Policy Brief

Incentives for Private Sector Development of an AIDS Vaccine

It has been over 20 years since HIV was identified as the cause of AIDS, yet the epidemic remains unchecked. Over 60 million people have been infected with HIV, with 14,000 people infected every day, making this the greatest health crisis of our time.

Treatment options have multiplied and are helping to slow the progression of the disease for some. But these must be combined with a comprehensive prevention program including a safe and effective HIV vaccine. Vaccines have been pivotal in controlling many diseases, and an HIV vaccine is scientifically possible.

A global commitment is needed to overcome both the scientific and the economic challenges that remain. This paper provides an overview of proposed solutions to the economic hurdles associated with research and development (R&D), primarily the lack of incentives for private industry.

I. Why does an incentives problem exist?

Private investment in R&D for an AIDS vaccine remains seriously inadequate – IAVI estimates that less than 20% of the $646 million spent on vaccine R&D in 2002 came from private sources, and this amount is likely to have declined even further in the past two years as the Phase III trial in Thailand of Vaxgen's candidate has wound down.[1]

In general, private spending on an AIDS vaccine is low because of the high risks and uncertain returns to investments in R&D for such a vaccine, as compared to other pharmaceutical products. There are several factors behind the high risks and uncertain returns, as perceived by both the large pharmaceutical companies and the smaller biotech firms today:

- The science of an HIV vaccine is complicated, with only modest progress so far on overcoming the scientific barriers to producing a vaccine that will consistently induce a strong immune response in humans.
- The research and product development process is very expensive, requiring more than a decade and hundreds of millions of dollars to bring a vaccine to market. Many small companies who are willing to take more risks on discovery and early testing often lack the capital and expertise.
- The public health and social benefits of an AIDS vaccine would be enormous. However, the financial benefits to a private company selling a vaccine globally are far less certain, given that more than 90% of HIV infections occur in developing countries where the ability to pay for a vaccine is limited. This lower or unpredictable financial return serves as a disincentive to invest in AIDS vaccine R&D.

What can be done to stimulate the private sector to discover, develop, and manufacture an AIDS vaccine, so that scientific and financial risks are reduced and the expected financial returns can be brought more into line with the very large health and social benefits of a vaccine that prevents HIV infection, illness, and death?

Topics covered inside **Page**

[1] IAVI, "Global Investment and Expenditures on Preventive HIV Vaccines: Methods and Results for 2002," July 2004.

Policy Brief #2/ September 2004

IAVI and its partners are currently exploring a range of mechanisms that could be used over the course of the product development cycle to address the key obstacles to private investment. Many of these mechanisms have either been tested or proposed to governments, industry, and donors.

"Push" mechanisms aim to reduce input costs and promote basic research. **"Pull"** mechanisms seek to reward output by improving (or creating) positive market conditions.

II. Push mechanisms - reducing the cost of R&D

Push mechanisms reduce the cost of R&D, and to a lesser degree, manufacturing of a vaccine. They focus on giving industry added incentives to invest in R&D inputs, generally by subsidizing the cost of these inputs. If these subsidies are targeted to high quality scientific research and product development, they can prove to be highly effective. It is inherently difficult for governments to pick "winners" in R&D, however, so there is always the risk of financial outlays without a successful outcome in terms of product development.

a. Funding Basic Scientific Research

Basic scientific research has an enormous positive impact as a global public good – everyone benefits from the positive results of the research, even though only some pay for it. However, there are almost no expected market returns to such research, so the private sector does not have strong incentives and public sector investment is critical.

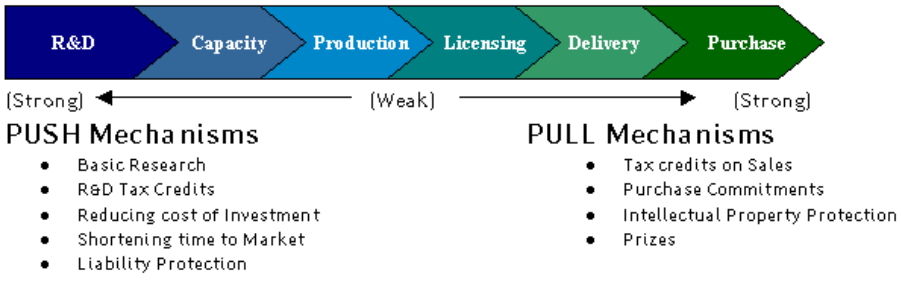
Basic research grants are allocated by national research authorities such as the National Institutes for Health in the US, the Medical Research Council in the UK, and the National Scientific Research Council in France.

