INTRODUCTION

Background to the G-FINDER survey

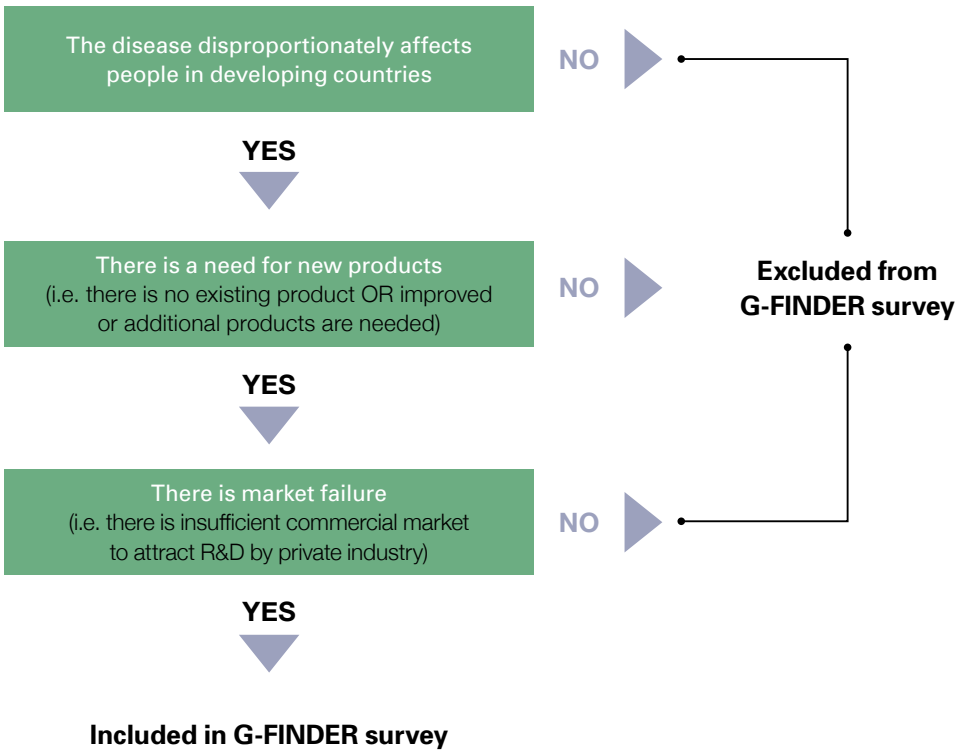
The first eight G-FINDER reports shed light on global investment into research and development (R&D) of new products to prevent, diagnose, manage or cure neglected diseases of the developing world each year since 2007. The ninth G-FINDER survey reports on 2015 investments.

The survey

WHICH DISEASES AND PRODUCTS ARE INCLUDED?

The scope of the G-FINDER survey is determined by applying three criteria (see Figure 1). Application of these criteria results in 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



Ebola and other African viral haemorrhagic fevers analysed separately

All product R&D is covered by the survey, 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 neglected diseases and products, but which have not yet been attached to a specific product for a specific disease.

We note that not all product types are needed for all diseases. For example, effective pneumonia management requires new developing-world specific vaccines, but does not need new drugs as therapies are either already available or in commercial development.

Funders were asked to only report investments *specifically* targeted at developing-country R&D needs. This is important to prevent neglected disease data being swamped by funding for activities not directly related to product development (e.g. advocacy and behavioural research); or by 'white noise' from overlapping commercial R&D investments (e.g. HIV/AIDS drugs and pneumonia vaccines targeting Western markets, and investments in platform stechnologies with shared applications for industrialised countries). As an example, G-FINDER defines eligible pneumonia vaccine investments by strain, vaccine type and target age group; while eligible HIV/AIDS drug investments are restricted to developing-country relevant products such as fixed-dose combinations (FDCs) and paediatric formulations.

The initial scope of G-FINDER diseases and eligible R&D areas was determined in the first survey year (2007) in consultation with an international Advisory Committee (AC) of experts in neglected diseases and neglected disease product development. A second round of consultations took place in year two. As a result of this process, for the 2008 survey, the typhoid and paratyphoid fever disease category was broadened to include non-typhoidal *Salmonella enterica* (NTS) and multiple *Salmonella* infections; while diagnostics for lymphatic filariasis were added as a neglected area.

In year seven, following a review by our AC (Annexe 2), the survey was expanded to include three additional diseases: cryptococcal meningitis, hepatitis C genotype 4 and leptospirosis. The AC review also decided that dengue vaccines no longer fit the criteria for inclusion in the G-FINDER survey given the emergence of a significant commercial market, and dengue vaccine R&D (including all previously reported investments) was removed from the scope of the survey. This does not affect other dengue products, which continue to be included.

In response to the 2014 West African Ebola epidemic, the survey scope was expanded again in year eight to capture investments in Ebola R&D for diagnostics, drugs and preventive vaccines, as well as basic research. On the advice of the AC, the scope of the hepatitis C category was also expanded to capture investment into R&D for two additional genotypes that disproportionately affect people in developing countries (genotypes 5 and 6).

