based HPD team as a Research Associate in February 2008. Prior to joining The George Institute, Lindsey worked as a healthcare policy consultant for The Lewin Group in Washington, DC. At Lewin, Lindsey's work involved health technology assessments for the Agency for Healthcare Research and Quality (AHRQ), clinical data analysis for the National Institutes of Health (NIH), and evidence-based reviews of pharmacogenomics for the US Department of Health and Human Services (DHHS). Lindsey received a Bachelor's of Applied Science in Biotechnology and a BA in Economics from the University of Pennsylvania, working part-time as a researcher at the Penn Center for Bioethics. She also received her MSc at the London School of Economics, where her graduate thesis explored the WTO TRIPS Agreement and its impact on the global pharmaceutical industry. Lindsey is an Honorary Research Fellow at the London School of Hygiene and Tropical Medicine.



Brenda Omune

RESEARCH ASSOCIATE

MBChB (Bachelor of Medicine, Bachelor of Surgery); MIPH (Master of International Public Health, Hons)

Brenda obtained her bachelors degree in Medicine and Surgery (MBChB) from the University of Nairobi, Kenya. After completing her degree, she was involved in the initial stages of enrolling, treating and following up of HIV patients through the comprehensive care clinic during the rolling out of anti-retroviral therapy (ART) in Kenya.

She then worked for several years as a casualty medical officer providing emergency care to both acutely ill patients and stable patients. She gained experience in clinical management of patients with infectious diseases including malaria, meningitis, pneumonia, tuberculosis and HIV/AIDS.

Brenda moved to Sydney in 2006 to pursue a Masters of International Public Health (Honours) from the University of Sydney. While completing her masters' degree, Brenda worked as a research assistant at the Critical Care and Trauma unit at The George Institute and at the Center for Health Informatics, UNSW. Brenda Omune joined the HPD team in June 2008.

REFERENCES

- 1 Hotez PJ, Molyneux DH, Fenwick A, Kumaresan J, Sachs SE et al (2007) Control of Neglected Tropical Diseases. *N Engl J Med* 357(10): 1018–1026.
- 2 Toreele E, Usdin M, Chirac P (2004) A needs-based pharmaceutical R&D agenda for neglected diseases. Geneva: World Health Organization. p.12. Available: <http://www.who.int/intellectualproperty/topics/research/Needs%20based%20R&D%20for%20neglected%20diseases%20Els%20Pierre%20Martine.pdf>. Accessed 5 December 2008.
- 3 IJsselmuiden C, de Haan S, Iacono SL, Kisia CN, Moomal H et al (2008) Alignment and Harmonisation in Health Research: AHA Study. Geneva: Council on Health Research for Development (COHRED). pp. 29–39. Available: http://www.cohred.org/AHA/files/resources/Synthesis_web.pdf. Accessed 4 December 2008.
- 4 de Francisco A (2004) Progress in measuring the 10/90 gap. In: Davey S, Jupp S, Mauroux C, editors. 10/90 Report on Health Research 2003-2004. Geneva: Global Forum for Health Research. pp. 107–126. Available: http://www.globalforumhealth.org/filesupld/1090_report_03_04/109004_chap_5.pdf. Accessed 4 December 2008.
- 5 HIV Vaccines and Microbicides Resource Tracking Working Group (2008) Sustaining the HIV Prevention Research Agenda: Funding for Research and Development of HIV vaccines, Microbicides, and Other New Prevention Options 2000-2007. New York: AIDS Vaccines Advocacy Coalition. pp. 1–38. Available: http://hivresourcetracking.org/content/RT_report_August2008.pdf. Accessed 18 December 2008.
- 6 Feuer C (2007) Tuberculosis Research and Development: A Critical Analysis of Funding Trends, 2005-2006. New York: Treatment Action Group.
- 7 Malaria R&D Alliance (2005) Malaria Research & Development: An Assessment of Global Investment. Seattle: Program for Appropriate Technology in Health (PATH). pp. 1–53. Available: http://www.malariavaccine.org/files/MalariaRD_Report_complete.pdf. Accessed 18 December 2008.
- 8 WHO (2001) Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization. p.89. Available: <http://whqlibdoc.who.int/publications/2001/924154550x.pdf>. Accessed 12 January 2009.
- 9 WHO Control of Neglected Tropical Diseases (NTD) (2008) Diseases covered by NTD Department. Available: http://www.who.int/neglected_diseases/diseases/en/. Accessed 11 December 2008.
- 10 WHO-based Special Programme for Research and Training in Tropical Diseases (TDR) (2008) Overview on diseases. Available: <http://www.who.int/tdr/svc/diseases>. Accessed 10 December 2008.
- 11 Sabin Vaccine Institute Global Network for Neglected Tropical Diseases (2008) The seven most common NTDs. Available: <http://gnntdc.sabin.org/about-ntds/factsheets>. Accessed 10 December 2008.
- 12 The PLoS Medicine Editors (2005) A new era of hope for the world's most neglected diseases. *PLoS Medicine* 2 (9): e323. Available: <http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pmed.0020323>. Accessed 19 December 2008.
- 13 Director, Office of AIDS Research, National Institutes of Health (NIH) (2002) National Institutes of Health Fiscal Year 2002 Plan for HIV-Related Research. Bethesda: National Institutes of Health.
- 14 Anderson J, MacLean M, and Davies C (1996) Malaria research: An audit of international activity. PRISM Report No. 7. London: Wellcome Trust Unit for Policy Research in Science and Medicine (PRISM). pp. 1–96. Available: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@sitedstudioobjects/documents/web_document/wtd003220.pdf. Accessed 12 January 2009.
- 15 WHO (2008) The Global Burden of Disease: 2004 update. Geneva: World Health Organization. pp.1–146. Available: http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf. Accessed 12 January 2009.
- 16 Carlton JM, Adams JH, Silva JC, Bidwell SL, Lorenzi H, et al (2008) Comparative genomics of the neglected human malaria parasite *Plasmodium vivax*. *Nature* 455(7214): 757–63. Available: <http://www.nature.com/nature/journal/v455/n7214/full/nature07327.html>. Accessed 13 January 2009.
- 17 Hotez PJ, Molyneux DH, Fenwick A, Ottesen E, Sachs SE et al (2006) Incorporating a Rapid-Impact Package for Neglected Tropical Diseases with Programs for HIV/AIDS, Tuberculosis, and Malaria: A comprehensive pro-poor health policy and strategy for the developing world. *PLoS Medicine* 3(5): e102. Available: <http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0030102>. Accessed 14 January 2009.
- 18 Wyeth (2008) Wyeth Receives FDA Fast Track Designation for its 13-valent Pneumococcal Conjugate Vaccine. Available: http://www.wyeth.com/news/archive?nav=display&navTo=/wyeth_html/home/news/pressreleases/2008/1228311291213.html. Accessed 19 January 2009.
- 19 Crump JA, Luby SP and Mintz ED (2004) The global burden of typhoid fever. *Bull World Health Organ* 82(5): 346–353. Available: <http://www.who.int/rpc/TFDisBurden.pdf>. Accessed 13 January 2009.
- 20 WHO (2008) Global leprosy situation, beginning of 2008. *Wkly Epidemiol Rec* 83(38): 293–300. Available: <http://www.who.int/wer/2008/wer8333.pdf>. Accessed 12 January 2009.