Research grants are focused on inputs, and are therefore considered the bluntest and least directed of all conventional incentives for new product development, yet they are still a fundamental building block in the search for new vaccines and pharmaceuticals. IAVI estimates that about 21% of the nearly $650 million currently spent on AIDS vaccines is public funding going to basic research, with another 43% for pre-clinical activities. Few of these resources end up being awarded to private companies – the majority goes to academic laboratories and intramural research activities carried out by national research authorities.

b. R&D Tax Credits

R&D tax credits reduce the cost of early research by allowing companies to deduct R&D expenditures from their tax liability. Tax credits also enable policymakers to be very specific about the type of R&D that can be claimed, such as in a US legislative proposal that offers a 100% R&D credit if a large pharmaceutical company partners with smaller biotechnology firms.[2]

Tax credits are only valuable to a company if it has some taxable earnings, however. This is the case for the larger biopharmaceutical companies, but so far a number of their representatives have indicated that tax benefits alone would not be a large enough inducement to them to shift their investments toward challenging R&D areas such as AIDS vaccines. The legislation approved recently in the UK to award tax



[2] *The Vaccines for the New Millennium Act of 2001*, introduced by Senator John Kerry (S. 895) and Rep. Nancy Pelosi (H.R. 1504).

benefits for research on new drugs and vaccines for AIDS, tuberculosis, and malaria needs to be evaluated to see if it has had an impact on the pace of R&D activity by the private sector.

Since many of the small "start up" biotech firms do not have sufficient earnings to be liable for current taxation, other inducements such as carry-forward tax credit provisions (which can be used in future years) or refunds in lieu of credits would be more appropriate for these smaller companies. Experience in the U.S. suggests that there were significant increases in R&D spending on "orphan" drugs (drugs for conditions affecting only small numbers of Americans and thus not commercially attractive) when carry-forward tax credits were instituted.[3]

c. Reducing the cost of capital to investors

A related way to induce expanded private investment in smaller companies involves provisions that lower tax liability to the investors. Tax incentives for potential investors have been used in other fields, but have not yet been tried for vaccine R&D – though they are contained in current draft legislation in the US aimed at stimulating rapid development of vaccines and drugs that can serve as bioterrorism countermeasures.

Limited Partnerships

Limited partnerships would allow companies to pass tax benefits – deductions on certain expenditures and losses – to the investors. This could be useful to small companies by offering an extra incentive to potential investors including venture capitalists, on top of the hoped-for return on sales of the future AIDS vaccine.

Special Class of Stock - Zero Capital Gains

A special class of stock could be created for AIDS vaccine research, with zero capital gains tax status. If an investor holds the stock for a certain period of time – say, three years – they pay no taxes on the capital gains from the sale of such stock. This too reduces the financial risk to investors, and could spur investment in vaccine R&D.[4]

d. Shortening time to market through expediting regulatory steps

In both the US and Europe, there are procedures for speeding up licensing by the regulatory authorities. In the US, the Food and Drug Administration has "fast track" and "priority review" procedures that can save vaccine developers money otherwise spent on processing regulatory dossiers, and thus boost returns by getting the product into the market faster. Priority review, for example, can cut approval time in the US by half, from 10-12 months, down to a maximum of six months.[5] These kinds of measures are most valuable for small companies that are less experienced with FDA processes and more influenced by relatively modest financial benefits associated with fast track and priority review. The European regulatory agency, the European Medicines Agency (EMEA), adopted a related measure, offering to provide expedited review and approval for vaccines and drugs that are likely to have their largest impact indeveloping countries. The expectation is that many countries in Africa and Asia will rapidly extend licenses for the same products once the EMEA has given its green light.

e. Reducing risks associated with liability

Concerns about legal liability can also have a negative impact on innovation. If companies fear they will be sued for alleged negative side effects of vaccines even after they are approved by the US and European regulatory authorities, this can act as a significant disincentive. Special liability protection therefore might have a positive effect on R&D spending decisions, by reducing the risk to companies of additional liability-related expenses.

One example of such protection is the National Vaccine Injury Compensation Program (VICP) approved in the US in 1988. The VICP is a no-fault compensation program that covers vaccines recommended by the US Centers for Disease Control for routine administration. The program has helped to reduce significantly the number of lawsuits filed against manufacturers, thus reducing liability risks, stabilizing costs, and promoting research spending.[6]

[3] Meyers, Abbey. Orphan Drug Development Conference: "Understanding the History of the Orphan Drug Act." September 2000. http://www.rarediseases.org/news/speeches/orp_drug

[4] Ibid.

