

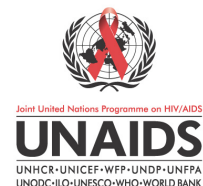
# TRACKING FUNDING FOR PREVENTIVE HIV VACCINE RESEARCH & DEVELOPMENT:

ESTIMATES OF ANNUAL INVESTMENTS AND EXPENDITURES  
2000 TO 2005

JUNE 2005

## HIV Vaccines and Microbicides Resource Tracking Working Group

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This report was prepared on behalf of the HIV Vaccines and Microbicides Resource Tracking Working Group by Gabrielle Lamourelle (IAVI), Polly Harrison (AMD), Jane Rowley (Consultant) and Mitchell Warren (AVAC).

## **ACKNOWLEDGEMENTS**

In 2002, UNAIDS established a Global Resource Tracking Consortium for AIDS composed of international experts, and in October 2004, an HIV Vaccines and Microbicides Resource Tracking Working Group was formed. This working group was tasked with generating better information on investments in research and development for vaccines and microbicides.

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 invaluable to the completion of this project.

Support for this project was provided by the Alliance for Microbicide Development (AMD), the AIDS Vaccine Advocacy Coalition (AVAC), the International AIDS Vaccine Initiative (IAVI) and the Joint United Nations Programme on HIV/AIDS (UNAIDS).

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## 1. INTRODUCTION

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In the 20 years since the identification of HIV as the cause of AIDS, the HIV pandemic has grown to be the greatest public health crisis facing the world since the 13th century. Over 65 million people have been infected with HIV to date, and each day another 14,000 people are infected.<sup>1</sup>

Clearly more needs to be done to expand access to prevention and treatment – but there is also an urgent need to simultaneously develop additional prevention methods. HIV vaccines and microbicides are two technologies currently under development that would provide people with new options for protecting themselves from HIV.

Accelerating the development and widespread use of preventive HIV vaccines and microbicides will require the active engagement of governments, international agencies, the private sector and community based organizations. Whilst significant research progress has been made, it is still a number of years before these two technologies will be licensed and widely used. However, the time to their being developed and in widespread use could be significantly reduced with increased and more efficient research and development (R&D) spending, accompanied by greater and sustained political commitment and action. This includes support for: conducting basic and applied research; running clinical trials; developing and sustaining clinical trial infrastructure; strengthening regulatory agencies; supporting process development to ensure that any licensed product can be manufactured at scale at a reasonable price; and establishing manufacturing capacity.

Over the past several years, a number of estimates have been made of global investments and expenditures on both preventive HIV vaccine and microbicide R&D,<sup>2</sup> but comparison of these estimates from year to year, from one technology to another, and across funders suffers from a lack of uniformity in how the estimates were generated.

In late 2004, the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Alliance for Microbicide Development (AMD), the AIDS Vaccine Advocacy Coalition (AVAC) and the International AIDS Vaccine Initiative (IAVI) established a collaborative project to track funding for HIV vaccines and microbicide R&D. Each of the organizations had been working separately to track funding levels and felt that working together would improve the quality and comparability of the data.

The specific objectives of this collaboration were to:

1. Develop a common approach for estimating global investment and expenditures by the public, philanthropic and commercial sectors to generate comparative annual data.
2. Generate estimates of annual global investment levels for each technology from 2000 to 2004 and preliminary estimates for 2005, as well as annual global expenditures by stage of product development from 2000 to 2004.
3. Monitor progress in the implementation of the Declaration of Commitment on HIV/AIDS, adopted at the United Nations General Assembly Special Session (UNGASS) on HIV/AIDS in 2001. This declaration contains a number of global and national indicators that are being monitored on an annual basis by UNAIDS and others. The second of the global commitment and action indicators,

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<sup>1</sup> UNAIDS/WHO (2004). *AIDS Epidemic Update 2004*. Geneva.

<sup>2</sup> Previous estimates include: a) IAVI (2004). *Global Investment and Expenditures on Preventive HIV Vaccines: Methods and Results for 2002*. New York, USA; b) UNAIDS (2003). *Progress Report on the Global Response to the HIV/AIDS Epidemic, 2003: Follow-up to the 2001 United Nations General Assembly Special Session on HIV/AIDS*. Geneva; c) Alliance for Microbicide Development (2004). *Funding for Microbicides: An Overview Chart*. Maryland, USA.; and d) AVAC (2004). *AIDS Vaccine Advocacy Coalition Report 2004*. New York, USA.

which is the specific focus of the work reported here, is the “Amount of public funds available for research and development of vaccines and microbicides.”<sup>3</sup>

This paper describes the methods developed to estimate annual investment and expenditures, and presents our estimates and analysis of the levels of public, philanthropic, and commercial investment in and expenditures on preventive HIV vaccine R&D. A companion paper will be released shortly that specifically examines funding for microbicide R&D.

In 2004, the public, philanthropic and commercial sectors invested a total of approximately US\$ 682 million (range US\$ 668 mn to US\$ 696 mn) in preventive HIV vaccines and current disbursement and commitment figures suggest that investment levels in 2005 will be higher than in 2004. This level of investment, however, is far short of the US\$ 1.2 bn a year that the Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise estimates is required to mount an accelerated search for a safe and effective vaccine.<sup>4</sup>

The vast majority of the funds invested are from the US public sector, which in 2004 committed US\$ 516 mn to HIV vaccine development, or 76% of the funds invested globally by the public, philanthropic and commercial sectors combined. The commercial sector, a key player in R&D for most other health products, was estimated to account for only 10% of global investment in HIV vaccine R&D.

Over the last five years there has been a substantial increase in overall funding for preventive HIV vaccine R&D. In particular, the level of investment from the non-commercial sector (i.e., the public and philanthropic sectors) almost doubled between 2000 and 2004. Funding from the commercial sector, however, has not kept pace – and, in fact, appears to have fallen between 2002 and 2004.

Total expenditures on preventive HIV vaccines in 2004 were estimated to be US\$ 686 mn or US\$ 4 mn more than investments. Most of these funds went towards basic and pre-clinical research (65% of the total) with clinical trials and cohort and site development accounting for 34%, and advocacy and policy development for 1%.

The figures presented in this report represent an improvement on previous efforts to track R&D funding for preventive HIV vaccines and provide a useful baseline against which future investments and expenditures can be compared. Collecting comparable and reliable international funding data, however, is a challenge. The development of better systems for reporting and collecting this sort of data at both the national and international levels, linked to efforts to estimate what level of funding is needed and can be absorbed, will help researchers and policy makers:

- Monitor current levels of effort;
- Identify trends in investment, spending, and research focus;
- Identify areas where more resources and effort need to be focused; and
- Assess the impact of public policies aimed at increasing investment in HIV vaccines.

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<sup>3</sup> UNAIDS (2003). *Progress Report on the Global Response to the HIV/AIDS Epidemic, 2003: Follow-up to the 2001 United Nations General Assembly Special Session on HIV/AIDS*. Geneva.

