KNOWLEDGE ECOLOGY INTERNATIONAL

The Big Idea: Prizes to Stimulate Drug Development

the Ruby Hutchison Memorial Address

Presented November 14, 2006
Revised 23 March 2007[1]

James Love, Knowledge Ecology International
Tim Hubbard, Wellcome Trust Sanger Institution

Table of Contents

Table of Contents 1
1. Introduction: The core idea 2
2. Background on prizes and their application to medical R&D 2
3. Shortcomings of current "price" incentive 4
4. Prize systems to simulate investments in medical innovation 9
5. Major issues in the design of prize funds 15
   5.1. Voluntary or non-voluntary? 15
   5.2. Relationship to the patent system 16
   5.3. Fixed total prize fund obligations, or obligation to pay fixed prize per QALY? 16
   5.4. Structure of prizes (and relationship to QALYs) 17
   5.5. Timing of payoff 19
   5.6. Size of the Prize Fund 21
   5.7. Valuation of inventions 21
   5.8. Allocation of set-asides for priority or neglected areas 22
   5.9. Treatment of follow-on innovation 22
   5.10. Transition from current to new system 23
6. Solving the global free-rider issue 23
7. Comparison of the prize fund approach to Advanced Purchase Commitments (APC) or Advanced Marketing Commitments (AMC) 24
8. The World Health Organization's International Working Group on Public Health, Innovation and Intellectual Property. 26
9. Prizes as an alternative to price discrimination for products. 28
10. Incremental or fundamental reform? 30
11. Conclusion 32
References 34

[1] This paper was presented as the Ruby Hutchison Memorial Address, on November 14, 2006, in Sidney Australia. Ben Krohmal provided helpful comments on an earlier draft. Additional comments are welcome.

1. Introduction: The core idea

The current system of financing research and development (R&D) for new medicines is deeply flawed by the impact of high prices on access to medicine, the wasteful spending on marketing and R&D for medically unimportant products, and the lack of investment in areas of greatest public interest and need. It can and should be replaced with something better.

The system for financing new drug development can be radically improved, spending spend less overall, aligning investment incentives more efficiently, while making drugs available to everyone at cheap generic prices.

Reforming the way we pay for R&D on new medicines involves a simple but powerful idea. Rather than give drug developers the exclusive rights to sell products, the government would award innovators money: large monetary "prizes" tied to the actual impact of the invention on improvements in health care outcomes that successful products actually deliver.

2. Background on prizes and their application to medical R&D

The idea of using prizes to stimulate innovation has a long history,[2] but in recent years, prize mechanisms have drawn new interest as a superior business model for the creation of medicines and some other knowledge goods.[3]

---

[2] See: Discussions in 1983. Brian Wright. "The Economics of Investment Incentives: Patents, Prizes, and Research Contracts". *American Economic Review*. 73: 691-707, 1998. Michael Kremer. "Patent Buyouts: A Mechanism for Encouraging Innovation". *Quarterly Journal of Economics* 113: 1137-67. 2001. Steven Shavell and Tanguy van Ypersele. "Rewards versus Rights". Journal of Law and Economics. 44: 525-547. Previously published as "Rewards versus Intellectual Property Rights". 1998 Harvard Law School, Olin Center for Law, Economics & Business, Discussion Paper No. 246, 2001. Nancy Gallini and Suzanne Scotchmer. "Intellectual Property: When is it the Best Incentive System?" University of California, Berkeley Working Paper E01-303., 2002. Paul Romer. "When Should We Use Intellectual Property Rights?" *The American Economic Review* vol. 92: 2, 2002. Lee Davis. "Should We Consider Alternative Incentives for Basic Research? Patents vs. Prizes". Paper for the Druid Summer Conference on Industrial Dynamics. Copenhagen, Denmark. 2003. Michael Abramowicz. "Perfecting Patent Prizes". *Vanderbilt Law Review*. 56: 114-236.

[3] In addition to papers mentioned above, see also: May 27, 2003. James Love. *From TRIPS to RIPS: A better Trade Framework to support Innovation in Medical Technologies*. Paper for the Workshop on Economic Issues Related to Access to HIV/AIDS Care in Developing Countries, Agence nationale de recherches sur le Sida, Marseille, France. August 22, 2003. Burton Weisbrod. "Solving The Drug Dilemma," *Washington Post*. 2003. James Love. *A New Trade Framework for Global Healthcare R&D*. Paper for Columbia University's Workshop on Access to Medicines and the Financing of Innovations in Heath Car. 2004. James Love and Tim Hubbard. "A New Trade Framework for Global Healthcare R&D". *PLOS Biology*. 2(2): e52 DOI: 10.1371/journal.pbio.0020052. June 25, 2004. Joseph DiMasi and Henry Grabowski. "Patents and R&D Incentives: Comments on the Hubbard and Love Trade Framework for Financing Pharmaceutical R&D". September 22, 2004. Dean Baker, "Financing Drug Research: What are the Issues?" Issue Brief, Center for Economic and Policy Research. January 17, 2005. Aidan Hollis. *An Efficient Reward System for Pharmaceutical Innovation*. January 2005. Thomas Pogge. "Human Rights and Global Health: A Research

This has been motivated in part by developments in information technologies, particularly the Internet, where vast knowledge goods and services are available for free, on the margin. These examples, which have been directly experienced and highly valued by millions of persons, are leading to new examinations of how other knowledge goods, including inventions of new drugs and vaccines, could be more widely shared.

In 2002, Aventis, the giant pharmaceutical firm, held a three-day scenario planning session in Ottrott-le-Haut, France, to consider what might happen if there were radical changes in the business models for new drug development. The meeting was authorized by the Aventis CEO and the company's board of directors, and included more than two dozen high-level Aventis executives and two critics of the existing regime of incentives: Tim Hubbard, Head of Human Genome Research for the Wellcome Trust Sanger Institute, and a leading proponent of placing genome research in the public domain, and James Love, then as Director of the Consumer Project on Technology and a proponent of compulsory licensing of patents on medicines in developing countries.

One product of this meeting was initially dubbed "Radical IPR Scenario # 1." It involved a proposal to eliminate marketing monopolies for new pharmaceutical drugs, in return for a system of large cash prizes. In order to ensure the entire world shared the costs of drug development, there would be a global treaty that set minimum levels of support for R&D, either through similar prizes funds, or other research projects, including open source research similar to the Human Genome Project.

When the Aventis scenario exercise concluded, some thought it offered a superior and plausible alternative to the current systems of paying for R&D for new medicines, and could be translated

---

Program". *Metaphilosophy*. 1/2(36). February 2, 2005, Representative Bernard Sanders, "Medical Innovation Prize Fund," *Congressional Record*, Extensions of Remarks, E149. May 18, 2005. Aidan Hollis. *An Optional Reward System for Neglected Disease Drugs*. June 21, 2005. Thomas Pogge on Online Opinion. *A New Approach to Pharmaceutical Innovations*. 2005. James Love and Tim Hubbard. "Paying for Public Goods" in *Code: Collaborative Ownership and the Digital Economy*. Edited by Rishab Aiyer Ghosh. MIT Press, Cambridge. 207-229. 2005. James Love. *Medical Innovation Prize Fund System of Remuneration. In Remuneration Guidelines for Non-Voluntary Use of a Patent on Medical Technologies*. James Love. WHO UNDP. 77-80 and 101-104. March 2006. James Love. "Measures to Enhance Access to Medical Technologies, and New Methods of Stimulating Medical R&D." Paper for the WIPO Open Forum on the Draft Substantive Patent Law Treaty (SPLT). April 18, 2006. Scott Woolley. "Prizes not Patents". *Forbes Magazine*. May 2006. James Love, "A New Initiative at the WHO, Prizes Rather than Prices." *Le Monde diplomatique*. May 2006. James Love, "Drug Development Incentives to Improve Access to Essential Medicines," *Bulletin of the World Health Organization*. 84(5). 2006. Kevin Outterson. "Patent Buy-Outs for Global Disease Innovations for Low and Middle-Income Countries." *American Journal of Law and Medicine*, Vol. 32. 2006. Joseph Stiglitz. "Give Prizes not Patents". *New Scientist*. December 23, 2006. Joseph Stiglitz. "Scrooge and Intellectual Property Rights: A Medical Prize Fund Could Improve the Financing of Drug Innovations," *British Medical Journal*. 333:1279-80.

into a broader global campaign for access to medical inventions. The campaign would focus on issues of fairness and economic efficiency. The new system was justified on both moral and economic grounds.

3. Shortcomings of current "price" incentive

It's not easy to summarize the complicated economics of the pharmaceutical industry, but some basic facts are helpful to review. According to the market research firm IMS, global sales for pharmaceutical products were $602 billion in 2005, or 1.35 percent of global GDP. Some experts believe that the current system of market monopolies for drug sales increased 2006 drug prices by $400 to $480 billion. In the U.S. market, brand name products are on average twelve times more expensive than generics when purchased from manufacturers.[4]

The hefty price premiums for patented brand name products are tolerated for one reason and one reason only: this is how we stimulate R&D for new medicines.

A simple but often overlooked question is: how much R&D do we get for the price premium? The International Federation of Pharmaceutical Manufacturers Associations (IFPMA) claims that global private sector investments in R&D were about $51 billion in 2005,[5] or less than 9 percent of global sales.[6] This is what we get for the $400 to $480 billion in higher prices. The patent system (as currently implemented) is a very expensive way to stimulate R&D. Consumers pay eight or nine dollars in higher prices to stimulate one dollar in R&D spending.

But what type of R&D does this buy? The granting of marketing monopolies creates big incentives to develop products that have modest (if any) medical benefits, when compared to existing medicines. If marketed heavily, such products can fetch high prices, so long as they are perceived to be roughly as good as another high-priced medicine. In some cases, products are

---

[4] In 2005, the U.S. market share for generic pharmaceutical products was 56 percent by volume, but only 9 percent by sales. On average, generic manufacturers sold products at only 8 percent of the price of branded products. Source: GPHA. Prices to consumers, which reflect pharmacy mark-ups and other distribution costs, have somewhat different relative prices, but still reflect large differences between patented and generic prices. Price premiums for "brand name" trademarks for medicines are also higher largely because of the long period of exclusive marketing rights, which associates the name of the product with the trademark, and presents entry barriers for generic products.

[5] Statement on IGWG Agenda Item 2.3: "Elements of the global strategy and plan of action, " Dr. Eric Noehrenberg, Director, International Trade and Market Policy, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). December 2006.

