



SAVING LIVES

Making the case for European investment in poverty-related and neglected disease R&D

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Deutsche Stiftung Weltbevölkerung (DSW)

Deutsche Stiftung Weltbevölkerung (DSW) is an international development organisation that focuses on the needs and potential of the largest youth generation in history. We are committed to creating demand for and access to health information, services and supplies, and to securing their right for a brighter future. We achieve this by engaging in advocacy, capacity development, and family planning initiatives, which make sure the youth of today are empowered to lead healthy and self-determined lives. With our headquarters in Hannover, Germany, DSW maintains four country offices in Ethiopia, Kenya, Tanzania, and Uganda, as well as liaison offices in Berlin and Brussels. DSW also advocates for investment in research and innovation to fight poverty-related and neglected tropical diseases – diseases that continue to disproportionately affect women and girls.

Policy Cures

Policy Cures is an independent not-for profit group based in Sydney, providing research, information, decision-making tools and strategic analysis for those involved in the creation of new pharmaceuticals for global health. The Policy Cures team has focused exclusively on product development related to global health since 2004, from R&D activities and portfolios, to developers, business models, funding, incentives, pricing and access issues.

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CONTENTS

Acronyms and Glossary	2
Executive Summary	4
Introduction	8
Key concepts	10
European public funding for PRND R&D	12
Funding from the EU	14
Funding from European Governments	15
How does the EU fund PRND R&D?	16
How do European Governments fund PRND R&D?	18
Which PRNDs are being funded?	19
Who does European public funding go to?	21
What type of research is being funded?	24
The benefits to global health as a result of EU investment	25
The impact of EU-funded tools	25
A pipeline of new products for the future	26
Capacity building	29
The benefits to Europe as a result of EU investment	30
Investing in Europe for jobs and growth	30
Investing in research excellence	31
Leveraging investment from the private sector	32
Investing in SMEs	32
Discussion	33
Appendix 1: Methodology	36
References	37





U.S. Army photo by Rick Scavetta

ACRONYMS AND GLOSSARY

CEWG	Consultative Expert Working Group on Research and Development: Financing and Coordination
DALY	Disability adjusted life year
DFID	United Kingdom Department for International Development
DG DEVCO	European Commission's Directorate-General for International Cooperation and Development
EDCTP	European & Developing Countries Clinical Trials Partnership
EMA	European Medicines Agency
ERC	European Research Council
EU	European Union
European Governments	EU's 28 member states plus Norway and Switzerland
European public funders	European Governments and European Union
EVI	European Vaccine Initiative
Framework Programmes	The EU's Framework Programmes for Research and Innovation, including Horizon 2020
GDP	Gross domestic product
HIV/AIDS	Human immunodeficiency virus / acquired immune deficiency syndrome
IMI	Innovative Medicines Initiative
LMIC	Low- and middle-income countries
MNC	Multinational pharmaceutical companies with revenues of over US\$10 billion per annum
MS	Member states of the EU



MSCA	Marie Skłodowska-Curie actions
NIDs	Neglected infectious diseases
PDP	Product development partnerships. Public health driven, not-for-profit organisations that typically use private sector management practices to drive product development in conjunction with external partners.
PRNDs	Poverty-related and neglected diseases
PS	Participating States, EDCTP
Public funders	Governments, government agencies, and government-affiliated research institutions. This category includes government research institutions, other research institutions and public sector pharmaceutical companies
R&D	Research and development
S&T	Science and technology
SC1	Societal Challenge 1: Health, Demographic Change and Wellbeing
SDGs	Sustainable Development Goals
SME	Small pharmaceutical and biotechnology firms with revenues of less than US\$10 billion per annum
TB	Tuberculosis
TBVI	TuBerculosis Vaccine Initiative
US	United States
VCP	Vector control product
WHO	World Health Organization



EXECUTIVE SUMMARY

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Poverty-related and neglected diseases (PRNDs) are infectious diseases that disproportionately affect the world's poorest populations. There is a dire lack of vaccines, diagnostics, drugs and other products that can address these diseases and lessen the burden. This dearth has arisen because there is insufficient commercial incentive for the private sector to invest in research and development (R&D). Since the market fails to innovate, public funding (funds from government organisations) is critical.

This report provides an in-depth analysis of European public funding for PRND R&D since 2007. It looks principally at European Union (EU) support for PRND R&D and how this compares with the direct investments made by European Governments (EU member states, Norway and Switzerland), as well as analysing the impact that this investment has had on global health, and the benefits it has created for Europe.

How much have European public funders invested in PRND R&D?

European public funders are significant contributors to global PRND R&D efforts, providing 20% of all public funding globally between 2007 and 2014. European Governments invested an average of €260 million each year during this period, while the EU provided around €100 million of grant funding to researchers annually.

The EU provides over a quarter of European public funding – an impressive figure, given that the annual budget of the EU is around 1% of the Gross National Income of its 28 Member States. Although this reflects positively on the EU's commitment to global health, it also reveals the relatively low level of contributions from European Governments, with every European country falling well below the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) target of dedicating 0.01% of GDP to PRND R&D.

Funding from both the EU and European Governments fell in four out of the five years between 2009 and 2014. EU funding increased markedly in 2015 as a result



Lucy Milmo/DFID

of significant new investment in Ebola research, but despite this increase it remains lower than both its 2009 peak and the 0.01% of GDP CEWG target. It is yet to be seen whether European Government funding for 2015 will reflect a similar Ebola-related boost.

Both European Governments and the EU have primarily focused on R&D for HIV/AIDS, malaria and TB. However, the concentration of funding on these three diseases has decreased considerably since 2007, outstripping the global trend towards more diversified funding of R&D across the spectrum of neglected diseases.

The EU has been increasingly funding more late-stage research, while European Governments have been moving in the opposite direction. Historically, both European Governments and the EU have directed around 30% of investment to basic research. This is changing: cuts to aid budgets have meant that many European Governments have been reducing their investments in product development partnerships (PDPs), whilst increasing funding for basic research. In contrast, the EU has increased its investment in product development – a trend accelerated by its recent Ebola investments, and which is likely to be sustained given the increased budget of the second European & Developing Countries Clinical Trials Partnership (EDCTP2).

The most striking difference between the EU funding and that of European Governments is in the type of organisations they fund. The EU primarily gives its funding directly to researchers in the public sector (including universities and other academic research institutes); just 12% of EU funding since 2007 went to industry and PDPs, the two groups most commonly responsible for later stage product development. In contrast, 41% of all European Government funding for PRND R&D was managed by PDPs – a proportion that increases to 85% when looking just at aid agency funding.

What research has been supported?

What are the global health benefits of EU investment in PRND R&D?

EU investment in PRND R&D has helped to deliver products that have already had an impact on global health, as well as a robust pipeline of products that have the potential to deliver significant benefits in the future. For example, EU funding contributed to the development of half of all new malaria drugs registered since 2000, and more than 1 in 10 of the most advanced candidates in the global PRND R&D pipeline are being developed with funding from the EU.

The EU's investment in capacity building recognises the importance of developing the talents of researchers from low- and middle-income countries (LMICs). It has invested heavily in both training researchers from LMICs as well as clinical trial infrastructure through the EDCTP and European Commission Directorate General for International Cooperation and Development (DG DEVCO). This investment, which has resulted in over 500 researchers being trained, is beginning to bear fruit, with 72% of EDCTP projects in 2015 being run by African scientists.

What are the benefits to Europe of EU investment?

The benefits of EU investment in PRND R&D accrue not only to global health, but also to European economies and researchers. Of every euro spent by the EU on PRND R&D, 80 cents is reinvested back into Europe – to laboratories, universities and companies that help deliver the objectives of the Framework Programmes (driving economic growth, creating jobs and securing Europe's global competitiveness). The EU's investment in PRND R&D under FP7, for example, directly created over 10,000 jobs in Europe.

Europe's long history of neglected disease R&D is maintained by research institutes that continue to contribute to basic research and product development for PRNDs.

The organisations are collaborating with other academic institutes as well as with industry and PDPs, contributing to Europe's scientific excellence. Collectively, European organisations are involved in 45% of the current pipeline of neglected disease products, most of which are being worked on in collaborations between multiple organisations.

EU funding for small and medium pharmaceutical and biotechnology companies (SMEs) leverages significant additional investment. SMEs rely on external investment to make it viable for them to conduct PRND R&D. But every euro invested by the EU in European SMEs for PRND R&D leverages an additional €4.33 in investment from these SMEs, foreign governments and philanthropic organisations.

Discussion

EU funding increased sharply in 2015, but this is welcomed with some caution. The increased budgets for the EDCTP and Horizon 2020, as well as the significant new investment in Ebola research through the IMI, are likely to see funding sustained at or above 2015 levels for the next two to three years. Beyond 2017/8, however, there are a number of factors that may exert downwards pressure on the quantum of funds directed to PRND R&D, including the UK's planned exit from the EU, and the winding down of Ebola investments. This would be a concerning outcome, given that the current level of EU funding remains lower than its 2009 peak, and is significantly less than the 0.01% CEWG target.

The extent to which the EU's significant financial contribution is accompanied by an ability to influence or coordinate funding from European Governments is unclear.

Greater coordination amongst European public funders would reduce the potential for duplication of effort, and increase the likelihood that PRND R&D investments will result in global health impact. But we see two separate funding spheres, with strikingly little overlap between the recipients of EU and European Government funding. This is healthy when it reflects complementary funding approaches, but without coordination can lead to duplication of effort.

There is room for improvement in achieving, measuring and communicating the impact of EU investments in PRND R&D. Taking into account both the relatively narrow scope of EDCTP1 and the limited number of new products approved for malaria, HIV/AIDS and TB since its establishment, the EDCTP has played a significant role in delivering the new health technologies approved since its inception. In malaria, for example, half of all new drugs approved since 2000 have relied on EDCTP-funded trials to support their registration. On the other hand, the impact of overall EU investment in PRND R&D on global health is harder to quantify; although European organisations are highly involved in the PRND pipeline, only a quarter of late-stage candidates have received EU funding. Both the achievement and the communication of impact could be improved by implementing more appropriate metrics for measuring the success of the EU's PRND R&D investments.

Recommendations

Given the proven benefits to global health and the European economy stemming from EU support for PRND R&D, as well as the potential of existing mechanisms, the EU and European Governments should increase their support for PRND R&D, and work to leverage their respective strengths:

1. Meeting funding targets:

- The EU and European Governments should collectively and individually work towards achieving the CEWG's PRND R&D funding target of 0.01% of GDP.
- Negotiations on the UK's exit from the EU should consider the importance of the continued participation of the UK Government and UK institutions in EU-funded research programmes, including the critical importance of UK Government funding to the EDCTP budget.

2. Improving synergies:

- The EU and European Governments should develop a comprehensive, complementary and unified strategy for global health R&D, focused on leveraging both synergies and differences in the way each group supports R&D. The strategy should set out aims and priorities, as well as a roadmap for achieving them that avoids duplication and makes full use of existing coordination mechanisms such as EDCTP2.

3. Focusing on impact:

- The EU and European Governments need to maintain their support for the whole product development cycle, and direct funding to the most promising projects and actors most likely to deliver.
- The EU should measure the success of all of its PRND R&D investments with metrics that are appropriate for evaluating global health impact, and regularly report against them to show the impact of its investments.





INTRODUCTION

Kate Holt/Africa Practice

Each year, poverty-related neglected diseases (PRNDs)* such as HIV/AIDS, TB and malaria cause 6.5 million deaths, and the loss of 353 million years of healthy and productive life in developing countries.¹ They are often chronic and can result in lifelong disabilities and deformities – the stigmatisation and social exclusion suffered is not captured by these figures.

Not only is there a moral imperative to reduce the human suffering caused by these diseases, but there is also an economic argument to lessen their burden: PRNDs are both a cause and a consequence of poverty in low- and middle-income countries (LMICs). Young adults in the prime of their productive lives are prevented from working. Children, weakened by malaria and diarrhoeal diseases, fail to attend school and to develop to their full potential. Health care systems, already struggling to meet the bare requirements of LMICs, carry the added costs of unnecessary illness.