<sup>4</sup> Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise (2005). *The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan*. PLoS Med 2: e25.

## 2. METHODS

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A broad definition of R&D was used for the analysis, and data were collated not only on product development efforts but also on support for: clinical trial preparations; community education; and advocacy and policy efforts directed at accelerating HIV vaccine development and use. We have not, however, included:

- R&D for vaccines with primarily therapeutic applications; or
- Research not directed primarily at preventive HIV vaccines and/or microbicides but that may have benefits or links to either of these products (e.g., platform technologies).

Two different types of resource flows were tracked: investments, defined as annual disbursements by funders; and expenditures, defined as the level of funding directly spent on R&D activities in a particular year. The main reasons for differentiating between these two 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 rise in the importance of public-private partnerships (PPPs) who require sufficient funds either banked or committed to enter into credible multi-year contracts.

All figures in the report are reported in current US dollars and have not been adjusted for inflation. Funding information provided in other currencies were converted into US dollars using the appropriate IMF annual average exchange rate,<sup>5</sup> except for those funds where we had access to the actual rate received.

### 2.1 ANNUAL INVESTMENT

Annual investment levels were estimated from the perspective of the funder. In other words, we have collated information on investment levels from primary funding organizations and the funds were allocated to the year in which they were actually disbursed irrespective of whether the funds were intended to be expended by the recipient in that year or in future years.

In developing these estimates, we distinguished between primary funders and intermediary organizations. Intermediary organizations are those who receive resources from multiple funders and use these resources to fund their own work as well as others. For example, IAVI and SAAVI (South African AIDS Vaccine Initiative) were classified as intermediary organizations. In order to avoid double counting, intermediary organizations were classified as recipients rather than funders. All identified primary funders of HIV vaccine R&D were allocated to one of three categories (see Table 1).

A four-step process was followed to estimate annual investment levels for both HIV vaccine and microbicide R&D (see Box 1). All primary funders were asked to provide data on annual disbursements,<sup>6</sup> as this gives a more accurate picture of annual investments than commitments or pledges made.<sup>7</sup> However, not all organizations were able to provide disbursement data and for these organizations commitment data were used instead.<sup>8</sup>

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<sup>5</sup> For investments made in 2005 the 2004 IMF annual average exchange rate was used ([www.imfstatistics.org](http://www.imfstatistics.org)).

<sup>6</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, 2004 to March 31, 2005 was treated as 2004 and the fiscal year July 1, 2004 to June 30, 2005 was treated as 2005.

<sup>7</sup> The Organization for Economic Cooperation and Development (OECD) makes a clear distinction between disbursements and commitments. Disbursements reflect the amount actually spent by a donor and record the actual release or transfer to a recipient of financial resources, goods or services valued at the cost to the donor. A commitment, on the other hand, is a firm obligation expressed in writing and backed by the necessary funds to provide a particular level of support.

<sup>8</sup> For example, the US National Institutes of Health (NIH) and Agency for International Development (USAID) figures are based on commitments and are charged against the year in which the commitments were made.

It should also be noted that many public sector and philanthropic agencies do not specifically track funding for HIV vaccine R&D. In these situations, the information provided was generally from a key word search conducted by the agency of projects funded or was based on the knowledge of the informant contacted. The former can lead to the identification of a number of projects where only a portion of each grant is directly related to HIV vaccines. In these cases, we reviewed the description of the project and estimated the percentage of the overall grant directly related to HIV vaccines. In addition, not all organizations were able to provide annual breakdowns of their grants. For these organizations, we allocated the total funds disbursed or committed equally over the duration of the grant.

In the case of commercial organizations, we initially asked them to provide us with information on their level of investment, excluding direct or indirect funding from the public sector or intermediary agencies, for the period 2000 to 2004 and their expected investment in 2005. It became clear, however, that given the time available for this study, we were going to have to scale back our expectations, as many of the companies contacted did not specifically track funding for HIV vaccine R&D and others were reluctant to share information on funding levels citing concerns about proprietary business issues. As a result, our industry estimates are presented as ranges for one year only (2004) and are based on the information provided by companies, publicly available documents and interviews with industry experts.

<b>Table 1. Public, Philanthropic and Commercial Sector Primary Funders</b>	
Public sector	<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>
Philanthropic sector	<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>
Commercial sector	<ul style="list-style-type: none"> <li>• Pharmaceutical companies</li> <li>• Biotechnology companies</li> </ul>

**Box 1: The process followed to estimate annual investments for both HIV vaccines and microbicides****Step 1: Identifying key funding agencies**

A list of all organizations involved in funding preventive HIV vaccine and microbicide R&D was drawn up based on funders identified in previous resource tracking efforts and supplemented by discussions with key individuals working in the HIV vaccine and microbicide fields. As new funders were identified, they were added to the list.

**Step 2: Collecting publicly available information**

For each of the funders identified, the publicly available information was reviewed for data on annual investment levels. Information sources consulted included: government reports, annual reports, US Securities and Exchange Commission (SEC) filings, published studies and articles, 'grey' literature, scientific presentations and website postings.

**Step 3: Contacting the funding agencies identified**Public sector:

Letters were written to all of the public sector funders identified asking them for information on funds disbursed since 2000 and future commitments in their local currency. Information requested included:

- Description of the projects or programs funded;
- Duration of grants/ contracts/ awards;
- Total funding committed;
- Funding disbursement by year since 2000; and
- Projected disbursement or future funding commitments by year.

Agencies contacted included national research funding agencies [e.g., Agence Nationale de Recherches sur le Sida (ANRS) in France and the Canadian Institutes of Health Research (CIHR)], overseas development agencies [e.g., the Department for International Development (DFID) in the UK and the Agency for International Development (USAID) in the US], and multilateral organizations (e.g., UNAIDS, The World Bank and The World Health Organization). Each national agency was also asked to suggest other national agencies that should be contacted.

Philanthropic sector:

Letters were written to all of the identified philanthropic funders known to have awarded more than US\$ 100,000 to either technology between 2000 and 2004. The letters were similar to those sent to public sector funders and asked for the same information. For smaller funders, disbursement estimates were based on information collated from intermediaries and internet searches and, where no information was readily available, the organizations were contacted directly.

In the case of corporate donations, data were only collected on cash donations. No attempt was made to include in-kind support such as goods, services, and donated staff time owing to the difficulties in valuing these contributions.

Commercial sector:

Each of the main companies identified was contacted in writing, in person or by phone and asked to provide information on its own internal funding (i.e., they were asked not to include funds received from external sources such as research agencies or intermediary organizations).

**Step 4: Reviewing, checking, and analysing the information collated**

The financial information received from each funder was reviewed against the project inclusion criteria and cross-checked. Any issues or questions were followed up with the funder. In the case of US agencies that track HIV vaccine funding explicitly, we have made use of their self-reported figures rather than examining each grant individually.

For those organizations that did not respond even after repeated follow-ups, annual disbursements were estimated based on publicly available information, supplemented by discussions with experts working in the field.