[6] The U.S. trade association PhRMA often presents data that suggests higher rates of investment in R&D, they are often misleading, because they don't take into account the fact that while most of the global R&D spending occurs in the United States, products are sold globally. PhRMA surveys systematically exclude R&D spending and sales by foreign subsidiaries of foreign pharmaceutical companies, and do not include revenues for non-PhRMA members.

simple reformulations of existing drugs, with only minor benefits in drug delivery.

Among experts, it is well known that most new drugs are not very important, because they don't offer significant improvements over existing medicines, and at the cost of unknown adverse reactions that will only emerge over time.

A recent study by the FDA Center for Drug Evaluation and Research (CDER) found that of the 1,284 new drug approvals (NDAs) from 1990 to 2004, only 289, or 22.5%, were for "priority" reviews, defined as a product that presents a "significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease."[7] Of the priority products, 183 (14.3 percent of the total NDAs) were classified by the FDA as new molecular entities (NMEs).

Not only are most new drug approvals for products not very important medically, but the costs of drug development for the so called "me-too" products are often more expensive. The largest costs for the development of new drugs are for clinical trials involving humans. A recent study of clinical trials by Love and Patel found that the number of patients enrolled in clinical trials is almost twice as large for products that don't have significant therapeutic benefits over existing drugs. This is not surprising. Once regulators like the U.S. FDA determine that products have few incremental benefits over existing medicines, they are likely to require more proof that the products don't cause harm to patients. Companies also need larger trials to claim that small differences in efficacy are statistically significant.

The companies who sell the products also admit that they invest in clinical trials that have little scientific value, largely for marketing purposes. Eve Slater, as Merck's Senior President for Clinical Testing, complained to the *Wall Street Journal* that post-marketing studies "are billowing out of control," with "a total lack of science" in some studies. When rivals offer studies that can be used to influence doctors and patients "you have to do it, too, or you are dead in the water," Slater said.[8]

One measure of the lack of scientific relevance of many of the clinical trials is found on the section of the FDA drug marketing label titled clinical trials. Weighted by the number of patients, the FDA cites less than half of the clinical trials that companies report having undertaken, as evidence to support the safety and efficacy of the products.[9]

This is the current system of stimulating R&D. In 2005, prices were $400 to $480 billion higher due to patent monopolies, in return for $51 billion in private sector R&D, and probably one half to two-thirds of the R&D investments were directed towards projects of almost no medical

---

[7] The FDA classification is prospective designation, and a post-approval evaluation may indicate proportions that are higher or lower.

[8] Robert Langreth, "Drug Marketing Drives Many Clinical Trials," *Wall Street Journa*l, November 16, 1998.

[9] Love and Patel, "Size of Clinical Trials for Priority and non-priority drug approvals," forthcoming.

significance.

What do these high prices do in terms of access? In a country with comprehensive healthcare insurance, where all new medicines are available through insurance, access would not suffer. Unfortunately, that does not describe the world we live in.

The situation is direst in developing countries, where access to medicines is often appalling. The World Health Organization's "essential medicines list" (EML) is limited to products that are "cost-effective." The most recent version of the list included only 14-patented products, 11 of which were for the treatment of AIDS, and only 3 for all other diseases.[10] AIDS drugs were only added to the list after activists launched a campaign for compulsory licenses on patents for AIDS drugs, and lobbied wealthy governments to fund the cost of treatment.

Major pharmaceutical companies routinely offer products in developing countries at high prices, not because they are concerned about re-importation to wealthy countries, but because the actual profit-maximizing prices are often those that target the elites who control the most income. A 2004 study of the pricing of Merck's asthma drug Singular found that it was only affordable for the wealthiest 10 percent of the South African population, the group that also controlled about half the country's income. Merck would have to decrease the price significantly to make the product affordable to even the top 20 percent of the population, let alone most people, and in doing so would have lower profits, even with more units sold.

In a 2004 meeting at the World Bank, a Novartis executive said the company considered India a country of 50 million potential customers, including only the 5 percent of the population with incomes comparable to Europeans. These stories are repeated all over the world, as illustrated by well-known disputes, such as over the prices of the heart disease drug Plavix in the Dominican Republic and Thailand, Pfizer's price of Norvasc in the Philippines, Pfizer's fluconazole in Honduras, or Tamilfu for government stockpiles, to mention only a few examples.[11]

Developing countries like Brazil and Thailand, with large populations of AIDS patients, find their political will to provide treatment challenged by the high prices for new second-line AIDS drugs, which eat up health care budgets.

---

[10] See March 2, 2007 letter to the WHO Expert Committee on the Selection and Use of Essential Medicines, http://www.keionline.org/index.php?option=com_content&task=view&id=25.

[11] Andrew Leonard, "Pfizer's Philippine follies, *Salon*, April 4, 2006. http://www.salon.com/tech/htww/2006/04/04/pfizer/index.html. May 14, 2002. Letter from French embassy to Sr. Hugo Guiliani Cury, Secretary of State of the Dominican Republic regarding proposed compulsory license for patents on the heart disease drug Plavix. Also: Gelders S, Ewen M, Noguchi N, Laing R. Price, *Availability and affordability; An international comparison of chronic disease medicines*. 2006. World Health Organization and Health Action International. WHO- EM/EDB/068/E/05.06/3000.

In developed economies the problems are less severe, but quite real. The United States reportedly has more than 50 million persons without health insurance, including many in the middle-class who face enormous challenges when diagnosed with severe illnesses. Some U.S. employers who provide insurance find ways to avoid hiring workers who will likely need expensive drugs. Public and private insurance companies everywhere try to limit access to some expensive new medicines.[12] Several governments have been in difficult negotiations over the high price of Gardasil, the new vaccine for the leading cause of cervical cancer.[13] In many OECD countries, reimbursements for very expensive drugs for cancer and other severe illnesses are restricted to limited uses, or in some cases are not available at all.[14]

There are many other important issues concerning current mechanisms to simulate R&D. For example:

- New antibiotics are needed to combat resistance to older drugs. But once they are developed, it is better if the drugs are only used when the older drugs fail, to reduce the risks of resistance to the new medicines. On the other hand, companies that hold the patents on such medicines have incentives to encourage product use, in order to increase sales.[15]

---

[12] See, for example, Robert E. Wittes, "Cancer Weapons, Out of Reach," *Washington Post*, June 15, 2004. Daniel Costello, "Setting a price for putting off death: A few more months of life may not be worth the costs of new cancer therapies, some argue." *LA Times*, March 18, 2007.

[13] "Glaxo May Face Resistance To Reimbursement," November 09, 2006, Dow Jones. Marie McCullough, "A downside to heralded HPV drug: Cost, access," *the Philadelphia Inquirer*, January 18, 2007, http://www.philly.com/inquirer/health_science/20070118_A_downside_to_heralded_HPV_drug__Cost__access.html. "The base price - $360 for three shots given over six months - makes it the most expensive of an ever-growing list of childhood vaccines. Private insurance coverage of Gardasil is in flux. Many physicians are complaining about under-reimbursement. And for the uninsured, free or discounted vaccines are very limited for women over 18." Linda A. Johnson for the Associated Press, "Cancer vaccine's price, insurance problems limiting patient access," Feb. 2, 2007.

[14] See cites in fn. 12. Also: James Love, "AstraZeneca tells New Zealand cancer patients they will withdraw cancer drug from the market to protest government pressures to lower prices," *the Huffington Post*, December 18, 2005. "Deal reached over cancer drug," tvnz.co.nz, Dec 19, 2005. Reinhard Angelmar, "NICE or Nasty?, Access and Reimbursement of Multiple Sclerosis Medicines in the UK," INSEAD Case Study 2006. "Roche: To Appeal UK Nice Tarceva Reimbursement Finding," Marc 9, 2007, *Dow Jones*. "The Basel-based pharmaceutical company plans to appeal the U.K. National Institute for Health and Clinical Excellence's, or NICE's, decision not to reimburse patients with lung cancer for Tarceva." Stephen B. Soumerai, "Benefits And Risks Of Increasing Restrictions On Access To Costly Drugs In Medicaid," Health Affairs, 23, no. 1 (2004): 135-146. Lars Rydéna, Graham Stokoeb, Gunter Breithardtc, Fred Lindemansd and Adriaan Potgietere, "Patient access to medical technology across Europe: on behalf of Task Force 2 of the Cardiovascular Round Table of the European Society of Cardiology," *European Heart Journal*, Volume 25, Number 7, page 611-616. S O Schweitzer, and S R Shiota, "Access and Cost Implications of State Limitations on Medicaid Reimbursement for Pharmaceuticals," *Annual Review of Public Health*, Vol. 13: 399-410, May 1992.

[15] Rudholm N., "Economic implications of antibiotic resistance in a global economy," *Journal of Health Economics*. 2002 Nov;21(6):1071-83. Laxminarayan, R., G.M. Brown, "Economics of Antibiotic Resistance: A theory of Optimal Use," *Journal of Environmental Economics and Management*, 42(2): 183-206, 2001.

- In many areas, products will be more useful if delivery systems or storage characteristics are improved, or medicines were used as co-formulated products or "cocktails," such as ritonavir with other protease inhibitors. Often these opportunities are discouraged by restrictive licensing policies set by parties holding blocking patents.

- A system that focuses on market exclusivity also suffers from over-investment in wasteful marketing activities, and often from the irrational prescribing practices that such marketing efforts promote. Company designs of clinical trials often avoid the types of comparisons between drugs that would be most useful in designing rational prescribing practices.

Special health problems that disproportionately impact the poor.

When marketing exclusivity is the reward, investors rationally target research investments to address the problems of patients who have highest incomes, and can pay the highest prices. The WHO's Commission on Intellectual Property, Innovation and Public Health (CIPIH) used a three category classification of diseases.[16] Type I diseases are those for which the burden is roughly the same everywhere, and there is a significant market in high-income countries. Examples of Type I diseases would include diabetes, heart disease, asthma and most non-communicable diseases. Type II diseases are those for which there is some disease burden and market in high-income countries, but where most patients are low-income persons living in low-income countries. Examples of Type II diseases would include AIDS or tuberculosis. Type III diseases are those that almost entirely afflict poor people living in poor countries. Examples of Type III diseases would include malaria or Chagas' disease. The CIPIH noted that under a system of incentives that targets prices (and incomes of patients), there is considerable under-investment in Type II and III diseases relative to need when measured on medical and social grounds, a problem that is widely discussed in the public health literature, and the subject of reports by periodic reports by the Global Forum for Health Research.[17]

Public health experts also note the special problems of treating patients in resource-poor settings,

---

Laxminarayan, R., "Fighting Antibiotic Resistance: Can Economic Incentives Play a Role?" *Resources,* No. 143 (Spring): 9-12, 2001.