The Sustainable Development Goals (SDGs) commit to ending the epidemics of these diseases. The goals recognise the link between health and development and call for support for research and development (R&D) of vaccines and medicines for diseases that primarily affect developing countries (Target 3b). Although progress was made through the Millennium Development Goals (the rate of new HIV infections has fallen dramatically, for example), these diseases still impose an unacceptable moral and economic burden.

Although there is a global desire to significantly reduce the burden of PRNDs and achieve SDG3, good intentions will fail to produce outcomes without sustained investment in R&D, because the tools required to eliminate these disease epidemics do not currently exist. Even the best-known (and best funded) diseases still have product gaps: effective vaccines, point of care diagnostics for low-resource settings and suitable treatments, particularly for vulnerable populations such as pregnant



Conor Ashleigh for AusAID

women and infants, are lacking for HIV/AIDS, malaria and TB. The products to address other neglected infectious diseases (NIDs) are even more scarce; most lack essential diagnostics and vaccines, and the only available drugs have suboptimal efficacy, toxicity and protocol complexity. R&D investment is required to discover and develop the appropriate products for PRNDs.

The primary reason that effective health technologies for PRNDs often don't exist is that these diseases disproportionately affect poor countries and people with insufficient means to afford the products. As a consequence, there is no commercial market that would provide a financial incentive to industry to invest in R&D. Since the market fails to drive innovation, funding from groups not driven by commercial incentives (i.e. public, philanthropic organisations) is critical.

Funding for PRND R&D also needs to reflect the specific needs of non-commercial disease product development. Unlike diseases that have a commercial market, where research is commercialised by industry after early stage / proof of concept, funding for PRND R&D needs to be available for the whole process, from basic and early stage research through clinical trials to support product registration to post-registration surveillance.

*PRNDs include: HIV/AIDS, malaria, TB, kinetoplastid diseases (Chagas' disease, leishmaniasis, sleeping sickness), diarrhoeal diseases (rotavirus, enterotoxigenic *E. coli*, cholera, *Shigella*, *Cryptosporidium*, enteroaggregative *E. coli*, *Giardia*), salmonella infections (non-typhoidal *S. enterica*, typhoid and paratyphoid fever (*S. typhi*, *S. paratyphi A*)), dengue, helminths (roundworm, hookworm, whipworm, strongyloidiasis and other intestinal roundworms, lymphatic filariasis, onchocerciasis, schistosomiasis, tapeworm), bacterial pneumonia and meningitis (*S. pneumonia*, *N. meningitidis*), leprosy, Buruli ulcer, trachoma, rheumatic fever, cryptococcal meningitis, hepatitis C (genotypes 4, 5, 6), leptospirosis, and Ebola.



KEY CONCEPTS

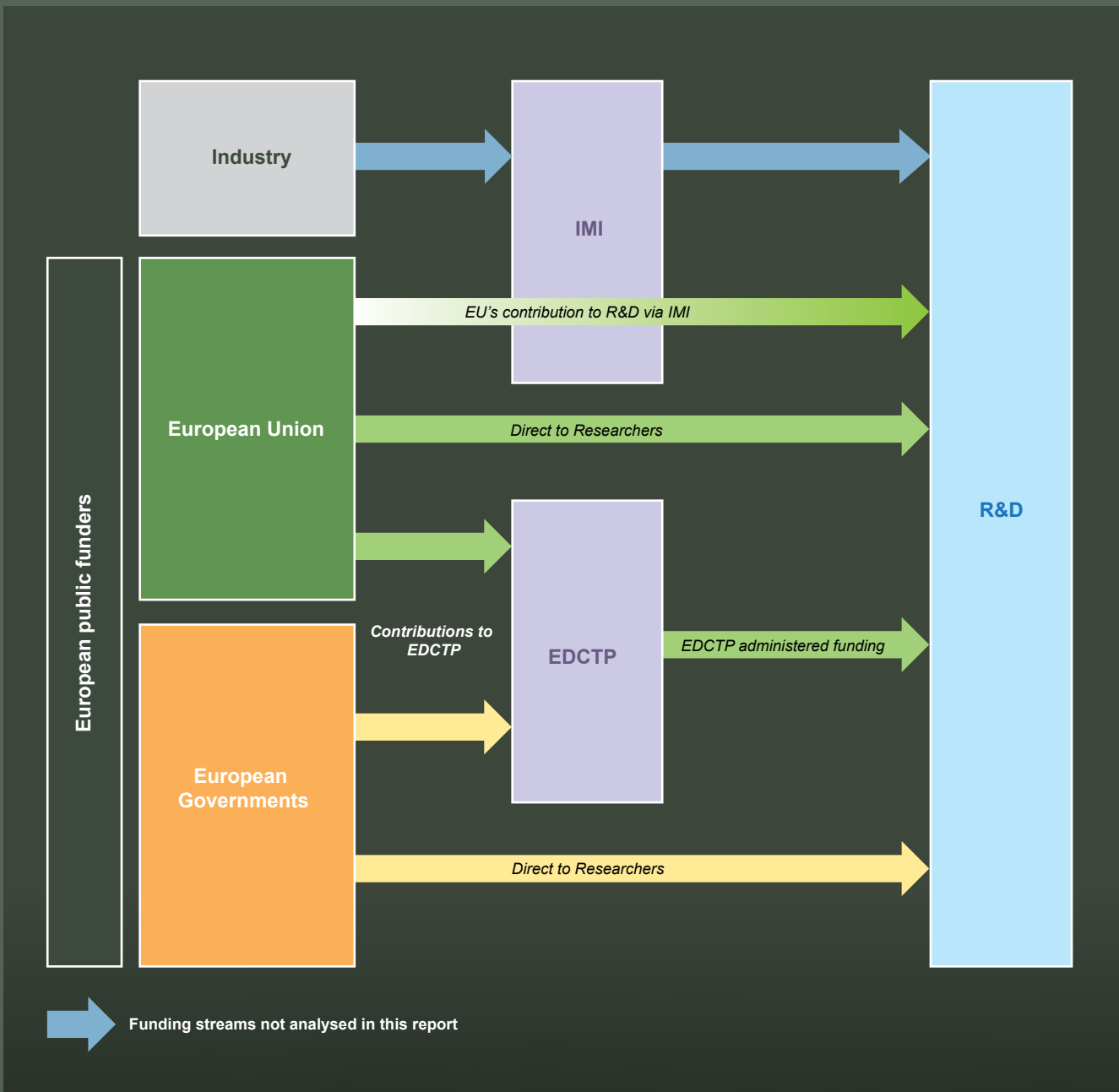
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This report provides an in-depth analysis of European public funding for PRND R&D since 2007. It looks particularly at European Union (EU) support for PRND R&D and how this compares with the direct investments of European Governments, as well as analysing the positive impact that this investment has had on global health, and the benefits it has created for Europe.

The term 'European public funding' is used to describe the collective investment from the EU and European Governments. In this report, we use the term European Governments to refer to the EU's 28 member states, as well as the governments of Norway and Switzerland (with these two countries responsible for 8% of all European Government PRND R&D investment between 2007 and 2014).

Because a large share of EU funding for PRND R&D is managed by the European & Developing Countries Clinical Trials Partnership (EDCTP), and provided as a single block grant, the analysis in this report is essentially divided into two parts. When looking at how much has been invested in PRND R&D since 2007 and through which mechanisms, as well as the trend over time, we have analysed the funding flows on the left-hand side of Figure 1. All other analysis (the breakdown by disease, recipient type and R&D stage, for example) looks at the right-hand side of Figure 1; 'EU funding' in this latter analysis includes all funding administered by the EDCTP, including the proportion that is contributed by EDCTP Participating States to the EDCTP's 'common pot'.

Figure 1 Funding streams†



KEY CONCEPTS

Funding data is from the G-FINDER survey, a survey conducted annually by Policy Cures that quantifies global investment into neglected disease R&D.² Pipeline data is from the Policy Cures data set for The Unrecognised Revolution in Global Health.³

Funding data for the EU covers the period 2007-2015, and includes unpublished data from the upcoming 2016 G-FINDER report. Data for European Governments and international comparators covers the period 2007-2014. Whenever combined totals or direct comparisons are made between EU and European Government funding, only the period 2007-2014 has been used.

All funding data is reported in 2015 euros (€). Further details can be found in Appendix 1: Methodology

† European Governments' investments in EDCTP-approved 'Participating States' Initiated Activities' is included in the 'Direct to Researchers' flow, not 'Contributions to EDCTP', as this funding is administered by the individual Government's, rather than by EDCTP. Industry also makes significant investment directly in R&D not shown in the diagram above.



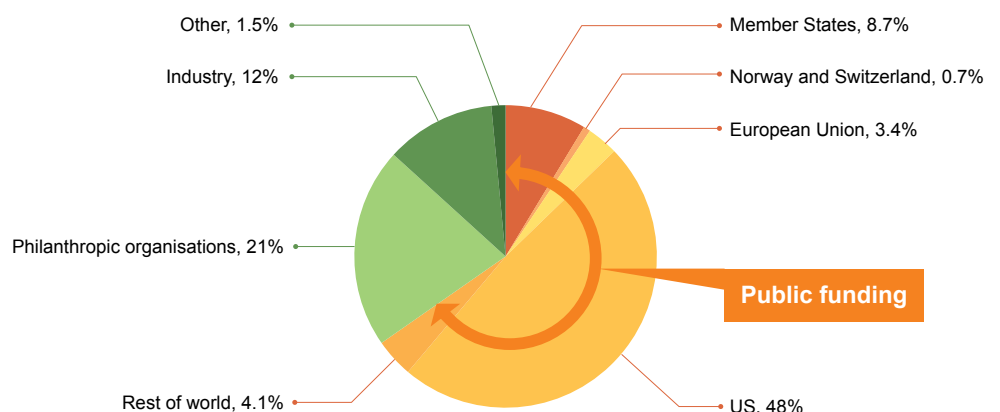
EUROPEAN PUBLIC FUNDING FOR PRND R

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Although contributing only a relatively small share of the global total, European public funders have demonstrated a serious commitment to funding of PRND R&D. In the eight years from 2007 to 2014, European public funders invested a total of €2.9 billion in PRND R&D, at an average of €363 million per year. This represents 13% of global funding for that period, and 20% of global public funding.

While the European contribution is dwarfed by that of the United States (US) Government – which provided nearly four times as much funding over the eight years – it should be recognised that European public funders invested more than three times as much as the rest of the world’s governments combined.

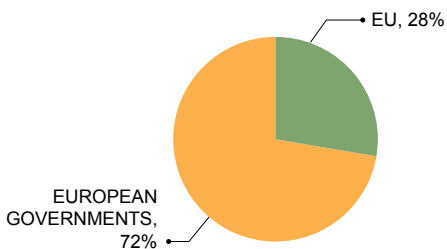
Figure 2 Who is funding PRND R&D? Share of global funding, 2007-2014





&D

Although around three-quarters (72%) of European public funding between 2007 and 2014 came directly from European Governments, this in turn means that the EU was responsible for 28% of all European public funding for PRND R&D during this period – an impressive figure, given that the annual budget of the EU is around 1% of the Gross National Income of its 28 Member States.



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FUNDING FOR PRND R&D 2007-2014

€2.9 billion

Collective total investment by European public funders

(Member State governments, Norway, Switzerland and the EU)

13%

of all global PRND R&D funding came from European public funders

€363 million

Average total annual investment by all European public funders

72%

of European public funding invested by European Governments

28%

of European public funding invested by the EU

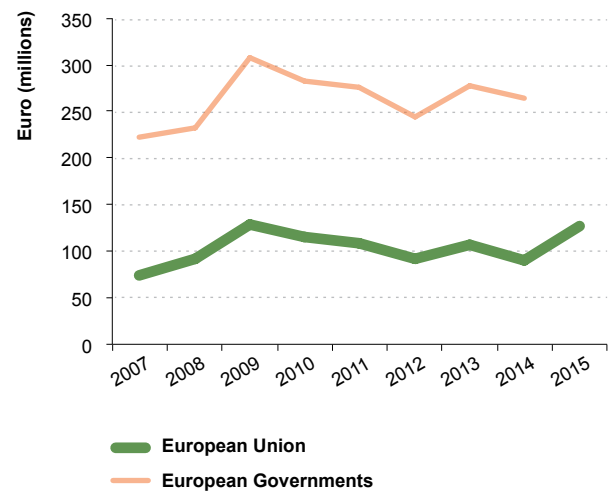
Funding from the EU

EU funding for PRND R&D has been relatively stable over the last nine years, averaging around €100 million per year since 2007. And, despite EU funding cycles being linked to the timing of its multiannual Framework Programmes for Research and Innovation (Framework Programmes), the trend in EU funding over time is almost identical to that of European Governments.