The estimates for each sector were then reviewed for consistency to ensure that similar definitions were used and to eliminate double counting.

## 2.2 ANNUAL EXPENDITURES

The total level of funding made available in a particular year and the level of funds actually spent in that year do not always match. For example, a funder may provide a large sum of money in one year for use in future years or a research programme may be delayed, postponing expenditures.

In estimating annual expenditures we distinguished between funding provided by primary funders to universities, not-for-profit organizations, or companies and funding they provided to "intermediary" organizations like IAVI and SAAVI. For each of the intermediary organizations we collated data on their annual expenditures. It should be noted that our annual expenditure estimates are first order estimates, and that actual annual expenditures could be higher or lower because non-intermediary expenditure estimates are based on disbursement figures rather than on actual expenditure data.

There is no agreed method for breaking down annual expenditures by type of activity or stage of product development. For this exercise, we have allocated expenditures into five categories. The first four categories are based on the US National Institutes of Health definitions<sup>9, 10</sup> (see Box 2 and Appendix 2 for more information). The allocation of funding across these categories was based on the information provided by the intermediaries and/or funders. When this information was not available, we reviewed the descriptions of the projects funded and, based on the description of each project, allocated the funds across the five expenditure categories.

<b>Box 2. The five categories used to classify preventive HIV vaccine expenditures</b>	
<b>Basic Research</b>	Studies to increase scientific knowledge through research on protective immune responses and host defenses against HIV that facilitate the development of preventive vaccines.
<b>Pre-clinical Research</b>	Research and development efforts directed at improving preventive vaccine design. This includes 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 vaccine candidates or concepts in domestic and international settings (including the costs of producing vaccine lots for clinical trials).
<b>Cohort and 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 and Policy Development</b>	Efforts directed at educating and mobilizing public and political support for preventive HIV vaccines and at addressing potential regulatory, financial, infrastructure and/or political barriers to their rapid development and use.

<sup>9</sup> National Institutes of Health (2000). *National Institutes of Health Fiscal Year 2002 Plan for HIV-Related Research*. Washington, DC.

<sup>10</sup> The NIH categories are: Basic, Pre-Clinical, Pediatric, Clinical Trials and Vaccine Preparedness. For the purposes of our estimates we have accepted the NIH breakdown of their expenditures by category. Funding classified as "pediatric" by NIH was allocated equally between pre-clinical research and clinical trials. Auditing and reclassifying the NIH data would have been a major exercise and was beyond the scope of this project.

## 2.3 DATA LIMITATIONS

Every effort was made to obtain a comprehensive set of data that was comparable across organizations and countries. The data presented in this report, however, are subject to a number of caveats.

### Missing or incomplete information:

Requests for information were directed to all public, philanthropic, and commercial organizations that were identified as providing funding for HIV vaccine R&D. However,

- We may have missed key funding organizations or developers.
- Public sector data collection efforts focused on national and international funding; information on state or provincial funding was not included in the estimates.
- Not all organizations provided financial information. For those that did not, annual investment and expenditure estimates were extrapolated based on information available in the public domain and expert opinions.
- Many private sector companies do not specifically track spending on HIV vaccines and hence do not have the relevant data readily available. In addition, many companies were reluctant to share financial information due to proprietary business concerns.

### Differences in definitions:

In our data analysis we tried to make the data collated consistent across funders and over time so that accurate trends and comparisons could be drawn. However,

- Not all funders reported disbursement data on a calendar year, but instead reported funding flows based on their own fiscal year and contracting mechanisms.
- The annual expenditure estimates are based on a combination of expenditure data from intermediary organizations and an estimate of non-intermediary expenditures.
- Most funders and intermediary organization do not break down their expenditures by type of activity or stage of product development and, if they do, they use their own definitions.
- Within a particular organization, changes may have occurred in how they classify funds over the five-year period studied.

### Sources of information and double counting:

Every attempt was made to reduce the potential for double counting and to distinguish between funders and recipients of funding. However,

- All financial information was “self reported” and not independently verified.
- A number of the pharmaceutical and biotechnology companies active in HIV vaccine and microbicide R&D receive either direct or indirect support from the public sector (e.g., the NIH, ANRS and the European Community [EC]) and intermediary organizations (e.g., IAVI and SAAVI) to finance their work. The data presented here reflect, to the best of our ability, only the direct expenditures by the companies of their own resources.

### 3. RESULTS

#### 3.1 TOTAL INVESTMENT

- In 2004, the public, philanthropic, and commercial sectors invested approximately US\$ 682 mn (range US\$ 668 mn to US\$ 696 mn) in preventive HIV vaccine R&D.

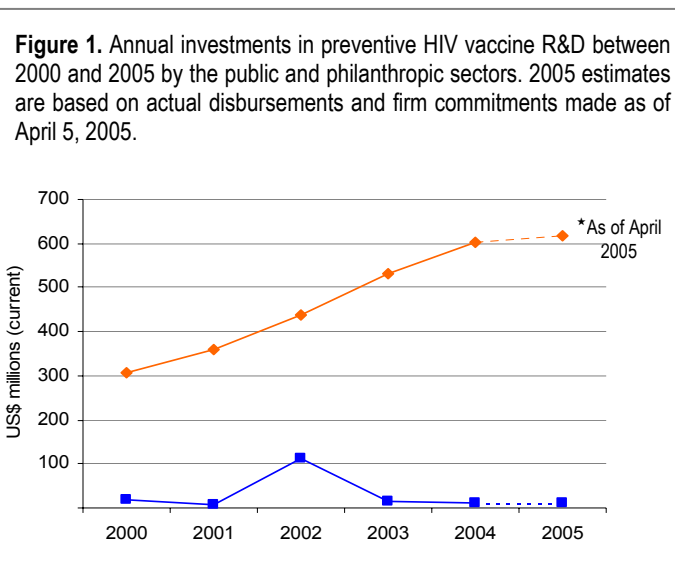
**Table 2.** Annual investment in preventive HIV vaccine R&D between 2000 and 2005 (current US\$ mn). The 2005 estimates represent actual disbursements and firm commitments made as of April 5, 2005.

	2000	2001	2002	2003	2004	2005
<b>Public Sector</b>						
- US	272	314	376	463	516	568
- Europe <sup>A</sup>	23	32	39	44	57	39
- Other <sup>B</sup>	10	12	21	24	28	8
- Multilaterals	2	2	2	2	2	2
<i>Total public</i>	307	359	436	532	602	617
<b>Philanthropic Sector</b>						
<i>Total philanthropic</i>	20	7	112	15	12	10
<b>Commercial Sector</b>						
- Pharmaceutical companies	-	-	-	-	59 (range 47 to 71)	-
- Biotechnology companies	-	-	-	-	9 (range 7 to 11)	-
<i>Total commercial</i>	-	-	-	-	68 (range 54 to 82)	-

<sup>A</sup> This figure includes funding from the European Commission.

