

# HIV Prevention Research & Development Investment in 2013

In a changing global development, economic,  
and human rights landscape

HIV VACCINES  
& MICROBICIDES  
RESOURCE TRACKING  
WORKING GROUP



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JULY 2014

## > Table of Contents

3	<b>1.0 Summary: Sustaining commitment to HIV prevention research and development in the context of broad global health and international development shifts</b>
5	Advocacy, policy and funding trends
8	Data collection and analysis methodology
15	<b>2.0 Global Investments in Preventive AIDS Vaccine Research and Development</b>
17	2.1 Funding Allocations for Preventive AIDS Vaccine Research and Development
18	2.2 Public Investments in Preventive AIDS Vaccine Research and Development
20	2.3 Philanthropic Investments in Preventive AIDS Vaccine Research and Development
20	2.4 Commercial-sector Investments in Preventive AIDS Vaccine Research and Development
21	<b>3.0 Global Investments in Microbicide Research and Development</b>
21	3.1 Funding Allocations for Microbicide Research and Development
23	3.2 Public Investments in Microbicide Research and Developments
24	3.3 Philanthropic Investments in Microbicide Research and Development
24	3.4 Commercial Investments and Contributions to Microbicide Research and Development
25	3.5 Investments in Rectal Microbicide Research and Development
25	3.6 Investments in Multipurpose Prevention Technology Research and Development
27	<b>4.0 Investments in Research and Development Related to Pre-exposure Prophylaxis</b>
29	<b>5.0 Investments in Research and Development Related to Treatment as Prevention</b>
30	<b>6.0 Investments in Follow-up Studies and Operations Research Related to Voluntary Medical Adult Male Circumcision</b>
31	<b>7.0 Investments in Research and Development and Operations Research Related to Female Condoms</b>
32	<b>8.0 Investments in Research Related to Vertical Transmission Prevention</b>
34	<b>9.0 Investments in HIV Prevention Research and Development Related to HSV-2 Prevention</b>
35	<b>10.0 Investment in HIV Cure and Therapeutic Vaccine Research and Development</b>
37	<b>11.0 Discussion and Conclusions: 2013 HIV prevention research and development investment conclusions and recommendations</b>
39	<b>Appendix: Methodology</b>
42	<b>Appendix: List of Acronyms</b>
43	<b>Appendix: Acknowledgements</b>

### LIST OF BOXES

4	<b>BOX 1:</b> A Changing Environment for HIV Prevention R&D
6	<b>BOX 2:</b> International Development Funding for HIV Prevention Research: Shifting paradigms and policies
8	<b>BOX 3:</b> United States Funding for HIV Prevention Research and Development: The story of the largest HIV prevention research funder
10	<b>BOX 4:</b> Enabling Environment Perspective: Human rights legislation and environmental factors inhibit HIV prevention research
16	<b>BOX 5:</b> Beyond RV144
17	<b>BOX 6:</b> Crowd-funding for AIDS Vaccine Research
19	<b>BOX 7:</b> Preventive AIDS Vaccine Research in South Africa: New partnerships and infrastructure development
28	<b>BOX 8:</b> Investment in Long-acting Injectables for Use as PrEP
32	<b>BOX 9:</b> WHO Recommendations
36	<b>BOX 10:</b> Toward a Cure Program Definition: US NIH eradication of viral reservoirs
36	<b>BOX 11:</b> Therapeutic Vaccine Research and Development
39	<b>BOX 12:</b> Data Collection Methods and Fluctuation in Investment Levels

## LIST OF FIGURES

- 3 **FIGURE 1:** Global HIV Prevention R&D Investment 2009 – 2013
- 4 **FIGURE 2:** HIV Prevention R&D Investment by Funder Type 2013
- 5 **FIGURE 3:** US Public-Sector Investment as a Proportion of Total HIV Prevention R&D Investment, 2009 – 2013
- 5 **FIGURE 4:** Investment by European Governments and the European Commission in HIV Prevention R&D 2009 – 2013
- 6 **FIGURE 5:** International Development Funding 2012-2013
- 7 **FIGURE 6:** Top Five Countries Investing in HIV Prevention R&D: Public-sector Investment 2012 – 2013
- 8 **FIGURE 7:** Top Philanthropies Investing in HIV Prevention R&D: Philanthropic-sector Investment 2012 – 2013
- 9 **FIGURE 8:** 2013 Investment in HIV Prevention R&D and Year-over-Year Change in Investment
- 10 **FIGURE 9:** Participants in HIV Prevention Trials 2013
- 11 **FIGURE 10:** HIV Prevention R&D Trial Participants by Region 2013
- 15 **FIGURE 11:** Preventive AIDS Vaccine Funding from 2000 – 2013
- 17 **FIGURE 12:** Preventive AIDS Vaccine Expenditures 2009 – 2013
- 18 **FIGURE 13:** Top Preventive AIDS Vaccine Funder Trends 2006 – 2013
- 21 **FIGURE 14:** Microbicide Funding 2000 – 2013
- 22 **FIGURE 15:** Microbicide Research and Development Expenditures for 2009 – 2013
- 23 **FIGURE 16:** Top Preventive Microbicide R&D Funder Trends 2006 – 2013
- 27 **FIGURE 17:** Investment in Pre-Exposure Prophylaxis 2005 – 2013
- 31 **FIGURE 18:** Funding for Female Condom R&D 2010 – 2013
- 35 **FIGURE 19:** Investment in Cure Research and Development 2012 – 2013
- 36 **FIGURE 20:** Investment in Therapeutic Vaccine Research and Development 2012 – 2013

## LIST OF TABLES

- 12 **TABLE 1:** Global Investment in HIV Prevention R&D: 2013 funding map
- 16 **TABLE 2:** Annual Investments in Preventive AIDS Vaccine R&D 2000 – 2013
- 18 **TABLE 3:** Preventive AIDS Vaccine Research and Development Categories 2009 – 2013
- 19 **TABLE 4:** Top Preventive AIDS Vaccine Funders for 2010 – 2013
- 20 **TABLE 5:** Philanthropic Investment in Preventive AIDS Vaccine R&D by Foundations and Commercial Philanthropy in 2013
- 20 **TABLE 6:** Estimated Commercial Engagement in Preventive AIDS Vaccine R&D by Company in 2013
- 22 **TABLE 7:** Annual Investments in Microbicide R&D 2006 – 2013
- 22 **TABLE 8:** Microbicide Research and Development Categories 2009 – 2013
- 24 **TABLE 9:** Top Microbicide Research and Development Funders for 2010 – 2013
- 28 **TABLE 10:** Annual Investments in PrEP R&D 2005 – 2013
- 29 **TABLE 11:** Annual Investments in Treatment as Prevention R&D 2011 – 2013
- 30 **TABLE 12:** Annual Investments in Male Circumcision R&D 2005 – 2013
- 33 **TABLE 13:** Funding for Vertical Transmission Prevention R&D 2008 – 2013
- 40 **TABLE 14:** Public, Philanthropic and Commercial Sector Primary Funders
- 40 **TABLE 15:** Categories Used to Classify Preventive AIDS Vaccine R&D Funding
- 41 **TABLE 16:** Categories Used to Classify Microbicide R&D Funding
- 41 **TABLE 17:** Classification of Other HIV Prevention R&D Funding
- 41 **TABLE 18:** Classification of Cure and Therapeutic Vaccine Funding

**SUMMARY**

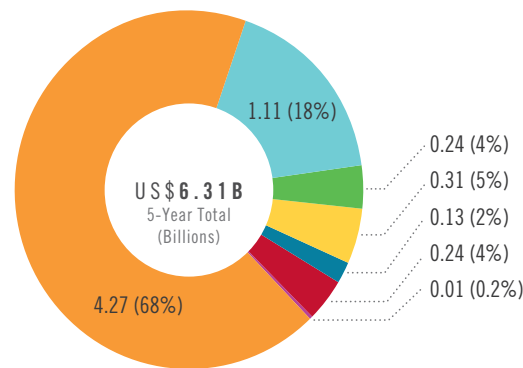
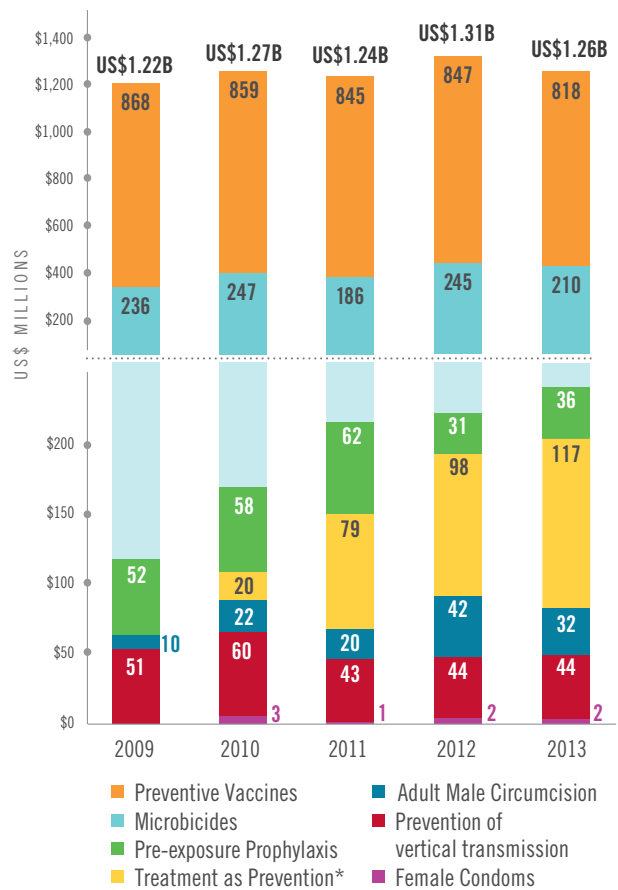
**Sustaining commitment to HIV prevention research and development in the context of broad global health and international development shifts**

In 2013, the reported funding for HIV prevention research and development (R&D) declined by US\$50 million, or four percent, compared to 2012, resulting in a 2013 total of US\$1.26 billion<sup>1</sup> (Figure 1). The 2013 decrease can be attributed largely to diminished United States (US) investment in all areas of HIV prevention research, as well as significantly reduced investment in some European countries. Changes in the international development landscape and the evolution of the HIV prevention research pipeline also played a role.

As the largest funder of HIV prevention R&D, the commitment of the US public sector has largely driven global HIV R&D and has shaped trends over the past decade. In the past five years, the US public sector has funded 70 percent of the total global investment in HIV prevention R&D (Figures 2 and 3), and in 2013 this percentage remained at 70 percent, US\$887 million. However, between 2012 and 2013, US public-sector funding declined nearly US\$38 million, or four percent, down from US\$925 million in 2012 (Table 1). The US National Institutes of Health (NIH) investment declined approximately US\$39 million (from US\$789 million in 2012 to US\$750 in 2013) and the US Agency for International Development (USAID) funding declined US\$2 million (from US\$87 million in 2012 to US\$85 million in 2013). These declines are primarily attributable to the sequestration policy that mandated across-the-

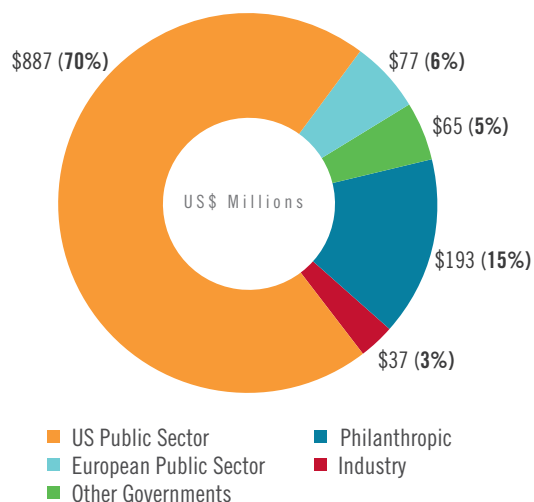
<sup>1</sup> The HIV prevention research total includes funding towards preventive AIDS vaccines, microbicides, pre-exposure prophylaxis (PrEP), treatment as prevention, voluntary medical male circumcision, female condom and prevention of vertical transmission research. Included within these categories is funding towards multipurpose prevention technologies and rectal microbicides. The HIV Vaccines & Microbicides Resource Tracking Working Group also tracks funding towards HSV-2, HIV cure and therapeutic vaccine research.

**FIG. 1 Global HIV Prevention R&D Investment 2009 – 2013 (US\$ millions)**



\*The Working Group began tracking funding for female condom and treatment as prevention research in 2010.

**FIG. 2 HIV Prevention R&D Investment by Funder Type 2013 (US\$ millions)**



board budget cuts, affecting all aspects of the US fiscal environment in 2013. HIV prevention research remains a fundamental component

of both US biomedical research support and international development policy (Box 3).

European and other public-sector funding also fell in 2013 (Box 2).<sup>2</sup> Investment by public-sector agencies in Europe declined ten percent, from US\$86 million in 2012 to US\$77 million in 2013 (Figure 4). Funding sources across the continent—including Belgium, Germany, the Netherlands, Spain, Sweden, Switzerland and the United Kingdom (UK)—decreased their support in 2013. Public-sector funding outside of US and Europe also declined by six percent, from US\$69 million in 2012 to US\$65 million in 2013.

Philanthropic funding decreased in 2014, as well, from US\$203 million in 2012 to US\$193 million in 2013. The two largest philanthropic donors, the Bill & Melinda Gate Foundation (BMGF) and the Wellcome Trust, maintained their support of HIV prevention R&D in 2013, with BMGF funding flatlining and the Wellcome

**BOX 1**

**A Changing Environment for HIV Prevention R&D**

The global funding and policy environment has shifted dramatically since the early 1990s. When HIV vaccine and microbicide research began in earnest, before the advent of life-saving antiretroviral treatments, AIDS was the foremost global health issue. The world was impelled to support research that might put an end to the epidemic. Today, with 9.7 million of the 35 million HIV-positive people living with the virus on treatment, and with deaths from AIDS declining, many may no longer see HIV prevention as the global health emergency and priority that it was even a decade ago. Efforts are now focused on increasing the percentage of HIV-positive people in low- and middle-income countries who can live with the virus on treatment.

At the same time, as living conditions and health care have improved in many low- and middle-income countries, morbidity and mortality from non-communicable diseases have also increased, and universal health insurance and health system quality have risen as dominant issues of concern. Parallel to this, the alleviation of poverty through economic empowerment has become a central theme of a new schema of global goals as expressed in the Millennium Development Goals (MDGs). There is, therefore, a new paradigm of health and development into which HIV prevention research must now find a place.

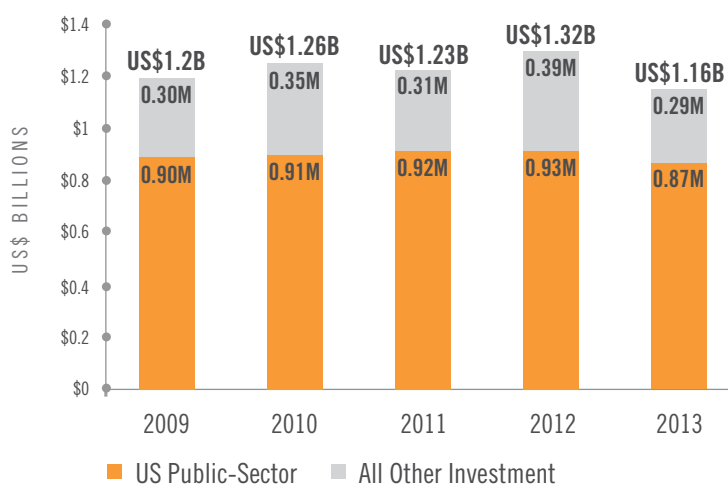
Changing dynamics of funding in all HIV R&D donor countries have shaped trends in 2013 and are expected to exert consequences for years to come. Recent budget battles in the US have caused funding cuts across all of HIV prevention R&D, and in early 2014 US NIH director Francis Collins called for new HIV research priorities in anticipation of tighter budgets over the next three to five years. These priorities will frame the future of US funding for every area of HIV prevention research.

European HIV R&D funding has also been affected by budget cuts in research and international development agencies. These have reduced HIV R&D investment by 20 percent since 2009, even as HIV remains a critical concern. The European Union (EU) Horizon 2020 initiative has set out new funding priorities for HIV research and, in May 2014, funding was approved for the second phase of the European & Developing Countries Clinical Trials Partnership (EDCTP2), laying out the path for future EU investment in HIV prevention research.

With several large funding programs coming to an end, and with revised programs and priorities taking their place, the future will present a vastly different funding environment for HIV prevention research—one with competing priorities, changing global economic dynamics and evolving research goals and needs.

<sup>2</sup> While overall official development assistance (ODA) from European Union (EU) countries that are members of the Organization for Economic Co-operation and Development (OECD) Development Assistance Committee (DAC) increased by US\$70.7 billion, or 5.25 percent, between 2012 and 2013, decreases in HIV prevention research investments from key donors such as the Netherlands, Norway and Sweden contributed to an overall decline in European funding. In the Netherlands, ODA in 2013 declined by 6.2 percent due to overall aid budget cuts, and a prioritization of “results-oriented support mechanisms and partnerships to increase the leverage of its development efforts.” While Sweden and Norway both increased their ODA in 2013 by 6.3 and 16.4 percent, respectively, Sweden prioritized bilateral aid, while Norway increased its development cooperation budget and disbursements specifically to Brazil. Outside of Europe, ODA fell in Canada by 11.4 percent. Canada’s expenditures for climate change and debt relief in 2012 and budget cuts affecting 2013 resulted in a significant decline. *Net Official Development Assistance from DAC and Other Donors in 2013.* [www.oecd.org/dac/stats](http://www.oecd.org/dac/stats).

**FIG. 3 US Public-Sector Investment as a Proportion of Total HIV Prevention R&D Investment, 2009 – 2013**



Trust increasing their support by US\$6 million (Figure 7). The greatest decline came from smaller philanthropic funders who either discontinued or reduced their support of HIV prevention R&D in 2013.

Investment has declined for HIV prevention options that have proven effective (i.e., voluntary medical adult male circumcision and female condoms), as investments go increasingly towards implementation of these tools. Conversely, investment has increased in support of treatment as prevention (TasP) and pre-exposure prophylaxis (PrEP), advancing these into successful implementation phases. Funding for HIV prevention options that are more upstream, such as vaccines and microbicides, is going toward the revitalization of a pipeline that has seen several large trials close out in the last few years. Investment has in part reflected this movement and the nature of funding clinical trials; the discontinuation of immunizations in the HIV Vaccine Trials Network’s HVTN 505 trial, the most recent ongoing AIDS vaccine efficacy trial and the completion of the Microbicide Trial Network’s VOICE study played a role in the decline of investments in 2013.

## Advocacy, policy and funding trends

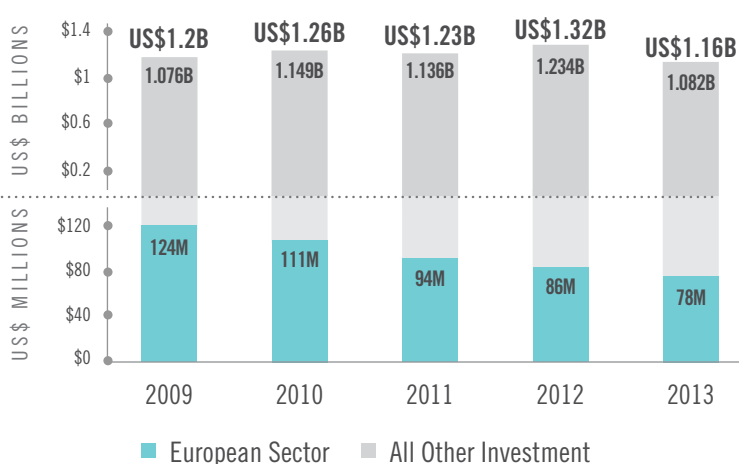
### The US public sector funds the majority of HIV prevention R&D.

