

Current and Proposed Incentive Mechanisms

GHTC Incentives & Innovative Financing Working Group

Existing Incentive Mechanisms

Advance Market Commitment (AMC)

Advance market commitments (AMCs) are a new initiative designed to spur vaccine innovation for developing country use. Donors provide money to guarantee a pre-determined price for a specific vaccine once it has been developed, assuring companies that a market will exist for that vaccine. In exchange for the guaranteed market, companies make binding commitments to provide the vaccine at a lower price once the donor funds have been depleted, ensuring long-term country access. Before the program is launched for a particular disease, an independent advisory group establishes the target product profile (TPP) for eligible vaccines as well as the price and availability.

Companies that develop the specified product would receive a proportion of the payment according to the percentage of the total purchase they supply. More than one company can fulfill a percentage of the market commitment—and thus receive a portion of the reward.

A pilot AMC for a late-stage pneumococcal vaccine was launched in 2007 with a US\$1.5 billion commitment from six donors – Italy, the United Kingdom, Canada, Norway, Russia, and the Bill and Melinda Gates Foundation. The GAVI Alliance, which is implementing the program, expects the final contract to be signed in late spring 2009. On April 3, 2009, the World Bank's Board of Executive Directors approved the financial platform of the pilot AMC. The \$1.5 billion donor subsidy will be placed on the balance sheet of the World Bank Group's International Bank for Reconstruction and Development (IBRD). The IBRD will provide financial management and administrative services regarding donor contributions, AMC commitments, and disbursements.

Discussion of a second AMC, potentially for an early stage product such as malaria or tuberculosis, is also underway among donors, but concrete plans are unlikely to emerge soon.

For more information, see www.vaccineamc.org.

Priority Review Vouchers (PRVs)

Enacted as part of the U.S. Food and Drug Administration Amendments Act of 2007 (FDAAA), the program awards a priority review voucher (PRV) to the sponsor of a newly approved drug or biologic that targets a neglected tropical disease. This voucher, which is transferable and can be sold, entitles the bearer to a priority review for any future new drug application—potentially shaving off four to twelve months from the standard FDA review. For applications accompanied by a voucher, FDA is required deem that product eligible for priority review, aiming to complete and act upon its review of the application within the six month window.

Products excluded from the program include combination products containing a product previously-approved by the FDA, pediatric formulations of previously-approved products, and diagnostics.

How the market ultimately values the voucher will be based on the perceived approval time saved and the anticipated sales of a new blockbuster product. Estimates from different sources vary, but most experts place the value of a PRV somewhere between US\$50 million and US\$500 million – enough to help offset the substantial risk and investment required for discovery and development of the neglected disease product.

The U.S. Food and Drug Administration awarded the first PRV to Novartis A.G. on April 8, 2009 for the antimalarial drug Coartem (artemether–lumefantrine).

For more information, see www.prvinfo.org.

Small Business Innovation Research (SBIR)

Under direction of the NIH, the SBIR program sets aside 2.5% of research and development (R&D) budgets of US government agencies to award to small businesses to fund research. The program was enacted in 1982, reauthorized from 2000 to 2008, and is currently set to expire in March 2009. Participating agencies include the Departments of Agriculture, Commerce, Defense, Education, Energy, HHS, Homeland Security, Transportation, EPA, NASA, and NSF. In 2007, approximately \$580 million were distributed through grants. Two types of grants are offered, Phase I grants (NIH R43) and Phase II grants (NIH R44). Phase I grants award up to \$100,000 for start-up phase research and Phase II grants award up to \$750,000, for up to two years, to expand Phase I results.

Under the program, a small business is defined as a for-profit company that is American-owned and independently operated by individuals. The principal researcher must be employed by the business, and the size of the company is limited to 500 employees. Companies that receive more than 50% venture capitalist funding (and thus are not owned solely by “individuals”) are ineligible to receive grants. The NIH, however, recently commissioned an analysis by the National Academies to review the impact of the “no venture capitalist funding” provision in the SBIR program.

Because the grants are small in comparison to the cost of drug and vaccine development, only small companies generally stand to benefit from the SBIR program. Work is underway to amend the SBIR program in order to improve its impact. National Academies Press recently published, *The Committee for Capitalizing on Science, Technology, and Innovation: An Assessment of the Small Business Innovation Research Program*, which provides an overall review of the program and makes recommendations for improvements. Some of the recommendations include maintaining the flexibility of the program, encouraging emerging talent (especially of women and minorities), and improving data collection and analysis. The full book is available here: http://books.nap.edu/openbook.php?record_id=11989&page=R1.