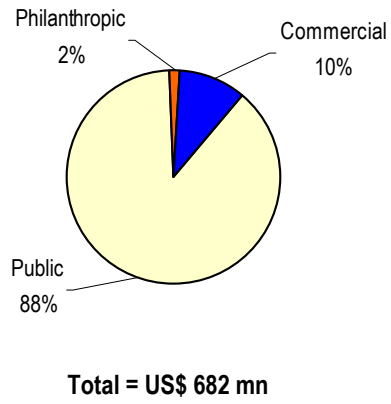
<sup>B</sup> Other includes all national public sector funding apart from funding from the US and Europe.

- Between 2000 and 2004 investment from non-commercial sources (the public and philanthropic sectors) almost doubled from US\$ 327 mn to US\$ 614 mn.
- By April 5, 2005 estimated disbursements and firm commitments from non-commercial sources for 2005 had already reached US\$ 627 mn.
- The 2005 estimate does not include the Requests for Proposals announced by the Bill & Melinda Gates Foundation in February 2005, which committed the Foundation to provide up to US\$ 360 mn over the next five years for HIV vaccine R&D. No awards have yet been announced and it is unlikely that any significant funding will be disbursed through this process in 2005.



- The peak in philanthropic funding in 2002 reflects a large grant made by the Bill & Melinda Gates Foundation to IAVI (see section 3.3).

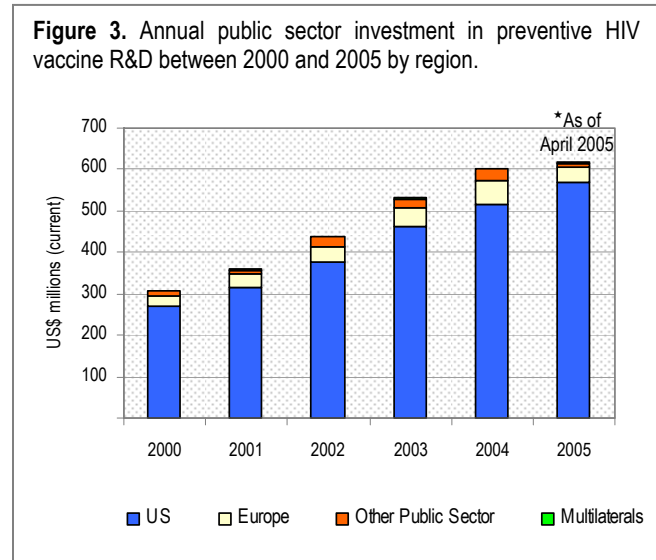
**Figure 2.** Sources of funding for preventive HIV vaccine R&D in 2004.



- In 2004, the public sector dominated funding for HIV vaccine R&D, accounting for 88% of total investment. The commercial sector accounted for 10% and the philanthropic sector for 2%.

### 3.2 PUBLIC SECTOR INVESTMENT

- In 2004, the public sector invested US\$ 602 mn in HIV vaccine R&D and by April 5, 2005 US\$ 617 mn had already been disbursed or committed for 2005.
- Public sector investment in the five years between 2000 and 2004 almost doubled from US\$ 307 mn to US\$ 602 mn.
- The United States dominates public sector funding. Between 2000 and 2004 the US accounted for 85 to 90% of public sector funding each year.
- In 2004, the US committed US\$ 516 million – about 86% of the total funds invested by the public sector. European national governments and the European Commission together accounted for just over 9%, whilst national governments from the rest of the world accounted for just under 5%. Multilaterals (WHO, UNAIDS and the World Bank) accounted for under 0.5%.



- Within the United States the main source of funding is the National Institutes of Health (NIH). The NIH accounted for 88% (about US\$ 452 mn) of US public sector funding in 2004, or 75% of total global public sector investment.

- 13 countries were identified that invested more than US\$ 1 mn of public sector funds in preventive HIV vaccine R&D in 2004. In comparison, in 2000 only 7 countries invested more than US\$ 1 mn. In addition, in 2004 the European Commission<sup>11</sup> invested around US\$ 12 mn, and WHO and UNAIDS together invested around US\$ 1.4 mn.

**Table 3.** National public sector investment in preventive HIV vaccine R&D by country in 2004. Within each category countries are listed alphabetically.

US\$ 50k to 500k	US\$ 500k to 1 mn	US\$ 1 mn to 5 mn	US\$ 5 mn to 10 mn	US\$ 10 mn to 25 mn	Over US\$ 25 mn
-Australia -China -Cuba -India -Thailand	-Brazil -Finland -Russia	-Denmark -France -Germany -Japan -Netherlands -Norway -Sweden	-Ireland -Italy -South Africa	-Canada -United Kingdom	-United States

- Three countries invested more than US\$ 10 mn from public sector sources in 2004 – Canada, the United Kingdom and the United States.

- Investment figures for individual years, however, do not necessarily reflect long-term donor commitment. In terms of total funds disbursed for HIV vaccine R&D between 2000 and 2004, the top five countries (excluding the EC) in descending order were: the United States, Canada, the United Kingdom, the Netherlands and France.

<sup>11</sup> This figure includes funding provided from the Directorate General for Research, the Directorate General for Development and the European and Developing Countries Clinical Trials Partnership (EDCTP).

**Table 4.** Per capita public sector investment in preventive HIV vaccine R&D by country in 2004.<sup>A</sup> Within each category countries are listed alphabetically.

US\$ 0.0001 to 0.01	US\$ 0.01 to 0.10	US\$ 0.10 to 0.25	US\$ 0.25 to 0.50	US\$ 0.50 to 1.00	US\$ 1.00 to 1.50	US\$ 1.50 to 2.00
-Brazil -China -India -Russia -Thailand	-Australia -Cuba -France -Germany -Japan	-Finland -Italy -South Africa -United Kingdom	-Denmark -Netherlands -Sweden	-Canada -Norway	(none)	-Ireland -United States

<sup>A</sup> Population size estimates are for the year 2003. Source: 2005 World Development Indicators, The World Bank.

- The United States and Ireland<sup>12</sup> were the two largest public sector investors in 2004 in terms of funds disbursed per capita.
- Levels of per capita investment for the United States and Ireland were more than four times the amount invested by any other countries, apart from Canada and Norway.

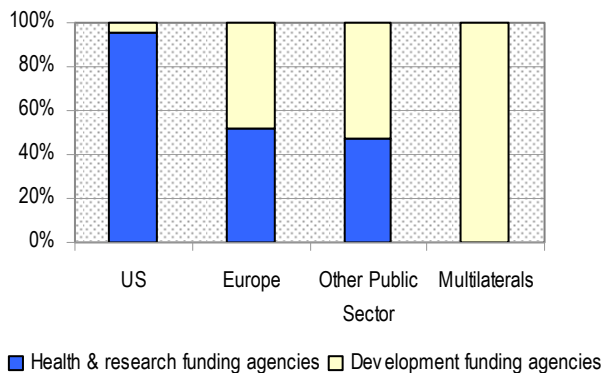
**Table 5.** Public sector investment in preventive HIV vaccine R&D in 2004 by country as a percentage of GDP.<sup>B</sup> Within each category countries are listed alphabetically.