Public-sector agencies in the US fund 70 percent of all HIV prevention research. Thus, when US investment decreases, so too does overall HIV prevention funding. With US\$85 billion in spending cuts from nearly all areas of the US budget, the crisis significantly affected all research funding in 2013, including HIV prevention R&D.

### Philanthropic organizations increasingly fund vital parts of HIV prevention research.

As public-sector support has come under increasing pressure, the funding of young investigators and new research proposals has waned, and an increasing number of conditions and stipulations have been placed upon existing grants. Philanthropic sources are often able to be more flexible than public-sector sources—supporting new, promising research and adapting more easily as research evolves. Foundations and charities dedicated to HIV prevention research enable innovative research and collaborations that may not always be funded through often restricted public-sector sources.

**FIG. 4 Investment by European Governments and the European Commission in HIV Prevention R&D 2009 – 2013**



## International Development Funding for HIV Prevention Research: Shifting paradigms and policies

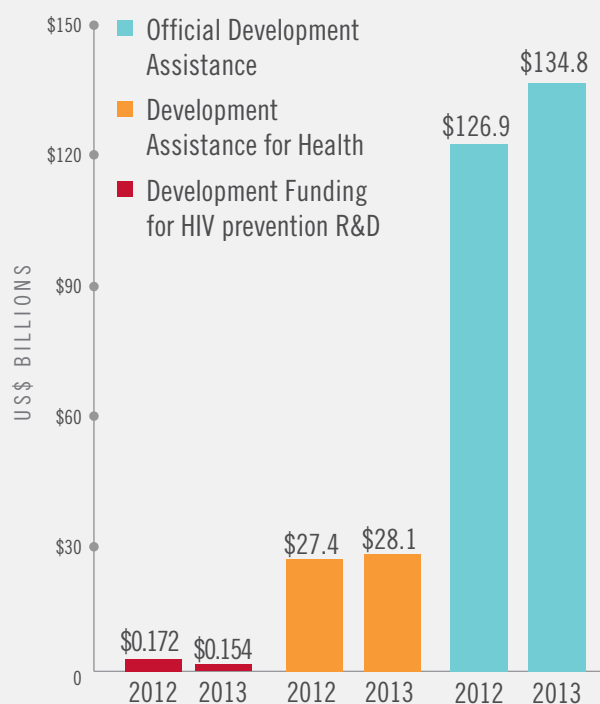
In 2013 foreign aid for development assistance reached a record high of \$134.8 billion, growing by six percent from US\$126.9 billion in 2012 (Figure 5).<sup>a</sup> With this growth came broad shifts in the international development institutional and policy environments of many funders which affected the support provided to HIV prevention research in 2013. While overall ODA grew in 2013, DAH flatlined, and development support towards HIV prevention research declined by ten percent.

The UK's ODA grew by 27.8 percent to US\$17.88 billion in 2013, for the first time reaching the international target to spend 0.7 percent of gross national income (GNI) on aid. The UK's DAH also increased in 2013; however, DFID revised its focus in 2013, choosing to shift investments from certain health areas and countries to others. In 2013 DFID announced US\$210 million in funding for nine five-year grants for public-private partnerships towards developing new drugs, vaccines, insecticides, diagnostics and microbicides, spanning a range of health areas. The five-year grants for AIDS vaccines and microbicides from 2013 to 2018 declined by a combined US\$60.8 million, from US\$91.3 million to US\$30.4 million in the previous five year grant cycle.

The reorganization of Canada's development agency into its department of foreign affairs and trade, a move intended to align the country's development aid with its trade and foreign policy objectives, could affect Canada's HIV prevention R&D funding. DAH from Canada dropped in 2013, as did funding for HIV prevention R&D, reflected in the decrease in DAH and in HIV prevention research funding in 2013.

<sup>a</sup> Organisation for Economic Co-operation and Development (OECD) data. [www.oecd.org/dac/stats](http://www.oecd.org/dac/stats).

FIG. 5 International Development Funding 2012 – 2013 (US\$ billions)



The infrastructure shifts seen in Canada are part of a larger trend toward moving the functions of international development agencies under the oversight of foreign affairs departments.

### Industry funding stayed almost flat and shifted to later development stages.

A very modestly increased investment from industry (by US\$2 million), combined with its focus on late stage product development and manufacturing expertise, has accelerated new HIV prevention products along the later stages of the pipeline toward rollout and impact.

With an increasing focus on later-stage research and implementation, as well as the support of therapeutic studies that have prevention applications for antiretroviral (ARV)-based prevention, the expertise and experience of industry is a much needed asset to the field in order to move products from the pipeline into the market.

### International development priorities are evolving.

2013 shifts of policy and strategy in the international development landscape had profound effects on HIV prevention research funding. While official development assistance (ODA) rose in 2013, and Development Assistance for Health (DAH) flatlined, many HIV prevention R&D donors either reprioritized their investments or shifted institutionally. The reorganization of Canada's development agency into its department of foreign affairs and trade, and a trend towards country-ownership models for the HIV/AIDS response could have profound effects on Canada's priorities, as reflected in the decrease in DAH and in HIV prevention research funding in 2013. While the UK's DAH increased

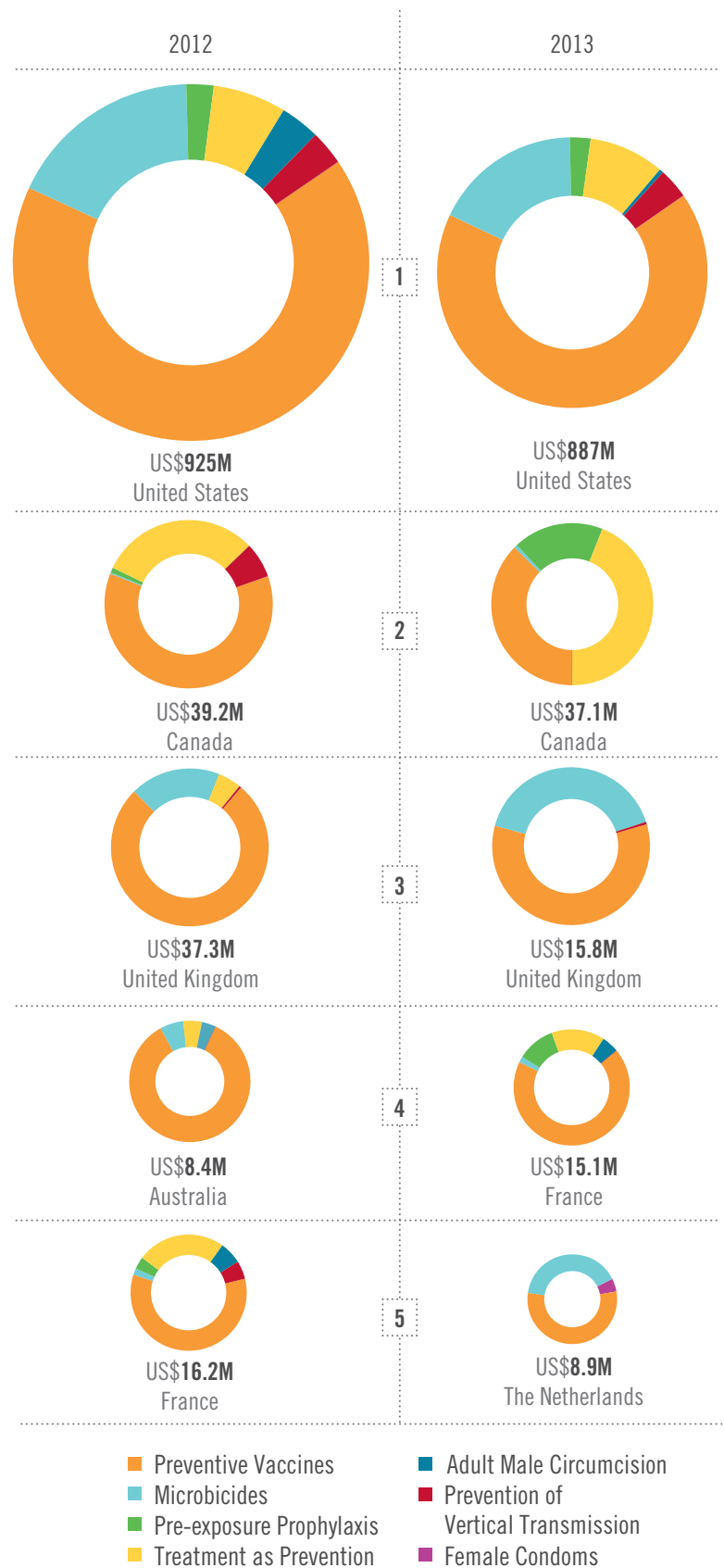


in 2013, the UK's Department for International Development (DFID) is recalibrating the countries and health areas it targets, resulting in repercussions in its 2013 overall support of product development partnerships, and thus in some of the HIV prevention research investments made through these partnerships. Similarly, other countries are undergoing structural and policy shifts in their ODA and DAH, focusing increasingly on bilateral aid and health indicators in a broader context of economic development. Development assistance has enabled a scaled-up response not only to the HIV epidemic, but also in R&D for medicines and vaccines for diseases primarily affecting poor and marginalized populations, including HIV therapeutics and prevention options. At the end of 2015, the Millennium Development Goals (MDGs) will expire and a new set of sustainable development goals (SDGs) will take their place. Although, the SDGs are still under development and the final goals are not yet set, a trend towards poverty alleviation and economic development has emerged.

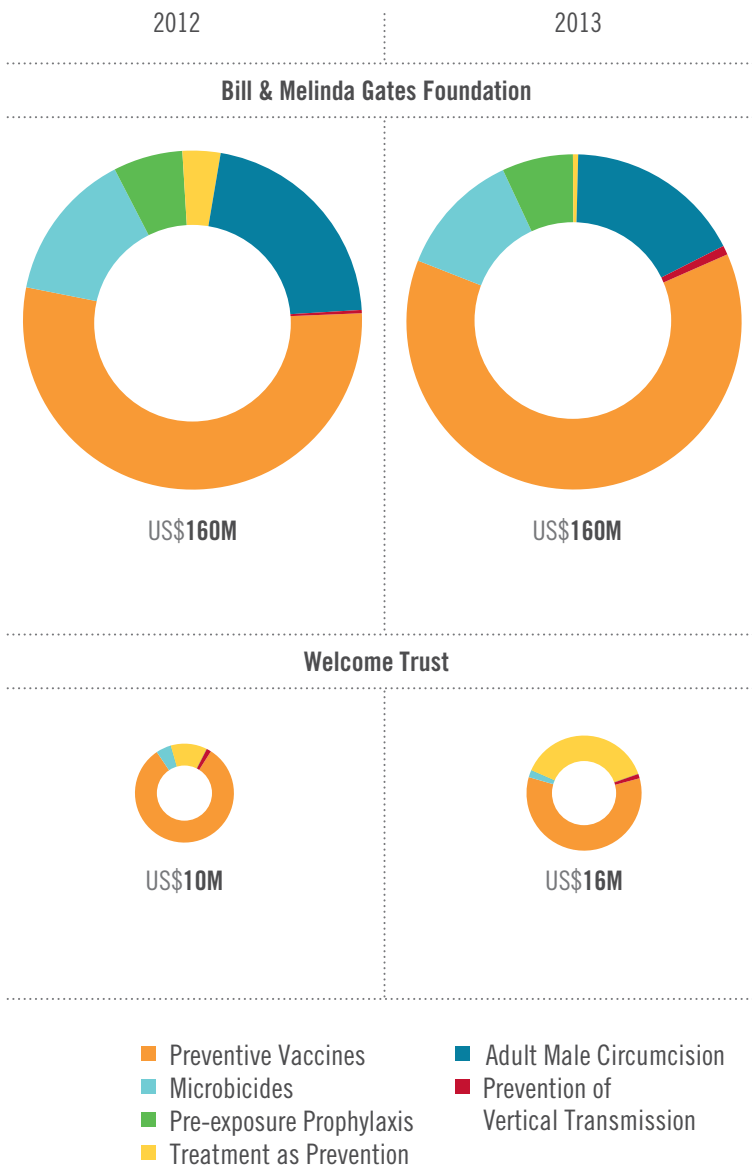
**The enabling environment has a profound effect on where trials take place and whether they are able to happen.**

HIV prevention research and development takes place within the larger public health, global health and human rights landscape (Figures 9, 10). US-based pre-exposure prophylaxis demonstration projects occur within the context of restrictions on syringe exchange programs and other limiting factors, and future vaccine and microbicide clinical trials in Africa must consider the human rights and gender equality implications of undertaking research in these settings. The HIV prevention field is grappling with how to incorporate new prevention options in their protocols while coordinating more resource-heavy trials that are expanded to the scale necessary in order to demonstrate efficacy, and it is also considering how research may be affected by the overall impact of health and rights in each trial setting, for each set of participants.

**FIG. 6 Top Five Countries Investing in HIV Prevention R&D: Public-sector Investment 2012 – 2013**



**FIG. 7 Top Philanthropies Investing in HIV Prevention R&D: Philanthropic-sector Investment 2012 – 2013 (US\$ millions)**



**Data collection and analysis methodology**

In order to generate investment estimates that can be compared from year to year, from one technology to another and across funding sources, the Working Group developed a systematic approach to data collection and collation during the first iteration of this collaborative project in 2004. The same methods were employed to generate the estimates of funding for R&D presented here.<sup>3</sup> Comprehensive

<sup>3</sup> See Appendix I for a detailed description.

**BOX 3**

**United States Funding for HIV Prevention Research and Development: The story of the largest HIV prevention research funder**

For over 30 years the US has been the largest funder of HIV prevention research (Figure 6). In 2013, US funding for HIV prevention research fell by over US\$44 million, from US\$925 million in 2012 to US\$887 million. What happened to cause this drop in investment?

In 2013, following contentious Congressional discussions on how to reduce the size of the federal budget, sequestration (automatic and mandated across-the-board cuts to all federally-funded programs) went into effect, impacting all agencies that invest in HIV prevention research, the NIH, USAID and the US Centers for Disease Control and Prevention (CDC) and the US Military HIV Research Program (MHRP).

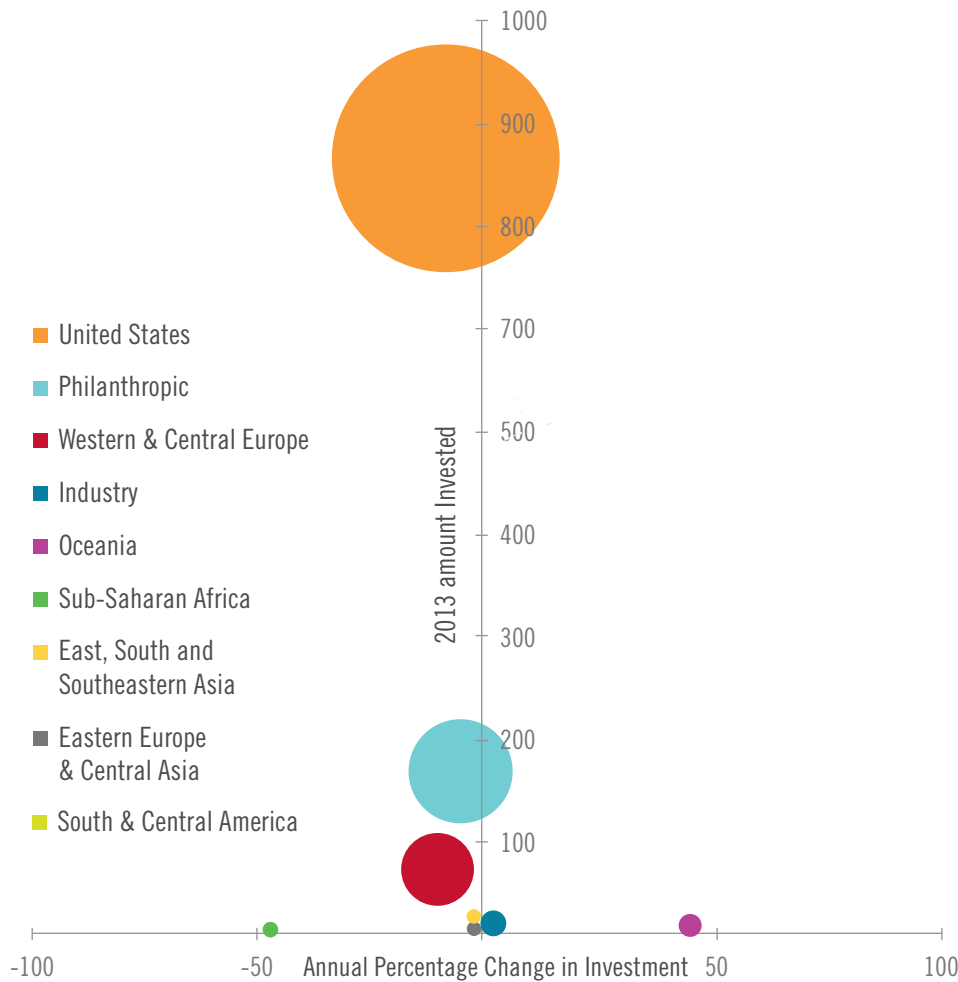
The NIH, the largest global funder of HIV prevention research, lost US\$153.7 million in AIDS research funding through these cuts. Two hundred eighty research grants went unfunded, including 31 dedicated to AIDS vaccine research.<sup>a</sup> Overall, the decline in NIH funding was four percent, from US\$789 million in 2012 to US\$755 million in 2013. The seven-percent decrease of NIH investment in AIDS vaccines was slightly higher than the overall decline. NIH funding for microbicide research declined 14 percent.

CDC’s HIV/AIDS, Viral Hepatitis, Sexually Transmitted Diseases and Tuberculosis Prevention account lost US\$62 million. The President’s Emergency Plan for AIDS Relief (PEPFAR) took the largest hit, funded in 2013 at US\$380 million below 2012 levels—the lowest since 2007. This is not indicative of a shift away from AIDS funding in general, but rather, a shift within AIDS funding strategy. USAID reprioritized funding in 2013 in order to meet the US pledge of US\$4 billion over three years towards the Global Fund to Fight AIDS, Tuberculosis and Malaria, with funding increasing by over 57 percent. Meanwhile, funding was shifted away from the R&D investments provided by PEPFAR.

While the President’s Fiscal Year 2014 budget request accounts for some of the loss in funding due to sequestration, it remains to be seen how and if HIV prevention research investment will recover in the years to come.

<sup>a</sup> amfAR. *The Effect of Budget Sequestration on Global Health: Projecting the human impact in fiscal year 2013*. March 2013. [www.amfar.org/the-effect-of-budget-sequestration-on-hiv/aids-in-the-united-states-projecting-the-human-impact-in-fiscal-year-2013](http://www.amfar.org/the-effect-of-budget-sequestration-on-hiv/aids-in-the-united-states-projecting-the-human-impact-in-fiscal-year-2013).