In the case of European Governments, the sharp increase in funding for PRND R&D in 2009 was the result of stimulus packages following the global financial crisis, which included increased investment in domestic R&D. EU funding also peaked in 2009, however it is unclear to what extent this was stimulus related, or whether it simply reflected the natural ramping up of investment in the first two years of FP7, its new Framework Programme (which began in 2007).

What is clear is that – prior to 2015 – EU funding had been trending downwards from its 2009 peak, falling by 7% per year on average. In 2015 it then increased sharply (up €37 million, 42%), which was entirely due to significant new investment in Ebola R&D; whether, and to what extent, an increase would have occurred if the West African Ebola outbreak had not happened will likely remain a mystery.

Figure 3 European public funding for PRND R&D, 2007-2015



Additional EU funding for PRND R&D

It is important to recognise that the totals reported above and throughout this report (for both the EU and European Governments) excludes funding that is not related to the development of new health technologies for developing country needs, or is not grant funding (e.g. loans or tax incentives). Although we recognise their importance, these investments are outside the scope of this report. In the EU context this includes, for example:

- non-grant funding (e.g. InnovFin, a debt-instrument to support the translation of semi-commercial research, such as in HIV/AIDS diagnostics);
- general training of, or support to, individuals from endemic countries in sub-Saharan Africa, which is not related to specific PRND research activities;
- research in diseases like TB or HIV/AIDS that is not relevant to LMICs (e.g. high-tech diagnostic approaches designed for use in European hospitals); and
- operational or health systems research not related to the development of new health technologies.

For this reason, the totals reported here may differ from those reported by the EU.

Funding from European Governments

Just like that of the EU, European Government funding for PRND R&D was relatively consistent over the eight years from 2007-2014, at an average of around €260 million per year. However, just like that of the EU and the US Government, European Government funding declined after its stimulus-related peak in 2009, with funding falling in four out of the following five years.

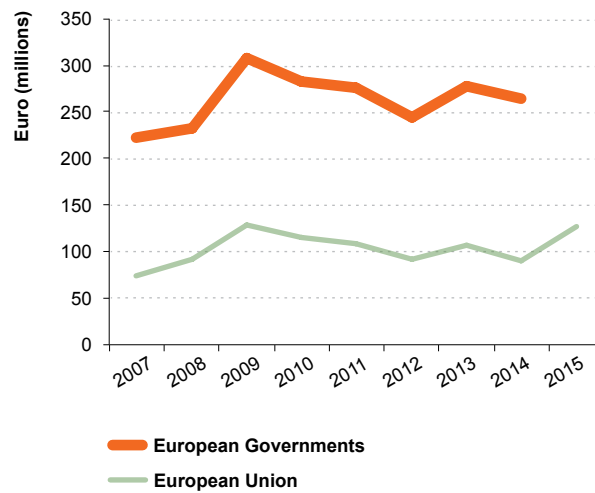
Somewhat concerningly, the rate of decline of European Government funding – averaging 3% per year

since 2009 – is double that of the US, despite the fact that European Governments already lag well behind the US in the funding they provide for PRND R&D. Not only is the collective contribution of European Governments only a quarter that of the US Government alone, but each Government's contribution as a proportion of their gross domestic product (GDP) is also far smaller than that of the US, as shown in Figure 5.

The UK is by far the biggest European Government funder, both in terms of proportion of GDP and in absolute value, having contributed a total of €871 million between 2007 and 2014. This accounts for over 40% of all European Government investment in PRND R&D. The UK is followed by France and Germany (€327 million, 15%, and €224 million, 10% respectively), and both of these countries have been increasing their investments over time. The Netherlands and Sweden round out the top five European countries. Beyond that, each country invested less than €100 million in public funding for PRND R&D over the eight year period.

Even when adding the proportion of the contributions that EU Member States make annually to the EU budget that will then be spent on PRND R&D, there is still not a single European country that comes close to the level of funding provided by the US, and all fall well short of the target of 0.01% of GDP proposed by the CEWG.^{†4}

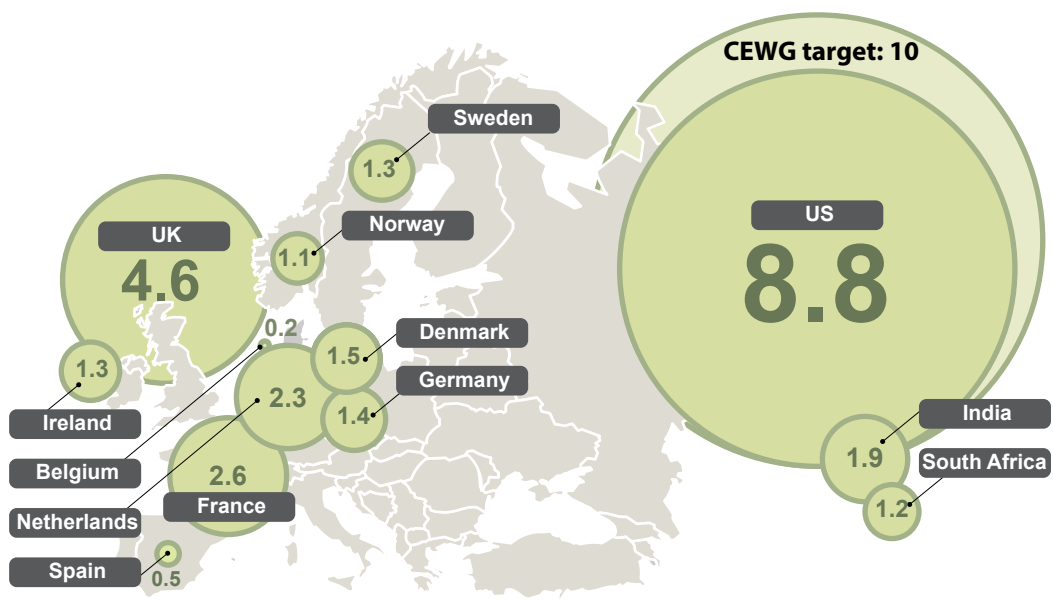
Figure 4 European public funding for PRND R&D, 2007-2014



† An index of 10 is equivalent to an investment of 0.01% of GDP. GDP figures taken from International Monetary Fund World Economic database. Excludes MS contributions to the EU

‡ The CEWG was established by the World Health Assembly (WHA) in 2010, and its recommendations have been endorsed by the WHA.

Figure 5 PRND R&D investment index as a proportion of GDP, 2014 †



How does the EU fund PRND R&D?

The EU stands apart from the majority of governments globally by having a single unifying programme through which it makes almost all of its research investments. The multi-annual Framework Programmes (FPs) are research and innovation schemes designed to drive economic growth, create jobs and secure Europe's global competitiveness; they are administered by the European Commission's Directorate-General for Research and Innovation, and funded from the central EU budget (which is derived from MS' contributions to the EU). Previously numbered 1-7, the current (and eighth) FP has been labelled Horizon 2020, and spans the period from 2014 to 2020.

The FPs cover all fields of research, from agricultural to zoological, and as such the EU's investment in PRND R&D in 2015 represented just 1.1% of the annualised expenditure of Horizon 2020. However, this is also equivalent to 13% of the annualised expenditure of the Work Programmes of Horizon 2020's thematic pillar on Health, Demographic Change and Wellbeing (called first Societal Challenge, or SC1) – representing a significant investment in global health.

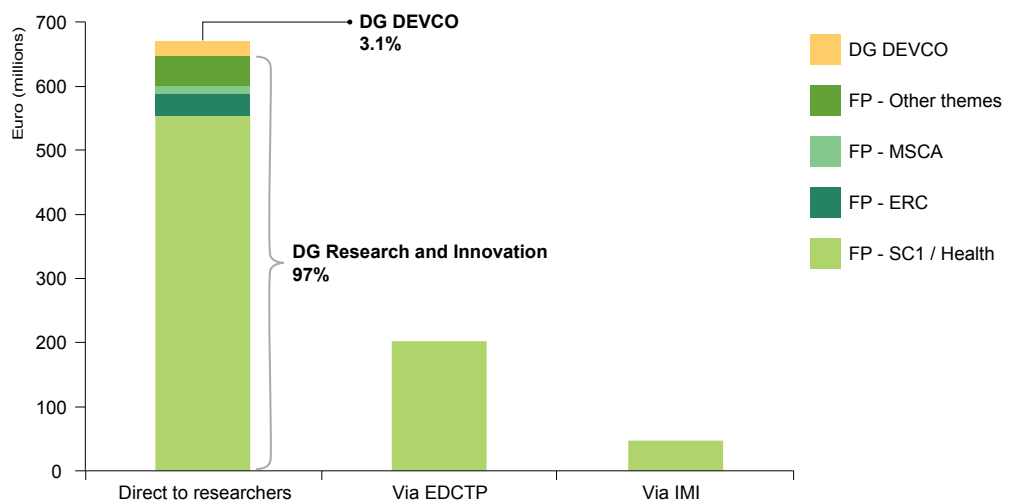
EU funding for PRND R&D is distributed to researchers in three ways:

1. Funding given directly to researchers – most EU funding for PRND R&D is given directly to researchers. In turn, the majority of this is awarded under the Work Programmes of SC1 (and SC1's equivalent predecessors, such as the Health theme of FP7), but also through the Marie Skłodowska-Curie actions (MSCA), European Research Council (ERA) and other non-health themes and inducement prizes[§] of the FPs. Outside of the FPs, funding for PRND R&D has also come from the European Commission's Directorate-General for International Cooperation and Development (DG DEVCO).[†]

2. Funding via the European & Developing Countries Clinical Trials Partnership (EDCTP) – a dedicated PRND R&D partnership between the EU, Participating States and third parties. The EU's contribution to the EDCTP falls under the SC1 budget, but is managed by the EDCTP Secretariat. See the box on the following page for a more detailed description of this initiative.

3. Funding via the Innovative Medicines Initiative (IMI) – a Joint Technology Initiative that focuses on the competitiveness of the European healthcare industry and brings together industry, academia and other participants in an effort to promote collaborative research. Like the EDCTP, the EU's contribution to IMI projects also falls under the SC1 budget.

Figure 6 EU PRND R&D funding distribution and source of funds, 2007-2015



§ To date, none of the prizes awarded have been within the scope of G-FINDER

† For an in-depth evaluation of DG DEVCO's support for research in partner countries, see the recent "Evaluation of the EU Support to Research and Innovation for Development in Partner Countries (2007-2013)"

The European & Developing Countries Clinical Trials Partnership

The EDCTP is the EU's dedicated PRND R&D funding initiative in partnership with European and sub-Saharan African States. Through the EDCTP, the EU and 28 Participating States (PS)** seek to reduce the burden of PRNDs by developing new or improved interventions and supporting clinical trials (Phases I-IV, with a focus on Phase II and III), implementation research and capacity-building. The EDCTP also acts as a coordinating platform for trials and promotes collaborative research.

The EDCTP is now in its second phase (2014-2024). The EU funds the EDCTP through Horizon 2020 – SC1, and has committed up to €683 million for this ten year period, on the condition this is equally matched by contributions from the European PS.⁵ Together with contributions from African PS and potential additional funding from third parties, the total budget could be up to €2 billion, four times that of EDCTP1.