Less than 0.0005	0.0005 to 0.001	0.001 to 0.002	0.002 to 0.003	0.003 to 0.004	0.004 to 0.005
-Australia -Brazil -China -Finland -France -Germany -India -Italy -Japan -Norway -Russia -Thailand	-Denmark -Netherlands -Sweden -United Kingdom	-Canada	(none)	-South Africa	-Ireland -United States

<sup>B</sup> GDP estimates are for the year 2003. Source: 2005 World Development Indicators, The World Bank. Note: no GDP data were available for Cuba for 2003.

- The United States and Ireland were the two largest public sector investors in 2004 as a percentage of GDP invested.
- Levels of investment as a percentage of GDP for the United States and Ireland were more than four times the amount invested by any other country apart from South Africa and Canada.

**Figure 4.** Funding sources for public sector investment in preventive HIV vaccines in 2004 by region.

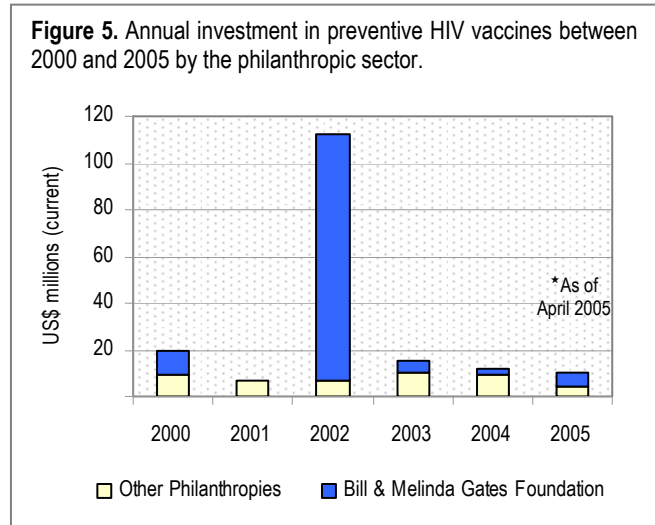


- The source of public sector funding for HIV vaccine R&D varies widely within countries. For example, in the United States 95% of the funding for HIV vaccine R&D in 2004 came from health and research funding agencies. This is quite different from many other countries where development funding sources are equally important. It is also quite different from the three multilateral agencies – UNAIDS, the World Bank and WHO – which provide primarily development funding.

<sup>12</sup> The 2004 investment figure for Ireland is slightly skewed by Development Cooperation Ireland's decision to disburse both their 2004 and 2005 funding to IAVI in the calendar year 2004.

### 3.3 PHILANTHROPIC SECTOR INVESTMENT

- In 2004, philanthropic funding totaled US\$ 12 mn or around 2% of the total funds disbursed.
- Levels of philanthropic funding have varied considerably over the period studied – from a low of US\$ 7 mn in 2001 to a high of US\$ 112 mn in 2002.
- The peak in 2002 reflects the multi-year US\$ 100 mn challenge grant awarded by the Bill & Melinda Gates Foundation to IAVI and that was disbursed in full to IAVI in 2002.



- Funding from the philanthropic sector is projected to increase substantially in the next few years as a result of three major Requests for Proposals to accelerate the development of an HIV/AIDS vaccine announced by the Bill & Melinda Gates Foundation in February 2005. These RFPs pledge up to US\$360 million over the next five years to support HIV vaccine research as part of the Global HIV/AIDS Vaccine Enterprise.

- In 2004, nine philanthropic organizations were identified who provided funding of more than US\$ 100,000 for HIV vaccine R&D. In addition, three companies also provided corporate donations of US\$ 100,000 or more.
- The largest philanthropic funder of HIV vaccine R&D is the Bill & Melinda Gates Foundation. Of the total cumulative funds disbursed by philanthropic organizations between 2000 and 2004, the Bill & Melinda Gates Foundation accounted for 75% or US\$ 123 mn of the US\$ 166 mn disbursed.

**Table 6.** Philanthropic investment in HIV vaccine R&D by organization in 2004. Within each category organizations are listed alphabetically.

US\$ 100k to 250k	US\$ 250k to 500k	US\$ 500k to 1mn	Over US\$ 1 mn
-Becton Dickinson and Company* -Deutsche AIDS Stiftung -Ford Foundation -Transnet* -Until There's A Cure Foundation	-American Foundation for AIDS Research (amfAR) -Bristol Myers Squibb Foundation	-Elizabeth Glaser Pediatric AIDS Foundation	-Bill & Melinda Gates Foundation -Eskom* -Starr Foundation -Wellcome Trust

\*Company donation rather than philanthropic organization

Note: because of differences in funding cycles, The Rockefeller Foundation, a long-term HIV vaccine supporter, is not included above.

### 3.4 COMMERCIAL SECTOR INVESTMENT

**Table 7.** Annual investment in preventive HIV vaccines by the commercial sector in 2002 and 2004 (current US\$). The 2004 estimates were generated by this project, while the 2002 figures are from a previous IAVI project.<sup>13</sup>

	2002	2004
Pharmaceutical Companies	US\$ 57 mn (58%) (range 48 to 67)	US\$ 59 mn (87%) (range 47 to 71)
Biotechnology Companies	US\$ 42 mn (42%) (range 36 to 49)	US\$ 9 mn (13%) (range 7 to 11)
<b>Total</b>	<b>US\$ 99 mn</b> (range 84 to 116)	<b>US\$ 68 mn</b> (range 54 to 82)

- In 2004, total commercial sector investment, excluding funding from external sources, was estimated to be US\$ 68 mn (range US\$ 54 mn to US\$ 82 mn).
- Total expenditures by the commercial sector, however, are considerably greater than this, as many of the companies active in HIV vaccine R&D receive programme funding from external sources such as public sector agencies (e.g., NIH and ANRS) or PPPs (e.g., IAVI and SAAVI).
- The 2004 estimate is considerably less than IAVI's estimate for 2002<sup>13</sup> of US\$ 99 mn (range US\$ 84 mn to US\$ 116 mn). The two estimates were generated using similar approaches but different people were involved in generating the estimates and hence they are not necessarily directly comparable.
- Much of the apparent drop in commercial investment between 2002 and 2004 is due to the completion of VaxGen's Phase III clinical trials and the subsequent shift in VaxGen's priorities from HIV vaccines to vaccines against bioterror agents. In 2002, VaxGen invested between US\$ 30 mn and US\$ 32 mn of their own funds on preventive HIV vaccines, whilst in 2004 they invested none.<sup>14</sup>
- The apparent drop in commercial investment between 2002 and 2004 was accompanied by a significant drop in the share of funding coming from biotechnology companies. In 2002, biotechnology companies accounted for 42% of commercial investment. By 2004, this figure had fallen to 13%. Again, much of this apparent drop is accounted for by the change in VaxGen's research focus.

