iavi Insights

POLICY BRIEF # 19
APRIL 2009

It is vital that we make every effort to support a policy environment that incubates the best ideas and encourages the best researchers to eventually defeat HIV and AIDS.

Spurring Innovation in AIDS Vaccine R&D: What Will It Take?

The comprehensive response mounted against HIV and AIDS needs to be sustained, and in many areas increased, to ensure continued scientific progress for all types of interventions and innovations, particularly in AIDS vaccines. Broad policy challenges currently facing the field include: How can the private sector, which has enormous research and development (R&D) capacity yet is only minimally involved in HIV prevention technologies, be better engaged? And how can funding mechanisms and organizational structures be more effectively designed to ensure innovation?

This policy brief is based on a paper presented to the collaborative aids2031 project's Science/Technology Working Group to explore strategies to spur innovation in HIV and AIDS prevention and treatment technologies. The brief provides an overview of existing and suggested strategies for promoting and supporting innovation in research for HIV and AIDS.

Push Mechanisms: Subsidizing Research

R&D incentives generally fall into two categories: push and pull mechanisms. Push mechanisms involve subsidies such as grants, tax credits and direct investment in product development programs. Such upfront funding mechanisms are relatively easy to implement and have proven to be politically feasible as well as beneficial in generating research discoveries.

However, push mechanisms also have a number of drawbacks. In general, push mechanisms rely on decision makers to pick winners, which may inadvertently elevate conventional wisdom over innovation. Push funding is also usually short term, often inflexible and typically targets researchers within geographic boundaries. These limitations belie the global and long-term nature of many scientific endeavors and the need for researchers to be able to rapidly reallocate resources in response to scientific developments.

Many funders have developed specific mechanisms to spur innovation. But crafting review processes that actually support this goal continues to be a challenge. Most grants, especially from public-sector agencies, have strict accountability procedures. This often limits grants to proven or evidence-based proposals, which may unintentionally squelch innovation. In response,

iavi International AIDS Vaccine Initiative

novel strategies have been adopted to balance supporting established researchers and promoting thinking that falls outside of the mainstream.

The US National Institutes of Health (NIH) has developed new programs to support innovation such as grants specifically for novel ideas, new methodologies and interdisciplinary approaches. The NIH is also supporting more first-time grantees over a longer period. For example, the Pioneer Award Program, launched in 2003 to support transformative approaches in biomedical and behavioral research, granted 16 awards in 2008 of US$ 2.5 million over five years per grantee.

The Grand Challenges Explorations program, launched in 2007 by the Bill and Melinda Gates Foundation, was established to support untested ideas and new researchers in global health. The first call for proposals drew 4,000 applications from more than 100 countries, with 12% from low- and middle-income countries and roughly 20% related to HIV and AIDS. The program awarded 104 grants in November 2008.

Similiarly, the International AIDS Vaccine Initiative (IAVI) created the IAVI Innovation Fund in 2007 to foster unconventional ideas from outside mainstream HIV and AIDS research. IAVI's fund uses an expedited review process to identify technologies for rapid advancement to clinical testing. At the end of 2008, the fund had supported six proposals totaling US$ 1.9 million.

R&D tax credits have also been proposed to leverage private-sector research capacity for neglected diseases. Successful tax credit programs include the US Orphan Drug Act of 1983, which includes a 50% tax credit on clinical trials for products designed for illnesses that affect fewer than 200,000 patients in the United States, as well as guaranteed seven-year market exclusivity. The Orphan Drug Act increased the number of products for rare diseases from 10 in the decade prior to the legislation to more than 200 in the first two decades of the act. However, general R&D tax credits may not be sufficient to induce research on neglected diseases by companies that usually focus on products aimed at more lucrative markets in higher-income countries. And small biotechs, with the most to contribute to early-stage R&D, may not produce sufficient taxable revenue to benefit from such tax credits.

Pull Mechanisms: Rewarding Success

While push mechanisms fund research inputs, pull mechanisms such as enhancements to intellectual property, advance purchase commitments and prizes aim to reward outputs. A number of challenges with this approach persist, including identifying in advance the specific outcomes desired, ensuring the credibility of rewards being paid and advance commitments being honored, and overcoming the lack of resources by potential innovators to carry their ideas forward.