EDCTP1 focused on Phase II and III TB, HIV/ AIDS and malaria trials in sub-Saharan Africa. Under EDCTP2, the partnership has widened its scope to also include other NIDs, and earlier clinical and later research. The focus remains on diseases that affect sub-Saharan Africa. EDCTP2 also seeks to involve industry, PDPs, philanthropic organisations and development agencies. In contrast to EDCTP1, which could not provide funding to PDPs or industry, now every public or private legal entity based in one of the PS can receive funding.⁶

** See the Methodology for a list of Participating States

†† All funding; not restricted to G-FINDER scope

Figure 7 European contributions to EDCTP grants, 2003-2015 ††5

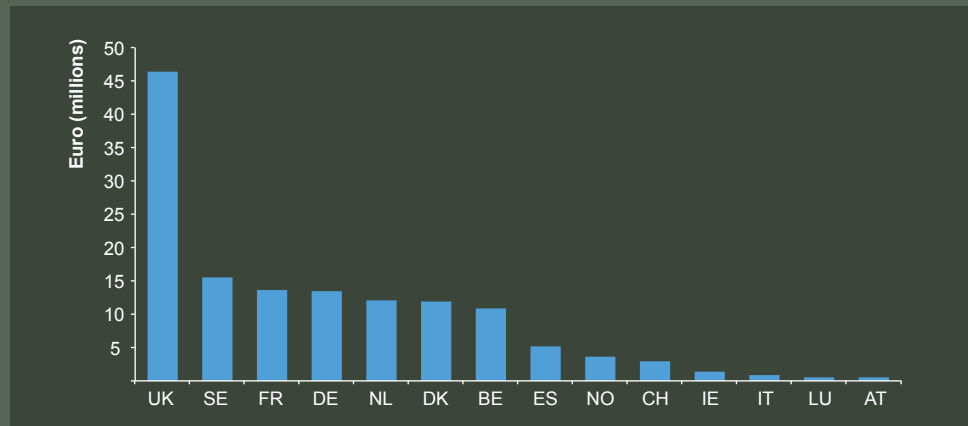
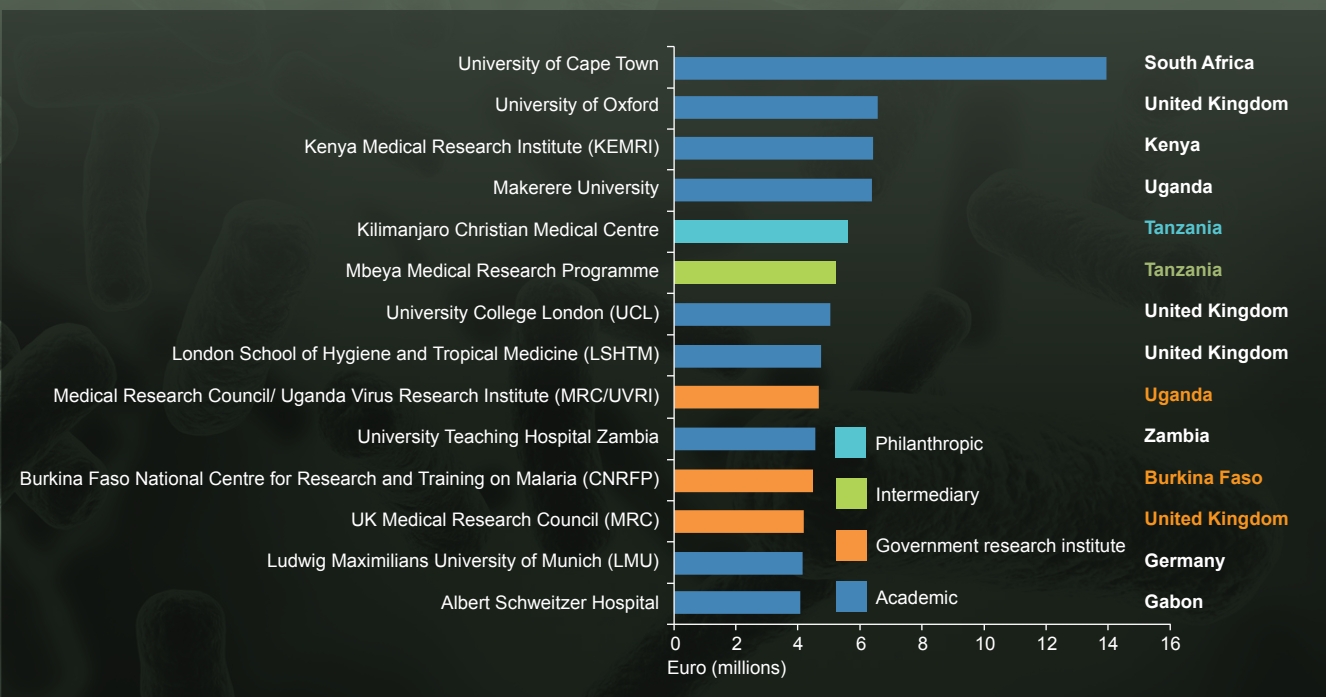


Figure 8 Top recipients of EDCTP administered funding, 2007-2015



How do European Governments fund PRND R&D?

Unlike the EU, which provides almost all its PRND R&D funding under the auspices of Horizon 2020, European Governments commonly have multiple strategies, avenues, and objectives for their PRND R&D investments – each of which will vary from country to country.

Regardless of the strategy or objectives, government funding for PRND R&D is primarily provided by two key types of funding agencies: science and technology (S&T) agencies and aid (international development) agencies.

S&T agencies

S&T agencies – such as the Medical Research Council in the UK (UK MRC) or Inserm in France – typically invest domestically, either in their own internal research programmes or by funding domestic academic research institutes, and mainly invest in basic and early-stage research.

Aid agencies

In contrast to S&T agencies, aid agencies – like the UK Department for International Development (DFID) or Swedish International Development Agency (SIDA) – have no imperative to invest domestically, and nor do they generally have the scientific expertise (or desire) to select and manage individual pipeline candidates. As a result, aid agencies overwhelmingly channel their funding through product development partnerships (PDPs). Because their focus is solely on health impact, aid agencies also tend to invest more in late-stage research, although many agencies also invest across the full spectrum of research, for example by providing core funding to PDPs.

Following the global financial crisis, and with austerity measures in place in many countries in Europe, there has been a clear trend towards declining aid agency funding (although the UK has been a notable exception), whilst S&T agency funding has increased or remained steady. This has had a clear impact on the nature of European Government funding for PRND R&D, which is discussed in more depth later in this report.



nuzree

Which PRNDs are being funded?

The EU and European Governments have very similar disease funding profiles, with the primary focus of both being on the three best known (and best funded) PRNDs: HIV/AIDS, TB and malaria. More than two-thirds (69%) of all European public investment in PRND R&D between 2007 and 2014 was in these three diseases. This is less concentrated than US Government funding, which is dominated by HIV investment (50% of all US Government investment is in HIV, with the 'top three' diseases receiving 80%) but broadly in line with public investment from the rest of the world (63% of all funding goes to HIV/AIDS, TB and malaria).

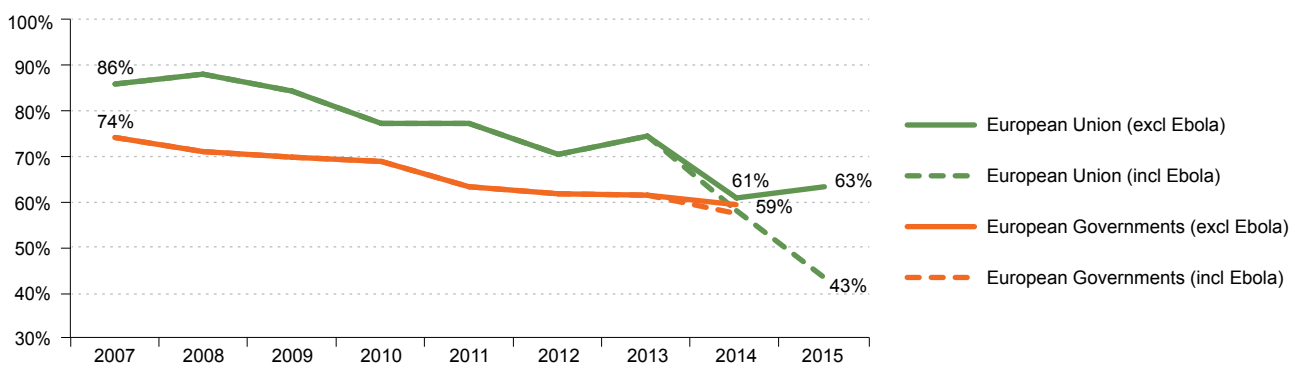
Table 1 EU and European Government funding of PRNDs R&D, 2007-2014

	Euro, m	European Union	European Governments	Euro, m	
27%	221	Tuberculosis	HIV/AIDS	602	29%
26%	208	HIV/AIDS	Tuberculosis	391	19%
24%	194	Malaria	Malaria	390	19%
7.0%	57	Can not be allocated to one disease	Can not be allocated to one disease	323	15%
5.7%	46	Kinetoplas	Kinetoplastids	144	6.8%
4.8%	39	Helminths (Worms & Flukes)	Diarrhoeal diseases	93	4.4%
1.6%	13	Diarrhoeal diseases	Helminths (Worms & Flukes)	50	2.4%
1.3%	11	Dengue	Bacterial Pneumonia & Meningitis	50	2.4%
0.8%	6.6	Buruli Ulcer	Salmonella infections	26	1.3%
0.5%	4.1	Ebola	Dengue	13	0.6%
0.4%	3.0	Hepatitis C (HCV 4, 5 and 6)	Ebola	8.9	0.4%
0.3%	2.6	Salmonella infections	Hepatitis C (HCV 4, 5 and 6)	4.6	0.2%
0.3%	2.5	Bacterial Pneumonia & Meningitis	Cryptococcal meningitis	2.5	0.1%
<0.1%	0.1	Leprosy	Buruli Ulcer	2.3	0.1%
			Trachoma	0.9	<0.1%
			Leprosy	0.6	<0.1%
			Rheumatic Fever	0.3	<0.1%

Interestingly, both the EU and European Governments have significantly reduced the share of their PRND R&D funding that goes to HIV/AIDS, TB and malaria over the last decade. In 2007, 86% of the EU's funding and 74% of European Governments' funding went to these three diseases; in 2014, this share was down to around 60% for both groups.

On the EU side, this dramatic reduction was entirely driven by increasing diversity in the funding awarded directly to researchers under FP calls. Although the expansion of the scope of EDCTP2 to include other NIDs will likely continue this trend, to date the EDCTP has only funded one NID project. The influx of new funding for Ebola R&D in 2015 (particularly through the IMI – see following page) further reduced this concentration, although this is likely to trend back towards the mean with time.

Figure 9 Proportion of annual PRND R&D funding directed to HIV/AIDS, TB and malaria



The EU response to Ebola

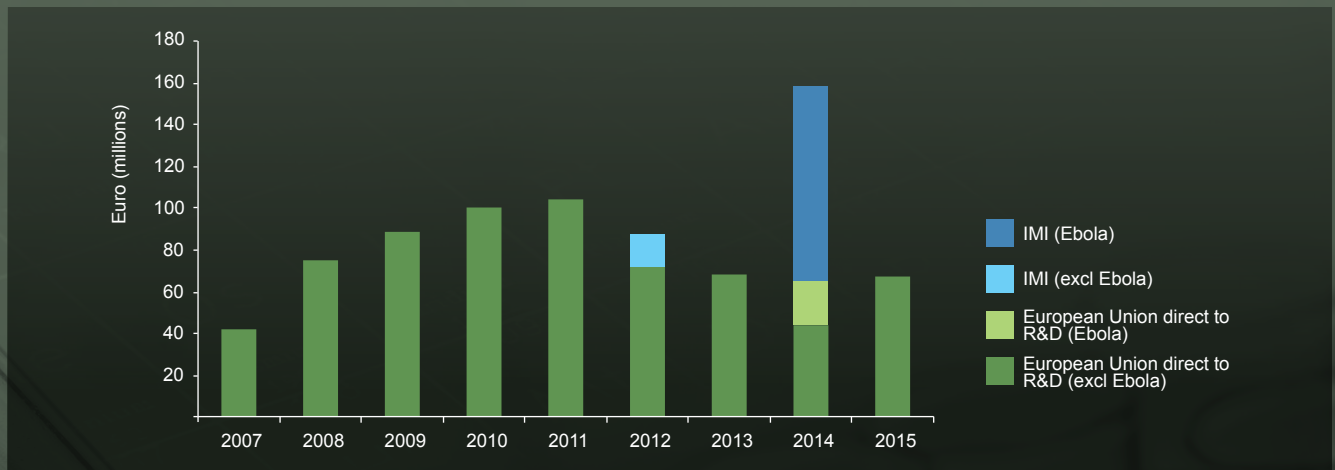
The outbreak of Ebola in West Africa reminded us of the devastating impact that an infectious disease can have on communities when vaccines, drugs, and diagnostic tools don't exist, and the health systems to utilise them are severely lacking. It also demonstrated that significant new funding for PRND R&D can be rapidly mobilised when the political commitment exists.