[16] This was taken from the earlier report of the WHO Commission on Macroeconomics and Health (CMH).

[17] *The 10/90 Report on Health Research 2003-2004,* the Global Forum for Health Research. P. Trouiller, P. Olliaro, E. Torreele, J. Orbinski, R. Laing, N. Ford, "Drug development for neglected diseases: a deficient market and a public-health policy failure." *The Lancet*, Volume 359, Issue 9324, Pages 2188-2194. G. Yamey and E. Torreele, "The world's most neglected diseases: Ignored by the pharmaceutical industry and by public-private partnerships," *BMJ.* 2002 Jul 27;325(7357):176-7. Hans Veeken, Bernard Pécoul (2000), Editorial: "Drugs for 'neglected diseases': a bitter pill," Tropical Medicine & International Health 5 (5), 309–311.

even for Type I diseases. For example, the lack of heat-stabilized insulin for diabetes is an enormous problem for patients living where reliable and convenient refrigeration is not available.

4. Prize systems to simulate investments in medical innovation

Economists have long seen prizes as a possible alternative to systems of exclusive marketing rights. In recent years, work on prizes was an academic backwater, seen more as a novelty than an important policy option. It was more than a decade after Brian Wright's widely read 1983 paper in the *American Economic Review*[18] that academic economists begin to display much interest in prizes. But by the late 1990s, as the impact of the internet and other new business models began to shake the technology sector, interest in new business models for knowledge goods began to grow.

Prizes are an appealing answer to a thorny dilemma. How can society ensure that knowledge goods, which are both costly to create and potentially "non-rival" in use, be shared freely? The patent system is a government intervention that makes a compromise. Inventors are given temporary legal monopolies. Goods are not shared for a period of time, and then they enter the public domain. The prize system is a way of rethinking the problem. If you can divorce the incentive for innovation from the product's price to consumers, knowledge goods, including the R&D for a new medicine, can be placed in the public domain immediately.

But if prizes replace prices as the relevant incentive, who determines the amount of the prize? This has been the major drawback to the use of the prize system. In many areas of the economy, there is a reluctance to abandon a system of prices determined by actual market transactions as the method of determining the value of a knowledge good.

Many of the academic papers on prizes focused on this problem, devising a variety of mechanisms and rules for setting the value of prizes, often seeking to mimic the outcomes of market transactions. For example, Michael Kremer's 1998 paper on patent buy-outs proposed a voluntary system for buying out patent rights by using auctions to determine values.[19]

Kremer soon began to focus on problems of R&D for medicines for diseases that primarily concern the poor, like malaria. But rather than a system of prizes or patent buy-outs, he called for large, government-funded programs to buy products at high prices. Kremer's proposals for "advanced purchase commitments" (APCs) or "advanced marketing commitments" (AMCs)

---

[18] Brian Wright, "The Economics of Investment Incentives: Patents, Prizes, and Research Contracts," *the American Economic Review*. 73: 691-707. 1983.

[19] Michael Kremer, "Patent Buyouts: A Mechanism for Encouraging Innovation," *Quarterly Journal of Economics*, November 1998, Vol. 113, No. 4, Pages 1137-1167.

were designed to address the problem of the poor not being able to pay the high prices for the drugs, and to tie the purchases to plans for delivering the products to patients. They were strictly voluntary, and did not seek to place inventions into the public domain. By maintaining the ability of drug developers to obtain high prices for products and control the patent rights, Kremer, Jeffrey Sachs and others were able to gain the support of the Gates Foundation and large pharmaceutical companies, groups that were anxious to show that tough intellectual property rules were consistent with development.

In May of 2001 in Montreux, the World Business Council for Sustainable Development (WBCSD) organized the first of two meetings between industry, academics and NGOs to discuss intellectual property rights in biotechnology and healthcare. This meeting sparked interest in new business models for drug development, including the use of prize funds, as well as other approaches to supporting "open source" medicines. The WBCSD effort led to the September 2002 Aventis scenario-planning exercise in Ottrott-le-Haut, on "Pharma Scenarios for Sustainable Healthcare," referred to above, where Tim Hubbard and James Love presented Radical IP Scenarios #1 and #2. At the heart of the proposals were two ideas.

1. The trade framework should no longer focus on standardized rules of minimum levels of intellectual property protection (such as the WTO TRIPS agreement and various WTO accession commitments, and bilateral and regional intellectual property trade agreements) or drug prices (such as the 1993 U.S./Thailand, 1999 U.S./E.U./Korea or 2005 U.S./Australia agreements on pharmaceutical prices). Instead, the focus would be on agreements between countries to support investments in R&D, providing a more flexible system for addressing the "free rider" issue that would recognize the value of different approaches, including both public and private sector investments, and "open" and "closed" science projects. In the 2002 proposal for the development of medicines, this would be closely tied to a country's GDP.
2. The primary "pull" incentive for private investment would no longer be the prospect of a marketing monopoly, but rather a system of prizes that rewarded the impact of the inventions on healthcare inventions. There would be a "separation" of the markets for the products and innovation. Innovations would enter the public domain, but innovators would profit when the inventions provided benefits to patients.

There was also work on proposals for new "competitive intermediaries" funded by mandatory employer/employee contributions to provide money for various open science projects.[20] These intermediaries would be similar to venture capital funds, but target investments in projects that yielded scientific rather than financial returns. Employers would be required to contribute, but would also be given the freedom to choose to which intermediaries they would give money. Proponents of this approach argue that employers would rationally target intermediaries that

[20] James Love and Tim Hubbard, "Paying for Public Goods" chapter in Code: Collaborative Ownership and the Digital Economy. Edited by Rishab Aiyer Ghosh. MIT Press, Cambridge, 2005. (pp. 207 - 229).

invested in the most promising advances in medical science, even when the investments were directed at basic or translational research, rather than final products.

Beginning in late 2002, the new paradigm proposals were presented at dozens of seminars and meetings, and were the subject of a Rockefeller-funded Bellagio series of meetings, as well as at three meetings at Columbia organized with Jeffrey Sachs and Joseph Stiglitz, and the main ideas were published in a number of papers.[21]

The initial reaction of the Aventis scenarios was positive but somewhat skeptical within the public health community, and largely negative among major pharmaceutical companies. However, interest in the proposals began to grow[22] when academic economists begin to publish similar ideas,[23] the major pharmaceutical companies began to mount attacks on the proposals, DiMasi and Grabowski, well known academic authors and industry advisors, co-authored a critique,[24] and a U.S. government health official asked the WHO to not discuss the ideas.[25]

In 2004, economist Aidan Hollis approached KEI (CPTech at that time) to explore ways to implement a system of prizes linked to health outcomes in a limited and voluntary fashion, focusing on R&D for neglected diseases. While recognizing the interest in exploring more limited applications of the prize fund approach, our preference was to focus attention on the possibility of a more radical change, targeting not only problems of so called "Type II and III" diseases, but as a model for any disease and any country, including in particular the U.S. market,

---

[21] May 27, 2003. James Love. *From TRIPS to RIPS: A Better Trade Framework to Support Innovation in Medical Technologies*. Paper for the Workshop on Economic Issues Related to Access to HIV/AIDS Care in Developing Countries, Agence nationale de recherches sur le Sida, Marseille, France. 2003. James Love. *A New Trade Framework for Global Healthcare R&D*. Paper for Columbia University's Workshop on Access to Medicines and the Financing of Innovations in Healthcare. 2003. Tim Hubbard and James Love. "Medicines Without Barriers". *The New Scientist*. 2004. Tim Hubbard and James Love. "We're Patently Going Mad: Lifesaving Drugs Must be Developed Differently - for All Our Sakes". *The Guardian*. 2004. James Love and Tim Hubbard. "A New Trade Framework for Global Healthcare R&D". *PLOS Biology*. 2(2): e52 DOI: 10.1371/journal.pbio.0020052. 2005. James Love and Tim Hubbard. "Paying for Public Goods". In *Code: Collaborative Ownership and the Digital Economy*. Edited by Rishab Aiyer Ghosh. MIT Press, Cambridge. 207-229. 2005. James Love. "Medical Innovation Prize Fund System of Remuneration". In: *Remuneration Guidelines for Non-Voluntary Use of a Patent on Medical Technologies*. James Love. WHO UNDP. 77-80 and 101-104. March 2006. James Love. "Measures to Enhance Access to Medical Technologies, and New Methods of Stimulating Medical R&D." Paper for the WIPO Open Forum on the Draft Substantive Patent Law Treaty (SPLT).

[22] Dean Baker was advocating a different approach that involved government-funded drug development companies, which he claimed was superior the prize fund approach. September 22, 2004. Dean Baker. "Financing Drug Research: What are the Issues?" Issue Brief, Center for Economic and Policy Research.

[23] Burton A. Weisbrod, "Solving the Drug Dilemma*," the Washington Post* on August 22, 2003.

[24] 2004. "Patents and R&D Incentives: Comments on the Hubbard and Love Trade Framework for Financing Pharmaceutical R&D" by Joseph A. DiMasi and Henry G. Grabowski

[25] October 30, 2003. William Steiger, US Department of Health and Human Services, letter to The Honorable J.W. Lee, M.D., Director-General, World Health Organization.

which is the most important in the world, and not as a voluntary system, but as a new incentive system that would replace government-imposed marketing monopolies.

In January 2005, Hollis and political scientist Thomas Pogge separately published papers that presented proposals for voluntary prize funds, and Congressman Bernard Sanders introduced an ambitious, non-voluntary prize fund system in the U.S. Congress based upon the Hubbard/Love/CPTech proposals.