FIG. 8 2013 Investment in HIV Prevention R&D and Year-over-Year Change in Investment (US\$ millions)



and consistent use of the methodology enables data comparisons across organizations, countries and years. The Working Group makes every effort to maintain a comparable data set, while allowing for the limitations inherent to global resource tracking. The primary limitation is that data collection largely depends on the response rate of public, private and philanthropic funders, and year-to-year variability is to a degree a reflection of this response rate. Funds were allocated to the year in which they were disbursed by

the donor, irrespective of whether the funds were expended by the recipient in that year or in future years.<sup>4</sup> Investment figures are rounded throughout the report. In order to minimize double-counting, the Working Group distinguished between primary funders and intermediary organizations. “Intermediary” organizations receive resources from multiple funders and use these resources to fund their own work, as well as the work of others. All figures in the report are reported in current US dollars and have not been adjusted for inflation.<sup>5</sup>

<sup>4</sup> Any instances in which funds were reported in the year they were spent rather than disbursed are clearly noted, with the rationale behind this decision indicated.

<sup>5</sup> Funding information in other currencies was converted into US dollars using the appropriate International Monetary Fund (IMF) annual average exchange rate for July 1, 2013, except for those funds where we had access to the actual rate received.

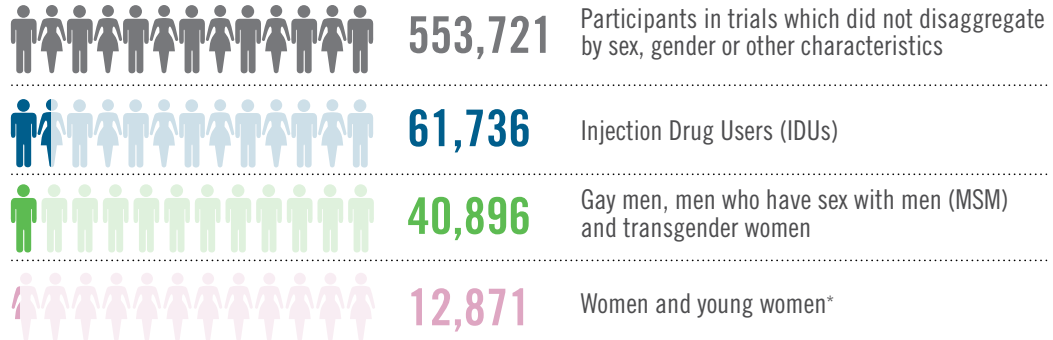
### Enabling Environment Perspective: Human rights legislation and environmental factors inhibit HIV prevention research

Prevention research still does not reflect the widespread consensus that the epidemic cannot be ended without focusing on disproportionately affected populations. Only six percent of trial participants in 2013 belonged to one of these populations (Figure 9 and 10). At the same time, these populations account for much higher proportions of new infections in priority research countries like Kenya and Nigeria.

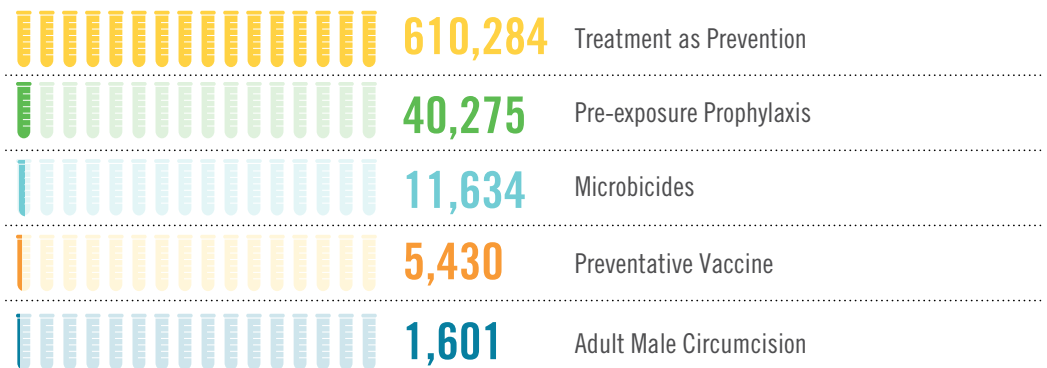
Of particular concern is a recent push to pass harsh anti-homosexuality laws in at least 11 countries in sub-Saharan Africa. Homosexuality is already illegal in those countries where 73 percent of 2013 research projects took place. If this trend continues, the research community will find it increasingly difficult to answer critical questions about how the prevention needs of affected populations can be met.

FIG. 9 Participants in HIV Prevention Trials 2013

#### Trial Participants by Population



#### Trial Participants by Prevention Option

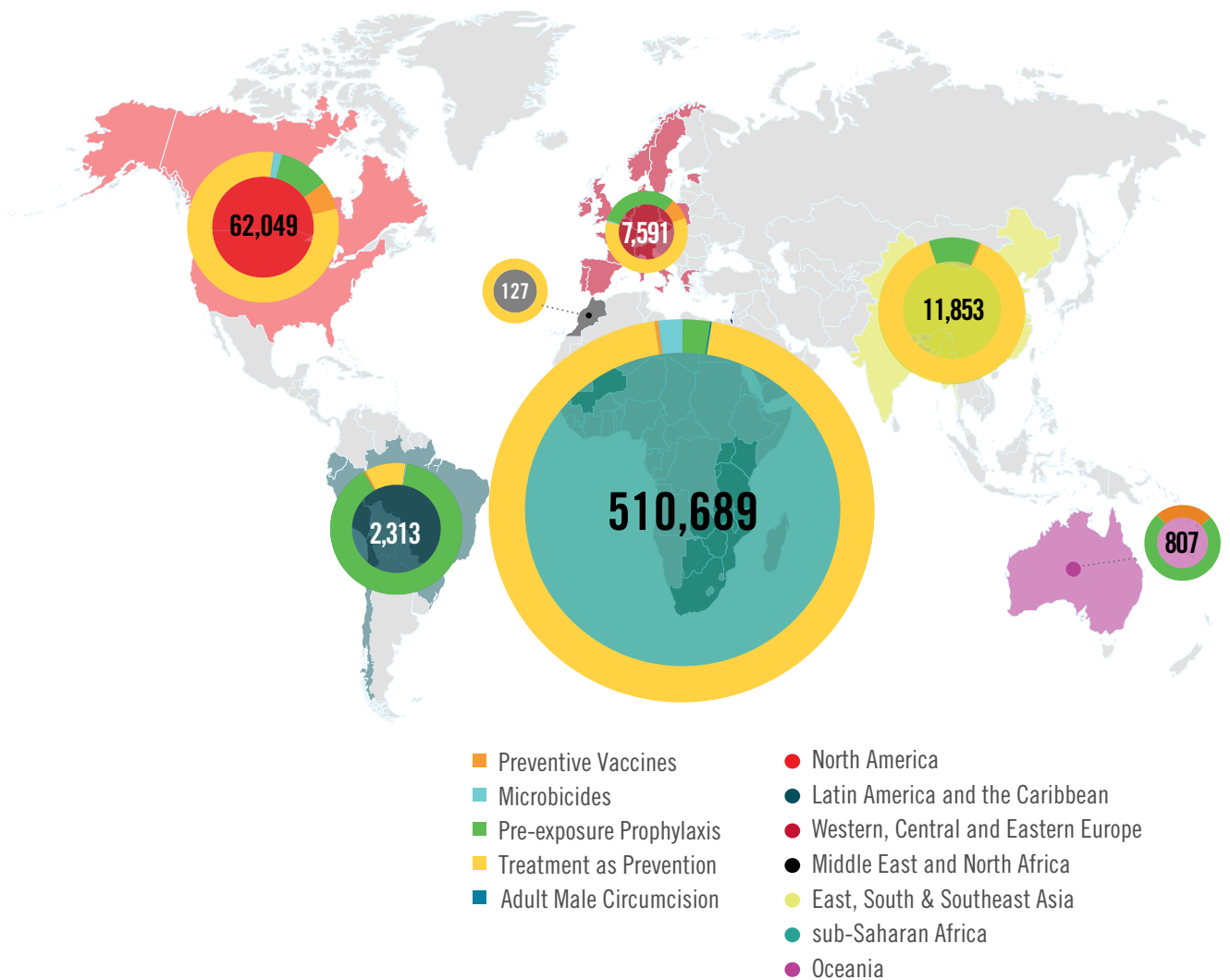


\* Includes trials which only enrolled women, or disaggregated by sex and gender.

Another major impediment to research on prevention options in these populations is the widespread disrespect for girls' and women's rights, resulting in challenges including violence against women, as well as criminalization of homosexuality, and the marginalization of injecting drug users and commercial sex workers. Gender-based violence, restricted access to education and secure income, and limited ability to make decisions about their sexual and reproductive lives are the realities many women face and the context in which many HIV prevention trials take place. All of these factors affect the ability of women to participate in HIV prevention trials, to continue participation once involved in trials, to use products and to actively engage in the research process. The factors that affect women's participation in clinical research are some of the very reasons it is vital that HIV prevention research for women continue. HIV/AIDS is the leading cause of death for women in their reproductive years, and for young women the HIV prevalence rate is twice that of young men. Products that address the needs of women need to be developed because of and in spite of the factors that affect the daily realities of women's lives.<sup>a</sup>

<sup>a</sup> UNAIDS. *UNAIDS Report on the Global AIDS Epidemic 2013*.

**FIG. 10 HIV Prevention R&D Trial Participants by Region 2013**



**Table 1: Global Investment in HIV Prevention R&D: 2013 funding map**

Funding Type	2012	2013	% Change 2012-2013	Funder	Total
US Public-Sector	925 million	887 million	-4%	NIH	750
				USAID/PEPFAR	85
				CDC	13.5
				MHRP	38.4
European Public-Sector	86 million	77 million	-10%	Belgium	1.1
				Denmark	4.4
				EC	25.1
				France	15.1
				Germany	0.3
				Ireland	2.6
				Italy	0.1
				Netherlands	8.9
				Norway	2.5
				Spain	0.2
				Sweden	0.1
				Switzerland	0.7
Other Governments	69 million	65 million	-6%	Australia	8.6
				Brazil	0.4
				Canada	37.1
				China	7.0
				Cuba	0.2
				India	1.9
				Japan	3.0
				Russia	0.1
				South Africa	4.0
				Taiwan	0.1
				Thailand	2.8
Philanthropic	203 million	193 million	-5%	BMGF	160.0
				Wellcome Trust	16.0
				Other	17.0
Industry	34 million	37 million	+9%	Commercial Sector	37.0
<b>Total</b>	<b>1.31 billion</b>	<b>1.26 billion</b>	<b>-4%</b>	<b>2013 HIV Prevention Option Totals</b>	<b>1.26 billion</b>
				<b>2012 HIV Prevention Option Totals</b>	<b>1.31 billion</b>
				<b>% Change 2012-2013</b>	<b>-4%</b>

<sup>a</sup> Where 100 percent increase in investment is noted, 2012 investment may not have been reported by funder and is not necessarily indicative of a 100 percent increase in funding from 2012. Similarly, where a 100 percent decrease in funding is noted, funder may not have reported investment for 2013. See appendix for detailed methodology section, including limitations of data collection.

2013 Totals in US\$ millions (2012 investment, percentage change<sup>a</sup>)

Preventive AIDS Vaccines			Microbicides			Pre-Exposure Prophylaxis			Treatment as Prevention			Male Circumcision			Female Condoms			Prevention of Vertical Transmission		
2013	2012	Change	2013	2012	Change	2013	2012	Change	2013	2012	Change	2013	2012	Change	2013	2012	Change	2013	2012	Change
518.2	557.0	-7%	111.2	130	-14%	14.2	9.8	+45%	64.8	57.3	+13%	1.2	1.0	+20%	0.15	0.3	-50%	40.0	33.2	+20%
27.3	28.7	-5%	42.8	43.2	-1%	1.0	2.2	-55%	11.25	11.25	0%	0.5	1.8	-72%	—	—	—	2.0	1.4	+43%
—	—	—	1.5	0.3	+400%	6.4	6.7	-4%	3.1	0	—	2.5	0	—	—	—	—	—	—	—
38.4	37.8	+2%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1.0	0.5	—	—	—	—	—	—	—	0.07	0.06	+17%	—	—	—	—	—	—	—	—	—
2.2	0.9	+144%	2.2	0.9	+144%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
16.2	8.4	+93%	8.9	14.0	-36%	—	—	—	—	—	—	—	—	—	—	—	—	—	0.8	—
10.3	9.0	+14%	0.25	0.3	-17%	1.6	0.5	+220%	2.2	2.0	+10%	0.7	1	-30%	—	—	—	0.01	0.8	-99%
—	—	—	—	—	—	—	—	—	0.3	2.4	-89%	—	—	—	—	—	—	—	—	—
1.3	1.2	+8%	1.3	1.2	+8%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	0.2	—	0.1	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
4.9	5.0	-2%	3.6	2	+80%	—	—	—	—	—	—	—	—	—	0.4	0	—	—	—	—
1.0	1.6	-38%	1.5	1.0	+50%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.2	1.3	-85%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.02	1.3	-98%	0.02	0.05	-60%	—	—	—	—	0.02	—	0.08	0.15	-47%	—	—	—	—	0.11	—
0.6	1.6	-63%	—	—	—	—	—	—	0.06	0.06	0%	—	—	—	—	—	—	—	—	—
6.1	20	-70%	9.1	7	+30%	—	—	—	0.5	0.12	+317%	—	—	—	—	—	—	0.1	0	—
7.2	4.8	+50%	0.7	0.5	+35%	0.3	0	—	0.4	0.5	-25%	0.03	0.12	-75%	—	—	—	—	6.6	—
0.4	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
16.3	15.0	+9%	0.2	10.0	-98%	0.1	0.4	-75%	20.3	13.0	+56%	0.03	0	—	—	—	—	0.2	0	—
7.0	7.0	0%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.2	0.08	+150%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1.5	1.5	0%	0.28	0.29	-3%	—	0.006	—	—	—	—	—	—	—	—	—	—	0.07	0.03	+133%
3.0	1.7	+76%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.1	0.1	0%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1.7	0.5	+240%	2.3	7.0	-67%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.1	0.1	0%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.4	0	—	1.6	1.3	+23%	—	—	—	0.8	0	—	—	—	—	—	—	—	—	—	—
100.4	86	+17%	19.2	22.9	-16%	10.9	10.6	+3%	0.80	5.8	-86%	27.2	34.2	-20%	—	—	—	1.4	0.5	+180%
7.7	8.2	-6%	0.3	0.5	-40%	—	—	—	7.7	1.2	+542%	—	—	—	—	—	—	0.2	0.2	0%
12.4	15.5	-20%	0.4	1.2	-67%	—	0.23	—	4.6	4.9	-6%	0.08	0.23	-65%	—	0.45	—	0.1	0.2	-50%
31	30	+3%	3	3	0%	1.7	1.3	+31%	—	—	—	—	—	—	1.6	1.6	0%	—	—	—
<b>818 million</b>			<b>210 million</b>			<b>36 million</b>			<b>117 million</b>			<b>32 million</b>			<b>2.2 million</b>			<b>44 million</b>		
847 million			245 million			31 million			98 million			41.6 million			2 million			43.8 million		
-3%			-14%			+16%			+19%			-23%			+10%			0%		







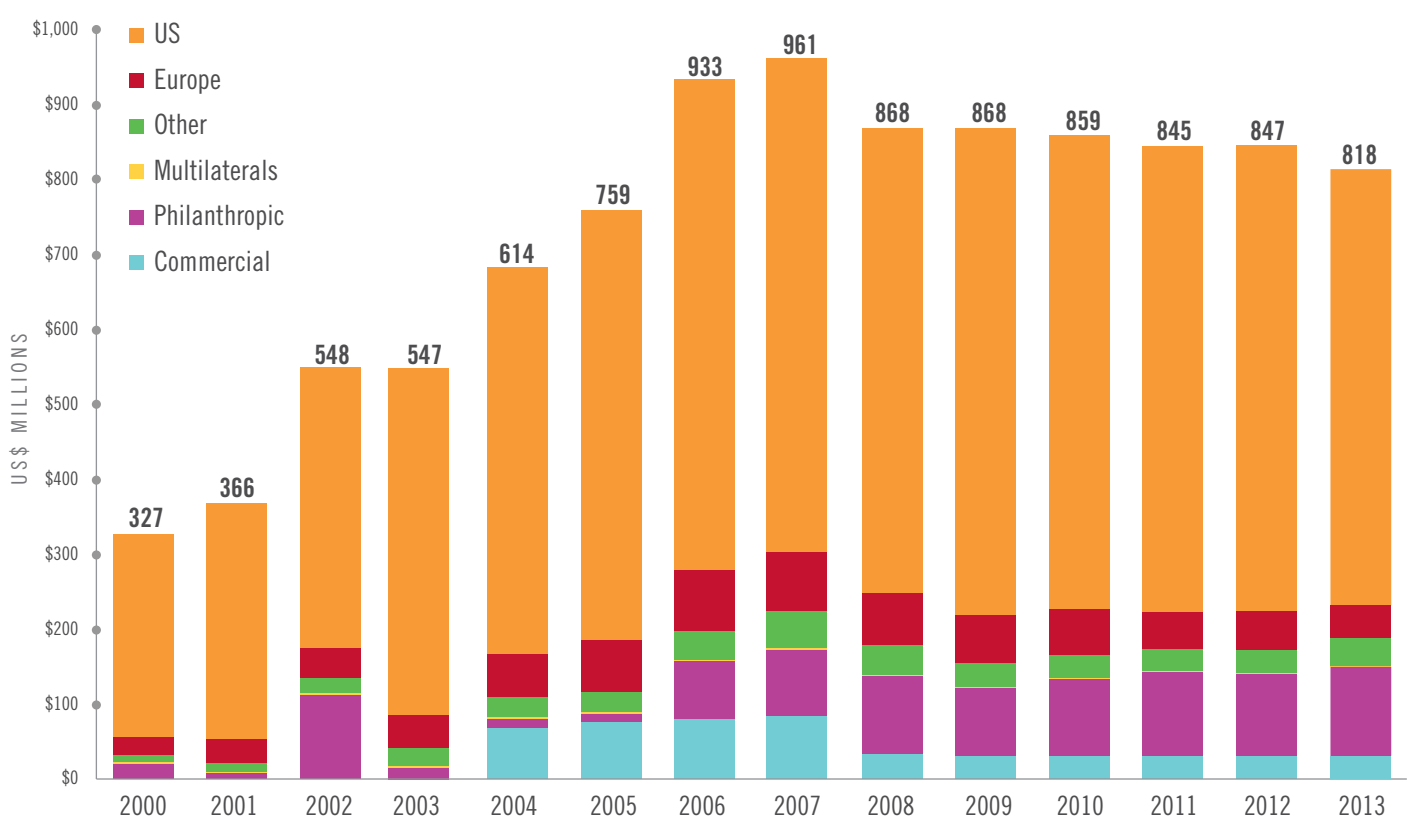
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## Global Investments in Preventive AIDS Vaccine Research and Development

In 2013, investments in global preventive AIDS vaccine R&D declined by US\$29 million, three percent, from US\$847 million in 2012 to US\$818 million in 2013 (Figure 11). 2013 saw the largest real decrease in preventive AIDS vaccine investment<sup>6</sup> since 2008, following five years in which funding had either declined or flatlined from a height of \$961 million in 2007 (Table 2). The substantial decrease in investment in 2013 was due primarily to the effects of mandated austerity measures taken by the US government, and in part to institutional and policy shifts within international development agencies in Europe and other countries.