[5] U.S. Food and Drug Administration, "Fast Track, Priority Review and Accelerated Approval." http://www.accessdata.fda.gov/scripts/cder/onctools/Accel.cfm

[6] U.S. Department of Health and Human Services, HRSA. "Background Information on VICP." http://www.hrsa.gov/osp/vicp/abdvic.htm

III. Pull mechanisms - Ensuring the market and rewarding success

"Nothing on the push side makes a difference if you don't have a market…" -- anonymous interviewee from industry.[7]

There are a variety of mechanisms that try to create a stronger market, spurring private sector investment in R&D by reducing uncertainties around the potential sales and profits from a new health technology like an AIDS vaccine. So-called "pull" mechanisms are those that reward outputs or successes. In this sense, they are well targeted, as public (or donor) funds are only awarded to the company once it produces a vaccine that meets certain pre-specified (and ideally, independently verified) criteria.

a. Tax credits for vaccine sales

One as yet untested idea involves tax credits on sales of an approved vaccine. The vaccine manufacturer would be relieved of having to pay sales or profit taxes on the sales of qualified vaccines to qualified organizations. This could substantially raise the financial returns on a successful vaccine.

b. Advance purchase commitments

Governments (or other sponsors such as foundations or international finance institutions) could promise to buy a predetermined quantity of vaccines at an agreed price, once the vaccine is developed to specified criteria. This could make the size of the market on an AIDS vaccine for developing countries as large, or larger, than the typical sales on the most important drugs and vaccines currently in the portfolio of the major biopharmaceutical companies – around $3-5 billion in total sales.

Recent work on the advance purchase or "advance contracting" approach[8] argues that such a mechanism is feasible using existing contract law and practice from other fields; that it could be made financially attractive to a range of large and small firms, substantially influencing their decisions to invest in R&D for vaccines to address the diseases of the developing worlds; and that governments, philanthropists such as Gates Foundation, and organizations such as the World Bank could effectively sponsor such a scheme under their existing budgeting procedures and financial regulations. The Center for Global Development's "Pull Mechanism's Working Group Final Report" suggests that advance contracting could be instrumental in bringing to market new vaccines that are at an advanced stage of product development, and could also help to accelerate development of vaccines that are earlier in the R&D pipeline (such as those for AIDS, malaria, and tuberculosis).

One of the key challenges surrounding advance contracting is to establish the credibility of the funding "sponsor" or sponsors, so that the contract truly binds them to pay a company once the vaccine is produced. Some companies may fear that donors, developing country governments, and activists could try to pressure a successful company to sell its vaccine at a lower price than agreed in the contract, on "humanitarian" grounds. From the sponsors' perspective, another issue is trying to figure out many years in advance what price to offer and what quantity of vaccines to commit to purchase, when costs and demand are hard to gauge.[9] The Center for Global Development's report maintains that these problems can be overcome. Nevertheless, it is unclear whether even a large advance contract for an AIDS vaccine would provide sufficient inducement to industry – big and small – to speed up its search for a vaccine.

Additional modeling of the advance contract idea as applied to an AIDS vaccine, and further dialogue with industry on the potential inducement of such a contract, need to be undertaken to test this idea further. The political attractiveness of such an advance financial commitment from donors – a multi-billion dollar pot of money for a company capable of producing an efficacious AIDS vaccine, in effect an "AIDS vaccine fund" – is potentially very powerful.

c. Tiered/Differential Pricing

In theory, tiered or differential pricing holds great promise for efficiency and equity while still providing sufficient returns to industry to spur R&D. A mechanism that facilitates charging different countries different prices for products based on their ability to pay increases overall social

[7] Collins, P. 3.
[8] "Pull Mechanisms Working Group Final Report," Center for Global Development, May 10, 2004.
[9] Kremer, PPT and England, P. 2.

welfare. However, this mechanism has several critical requirements.

- There must be demand for the particular product in a high-income market. Without the high-income markets to pay higher prices, prices will be prohibitively high in low-income markets, and/or R&D costs will not be recouped.
- The market segmentation must be firm and non-porous. Reimportation of cheaper drugs from a low-income market to a high-income market will erode the mechanism.
- Developed countries must be willing to accept higher prices. This willingness to pay is difficult to guarantee, however. Tiered pricing can be unpopular with consumers in high-income countries, making it politically challenging. Industry, in turn, may fear that high-income countries will use the lower prices to extract price concessions in high-income markets.