On February 24, 2005, 162 leading scientists, academic law professors, economists, NGOs, members of parliaments, government officials and others wrote the WHO Executive Board and the WHO Commission on Intellectual Property, Innovation and Health (CIPIH) to request that they evaluate a proposal for a New Global Medical R&D Treaty.[26] The February 24, 2005 proposal was ambitious, offering a complete alternative to the exiting trade framework involving TRIPS and TRIPS-plus measures on intellectual property rights and drug prices. In addition to creating new global minimum requirements to support medical R&D, it created a system of identifying and rewarding investments in priority research, open research, technology transfer, and the preservation and dissemination of traditional medical knowledge.[27]

With respect to new incentives based upon prizes, Hollis proposed rewards for inventions that treated neglected diseases, with the amount of the rewards determined by the supply of innovations that improved Quality Adjusted Life Years (QALYs) in a competition for a fixed prize fund, an approach similar to the one being proposed for a bill in the U.S. Congress by Representative Sanders.

Pogge proposed an international agreement that would be an open-ended commitment to reward QALYs at a fixed rate or dollar per QALY, an approach that we had rejected because of the difficulty of independently determining rates for QALYs and the uncertainty of budget outlays. Like Hollis, Pogge's proposal was voluntary, and innovators could choose to protect inventions as monopolies rather than participate in the prize program. Unlike Hollis, Pogge's proposal was not limited to particular diseases.

On January 26, 2005, Representative Bernard Sanders (now a Senator from Vermont) introduced HR 417 in the 109th Congress under the title the Medical Innovation Prize Fund Act. Sanders based his bill on the proposals championed by Hubbard and Love. HR 417 was the first practical illustration of how a prize fund would operate, and it was the most ambitious. It had a budget,

[26] 24 February 2005, letter to World Health Assembly Executive Board and World Health Organization Commission on Intellectual Property, Innovation and Health, Request to Evaluate Proposal for New Global Medical R&D Treaty. Andrew Jack, "WHO Members Urged to Sign Kyoto-style Medical Treaty". *Financial Times*, February 25, 2005. http://news.ft.com/cms/s/67e10ff8-86d4-11d9-8075-00000e2511c8.html.

[27] One novel and controversial aspect of the proposal was the creation of a system of tradable credits for investments in these projects, influenced in part by suggestions from Columbia economist Joshua Zivin, then with the Council of Economic Advisors.

initially set at .5 percent of the U.S. GDP, and a management structure. It addressed a number of practical issues. These are some highlights:

HR 417 does not do away with the patent system. Innovators can still get patents, and use patents to protect inventions, up until the point when a product is registered for sale. At that point, however, rewards for the invention from the prize fund replace the exclusive rights of patent as the incentive mechanism. In effect, it changes the way the patent system works, and provides a new system of intellectual property incentives.

HR 417 was not a strict "QALY" proposal. A management structure would administer the prizes, under a set of general rules, including consideration of:

(1) The number of patients who benefit from a drug, biological product, or manufacturing process including (in cases of global neglected diseases, global infectious diseases, and other global public health priorities) the number of non-United States patients.
(2) The incremental therapeutic benefit of a drug, biological product, or manufacturing process, compared to existing drugs, biological products, and manufacturing processes available to treat the same disease or condition.
(3) The degree to which the drug, biological product, or manufacturing process addresses priority health care needs, including:
    a. Current and emerging global infectious diseases;
    b. Severe illnesses with small client populations (such as indications for which orphan designation has been granted under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb)); and
    c. Neglected diseases that primarily afflict the poor in developing countries.
(4) Improved efficiency of manufacturing processes for drugs or biological processes.

Companies who registered new medicines with the U.S. FDA would compete for rewards by providing evidence that inventions benefit patients, as measured by *improved* health outcomes.

The rewards would be paid annually, over a ten-year period of time (because information about the safety and efficacy of new medicines emerges over time).

In cases where a new invention is based upon an earlier invention, HR 417 allows for sharing of rewards, so that a follow-on invention may completely replace an existing medicine, but the earlier product could still receive prize money, even with a zero market share, if the second product was based upon its technology. The aim is to give the correct incentives for products which are both first- and second-movers, since both are important.

In the next version, the prize fund will seek to address the issue of products that are registered at nearly the same time, an issue raised by Dean Baker in discussions on the bill.

The amount of the reward for a particular drug would be determined by supply and demand. The size of the prize fund constitutes the "demand" for innovations. Companies (or non-profit developers) would enter the market to supply such innovations so long as the expected returns (the expected share of the prize fund rewards) are greater than the expected R&D costs.

The size of the prize fund is important, and the basic structure of HR 417 accommodates changes in views concerning the needed magnitude of incentives. If the government wants to stimulate more private investment in R&D, it can increase the size of the prize fund administratively, for example, from 50 basis points to 70 or 100 basis points of GDP. The amount of private investment in R&D thus becomes a matter of public policy. The size of the prize fund can be increased or decreased, and it has nothing to do with the price of the products themselves.

The policy-making board has the authority to determine many of the details of the prize fund reward system later, within certain parameters. As noted, rewards would be based upon evidence that inventions provide "incremental" benefits. No "single drug, biological product, or manufacturing process" could receive more than *five percent* of the total rewards in any given year. There were also certain "set-asides" for special public health problems or needs. These included the following initial minimum allocations:

4 percent for global neglected diseases;

10 percent for orphan drugs; and

4 percent global infectious diseases and other global public health priorities, including research on AIDS, AIDS vaccines, and medicines for responding to bio-terrorism.

The break in the link between the price of the product and the reward to the drug developer has many benefits, including the following:

1. Patients who need drugs and third parties that pay for medicines through insurance would no longer restrict access to medicines because of high prices. Formularies for medicines would not longer be based upon drug prices, but rather the medical qualities of the medicines.

2. Like in India for more than thirty years, drug manufactures would be able to sell any product. They would no longer have incentives to manufacture and sell inferior medicines.

3. By removing legal monopolies, companies that are efficient and have a good reputation for quality would have an edge.

4. Incentives for marketing would be radically changed. Marketing of a product like Vioxx to patients who did not need the drug, as was done by Merck, would not be profitable, because the prizes would only reward incremental health care benefits. Marketing could also not move the price for the product itself, because of competition among generic suppliers. Only evidence of benefits would generate rewards, making it less profitable to market medicines as if they are fashion accessories or magic potions.

5. Major issues in the design of prize funds

There are a number of important issues in the design of a prize fund. Many of these are usefully discussed in Steven Shavell and Tanguy van Ypersele's influential 1998 and 2001 papers on prizes,[28] as well as a growing literature of economists and law professors on prizes.[29]

5.1. Voluntary or non-voluntary?

Love and Hubbard have argued for a non-voluntary replacement of prizes for marketing monopolies, but have also considered the possibility of voluntary mechanisms in the recent deliberations in the WHO's Intergovernmental Working Group (IGWG) on Intellectual Property Rights, Innovation and Public Health.[30]

Hollis and Pogge have proposed voluntary prize mechanisms largely because they believe such mechanisms would be politically appealing to the existing pharmaceutical industry, which could choose between monopoly profits and the prize reward system.[31] Some have even proposed that

[28] Steven Shavell and Tanguy van Ypersele. "Rewards versus Rights". *Journal of Law and Economics*. 44: 525-547. Previously published as "Rewards versus Intellectual Property Rights". 1998 Harvard Law School, Olin Center for Law, Economics & Business, Discussion Paper No. 246.

[29] Lee Davis. Intellectual Propert Rights, Strategy and Policy. Economics of Innovation and New Technology. (13)5: 399-415. 2004. Lee Davis and Jerome Davis. How Effective Are Prizes as Incentives to Innovation? Evidence from Three 20th Century Contests. Paper for the Druid Summer Conference on Industrial Dynamics, Innovation and Development. Elsinore, Denmark. 2004. Michael Abramowicz. Perfecting Patent Prizes. Vanderbilt Law Review. 56: 114-236.2003. Paul Romer. When Should We Use Intellectual Property Rights? The American Economic Review 92:2. 2002. Lee Davis. Should We Consider Alternative Incentives for Basic Research? Patents vs. Prizes. Paper for the Druid Summer Conference on Industrial Dynamics. Copenhagen, Denmark. 2002. Nancy Gallini and Suzanne Scotchmer. Intellectual Property: When is it the Best Incentive System? University of California, Berkeley Working Paper E01-303. 2001. Steve Calandrillo. An Economic Analysis of Intellectual Property Rights. Fordham Intellectual Property, Media & Entertainment Law Journal. 9: 301-360. 1998.

[30] Submission of CPTech to IGWG, 15 November 2006.

[31] Hollis also considers making the voluntary prizes an alternative to tough price controls.

prizes be a supplement rather than replacement for marketing monopolies.

The differences between the voluntary and non-voluntary systems are most significant in cases where existing markets are large, such as for type I diseases, in OECD countries. For type III and some type II diseases, or for innovations that adapt medicines for resource-poor settings, a strong prize system might be the only significant reward for innovators in developing countries.

Voluntary prize mechanisms would also be the most expensive, since companies could opt for the larger sum between monopoly profits or the prizes, or in some proposals, for both. In such situations the result would either be high prices or larger prizes to encourage the adoption of prizes rather than monopoly profits. Voluntary mechanisms also do not address many well-known pricing abuses and access problems, if the patent owner chooses the monopoly over the prize. For these reasons, the non-voluntary option will provide greater benefits and likely generate more support from the persons who actually pay for medicines (consumers, employers, insurers, governments).

5.2. Relationship to the patent system

The prize system is often presented to the public as an alternative to the patent system, but it need not be. In many of the proposals for voluntary prize mechanisms, patent owners effectively choose whether or not to license patents for the uses tied to the prize payments. In some proposals, prizes would simply supplement the benefits of strong patent protection, and not replace the patent monopoly.[32] Other proposals would have prizes co-exist with a weaker patent system. An example of the later is HR 417 from the 109th Congress, a legislative proposal by Bernard Sanders to create a Medical Innovation Prize Fund in the United States. HR 417 did not eliminate patents on medicines, but once the FDA approves products, the patent would no longer prevent generic competition for the patented invention. Inventors would effectively use patents to make claims on the prize fund, rather than to create monopolies for products. But HR 417 did not limit the prize fund payments to only patented inventions. Any new product would qualify, including one that was developed without patents, such as paclitaxel, the unpatented cancer drug developed by the NIH.

5.3. Fixed total prize fund obligations, or obligation to pay fixed prize per QALY?

Hubbard and Love, as well as Hollis, proposed fixed prize funds with payments divided among innovators on the basis of the relative merits of each innovation. Pogge proposed a fixed

[32] This is a possibility that seems to be suggested by Stiglitz in his BMJ article.

payment per QALY, with an open-ended obligation to pay for prizes.