After further consultation with the AC, a new grouped disease category was incorporated in this year's survey: African viral haemorrhagic fevers (VHFs). In addition to Ebola, this new category allowed respondents to report R&D funding for Marburg and Other and/or multiple African VHFs. Because of the unique nature of the Ebola threat and global response – evidenced by the significant influx of private sector investment seen in this year's survey – R&D funding for Ebola and other African VHFs has been analysed separately in order not to distort the main neglected disease analysis.

The scope of G-FINDER neglected diseases, products and technologies included in year nine is shown in Table 1.

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

Disease		Basic research	Drugs	Vaccines (Preventive)	Vaccines (Therapeutic)	Microbicides	Vector control products	Diagnostics
HIV/AIDS		R	R	Y		Y		Y
Tuberculosis		Y	Y	Y	Y			Y
Malaria	*P. falciparum*	Y	Y	Y			Y	Y
	P. vivax	Y	Y	Y			Y	Y
	Other and/or unspecified malaria strains	Y	Y	Y			Y	Y
Diarrhoeal diseases	Rotavirus			R				
	Cholera	Y	R	Y				Y
	Shigella	Y	R	Y				Y
	Enterotoxigenic *E. coli* (ETEC)			Y				Y
	Cryptosporidium	Y	R	Y				Y
	Enteroaggregative *E.coli* (EAggEC)			Y				Y
	Giardia							Y
	Multiple diseases	Y	R	Y				Y
Kinetoplastids	Leishmaniasis	Y	Y	Y	Y			Y
	Sleeping sickness	Y	Y	Y			Y	Y
	Chagas' disease	Y	Y	Y	Y		Y	Y
	Multiple diseases	Y	Y	Y	Y		Y	Y
Dengue		Y	Y				Y	Y
Bacterial pneumonia & meningitis	*S. pneumoniae*			R				Y
	N. meningitidis			R				Y
	Both bacteria							Y
Helminth infections	Schistosomiasis (bilharziasis)	Y	Y	Y			Y	Y
	Lymphatic filariasis (elephantiasis)	Y	Y				Y	Y
	Onchocerciasis (river blindness)	Y	Y	Y			Y	Y
	Hookworm (ancylostomiasis & necatoriasis)	Y	Y	Y				
	Tapeworm (cysticercosis/taeniasis)	Y	Y				Y	
	Strongyloidiasis & other intestinal roundworms	Y	Y	Y				Y
	Whipworm (trichuriasis)	Y	Y					
	Roundworm (ascariasis)	Y	Y					
	Multiple diseases	Y	Y	Y			Y	Y
Salmonella infections	Typhoid and paratyphoid fever (*S. typhi, S. paratyphi A*)	Y	Y	Y				Y
	Non-typhoidal *S. enterica (NTS)*	Y	Y	Y				Y
	Multiple *Salmonella* infections	Y	Y	Y				Y
Hepatitis C (genotypes 4, 5 & 6)			R	Y				Y
Leprosy		Y	Y					Y
Cryptococcal meningitis			Y					
Trachoma				Y				Y
Rheumatic fever				Y				
Buruli ulcer		Y	Y	Y				Y
Leptospirosis								R
Platform technologies (non-disease specific)		General diagnostic platforms			Adjuvants and immunomodulators		Delivery technologies and devices	
			R			R		R
African viral haemorrhagic fevers (VHFs)	Ebola	Y	Y	Y				Y
	Marburg	Y	Y	Y				Y
	Other and/or multiple African VHFs	Y	Y	Y			Y	Y

'R' denotes a restricted category where only some investments are eligible, as defined in the neglected disease R&D scope document
'Y' denotes a category where a disease or product is included in the survey

WHAT TYPES OF INVESTMENTS ARE INCLUDED?

G-FINDER quantifies neglected disease investments in the following R&D areas:

- 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 are outside the scope of G-FINDER. We also exclude investment into non-pharmaceutical tools such as bednets or circumcision, and general therapies such as painkillers or nutritional supplements, as these investments cannot be ring-fenced to neglected disease treatment only.

HOW WAS DATA COLLECTED?

Two key principles guided the design of the G-FINDER survey. We sought to provide data in a manner that was consistent and comparable across all funders and diseases, and as close as possible to 'real' investment figures.

G-FINDER was therefore designed as an online survey into which all organisations entered their investment data in the same way according to the same definitions and categories, and with the same inclusion and exclusion criteria. All funders were asked to only include disbursements, as opposed to commitments made but not yet disbursed; and we only accepted primary grant data. The exception was the United States National Institutes of Health (US NIH), for whom data was collected by mining the US NIH's Research Portfolio Online Reporting Tools (RePORTER) and Research, Condition, and Disease Categorization (RCDC) process.