<sup>13</sup> See IAVI (2004). *Global Investment and Expenditures on Preventive HIV Vaccines: Methods and Results for 2002*. New York, USA.

<sup>14</sup> This figure does not include the 2002 investments made in building a manufacturing plant by Celltrion, a joint venture wholly owned by VaxGen, Inc. and several South Korean investors. In total US\$ 122 mn was committed in February 2002 (of which US\$ 7 mn was spent in that year), to build two large-scale multi-use bio-manufacturing plants capable of the production of AIDS VAX® and other bio-manufactured products.

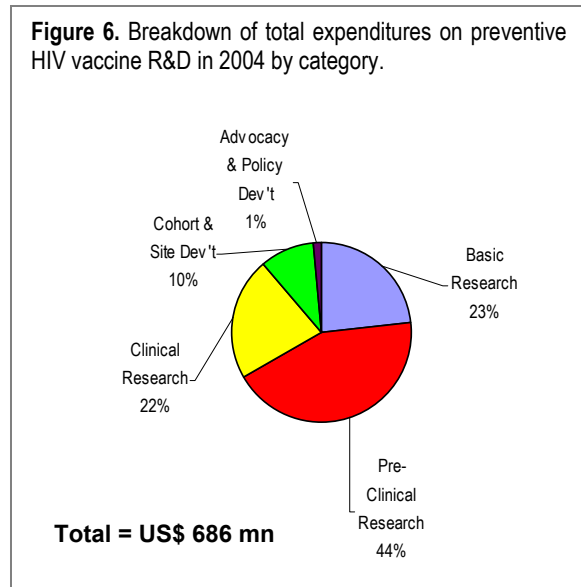
- Four companies were identified that were estimated to have invested more than US\$ 5 mn of their own funds in preventive HIV vaccine R&D in 2004.
- The vast majority of the companies engaged in HIV vaccine R&D receive extensive program support from public sector agencies or intermediaries, and their own investments are generally small and supplementary to the funding they receive from these external sources. In total, we estimated that there were 27 companies who invested US\$ 25,000 or more of their own funds in HIV vaccine R&D in 2004.

**Table 8.** Commercial investment in preventive HIV vaccine R&D by company in 2004. Within each category companies are listed alphabetically.

US\$ 25,000 to 1 mn	
<ul style="list-style-type: none"> <li>• Advanced BioScience Laboratories</li> <li>• AlphaVax Human Vaccines Inc.</li> <li>• AVANT Immunotherapeutics, Inc.</li> <li>• Bavarian Nordic</li> <li>• Berna Biotech Ag</li> <li>• Bioption AB</li> <li>• Bioqual Inc.</li> <li>• Cobra Biomanufacturing plc</li> <li>• Crucell N.V.</li> <li>• Epimmune Inc.</li> </ul>	<ul style="list-style-type: none"> <li>• EpiVax, Inc.</li> <li>• GenVec, Inc.</li> <li>• GeoVax, Inc.</li> <li>• Globeimmune, Inc.</li> <li>• Impfstoffwerk Dessau Tornau GmbH</li> <li>• Maxygen, Inc.</li> <li>• PAREXEL International Corporation</li> <li>• Progenics Pharmaceuticals, Inc.</li> <li>• Therion Biologics Corporation</li> <li>• Vical Inc.</li> </ul>
US\$ 1 mn to 5 mn	
<ul style="list-style-type: none"> <li>• FIT Biotech Oyj Plc.</li> <li>• GlaxoSmithKline plc</li> </ul>	<ul style="list-style-type: none"> <li>• Targeted Genetics Corporation</li> </ul>
US\$ 5 mn to 10 mn	
<ul style="list-style-type: none"> <li>• Chiron Corporation</li> <li>• Sanofi Pasteur (formerly Aventis Pasteur)</li> </ul>	<ul style="list-style-type: none"> <li>• Wyeth-Ayerst Lederle Inc.</li> </ul>
Over US\$ 10 mn	
<ul style="list-style-type: none"> <li>• Merck &amp; Co., Inc.</li> </ul>	

### 3.5 ANNUAL EXPENDITURES

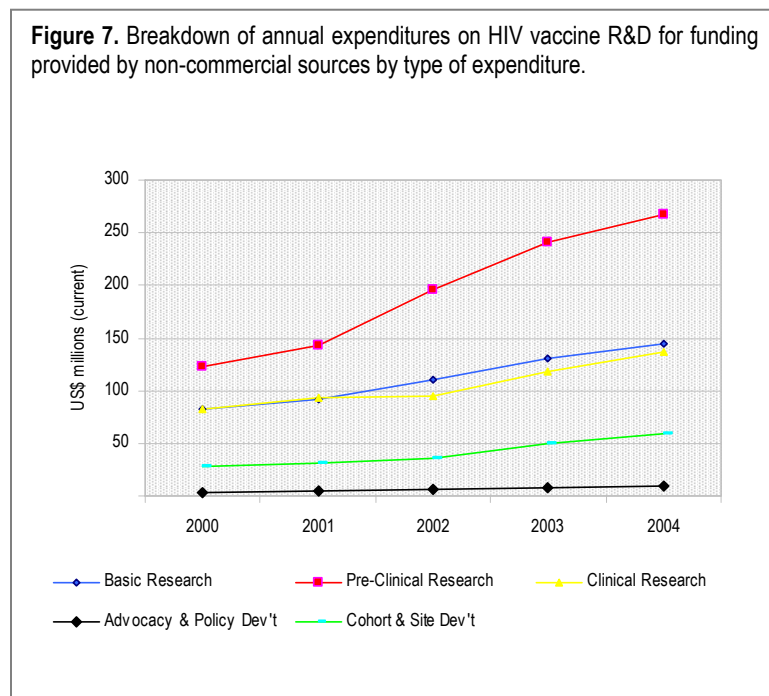
**Figure 6.** Breakdown of total expenditures on preventive HIV vaccine R&D in 2004 by category.



- In 2004, total expenditures by the public, philanthropic and commercial sectors on HIV vaccine R&D were estimated to be US\$ 686 mn.
- In 2004, annual expenditures were estimated to be greater than annual investments by a total of US\$ 4 mn, or 0.5% of total investments. This is unlike earlier years when estimated annual investments were greater than expenditures.
- The last five years have seen a rise in the importance of intermediary organizations, and in particular PPPs such as IAVI and SAAVI, in the development of new public health technologies like HIV vaccines. IAVI is the largest of the PPPs working on HIV vaccines and in 2004 accounted for 10% of global expenditures, or just under US\$ 70 mn.

- Basic research and pre-clinical research together were estimated to account for 67% of the funds spent in 2004. In comparison, support for clinical trials accounted for 22%, cohort and site development for 10%, and advocacy and policy development for 1%.