The preventive AIDS vaccine field grappled with difficult questions in 2013. In April 2013, HVTN 505, the only ongoing efficacy trial, halted immunizations of its DNA-adenovirus type 5 (Ad5) vaccine regimen because its Data Safety and Monitoring Board (DSMB) found that the vaccine did not prevent HIV infection, nor did it reduce viral load among vaccine recipients who became infected with HIV. The US-based trial, which was funded by the NIH's National Institute of Allergy and Infectious Diseases (NIAID), was estimated to cost between US\$75 and US\$80 million and intended to run from 2009 to 2015. Researchers and funders

FIG. 11 Preventive AIDS Vaccine Funding from 2000 – 2013 (US\$ millions)



<sup>6</sup> While percentage declines have been higher in previous years, the dollar value of the decline between 2012 and 2013 is the highest in the the past five years.

**Table 2: Annual Investments in Preventive AIDS Vaccine R&D 2000 – 2013 (US\$ millions)<sup>a</sup>**

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>US</b>	272	314	376	463	516	574	654	659	620	649	632	615	623	584
<b>Europe</b>	23	32	39	44	57	69	82	79	69	65	61	48.5	52	44
<b>Other</b>	10	12	21	24	28	27	38	49	41	31	32	30	31	38
<b>Multilaterals</b>	2	2	2	2	2	2	2	2	1	1	1	0.5	0.5	0.5
<b>Total Public</b>	307	359	436	532	602	672	776	789	731	746	726	702	707	667
<b>Total Philanthropic</b>	20	7	112	15	12	12	78	88	104	92	103	113	110	120.5
<b>Total Commercial</b>	–	–	–	–	68	75	79	84	33	30	30	30	30	31
<b>Total Global Investment</b>	<b>327</b>	<b>366</b>	<b>548</b>	<b>547</b>	<b>682</b>	<b>759</b>	<b>933</b>	<b>961</b>	<b>868</b>	<b>868</b>	<b>859</b>	<b>845</b>	<b>847</b>	<b>818</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

met in September of 2013 to discuss the future for adenovirus platforms for preventive AIDS vaccines, leading to the April 2014 publication by Dr. Anthony Fauci and colleagues at the NIAID of recommendations on moving forward with research on adenovirus-vectored vaccines. While no clinical trials using an Ad-5 based regimen are planned or enrolling, other adenovirus vectors-based vaccines have showed promise. Progress is being made with an Ad26-based vaccine set to begin a Phase I clinical trial in late-2014, to be funded by Janssen and NIAID.

The Pox-Protein Public-Private Partnership (P5) is funding and organizing a follow-up to the RV144 trial, where a pox-protein vaccine regimen

was shown to reduce the risk of HIV infection by 31.2 percent after three years of follow-up, proving for the first time that a preventive AIDS vaccine is possible. Organizational and financial support for the P5 comes from NIAID, the Bill & Melinda Gates Foundation, the US Military HIV Research Program, Sanofi Pasteur, Novartis Vaccines and Diagnostics and the South African Medical Research Council (Box 4).

More than 30 other vaccine candidates were in the pipeline in 2013, most in early-stage trials. Basic research is ongoing to identify vaccine antigens that would stimulate immune systems to create broadly-neutralizing antibodies. Early-stage passive immunization trials supported by

**BOX 5**

**Beyond RV144**

Building on the results of the RV144 trial in Thailand, follow-on studies advanced throughout 2013:

- RV306, the follow-up study to RV144, began in September 2013, evaluating the RV144 vaccine regimen, comparing additional vaccine boosts and gathering more immunogenicity data in Thailand.
- In March 2014, data from the RV305 trial in Thailand showed that the magnitude of immune responses increased with the re-boost vaccination of RV144 participants three years after their last dose of primary vaccination. How long these responses persist continues to pose a question for further research.
- In August 2013, Thailand announced its commitment to support a future efficacy study at the AVEC (AIDS Vaccine Efficacy Consortium) Summit for an AIDS-Free Generation in Thailand and assist in establishing a flexible biologics manufacturing capability that could

support preventive AIDS vaccine production in Thailand. AVEC hopes to finalize plans for the protein development in 2014, so plans for an efficacy study can proceed and enrollment can potentially begin in 2017.

- Led by the NIAID-funded HIV Vaccine Trials Network (HVTN), a Phase I trial, HVTN 097, started in South Africa in June 2013 using the same regimen that was tested in RV144. The HVTN is planning Phase II and Phase III trials to begin in 2015 that will move to potentially license an ALVAC protein prime boost similar to RV144. The efficacy trial, HVTN 702, is expected to enroll more than 5,000 volunteers in late-2016.
- At the same time, the HVTN is developing a suite of studies in Southern Africa with different pox-protein combinations in a series of phase I and II trials. HVTN 701 is a two-part trial design with Part A Phase I trial for safety and immunogenicity, and Part B Phase IIb testing safety, immune responses and efficacy. The trial is tentatively scheduled to begin in 2015 for Part A and late-2016 to Part B.

## Crowd-funding for Preventive AIDS Vaccine Research

In early-2014, the US-based Immunity Project posted a video online asking the public to crowd-fund AIDS vaccine research with the message, “In a few short years we can be distributing our vaccine to the millions who need it most. So pledge now to make a difference, and together let’s end HIV/AIDS and save millions of lives.”

The Immunity Project, launched with US\$20,000 backing from the technology-startup Accelerator Y Combinator, has raised US\$462,570 through crowd-funding and has partnered with the Until There’s A Cure non-profit organization. The project is looking to find epitopes that are targeted by HIV elite-controllers and use these epitopes in a vaccine to produce a protective T-cell response.

Crowd-funding, the use of small amounts of capital from a large number of individuals to finance a new business venture, is a relatively new financing mechanism. Crowd-funding is being used by some scientists to appeal to the public to fund their research and studies. As US public-sector budgets for biomedical research decline across all areas of research, young scientists and new research projects find it increasingly difficult to obtain funding, and crowd-funding could potentially provide a way to jumpstart innovative research.

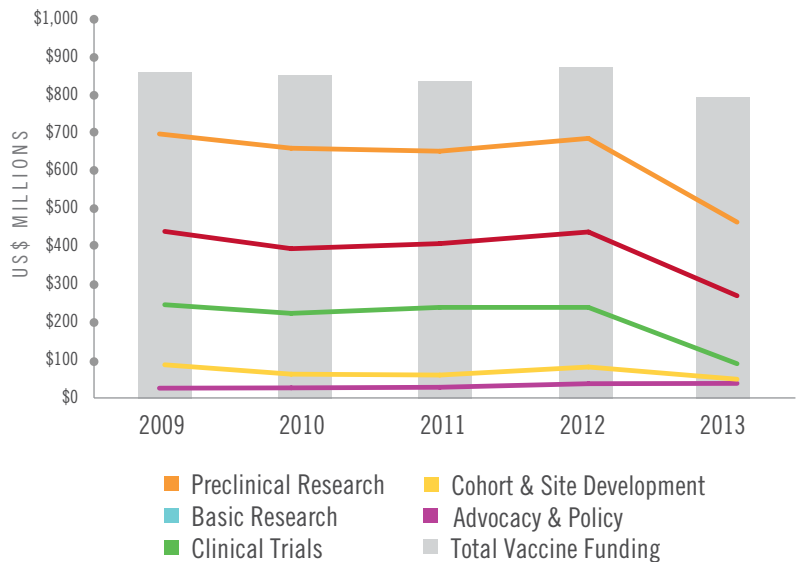
The largest US site devoted to crowd-funding, Kickstarter, does not allow medical research projects, as most basic scientific research does not fit into their guidelines, which specify that projects must have “a clear end, like making an album, a film or a new game.” The long-term, often uncertain path of developing an AIDS vaccine does not adhere to such guidelines. Crowd-funding is largely dependent upon communications with the public, and publicizing AIDS vaccine development is complicated and potentially risky or even dangerous, since references to near-term advances can prove erroneous or misleading.

the NIH, and a vectored immunoprophylaxis trial led by the International AIDS Vaccine Initiative (IAVI), are underway, and could lead to testing of the concept that broadly-neutralizing antibodies can reduce the risk of HIV infection. Vaccine candidates using replicating vectors are also showing promising results, with IAVI’s Sendai virus vaccine currently in a phase I study in Kenya, Rwanda and the UK. China’s National Center for AIDS/STD Control and Prevention and China CDC are currently testing a replicating Tian Tan vaccine in a Phase II study.

## 2.1 Funding Allocations for Preventive AIDS Vaccine Research and Development

In 2013, spending by the public and philanthropic sectors on preventive AIDS vaccine R&D was allocated to five categories (Figure 12): basic research (41 percent); preclinical research (42 percent); clinical trials (11 percent); cohort and site development (three percent); and advocacy and policy (three percent). In 2013, the distribution of investment among the five categories shifted for the first time in five years (Figure 12). With no large efficacy trials starting or ongoing for the last three quarters of 2013, funding for clinical trials decreased by 52 percent, which led in part to the decrease in overall funding. As basic research efforts scaled up, funding for basic research increased by 46 percent (Table 3). Further information about the categories used to define R&D can be found in Table 13 of the Methodology section of the Appendix.<sup>7</sup>

FIG. 12 Preventive AIDS Vaccine Expenditures 2009 – 2013 (US\$ millions)<sup>a</sup>



<sup>a</sup> Total expenditure is a subset of total investment.

<sup>7</sup> With the exception of “policy and advocacy,” these are the categories used by the NIH to classify allocations for AIDS vaccine research. Because not all data from funders can be parsed according to these five categories, these percentages were estimated based on a US\$560 million subset that allowed for determining allocations. These expenditure estimates do not include therapeutic vaccines.

**Table 3: Preventive AIDS Vaccine Research and Development Categories 2009 – 2013**

R&D Categories	2009	2010	2011	2012	2013
Basic research	29%	27%	27%	28%	41%
Preclinical research	37%	41%	39%	40%	42%
Clinical trials	23%	25%	28%	23%	11%
Cohort and site development	10%	6%	5%	7%	3%
Advocacy and policy	1%	1%	1%	2%	3%

## 2.2 Public Investments in Preventive AIDS Vaccine Research and Development

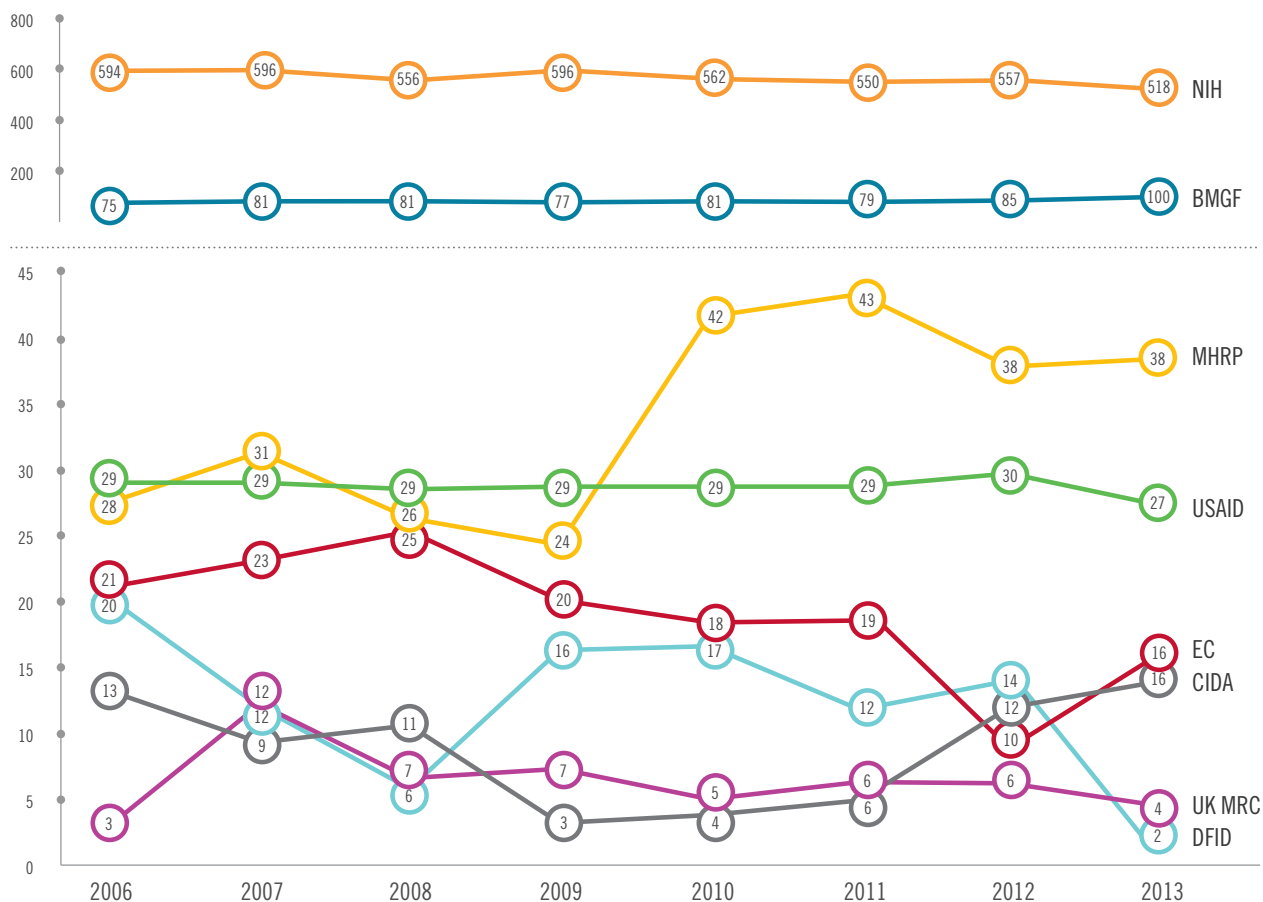
In 2013, public-sector AIDS vaccine research funding declined to its lowest level since 2005, at US\$667 million. Public-sector funding made up 81 percent of total AIDS vaccine funding in 2013, nearly the same proportion as in every year of the past decade. This is due to the fact that the rise and fall in total HIV prevention research investment is largely dependent on public-

sector funding trends. The negative effects of the US budget-cuts and shifts in policy toward international development funding resulted in a US\$40 million decrease in 2013 investments, down from US\$707 million in 2012.

US government agencies alone accounted for 70 percent of total AIDS vaccine R&D funding, with the US NIH contributing 62 percent of the total—slightly lower than 2012 percentages. As the largest funder (Table 4), US investments not only set the year-to-year investment trend, but support the majority of ongoing research across all categories. With the significant budget cuts to all US agencies supporting AIDS vaccine research, 31 AIDS vaccine projects were left unfunded.

While international development agencies decreased their funding for AIDS vaccine research in 2013 overall—including declines in investments in the UK, Norway, Belgium and Denmark—investment by the European Union (EU) actually increased. 2013 was the last year of

**FIG. 13 Top Preventive AIDS Vaccine Funder Trends 2006 – 2013 (US\$ millions)**



**Table 4: Top Preventive AIDS Vaccine Funders for 2010 – 2013 (US\$ millions)<sup>a,b</sup>**

2010 Rank	Funder	Amount	2011 Rank	Funder	Amount	2012 Rank	Funder	Amount	2013 Rank	Funder	Amount
1	NIH	561.6	1	NIH	550.4	1	NIH	557	1	NIH	518.2
2	BMGF	80.9	2	BMGF	78.5	2	BMGF	86.0	2	BMGF	100.4
3	MHRP	41.6	3	MHRP	43.3	3	MHRP	37.8	3	MHRP	38.4
4	USAID	28.7	4	USAID	28.7	4	USAID	28.7	4	USAID	27.3
5	EC	19.9	5	DFID	11.8	5	DFID	14.0	5	CHVI <sup>c</sup>	14.7
6	China	18.3	6	EC	10.3	6	CHVI <sup>19</sup>	12.0	6	EC	12.8
7	DFID	16.6	7	Ragon Foundation	10.0	7	Ragon Foundation	10.0	7	Ragon Foundation	10.0
8	Ragon Foundation	10.0	8	ANRS	7.3	8	EC	8.4	8	Wellcome Trust	7.7
9	ANRS	6.6	9	China	6.9	9	Wellcome Trust	8.2	9	China <sup>e</sup>	7.0
10	Wellcome Trust	5.1	10	Wellcome Trust	6.5	10	China	7.0	10	NHMRC	6.8
11	UK MRC	5.0	11	UK MRC	6.2	11	UK MRC	6.2	11	ANRS	5.3
12	EDCTP	4.5	12	CHVI	5.8	12	Institute Pasteur	4.8	12	Netherlands	4.9
13	CIDA	3.8	13	CIDA	4.9	13	Netherlands	4.8	13	Institute Pasteur	4.8
14	AECID	3.6	14	NMHC	3.9	14	NHMRC	4.4	14	UK MRC	4.4
15	NORAD	2.5	15	Netherlands	3.8	15	ANRS	4.0	15	EDCTP	3.4

<sup>a</sup> See appendix for list of acronyms.

<sup>b</sup> A portion of the significantly lower contribution to AIDS vaccine R&D by DFID in 2013 can be attributed to a difference in funding cycles: a £5 million disbursement was recognized as 2012 funding due to Working Group Methodology.

<sup>c</sup> Participating CHVI Government of Canada departments and agencies are: the Canadian International Development Agency (CIDA), the Public Health Agency of Canada (PHAC), Industry Canada, the Canadian Institutes of Health Research (CIHR) and Health Canada. CIHR grants are reported separately.

<sup>d</sup> Amounts converted from euros to US dollars are subject to exchange rate variations. Amounts are converted using the IMF annual average exchange rate for July 1, 2013.

<sup>e</sup> The Working Group could not obtain a response from China for investments made in 2012 and 2013; thus, an estimate was developed and sent to China's National Center for AIDS/STD Control and Prevention. The estimate was developed based on public information submitted by the National Center for AIDS/STD Control and Prevention and China's Center for Disease Control and Prevention on clinicaltrials.gov, regarding a Phase II preventive AIDS vaccine trial started in August 2012, as well as other basic research underway.

the EU's Seventh Framework Programme for Research (FP7). Of the total €10.8 billion (US\$14 billion, July 1, 2013)<sup>8</sup> budget for research and innovation in 2013, the EU allocated €8.1 billion (US\$10.6 billion, July 1, 2013) to proposals under the EU's FP7. As the largest amount of funding allocated since the inception of the FP7, funding for preventive AIDS vaccine research in 2013 increased by 52 percent, or €3.4 million (US\$4.4 million, July 1, 2013). Additionally, preparations are underway for a second phase of the European & Developing Countries Clinical Trials Partnership program (EDCTP2), set to run from 2014 to 2024 as part of the EU's Horizon 2020 research funding program. The first phase of EDCTP provided €38.4 million (US\$50 million, July 1, 2013) to AIDS vaccine research from 2003-2012. The next phase of EU funding, Horizon 2020, is set to begin in 2014, with funding for "personalizing health and care," including work on vaccine platforms for HIV.

**BOX 7**

**Preventive AIDS Vaccine Research in South Africa: New partnerships and infrastructure development**

In late-2013, the South African Medical Research Council (MRC) and the University of Cape Town established a partnership with the BMGF to develop new therapeutics, vaccines and other biotechnologies to fight HIV, tuberculosis (TB), and malaria. The partnership is a North-South co-funding arrangement backed by both the BMGF and South Africa's Department of Science and Technology and Department of Health.