Participating multinational pharmaceutical companies (MNCs) agreed to provide full data on their neglected disease investments. However, as these companies do not operate on a grant basis, the reporting tool was varied. 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 ninth G-FINDER survey was open for a six-week period from June to July 2016, during which intensive follow-up and support for key recipients led to a total of 9,070 entries being recorded in the database for financial year 2015.

With the exception of grants from major key funders, in particular the US NIH, all entries over $0.5m (i.e. any grant over 0.01% of total funding) were verified against the inclusion criteria and crosschecked for accuracy. Cross-checking was conducted through automated reconciliation reports that matched investments reported as disbursed by funders with investments reported as received by intermediaries and product developers. Any discrepancies were resolved by contacting both groups to identify the correct figure. 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). Industry data was aggregated for MNCs and for small pharmaceutical and biotechnology companies (SMEs) in order to protect their confidentiality.

WHO WAS SURVEYED?

A total of 185 organisations participated directly in the G-FINDER survey, reporting data on behalf of a total of 209 organisations. This meant that we received data for more organisations than the previous year, despite targeting our survey follow-up to increase efficiency.

G-FINDER is primarily a survey of funding, and thus of funders. In its ninth year, 143 funders in 29 countries around the world participated in the survey. These included:

- Public, private and philanthropic funders in:
  - High-income countries (HICs) that are part of the Organisation for Economic Co-operation and Development (OECD)
  - European Union (EU) member states and the European Commission (EC)
- Public funders in three Innovative Developing Countries (IDCs) (Brazil, India and South Africa)
- Public funders in an additional three middle-income countries (MICs) (Colombia, Mexico and Thailand)
- Private sector funders in two MICs (Brazil and India)

G-FINDER also surveyed a wide range of funding intermediaries, product development partnerships (PDPs), and researchers and developers who received funding. Data from these groups was used 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.

HOW WERE CHANGES IN PARTICIPATION MANAGED?

It is important when comparing figures between survey years to distinguish between real changes in funding and *apparent* changes due to fluctuating numbers of survey participants. Funding figures have therefore been broken down to distinguish between:

1. Increases or decreases reported by repeat survey participants – called YOY funders – which represent real funding changes
2. Changes associated with irregular survey participants. These include increases reported by new survey participants and decreases due to non-participation by organisations that provided data to G-FINDER in previous years but which were lost to follow-up. These do not represent true changes in neglected disease funding, but rather are related to expansion or contraction of G-FINDER's data capture.

Reading the findings

The ninth G-FINDER survey collected data on financial year 2015 investments. Throughout the text, we refer to survey years as follows: 2007 refers to financial year 2007 (year one of the survey), 2008 refers to financial year 2008 (year two of the survey) and so on up to the current year (financial year 2015, year nine of the survey).

Any changes in funding (increases or decreases) noted in the report refer only to those organisations that participated across all years of the survey, i.e. YOY funders. Any real new funding streams, for example the introduction of the Global Health Innovative Technology Fund (GHIT), are also included in YOY analysis. YOY amounts reported in previous years may not always match the YOY amount reported in year nine due to dropouts (i.e. loss to follow-up).

All funding is reported in constant 2015 US dollars

As in previous G-FINDER reports, all funding data has been adjusted for inflation and converted to US dollars (US$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations, thus allowing accurate comparison of YOY changes. In line with the new approach to financial reporting implemented in year seven, the base year of the survey for inflation adjustment purposes has been updated to the current financial year of the survey, and so all funding data is reported in 2015 US$. As a result of this rebasing, historical G-FINDER data for the years 2007 to 2014 presented in this report will differ from the figures published in previous G-FINDER reports.

Unless noted otherwise, all DALY (disability-adjusted life year) and mortality figures in the report specifically represent low- and middle-income country (LMIC) figures and are taken from the Global Burden of Disease Study 2015 (GBD 2015),[1] which represent the most comprehensive and recent figures available. We note that some of the GBD 2015 methodologies have been updated compared to previous GBD studies,[2] so the figures quoted in this report may not be directly comparable to the figures published in previous G-FINDER reports. Due to the level of detail in GBD 2015, figures for bacterial pneumonia & meningitis reflect only DALYs and mortality related to pathogens that are within G-FINDER scope. In some cases, GBD 2015 estimates are different from those derived using other methods or published by other groups, however they allow the most consistent approach across diseases.

For brevity, we use the terms 'LMICs' and 'developing countries' (DCs) to denote low- and middle income countries and 'HICs' to denote high-income countries as defined by the World Bank.[3] IDCs refers to developing countries with a strong R&D base (Brazil, India and South Africa) who participated in the G-FINDER survey. MNCs are defined as multinational pharmaceutical companies with revenues of over $10bn *per annum*.

Around 1.6% ($53m) 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.

A further 4.1% ($132m) was given as core funding to R&D organisations that work in multiple disease areas, for example, the European and 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.

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 methodological choices (see Online annexe A for further details).