

INTRODUCTION

Background to the G-FINDER survey

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development (R&D) of new products to prevent, diagnose, control or cure neglected diseases in developing countries. It provides an up-to-date analysis of how R&D investments are being allocated across diseases and product types, funding trends over time, and where the potential gaps lie. G-FINDER is the primary source of neglected disease R&D funding data for both the World Health Organization's (WHO) Global Observatory on Health R&D and Donor Tracker, and helps support the work of many other groups in the broader global health community.

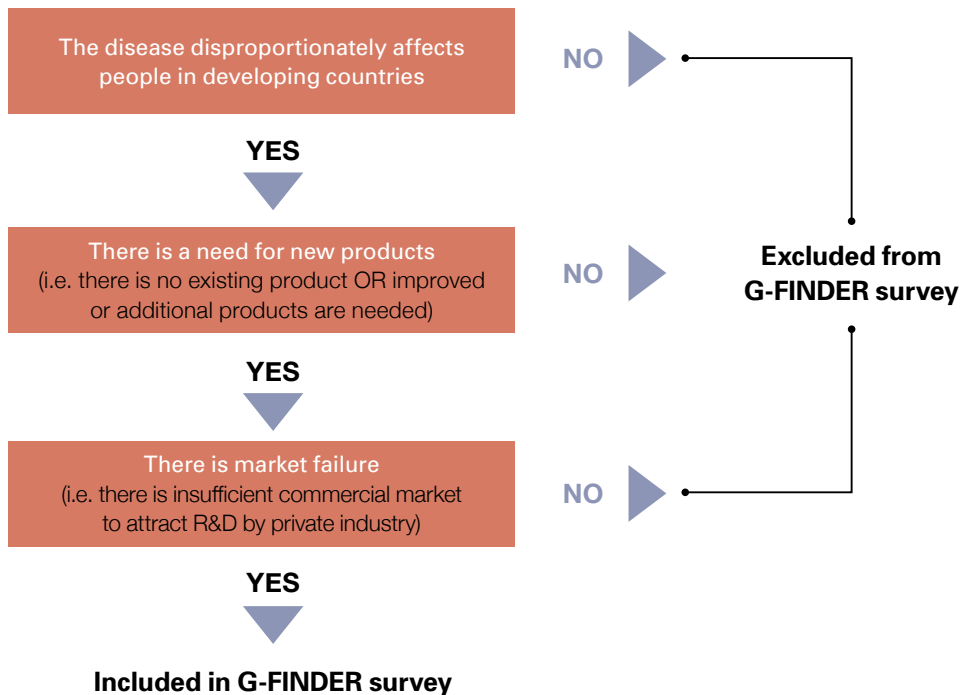
This is the tenth annual G-FINDER report; in addition to the previous nine years of funding data, it reports on investments made in financial year 2016, referred to as 2016 in the text.

The survey scope

DEFINING NEGLECTED DISEASES AND PRODUCTS

The scope of the G-FINDER survey is determined in consultation with the G-FINDER Advisory Committee, which is made up of a broad cross-section of international experts in neglected diseases and product development (see Annexe 1 for the list of current Advisory Committee members). When defining the G-FINDER scope at the project's inception, and at all subsequent reviews, three key criteria (see Figure 1) have been applied in order to establish a list of neglected diseases and products for which R&D would cease or wane if left to market forces.

Figure 1. Filter to determine G-FINDER inclusions



Although all relevant product types – drugs, vaccines (preventive and therapeutic), diagnostics, microbicides and vector control products (pesticides, biological control agents and vaccines targeting animal reservoirs) – as well as basic research were considered for all diseases, it is important to note that not all product types are included in the G-FINDER scope for all diseases, and some are included only with restrictions. For example, pneumonia drugs are excluded because there is a sufficient commercial market; while pneumonia vaccine investments are only included if they meet G-FINDER requirements for strain, vaccine type and target age group.

Platform technologies (adjuvants, diagnostic platforms and delivery devices) are also included in the scope of G-FINDER. Platform technologies can potentially be applied to a range of neglected diseases and products, but have not yet been attached to a specific product for a specific disease.

Investments that do not meet the G-FINDER scope are excluded from the results. This includes activities such as advocacy and behavioural research, which are important and critical to effect change, however are distinct from product development and fall outside the G-FINDER criteria.