The BMGF is contributing US\$11.7 million to the MRC for its Strategic Health Innovation Partnerships unit over three years to develop vaccines for HIV and TB. In addition to the funding from BMGF, the unit will receive US\$13.1 million from the South African Department of Science and Technology and US\$6.0 million from the South African Department of Health.

In October 2013, the HVTN opened an AIDS vaccine laboratory in Cape Town, South Africa. The Cape Town HVTN Immunology Laboratory will analyze blood samples from trial participants in follow-up trials to RV144 that are taking place in South Africa. The laboratory received approximately US\$3.5 million in funding from the BMGF in 2013.

<sup>8</sup> Commercial funding figures are based upon a review of AIDS vaccine programs at each company. In recent years, fewer companies have been willing to provide actual investment figures for their programs. Where companies decline to report financial information, the Working Group develops estimates for companies based upon interviews with company staff and third parties, and publicly filed documents. The amounts described here are estimated investments of companies' own funding and do not include the financial support that many of these companies receive from the public-sector and through public-private partnerships. Additionally, estimated amounts for private sector funders are not included in the list of top funders.

**Table 5: Philanthropic Investment in Preventive AIDS Vaccine R&D by Foundations and Commercial Philanthropy in 2013 (US\$ millions)**

Amount	Investors
US\$100.4 million	BMGF
US\$5-US\$10 million	Ragon Foundation, Wellcome Trust
US\$1 to US\$5 million	None in 2013
US\$500,000 to US\$1 million	New York City Economic Development Corporation, Obra Social Fundación “La Caixa”
US\$250,000 to US\$500,000	Robert Wood Johnson Foundation,
<US\$250,000	amfAR, Broadway Cares/Equity Fights AIDS, Emmes, James B. Pendleton Charitable Trust, GSK

### 2.3 Philanthropic Investments in Preventive AIDS Vaccine Research and Development

Investment from the philanthropic sector increased by US\$10.5 million in 2013, from US\$110 million in 2012 to US\$120.5 million, or 15 percent of the total funds disbursed for preventive AIDS vaccine R&D (Table 5). The BMGF has been the top philanthropic funder in this area for over a decade, investing US\$100.4 million in 2013, 83 percent of all philanthropic funding and 17 percent more than in 2012—its highest level of funding since the foundation began investing in AIDS vaccine research. The Ragon Foundation and the Wellcome Trust ranked second and third, at US\$10 million and US\$7.7 million, respectively, in 2013.

### 2.4 Commercial-sector Investments in Preventive AIDS Vaccine Research and Development

Commercial-sector funding for preventive AIDS vaccine R&D totaled US\$31 million in 2013,

**Table 6: Estimated Commercial Engagement in Preventive AIDS Vaccine R&D by Company in 2013 (US\$ millions)**

Amount	Investors
US\$5 million to US\$10 million	Crucell, Novartis International AG, Sanofi Pasteur
US\$1 million to US\$5 million	ESTEVE, GSK, Merck, Mymetics
US\$100,000 to US\$1 million	Advanced BioScience, Argos Therapeutics, Bionor Immuno, FIT-Biotech, Genvec, GeoVax, Ichor, Inovio Pharmaceuticals, Vical

making up approximately three percent of the total global investment in AIDS vaccine R&D (Table 6). Several large pharmaceutical companies have historically invested in preventive AIDS vaccine research, and biotechnology firms are increasingly engaging in R&D efforts, yet apart from a few companies, commercial-sector engagement has waned significantly in recent years.

Multinational pharmaceutical companies engaging in substantial research efforts include Sanofi Pasteur, Novartis International AG, GlaxoSmithKline (GSK) and Crucell, a Janssen pharmaceutical company of Johnson & Johnson. Each has participated in public-private partnerships, contributing expertise to the development and manufacture of vaccines.

Sanofi Pasteur, Novartis and GSK are also supporting the P5, to build on the success of the RV144 HIV vaccine trial. Sanofi Pasteur is contributing its expertise and its vaccine, ALVAC, to the partnership. Novartis is also contributing expertise, its protein, gp120, and an adjuvant, MF59.

Crucell, Beth Israel Deaconess Medical Center and Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology and Harvard, and the US MHRP at the Walter Reed Army Institute of Research collaborated on a preclinical study showing promising results of an adenovirus 26 (Ad26) vaccine in 2012, which is now being tested in early clinical trials. Later stage trials of the vaccine are currently being planned.

Programs by Merck and GSK have scaled back from prior years and biotechnology research is largely conducted with funding from the US public sector. In early 2014, GSK acquired Novartis' vaccine businesses (currently marketed products), with the transaction expected to be completed by the first half of 2015 and with around 70 percent of GSK's revenues focused on four areas (respiratory, HIV, vaccines and consumer healthcare). GSK stated that the acquisition would strengthen their manufacturing network and reduce supply costs. The move may affect GSK's R&D investment in AIDS vaccines, among other HIV-related research.

# 3.0

## Global Investments in Microbicide Research and Development

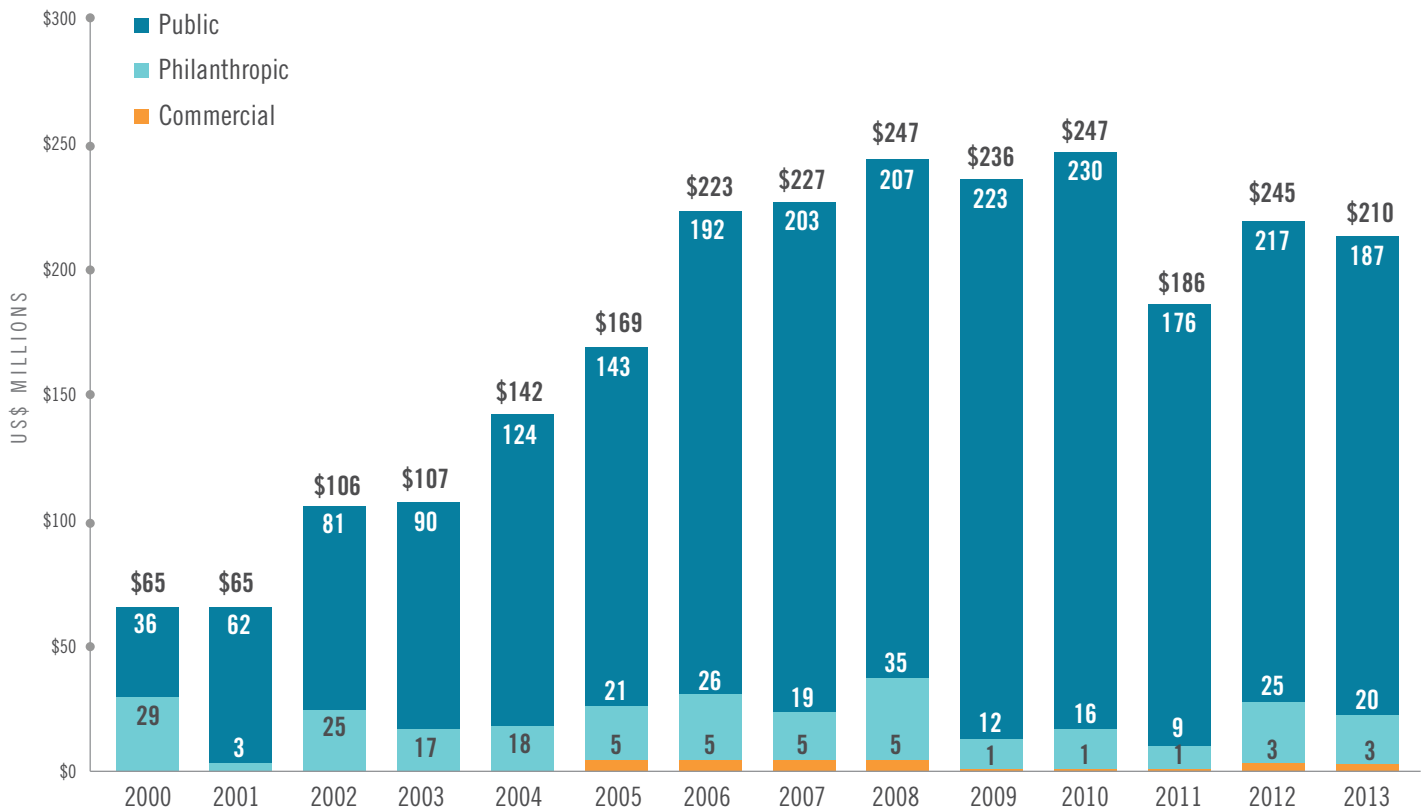
Global investment in microbicide R&D fell in 2013 by US\$35 million, to a total of US\$210 million (Figure 14). Of that 2013 total, the public sector provided US\$187 million (89 percent), the philanthropic sector provided US\$20 million (10 percent) and the commercial sector gave US\$3 million (one percent). Funding decreased in all sectors in 2013, with the largest reductions in funding coming from US public-sector agencies, whose participation fell by US\$18 million in 2013, due largely to substantial reductions in NIH and USAID funding. Still, the US public sector remained the largest source of microbicide investment overall, funding 74 percent of the 2013 total (Table 7).

The philanthropic sector also reduced its funding in 2013, with the largest philanthropic funder, BMGF, decreasing funding by nearly US\$4 million. Additionally, some philanthropic funders that had invested in microbicide research in previous years did not do so in 2013.

### 3.1 Funding Allocations for Microbicide Research and Development

In 2013, expenditures on microbicide R&D were allocated across the following seven categories (Figure 15): basic mechanisms of mucosal transmission (10 percent); preclinical testing (20 percent); formulations and modes

FIG. 14 Microbicide Funding 2000 – 2013 (US\$ millions)

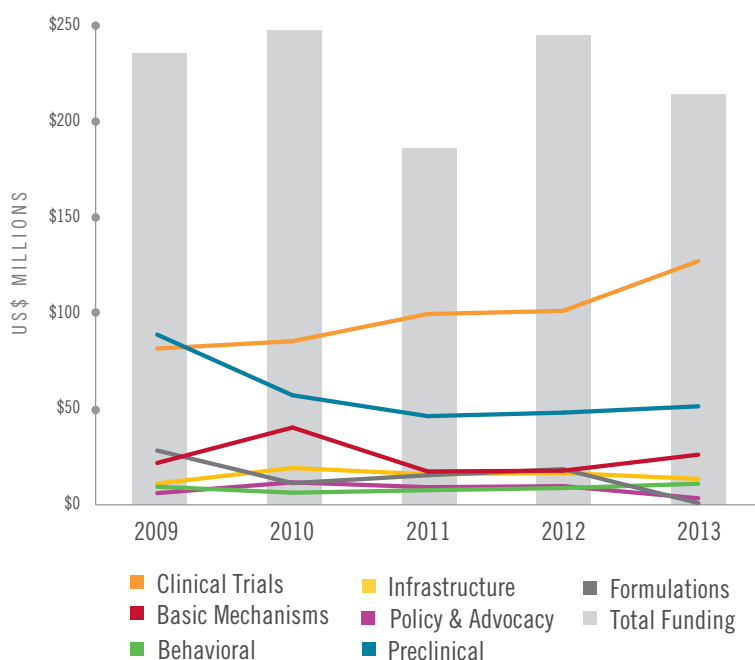


**Table 7: Annual Investments in Microbicide R&D 2006 – 2013 (US\$ millions)<sup>a</sup>**

	2006	2007	2008	2009	2010	2011	2012	2013
<b>US</b>	129.7	139.8	154.4	172.6	181.7	148	173	155
<b>Europe</b>	56.3	59.6	39.9	44.4	40.3	16	27	27
<b>Other</b>	4.7	3.4	12.1	5.7	8.3	12	17	5
<b>Multilaterals</b>	1.4	0.2	0.2	0.2	0.1	0.1	0.1	0.1
<b>Total Public</b>	192.1	203	206.6	222.9	230.4	176	217	187
<b>Total Philanthropic</b>	26.2	19	34.6	11.8	15.9	9	25	20
<b>Total Commercial</b>	4.5	4.5	2.5	1	1	1	3	3
<b>Total Global Investment</b>	<b>222.8</b>	<b>226.5</b>	<b>243.7</b>	<b>235.7</b>	<b>247.3</b>	<b>186</b>	<b>245</b>	<b>210</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

**FIG. 15 Microbicide Research and Development Expenditures for 2009 – 2013 (US\$ millions)**



of delivery (10 percent); clinical trials (50 percent); microbicide behavioral and social science research (four percent); microbicide research infrastructure (five percent); and policy and advocacy (one percent). Funding allocations for clinical trials increased by 23 percent in 2013, reflecting two ongoing Phase III studies of the dapivirine ring (Table 8). Further information about the categories used to define R&D can be found in Table 14 of the Methodology section of the Appendix.

**Table 8: Microbicide Research and Development Categories 2009 – 2013**

R&D Categories	2009	2010	2011	2012	2013
<b>Basic mechanisms of mucosal transmission</b>	9%	18%	8%	11%	<b>10%</b>
<b>Preclinical testing</b>	36%	25%	22%	28%	<b>20%</b>
<b>Formulations and modes of delivery</b>	11%	5%	7%	14%	<b>10%</b>
<b>Clinical trials</b>	34%	36%	48%	32%	<b>50%</b>
<b>Behavioral and social science research</b>	4%	2%	3%	3%	<b>4%</b>
<b>Research infrastructure</b>	4%	8%	7%	10%	<b>5%</b>
<b>Advocacy and policy</b>	2%	4%	4%	2%	<b>1%</b>



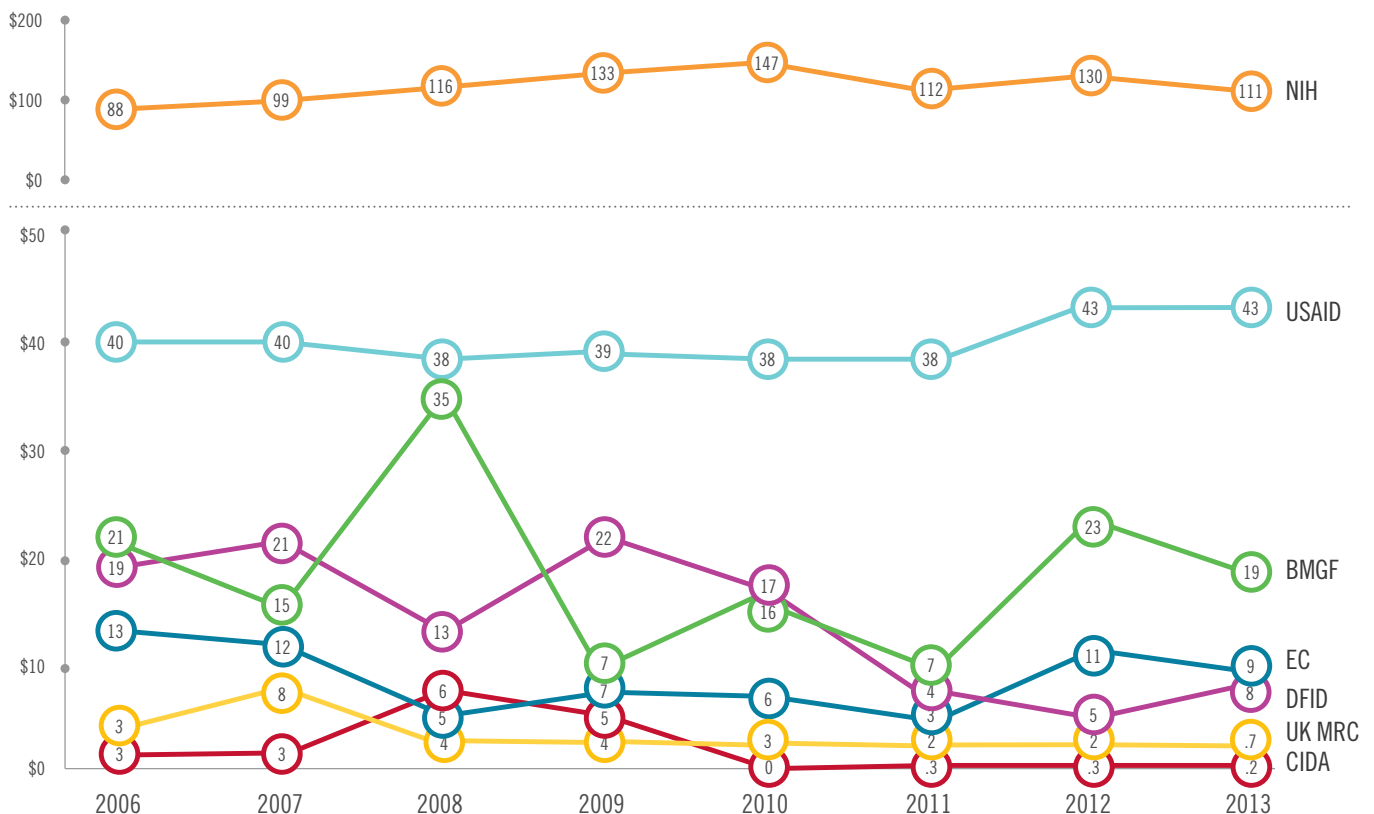
### 3.2 Public Investments in Microbicide Research and Development

Public-sector investment accounted for 89 percent of combined global funding for microbicide research, development and advocacy in 2013. While the US remained the primary source of funding, European national governments and the European Commission (EC) together accounted for US\$27 million, flatlining from the year before (Figure 16). Still, due to diminished budgets for research in general, European investment in microbicide R&D continued to lag behind the levels of earlier years, and its future is unclear. 2013 was the final year of the FP7, the EC Framework strategy for research and innovation under which microbicide R&D has been funded since 2007. The Horizon 2020 initiative, the next iteration of the Framework strategy launched in early 2014, has a US\$82.5 billion budget; however, it is still unclear if any of this funding will go to new microbicide research.

Trial results reported in 2013 also affect the funding picture for microbicide R&D going forward. The NIH-funded VOICE (MTN 003) trial results in early 2013 indicated that none of the study interventions—daily oral tenofovir, daily oral TDF/FTC and daily 1% tenofovir gel—provided protection against HIV and that levels of adherence to product use by the women involved in the trial were insufficient to permit evaluation of the products' efficacy. These two conclusions and their interrelationships are being explored in a series of secondary analyses and at least one follow-up trial.

The ongoing FACTS 001 trial, funded by the BMGF, the South African Department of Science and Technology, South African National Department of Health and USAID, is scheduled to release results in 2014 on the safety and effectiveness of 1% tenofovir gel. Intended as a confirmatory trial, FACTS 001 may well prove to be the final arbiter of the future of tenofovir gel for vaginal protection from HIV infection, although its potential for rectal application will remain to be determined.