Prizes have been used throughout history as incentives to solve scientific problems such as determining longitude at sea or encouraging private space flight (Table 1). More recent efforts have focused on public health

Funding for Innovation: What Works

IAVI examined a number of innovation-funding initiatives in diverse health fields and identified similarities in approach, philosophy and process:

- *First, these mechanisms sought to respond to the state of the science in each particular field such as the lack of major therapeutic breakthroughs or the insularity of a specific research community.*
- *Second, the initiatives targeted a particular funding niche, typically focusing on early-stage or translational research, to move candidates quickly through the pipeline.*
- *Third, the mechanisms relied on relatively rapid and fairly standardized evaluation processes, although there were some distinctive features such as matching domestic proposals with international reviewers (and vice versa) to avoid political or competitive pressures and including patients active in disease-specific advocacy organizations to evaluate applications.*

These initiatives have led to an impressive number of peer-reviewed publications, subsequent funding and licensing agreements. Two key lessons were learned:

- *Focus on novelty, but don't try to define it. Don't require proof of principle or preliminary data, and don't try to define or limit research priority areas a priori.*
- *Be careful how you review. Decisions stemming from independent assessments are more likely than committees to fund the most innovative ideas.*

challenges such as new diagnostic tools for tuberculosis. History shows that prizes often generate R&D investments far exceeding the actual prize, suggesting that prizes may act as an intellectual challenge as much as a financial enticement. Effective prize competitions must define a challenging yet achievable goal, outline clear measures of success, include a credible commitment to pay out and have an impartial process for judging and evaluating success.

However, critics have cited the all-or-nothing competitive nature of prizes as a potential weakness. In response, prize proponents have suggested a number of options such as prizes that reward intermediate achievements and a percentage of the prize for work that may have contributed to solving the challenge.

A recent example of a prize competition meant to spur innovation in public health is InnoCentive, which is based on an approach used by the open-source software community. InnoCentive charges individual companies a fee to post problems for researchers to solve on its website with specifications for an acceptable solution, a timeline and the prize amount.

Another pull mechanism involves the use of contracts for the purchase of a particular product once it is developed. This approach addresses a widespread perception that buyers are unwilling or unable to purchase products intended primarily for low- and middle-income countries. A recent example is the US$ 1.5 billion advance market commitment (AMC) launched in 2007 by the Bill and Melinda Gates Foundation and several donor governments to purchase a minimum amount of pneumococcal vaccines at a pre-set price. It remains to be seen whether the mechanism can promote early-stage innovation and investments, but advocates are hopeful that AMCs can be applied to other diseases such as HIV and AIDS. A primary challenge of contracts such as AMCs is ensuring that the contract is large enough to incentivize companies to make the enormous upfront investment. Another key issue is ensuring the credibility of the contract given the downstream and long-term nature of AMCs, especially in the case of public-sector funding institutions that depend on year-to-year appropriations.

Regulatory approaches are another strategy that has been proposed to encourage the development of drugs and vaccines for neglected diseases. In 2007, the US Congress established a voucher program that allows the sponsor of a new drug or vaccine for tropical diseases to obtain prioritized regulatory review that can be applied to other products or transferred or sold to another entity. This would allow a new product to enter the market up to a year sooner; estimates value an expedited review at more than US$ 300 million. However, it is difficult to accurately valuate a prioritized regulatory review because it is hard to know whether a drug will be a blockbuster. And this mechanism's value in increasing R&D for neglected diseases has yet to be seen in practice. Also, a number of critical issues remain unresolved, including timing, matching buyers and sellers of vouchers, and the challenge of securing the upfront resources required to undertake innovative scientific work prior to being awarded a voucher for success.

Table 1

Prizes for Specific Solutions

DATE PRIZE ESTABLISHED	NATURE OF CHALLENGE (SPONSOR)	PRIZE OFFERED / 2008 US$ VALUE	SOLUTION NOTES
1714	Determine longitude at sea (British government)	£20,000 /$3.65 million	Multiple solvers; over £100,000 awarded
1919	Solo flight from New York to Paris (Raymond Orteig, hotel magnate)	$25,000 /$316,000	Total investment by competitors about 16 times the prize amount
1990	Develop (and sell) super-efficient refrigerator (consortium of 24 utility companies)	$30 million /$41 million	14 entrants; some success, but winner failed to meet sales requirement to claim full prize
1994	Develop accurate diagnostic test for sexually transmitted infections (Rockefeller Foundation)	$ 1 million/$ 1.3 million	Unsolved
1995	Private space flight (X prize, funded by Amir and Anousheh Ansari, aerospace entrepreneurs)	$10 million /$12 million	Total investment of competitors $100 million
2006	Improved movie recommendations (Netflix)	$1 million /$1.1 million	Partially Solved

Beyond Push and Pull: Other Innovation Mechanisms

The broad range of strategies to spur innovation noted above underscores the considerable thought devoted to developing ways to organize and incentivize research.