Shortly after the World Health Organization (WHO) declared the outbreak to be a public health emergency of international concern, the EU announced nearly €120 million in new projects for Ebola R&D. Most of this announced funding (€94 million) came from the IMI's Ebola+ initiative, with the remainder coming from specific Work Programme calls under SC1 of Horizon 2020.

Unfortunately, the Ebola funding announced under the Work Programme calls appears to have come at the expense of new projects for other PRNDs: Ebola accounted for a third of all funding for new Work Programme projects initiated in 2014, but the total value of new PRND projects initiated in 2014 remained identical to the preceding year.

In contrast to the Work Programme funding, the large IMI investment can be considered 'new' EU money for PRND R&D, as the initiative has rarely been used for PRND R&D projects (the only other in-scope project is PreDiCT-TB, launched in 2012, which focuses on preclinical research for TB drugs). This IMI investment also leverages matching in-kind contributions from industry partners, effectively doubling the EU's investment.

Figure 10 Impact of Ebola on value of announced PRND projects – IMI and EU direct to R&D ^{##}



The EU's role in Ebola R&D was not limited to that of funder; it also made an appeal to European Governments for research coordination. It worked with WHO and the European Medicines Agency (EMA) and produced a report on global research efforts.⁷ European Governments, however, made 82% of their investments domestically, and there was little co-investment in EU projects.

The only structure that allows co-investment from European Governments and the EU is the EDCTP. In March 2015, the EU urged the EDCTP to mobilise funding from the Participating States,⁸ but there was no EDCTP investment in Ebola product R&D reported in 2015. The EDCTP provided some funding for Ebola-specific capacity building; it also made a non-disease-specific call for new diagnostics, but the successful grants under this call were for non-Ebola research. As a result, all of the EU's funding for product development-focused Ebola R&D was directed through the IMI and the SC1 Work Programmes of Horizon 2020, neither of which is designed to facilitate European Government co-funding.

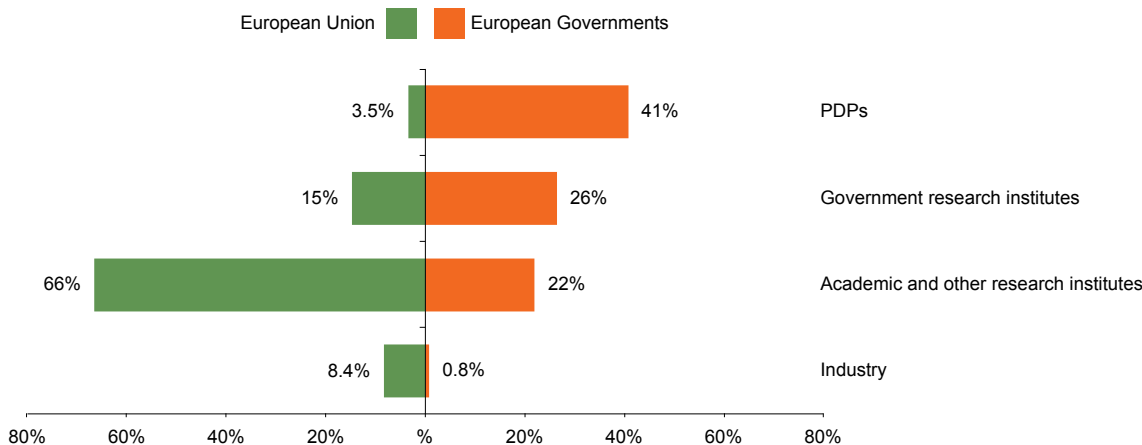
^{##} EDCTP funding not included. Appendix 1: Methodology explains difference between announced value and expenditure

Who does European public funding go to?

Although the EU and European Governments have similar disease priorities, the types of organisations they fund to carry out this research are very different.

The EU invests much like a typical S&T agency, selecting individual projects to fund, and directing the vast majority of its investment to public sector research organisations – primarily academic or other research institutes, but also government research institutes – which typically specialise in basic and early-stage development. Just 12% of EU funding goes to industry and PDPs, the two groups most commonly responsible for later stage product development.

Figure 11 Types of recipient, 2007-2014



In contrast, European Governments invest heavily in PDPs; PDPs received 41% of all European Government investment over the same period – a proportion that increases to 85% of all aid agency investment. As a result (because PDPs act as the intermediary between government and industry), European Governments actually give less direct funding to the pharmaceutical industry than the EU does; industry received less than 1% of European Government funding for PRND R&D between 2007 and 2014.

Given the fact that PDPs are involved in the development of approximately 40% of PRND products in the pipeline, the fact that the EU essentially does not fund PDPs (they received only 3.5% of EU PRND R&D investment) is notable. But what is perhaps more interesting, is that when it does fund PDPs, the EU almost exclusively funds the two Europe-based PDPs partly established by the EU^{§§} (the TuBerculosis Vaccine Initiative⁹ and the European Vaccine Initiative), and that there is very little overlap between this PDP investment and that of European Governments.

These differences in funding preferences are clearly reflected in the list of top recipients of European public funding: there is almost no overlap between the top recipients of EU funding and those of European Government funding.

^{§§} The TuBerculosis Vaccine Initiative was established under the FP7 project ESI-TBVI. The European Vaccine Initiative grew out of the European Malaria Vaccine Initiative, a collaboration between the EC and the governments of Denmark, Ireland, The Netherlands, Norway and Sweden.

Figure 12 Direct investment in PDPs, 2007-2014

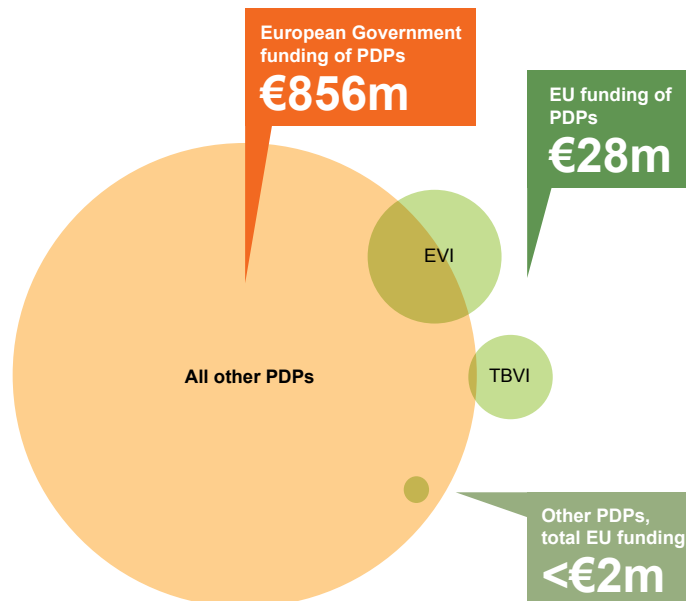
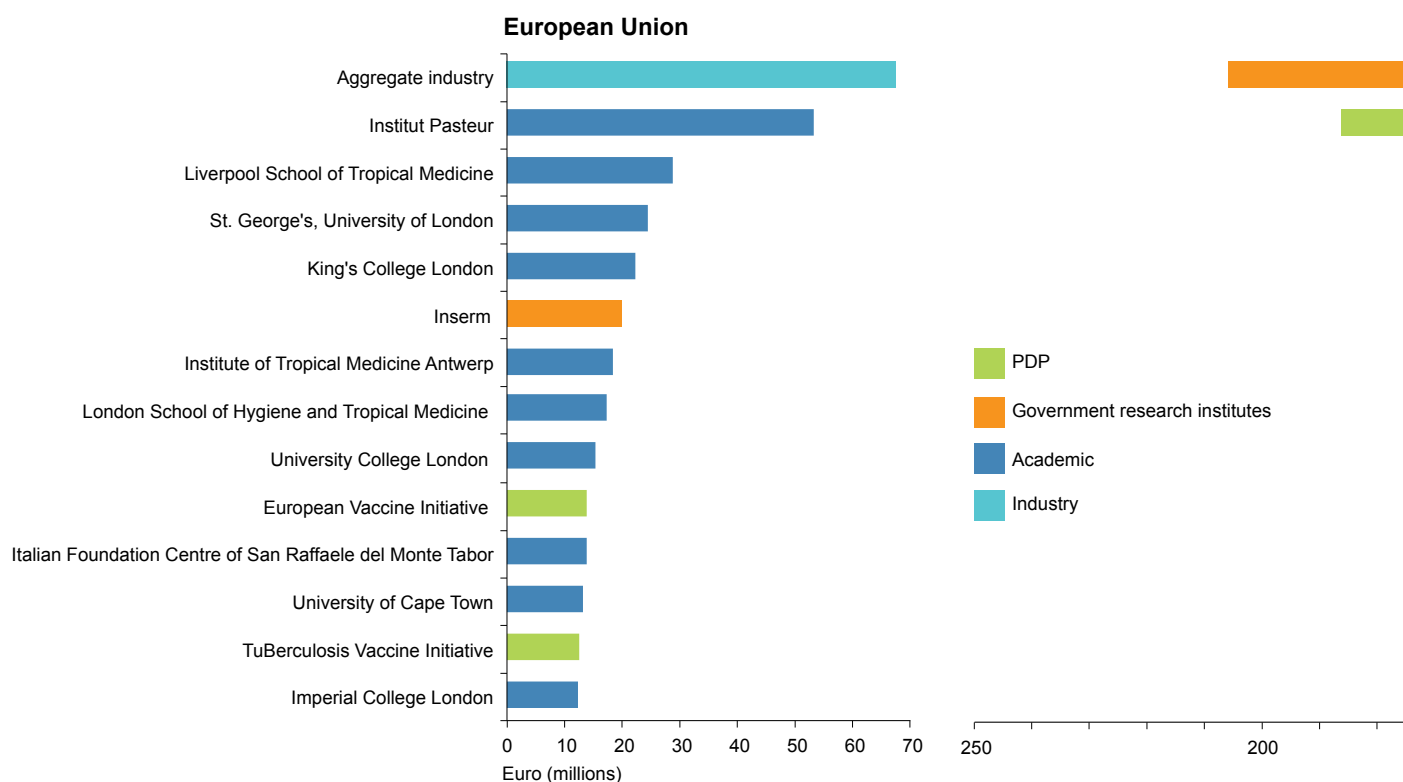


