Investing in AIDS Vaccines: Estimated Resources Required to Accelerate R&D

The International AIDS Vaccine Initiative (IAVI) has called on the G8 to significantly increase spending on the global effort to develop and deliver a preventive vaccine against AIDS suitable for use in developing countries. This paper sets out our assessment of the total level of spending needed for AIDS vaccine research and development (R&D) in the coming years and the gap between current and projected spending, based upon IAVI policy research findings. It should be read alongside the paper *Tracking Funding for Preventive HIV Vaccine Research and Development: Estimates of Annual Investments and Expenditures 2000 to 2005*, prepared by a consortium of organizations including the Alliance for Microbicide Development, the AIDS Vaccine Advocacy Coalition, IAVI, and UNAIDS (June 2005).

The figures presented here should be viewed as our current best estimates. We will continue to refine them as new evidence becomes available and through discussion with relevant experts and representatives of donor organizations and industry.

The potential for accelerating vaccine development

There are three main ways to accelerate the timeline and improve the probability for discovery and development of an AIDS vaccine. The first is to enhance the quality of those candidates and their chances of successfully progressing through the pipeline, through improvements in applied research and in techniques supporting vaccine testing, such as laboratory standards. The second is to increase the number of high-quality, viable candidate vaccines entering and moving through the product development pipeline, from Phase I safety studies to Phase III efficacy trials and licensure. Third is to reduce the time it takes to move a candidate vaccine through a phase, for example by recruiting volunteers faster and obtaining regulatory approvals in a more expeditious way.

Raising these “transition probabilities”, increasing the number of viable candidate AIDS vaccines entering the pipeline, and lowering the “time in phase” would have a substantial positive impact in accelerating the emergence of a successful vaccine. Doing all three of these actions simultaneously could move forward the advent of a vaccine by several years.

We estimate below that to achieve this expansion of viable vaccine candidate throughput, raise the overall quality of the pipeline, and shorten time in phase, R&D spending needs to rise from the current (2004) level of around US$690 million a year[1] to approximately US$1.15 to US$1.2 billion a year. Recent new commitments from two sources have helped to close the gap from around US$500 million to slightly less than US$400 million (see Table on page 3). Still, this is a significant shortfall that needs to be met from additional investments. We break down the additional funding required into components for basic and applied research, product development, and national infrastructure and capacity building in developing countries—although we also understand there is some overlap between these categories, particularly the first two.

[1] Alliance for Microbicide Development, AIDS Vaccine Advocacy Coalition, International AIDS Vaccine Initiative, and Joint United Nations Programme on HIV/AIDS. *Tracking Funding for Preventive HIV Vaccine Research and Development: Estimates of Annual Investments and Expenditures 2000 to 2005.* June 2005.

These figures are broadly consistent with the earlier estimates from IAVI and those in the "scientific blueprint" of the AIDS Vaccine Enterprise, which proposed a doubling of current spending.

The impact of accelerating the timeline for a successful AIDS vaccine, in terms of infections averted, lives saved, and economic benefits for poor countries in Africa, Asia, and Latin America, would be immense. It is expected that around 13-19 million new HIV infections will occur over a 3-year period at current rates of transmission,[2] with more pessimistic scenarios suggesting this figure could rise as high as 30 million.[3] Even if an AIDS vaccine only cuts transmission by a quarter or a third, its health and economic effects would be huge.

Resource needs analysis

The baseline: vaccine spending today

IAVI studies of global AIDS vaccine R&D expenditure suggest that in 2004, about US$685 million was spent in the search for an AIDS vaccine (see Table on page 3). Of this amount, about US$150 million (22%) was devoted to product development, and another US$75 million (11%) went to other activities including building trials capacity in developing countries.

The balance of US$460 million was allocated to basic and applied research, but only a small share of this went to the kind of goal-directed, collaborative work on the key unanswered scientific questions that is now being proposed. While it is vitally important for national health research authorities to continue to support a wide range of investigator-initiated basic research that can lead to new scientific knowledge about HIV and novel ideas that can be translated into better vaccine design, this basic research must also be complemented with more efforts and increased resources to address key applied research questions (e.g., how to elicit broadly neutralizing antibody responses) and to prioritize, develop and test promising vaccines efficiently in field trials.

Enhancing and feeding the pipeline: goal-directed research

In order to generate suitable candidate vaccines to enter the product development pipeline and pass successfully through the various trial phases, there needs to be more investment in basic and pre-clinical stages of research. As mentioned earlier, while a part of this spending should continue to go to basic investigator-initiated research sponsored by national health bodies such as NIH, MRC, and ANRS, a significant share of new investment should be channelled to large collaborative goal-directed research. This is the approach taken by IAVI through its "neutralizing antibody consortium" and now being pursued by the AIDS Vaccine Enterprise.