A comprehensive explanation of all inclusions, exclusions and restrictions is outlined in the detailed G-FINDER R&D scope document, which is available online. A matrix summarising the neglected diseases, products and technologies included in this year's G-FINDER report is shown in Table 1.

CHANGES TO THE G-FINDER R&D SCOPE FOR NEGLECTED DISEASES

Although it is important to maintain a consistent scope in order to allow comparable, long-term analysis of multi-year R&D funding trends, the scope of the G-FINDER survey is reviewed annually in consultation with the Advisory Committee.

In year two of the G-FINDER survey (FY2008), the typhoid and paratyphoid fever disease category was expanded to include non-typhoidal *Salmonella enterica* (NTS) and multiple *Salmonella* infections, and R&D for lymphatic filariasis diagnostics was added.

In FY2013 (the seventh survey year), the survey was expanded to include three additional diseases: cryptococcal meningitis, hepatitis C (genotype 4) and leptospirosis. Dengue vaccines were determined to no longer fit the criteria for inclusion in the G-FINDER survey given the emergence of a commercial market, and dengue vaccine R&D funding (including all previously reported investment) was removed from the survey. All other dengue product areas were retained.

In FY2014 (the eighth survey year), the hepatitis C category was expanded to capture investment in R&D for two additional genotypes (genotypes 5 and 6) that disproportionately affect people in developing countries.

This year (FY2016, the tenth year of the survey), the bacterial pneumonia & meningitis category was expanded to include developing country-focused basic research for both *Streptococcus pneumoniae* (*S. pneumoniae*) and/or *Neisseria meningitidis* (*N. meningitidis*). Developing country-specific research into therapeutic vaccines for HIV/AIDS was also added as a restricted category, reflecting emerging research into broadly neutralising anti-HIV antibodies (bNAbs) and their potential use in developing countries.

Table 1. G-FINDER neglected diseases, products and technologies

Disease		Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products
HIV/AIDS		Restricted	Restricted	✓	Restricted	✓	✓	-
Malaria	<i>P. falciparum</i>	✓	✓	✓	-	✓	-	✓
	<i>P. vivax</i>	✓	✓	✓	-	✓	-	✓
	Multiple and/or other malaria strains	✓	✓	✓	-	✓	-	✓
Tuberculosis		✓	✓	✓	✓	✓	-	-
Diarrhoeal diseases	Rotavirus	-	-	Restricted	-	-	-	-
	<i>Shigella</i>	✓	Restricted	✓	-	✓	-	-
	Cholera	✓	Restricted	✓	-	✓	-	-
	<i>Cryptosporidium</i>	✓	Restricted	✓	-	✓	-	-
	Enterotoxigenic <i>E. coli</i> (ETEC)	-	-	✓	-	✓	-	-
	Enteroaggregative <i>E. coli</i> (EAggEC)	-	-	✓	-	✓	-	-
	<i>Giardia</i>	-	-	-	-	✓	-	-
	Multiple diarrhoeal diseases	✓	Restricted	✓	-	✓	-	-
Kinetoplastids	Leishmaniasis	✓	✓	✓	✓	✓	-	-
	Sleeping sickness (HAT)	✓	✓	✓	-	✓	-	✓
	Chagas' disease	✓	✓	✓	✓	✓	-	✓
	Multiple kinetoplastid diseases	✓	✓	✓	✓	✓	-	✓
Dengue		✓	✓	-	-	✓	-	✓
Bacterial pneumonia & meningitis	<i>S. pneumoniae</i>	Restricted	-	Restricted	-	✓	-	-
	<i>N. meningitidis</i>	Restricted	-	Restricted	-	✓	-	-
	Both <i>S. pneumoniae</i> and <i>N. meningitidis</i>	Restricted	-	-	-	✓	-	-
Salmonella infections	Typhoid and paratyphoid fever (<i>S. Typhi</i> , <i>S. Paratyphi A</i>)	✓	✓	✓	-	✓	-	-
	Non-typhoidal <i>S. enterica</i> (NTS)	✓	✓	✓	-	✓	-	-
	Multiple <i>Salmonella</i> infections	✓	✓	✓	-	✓	-	-
Helminth infections (worms & flukes)	Schistosomiasis (bilharziasis)	✓	✓	✓	-	✓	-	✓
	Lymphatic filariasis (elephantiasis)	✓	✓	-	-	✓	-	✓
	Onchocerciasis (river blindness)	✓	✓	✓	-	✓	-	✓
	Hookworm (ancylostomiasis & necatoriasis)	✓	✓	✓	-	-	-	-
	Tapeworm (taeniasis/cysticercosis)	✓	✓	-	-	-	-	✓
	Whipworm (trichuriasis)	✓	✓	-	-	-	-	-
	Strongyloidiasis & other intestinal roundworms	✓	✓	✓	-	✓	-	-
	Roundworm (ascariasis)	✓	✓	-	-	-	-	-
	Multiple helminth infections	✓	✓	✓	-	✓	-	✓
Hepatitis C (genotypes 4, 5 & 6)		-	Restricted	✓	-	✓	-	-
Leprosy		✓	✓	-	-	✓	-	-
Cryptococcal meningitis		-	✓	-	-	-	-	-
Buruli ulcer		✓	✓	✓	-	✓	-	-
Leptospirosis		-	-	-	-	Restricted	-	-
Trachoma		-	-	✓	-	✓	-	-
Rheumatic fever		-	-	✓	-	-	-	-