Figure 13 Top recipients, European Union and European Governments, 2007-2014



Collaborating for an effective TB vaccine

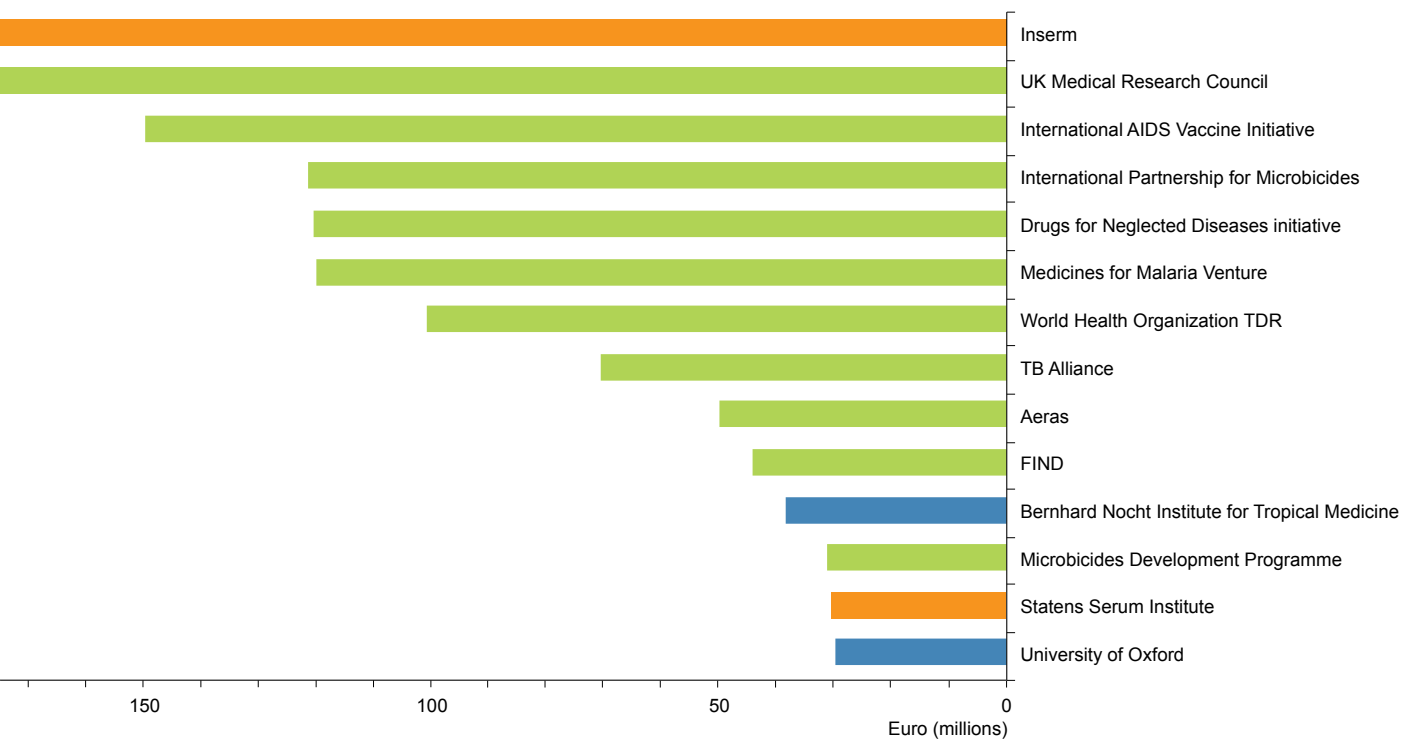
TB is the second biggest killer and fourth-highest cause of morbidity of all the PRNDs, resulting in 1.3 million deaths and 49 million DALYs each year in LMICs. And unlike the global epidemics of HIV and malaria, the number of new cases of TB each year is on the rise.¹⁰

With the growing emergence of multi-drug resistant TB and extensively drug-resistant TB and only two new drugs registered for TB in the last 50 years, an effective vaccine is likely to be the only tool capable of ending the TB epidemic. Unfortunately the existing TB vaccine (BCG, developed in 1921), although effective against disseminated TB in children, does not protect against primary infection or reactivation.¹¹ A new vaccine is desperately needed.

Aeras, a US-based PDP, was established in 1997 with the goal of developing a new, effective TB vaccine that would be affordable and accessible to all those who need it. Since then, Aeras has received significant funding from aid agencies in EU Member States, including UK DFID and the Dutch Directorate-General of Development Cooperation (DGIS). However, although it has collaborated with the EDCTP on clinical trials of its vaccine candidates, Aeras has never received funding from the EU.

Under FP5 and FP6, EU funding for TB vaccine R&D had instead been channelled towards traditional European research collaborations. This changed in 2008 with the FP7 project ESI-TBVI, which created the TuBerculosis Vaccine Initiative (TBVI), a Europe-based PDP established to ensure 'appropriate linkage between EC supported projects and global initiatives aiming at the development of new TB vaccines.'⁹ TBVI

European Governments



was tasked with coordinating the EU's TB vaccine R&D efforts under the NEWTBVAC project, and has been the main vehicle for EU funding for TB vaccine R&D ever since. But although European Governments have provided some funding to TBVI, the majority of their PDP funding for TB vaccine R&D has gone to Aeras.

To avoid the potential for funding duplication between the EU and its Member States, and to capitalise on their different strengths, TBVI and Aeras have developed a model for R&D coordination. The two PDPs have a memorandum of understanding to collaborate on funding, advocacy efforts, and the technical evaluation of vaccine candidates, with TBVI primarily responsible for management of early-stage research efforts and Aeras focused on advancing these candidates through later stages of development.



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What type of research is being funded?

Historically, the EU has been considered a typical S&T agency funder. Unlike European Governments, where aid agency funding for late-stage product development (particularly via PDPs) complements the basic and early-stage research investments of S&T agencies, EU funding was less balanced, primarily going to basic and early-stage research conducted by academic researchers.

This characterisation remains true in part: the EU does resemble an S&T agency in the type of recipients it funds, with the vast bulk of its funding going to academic and other public sector research institutes. But taking the period from 2007-2014 as a whole, the distribution of the EU's funding across the research spectrum is almost identical to that of European Governments; both groups invested around 30% of their total PRND R&D funding in basic research, with the remainder to product development.

The overall similarity of EU and European Government funding across the research spectrum reflects two key underlying trends: declining aid agency funding has led to basic research making up an ever-growing share of European Government funding; and the EU has been increasing its funding for product development, including for late-stage research, whilst investing less in basic research. And this is not solely via the EDCTP and the IMI; although three quarters (74%) of all FP7 funding for PRND R&D given directly to researchers (i.e. excluding EDCTP and IMI) was for basic and early-stage research, the amount invested in clinical (late-stage) development has been increasing sharply.

Table 2 Forces affecting research stage








	European Union	European Governments
Basic research	 Declining investment	 Increasing investment through S&T agencies (vs. aid agencies), leading to increased investment in early-stage academic research
Product development	 Large IMI investment in late-stage Ebola projects, 2014+	 Reducing aid agency investment (with the exception of DFID), resulting in less investment in PDPs, and a reduction in product development investment
	 Increase in EDCTP budget likely to increase late-stage investment in coming years	
	 Investment in multinational pharmaceutical companies (MNCs) doing late-stage Ebola research	
	 Increasing EU direct investment in academics that are doing late-stage research	

Figure 14 Investment by research stage, European Union

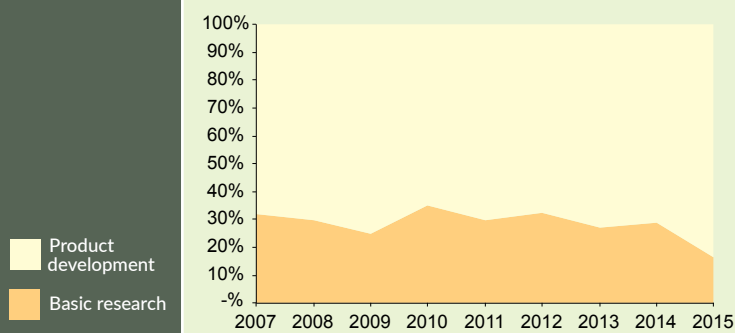
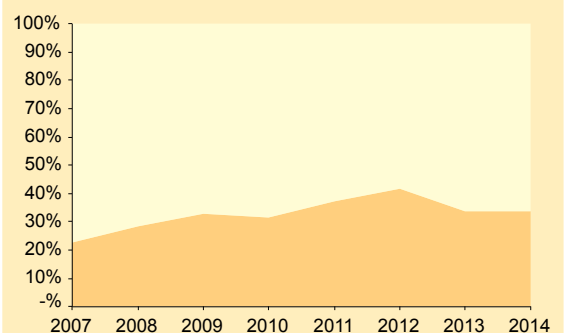


Figure 15 Investment by research stage, European Governments





THE BENEFITS TO GLOBAL HEALTH AS A RESULT OF EU INVESTMENT

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The impact of EU-funded tools

Any evaluation of the EU's contribution to delivering new products for PRNDs needs to take into account the state of science for the diseases which are (or have been) the EU's primary focus; vaccines for HIV and TB are still a distant prospect, just one (partially effective) malaria vaccine has ever been developed, and only two new drugs for TB have been approved in the last 60 years, neither of which were developed primarily for LMIC markets. With this in mind, the EDCTP in particular has actually played quite a significant role in delivering new health technologies for PRNDs. In malaria, for example, half of all new drugs approved since 2000 have relied on EDCTP-funded trials to support their registration.

● Pyramax Granules

Nine out of every ten malaria deaths globally occur in Africa, and 86% of these are in children younger than five. But until recently, there has been no first-line malaria drug designed specifically for children; instead, tablets designed for adults had to be crushed, and the appropriate dose decided by guesswork.

Pyramax (pyronaridine-artesunate) Granules, developed by Shin Poong Pharmaceutical in collaboration with the Medicines for Malaria Venture (MMV), a Switzerland-based PDP, is a once-daily, 3-day treatment for uncomplicated malaria in children. In November 2015, it became the first paediatric antimalarial drug to receive a positive opinion under the EMA's Article 58 process, which is designed to provide regulatory guidance on products not intended for use in Europe. In March 2016 it was added to the World Health Organization's (WHO) list of prequalified medicines.

EDCTP funding was critical to achieving these approvals. Along with MMV, the EDCTP was the primary funder of a large Phase IIIb/IV safety and efficacy study with patients

EDCTP funding was instrumental in delivering a new and effective malaria drug designed specifically for the needs of children – who represent 86% of all malaria deaths in Africa

THE BENEFITS TO GLOBAL HEALTH AS A RESULT OF EU INVESTMENT

from Mali, Burkina Faso and Guinea. Led by the West African Network for Clinical Trials of Antimalarial Drugs (WANECAM), this trial provided safety and efficacy data to the EMA to support its approval of the drug.¹²

● LabDisk

Rapid and accurate diagnosis of malaria and other infectious diseases is critical to appropriate and successful treatment. The development and widespread availability of rapid diagnostic tests (RDTs) for malaria has meant that malaria can now be diagnosed quickly and cheaply in the field, without the need for laboratories or highly-trained health professionals. But malaria is only one of the many possible causes of febrile illness; not only do many of these other diseases lack suitable RDTs, but the focus on screening for a single infection (particularly in the case of epidemics like Ebola) leads to significant under-diagnosis of other infections.

Under FP7, the EU invested €3 million in the DiscoGnosis project, which resulted in the development of the LabDisk, a tool that can diagnose malaria and other febrile infectious diseases simultaneously in just an hour – allowing faster point-of-care treatment and precise drugs administration that will not only save lives but also deliver economic benefits.

Not only is accurate diagnosis critical to successful treatment; but the economic costs of misdiagnosis can be enormous. One study in Sudan suggested that the cost of diagnosis and treatment of malaria in Sudan in one year was US\$100 million, and yet only US\$14 million of this was related to true malaria cases.¹³ In addition, the potential to expand this technology to other emerging infectious diseases (such as Zika), holds enormous potential for health outcomes and economic savings.

A pipeline of new products for the future

As well as the benefits to global health that have already been realised, EU investment in PRND R&D has helped to deliver a robust pipeline of products that have the potential to deliver significant impact in the future. At least 13% of the 133 most advanced pipeline candidates (those in Phase II and III clinical trials) have received funding from the EU. The true proportion is likely to be even higher, as investments in basic and early-stage research are often hard to link to individual candidates as they become further advanced.

Developed with FP7 funding, the LabDisk can diagnose malaria and other febrile infectious diseases simultaneously in just an hour

THE BENEFITS TO GLOBAL HEALTH AS A RESULT OF EU INVESTMENT



Wikimedia

Highlighted below are three examples of EU-funded pipeline candidates that could help make significant inroads in the fight against PRNDs.

● Olyset Duo

Although 3.2 billion people globally are still at risk of contracting malaria, global efforts to eliminate the disease have reduced malaria mortality by 60% since 2000.¹⁰ In Africa, where 90% of deaths from malaria occur, two-thirds of this dramatic reduction in malaria deaths has been attributed to the effective use of insecticide treated nets.¹⁰

However, the rapid spread of insecticide resistance in mosquitoes threatens these gains. The AVECNET consortium, led by the Liverpool School of Tropical Medicine, a leader in malaria vector control and home to the vector control PDP Innovative Vector Control Consortium (IVCC), was funded under FP7 to conduct R&D for malaria vector control. The consortium is developing a long-lasting insecticidal bed net that would address the threat of insecticide resistance through the use of a novel combination of insecticides. The Olyset Duo net is being developed in partnership with the Sumitomo Corporation of Japan and IVCC, and is currently in clinical trials in Burkina Faso.