**Figure 7.** Breakdown of annual expenditures on HIV vaccine R&D for funding provided by non-commercial sources by type of expenditure.



- Trends in expenditures of funding from non-commercial sources (i.e., public and philanthropic sector funding) indicate an almost doubling of expenditures between 2000 and 2004 – increasing from US\$ 318 mn to US\$ 618 mn.
- The allocation of funds across the five expenditure categories for non-commercial funding has remained fairly constant over the last five years.

## 4. DISCUSSION

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There is increasing scientific confidence that it will be possible to develop a safe and effective preventive HIV vaccine. However, there are many scientific challenges ahead and ensuring that an HIV vaccine is developed in a timely fashion will require increased global collaboration and coordination.<sup>15</sup> It will also require the investment of significantly more resources. Given the many uncertainties in developing new technologies, it is impossible to say exactly how much money will be required to develop an effective HIV vaccine.<sup>16</sup> The targeted investment of significantly more resources, however, should increase the likelihood of success. In a recent paper, the Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise estimated that an accelerated search for a safe and effective HIV vaccine would require about US\$ 1.2 bn a year.<sup>17</sup>

This paper presents information on both annual investment and expenditures for preventive HIV vaccine R&D for 2000 to 2004 and preliminary investment estimates for 2005 generated through a collaborative project involving AMD, AVAC, IAVI, and UNAIDS. This collaboration has generated a great deal of information on funding flows for HIV vaccine and for microbicide R&D<sup>18</sup> that can be used to monitor levels of effort and to identify trends in investment, spending and research focus.

The data were generated primarily through direct contact with funding agencies and intermediary organizations. Each organization was asked to provide information on the funds it disbursed over the last five years and to provide details of the specific projects funded. This approach, whilst time-consuming, provides the necessary detail to ensure data comparability across funders and over time. Nevertheless there are gaps, reflecting both missing and incomplete information, and we hope to improve the comprehensiveness of the data in future years.

Data for the public and philanthropic sectors are more comprehensive than the data for the commercial sector. This reflects both how companies track their own funding and corporate concerns about divulging proprietary information. Future estimates would benefit from a stronger collaboration with industry to find creative solutions to track commercial sector investments and to track the level of funding the commercial sector receives directly from public and philanthropic sources and from intermediary agencies. This sort of information is essential if these figures are to be used for assessing the impact of public policies on private sector investment.

Future work in this area would also benefit from additional effort being directed at collating more detailed information on the breakdown of expenditures and sub-dividing some of the expenditure categories, such as pre-clinical research, that cover a wide range of topics. Collection of this type of information, combined with estimates of funding needs and absorptive capacity, should help identify areas where more resources and effort need to be focused.

In 2004, the public, philanthropic and commercial sectors combined invested approximately US\$ 682 million (range US\$ 668 mn to US\$ 696 mn) in preventive HIV vaccine R&D, or around 0.5% of the total funds invested globally in health R&D.<sup>19</sup> This represents a significant increase in total investment in the last five years – especially from the public sector – but a figure that is still far short of the estimated US\$ 1.2 bn required annually for an accelerated global search.

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<sup>15</sup> Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise. (2005). *The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan*. PLoS Med 2: e25.

<sup>16</sup> The Bill & Melinda Gates Foundation and IAVI are supporting a joint project looking at future funding needs. Results are expected to be available mid-2005.

<sup>17</sup> Coordinating Committee of the Global HIV/AIDS Vaccine Enterprise. (2005). *The Global HIV/AIDS Vaccine Enterprise: Scientific Strategic Plan*. PLoS Med 2: e25.

<sup>18</sup> A companion report on investments and expenditures on microbicide R&D will be released shortly by the HIV Vaccines and Microbicides Resource Tracking Working Group.

<sup>19</sup> This estimate is based on the 2001 figure for global investments in health research and development (US\$ 105.9 bn) generated by the Global Forum and extrapolated to 2004 using their estimated annual growth rate of US\$ 7.0 bn per year for 1998 to 2001. For more information see: Global Forum for Health Research (2004). *Monitoring Financial Flows for Health Research*. Volume 2.

Over the last five years there has been a substantial increase in funding for preventive HIV vaccine R&D. In particular, the level of investment from the non-commercial sector (i.e., the public and philanthropic sectors) nearly doubled between 2000 and 2004, and current commitment and disbursement figures suggest that investment levels in 2005 will be markedly higher than in 2004. This increase in non-commercial funding reflects both increased contributions from existing donors and a growth in the number and geographical distribution of funders as new donors are engaged in supporting this important work. Commercial sector funding, on the other hand, has not kept pace – and appears to have declined between 2002 and 2004.

The US public sector is the largest funder of preventive HIV vaccine R&D and in 2004 committed US\$ 516 mn to HIV vaccine development, or 76% of the total funds invested by the public, philanthropic and commercial sectors combined. The commercial sector, a key player in R&D for most other health products, was estimated to account for only 10% of global HIV vaccine R&D investment.

Total expenditures on preventive HIV vaccines in 2004 were estimated to be US\$ 686 mn or US\$ 4 mn more than investments. Of the funds spent in 2004, most went towards basic and pre-clinical research (67% of the total), with clinical trials and cohort development accounting for 32%, and advocacy and policy development for 1%.

The significant increase in funding for preventive HIV vaccines and for microbicides over the last five years has coincided with a dramatic increase in the overall financial commitment to the HIV/AIDS field in general. While the HIV Vaccines and Microbicides Resource Tracking Working Group has not collected data on overall financial commitments to HIV/AIDS, anecdotal evidence suggests that funders have increased funding for the development of preventive HIV vaccines and microbicides in addition to – not at the expense of – their commitments to expanding access to the prevention and treatment tools already available.

## APPENDIX 1: FUNDING INSTITUTIONS AND DEVELOPERS INCLUDED IN THE HIV VACCINE ESTIMATES

### Public sector – Countries

- Australia
- Brazil
- Canada
- China
- Cuba
- Denmark
- European Commission
- Finland
- France
- Germany
- India
- Ireland
- Italy
- Japan
- The Netherlands
- Norway
- Russia
- South Africa
- Sweden
- Thailand
- United Kingdom
- United States

### Public sector - Multilaterals

- Joint United Nations Programme on HIV/AIDS (UNAIDS)
- World Bank
- World Health Organization

### Philanthropic sector – Foundations, Trusts and NGOs

- American Foundation for AIDS Research
- Bristol Myers Squibb Foundation
- Broadway Cares/Equity Fights AIDS
- Crusaid
- Deutsche AIDS Stiftung
- Ford Foundation
- Bill & Melinda Gates Foundation
- Elizabeth Glaser Pediatric AIDS Foundation
- Gill Foundation
- John & Marcia Goldman Foundation
- Phoebe W. Haas Charitable Trust B
- Henry M. Jackson Foundation
- John M. Lloyd Foundation
- John D. and Catherine T. MacArthur Foundation
- James S. McDonnell Foundation
- Mercury Phoenix Trust
- NY Community Trust
- Overbrook Foundation
- Parthenon Trust
- James B. Pendleton Trust
- Perls Foundation
- Rockefeller Foundation
- San Francisco AIDS Foundation
- Starr Foundation
- Stichting Aids Fonds
- Tides Foundation/John Lee Fund
- Until There's A Cure Foundation
- Vanderbilt Family Foundation
- Wellcome Trust

### Philanthropic sector - Corporate donors

- Becton, Dickinson, and Company
- Eskom International Inc.
- Impala Platinum Holdings Limited
- TransNet Corporation

### Commercial sector - Pharmaceutical companies

- GlaxoSmithKline plc
- Merck & Co. Inc.
- Sanofi Pasteur (formerly Aventis Pasteur)
- Wyeth-Ayerst Lederle Inc.