There are three major reasons why we support the fixed total prize fund approach:

First, it provides greater ability to control and predict government budget outlays. This is a major issue for the governments that will have to pay the prizes.

Second, by fixing the size of the prize fund, the marginal cost of using an innovation is zero, since it does not change the annual budget for the prize payments. This is essential for the elimination of *price-sensitive* medical formularies.

Third, by fixing the size of the prize fund, the developers of products will have an incentive to lobby for fair and efficient methods of valuing inventions. If too much money is given to one inventor, prizes available for everyone else are smaller.

5.4. Structure of prizes (and relationship to QALYs)

Hollis and Pogge propose a strictly proportional link to QALYs as the standard for measuring benefits and allocating prize fund awards. The flaw of this is that it over-rewards products with very large QALYs at the expense of other valuable product with much lower QALYs. We believe rewards partly but not exclusively be linked to QALYs, to ensure the development of a broader range of products, and to address other R&D objectives.

First, how would a strictly proportional QALY payout work? In the Hollis formulation, if three drug developers were responsible for 1,000; 2,000; and 7,000 QALYS, the total number of QALYs would be 10,000 and the shares of the fund would be divided as follows: 1,000/10,000 = 0.1; 2,000/10,000 = 0.2; and 7,000/10,000 = 0.7.

We prefer a system where the administrators of a prize fund have the flexibility to consider different approaches, rather than only one that is strictly proportional to QALYs.[33]

[33] The approaches used can also be transparent and predictable, although the issue of predictability has to be placed into perspective. In a world with strong exclusive rights and prices completely unfettered by government regulation, patent owners still face considerable uncertainty, given the well known risks that unanticipated averse effects or the emergency of superior alternatives will reduce demand for products. And methodologies for government reimbursement programs that involve impendent evaluation of the value of medicines are also constantly being changed in response to lobbying by right-owners and new thinking by academic researchers and policy makers. Add to this, the stochastic nature of the R&D process itself. These risks are not by themselves problematic, if capital markets are efficient, and if investors believe that the overall level of funding will be large, rather than small.

Larger QALYs are associated with both the efficacy of the products and the number of patients who use them. Diseases like breast cancer, heart disease, diabetes and asthma have very large patient populations. Some diseases or conditions have very few patients. In the current market, governments and private insurers are willing to pay higher prices for products that have relatively small client populations, such as the high prices paid for Gleevec (STI571) or Ceredase (Alglucerase), medicines used to treat diseases classified as "orphans" by the U.S. FDA.

The arguments for paying higher prices for products with smaller client populations are several, including the fact that the costs of drug development are normally not strongly tied to the size of the potential market. There are also benefits in having new medicines on the market because they may later be used for new indications, as has been the case for medicines such as AZT (originally developed for cancer, now used for AIDS), Viagra (originally developed for heart disease, now used to enhance erections) or ritonavir (originally developed as a standalone protease inhibitor, now used as a booster of protease inhibitors).

It is possible to simulate prize fund payments and development costs to better understand the consequences of different reward designs.

For a simple example, consider a world where the risk-adjusted cost of drug development is fixed at $200 million, the size of the prize fund is $2 billion, and there are 5 potential candidates for R&D, expecting to yield 1,000; 2,000; 3,000; 7,000 and 25,000 QALYs. If the prizes were allocated with a strictly proportional payout per share of QALYs, as proposed by Hollis and Pogge, only two the projects would be brought to market. If the prize fund were allocated half on the basis of QALYs and half for bringing a new product for market, all five projects would be brought to market.

Table 1
Two prize payments methods compared
2,000 prize fund, 200 fixed R&D cost

		Prize Payments		
	QALYs (000)	*Rewards Proportional to QALYs*	*Rewards Proportional to QALYs (only feasible projects)*	*Half allocated proportional to QALYs, half for successful new drugs*
Projects	1	53		226
	2	105		253

	3	158		279
	7	368	438	384
	25	1,316	1,563	858
Totals	38	2,000	2,000	2,000

The above is just a simple illustration of a prize fund structure that levels out the rewards somewhat, giving relatively larger prizes to the projects associated with fewer QALYs and less to projects with more QALYs, which could ensure that more projects are undertaken.[34] In the real world, it is much more complicated to model. Risk-adjusted costs are themselves a function of the expected payoffs (companies will take larger gambles or spend more on known risks if the expected payoffs are higher), for example, but the basic point is quite important. The fact that we currently accept much higher prices for products with smaller client populations provides some evidence that the market itself seeks to accommodate the issue of high fixed-development costs.

More sophisticated modeling is possible for the relationship to R&D costs and QALYs, and also for consideration of other approaches, such as option pricing models, to address the valuation of new antibiotics or products developed for potential health threats, such as medicines and vaccines for avian flu, SARS or bio-terrorism.

Some issues of prize fund design can also be addressed through instruments like caps on shares given to any one product, or set-asides for special categories of medicines, approaches already incorporated in HR 417.

5.5. Timing of payoff

It is very difficult to know what the benefits of a product will be when it is first placed on the market. We recommend prizes be paid out over time, as more is known about utilization, safety and efficacy of products. The Sanders bill uses a 10-year period for evaluation, with payments made annually, given the evidence available for that year, a system that approximates the existing effective term of marketing monopolies. A longer period could be used, but periods too long may not be desirable, given the high discount rates for the private investors.

Under the current system of incentives linked to marketing monopolies, governments issue 20-year patents on products, processes or uses of products, and exclusive rights in pharmaceutical

[34] For a different view, see: Aidan Hollis, "Determining rewards in a prize fund," *Drug Development*, July 08, 2006..

test data,[35] orphan product exclusive marketing protections, various *sui generis* programs to extend patent terms and other legal barriers to entry. Table 2 looks at the current (February 2007) status of new molecular entities that were approved for marketing by the U.S. FDA from 1990 to 2005.

Table 2
Status of competition: NMEs approved by FDA from 1990 to 2005
Orange Book Status as of February 2007

Year of FDA approval	Monopoly seller	Facing competition	Withdrawn	Facing competition or withdrawn	Year on the market
1990	50%	27%	23%	50%	17
1991	20%	57%	23%	80%	16
1992	31%	42%	27%	69%	15
1993	52%	28%	20%	48%	14
1994	59%	14%	27%	41%	13
1995	67%	27%	7%	33%	12
1996	79%	13%	8%	21%	11
1997	56%	13%	31%	44%	10
1998	83%	7%	10%	17%	9
1999	80%	9%	11%	20%	8
2000	89%	7%	4%	11%	7
2001	100%	0%	0%	0%	6
2002	88%	0%	12%	12%	5
2003	95%	0%	5%	5%	4
2004	94%	3%	3%	6%	3
2005	92%	8%	0%	8%	2
1990-1994	41%	35%	24%	59%	
1995- 1999	73%	13%	13%	27%	
2000- 2005	93%	3%	4%	7%	

Source: Julie Patel and Michael Palmedo, February 2007

[35] Judit Rius Sanjuan, James Love, Robert Weissman: "Protection of Pharmaceutical Test Data: A Policy Proposal" (November, 2006).

5.6. Size of the Prize Fund

The 2005 Sanders proposal would create a prize fund of 50 basis points of U.S. GDP. Love's 2005 WHO publication on remuneration for non-voluntary use of patents simulated a lower rate for countries, starting with a top rate of 20 basis points for high income countries, and reducing that rate according to rankings on the UNDP human development index.[36] Pogge's 2005 papers recommended a global prize fund of approximately 10 basis points of world GDP.

The size of a prize fund should be related to its objectives, and seen in the broader context of other efforts to fund R&D. If the prize fund were the only source of R&D funding, it would have to be very large. If prizes co-exist with other instruments to finance R&D, such as patent monopolies, public sector R&D funding, employer contributions to research funds[37], UNITAID-type global transactions taxes, or other sources, then the prize fund might be smaller. Holding all other R&D funding options constant, the larger the prize fund, the more investment it will stimulate.

In looking at the appropriate size of a prize fund, there are several factual and policy issues that should be considered, including the current levels and composition of investment in R&D for new medicines by the public and private sector, the anticipated risk and profit premiums (discount rates) for attracting private investment, and the opportunities for the public sector to strategically subsidize some aspects of drug development costs, such as for clinical trials. Governments will also be making implicit or explicit assumptions about the elasticity of supply of improved health care outcomes. To the degree that greater investments in R&D for new medicines have high yields in terms of improved outcomes, they are economically efficient and attractive uses of scarce resources.

5.7. Valuation of inventions

The government of Australia, a country with a population just over 20 million persons, evaluates the "value" of medicines in order to set reimbursements for its Pharmaceutical Benefit Scheme (PBS). Other governments do things that are quite similar. In the U.K., evaluation of benefits is by the National Institute of Clinical Excellence (NICE). In Australia, the U.K., Canada, New Zealand and in many OECD countries, governments are making decisions on the allowed reimbursement rates for new medicines. The U.S. Congress is asking the U.S. Federal government to do the same. Private insurance companies also have to decide if or how much they will reimburse medicines. Explicitly or implicitly, these evaluations are based upon evidence of the pharmoeconomic benefits of the products.

---

[36] Base rate * (178 – rank of HDI)/177.

[37] "Paying for Public Goods," section on Supporting Health Care R&D.

Logically, there is very little difference between determining the value of a reimbursement and determining the value of a prize. If one can be done, so can the other.

The basic tools for valuation are already at hand, filling volumes of specialized journals, but there is room for considerable improvement, particularly in terms of the evidence now collected from clinical trials.

5.8. Allocation of set-asides for priority or neglected areas

As described above, the Sanders bill recognizes that policy makers want to address certain health problems, and that this extends to the systems to stimulating R&D on new medicines. For example, in the United States and Europe, special marketing exclusivity provisions are provided for products with small markets (sometimes referred to as "orphan" products following the U.S. passage of the "Orphan Drug Act" in 1982). The Sanders bill created initial set-asides for three categories of priority research:

4 percent for global neglected diseases;

10 percent for orphan drugs; and

4 percent for global infectious diseases and other global public health priorities, including research on AIDS, AIDS vaccines, and medicines for responding to bio-terrorism.

The bill allows the set-aside percentages to be modified by the board that administers the prize fund.