Preliminary data has shown superior personal protection over WHO recommended single insecticidal bed net and reduced mosquito egg development.^{16,17} Although eliminating malaria is likely to require a combination of tools, including new drugs and diagnostics, and possibly an effective vaccine, a product like the Olyset Duo that can reduce the fertility of mosquitoes in areas of high insecticide-resistance will be a critical component of this toolbox.

● BERENICE

Chagas' disease is a silent killer spread by the 'kissing bug'; the initial, acute infection often has no symptoms, but the chronic stage can result in cardiac failure and death if left untreated. Although most commonly found in Latin America, it is estimated that 6-7 million people globally are infected with the causative agent, *Trypanosoma cruzi*.¹⁸

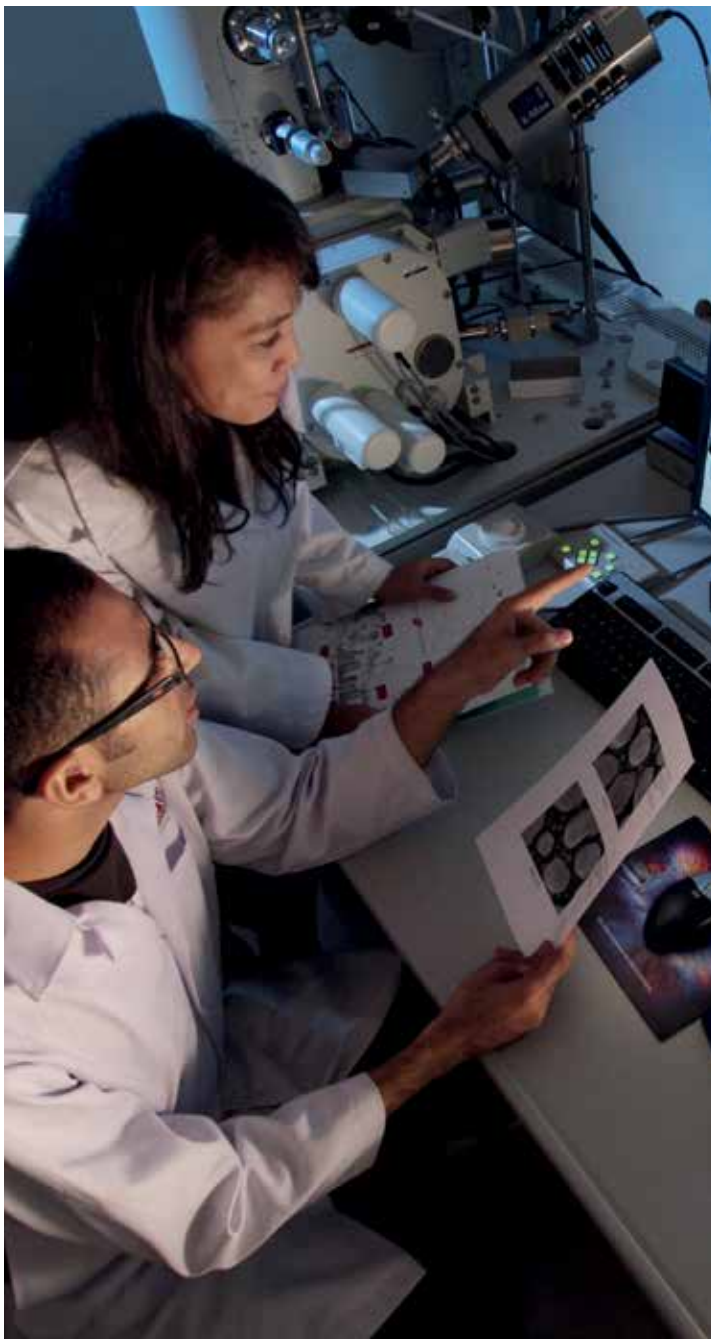
There are currently two drugs used to treat Chagas' disease (benznidazole and nifurtimox), and both have a high cure rate if given in the



CDC Global

early, acute phase. But because this stage is often asymptomatic, treatment is often not started until the chronic stage of the infection, when they will be ineffective in 1 out of 3 cases.¹⁸ Add to this the fact that 4 in every 10 people who receive these drugs experience extreme side effects due to their toxicity, and that the treatment is unsuitable for pregnant women, and the need for a new Chagas' drug is clear.

The EU, under the Low-Cost Interventions for Disease Control in Resource Poor Settings call of FP7, provided €3 million to the BERENICE consortium to develop improved treatments for Chagas' disease. The consortium is developing nano-encapsulation of benznidazole to reduce its toxicity while decreasing its cost.¹⁹ Together with better diagnostic tools, a more effective and better tolerated drug such as this would not only save the lives of Chagas' disease patients, but would also save significant sums of money: in Colombia alone, the annual cost of medical care for all Chagas' patients was estimated at US\$267 million in 2008, and the cost of vector control efforts an additional US\$5 million annually.



felixioncool

This is an unusual example of EU funding, as the consortium includes two research organisations and a biotechnology company from South America, where Chagas' is endemic. The funding eligibility for the progression of this project, if successful, is unclear, as any future clinical trials will need to be conducted in South America. Indeed, the EU typically funds drug trials through the EDCTP rather than through Work Programmes, but a South American trial would fall outside of the remit of the EDCTP.

● TaMoVac

Along with the dramatic reduction in malaria deaths over the last decade, the sustained decline in HIV/AIDS-related deaths and new infections over the same period has been one of the success stories of global efforts to combat PRNDs. Despite these efforts, it is estimated that 1.3 million people died from HIV/AIDS in 2013,¹ and after three decades of R&D efforts, there is still no cure for HIV/AIDS and no vaccine to prevent transmission. The constantly mutating virus, and dearth of animal models present challenges to vaccine development. Yet an effective vaccine remains the goal for cost-effective, sustainable prevention.

The TaMoVac consortium has been involved in HIV/AIDS vaccine clinical trials in East Africa. It has been co-funded by the EDCTP, building upon previous investment in capacity building and clinical trial networks. Preliminary data from clinical trials has shown excellent tolerability and enhanced immune response with their HIV-1 DNA vaccine candidate.²⁰ Further intradermal administration of this vaccine candidate has opened up a new avenue for HIV vaccine development.²⁰

The health and socio-economic impact of an even



mwooten

partially effective HIV vaccine would be enormous. Modelling predicts that a vaccine that provides protection only in 70% of cases would still essentially halve the number of new HIV cases annually after one decade, be highly cost-effective in even the poorest countries, and save \$1.5 billion per year by 2070.²¹

Capacity building

Europe has a longstanding commitment to knowledge and technology transfer to LMICs to strengthen local capacity in the fight against PRNDs, particularly in Africa, and the EU is representative of this trend. For more than a decade, the EU has been investing in capacity building for clinical trials in sub-Saharan African countries through the EDCTP, and has also contributed towards capacity building in African countries through DG DEVCO.

Between 2003 and 2013, 17% of EDCTP funding was invested in capacity building in sub-Saharan Africa – a figure that is projected to have increased to 26% in 2015.^{22,23} As a result of this investment, more than 516 senior and junior scientists from 31 sub-Saharan African countries have been trained,²⁴ and by 2015, 72% of EDCTP funded grants were run by African scientists.²⁵ It has also established a joint fellowship programme with the European pharmaceutical industry to train African scientists at European companies.²⁶

The EDCTP has established four Regional Networks of Excellence. Each centre has six laboratories that run world class clinical trials and promote sub-regional scientific collaborations. This investment has had the added benefit of attracting funding for PRNDs from completely new sources: one of the four Regional Networks of Excellence, the Central African Network on TB, HIV/AIDS and malaria, has secured funding from a local oil company to conduct malaria research.⁵ More recently, EDCTP funding led to the establishment of the Pan-African Clinical Trials Registry, which has become the WHO-recognised primary clinical trial registry in Africa.²⁷

In addition to the investments made by the EDCTP, support for capacity building in Africa has also come from outside the Framework Programmes. DG DEVCO funded the WHO Special Programme for Research and Training in Tropical Diseases to create the African Network for Drugs and Diagnostics Innovation (ANDI). ANDI promotes South-South and South-North partnerships to address local health needs and builds capacity to support locally sustainable R&D development for medicines.



THE BENEFITS TO EUROPE AS A RESULT OF EU INVESTMENT

Jim Holmes for AusAID

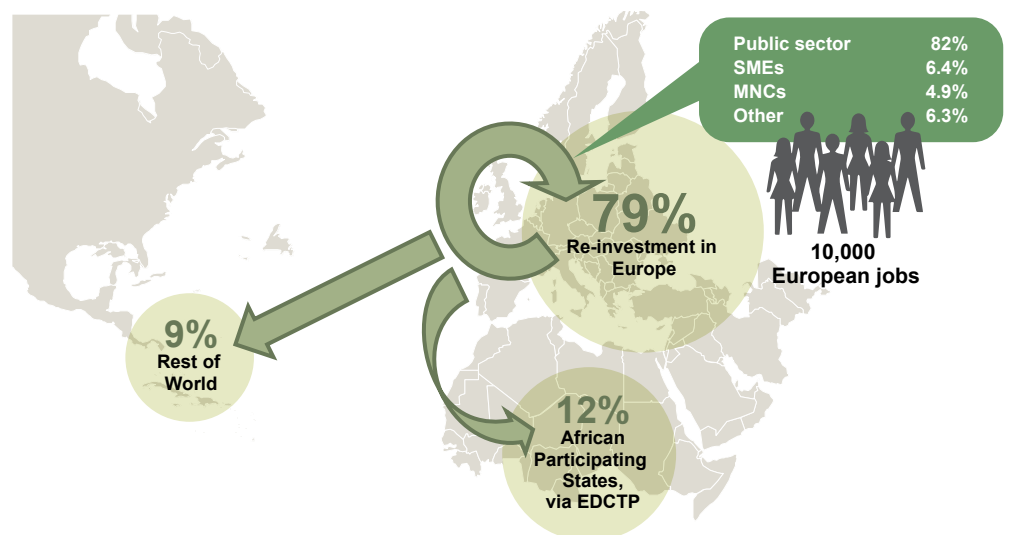
THE BENEFITS TO EUROPE AS A RESULT OF EU INVESTMENT

The EU's investment in PRND R&D is not only helping to deliver new vaccines, drugs and diagnostics that will benefit populations in LMICs, but has also resulted in investment within Europe that produces both immediate benefits (e.g. jobs), and durable structural changes (e.g. a vibrant industry).

Investing in Europe for jobs and growth

Almost 80% of the EU's investment in PRND R&D is re-invested in Europe. The recipients of this investment are researchers and product developers in European laboratories, universities and companies.

Figure 16 Geographic distribution of EU funding



As a result of the EU's investment in PRND R&D through FP7, more than 10,000 European research jobs have been created.*** It should also be noted that this figure only includes the new jobs created directly as a result of the EU's investment; when considering the additional investment leveraged from the private sector and from other sources (including European Governments and from outside Europe), the number of jobs created would be significantly higher.

Investing in research excellence

The European research sector has a long and rich history of being at the forefront of explorations in infectious diseases. Institutions that were established hundreds of years ago have made some of the key scientific breakthroughs in PRND research. Investment in these organisations continues, providing the backbone to Europe's research industry.

Institut Pasteur	<ul style="list-style-type: none"> • A private, non-profit foundation based in Paris, France • Diverse disease focus, with products in the pipeline for helminths, hepatitis C, TB, malaria, leptospirosis and diarrhoeal diseases • Receiving funds from the EU through FP7 for pre-clinical and Phase 1 testing of a synthetic glycoconjugate vaccine for <i>Shigella</i>, in its role as coordinator for STOPENTERICS project
Statens Serum Institute	<ul style="list-style-type: none"> • A public enterprise under the Danish Ministry of Health • Part of the long-running, EU-funded TBVAC2020 consortium developing the pipeline for TB vaccines, coordinated by TBVI • Conducting malaria and TB vaccine trials with funding from the EDCTP
Swiss Tropical & Public Health Institute	<ul style="list-style-type: none"> • A public organisation associated with the University of Basel, Switzerland • Malaria, kinetoplastid, helminth and Buruli ulcer products in the pipeline • Co-lead of the EDCTP-funded TB CHILD consortium developing a sputum-independent TB diagnostic • Part of a Drugs for Neglected Diseases Initiative (DNDi) consortium developing a promising sleeping sickness drug, fexinidazole
London School of Hygiene and Tropical Medicine	<ul style="list-style-type: none"> • A public research university associated with the University of London • Awarded €57 million by the IMI for EBOVAC1 - the development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen, in a consortium with Janssen • A number of early-stage candidates in the pipeline, for bacterial pneumonia & meningitis, leishmaniasis and malaria

European organisations are involved in the development of 45% of the 494 products currently in the global PRND pipeline. These products are being developed by research institutes, industry and PDPs, with considerable collaboration between the three groups. There is further collaboration within each organisation group, with almost all products being a joint effort between parties.