InnoCentive Challenges

InnoCentive, Inc. is a global, online marketplace that connects organizations in need of innovation with academics, scientists, and other innovators looking to solve problems.

TB Alliance Challenge on InnoCentive

In the spring of 2008, the Global Alliance for TB Drug Development (TB Alliance) and InnoCentive, Inc. announced a challenge seeking methods for accelerating and simplifying the manufacturing process for a promising new TB drug candidate. Specifically, the challenge asked contestants to propose more cost-effective and efficient methods for manufacturing the Phase II TB drug candidate PA-824. On December 3, 2008, two solvers (one based in India and one based in China) were each awarded US\$20,000 for their solutions. The Challenge was supported by the Rockefeller Foundation.

To read the press release announcing the completion of the TB Alliance challenge, see: <http://www.innocentive.com/crowd-sourcing-news/2008/12/04/two-innocentive-solvers->

[win-40000-for-devising-new-methods-to-cost-effectively-manufacture-tuberculosis-drug-candidate/](#).

IAVI Challenge on InnoCentive

In December 2008, the International AIDS Vaccine Initiative (IAVI) posted a US\$150,000 challenge through InnoCentive, Inc. According to IAVI's website, the challenge "seeks proposals for and a sample of the protein that will provide researchers with new avenues for furthering HIV vaccine design and development." The challenge was posted through February 28, 2009, and is funded by the Rockefeller Foundation, an InnoCentive partner.

For more information, see <http://www.iavi.org/viewfile.cfm?fid=50153>.

Affordable Medicines Facility – Malaria (AMFm)

The Affordable Medicines Facility – Malaria (AMFm) is a \$225 million innovative financing mechanism for funding malaria treatment that was launched April 17, 2009. Because effective treatment is unaffordable or unavailable to 60% of the people who purchase malaria medicines through the private sector, the AMFm seeks to make artemisinin-based combination therapies (ACTs) affordable to all patients who need them. The AMFm plans to promote the use of affordable, effective antimalarials by reducing consumer prices through price negotiations and subsidies; it is possible that prices could be reduced to as low as \$0.20-\$0.50 per patient.

In September 2007, the concept of the AMFm was approved by the Board of the Roll Back Malaria (RBM) Partnership, and RBM invited the Global Fund for AIDS, TB and Malaria to host the program. Financial support for the \$225-233 million cost of medicines over the first two years of the scheme will be shared by Britain and UNITAID -- a French initiative supported by Norway and 27 other nations to finance drugs and diagnostics against HIV/AIDS, malaria and tuberculosis. Technical support will come from the Roll Back Malaria Partnership, a group of public and private institutions such as the World Bank, UNICEF, the Dutch government, the Bill and Melinda Gates Foundation and the Clinton Foundation. It will initially be offered to 11 countries (Benin, Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Rwanda, Senegal, Tanzania and Uganda). After two years, providing it is successful, a decision will be taken on whether to expand it globally.

To read the press release about the AMFm launch, see:
<http://www.rollbackmalaria.org/docs/press/prRBM2009-04-17.pdf>

Proposed/Theoretical Incentive Mechanisms

R&D Tax Credits

Tax credits are a popular incentive mechanism in many fields. In the case of drug development, the Orphan Drug Act currently offers a 50% tax credit for the cost of conducting human clinical testing.

Genzyme is currently working on a proposed bill for a Neglected Disease Tax Credit. This bill would provide a fifty percent tax credit for pre-clinical (before human clinical testing) research expenditures incurred for the development of neglected diseases. The tax credit will be provided only on the condition that the company donate the rights to the neglected disease treatment to an organization whose purpose is to research, administer, or develop treatments for neglected diseases.

In the draft stage of the bill, the 50% tax credit is non-refundable or tradable. Thus, only profitable pharma and biotech companies could benefit. If the tax credit were refundable or salable, it may be of greater value to a broader spectrum of industry.

In fall 2008, Genzyme informed the Incentives and Innovative Financing Working Group that the bill would be introduced in the House in early 2009. Because tax legislation is rarely passed alone, the bill will likely be packaged with other tax legislation expected to be considered.