### Commercial sector - Biotechnology companies

- Advanced BioScience Laboratories
- AlphaVax Human Vaccines Inc.
- AVANT Immunotherapeutics, Inc.
- Bavarian Nordic
- Berna Biotech Ag
- Bioption AB
- Bioqual Inc.
- Chiron Corporation
- Cobra Pharmaceuticals Plc
- Crucell N.V.
- Epimmune Inc.
- EpiVax, Inc.
- FIT Biotech Oyj Plc.
- GenVec, Inc.
- Globelimmune, Inc.
- GeoVax, Inc.
- Impfstoffwerk Dessau Tornau GmbH
- MaxyGen, Inc.
- PAREXEL International Corporation
- Progenics Pharmaceuticals, Inc.
- Targeted Genetics Corporation
- Therion Biologics Corporation
- VaxGen, Inc.
- Vical Inc.

### Intermediary agencies

- Aaron Diamond AIDS Research Center
- African AIDS Vaccine Programme
- Canadian Network for Vaccines and Immunotherapeutics
- Harvard AIDS Institute
- International AIDS Vaccine Initiative
- South African AIDS Vaccine Initiative

**APPENDIX 2: DESCRIPTIONS OF THE FIVE EXPENDITURE CATEGORIES**

CATEGORY	EXAMPLES OF THE TOPICS INCLUDED
<b>BASIC RESEARCH</b>	<ul style="list-style-type: none"> <li>• Defining mechanisms of systemic/mucosal immunity to facilitate the development of preventive HIV vaccines</li> <li>• Seeking correlates of immune protection for HIV-infected/highly-exposed but seronegative individuals</li> <li>• Developing <i>in vitro</i> tools to analyze vaccine responses</li> </ul>
<b>PRE-CLINICAL RESEARCH</b>	<ul style="list-style-type: none"> <li>• Supporting novel vaccine design and testing for safety/ immunogenicity</li> <li>• Fostering collaboration for novel vaccine designs (e.g., producing pilot lots and conducting comparative animal testing)</li> <li>• Optimizing vaccine characteristics for broad international use (e.g., cheap, easy to produce/administer, stable)</li> <li>• Improving or modulating immune responses (e.g., development of improved adjuvants and delivery methods, cytokines, chemokines, and other strategies)</li> <li>• Supporting testing in animal models and looking at <i>in vitro</i> correlates of <i>in vivo</i> protective response and impact on vaccine-induced immunity from: formulation, site of delivery, regimen, nature/timing/phenotype/route of infectious virus challenge, genetic factors, age, viral mutation/variation, mucosal/genital/hormonal co-factors</li> <li>• Developing reagents and standardized methods to assess vaccine-induced immune response in animals and humans (e.g., developing, refining, standardizing and validating assays to distinguish responses due to immunization vs. infection)</li> <li>• Conducting research on safety and regulatory considerations of vaccines in development (e.g., research on vaccines that use tumor/continuous cell lines or vectors that could integrate)</li> </ul>
<b>CLINICAL TRIALS</b>	<ul style="list-style-type: none"> <li>• Supporting Phase I and II trials that study immunogenicity and address strain selection to provide data for decisions on proceeding to Phase III</li> <li>• Developing strategies for retention and follow-up of participants to meet pre-defined endpoints</li> <li>• Supporting large-scale efficacy trials of vaccines meeting Phase III criteria that are ethical and minimize social and economic harm to volunteers</li> <li>• Conducting behavioral research during clinical trials including but not limited to risk assessment and factors affecting adherence to protocol</li> <li>• Coordinating trial research with pre-clinical, therapeutics, and other relevant research, including studies designed to permit validation of preclinical assays</li> </ul>
<b>COHORT &amp; SITE DEVELOPMENT</b>	<ul style="list-style-type: none"> <li>• Identifying potential sites and populations for trials (e.g., assessing seroincidence and viral subtypes as well as genetic and other factors that may affect trial results)</li> <li>• Developing and maintaining personnel (including social and behavioral scientists) and laboratory infrastructure in potential trial sites to conduct trials</li> <li>• Developing regional or central laboratory capacity that could serve a group of trial sites and also provide standardized GLP-quality storage of specimens for comparative analyses during and after trials</li> <li>• Working with host governments, regulatory bodies, local agencies, vaccine manufacturers, multilaterals to plan, prepare and conduct trials</li> <li>• Developing relationships with communities and community organizations in potential sites</li> <li>• Exploring innovative trial designs to minimize time and costs without compromising participant safety (e.g., using serodiscordant couples or secondary endpoints)</li> </ul>
<b>ADVOCACY &amp; POLICY DEVELOPMENT</b>	<ul style="list-style-type: none"> <li>• Developing and supporting public education efforts</li> <li>• Developing and supporting policy research and development directed at accelerating the development and rapid use of HIV vaccines</li> <li>• Exploring alternative strategies for supporting R&amp;D efforts and the purchase of HIV vaccines</li> <li>• Supporting ongoing national and international advocacy efforts</li> <li>• Supporting analysis and modeling to anticipate resource needs, potential demand for product, costs of product and distribution, and epidemiological impact</li> </ul>

## HIV Vaccines and Microbicides Resource Tracking Working Group

AIDS Vaccine Advocacy Coalition (AVAC) [www.avac.org](http://www.avac.org)  
Alliance for Microbicide Development (AMD) [www.microbicide.org](http://www.microbicide.org)  
International AIDS Vaccine Initiative (IAVI) [www.iavi.org](http://www.iavi.org)  
Joint United Nations Programme on HIV/AIDS (UNAIDS) [www.unaids.org](http://www.unaids.org)

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For more information on HIV vaccines, please contact the AIDS Vaccine Advocacy Coalition ([avac@avac.org](mailto:avac@avac.org)) or the International AIDS Vaccine Initiative ([publicpolicy@iavi.org](mailto:publicpolicy@iavi.org)).

For more information on microbicides, please contact the Alliance for Microbicide Development ([info@microbicide.org](mailto:info@microbicide.org)).

For more information on UNAIDS resource tracking activities, please contact the UNAIDS Resource Tracking Unit ([rtpdata@unaids.org](mailto:rtpdata@unaids.org)).