Given the multiple challenges faced by a formal system of tiered pricing, some potential mechanisms may improve the feasibility, including strict prohibition of parallel imports or employing confidential discounts and rebates.

d. Patents and market exclusivity – intellectual property incentives

Extending patents (e.g., in the US, adding to the typical 20 year period of intellectual property protection) or granting market exclusivity (in the US, a shorter period of protection given by the Food and Drug Administration) create a large and relatively predictable revenue stream for vaccine manufacturers. In this regard, they are seen as powerful pull incentives for industry. Since these types of mechanisms do not require direct funding guarantees or actual financial outlays by governments, they avoid the credibility issues surrounding advance purchase commitments. Despite their simplicity and potential potency as incentives for R&D on AIDS vaccines, patents and exclusivity have not been politically popular in the US and Europe, as they tend to be opposed by consumer groups (who often try to drive down prices on drugs) and by those who believe that pharmaceutical industry earns excessive profits in general.

Standard patent extension and market exclusivity alone may have limited value for an AIDS vaccine, since manufacturers may find it difficult to sell such a vaccine in developing country markets at a price that is above their average cost of production (this is where an advance purchase commitment could make a difference). It could be useful in developed country markets, however, where individuals, insurance schemes, and governments will be able to pay a higher price for vaccination.

An alternative incentive on intellectual property would be to allow a company that successfully manufactures an AIDS vaccine to obtain a patent extension on another drug or vaccine in its portfolio, such as a cholesterol drug or an anti-depressant. This kind of "wild card" patent transfer could amount to a very substantial financial reward for the company – some company executives have mentioned it privately as a potentially powerful inducement to invest in AIDS vaccine R&D. For smaller biotech companies that do not have other profitable products, such patent transfer would not be meaningful. To spur innovation among these smaller biotechs, legislation could allow the firm successful in producing an AIDS vaccine to sell its patent extension to another company that has profitable products.[10]

To make patent extensions and exclusivity more politically palatable, some advocates have proposed that profit caps could be imposed – above certain levels of profit, the exclusivity would be rescinded; or that industry could be required to invest a percentage of their earnings back into R&D for other drugs and vaccines for AIDS, malaria, etc.

e. Prizes

The idea of offering a financial "prize" or reward to a company that discovers or manufactures an AIDS vaccine seems appealing. Such a prize would reward results, and could therefore be a straightforward and efficient mechanism to spur a specific vaccine innovation. There are some examples of successful prizes in other areas, such as energy-conserving home appliances,[11] but various studies suggest that a prize for an HIV vaccine and other medical technology breakthroughs is unlikely to be an effective stimulus to increased R&D.[12]

[10] Collins, Chris. Policy Monograph, April 2001. "The Policy of AIDS Vaccines: Exploring Legislative Options for Advancing AIDS Vaccine Research and Delivery. AIDS Policy Research Center & Center for AIDS Prevention Studies, AIDS Research Institute, University of California San Francisco. P. 34.

[11] Kremer, and Glennerster (2000).

IV. Conclusion

A combination of carefully designed, adequately funded, and politically backed measures – both pushing and pulling – could have an significant effect on the level of R&D spending for AIDS vaccines, on the quality and effectiveness of this research and product development effort, and ultimately on the speed with which an efficacious vaccine for all regions is produced and made accessible to those who need it.

To be effective, the mix of push and pull measures should stimulate not only the large biopharmaceutical companies but also the smaller biotechnology companies that have been an important source of technical innovation in recent years. It is vital both to evaluate these proposals further and to discuss them with industry and governments and model their detailed working and effects.

IAVI anticipates that a comprehensive package of push and pull inducements would cost governments and taxpayers billions of dollars in tax relief and guaranteed purchase funding. But the economic and social "returns" on an AIDS vaccine are so large that they dwarf the costs involved – UNAIDS estimates that $20 billion will be needed for prevention and care in low and middle-income countries by 2007.[13] Bold and imaginative steps need to be taken by world leaders today to create strong incentives for industry to invest in finding a vaccine that prevents the spread of AIDS.

[12] Batson, Amie "World Bank Task Force on Accelerating the Development of an HIV/AIDS Vaccine for Developing Countries." HIV Vaccine Industry Study October-December 1998. 20 March 2000.

[13] UNAIDS 2004 Report on the Global AIDS Epidemic.

About IAVI: IAVI (www.iavi.org) is a global not-for-profit organization working to accelerate the development of a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 23 countries, IAVI and its network of collaborators research and develop vaccine candidates. IAVI also works to assure that a vaccine will be accessible to everyone who needs it. IAVI's major financial supporters include the Bill & Melinda Gates Foundation; the Rockefeller, Sloan and Starr foundations; the World Bank; BD (Becton, Dickinson & Co.); the European Union; and the governments of Canada, Denmark, Ireland, the Netherlands, Norway, Sweden, the United Kingdom and the United States.

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The Policy Brief series outlines key public policy issues in the research, development and eventual distribution of HIV vaccines.
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