Transferable Market Exclusivity (“Wild Card Patents”)

Under transferable market exclusivity, a company that successfully develops a product for a neglected disease could be granted a patent extension on a product of their choice. Patent extensions have been used successfully under the Orphan Drug Act and the Pediatric Exclusivity program, spurring new industry innovation. Studies of the Orphan Drug Act have shown that the single most valuable aspect of the act was guaranteed market exclusivity. On the other hand, *non-transferable* patent extensions on products for diseases of the developing world are of limited value if there is little to no market for the product. A *transferable* patent extension applied to a product of the company’s choosing, however, can have substantial value and could be a significant incentive for new innovation.

While the concept has been proposed in previous legislation, it has been viewed as highly controversial by both sides of the aisle. Some have raised concerns that the benefit to companies from the additional market exclusivity would be unnecessarily large. Moreover, many are concerned about the additional cost born by consumers. For example, if a company developed a drug eligible to receive transferable exclusivity, and chose to apply the patent extension to a cardiovascular disease drug, then those patients who use the new drug would bear the burden of the additional cost from the extended patent life of the product (and hence the delay in lower cost generic substitutes). Recently, a major push for transferable exclusivity has come from advocates concerned about the need to create incentives for the development of new antibiotics.

Innovation Inducement Prizes – Additional Proposals

Prizes have been proposed by a number of organizations to spur biopharmaceutical innovation for global health. Prizes have been used effectively in other fields, and successful contests have resulted in the development of canned goods and the completion of the first trans-Atlantic flight. There are a number of variations in the kinds of prizes that could be offered and each serves a different purpose. A few criteria remain constant between the categories. First, for the prize system to work well, the objective must be clearly defined. Second, awarding any type of prize requires a committee to evaluate submissions and select the winner.

- A. First-to-succeed prize – This type of prize rewards the first innovator to achieve the stated goal.
- B. Intermediate prize (milestone-based “pull” incentive) – This type of prize would be awarded based on the completion of a previously-defined condition that would bring development closer to a successful product. At times, this prize would be awarded based on reaching a target “milestone.” An intermediate prize may also seek to solve a scientific puzzle. The InnoCentive challenges are examples of intermediate prizes.
- C. Best Progress – This type of prize would reward the innovator who had advanced most successfully towards reaching a goal. Judging this type of prize would require an extremely clear aim and impartial judges.

In 2008, the governments of Bolivia and Barbados made five different prizes proposals to the WHO IGWG for prizes for innovation: (1) for the development of a low cost rapid diagnostic test for tuberculosis, (2) for new treatments for Chagas disease, (3) for new cancer treatments in

developing countries, (4) for a priority medicines and vaccines prize fund and (5) for a licensed products prize fund for donors. It is expected that these proposals will be discussed by the WHO Expert Group on R&D financing in June 2009.

On the U.S. legislative front, Senator Bernie Sanders (D-VT) introduced the Medical Innovation Prize Act (S.2210) to the Senate in 2005 and later re-introduced a revised version of the bill in 2007. The bill is based on de-linking the cost of R&D from the price of the drug by creating an annual prize fund of US\$80 billion that would remunerate drug developers. The Sanders bill set aside US\$6.4 billion for neglected diseases, global infectious diseases such as HIV/AIDS, and medicines needed to respond to bio-terrorism. The Sanders bill sought to eliminate exclusive marketing monopolies of biopharmaceutical products. The bill proposed that patents would be used to establish entitlement to a payment from the prize fund, but would no longer establish market exclusivity. The Sanders bill would create a competitive generics market for new pharmaceutical products while providing abundant financing for innovators.

For a full text of the Medical Innovation Prize Act of 2007, see:
http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_bills&docid=f:s2210is.txt.pdf

X PRIZE for TB Diagnostics

The X PRIZE Foundation received a planning grant from the Bill & Melinda Gates Foundation to develop the concept of an X PRIZE (including fundraising for the prize) for effective diagnosis of tuberculosis in the developing world. In under-developed regions, roughly 60% of tuberculosis patients have access to only primitive, peripheral health clinics with scarce resources. An effective tuberculosis diagnostic could potentially save millions of lives.

The most commonly used diagnostic method in developing countries is smear microscopy, which has a sensitivity of about 40%. Consequently, many people—especially those who have latent TB, suffer from extrapulmonary TB, are in the early stages of infections, or are co-infected with HIV—are under diagnosed and under treated.