- 21 WHO (2008) Buruli ulcer progress report, 2004—2008. *Wkly Epidemiol Rec* 83(17): 145—154. Available: <http://www.who.int/wer/2008/wer8317.pdf>. Accessed 13 January 2009.
- 22 IMF (2008) World Economic and Financial Surveys. World Economic Outlook Database. Available: <http://imf.org/external/pubs/ft/weo/2008/02/weodata/index.aspx>. Accessed 16 January 2009
- 23 Moran M, Guzman J, Ropars A, Jorgensen M, McDonald A et al (2007) The malaria product pipeline: Planning for the future. London: The George Institute for International Health. pp. 1—94. Available: http://www.thegeorgeinstitute.org/shadomx/apps/fms/fmsdownload.cfm?file_uuid=1ABDE79C-DA73-20B3-D6E1-F7AF25011EC9&siteName=iih. Accessed 19 December 2008.
- 24 Pekar N, editor (2001) *The Economics of TB Drug Development*. New York: Global Alliance for TB Drug Development. Available: http://www.tballiance.org/downloads/publications/TBA_Economics_Report.pdf. Accessed 16th January 2009
- 25 DiMasi JA, Hansen RW, Grabowski HG (2003) The price of innovation: new estimates of drug development costs. *J Health Econ* 22:151—185. Available: <http://www.cptech.org/ip/health/econ/dimasi2003.pdf>. Accessed 16 January 2009
- 26 Serdobova I, Kieny MP (2006) Assembling a Global Vaccine Development Pipeline for Infectious Diseases in the Developing World. *Am J Public Health* 22 (9): 1554—1559. Available: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1551949>. Accessed 16 January 2009
- 27 Moran M, Ropars AL, Guzman J, Diaz J and Garrison C (2005) *The new landscape of neglected disease drug development*. London: *London School of Economics and The Wellcome Trust*. Available: http://www.thegeorgeinstitute.org/shadomx/apps/fms/fmsdownload.cfm?file_uuid=F2B06396-EEA0-851E-3049-C9A030AEDE0F&siteName=iih. Accessed 19 December 2008.
- 28 Organisation for Economic Co-operation and Development (2007) Main science and technology indicators database. Available: <http://lysander.sourceoecd.org/vl=3010314/cl=12/nw=1/rpsv/cw/vhosts/oecdstats/16081242/v207n1/contp1-1.htm>. Accessed 7 December 2007.
- 29 International Monetary Fund (2007) IMF exchange rates database. Available: <http://www.imf.org/external/np/fin/ert/GUI/Pages/CountryDataBase.aspx>. Accessed 7 December 2007.