In recent years, a number of consortia and centers of excellence have been established to bring together different disciplines to solve global health problems. Examples of innovative organizational models include the NIH's Research Teams for the Future initiative and the Neutralizing Antibody Consortium, convened by IAVI to focus on a specific scientific hurdle in AIDS vaccine development. These efforts link researchers to central facilities and enable members to share ideas, data and results. Models such as these are relatively new and their progress should be monitored closely.

Given the long-term nature of AIDS vaccine research, ongoing efforts to involve new scientists will be required to replenish the field with new thinking. Mechanisms such as the Grand Challenges Explorations and prizes that focus on new and untested ideas are seen as potential ways of enticing young scientists to the field by offering improved opportunities for funding and prestige.

Sustaining the Innovation Momentum for New HIV and AIDS Technologies

The above discussion highlights not only the need for innovation in HIV and AIDS technologies but also the many challenges in supporting that innovation. No single mechanism will perfectly identify, fund, organize and implement innovative ideas. Nonetheless, we must maximize the odds that risky ideas will come to fruition, while acknowledging that some of those ideas will fail. In looking forward, we propose the following three steps for continued innovation in HIV and AIDS research:

1. Analyze the results of new funding mechanisms and organizational arrangements

Several new programs have been established with the explicit goal of identifying and supporting innovative research efforts. As many of these programs have only recently been implemented, it is too soon to tell which, if any, will promote the innovation necessary to move the AIDS vaccine field forward. Programs such as the NIH's new efforts to fund novel research ideas, the US government's priority review vouchers, the pilot AMC, and organizational approaches such as consortia-based research should be carefully monitored to gauge progress and identify successful elements in order to apply lessons more broadly and make adjustments.

2. Consider prize competitions to generate new ideas

A carefully implemented prize competition could be a great boost to the AIDS vaccine field, which is in need of novel thinking from researchers both within and outside traditional AIDS and vaccine research circles. It is important that we apply lessons learned from past competitions such as defining a goal without specifying solutions and considering prizes for interim accomplishments that address specific scientific challenges faced by the field.

3. Consider new sources of funding for innovation in HIV and AIDS research

New opportunities to expand and diversify the current funding base while ensuring long-term sustainability should be explored. For example, private capital markets and extending the mandates of existing multilateral mechanisms–such as the Global Fund or GAVI–to directly fund R&D could expand the resource base for innovation.

The search for HIV and AIDS prevention tools such as vaccines will continue to be an enormous test of our ability to innovate. It is vital that we make every effort to support a policy environment that incubates the best ideas and encourages the best researchers to eventually defeat HIV and AIDS.

iavi International AIDS Vaccine Initiative

IAVI gratefully acknowledges the generous support provided by the following major donors.*

Alfred P. Sloan Foundation
Basque Autonomous Government
Becton, Dickinson and Company (BD)
Bill & Melinda Gates Foundation
Bristol-Myers Squibb (BMS)
Broadway Cares/Equity Fights AIDS
Canadian International Development Agency
Continental Airlines
European Union
Foundation for the National Institutes of Health
Google Inc.
The Haas Trusts
Henry Schein, Inc.
Irish Aid
James B. Pendleton Charitable Trust
The John D. Evans Foundation
Kathy Bole & Paul Klingenstein
Merck & Co., Inc.
Ministry of Foreign Affairs and Cooperation, Spain
Ministry of Foreign Affairs of Denmark
Ministry of Foreign Affairs of The Netherlands
Ministry of Foreign Affairs of Sweden
The New York Community Trust
Norwegian Royal Ministry of Foreign Affairs
Pfizer Inc
The Rockefeller Foundation
Swedish International Development Cooperation Agency
U.K. Department for International Development
Until There's a Cure Foundation
The U.S. President's Emergency Plan for AIDS Relief through the U.S. Agency for International Development
The William and Flora Hewlett Foundation
The World Bank through its Development Grant Facility

And many other generous individuals from around the world.

* As of 04/08

THE INFORMATION CONTAINED IN THIS BRIEF IS DRAWN FROM IAVI POLICY WORKING PAPER #17, SPURRING INNOVATION FOR THE DEVELOPMENT OF HIV AND AIDS TECHNOLOGIES. *THE VIEWS EXPRESSED ARE THOSE OF THE AUTHORS AND DO NOT NECESSARILY REFLECT THE OFFICIAL POLICY OR OPINION OF THE WIDER aids2031 INITIATIVE OR PARTNER ORGANIZATIONS.*

IAVI's policy brief series outlines key public policy issues in the research, development, and eventual distribution of AIDS vaccines.

April 2009

iavi Insights