FIG. 16 Top Preventive Microbicide R&D Funder Trends 2006 – 2013 (US\$ millions)



**Table 9: Top Microbicide Research and Development Funders for 2010 – 2013 (US\$ millions)<sup>a</sup>**

2010 Rank	Funder	Amount	2011 Rank	Funder	Amount	2012 Rank	Funder	Amount	2013 Rank	Funder	Amount
1	NIH	147.0	1	NIH	111.8	1	NIH	129.9	1	NIH	111.2
2	USAID	38.0	2	USAID	36.0	2	USAID	43.2	2	USAID	42.8
3	DfID	16.5	3	South African DST/DOH	10.0	3	BMGF	22.9	3	BMGF	19.2
4	BMGF	15.7	4	BMGF	7.0	4	EC	13.6	4	DFID	8.4
5	EC	6.7	5	DfID	3.2	5	CHV19	9.2	5	EC	6.7
6	China	3.6	6	Netherlands	2.7	6	South Africa <sup>b</sup>	7.0	6	Netherlands	3.6
7	UK MRC	3.4	7	NORAD	2.5	7	DFID	4.7	7	South Africa DST/DOH	2.3
8	NORAD	3.3	8	Wellcome Trust	1.6	8	UK MRC	2.2	8	Denmark	2.2
9	EDCTP	2.0	9	Irish Aid	1.4	9	Netherlands	1.7	9	EDCTP	2.2
10	Spain	1.9	10	UK MRC	1.3	10	Ireland	1.2	10	Norway	1.5
11	Netherlands	1.7	11	Denmark	0.9	11	Norway	1.0	11	US CDC	1.5
12	Denmark	1.7	12	NHMRC	0.6	12	OPEC	1.0	12	Ireland	1.3
13	Germany	1.3	13	OFID	0.5	13	Denmark	0.9	13	UK MRC	0.8
14	Irish Aid	1.1	14	Spain	0.4	14	NHMRC	0.5	14	NHMRC	0.5
15	CDC	0.7	15	ARC	0.4	15	Wellcome Trust	0.5	15	Wellcome Trust	0.3

<sup>a</sup> See appendix for list of acronyms.

<sup>b</sup> Figure includes South African DST and DOH, as well as other local sources of funding.

The microbicide development pipeline continues to generate new approaches. Furthest along is the monthly dapivirine vaginal ring now in safety and effectiveness trials supported by the NIH: the Microbicide Trials Network (MTN) ASPIRE study (MTN 020) and the parallel International Partnership for Microbicides (IPM) Ring Study (IPM 027). Other microbicide candidates in the earlier stages of the R&D pipeline that are receiving considerable attention include rectal microbicides, films, vaginal tablets and multipurpose technologies (MPTs).

The Combined Highly Active Anti-Retroviral Microbicides (CHAARM) project, a large collaboration co-funded by the EU under the FP7 at a level of US\$15.2 million over five years—US\$3.1 in 2013—continues its wide-ranging basic research into specifically targeted ARV combinations for topical application. CHAARM funding under the FP7 is set to end by December 2014, but funding for the project is expected to continue under the Horizon 2020 funding scheme.

### 3.3 Philanthropic Investments in Microbicide Research and Development

In 2013, the philanthropic sector as a whole provided US\$20 million (nine percent) of the funds disbursed for microbicide R&D, decreasing by US\$5 million from 2012. Similarly to the past five years, almost all philanthropic funding came from the BMGF, with the Wellcome Trust as the second largest donor. The majority of the decrease was a result of the BMGF funding decreasing by US\$3.7 million.

### 3.4 Commercial Investments and Contributions to Microbicide Research and Development

A relatively small number of biotechnology companies, through a variety of grant and contract mechanisms, continue to work on both ARV- and non-ARV-based microbicide candidate products.

Perhaps the most significant contributions from the private sector to microbicide R&D have been royalty-free transfers of ARVs for use as active agents in microbicide products.

CONRAD and the Population Council have received royalty-free licenses and material transfers from pharmaceutical companies, including licenses to develop ARVs as components of combination products. And in 2004, Janssen and IPM formed a public-private partnership to develop, manufacture and commercialize dapivirine (TMC 120) in developing-world settings. In early 2014, Janssen and IPM announced an expansion of that collaboration, under which Janssen gave IPM the exclusive worldwide rights to develop and commercialize dapivirine as a microbicide for HIV prevention and/or in combination with other anti-infective or contraceptive agents as multipurpose prevention technologies (3.6).

Microbicide developers also continue to receive product information, technical support and advice from commercial partners. Such in-kind contribution of companies is not readily quantifiable, but it continues to include a range of expertise and support, including: legal support for material transfer agreements and licenses; regulatory and scientific advice; access to preclinical toxicology studies and clinical safety or surveillance data; drug and product supplies; advice on manufacture of microbicide delivery systems; participation in development meetings and teleconferences; and timeline guidance.<sup>9</sup>

### **3.5 Investments in Rectal Microbicide Research and Development**

In 2013, R&D for rectal microbicides was funded at approximately US\$3.4 million, the same level as in 2012. Between 2001 and 2013, global spending on rectal microbicide research totaled nearly US\$38 million. In 2013, funding came predominantly from the US and was dedicated to support for both preclinical

development and clinical testing of rectal microbicides.

Funded by the NIH, the Combination HIV Antiretroviral Rectal Microbicide Program (CHARM) is a five-year, US\$11 million, multi-center grant intended to advance rectal microbicide candidates from discovery into early clinical development. The most advanced work on rectal microbicides is the MTN Phase II trial of tenofovir gel in gay men, men who have sex with men (MSM) and transgender women which began in late-2013 at US sites and in early-2014 at sites in Peru, South Africa and Thailand. The trial is the first Phase II rectal microbicide study and the first rectal microbicide study in sites outside the US. Both CHARM and the MTN are also evaluating maraviroc for rectal use and clinical evaluations of maraviroc products started in late 2013.

### **3.6 Investments in Multipurpose Prevention Technology Research and Development**

Women worldwide confront two major and often concurrent reproductive health challenges: the need for contraception and the need for protection against sexually transmitted infections (STI), importantly but not exclusively HIV/AIDS. While conception and infection occur at the same anatomical site via the same mode of transmission, there are no reproductive health technologies to date that *simultaneously* address that reality. Available single-indication technologies are either contraceptive or anti-infective, limited in number, or require different modes of administration and management, and therefore do not fully respond to pivotal events in many women's lives.

By way of possible remedy, multipurpose prevention technologies (MPTs)<sup>10</sup> are being designed to address two or more sexual and reproductive health indications simultaneously, combining protection against unintended

<sup>9</sup> Quantifying in-kind contributions, technical assistance, IP transfers and other non-direct financial contributions is challenging for pharmaceutical companies; thus, it is often not possible for companies to report this information to the Working Group.

<sup>10</sup> PF Harrison, A Hemmerling, J Romano, KJ Whaley, B Young Holt. *Developing Multipurpose Reproductive Health Technologies: An integrated strategy*. AIDS Research and Treatment 2013, Article ID790154. [dx.doi.org/10.1155/2013/790154](https://doi.org/10.1155/2013/790154).

pregnancy and at least one sexually transmitted infection (as determined by country epidemiological profile). A number of MPTs, in sustained-release forms, combine prevention of unintended pregnancy and HIV and, in some cases, herpes simplex virus (HSV-2). Intravaginal rings (IVR), long-acting injectables, and “on-demand”/pericoital formulations with various targets are in the preclinical and early-clinical stages. These include:

- A 60-day IVR delivering the ARV dapivirine and hormonal contraceptive levonorgestrel (LNG);
- A 90-day IVR delivering LNG and tenofovir;
- IVR or on-demand formulations combining MIV-150, LNG, zinc acetate, and carrageenan;
- An MZL combination topical gel; and
- The “one size fits all” SILCS diaphragm, delivering nonhormonal contraceptive gel and/or 1% tenofovir gel.

The pipeline of MPT components and combination options is substantial and growing. However, it is new, uncharted and complex R&D terrain, such that MPT development has been rightly described as “a high-risk/high-gain, expensive process” that faces a plethora of basic scientific questions and challenges regarding formulation, regulatory requirements, manufacturing, costs, market, acceptability, adherence and, inevitably, funding.

To address this considerable complexity, consensus has been reached with regards to several points. First, donor collaboration on investment decisions will be essential to the advancement of MPTs, particularly in the current funding environment. Second, such collaboration must be informed by an objective process of prioritization. This process is to be based on a set of “Target Product Profiles”

(TPP) that describe the public health impact potential of MPT classes and/or individual candidates, adapted to individual country or regional settings, along with the associated R&D parameters. Identification of the relevant TPPs took place during 2013 through a series of carefully designed consultations and regional meetings.<sup>11</sup> Forthcoming clinical data from the FACTS tenofovir studies, ASPIRE trial and IPM Ring Study will be of certain consequence for MPT product development strategies and investments, as will the ongoing conversations about the critical relationships among antiretroviral therapy (ART), contraception, and HIV.

Current MPT R&D resides largely in the hands of CONRAD, IPM, PATH and the Population Council, with a number of smaller developers (e.g., Female Health Company, FHI360, Mapp Biopharmaceutical, Osel, ReProtect, Starpharma) and institutional groups (e.g., Microbicide Trials Network, Queens University of Belfast, University of Utah) working on individual MPT components and/or discrete research questions. These are variously supported by the BMGF, NIH Division of Acquired Immunodeficiency Syndrome (DAIDS) and USAID. Other funding sources include the Dutch Ministry of Foreign Affairs, the Swedish International Development Cooperation Agency (SIDA) and the South African Department of Science & Technology. The advocacy work of the Coalition Advancing Multipurpose Innovations (CAMI) is supported primarily by BMGF and USAID; CAMI has also received small contributions from the Mary Wohlford Foundation, NIH Office of AIDS Research (OAR) and the Wellcome Trust.

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<sup>11</sup> J Romano, J Manning, A Hemmerling, E McGrory, B Young Holt. *Prioritizing Multipurpose Prevention Technology Development and Investments Using a Target Product Profile*. *Antiviral Research* 100 (2013) 532-538. [dx.doi.org/10.1016/j.antiviral.2013.09.016](https://doi.org/10.1016/j.antiviral.2013.09.016).

# 4.0

## Investments in Research and Development Related to Pre-exposure Prophylaxis

Global public, philanthropic and commercial investment in PrEP increased to US\$36 million in 2013, bringing the total investment over the past eight years to US\$333 million (Figure 17). Investment increased by US\$5 million in 2013 due in part to a number of new demonstration and implementation projects that began in late 2012 and early 2013 focused on the use of PrEP in different settings (Table 10). Additionally, the initiation of several studies testing long-acting PrEP formulations in 2013 also resulted in an increase of investment in clinical trials.

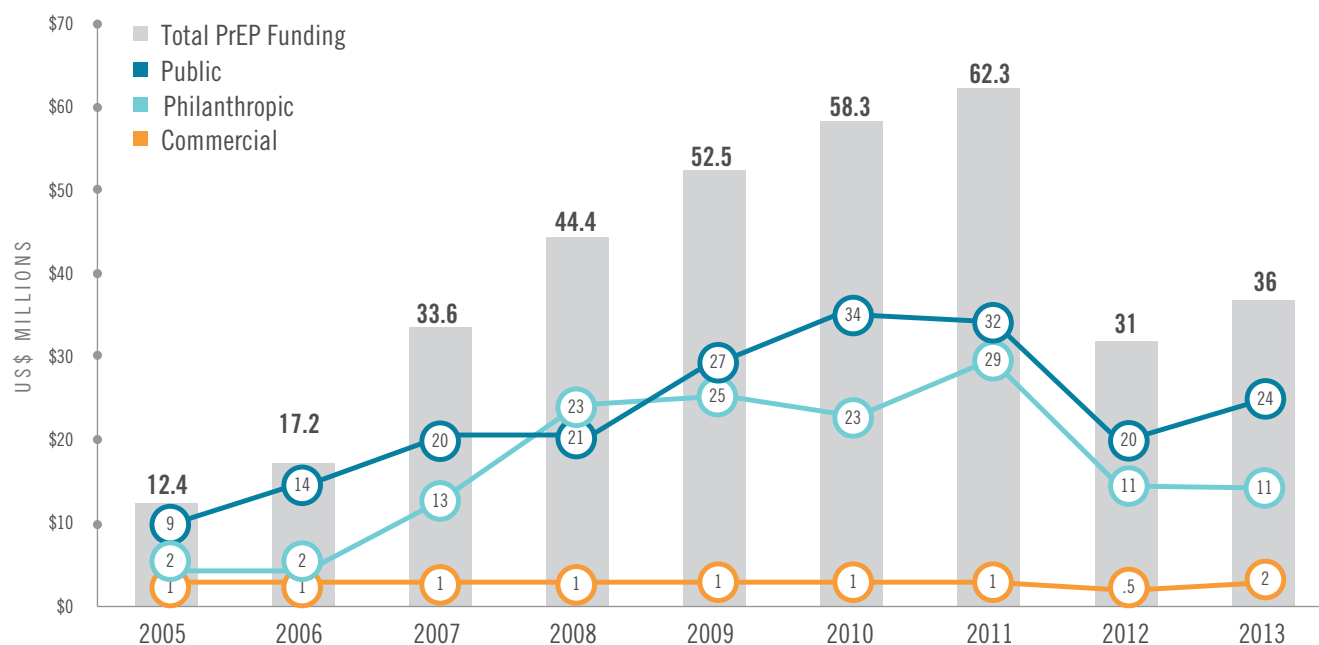
In July 2012, based on evidence from several trials, the US Food and Drug Administration (FDA) approved daily oral tenofovir (TDF/FTC, marketed as Truvada) for use as PrEP for HIV prevention in HIV-negative women and men. Daily TDF/FTC has proven effective at reducing risk of HIV via sexual exposure in heterosexual men and women, gay men and other MSM and transgender women. The FDA decision led to preparation for and initiation

of demonstration projects and follow-on trials to better assess and understand how to rollout PrEP for prevention. More than ten demonstration projects began in 2013 alone, with additional projects slated to begin in the coming years.

In June 2013, results from the Bangkok Tenofovir Study (BTS) were published, showing that a daily dose of oral tenofovir reduced the risk of HIV infection in a population of IDUs by 49 percent overall. The study began in 2005 and enrolled more than 2,400 men and women. The follow-up study to the BTS is ongoing, funded by the US CDC and the Thailand Ministry of Public Health.

Ongoing studies are exploring different dosing strategies, including intermittent, time-driven and exposure-based use of PrEP. New PrEP strategies are also in development, including testing of long-acting TMC278 (Box 8) and, in another trial, maraviroc as an HIV prevention agent together with TDF and FTC.

FIG. 17 Investment in Pre-Exposure Prophylaxis 2005 – 2013 (US\$ millions)



**Table 10: Annual Investments in PrEP R&D 2005 – 2013 (US\$ millions)<sup>a</sup>**

	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>Public</b>	8.7	13.5	19.7	20.6	26.6	33.8	32.3	19.6	23.6
<b>Philanthropic</b>	2.4	2.4	12.6	22.5	24.6	23.2	28.7	10.9	10.9
<b>Commercial</b>	1.3	1.3	1.3	1.3	1.3	1.3	1.3	0.5	1.7
<b>Total Global Investment</b>	<b>12.4</b>	<b>17.2</b>	<b>33.6</b>	<b>44.4</b>	<b>52.5</b>	<b>58.3</b>	<b>62.3</b>	<b>31</b>	<b>36</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

**BOX 8**

**Investment in Long-Acting Injectables for Use as PrEP**

Long-acting ARV injectables are being studied as a new option for both HIV prevention and treatment. A long-acting ARV injectable is an antiretroviral (ARV) drug that is delivered via an injection and persists in the body for an extended period of time. In 2013, investment in preclinical and clinical research towards long-acting injectables for use as PrEP reached US\$7.8 million. US\$2.2 million came from the NIH, US\$4.9 million from the BMGF and US\$0.72 million from industry.

Several long-acting injectable products are currently in the pipeline. Janssen's TMC278 (rilpivirine) is in a Phase I study, and PATH, Janssen and the NIH are advancing the

product to a Phase II trial in 2014. After completing Phase I studies in 2013, GlaxoSmithKline's GSK744 started in a Phase II study in 2014. TaiMed Biologics Inc., the Aaron Diamond AIDS Research Center and Rockefeller University completed a Phase I study of Ibalizumab, a monoclonal antibody, in 2012.

As potentially marketable products, long-acting injectables have a relatively high investment from industry. While the exact amount invested cannot be quantified,<sup>a</sup> the investment in long-acting injectables for use as PrEP goes beyond that of trials with prevention indications. Research on these products for therapeutic purposes has provided information that greatly aided in their development for prevention.

<sup>a</sup> Industry responses to the AIDS Vaccine & Microbicide Resource Tracking Working Group's annual survey are low, with only two pharmaceutical companies and five biotechnology companies responding with investment figures.

## 5.0 Investment in Research and Development Related to Treatment as Prevention

Investment in research into the early initiation of AIDS treatment drugs as a prevention strategy has continued to increase since the Working Group began tracking funding towards the HIV prevention modality in 2010. Countries continue to include treatment as prevention in national strategies as models show that it could dramatically alter the course of the epidemic. Ongoing research seeks to answer questions about how best to implement treatment as prevention programmatically, and to address implementation in specific populations and settings. Total global investment in treatment as prevention R&D in 2013 was US\$117 million in 2013, an increase of US\$19 million from 2012 (Table 11).

Public-sector agencies from the US provided a significant portion of funding, with more than US\$64.8 million from the NIH, US\$3.1 million from the CDC and US\$11.25 million for combination prevention studies from PEPFAR. US NIH funding is supporting ongoing trials in Botswana, South Africa, Tanzania, Thailand, Zambia and Zimbabwe, as well as combination prevention trials in South Africa and Uganda.

In 2013, the Government of British Columbia invested nearly US\$20 million in its Stop HIV/AIDS campaign, an increase of US\$8 million from 2012. European public-sector funding came from France, Belgium, Germany, Switzerland and the UK. France's National Agency for Research on AIDS and Viral Hepatitis (ANRS) is funding the Start ART trials, focusing on the acceptability and feasibility of treatment and prevention at the individual and community levels. China is also funding

**Table 11: Annual Investments in Treatment as Prevention R&D 2011 – 2013 (US\$ millions)<sup>a</sup>**

	2011	2012	2013
<b>US</b>	55	68.6	79
<b>Europe</b>	4.7	4.6	3
<b>Other</b>	13.5	13	21.5
<b>Total Public</b>	73.2	86.2	103.5
<b>Philanthropic</b>	6.2	11.8	13.1
<b>Total Global Investment</b>	<b>79.4</b>	<b>98</b>	<b>117</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

large-scale implementation efforts in treatment as prevention.<sup>12</sup>

The majority of philanthropic funding came from the BMGF, the Dream Fund of the Dutch Postcode Lottery, Médecins Sans Frontières (MSF) and the Wellcome Trust. The Dream Fund of the Dutch Postcode Lottery is funding the MaxART trial taking place in Swaziland and sponsored by STOP AIDS NOW! and the Clinton Health Access Initiative (CHAI).

While there is no direct commercial investment in R&D for treatment as prevention, substantial quantities of ARV drugs have been donated for clinical trials. In the HIV Prevention Trials Network's HPTN 052 trial, for example, study drugs are being donated by Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GSK and Merck & Co. For the MaxART trial, Mylan is donating first-line and second-line ARVs, and will be providing additional support to the trial in 2014.

<sup>12</sup> China did not report 2013 funding levels for treatment as prevention research.

## Investments in Follow-up Studies and Operations Research Related to Voluntary Medical Adult Male Circumcision

Global public-sector and philanthropic investment in R&D and operations research related to voluntary medical adult male circumcision (VMMC) totaled nearly US\$32 million in 2012, a decrease of 42 percent from 2011 (Table 12).<sup>13</sup> The BMGF funded the majority of VMMC research, at US\$27.2 million, and the US public sector was the second largest funder, with the CDC contributing US\$2.5 million and the NIH investing US\$1.2 million.