Other investment applicable to more than one neglected disease

Platform technologies			
General diagnostic platforms	Adjuvants and immunomodulators	Delivery technologies and devices	Core funding of a multi-disease R&D organisation
Restricted	Restricted	Restricted	✓

HANDLING OF EMERGING INFECTIOUS DISEASES

In response to the 2014 West African Ebola epidemic, the FY2014 (year eight) G-FINDER survey scope was expanded to capture investments in Ebola R&D for diagnostics, drugs and preventive vaccines, as well as basic research. For FY2015 (year nine), the survey scope was further expanded to include other African viral haemorrhagic fevers (VHFs). In addition to Ebola, this new category allowed respondents to report R&D funding for Marburg and other African VHFs.

Because of the unique nature of the Ebola threat and global response, and its distorting effect on analysis of the R&D funding landscape for neglected diseases, R&D funding for Ebola and other African VHFs was analysed separately in the year nine G-FINDER report.

The separation of emerging infectious diseases (EIDs) and neglected diseases was formalised this year. For the FY2016 (year ten) survey, a separate scope definition was developed to identify investments in R&D for all priority EIDs identified in the WHO R&D Blueprint for action to prevent epidemics. EID data is not included in this G-FINDER neglected disease report, and will be reported separately.

TYPES OF RESEARCH INCLUDED

The purpose of G-FINDER is to track and analyse global investment in the research and development of new health technologies for neglected diseases. It does not, and is not intended to, capture investment in the entire spectrum of neglected disease research. There is a broad range of research activities that are extremely important for improving global health, but which are excluded from this report because they are not related to the development of new tools for neglected diseases, including health systems and operations/implementation research (for example, research into health systems or policy issues, or research into the programmatic delivery of non-product interventions, or existing health technologies), and sociological, behavioural and epidemiological research not related to the development of new health technologies. We also exclude investment into non-pharmaceutical tools such as untreated bed nets, or interventions such as circumcision. General therapies such as painkillers or nutritional supplements are excluded, as these investments cannot be ring-fenced to neglected disease treatment only. Investment that is not research-related is similarly excluded: although we recognise the vital importance of activities such as health programme delivery, advocacy, routine disease surveillance programmes, community education and general capacity building to address neglected diseases, investment in these activities falls outside the scope of G-FINDER.

G-FINDER quantifies neglected disease R&D investments into two overarching categories, each broken down into a number of further categories:

- Basic and early stage research, including:
 - Basic research
 - Product discovery and pre-clinical development
- Clinical and field development and post registration studies, including:
 - Baseline epidemiology in preparation for product trials
 - Clinical or field product development
 - Phase IV/pharmacovigilance studies of new products

A detailed explanation of what types of R&D activities are included in each of these categories, as well as specific inclusions and exclusions related to the G-FINDER scope, is provided in the G-FINDER neglected disease R&D scope document, which is available online.

Survey methodology

DATA COLLECTION

Over the past decade, the G-FINDER survey has operated according to two key principles: capturing and analysing data in a manner that is consistent and comparable across all funders and diseases; and presenting funding data that is as close as possible to 'real' investment figures.