*** Following the methodology of the NEMESIS model ²⁸

Leveraging investment from the private sector

The majority of global PRND research activity that is conducted by industry is conducted in Europe – European companies invest twice as much as their American counterparts. Three European pharmaceutical companies (GlaxoSmithKline, Sanofi and Novartis) lead the field in terms of industry involvement in the PRND product pipeline – collectively, these three companies are involved in the development of almost fifty new product candidates, representing more than 10% of the global pipeline.

While the EU's support of European MNCs is a fraction of what the companies invest themselves, it is unlikely that the industry could persist in an economy devoid of the ecosystem of innovation, discovery and collaboration that develops as a result of publicly supported research institutes and SMEs.

Public investment develops the elements needed for productive collaboration – a pool of talented researchers and high-quality research institutes that can support and feed innovative SMEs, and MNCs that have the scale and expertise to develop products through to registration.

Investing in SMEs

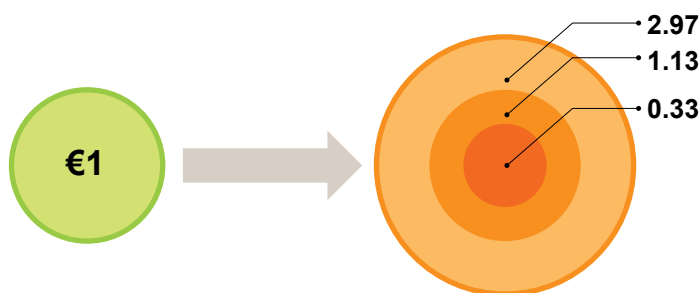
The structure of general EU funding for R&D is focused on maintaining a vibrant SME landscape, with key measures specifically designed to increase SME participation and competitiveness, such as the consortium nature of EU funding, the SME Instrument,²⁹ and a specific SME funding target for Framework Programmes.

However, the SME instrument (and many other tailored mechanisms, especially those that utilise debt-financing rather than grants) are less useful for PRND R&D because of the lack of commercial return. The SME instrument has funded less than €2 million for a total of seven PRND R&D projects between 2007 and 2015, and most of these projects were answering the call for “Clinical research for the validation of biomarkers and/or diagnostic medical devices”, and resulted in R&D for diagnostics for diseases that have some commercial market (TB, HIV/AIDS, malaria).

In a similar vein, the percentage of PRND R&D funding that is awarded to SMEs under the Framework Programmes is currently well below the target of 20% for the Societal Challenges and “Leadership in Enabling and Industrial Technologies” sections of Horizon 2020.³⁰ The average achieved rate under FP7 was 6%. This has increased to 10% in the early years of Horizon 2020 – a trend that would be expected to continue following the revised eligibility requirements for EDCTP2, which allow EDCTP2 to fund SMEs (something that was not possible under EDCTP1).

Despite the challenges of offering suitable and workable incentives and structures for SME investment in PRND R&D, the EU has invested €46 million in SMEs over nine years, funding a total of around 100 companies, of which only €2 million was provided through the SME instrument.

Figure 17 Leveraged PRND R&D investment from EU funding to SMEs



This is notable, as investing in SMEs leverages significant additional funding. For every €1 that the EU invests in European SMEs for PRND R&D, €2.97 is invested by these SMEs, €1.13 is invested by international organisations (mostly public and philanthropic) and €0.33 by European Governments.



DISCUSSION

Corporal Paul Shaw/MOD

Sustainability of current EU funding levels

The decline in EU funding following its peak in 2009 seems to have reversed, but this is welcomed with some caution. Increased budgets for EDCTP2 and Horizon 2020, as well as the significant new investment in Ebola research through the IMI, are likely to sustain funding levels for the next two to three years. Beyond 2017, however, there are three factors that may exert downwards pressure on funding for PRND R&D.

Firstly, it is unlikely that the significant 'new' EU investment in PRND R&D under the IMI Ebola+ initiative will continue to be dedicated to PRND R&D once these Ebola projects have finished; in the absence of Ebola or another similar emerging infectious disease threat, IMI funding for PRND R&D will likely revert to previous (low) levels.

Secondly, the mid-term review of the 2014-2020 Multi-annual Financial Framework (MFF) will be completed by 2017. The outcomes of this review will determine the available funding for each of the MFF priority funding areas for the period 2017-2020, as well as informing the shape of the next MFF. With all European Governments (and the European Union as a whole) currently well below the CEWG PRND R&D funding target of 0.01% of GDP, any cut in the funding available for PRND R&D would be a backwards step. At the same time, there are a number of competing threats – such as the ongoing migrant and refugee crisis – currently putting significant pressure on the MFF envelope.

Finally, the UK's planned exit from the EU and the uncertainty of its continued role in European research programmes are of particular concern. Not only are there implications for collaboration and free movement of researchers, but the budgets of Horizon 2020 and the EDCTP could also be affected, depending on the negotiated scenario. The importance of UK Government funding to the EDCTP budget is hard to overstate: it provides a quarter of all Participating States' contributions to the EDCTP

(which in turn dictate the size of the EU contribution to the EDCTP). Unless the UK maintains its role as a Participating State – which is only possible if associated to Horizon 2020 – the EDCTP’s budget risks being significantly reduced.

The EU’s leadership role

The EU’s financial contribution to European public funding to PRND R&D is impressive; it was the source of 28% of all European public funding to this field over the period 2007-2014. But the extent to which it has been able to influence or coordinate funding from European Governments is less clear. Greater coordination amongst European public funders would reduce the potential for duplication of effort, and increase the likelihood that PRND R&D investments will translate into global health impact. But the impression of two separate spheres of funding remains: the lack of overlap between the recipients of direct EU/IMI funding and those of European Governments, for example, is striking.

Coordination is a two-way street, and the onus is equally on European Governments to align with the EU’s funding agenda. There are also structural limits to the EU’s capacity to promote financial coordination; for example, the EDCTP is the only EU funding mechanism that explicitly encourages co-funding by European Governments (either as pooled funding, or as Participating States’ Initiated Activities). The scope and eligibility restrictions of EDCTP1 limited its ability to fulfil its coordinating potential, but EDCTP2 has been designed to address these limitations (although we note that it is still restricted to diseases that affect sub-Saharan Africa, and only participants from defined countries are eligible for funding). The upcoming mid-term evaluation of EDCTP2 will provide a timely opportunity to review the impact of these changes.

Maximising impact from EU investments

Although European organisations are highly involved in the PRND pipeline, only a quarter of late-stage candidates are known to have received EU funding. The fact that PDPs – who are involved in the development of over half of all candidates in the pipeline – receive minimal funding from the EU is one explanation for this, as is the historical ‘bias’ towards funding early-stage research, and the limited scope of EDCTP1 (which extended only to HIV, TB and malaria).



Possible

Within the scope of EDCTP1 – and taking into account the limited number of new products approved for these three diseases since its establishment – the EDCTP has actually played a much larger role than might be expected based on the numbers above. In malaria, for example, half of all new drugs approved since 2000 have relied on EDCTP-funded trials to support their registration.

One step to achieving impact – and being able to communicate it – is to ensure that it is measured appropriately. Currently, the outcomes of much of the PRND R&D conducted under Horizon 2020 are measured using the same metrics as other research, which are often a poor proxy for actual global health impact. The high-level indicators for EDCTP2 are a step in the right direction, but could still be considered either modest (by the end of the programme to have delivered at least one new medical product) or vague (to have progressed the clinical development of at least 20 candidate products).

The benefits to Europe of EU investment in PRND R&D, on the other hand, are clear. Horizon 2020 is measurably delivering on its aim of driving economic growth, creating jobs and improving competitiveness, with thousands of jobs and a vibrant industry generated by FP investment. In the face of increasing pressure on the public wallet, this should not be forgotten.

Recommendations

Given the proven benefits to global health and the European economy stemming from EU support for PRND R&D, as well as the potential of existing mechanisms, the EU and European Governments should increase their support for PRND R&D, and work to leverage their respective strengths.

1. Meeting funding targets:

- The EU and European Governments should collectively and individually work towards achieving the CEWG's PRND R&D funding target of 0.01% of GDP.
- Negotiations on the UK's exit from the EU should consider the importance of the continued participation of the UK Government and UK institutions in EU-funded research programmes, including the critical importance of UK Government funding to the EDCTP budget.

2. Improving synergies:

- The EU and European Governments should develop a comprehensive, complementary and unified strategy for global health R&D, focused on leveraging both synergies and differences in the way each group supports R&D. The strategy should set out aims and priorities, as well as a roadmap for achieving them that avoids duplication and makes full use of existing coordination mechanisms such as EDCTP2.

3. Focusing on impact:

- The EU and European Governments need to maintain their support for the whole product development cycle, and direct funding to the most promising projects and actors most likely to deliver.
- The EU should measure the success of all of its PRND R&D investments with metrics that are appropriate for evaluating global health impact, and regularly report against them to show the impact of its investments.

APPENDIX 1: METHODOLOGY

Data collection

The source of investment data for this report is the G-FINDER survey, a survey conducted annually by Policy Cures that identifies global investment into neglected disease research and development. It covers 35 neglected diseases, across 142 product areas for these diseases, including drugs, vaccines, diagnostics, microbicides and vector control products as well as platform technologies (e.g. adjuvants, delivery technologies, diagnostic platforms). Further information is available at [http://policycuresresearch.org/downloads/Y8 GFINDER full report web.pdf](http://policycuresresearch.org/downloads/Y8_GFINDER_full_report_web.pdf).

The data includes all types of product-related R&D, including basic research, discovery and preclinical, clinical development, Phase IV and pharmacovigilance studies, and baseline epidemiological studies.

Survey recipients are asked to enter grant-by-grant expenditures incurred during their financial year. Only expenditures are included, as opposed to commitments made but not yet disbursed or 'soft' figures such as in-kind contributions, costs of capital, or funding estimates. Funding from the European Union and the Innovative Medicines Initiative is reported to the survey in multi-year project totals ("announced value"). For the G-FINDER survey, these totals are divided by the project duration and annualised, to provide the best estimate of annual expenditure. Conversely, Figure 10 illustrates the announced value, rather than the annualised value.

All figures in the report have been adjusted for inflation and are reported in 2015 Euro (€). All reported data has been adjusted for inflation using consumer price index estimates from the Organisation for Economic Co-operation and Development (OECD) and the International Monetary Fund (IMF). Data entered by survey participants in their local currency has been converted to Euro based on the 2015 average annual exchange rate as reported by the IMF.

Global PRND R&D funding data from 2007 to 2014 has been analysed for this report. The EU has kindly provided 2015 G-FINDER data ahead of schedule, allowing us to include this data where appropriate.

Country inclusions

The term "European Governments" refers to public funding from the EU Member States (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom), Norway and Switzerland.

The current EDCTP Participating States are:

- 14 European countries – Austria, Denmark, Finland, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, UK; and
- 14 African countries – Burkina Faso, Cameroon, Congo, Gabon, The Gambia, Ghana, Mali, Mozambique, Niger, Senegal, South Africa, Tanzania, Uganda and Zambia.

Limitations

The key limitation concerns potential gaps in the financial investment data. In particular, the G-FINDER data does not capture investments made by smaller European funders of PRND R&D who do not participate in the survey. Funders who have participated in G-FINDER can be viewed using the G-FINDER Public Search Tool, available at <https://gfinder.policycures.org/PublicSearchTool/>

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