With the World Health Organization (WHO) recommending full implementation, and with a target set to provide circumcisions for 20 million men in 14 African countries by 2015, VMMC is currently in an implementation phase.<sup>14</sup> Data from Kenya, South Africa and Uganda have already shown that male circumcision reduces the individual risk of HIV infection by 60 percent.<sup>15</sup> Study results released in 2011 by France's ANRS Orange Farm study showed that rollout in the southern and eastern regions of Africa was able to significantly decrease the community level of HIV in high-prevalence areas,<sup>16</sup> and additional results from 2013 confirmed the effectiveness of VMMC in reducing the risk of HIV infection.<sup>17</sup>

Ongoing research in 2013 funded by the NIH at a level of US\$1.2 million (a decrease

of US\$3 million from 2012) focused on the socio-behavioral aspects of VMMC, such as public outreach campaigns for effective implementation of circumcision programs and risk compensation studies, and continuing R&D related to the effect of circumcision on HIV risk.

The largest funder of VMMC implementation research remains the BMGF, which increased its investment from 2012 to 2013 by US\$7 million—accounting for most of the 2013 investment increase in this area. BMGF grants focused on the monitoring of scale-up, demand creation and delivery.

Investors also focused on PrePex and the Shang Ring, new devices that were shown in 2011 to be safe and effective, both requiring less surgical skill than traditional male circumcision techniques. Studies to confirm the results of evaluations of PrePex and the Shang Ring were ongoing in 2013 in Zambia, Rwanda and Kenya, supported by funds from the BMGF and USAID. In June 2013, PrePex received prequalification from WHO. Three other devices—the Shang Ring, Plastibell and Tara KLamp—are in the WHO prequalification process, but have not yet been approved.

**Table 12: Annual Investments in Male Circumcision R&D 2005 – 2013 (US\$ millions)<sup>a</sup>**

	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>Public</b>	6.9	4.8	6.2	7.5	5.0	6.1	7.2	5.0	23.6
<b>Philanthropic</b>	4.3	2.9	4.3	2.1	16.7	14.2	34.4	27.2	10.9
<b>Total Global Investment</b>	11.2	7.7	10.5	9.6	21.7	20.3	41.6	32.0	1.7
<b>Total Global Investment</b>	<b>12.4</b>	<b>17.2</b>	<b>33.6</b>	<b>44.4</b>	<b>52.5</b>	<b>58.3</b>	<b>62.3</b>	<b>31</b>	<b>36</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

<sup>13</sup> Full definition of research area included in Appendix.

<sup>14</sup> PEPFAR Male Circumcision Technical Working Group. *Joint Strategic Action Framework to Accelerate the Scale-Up of Voluntary Medical Male Circumcision for HIV Prevention in Eastern and Southern Africa*. UNAIDS and WHO (November 2011). [www.pepfar.gov/documents/organization/178294.pdf](http://www.pepfar.gov/documents/organization/178294.pdf).

<sup>15</sup> B Auvert, D Taljaard, E Lagarde et al. *Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 trial*. *PLoS Medicine* 2:11(November 2011).

<sup>16</sup> B Auvert, D Taljaard, D Rech et al. *Effect of the Roll-out of Male Circumcision in Orange Farm (South Africa) on the Spread of HIV (ANRS-12126)*. IAS (Rome, 2011), Abstract WELBC02.

<sup>17</sup> CM Liu, BA Hungate, AAR Tobian et al. *Male Circumcision Significantly Reduces Prevalence and Load of Genital Anaerobic Bacteria*. *mBio* 4:2(2013).



# 7.0

## Investments in Research and Development and Operations Research Related to Female Condoms

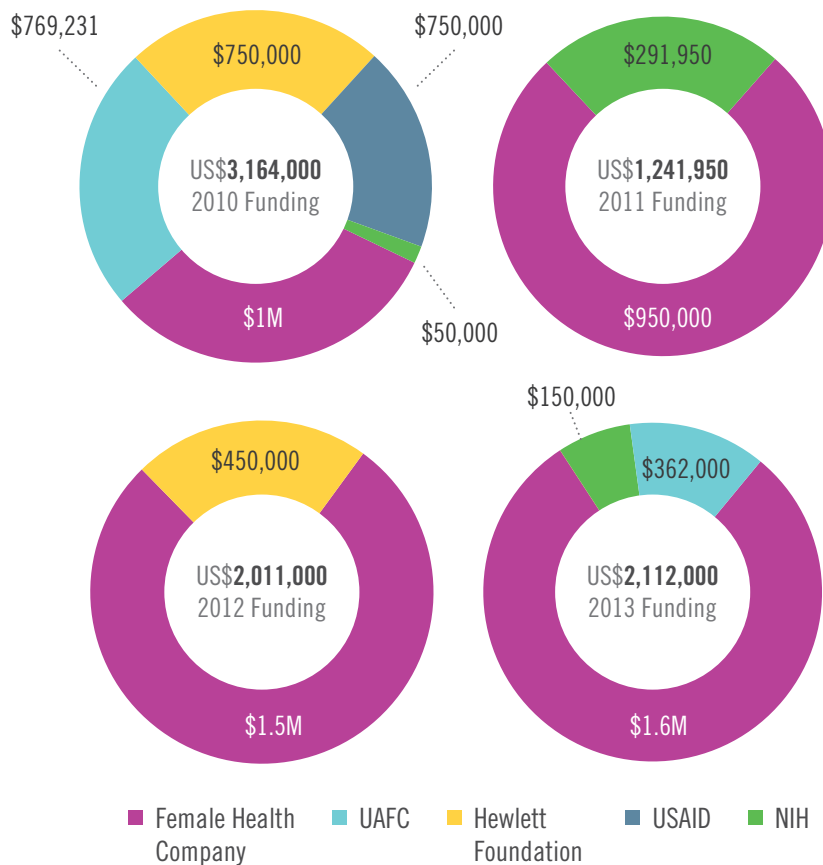
In 2013, global investment related to female condom R&D totaled US\$2.2 million (an increase of US\$200,000 over 2012), from the Female Health Company and the Universal Access to Female Condoms (UAFC) Joint Programme, funded by the Netherlands Ministry of Foreign Affairs (Figure 18).

Between 2000 and 2013, approximately US\$128 million was spent procuring 190 million female condoms through donor funding.<sup>18</sup> Two female condoms are currently prequalified by the WHO, the FC2 and Cupid1. Two other

designs, the Cupid2 and the Hindustan Lifecare Ltd. (HLL), were in a functionality study in 2013 with UAFC support, looking at safety, acceptability and performance. The results of the study will inform a product dossier submitted for WHO prequalification.

Other products were also submitted for WHO prequalification in 2013. The Shanghai Dahua Medical Apparatus Company in China tested its O'lavie female condom in a study in 2013, and the product is under review for WHO prequalification.

FIG. 18 Funding for Female Condom R&D 2010 – 2013 (US\$ millions)



<sup>18</sup> This does not include purchases made through government funding and in private sector markets.

## Investments in Research Related to Vertical Transmission Prevention

Funding for research related to prevention of vertical transmission of HIV from mother to child at birth and during breastfeeding increased nominally between 2012 and 2013, from US\$43.8 million to US\$44 million. The public sector accounted for most of this funding, with the US, through NIH and USAID, contributing nearly 95 percent (Table 13).

In July 2013, the WHO issued new guidelines on treatment for preventing mother-to-child transmission and on HIV and breastfeeding. These 2013 guidelines recommend that countries follow Option B+, and in countries where this is not feasible, Option B (Box 9). Option B+ recommends that all HIV-infected pregnant and breastfeeding women are eligible for lifelong antiretroviral therapy (ART) regardless of CD4 count. The largest research grants towards vertical transmission prevention R&D in 2013 continued to look at program optimization in order to meet the WHO recommendations.

Benefits of Option B+ include provision of more effective treatment regimens for pregnant women, reduction in vertical transmission through early treatment access, reduced morbidity and mortality of those on treatment and fewer orphans and vulnerable children. Combining these benefits, PEPFAR funded the Futures Group to look at the long-term effects of implementing Option B+, and projections showed that vertical transmission can be nearly eliminated. However, the question remains as to how countries will fund Option B+.

Additional research endeavors are exploring: the ways ARVs function in prevention of vertical transmission, both at birth and through breastfeeding; retention and recruitment of women and infants in prevention of vertical transmission; and basic research, such as functional correlates of vertical transmission and mechanisms of transmission in breast milk.

### BOX 9

#### WHO Recommendations

**Option B+:** Provide all HIV-positive pregnant or breastfeeding women with a course of antiretroviral drugs to prevent mother-to-child transmission. A triple-drug antiretroviral regimen should be taken throughout pregnancy, delivery and breastfeeding, and continuing for life, regardless of CD4 count or clinical stage.

**Option B:** Provide all HIV-positive pregnant or breastfeeding women with a course of antiretroviral drugs to prevent mother-to-child transmission. A triple-drug antiretroviral regimen should be taken throughout pregnancy and delivery. If the mother is breastfeeding, she

should also continue to take the triple-drug antiretroviral regimen until one week after breastfeeding has finished.

Pregnant women who are eligible to receive antiretroviral treatment for their own health, based on their CD4 count or clinical stage, should continue taking HIV treatment for life. Eligibility is determined at a country level. WHO recommends that women with a CD4 count of  $\leq 500$  cells/mm<sup>3</sup> (or clinic stage three or four) should continue taking antiretroviral treatment for life. This course of medication should be permanent and taken every day in order to postpone the development of HIV into AIDS.

<sup>a</sup> WHO. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach* (June 2013). See more at <http://www.avert.org/who-guidelines-pmtct-breastfeeding.htm#sthash.e2XzvePo.dpuf>.

**Table 13: Funding for Vertical Transmission Prevention R&D 2008 – 2013 (US\$ millions)<sup>a</sup>**

		2008	2009	2010	2011	2012	2013
<b>PUBLIC SECTOR</b>							
<b>France</b>	ANRS	3,429,355	1,820,086	418,890	203,100	816,969	10,589
	Institute Pasteur	0	0	0	384,900	0	0
<b>Canada</b>	CHVI	0	0	0	3,956,400	6,556,557 <sup>19b</sup>	0
	CIDA	0	0	1,250,000	570,600	[Included in CHVI figure]	0
	CIHR	0	0	0	634,000	88,489	169,417
<b>US</b>	CDC	1,716,928	488,132	0	0	0	0
	NIH	8,533,594	44,101,000	55,348,000	34,012,000	33,154,000	39,961,000
	USAID	0	0	1,600,000	2,225,000	1,400,000	2,000,000
<b>Sweden</b>	SIDA	128,041	263,158	1,127,820	102,800	0	0
	SRC	0	0	0	0	108,133	0
<b>UK</b>	MRC	374,600	448,105	0	448,000	0	113,543
	EDCTP	3,393,500	3,393,500	0	0	815,145	0
<b>India</b>	DBT	0	0	0	0	34,135	74,384
<b>Total public</b>		<b>17,576,018</b>	<b>50,513,981</b>	<b>59,744,709</b>	<b>42,613,680</b>	<b>42,973,428</b>	<b>42,242,960</b>
<b>PHILANTHROPIC SECTOR</b>							
<b>Total philanthropic</b>		<b>3,641,800</b>	<b>904,065</b>	<b>0</b>	<b>500,700</b>	<b>841,956</b>	<b>1,652,449</b>
<b>Total global investment</b>		<b>21,217,800</b>	<b>51,418,000</b>	<b>59,744,700</b>	<b>43,114,344</b>	<b>43,815,384</b>	<b>43,981,381</b>

<sup>a</sup> Data submitted in currency other than US\$ is converted using a 1 July 2013 conversion rate; otherwise, inflation is not taken into account.

## Investments in HIV Prevention Research and Development Related to HSV-2 Prevention

Prevention of herpes simplex virus type 2 (HSV-2) infections in HIV-negative people may prove to be an effective element in an HIV prevention strategy. While HSV-2 suppression with acyclovir and its analogues has not been shown to affect HIV acquisition, research on other therapeutic and prophylactic methods is ongoing and some basic questions continue to be pursued.

In 2013, a total of US\$5.8 million was provided for HSV-2 vaccine research from the US NIH, an increase of US\$3.5 million over 2012. As in previous years, commercial investors were often subsidized by public-sector institutions, such as the US NIH. Pharmaceutical and biotechnology companies investing in HSV-2 vaccine R&D include Agenus Inc., GSK, Genoccea Biosciences, Juvaris and Vical.

Genoccea presented promising data on a Phase I/IIa trial of its HSV-2 protein subunit vaccine and is continuing research. In 2013,

Genoccea filed an initial public offering in an effort to raise US\$75 million. Genoccea's most recent funding came from the BMGF. GSK's venture arm, SR One, is also a top investor in the biotech company. GSK's vaccine, containing a glycoprotein D (gD-2) did not show efficacy in a Phase II trial ending in 2012. Efforts to prevent HSV-2 using gD-2 subunit vaccines were ongoing for over 20 years with nearly US\$100 million invested in the research.<sup>19</sup> gD-2 is one of the proteins in Genoccea's vaccine and the other is infected cell protein.

Agenus Inc. also has an HSV-2 vaccine, presenting results in November 2013 from a Phase II study of Herpy, a recombinant therapeutic vaccine. Vical, with NIH funding, is developing a plasmid DNA-based vaccine to inhibit recurring lesions in patients latently infected with HSV-2. The program advanced to a Phase I/II trial in December 2013 after promising preclinical results.

<sup>19</sup> WP Halford, R Puschel, E Gershburg, A Wilber, S Gershburg, et al. *A Live-Attenuated HSV-2 ICPO—Virus Elicits 10 to 100 Times Greater Protection against Genital Herpes than a Glycoprotein D Subunit Vaccine*. PLoS ONE 6:3 (2011) e17748. Doi:10.1371/journal.pone.0017748.

# 10.0

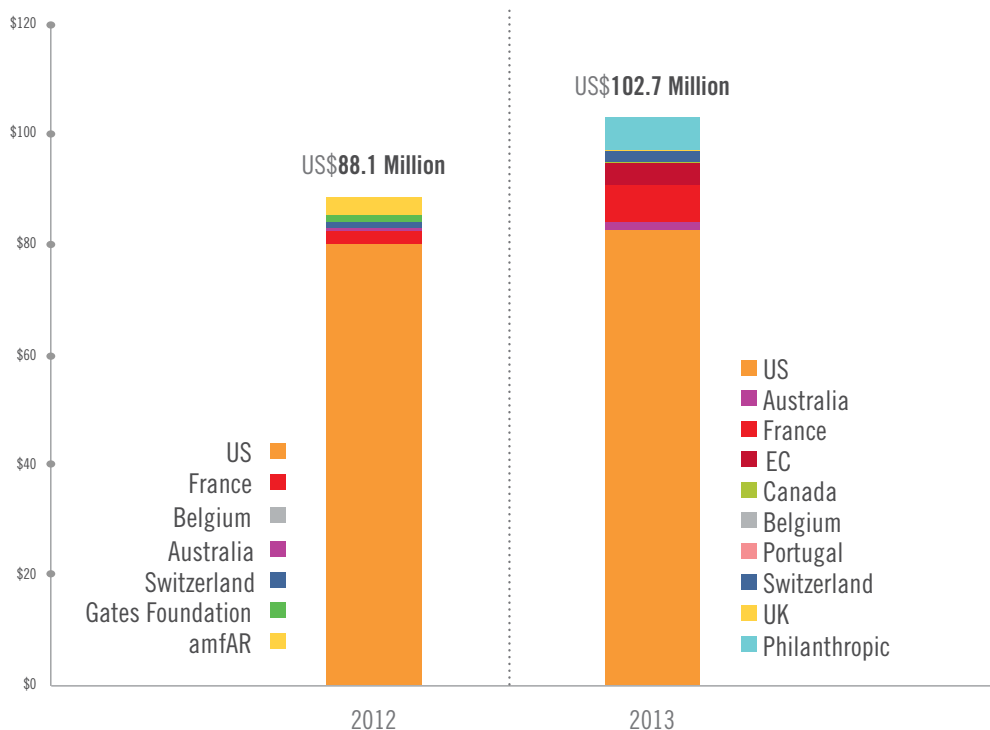
## Investment in HIV Cure and Therapeutic Vaccine Research and Development

In 2013, the US, through the US NIH, contributed the majority of public funding, with Australia, Canada, the EU and France also contributing significantly to HIV cure research (Box 10). Fifteen different funders of cure research from across the globe were identified in 2012 and 16 in 2013 (Figure 19).<sup>20</sup> US investment is expected to increase in future years after President Obama announced in 2013 that \$100 million of funding for the NIH would be reprioritized to launch a new HIV Cure Initiative.

In 2012, non-US countries invested eight percent of global HIV cure research funding, while in 2013, it is noted that the rest of the

world increased their investment proportionally, resulting in 13 percent of global HIV cure research funding. This indicates encouragingly that HIV cure research investment is expanding, and that non-US countries are increasing their funding. There is investment in several international collaborations, such as the Collaborative HIV Eradication of Viral Reservoirs (CHERUB) in the UK, the amfAR Research Consortium on HIV Eradication (ARCHE), the International AIDS Society (IAS)/ANRS Young Investigator Award Program and the Martin Delaney Collaboratories.

FIG. 19 Investment in Cure Research and Development 2012 – 2013 (US\$ millions)



<sup>20</sup> Investment figure for 2013 does not reflect BMGF investment in HIV cure research which is not disaggregated from HIV vaccine investment. Subsequent iterations of the Working Group's report will include BMGF investment in HIV cure research.

### Toward a Cure Program Definition: US NIH eradication of viral reservoirs<sup>a</sup>

Research conducted on viral latency, elimination of viral reservoirs, immune system and other biological approaches, as well as therapeutic strategies that may lead to either a functional (control of virus rather than elimination, without requirement for therapy) or sterilizing (permanent remission in absence of requirement for therapy) cure of HIV infection.

**Pathogenesis studies:** Basic research on viral reservoirs, viral latency, and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.

**Animal models:** Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.

**Drug development and preclinical testing:** Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system.

**Clinical trials:** Studies to evaluate lead compounds, drug regimens and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.

**Therapeutic vaccines:** Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.

**Adherence/compliance:** Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

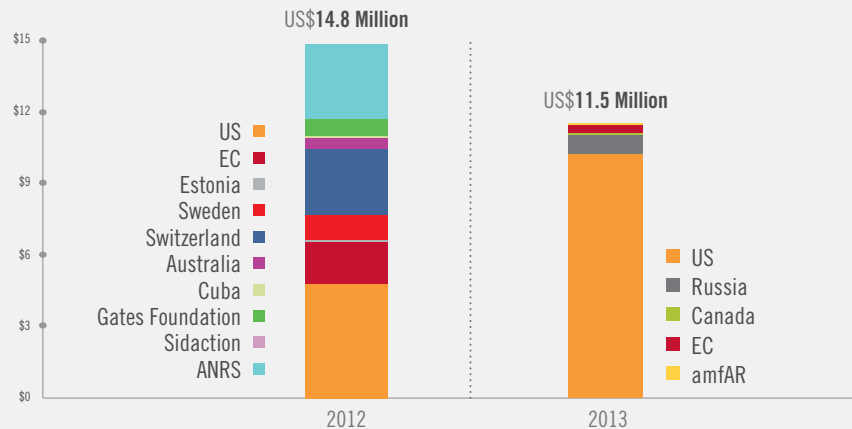
<sup>a</sup> Department of Health and Human Services National Institutes Of Health Office of AIDS Research. *Trans-NIH AIDS Research Budget FY2014*. [http://www.oar.nih.gov/budget/pdf/2014\\_OAR\\_CJ\\_Trans-NIH.pdf](http://www.oar.nih.gov/budget/pdf/2014_OAR_CJ_Trans-NIH.pdf).