G-FINDER was originally designed as an online survey. An online survey platform was developed to capture grant data and is still used by the majority of survey participants. An offline grant-based reporting tool is also available. Industry (pharmaceutical companies and biotechnology firms) investment in R&D is not grant-based, so the reporting tool has been tailored for these participants. Instead of grants, companies enter the number of staff working on neglected disease programmes, their salaries, and direct project costs related to these programmes. Companies are required to exclude 'soft figures' such as in-kind contributions and costs of capital.

For some organisations with very large datasets, the online survey and equivalent offline reporting tool are difficult to use. The G-FINDER team was therefore asked to use publicly available databases to identify the relevant funding. For the US National Institutes of Health (NIH), grants were collected using the Research Portfolio Online Reporting Tools (RePORTER) and the Research, Condition and Disease Categorization (RCDC) process. For the Biomedical Advanced Research and Development Authority (BARDA), funding information was identified using the international and domestic 'Project Maps' retrieved from the Medical Countermeasures website. Funding from the European Commission (EC)[^] was retrieved from the Community Research and Development Information Service (CORDIS) public database and Innovative Medicines Initiative's (IMI) online project list. Supplementary data was provided by the EC.

All participating organisations were asked to only include disbursements (or receipts), rather than commitments made but not yet disbursed. In general, only primary grant data was accepted; the only exception is in the case of data collection collaborations between G-FINDER and other R&D funding surveys, such as AVAC. Data from all sources was subject to verification using the same processes and inclusion criteria.

VALIDATION

All entries over \$0.5m were verified against the inclusion criteria. Cross-checking was conducted using automated reconciliation reports – which match investments reported as disbursed by funders with investments reported as received by intermediaries and product developers – followed by manual grant-level review of the report outputs. Any discrepancies were resolved by contacting both groups to identify the correct figure. For grants from the US NIH, funding data was supplemented and cross-referenced with information received from the Office of AIDS Research (OAR) and the National Institute of Allergy and Infectious Diseases (NIAID).

UNSPECIFIED FUNDING

Around 2.3% (\$73m) of funding was reported to the survey as 'unspecified', usually for multi-disease programmes where funds could not easily be apportioned by disease. A proportion of funding for some diseases was also 'unspecified', for instance, when funders reported a grant for research into tuberculosis (TB) basic research and drugs without apportioning funding to each product category. This means that reported funding for some diseases and products will be slightly lower than actual funding, with the difference being included as 'unspecified' funding.

[^] The term 'EC' used here and throughout the report refers to funding from the European Union budget that is managed by the European Commission or related European Union partnerships and initiatives, such as the European & Developing Countries Clinical Trials Partnership (EDCTP) and Innovative Medicines Initiative (IMI)

A further 4.2% (\$136m) was given as core funding to R&D organisations that work in multiple disease areas, for example, the European & Developing Countries Clinical Trials Partnership (EDCTP) and the Foundation for Innovative New Diagnostics (FIND). As this funding could not be accurately allocated by disease it was reported as unallocated core funding. In cases where grants to a multi-disease organisation were earmarked for a specific disease or product, they were included under the specific disease-product area.

DATA AGGREGATION

All pharmaceutical industry funding data has been aggregated and anonymised for confidentiality purposes. Rather than being attributed to individual companies, pharmaceutical company investment is instead reported according to the type of company, with a distinction made between multinational pharmaceutical companies (MNCs) and small pharmaceutical and biotechnology companies (SMEs).

INFLATION ADJUSTMENTS

Funding data has been adjusted for inflation and converted to US dollars (US\$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations, allowing accurate comparison of annual changes. Due to these adjustments, historical G-FINDER data in tables and figures in this report will differ to data in previous G-FINDER reports. All funding data in this report is in 2016 US\$.

LIMITATIONS

While the survey methodology has been refined over the past decade, there are limitations to the data presented, including survey non-completion, time lags in the funding process, an inability to disaggregate some investments, and non-comparable or missing data. Please see the G-FINDER methodology document, available online at www.policycuresresearch.org/g-finder-2017, for a more in-depth discussion of these limitations.

Reading the G-FINDER report

STRUCTURE

The G-FINDER report is structured in four main parts: 1) analysis of funding by neglected disease; 2) analysis of neglected disease funders; 3) analysis of funding flows; and 4) discussion of key findings.