5.9. Treatment of follow-on innovation

One of the most important aspects of any incentive mechanisms for new medicines concerns the treatment of follow-on inventions. The most risky investments and the most difficult science are often for the first product in a therapeutic class. It is often not difficult to engineer around the first product and introduce additional molecules that use similar mechanisms for treatments. Moreover, the later products are often better than the first, in terms of efficacy or safety. Even when the differences are small, for example, between Zocor and Lipitor, it may be rational to switch patients to the newer product. This can radically reduce the market share of the product that established the value of the approach. An incentive system needs to provide incentives to both early movers and the follow-on inventions that improve upon the early entrant. HR 417

addresses this issue as follows:

> In cases where a new drug, biological product, or manufacturing process offers an improvement over an existing drug, biological product, or manufacturing process and the new drug, biological product, or manufacturing process competes with or replaces the existing drug, biological product, or manufacturing process, the Board shall continue to make prize payments for the existing drug, biological product, or manufacturing process to the degree that the new drug, biological product, or manufacturing process was based on or benefited from the development of the existing drug, biological product, or manufacturing process.

In short, under HR 417 the prize payments for the new product will reflect the incremental value of the improvements and the early entrant will continue to receive prize payments even if its market share falls to zero.

5.10. Transition from current to new system

The 2005 Sanders Bill proposed an immediate transition to the new system. In the first year, 90 percent of the prize payments would be given to products already on the market. The share allocated to the older products would be reduced by 9 percent each year.

6. Solving the global free-rider issue

The current global system for stimulating medical R&D relies extensively on a complex and growing web of global trade agreements to ensure minimum levels of intellectual property protection and in some cases, minimum prices for medicines. These include the WTO TRIPS accord and the many bilateral and regional trade agreements that that provisions on intellectual property of drug pricing. [38]

Global agreements that seek only to enhance the exclusive marketing rights for medicines are highly imperfect instruments to address concerns about the equitable distribution of the costs of medical R&D. These obligations are focused not on R&D itself, but on the intermediate measures that will influence drug prices. In practice, countries with very similar systems of intellectual property protection often pay very different amounts for medicine. In most countries, reimbursements for medicines are tied to drug prices. Despite fairly similar

[38] Such as the 1999 U.S./Korea and E.C./Korea agreements, and the more recent efforts by the E.C. to set minimum reimbursements in Turkey, or the U.S. efforts to undermine price negotiations or increase reimbursements in Australia, Malaysia, Canada, Germany, Thailand, and elsewhere.

intellectual property regimes, one observes very different outcomes in terms of actual outlays among developed economies, such as the United States, Canada, France, Germany, Australia, Korea and New Zealand. The same is true for developing economies, where the different cultures, traditions and levels of states' support for reimbursing purchases of medicines lead to quite different outcomes in countries like Kenya, India, South Africa, Brazil, Costa Rica, the Philippines, and Thailand.

To the extent that the current global framework does increase global outlays in patented medicines, it is quite inefficient, raising global outlays from $400 to $500 billion in 2005, for only $51 billion in private sector outlays on R&D, little of which was invested in products that were medically important. High drug prices have created a pervasive and harmful culture of rationing of medicines, as evidenced by the paucity of patented medicines on the WHO essential drugs list, and the extensive efforts by governments and private insurance companies to justify limiting reimbursements for new medicines.

The current global framework also completely ignores global obligations to support investments in basic research, public goods like the Human Genome Project, investments in emerging public health threats, high risk translational research, diseases that primarily afflict poor people living in poor countries, or the types of clinical trials that would best evaluate the benefits and risks of existing medicines.

A shift from prices to prizes would require a new global framework to address the legitimate problems of sharing the costs of research and development for new products. The proposal to the WHO in February 2005 was one effort to address this issue. It presented a global framework that recognized the importance of both public and private sector investments in R&D, and it offered a framework for obligations and incentives to invest in projects and areas of public interest. The new global framework focuses on R&D directly, rather than the flawed mechanisms of high drug prices. It is entirely consistent with a shift from prices to prizes as the primary "pull" mechanism to stimulate medical R&D.

7. Comparison of the prize fund approach to Advanced Purchase Commitments (APC) or Advanced Marketing Commitments (AMC)

While prize mechanisms are beginning to attract more attention, in some circles a related but somewhat different approach is better known. Largely because of the effective advocacy of Michael Kremer and Jeffrey Sachs, and the support from Bill Gates and large pharmaceutical companies, there has been considerable work to explore the possible role of "advanced purchase commitments" (APCs) or "advanced marketing commitments (AMCs). First proposed by Kremer and Sachs as mechanism for stimulating "greenfield" R&D on new vaccines for malaria and other illnesses of the poor, APCs and AMCs are now largely discussed in the context of "late

stage" R&D on products that are already far into the pipeline.

The APC and AMC approaches both embrace the notion that prices should continue to be the main signal for investors, even when patients are poor. They do not change the nature of price-sensitive formularies. They do not move toward a world where the prices of innovation are zero on the margin. They do make a political statement: the price system works well when you have enough money to pay for it.

The most appealing argument in favor of the APC/AMC approaches is that they link the R&D incentive to the delivery of the products to patients. However, there is no reason why a prize would not do the same thing, so long as prizes reward actual outcomes. In important ways, prizes would create more sustainable systems of finance. In the APC/AMC approaches, governments or donors would spend large sums of money, billions of dollars in many proposals, to buy products at high prices and then deliver them to the poor. The developer of the products has no obligation to transfer the invention to the public domain and indeed, no incentive to develop products that are particularly inexpensive to manufacture. When the APC/AMC payments stop, or even before they begin, the developer can charge whatever it wants, assisted by the fact that the governments or donors have deliberately established a high price.

The APC/AMC requires a specification of the products eligible for purchases. In some versions, the prices are determined before the products are fully developed. This feature of the APC/AMC creates considerable problems, as governments and donors are expected to anticipate technologies best suited to the health care objectives, and to the prices that will stimulate development of such technologies. This introduces the need for considerable information and judgment, as well as presents the possibility that the APC/AMC will be tailored for specific companies, just as a job description can be designed for a single applicant.

For many of these reasons, advocates of the APC/AMC approach have moved away from assertions that the mechanism should use "greenfield" R&D ventures, and now propose that the focus be placed on "late stage" R&D projects. How "late" would that be? If products are indeed "fully cooked" and ready for commercialization, the APC/AMC becomes simply a negotiation over a price in a procurement. If the APC/AMC approach is too early, it risks the inefficiencies associated with similar central planning exercises.

The prize fund approach would suffer from these same problems if it were too closely tied to a special technological standard, and to a lesser but important extent, if tied to a narrow disease category.

Hubbard/Love, Hollis, Pogge, Sanders, Weisbrod and some others have advocated an approach that is not tied to technology standards, but rather to improved health outcomes themselves, leaving the question of the technology itself to the developer. We all have proposed systems that

are quite broad in terms of disease coverage. In our view, the objectives of the proponents of the APC/AMC approach would be better served by a system of prizes. A system of prizes would create or enhance the incentives for R&D that lead to better health outcomes, with the benefit of providing incentives to create products for which the costs of manufacturing and delivery are minimized. Also, if the prizes are implemented within a fixed budget (as is advocated by Hubbard/Love, Hollis and Sanders), it would ensure that products would benefit from marginal cost pricing.

8. The World Health Organization's International Working Group on Public Health, Innovation and Intellectual Property.

In May 2006, the World Health Assembly adopted resolution WHA 59.24, which created a new Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (referred to by the WHO internally as PHI/IGWG). This resolution combined two resolutions, one that concerned the recently completed report of the WHO's Commission on Intellectual Property, Innovation and Public Health (CIPIH), and another concerning a "Global Framework on Essential Health Research and Development" that had been first sponsored by Kenya on November 16, 2005, and later co-sponsored by Brazil.

Under WHA 59.24, the WHA decided:

> (1) to establish, in accordance with Rule 42 of the Rules of Procedure of the World Health Assembly, an intergovernmental working group open to all interested Member States to draw up a global strategy and plan of action in order to provide a medium-term framework based on the recommendations of the Commission. Such a strategy and plan of action aims at, inter alia, securing an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries, proposing clear objectives and priorities for research and development, and estimating funding needs in this area;

The first meeting of the PHI/IGWG took place in December 2006. In February 2006, Bangladesh and Bolivia submitted papers to the PHI/IGWG calling for consideration of new methods of stimulating investments in medical R&D, including the use of prizes. The Bangladesh submission said:

> We note with great interest a shift in the global policy discussion, away from the status quo of TRIPS compliant patent regimes for medicines and toward new models for rewarding innovation, such as prize funds. The prize fund model separates the incentives for innovation from the prices of medicines. Innovation would be rewarded directly from

> nationally, regionally or globally managed prize funds based on improvements in health care outcomes, while ensuring low prices for medical innovations from generic competition immediately upon market entry.

The Bolivian submission echoed these themes, calling for the de-linking of R&D incentives from the prices of products, and called for the PHI/IGWG to evaluate the plausibility of creating a new system of prizes to reward development of essential medicines that improve health care outcomes:

> Desvincular precios de los incentivos a la investigación y desarrollo (I+D)
>
> Un numero creciente de economistas, expertos en salud, y empresas del sector privado están examinando los beneficios de cambiar la naturaleza de los incentivos privados para la investigación y desarrollo, para que no se vinculen a los precios de los medicamentos. Destacamos en particular el trabajo sobre premios (recompensas) de Tim Hubbard, James Love, Aidan Hollis, Thomas Pogge, y Joseph Stiglitz.
>
> Sugerimos al IGWG evaluar la factibilidad de la creación de un sistema nuevo de premios para recompensar el desarrollo de medicamentos esenciales. Estos premios podrían recompensar las invenciones que mejoren las resultas.

The PHI/IGWG is focusing on new approaches to R&D for Type II and III diseases. The position of the large pharmaceutical industry has recently become more receptive to the consideration of prizes in this area. For example, in a January 11-12 meeting in New York on "Overcoming the gaps in TB drug development," organized by MSF, the meeting participants adopted this statement on support for new approaches to R&D.

> The TB community must engage in the World Health Organization's Intergovernmental Working Group on Innovation, Intellectual Property and Public Health to establish a global R&D framework to help design new ways of setting R&D priorities and financing. With respect to TB drug development, participants of the New York symposium support current discussion at the WHO for a treaty on essential health R&D that addresses the question of who pays for essential medical R&D and de-links incentives from drug prices, instead rewarding the impact of inventions according to health care outcomes.[39] [Emphasis added]

The New York statement on R&D was supported by the industry participants in the event. A representative from Novartis attending the event said that the current incentive systems do not work for diseases like TB, and that they we willing to look at alternatives, a view later shared by

[39] Conference Statement: NO TIME TO WAIT: Overcoming the gaps in TB drug development. 12 January 2007. Press Release: Tuberculosis Experts Outline Proposals to Speed Up Drug Development, January 12, 2007.

a representative from the IFPMA in a Geneva event on intellectual property rights and access to medicine, and echoed privately by a number of industry officials. These industry officials are unwilling, however, to endorse the prize model as the primary mechanisms to support R&D for Type I diseases.