### Therapeutic Vaccine Research and Development

Therapeutic vaccine research is defined by the Working Group as studies that increase scientific knowledge through research on protective immune responses and host defenses against HIV—now included by the OAR in a subcategory under the umbrella of cure research. While in the past the Working Group has distinguished these studies from those

that focus on cure research [as defined in Box 10], the OAR has included these studies as a subcategory under the umbrella of cure research. The Working Group listed three NIH grants toward therapeutic vaccine research in 2013, totaling US\$6.6 million. Overall investment in therapeutic vaccine research decreased by US\$7.5 million from 2012 to 2013, resulting in a total of US\$6.9 million (Figure 20). This decline was offset by an expansion of various non-vaccine-based therapeutic approaches as part of cure research.

FIG. 20 Investment in Therapeutic Vaccine Research and Development 2012 – 2013 (US\$ millions)



## 2013 HIV Prevention Research and Development Investment Conclusions and Recommendations

Considering the 2013 funding patterns identified by the Working Group in this report and the science that funding has supported, the following conclusions regarding the state of HIV prevention R&D investments are advanced:

### **The US is funding the majority of HIV prevention R&D.**

US budgets were inevitably cut in 2013 and it is likely that US funding for HIV prevention research will continue to come under pressure in subsequent years. The investment trends highlighted throughout this report show declines in nearly every category of HIV prevention R&D. These declines are not unique to the HIV prevention field, or to the HIV field. Research budgets in the US have been cut across the board. By relying so heavily on US funding, the decision as to whether or not HIV prevention options start and continue, from research to rollout, is often determined by the economic, international development and research priorities of a limited set of actors.

### **Philanthropic support funds vital parts of HIV prevention research.**

A small number of funding sources provide the bulk of support from the philanthropic sector, and this support is increasingly important in the face of declining public sector support. Philanthropic sources provide support for research all along the HIV prevention pipeline—from early stage research to implementation and rollout of proven HIV prevention technologies—often funding projects that are outside the scope of public sector proposal calls.

### **Industry investment is key, especially at later stages of the HIV prevention pipeline.**

Industry collaboration and support was essential in developing vaccines and drugs used in trials that showed promising results in the past five years. RV144, CAPRISA iPrEx and HPTN 052 all had successful collaborations with industry. While HIV prevention R&D by pharmaceutical companies has not increased, the private sector is a critical part of the field in moving products from the pipeline into the market.

### **International development priorities are evolving.**

Structural changes placing foreign affairs at the helm of international development departments led to changes in funding of single-disease biomedical research. The overall trend towards funding country-ownership models and near-term outcomes affected funding for HIV prevention research. Economic development and poverty alleviation are high on the agenda in the upcoming Sustainable Development Goals, and central to the European Union's new funding program, Horizon 2020. HIV prevention research is intimately tied to economic development and anti-poverty priorities. HIV continues to claim 1.6 million lives and infect 2.3 million people annually. The economic effect of the epidemic has been well documented in high-incidence settings. Just as the introduction of ARVs helped to alleviate the economic burden faced in these settings, HIV prevention technologies have the potential to reduce the burden of the epidemic on an economy. *The Lancet's Global Health 2035*

Commission,<sup>21</sup> launched in late-2013, re-visited the case for investing in health, concluding that increased health leads to greater economic development. In making this case, the authors cite data showing that the value of eradicating AIDS in Africa would be nearly the value of the annual economic output of the entire continent.<sup>22</sup>

**The enabling environment provided by a human rights context has a profound effect on where trials take place and if they are able to happen.**

HIV prevention research is taking place in an increasingly changing and challenging environment. Uganda and Nigeria recently

passed anti-homosexuality laws, and India's Supreme Court is reviewing its 2009 decision to overturn the law criminalizing homosexuality. Similar legislation has been proposed in countries across Africa. Additionally, laws criminalizing sex workers and IDUs proliferate globally. Research has already been affected by these environmental changes as the world moves farther away from a legal environment framed by a human rights approach. To successfully test and roll out HIV prevention technologies, research needs to take place in those communities hardest hit by the HIV epidemic.

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<sup>21</sup> D Jamison, L Summers et al. *Global Health 2035: A world converging within a generation*. The Lancet 382:9908 (December 2013). Doi:10.1016/S0140-6736(13)62105-4.

<sup>22</sup> TJ Philipson, RR Soares. *The Economic Cost of AIDS in Sub-Saharan Africa: A reassessment*. In: G Lopez-Casanovas, B Rivera, L Currais, eds., *Health and Economic Growth: Findings and policy implications*. Cambridge, MA: The MIT Press, 2005: 315–38.



This report was prepared by Emily Donaldson (AVAC), with contributions from Kevin Fisher (AVAC), Reuben Granich (UNAIDS), Thomas Harmon (IAVI), Polly Harrison (AVAC) and Mitchell Warren (AVAC) of the HIV Vaccines and Microbicides Resource Tracking Working Group (herein referred to as “the Working Group”), with contributions from Julien Burns and Emily Hayman. The Working Group developed and has utilized a systematic approach to data collection and collation since 2004. These methods

were employed to generate the estimates of funding for R&D presented in this report. A detailed explanation of the methodology can be found on the Working Group website ([www.hivresourcetracking.org](http://www.hivresourcetracking.org)). The two sets of categories used to describe different R&D activities—one for AIDS vaccines and one for HIV microbicides—were derived from those developed by the US NIH and are shown in the following tables.

**BOX 12****Data Collection Methods and Fluctuation in Investment Levels**

HIV prevention R&D investment figures are collected annually by the AIDS Vaccines & Microbicides Resource Tracking Working Group through an email survey. For the present report, the Working Group reached out from January to May 2014 to 300 funders in the public, philanthropic and commercial sectors and collected information on 596 grants and line-item investments that the Group allocated to HIV prevention R&D.

Two different types of resource flows were tracked: investments, defined as annual disbursements by funders; and, when available, expenditures, defined as the level of resources directly spent on R&D activities by funding recipients in a particular year. The main reasons for differentiating between these two resource flows were: (1) some funders may forward fund (i.e., disburse funding in one year to be expended over multiple years); (2) research projects may be delayed; and (3) the increasingly important product development public-private partnerships (PDPs) often receive funds in one year but expend them over a period of time or may hold funds to sustain multi-year contracts.

Investment figures were based on estimates of the level of funds disbursed each year and generated from the perspective of the funder.<sup>a</sup> As such, funds were allocated to the year in which they were disbursed by the donor, irrespective of whether the funds were expended by the recipient in that year or in future years.<sup>b</sup>

In order to minimize double-counting, the Working Group distinguished between primary funders and intermediary organizations. “Intermediary” organizations receive resources from multiple funders and use these resources to fund their own work, as well as the work of others. All identified primary funders were categorized as public (such as government research bodies, international development agencies and multilaterals), philanthropic (such as foundations, charities and corporate donors), or commercial (pharmaceutical and biotechnology companies) sector funders.

While limitations exist in developing a method for breaking down funding allocations by type of activity or stage of product development, the Working Group allocates resources identified into categories based on NIH definitions.<sup>c</sup> As the largest funder of HIV prevention R&D and thus, with the majority of grants towards HIV prevention research allocated based on NIH definitions, this allows for the most accurate possible analysis of the largest portion of grants. For grants received outside of NIH funding, the allocation of funding was based on the information provided by the intermediaries or funders. When this information was not available, the Working Group reviewed the descriptions of the projects funded and, based on the description of each project, allocated the funds across the expenditure categories.

All figures in the report are given in current US dollars and have not been adjusted for inflation. Funding information in other currencies was converted into US dollars using the

*Continues on the next page >*

<sup>a</sup> Organizations were asked to provide data based on the calendar year if possible and, if not, by their fiscal year. For organizations for which the fiscal year and the calendar year did not match we treated the fiscal year as equivalent to the calendar year in which it predominantly occurs. For example, the fiscal year April 1, 2013 to March 31, 2014 was treated as 2013 and the fiscal year July 1, 2013 to June 30, 2014 was treated as 2014.

<sup>b</sup> Any instances in which funds were reported in the year they were spent rather than disbursed are clearly noted, with the rationale behind this decision indicated.

<sup>c</sup> See Appendix for expenditure categories.

appropriate International Monetary Fund (IMF) annual average exchange rate for July 1, 2013, except for those funds where we had access to the actual rate received.

Every effort was made to obtain a comprehensive set of data that was comparable across organizations and countries. However, the data presented in this report are subject to a number of limitations:

- Requests for information were directed to all public, philanthropic and commercial organizations that were identified as providing funding for HIV prevention R&D. However, not all entities contacted responded or provided financial information with their response. For the private sector, annual investment and funding estimates were

extrapolated based on qualitative data collection on R&D programs and expert opinions.

- The Working Group provides R&D allocation definitions in the survey sent to funders. However, most funders and intermediary organizations do not break down their expenditures and investments by type of activity or stage of product development, and definitions often vary between funders.
- The Working Group attempted to reduce the potential for double-counting and to distinguish between funders and recipients of funding. However, all financial information is “self-reported” by organizations and not independently verified.

**Table 14: Public, Philanthropic and Commercial Sector Primary Funders**

Total Responders: 120	
Sector	Type of Responders
<b>Public</b>	<ul style="list-style-type: none"> <li>• National governments (including government research bodies, international development assistance agencies and other government funding agencies)</li> <li>• European Commission</li> <li>• Multilateral agencies</li> </ul>
<b>Philanthropic</b>	<ul style="list-style-type: none"> <li>• Private, not-for-profit organizations (e.g., foundations, trusts and non-governmental organizations)</li> <li>• Charities</li> <li>• Corporate donations</li> <li>• Individual gifts and bequests</li> </ul>
<b>Commercial</b>	<ul style="list-style-type: none"> <li>• Pharmaceutical companies</li> <li>• Biotechnology companies</li> </ul>

**Table 15: Categories Used to Classify Preventive AIDS Vaccine R&D Funding**

Category	Definition
<b>Basic Research</b>	Studies to increase scientific knowledge through research on protective immune responses and host defenses against HIV.
<b>Preclinical Research</b>	R&D efforts directed at improving preventive AIDS vaccine design. These include vaccine design, development and animal testing.
<b>Clinical Trials</b>	Support for Phase I, II and III trials testing the safety, immunogenicity and efficacy of suitable preventive AIDS vaccine candidates or concepts in domestic and international settings (including the costs of producing candidate product lots for clinical trials).
<b>Cohort &amp; Site Development</b>	Support to develop the strategies, infrastructure and collaborations with researchers, communities, government agencies, regulatory agencies, NGOs and industry necessary to identify trial sites, build capacity, ensure adequate performance of trials and address the prevention needs of at-risk populations in trial communities.
<b>Advocacy &amp; Policy Development</b>	Efforts directed at educating and mobilizing public and political support for preventive AIDS vaccines and at addressing potential regulatory, financial, infrastructure and/or political barriers to their rapid development and use.

**Table 16: Categories Used to Classify Microbicide R&D Funding**

Category	Definition
<b>Basic Mechanisms of Mucosal Transmission</b>	Elucidate basic mechanisms of HIV transmission at mucosal/epithelial surfaces that are important for microbicide research and development in diverse populations.
<b>Discovery, Development &amp; Preclinical Testing</b>	R&D efforts directed at the discovery, development and preclinical evaluation of topical microbicides alone and/or in combination.
<b>Formulations &amp; Modes of Delivery</b>	Develop and assess acceptable formulations and modes of delivery for microbicides, bridging knowledge and applications from the chemical, pharmaceutical, physical, bioengineering and social sciences.
<b>Clinical Trials</b>	Conduct clinical studies of candidate microbicides to assess safety, acceptability and effectiveness in reducing sexual transmission of HIV in diverse populations in domestic and international settings.
<b>Microbicide Behavioral &amp; Social Science Research</b>	Conduct basic and applied behavioral and social science research to inform and optimize microbicide development, testing, acceptability and use domestically and internationally.
<b>Microbicide Research Infrastructure</b>	Establish and maintain the appropriate infrastructure (including training) needed to conduct microbicide research domestically and internationally
<b>Policy &amp; Advocacy</b>	Efforts directed at educating and mobilizing public and political support for microbicides and at addressing potential regulatory, financial, infrastructure and/or political barriers to their rapid development and use.

**Table 17: Classification of Other HIV Prevention R&D Funding**

Category	Definition
<b>Pre-exposure Prophylaxis</b>	Includes biomedical R&D, follow-on studies, demonstration projects and operations research for implementation.
<b>Treatment as Prevention</b>	Includes research focused on the primary outcome of transmission at all CD4 levels.
<b>Male Circumcision</b>	Includes operations research for implementation, as well as biomedical R&D. <sup>a</sup>
<b>Prevention of Vertical Transmission</b>	Includes operations research related to prevention of vertical transmission from mother to child at birth and during breastfeeding.
<b>HSV-2 Vaccine</b>	Includes research related to prevention of HSV-2 infections in HIV-negative people via an HSV-2 vaccine.
<b>Female Condom</b>	Includes R&D work focused on product development efforts, community education and advocacy and demonstration studies.

<sup>a</sup> While the Working Group tracks investment in R&D and operations research for adult male circumcision, it does not track investment in rollout and scale-up of the procedure. In the context of this report, "male circumcision" refers specifically to voluntary adult male circumcision (VMMC) performed for the purposes of reducing transmission of HIV and other sexually transmitted diseases. "Operations research" aims to develop solutions to current operational problems of specific health programs or specific service delivery components of the health system. "Implementation research" aims to develop strategies for available or new health interventions in order to improve access to and use of these interventions by the populations in need. Definitions from JHF Remme et al. *Defining Research to Improve Health Systems*. PLoS Med 7:11 (16 November 2010).

**Table 18: Classification of Cure and Therapeutic Vaccine Funding**

Category	Definition
<b>Cure</b>	Includes research conducted on viral latency, elimination of viral reservoirs, immune system and other biological approaches, as well as therapeutic strategies that may lead to either a functional (control of virus rather than elimination, without requirement for therapy) or sterilizing (permanent remission in absence of requirement for therapy) cure of HIV infection.
<b>Therapeutic Vaccine</b>	Includes research into vaccines for HIV-positive individuals designed to enhance immune responses to HIV to better control the infection.

## APPENDIX List of Acronyms

<b>AECID</b>	Spanish Agency for International Development Cooperation	<b>IRMA</b>	International Rectal Microbicides Advocates
<b>amfAR</b>	American Foundation for AIDS Research	<b>MHRP</b>	US Military HIV Research Program
<b>ANRS</b>	National Agency for Research on AIDS and Viral Hepatitis (France)	<b>MPT</b>	Multipurpose Technology
<b>ARC</b>	Australian Research Council	<b>MSF</b>	Médecins Sans Frontières
<b>ARCHE</b>	amfAR Research Consortium on HIV Eradication	<b>MSM</b>	Men who have sex with men
<b>ART</b>	Anti-retroviral therapy	<b>MRC</b>	UK Medical Research Council
<b>ARV</b>	Anti-retroviral	<b>MTN</b>	Microbicide Trials Network
<b>BMGF</b>	Bill & Melinda Gates Foundation	<b>NHMRC</b>	Australian National Health & Medical Research Council
<b>CDC</b>	US Centers for Disease Control and Prevention	<b>NIAID</b>	US National Institute of Allergy and Infectious Diseases
<b>CHAARM</b>	Combined Highly Active Anti-Retroviral Microbicides Project	<b>NIH</b>	US National Institutes of Health
<b>CHARM</b>	Combination HIV Antiretroviral Rectal Microbicide Program	<b>NSC</b>	National Science Council of Taiwan
<b>CHAI</b>	Clinton Health Access Initiative	<b>OAR</b>	US NIH Office of AIDS Research
<b>CHVI</b>	Canadian AIDS Vaccine Initiative	<b>OFID</b>	OPEC Fund for International Development
<b>CIDA</b>	Canadian International Development Agency	<b>P5</b>	Pox-Protein Public-Private Partnership
<b>CIHR</b>	Canadian Institutes of Health Research	<b>PDP</b>	Product development partnership
<b>DBT</b>	Department of Biotechnology at India's Ministry of Science and Technology	<b>PEPFAR</b>	US President's Emergency Plan for AIDS Relief
<b>DFID</b>	UK Department for International Development	<b>PHAC</b>	Public Health Agency of Canada
<b>DST</b>	Department of Science and Technology, South Africa	<b>PMTCT</b>	Prevention of mother-to-child transmission
<b>EC</b>	European Commission	<b>PrEP</b>	Pre-exposure prophylaxis
<b>EDCTP</b>	European and Developing Countries Clinical Trials Partnership	<b>R&amp;D</b>	Research & development
<b>EGPAF</b>	Elizabeth Glazer Pediatric AIDS Fund	<b>SA DOH</b>	South African Department of Health
<b>FACTS</b>	Follow-on African Consortium for Tenofovir Studies	<b>SIDA</b>	Swedish Agency for International Cooperation Development
<b>FDA</b>	US Food and Drug Administration	<b>SRC</b>	Swedish Research Council
<b>FHI</b>	Family Health International, US	<b>START</b>	Strategic Timing of AntiRetroviral Treatment (START) study
<b>FHI 360</b>	Prevention Trials Network	<b>TDF</b>	Tenofovir
<b>HVTN</b>	HIV Vaccine Trials Network	<b>TDF/FTC</b>	Tenofovir/Emtricitabine
<b>IAVI</b>	International AIDS Vaccine Initiative	<b>UK</b>	United Kingdom
<b>ICMR</b>	Indian Council of Medical Research	<b>UNAIDS</b>	Joint United Nations Programme on HIV/AIDS
<b>IPM</b>	International Partnership for Microbicides	<b>US</b>	United States
		<b>USAID</b>	US Agency for International Development
		<b>VOICE</b>	Vaginal and Oral Interventions to Control the Epidemic
		<b>VMMC</b>	Voluntary Medical Male Circumcision
		<b>VRC</b>	US Vaccine Research Center
		<b>WHO</b>	World Health Organization

## APPENDIX Acknowledgements

The Working Group would like to thank the many individuals from the public, philanthropic and commercial sectors who provided us with information and whose participation was essential to the completion of this project. The Working Group would like to first thank the following individuals and organizations:

**Donna D. Adderly**, Office of AIDS Research, National Institutes of Health  
**Bobbie Annonson**, The Female Health Company  
**Mireia Manent Blanch**, Institut de Recerca de la Sida  
**Christian Brander**, IrsiCaixa-HIVACAT-ICREA  
**Doris Brauer**, Federal Ministry for Economic Cooperation and Development, Germany  
**Kim Brehm**, William and Flora Hewlett Foundation  
**Gabrielle Breugelmans**, European & Developing Countries Clinical Trials Partnership  
**Adam Brush**, Centers for Disease Control and Prevention  
**Monika Ciesielczyk**, US Military HIV Research Program  
**Kent Cozad**, amfAR, The Foundation for AIDS Research  
**Christine Cryan**, Public Health Agency of Canada  
**Brendan Curran**, Canadian Foundation for AIDS Research  
**Lauren Dolak**, International Partnership for Microbicides  
**Cristina de Carvalho Eriksson**, Regional HIV & AIDS Team for Africa, Embassy of Sweden  
**Inger Florin**, Swedish Foundation for Strategic Research  
**Jessica Fredin**, Australian Research Council  
**Alexis Gilbert**, Wellcome Trust  
**Melanie Glaettli**, Swiss National Science Foundation  
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