YEARS

Throughout the text, references to years, other than survey years, refer to financial years.

YEAR-ON-YEAR CHANGES

It is important when comparing figures between survey years to distinguish between genuine changes in funding and apparent changes due to fluctuating numbers of survey participants. Therefore, to clearly demonstrate genuine funding changes, any increases or decreases in funding explicitly described in the report rely only on data from organisations that have participated in every year of the survey, referred to as 'year-on-year (YOY) funders'. New funding streams, for example the introduction of the Global Health Innovative Technology Fund (GHIT), are also included in YOY analysis. The YOY amounts reported may not always match the YOY amounts reported in previous years due to participation changes.

COUNTRY GROUPINGS

For brevity, we use the terms 'LMICs' and 'developing countries' to denote low- and middle-income countries and 'HICs' to denote high-income countries as defined by the World Bank.¹ Innovative developing countries (IDCs) are developing countries with a strong R&D base, which in the context of this report refers to Brazil, India and South Africa.

BURDEN OF DISEASE FIGURES

Estimating the burden of disease is a complex process, and estimates may differ substantially between sources depending on the data and methodology used. This report presents disease burden estimates from two key sources: the Institute for Health Metrics and Evaluation's (IHME) Global Burden of Disease Study 2015 (GBD 2015),² and the World Health Organization's Global Health Estimates 2015 (GHE 2015).³ Estimates of mortality and disability-adjusted life years (DALYs) in LMICs from GBD 2015 are presented for all G-FINDER neglected diseases, where available. Estimates of global and LMIC mortality from GHE 2015 are also included, where available. We note some GBD 2015 estimates may differ from those published in previous G-FINDER reports due to updates to IHME's methodology.⁴

Pathogen specific diagnosis for diarrhoeal diseases, and bacterial pneumonia & meningitis is challenging, which affects estimates for burden of disease. The diarrhoeal disease group in GBD 2015 is presented by cause and includes diseases outside the scope of G-FINDER, and does not include estimates for *Giardia*. Therefore, estimates of mortality and DALYs for the diarrhoeal disease group presented in this report have been calculated by subtracting pathogens identified by aetiology as out of scope from the GBD 2015 diarrhoeal disease grouping by cause totals. GBD 2015 includes an 'Other meningitis' aetiology category that is not disaggregated to a level where it can be established what proportion of the data falls in or out of the scope of G-FINDER. Estimates of mortality and DALYs for bacterial pneumonia & meningitis presented in this report include 'Other meningitis', and may therefore include some burden of disease caused by pathogens outside the scope of G-FINDER. For helminth infections (worms and flukes), GBD 2015 figures presented in this report do not include estimates for strongyloidiasis.

The latest G-FINDER survey

The tenth G-FINDER survey was open for a seven-week period from June to July 2017. Intensive follow-up and support for key participants led to a total of 10,144 recorded entries in the database for financial year 2016.

PARTICIPANTS

G-FINDER is primarily focused on funding, and therefore the emphasis is on surveying funding organisations. A total of 187 organisations participated in the G-FINDER survey in 2017, reporting on behalf of 194 organisations. 123 of the 187 direct participants were funders. A wide range of funding intermediaries, product development partnerships (PDPs), and researchers and developers who received funding also participated. Data from funding recipients was used to collect data on investments from funders who did not participate in the survey; to better understand how and where R&D investments were made; to track funding flows through the system; to prevent double counting; and to verify reported data.

Participants originated from 32 countries. Organisations included:

- Public, private and philanthropic funders from 21 HICs
- The EC
- Public funders in three IDCs (Brazil, India and South Africa)
- Public funders in an additional four MICs (Argentina, Colombia, Mexico and Thailand)
- Private sector funders in two MICs (Brazil and India)
- Academic organisations from six MICs.