9. Prizes as an alternative to price discrimination for products.

Some critics of prizes have suggested that forms of price discrimination are a preferred method to promote access, because they are less disruptive of the current paradigms. However, price discrimination approaches can be difficult to implement in practice, often yield unsatisfactory results, and present conflicts with other policy objectives, such as the free movement of goods.

Price discrimination in medicines and vaccines is already persuasive. U.S. consumers generally pay more for patented pharmaceutical products than do consumers in Australia, Canada, New Zealand or Europe. Consumers in the Philippines generally pay higher prices for medicines than do consumers in Thailand. Prices in Northern European countries historically have been higher than prices in Southern European countries. Prices are quite different from country to country, and also within countries. Some of the price differences have nothing to do with the ability to pay.[40] For example, uninsured patients in the U.S. lack the ability to bargain, and often pay higher prices than do patients that have insurance, despite their lesser ability to pay. Because of inefficient distribution systems, consumers in Indonesia pay higher prices for generic antibiotics than do consumers in Canada.

In other cases, price discrimination is a rough but imperfect effort to extract higher prices from different classes of consumers. An example of this would be the two tiers of pricing of medicines between the public and private sector in some countries. But price discrimination is plagued with problems. It is difficult to monitor the ability of different groups to pay for medicines, and often companies simply target the highest price consumers. In developing countries, it is often the case that products are priced to sell to only the wealthiest 5 to 20 percent of consumers. The putative rationale for such policies is that it is costly if not impossible to prevent the rich from buying lower priced products that are affordable for the poor. The same argument is made with regard to pricing of products between rich and poor countries. Even information about price differences can lead to indirect price controls, through reference price mechanisms, for example, not to mention the theoretical possibility of parallel trade between

[40] See, for example, the many examples in Susanne Gelders, Margaret Ewen, Nakae Noguchi, Richard Laing, "Price, availability and affordability: An international comparison of chronic disease medicines," Background report prepared for the WHO Planning Meeting on the Global Initiative for Treatment of Chronic Diseases held in Cairo in December 2005. WHO-EM/EDB/068/E.

countries.

One area where price discrimination is being severely challenged is in the European Union. Today there are 27 member states in the European Union. Incomes between states are quite different. The average per capita income for these countries was $26,460 in 2004. 10 member states with a population of more than 100 million persons have average incomes that are less than half of this. The European Union is now struggling with a dilemma. The policy of a unified market is creating huge problems for access to medicines, within Europe.

Table 3

EU Member State	Population in millions	GDP/POP
Bulgaria	7.8	$ 3,090
Romania	21.8	3,358
Latvia	2.3	5,913
Poland	38.6	6,277
Lithuania	3.4	6,559
Slovakia	5.4	7,611
Estonia	1.3	8,615
Hungary	10.1	9,970
Czech Republic	10.2	10,490
Malta	0.4	13,250
Slovenia	2.0	16,100
Portugal	10.4	16,125
Greece	11.1	18,486
Cyprus	0.8	19,250
Spain	42.6	24,411
Italy	58.0	28,928
Germany	82.6	33,179
Belgium	10.4	33,875
France	60.3	33,940
Austria	8.2	35,646
United Kingdom	59.5	35,704
Netherlands	16.2	35,741
Finland	5.2	35,750
Sweden	9.0	38,489
Ireland	4.1	44,293
Denmark	5.4	44,704
Luxembourg	0.5	63,800

A switch from prices to prizes would allow the members of the European Union to reconcile the need for incentives for new drug development with access to medicine and the EU policy of a single market for the products.

Prizes would be a particularly appropriate paradigm for Europe, where governments and employers already are providing extensive social insurance for pharmaceutical products, prices are already often determined by negotiations, and the free movement of goods is a core value. A system of prizes for Europe would also help address the troubling movement toward rationing for new medicines, particularly for the most expensive new medicines for severe illnesses.

This is also true in the larger global market, where the problems of limiting parallel trade and other diversions of medicines are making it more difficult to consider price discrimination as a viable strategy to protect consumer and promote access.

10. Incremental or fundamental reform?

There are two assumptions implicit in proposals that consider prize mechanisms only as special and limited programs to deal with areas of complete market failure, such as neglected diseases or sales to populations with almost no ability to pay. One is that the current system is functioning reasonably well, and it would not be prudent to change without more evidence that the alternative would work. The second is that it is politically difficult, if not impossible, to introduce a radical change in the way that R&D is financed for Type I diseases or for high-income markets, given the political power of the incumbent pharmaceutical companies. While we support even limited efforts to experiment with the use of prizes to stimulate medical R&D, including those being considered today by the WHO's Intergovernmental Working Group (IGWG) on Public Health, Intellectual Property and Innovation, we have considered and rejected both assumptions against a broader and more radical reform.

Tying the incentive for R&D to the price of products fundamentally flaws the current system of financing R&D for new medicines. It has led to appalling disparities of access to medicines, well-known pricing abuses in both high- and low-income countries, massive waste in terms of excessive marketing of products and investments in medically unimportant products, and under-investment in products that have the greatest medical benefits. Prices for new medicines treating severe illnesses are very aggressive, which leads to increasing rationing of access, even in the high-income countries. The existence of high prices in the United States and other high-income countries is leading to enormous pressures on other countries to accept high prices, through such measures as new intellectual property norms, exercised both formally and informally.

The intellectual property norms incorporated into the 1995 WTO TRIPS agreement were at the time considered to be quite tough. WTO members were obligated to provide 20-year patents on

pharmaceutical products, and to abide by a set of rules when using compulsory licensing or other exceptions to patent rights. However, subsequent analysis and debate over the TRIPS agreement has shown that TRIPS itself can be a fairly flexible instrument, if WTO members are willing to use the various exceptions and limitations to rights that are allowed in the agreement. These flexibilities include the ability to grant non-remunerative exceptions to patent rights in certain cases, to embrace relatively high standards for patentability, and to grant non-voluntary authorizations to use patents, subject to "adequate" remuneration.

Even before the TRIPS agreement came into force, the United States and other high-income countries sought a number of new bilateral, regional and multilateral agreements on intellectual property rights and drug pricing that go far beyond the 1995 TRIPS obligations. The Clinton Administration continued an aggressive "TRIPS plus" trade policy that was not modified until AIDS activists aggressively disrupted the presidential campaign of Al Gore in 1999.[41] The U.S. trade policy was then somewhat moderated, with formal changes announced by President Clinton on December 1, 1999,[42] followed by an executive order on AIDS and sub-Saharan Africa in May 2000.[43] But as important as the changes in policy were, they were fairly limited, and in practice did not extend greatly beyond policies relating to a single disease, AIDS, and were limited when applied even to AIDS outside of Sub-Saharan Africa. For example, President Clinton's trade team negotiated a 1999 agreement with Korea setting mandatory minimum price reimbursements for innovative medicines (the A-7 pricing agreement), and a 2000 FTA agreement with Jordan that dramatically narrowed the grounds under which Jordan could issue compulsory licenses on patents, as well as the protection of pharmaceutical test data and other provisions.

The 2000 USTR 301 report to Congress was the first to abide by the new program to address public health concerns. While it had been moderated, it still contained a number of citations for inadequate intellectual property protection on medicines, including complaints about failures to adopt intellectual property protections of pharmaceutical test data that go beyond WTO TRIPS obligations for Argentina, Chile, Hungary, India, Israel, Korea, Lithuania, Poland, Romania and Uruguay. On January 9, 2001, days before leaving office, President Clinton asked the WTO to bring trade sanctions against Brazil for a compulsory licensing statute, at a time when Brazil was considering issuing a compulsory license for the patents on the AIDS drug efavirenz (EFV).[44]

---

[41] Bob Davis, "Gore Hopes New AIDS Pact Will Help Shake Protesters," *Wall Street Journal*, August 12, 1999. For a personal account, see: Mark Milano, "Personal Perspective: Zapping for Drugs," *The Body*, Fall 2006. http://www.thebody.com/cria/fall06/zapping.html?m172o.

[42] "President Clinton Announces New Cooperative Effort To Help Poor Countries Gain Access To Affordable Medicines, Including For Hiv/Aids Treatment," December 1, 1999, http://clinton4.nara.gov/WH/New/WTO-Conf-1999/factsheets/fs-012.html.

[43] Executive Order 13155 - Access to HIV/AIDS Pharmaceuticals and Medical Technologies. May 10th, 2000. Neil Lewis, "Clinton Issues Order to Ease Availability of AIDS Drugs in Africa," *New York Times*, May 11, 2000.

[44] WT/DS199/3 9 January 2001 (01-0093), Brazil - Measures Affecting Patent Protection, Request for the

President Bush took office initially sympathetic to some measures to balance trade polices on intellectual property protection, notably by deciding to keep the Clinton Executive Order on AIDS and Africa, and by participating constructively in the 2001 WTO negotiations that led to the widely praised Doha Declaration on TRIPS and Public Health. But by 2002, extensive lobbying and vast campaign contributions by the pharmaceutical industry led to changes in trade policy, and were followed by the launching of a plethora of new bilateral and regional trade negotiations that sought tough TRIPS-plus measures, as well as new trade agreements on drug pricing. The European Union and other high-income countries also pursued similar agreements.

Perhaps much more important than the formal agreements are the arm-twisting and pressuring of countries to prevent them from using the flexibilities existing in both the TRIPS and the new TRIPS plus trade measures. In addition to the enormous power of the various threats and efforts to link pharmaceutical policies to broader trade and foreign policy considerations, countries North and South faced considerable in-country lobbying by pharmaceutical companies, and consistently inaccurate, biased, and pro-industry press coverage and academic commentary, which created effective soft norms against the use of TRIPS flexibilities or effective price controls. Even aggressive price negotiations are branded as "piracy" and theft of intellectual property. The most recent example of this dynamic is the bitter debate over the recent decision by Thailand to issue compulsory licenses on medicines for AIDS and heart disease.