The need for a tuberculosis diagnostic prize was recognized by the Advisory Council of the X PRIZE Foundation's Life Sciences Group. The idea was also independently explored by a classroom of students at the X PRIZE Foundation's X PRIZE Lab @ MIT. The Lab is a semester long class that focused on Health Care in the Developing World in the spring of 2008. As part of an ongoing project, several students discussed a need for a prize in this area, leading to combined discussions with the Gates Foundation, which resulted in the grant.

For more information, please see <http://www.xprize.org/future-x-prizes/tuberculosis-diagnostics>

Health Impact Fund (HIF)

Thomas Pogge and Aidan Hollis of Incentives for Global Health (IGH) proposed the Health Impact Fund (HIF) to reward pharmaceutical innovation according to a product's impact on health. The fund would complement the traditional patent monopoly system, rather than replace it, by allowing companies to choose whether to register a patented product with the HIF or to pursue a traditional market-based profit. Companies participating in the HIF would agree to sell their product at a low price (based on the manufacturing price), in exchange for a portion of the HIF over a fixed period of time.

The proposed HIF would not be limited to developing world diseases. Any patented drug or vaccine would be eligible to register for the fund. The fund will have a fixed disbursement per

annum, which will be divided between the registered firms in proportion to the assessed global health impact of each product in the preceding year.

The fund would be financed through the annual contributions of multiple governments and donors. Estimates indicate that roughly six billion dollars per year would be necessary to serve as an incentive. The HIF's architects propose that donating countries commit a fixed share of their gross national income (suggested 0.03 percent), allowing the HIF to grow with the global economy.

One disadvantage of the HIF is that drug companies will be unable to predict in advance the amount of their reward. It will depend both on the "global health impact of the product," which will be determined by evaluating both access and effectiveness, the number of other products registered with the HIF for that year, *and* the health impact of the other products. The number of variables considered in determining the amount of the payout would likely discourage companies from trusting the fund as a reliable incentive for expensive R&D.

Track II Patents

Patents currently allow companies to gain market exclusivity (track I). The idea behind track II patents is to create an option for scientists or companies to be rewarded for a new product in proportion to the impact that it affects health (track II). The purpose of track II patents is not to replace the traditional patent monopoly system, but to provide a profitable alternative for products with no market value.

The Health Impact Fund is an example of a Track II patent initiative. To the best of our knowledge, no other track II patent proposals exist.

A Fund for R&D for Neglected Diseases (IFPMA/Novartis/Dalberg proposal)

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) proposed development of a fund that provides additional financing for R&D for neglected diseases (defined as the 10 neglected diseases identified by WHO/TDR) in order to address the need for sustainable funding in this area. The fund would seek to raise new funding for global health R&D, outside of what already exists for PDP financing. The financing would be focused across disease categories and various stages of the research pipeline, allowing more drugs and diagnostics (although not vaccines) to enter financed clinical trials. The goal is to finance drugs or diagnostics that have the most impact. Under the proposal, funding would go to a variety of research organizations – PDPs, academia, industry, CROs, developing countries.

In addition to IFPMA, the fund is being advocated and championed by Novartis. In addition, Dalberg Global Development Advisors have provided expertise in developing the proposal. Many decisions related to governance/administration have yet to be outlined. Outstanding questions include: who would manage the fund? Who would serve as the leading donors?

Industry R&D Facilitation Fund (IRFF)

The IRFF, proposed by Mary Moran at The George Institute, is a fund proposed to provide continued financial support to existing PDPs. Moran argues that PDPs have proven to be the most effective way of creating drugs for neglected diseases. She and her colleagues measure effectiveness using the following criteria: (1) the health impact of drugs produced; (2) the level of "breakthrough innovation" achieved—that is, those companies that develop completely new drugs; (3) the amount of time taken to develop the drugs; and (4) the cost-effectiveness of the R&D process.

The rationale for the IRFF is that if PDPs continue to contract with industry as they do now, their funds will eventually be depleted. Rather than allow PDPs to be limited by current funding, the

IRFF would reimburse PDPs for payments already made to industry, thus allowing PDPs to continue indefinitely. Moran estimates that the IRFF would require a contribution each year of \$7 million USD per OECD country, eventually capping at a total \$200 million per year.