To build the scientific knowledge that will generate a more robust and higher quality stream of new vaccine products, an increase in basic and applied research funding of around US$265-290 million a year is needed, as compared to the spending that took place in 2004. Because US$90 million a year of new investment (US$450 million over five years) in this area has recently been announced by the Bill and Melinda Gates Foundation and the NIH, this leaves a balance of US$175-200 million in additional funding that is needed for research.

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[2] Estimated at 4.3-6.4 million during 2004. UNAIDS. *AIDS Epidemic Update.* December 2004.

[3] Potentially 10 million a year. Eberstadt, N. *Foreign Affairs.* November/December 2002.

Expanding the pipeline: product development

Doubling the number of viable and promising candidate vaccines in product development would require an increase of about US$175-200 million a year.[4] This would enable product development organizations including large vaccine companies and smaller biotechs, national research bodies, and public-private partnerships like IAVI to finance the throughput of a pipeline with about 10-20 vaccine candidates introduced each year for phase I trials. Recent new investments by the Bill and Melinda Gates Foundation to foster development of T-cell vaccines averaging US$30 million a year for five years help to close the remaining gap to US$145-170 million.

Supporting the pipeline: capacity-building

An expanded product development pipeline will put pressure on existing scientific, managerial and clinical trials capacity in developing countries, where many of the smaller phase I and II trials and most of the larger phase III trials will need to take place. We estimate that in the medium term another US$ 25 million a year could be invested in capacity-building in order to minimise the risk of future product development bottlenecks, while enhancing the participation of developing country scientists and communities in vaccine R&D. This is an area where IAVI and others, such as the US HIV Vaccine Trials Network (HVTN), the European and Developing Countries Clinical Trial Partnership (EDCTP), and the South African AIDS Vaccine Initiative (SAAVI) are actively working.

Current global expenditures on AIDS vaccine R&D and estimated resource gap

	2004 global expenditures (US$ millions)[5]	Required total annual funding 2006- (US$ m)	Total annual gap (US$ millions)	Announced new commitments (US$ m/year)	Remaining gap (US$ m/year)
Basic and goal-directed research	460	725-750	265-290	90[6,7]	175-200
Product development	151	325-350	175-200	30[8]	145-170
Capacity, infrastructure and policy	75	100	25	0	25
Total	**686**	**1150-1200**	**464-514**	**120**	**344-394**

[4] There is an issue around whether current reported figures on AIDS vaccine product development spending reflect the full costs of this phase of vaccine R&D, as the financial cost accounting systems of various research bodies and private companies may not capture accurately the true economic costs involved.

[5] Alliance for Microbicide Development, AIDS Vaccine Advocacy Coalition, International AIDS Vaccine Initiative, and Joint United Nations Programme on HIV/AIDS. *Tracking Funding for Preventive HIV Vaccine Research and Development: Estimates of Annual Investments and Expenditures 2000 to 2005.* June 2005. Note that the figures shown here are derived from the classification of expenditure used in the paper into basic research, pre-clinical research, clinical trials, cohort development and clinical trial infrastructure, and vaccine education, advocacy and policy development.

[6] US National Institutes of Health RFA for Center for HIV/AIDS Vaccine Immunology: US$14.9 m in FY2005 and up to US$49 m/year subsequently over a total of up to seven years. http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-04-051.html.

[7] Bill and Melinda Gates Foundation RFPs for Vaccine Discovery (Antibodies) Consortia/Centers and Vaccine Immune Monitoring Consortia/Centers totaling US$210 million over five years. http://www.gatesfoundation.org/GlobalHealth/HIVAIDSTB/HIVAIDS/Vaccines.htm

[8] Bill and Melinda Gates Foundation RFPs for Vaccine Discovery (T-Cells) Consortia/Centers totaling US$150 million over five years. http://www.gatesfoundation.org/GlobalHealth/HIVAIDSTB/HIVAIDS/Vaccines.htm

Conclusion

There is a funding gap for AIDS vaccine R&D of about US$345-395 million a year, over and above current and recently announced spending. Such a level of investment might bring forward the time to emergence of a successful vaccine by a significant number of years, in part by expanding and diversifying the pipeline, and in part by enhancing the selection and assessment of vaccine candidates and thus the chances of being successful. The most immediate need is for increased investment in targeted areas of applied research, strengthening the product development pipeline, and expanding capacity in developing countries. All of this additional spending must be complemented by a continuation of tried and tested mechanisms to support investigator-initiative basic research.

IAVI urges the G8 nations to commit collectively to increase the level of R&D expenditure, pledge individually to higher financial contributions, and work with other non-G8 donors to close this gap. IAVI recognizes that a doubling of current AIDS vaccine spending will have to be phased in over several years but calls on the G8 to start the process at this year's Gleneagles Summit and move progressively toward this target over time. The current magnitude of the AIDS pandemic and the potential of an effective vaccine to end it make this an historic opportunity for G8 leadership.