ONLINE SEARCH TOOL

All of the data behind the G-FINDER report is available through the online search tool at <https://gfinder.policycuresresearch.org/PublicSearchTool>

Table 2. Disease and product R&D funding 2016 (US\$ millions)

Disease or R&D area	Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products	Unspecified	Total
HIV/AIDS	169.87	24.26	724.29	9.18	28.91	124.59		21.21	1,102.30
Malaria	138.90	218.11	115.54		20.53		59.89	23.42	576.40
<i>P. falciparum</i>	68.78	89.76	73.98		8.04		6.99	7.11	254.66
<i>P. vivax</i>	9.73	59.49	7.02		5.97		0.47	0.48	83.15
Multiple and/or other malaria strains	60.40	68.87	34.54		6.53		52.42	15.83	238.58
Tuberculosis	151.84	262.19	74.34	5.81	51.33			22.60	568.11
Diarrhoeal diseases	34.14	6.83	84.75		11.90			7.78	145.39
Rotavirus			37.94					0.92	38.86
<i>Shigella</i>	5.67	0.42	15.44		1.36			0.99	23.89
Cholera	15.19	0.54	6.46		1.10			0.07	23.37
<i>Cryptosporidium</i>	6.24	5.74	1.01		0.25			0.26	13.50
Enterotoxigenic <i>E. coli</i> (ETEC)			9.18		0.41			0.09	9.68
Enterotoxigenic <i>E. coli</i> (EAggEC)			0.54		0.21			0.08	0.82
<i>Giardia</i>					0.02			0.12	0.14
Multiple diarrhoeal diseases	7.04	0.12	14.19		8.56			5.25	35.16
Kinetoplastids	50.30	61.10	6.40	2.00	4.70		0.78	5.88	131.17
Leishmaniasis	15.81	14.35	4.91	0.30	1.79			4.09	41.25
Sleeping sickness (HAT)	19.00	13.88	0.59		0.96		0.72	1.39	36.54
Chagas' disease	12.07	7.85	0.89	1.70	1.93		0.06	0.05	24.55
Multiple kinetoplastid diseases	3.43	25.02	0.01	-	0.02		-	0.35	28.82
Dengue	49.92	28.43			9.38		19.73	5.36	112.82
Bacterial pneumonia & meningitis	9.29		81.39		0.86			-	91.55
<i>S. pneumoniae</i>	7.52		57.87		0.71			-	66.10
<i>N. meningitidis</i>	0.98		23.52		0.07			-	24.58
Both <i>S. pneumoniae</i> and <i>N. meningitidis</i>	0.79				0.08			-	0.87
Salmonella infections	45.49	3.77	36.84		4.22			1.14	91.46
Typhoid and paratyphoid fever (<i>S. Typhi</i> , <i>S. Paratyphi A</i>)	31.13	2.99	34.53		2.77			-	71.42
Non-typhoidal <i>S. enterica</i> (NTS)	2.96	0.48	0.41		0.81			-	4.66
Multiple <i>Salmonella</i> infections	11.40	0.30	1.91		0.64			1.14	15.38
Helminth infections (worms & flukes)	29.49	30.90	7.70		2.46		0.10	3.90	74.56
Schistosomiasis (bilharziasis)	10.13	2.90	2.24		1.45		0.07	1.58	18.37
Lymphatic filariasis (elephantiasis)	6.64	7.27			0.12		0.02	1.78	15.82
Onchocerciasis (river blindness)	1.31	7.36	0.45		0.65		0.02	0.48	10.25
Hookworm (ancylostomiasis & necatoriasis)	0.27	0.85	2.71					0.05	3.87
Tapeworm (taeniasis/cysticercosis)	1.76	1.85					-	-	3.61
Whipworm (trichuriasis)	0.87	0.94						-	1.81
Strongyloidiasis & other intestinal roundworms	0.68	0.47	<0.01		0.24			-	1.39
Roundworm (ascariasis)	0.83	0.45						-	1.28
Multiple helminth infections	7.01	8.82	2.30		-		-	0.02	18.15

Disease or R&D area	Basic research		Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products	Unspecified	Total
		Drugs							
Hepatitis C (genotypes 4, 5 & 6)		11.92	3.47		6.95			0.03	22.37
Leprosy	6.57	0.18			0.39			3.91	11.06
Cryptococcal meningitis		5.64							5.64
Buruli ulcer	1.05	1.17	-		0.48			0.05	2.76
Leptospirosis					2.31				2.31
Trachoma			1.19		0.22			0.76	2.18
Rheumatic fever			1.18					0.10	1.28
Core funding of a multi-disease R&D organisation									135.99
Unspecified disease									73.18
Platform technologies	General diagnostic platforms		Adjuvants and immunomodulators		Delivery technologies and devices				
	18.30		17.68		16.23				52.21
Total R&D funding									3,202.74

- No reported funding

Category not included in G-FINDER