Without a more fundamental reform in developed economies, it unlikely that poor people in developing countries will be allowed to use the existing flexibilities in trade agreements. In this sense, the more radical reforms may be needed for a sustainable solution to the global problem of access.

11. Conclusion

In this article we have argued that it is possible to construct a viable new system to finance innovation in a way that maximizes access to new inventions while continuing to exploit commercial competitive market incentive mechanisms.

- The prize mechanisms should be thought of as part of a larger ecosystem of financing of medical R&D, and should be implemented in combination with other instruments, such direct or indirect government funding of basic research, non-profit product development partnerships (PDPs), clinical trials, and other traditional and non-traditional types of funding R&D. What the prizes offer uniquely is an alternative to the marketing monopoly as an incentive for private investment.

Establishment of a Panel by the United States.

- When implemented properly, Prize based models can directly reward successful R&D projects, while permitting marginal cost pricing of products, and avoiding the trap of overly bureaucratic and centralized decision-making.

- By decoupling the rewards for successful R&D investment from the sales of products, the new model will permit governments to create more efficient and useful incentives for R&D that focus on inventions that improve health outcomes.

- Prize mechanisms can be implemented in ways that are consistent with a robust patent system, but are best implemented in systems where the patent system is used to establish ownership of inventions and thus claims on the prize rewards, rather than through exclusive rights to market products.

- It is important that those incentives are linked to broad research priorities, and not be overly prescriptive in terms of diseases, mechanisms or technologies.

- By eliminating marketing monopolies on products, there is an opportunity for much greater efficiency through unrestricted competition to manufacture the resulting medical products.

- The elimination of marketing monopolies, the de-coupling of R&D incentives from prices, and the creation of an evidence based reward system linked to changes in health outcomes, will lead to significant reductions in expenditures to market products, the area of the largest waste in the current system.

- It is important that the total obligations to finance the reward payment are not directly tied to utilization, but rather measures of a country's ability to contribute to global R&D costs, so that countries do not have incentives to limit access to products in order to control budget outlays on innovation rewards.

- Prize mechanisms can be introduced in areas where the markets are functioning the poorest, such as for diseases that primarily affect poor people living in poor countries. But the largest benefit will come from the adoption of prize mechanisms in higher income markets, such as the United States, both because improvements in the efficiency of R&D incentives in high income countries are important for the development of medicines used everywhere, and also because pricing norms in high income countries are forcefully exported to developing countries, creating enormous hardships.

- Whilst additional detailed modeling will be required to improve reward structures and evaluation criteria, these efforts are feasible, and not materially different from efforts by

governments or insurance companies to determine acceptable reimbursements for insured products.

- A shift to a new system of incentives that relies upon prizes rather than prices will also require a shift to a new global trade framework that focuses less on intellectual property rights and more on country contributions to mechanisms that support R&D, including but not limited to prize incentive mechanisms.

The major challenge to switching financing systems for medical innovation on a global scale depends on whether there is sufficient political leadership.

References

Abramowicz, Michael. "Perfecting Patent Prizes." *Vanderbilt Law Review* vol. 56: 114 236.

Angelmar, Reinhard. "NICE or Nasty? Access and Reimbursement of Multiple Sclerosis Medicines in the UK." INSEAD Case Study 2006.

Baker, Dean. Issue Brief. "Financing Drug Research: What are the Issues?" Center for Economic and Policy Research. 22 Sept. 2004.

Calandrillo, Steve. "An Economic Analysis of Intellectual Property Rights." *Fordham Intellectual Property, Media & Entertainment Law Journal* vol. 9: 301-360.

Clinton, President William, Access to HIV/AIDS Pharmaceuticals and Medical Technologies: Executive Order 13155. 10 May 2000.

Costello, Daniel. "Setting a Price for Putting off Death: A Few More Months of Life May Not Be Worth the Costs of New Cancer Therapies, Some Argue." *LA Times* 18 Mar. 2007.

Davis, Bob. "Gore Hopes New AIDS Pact Will Help Shake Protesters." *Wall Street Journal* 12 Aug. 1999.

Davis, Lee, Jerome Davis. "How Effective Are Prizes as Incentives to Innovation? Evidence from Three 20th Century Contests." Druid Summer Conference on Industrial Dynamics, Innovation and Development Elsinore, Denmark, 2004.

Davis, Lee. "Intellectual Property Rights, Strategy and Policy." *Economics of Innovation and New Technology* vol. (13)5: 399-415.

Davis, Lee. "Should We Consider Alternative Incentives for Basic Research? Patents vs. Prizes." Paper for the Druid Summer Conference on Industrial Dynamics, Copenhagen, Denmark, 2003.

DiMasi, Joseph and Henry Grabowski. "Patents and R&D Incentives: Comments on the Hubbard and Love Trade Framework for Financing Pharmaceutical R&D." 22 September 2004.

Dow Jones. "Glaxo May Face Resistance To Reimbursement." 9 Nov. 2006.

Dow Jones. "Roche: To Appeal UK Nice Tarceva Reimbursement Finding." 9 Mar. 2007.

Gallini, Nancy and Suzanne Scotchmer. "Intellectual Property: When is it the Best Incentive System?" *Working Paper E01-303*. 2001 University of California, Berkeley.

Gelders, S.; Ewen, M.; Noguchi, N.; Laing R.; Price. "Availability and affordability: An international comparison of chronic disease medicines." World Health Organization and Health Action International 2006. WHO-EM/EDB/068/E/05.06/3000.

Hollis, Aidan. "Determining Rewards in a Prize Fund." *Drug Development* 8 Jul. 2006.

Hollis, Aidan. "An Efficient Reward System for Pharmaceutical Innovation." January 2005.

Hollis, Aidan. "An Optional Reward System for Neglected Disease Drugs." 18 May 2005.

Hubbard, Tim and James Love. "Medicines Without Barriers." *The New Scientist* 2004.

Hubbard, Tim and James Love. "We're Patently Going Mad: Lifesaving Drugs Must Be Developed Differently - for

All Our Sakes." *The Guardian* 2004.
Jack, Andrew. "WHO Members Urged to Sign Kyoto-style Medical Treaty." *Financial Times* 25 Feb. 2005. See also: http://news.ft.com/cms/s/67e10ff8-86d4-11d9-8075-00000e2511c8.html.
Johnson, Linda A. "Cancer Vaccine's Price, Insurance Problems Limiting Patient Access." *Associated Press* 2 Feb. 2007.
Kremer, Michael. "Patent Buyouts: A Mechanism for Encouraging Innovation." *Quarterly Journal of Economics* vol. 113, no. 4: 1137-1167.
Langreth, Robert. "Drug Marketing Drives Many Clinical Trials." *Wall Street Journal* 16 November 1998.
Laxminarayan, R. "Fighting Antibiotic Resistance: Can Economic Incentives Play a Role?" *Resources* no. 143 spring 2001: 9-12.
Laxminarayan, R., G.M. Brown. "Economics of Antibiotic Resistance: A Theory of Optimal Use." *Journal of Environmental Economics and Management* 42(2): 183-206.
Leonard, Andrew "Pfizer's Philippine Follies." *Salon* 4 April 2006. See also: http://www.salon.com/tech/htww/2006/04/04/pfizer/index.html.
Lewis, Neil. "Clinton Issues Order to Ease Availability of AIDS Drugs in Africa." *New York Times* 11 May 2000.
Love, James and Julie Patel. "Size of Clinical Trials for Priority and non-Priority Drug Approvals." forthcoming.
Love, James and Tim Hubbard. "Paying for Public Goods." *Code: Collaborative Ownership and the Digital Economy*. Ed. Rishab Aiyer Ghosh. Cambridge, MA: MIT Press, 2005: 207-229.
Love, James and Tim Hubbard. "A New Trade Framework for Global Healthcare R&D." *PLOS Biology,* June 25, 2004. 2(2): e52 DOI:10.1371/journal.pbio.0020052.
Love, James. "A New Initiative at the WHO, Prizes Rather than Prices." *Le Monde diplomatique* May 2006.
Love, James. "AstraZeneca Tells New Zealand Cancer Patients They Will Withdraw Cancer Drug from the Market to Protest Government Pressures to Lower Prices." *The Huffington Post* 18 Dec. 2005.
Love, James. "A New Trade Framework for Global Healthcare R&D." Workshop on Access to Medicines and the Financing of Innovations in Healthcare. Columbia University, 2003.
Love, James. "Drug Development Incentives to Improve Access to Essential Medicines." *Bulletin of the World Health Organization* vol. 84(5) 2006.
Love, James. "From TRIPS to RIPS: A Better Trade Framework to Support Innovation in Medical Technologies." Workshop on Economic Issues Related to Access to HIV/AIDS Care in Developing Countries. Agence nationale de recherches sur le Sida, Marseille, France, 22 Aug. 2003.
Love, James. "Medical Innovation Prize Fund System of Remuneration." Remuneration Guidelines for Non-Voluntary Use of a Patent on Medical Technologies. WHO UNDP March 2006: 77-80 and 101-104.
Love, James. "Measures to Enhance Access to Medical Technologies, and New Methods of Stimulating Medical R&D." Paper for the WIPO Open Forum on the Draft Substantive Patent Law Treaty (SPLT) 18 April 2006.
McCullough, Marie. "A Downside to Heralded HPV Drug: Cost, Access." *The Philadelphia Inquirer* 18 Jan. 2007.
Milano, Mark. "Personal Perspective: Zapping for Drugs." *The Body* Fall 2006. (See also: http://www.thebody.com/cria/fall06/zapping.html?m172o).
Outterson, Kevin. "Patent Buy-Outs for Global Disease Innovations for Low and Middle-Income Countries." *American Journal of Law and Medicine* vol. 32, 2006.
Pogge, Thomas. "A New Approach to Pharmaceutical Innovations." *Online Opinion*. 21 June 2005.
Pogge, Thomas. "Human Rights and Global Health: A Research Program." *Metaphilosophy* 1/2(36).
Romer, Paul. "When Should We Use Intellectual Property Rights?" *The American Economic Review* vol. 92, 2002: 2.
Rudholm, N. "Economic Implications of Antibiotic Resistance in a Global Economy." *Journal of Health Economics* 21 Nov. 2002 vol. 21(6): 1071-83.
Rydéna, Lars, Graham Stokoeb, Gunter Breithardtc, Fred Lindemansd, Adriaan Potgietere. "Patient Access to Medical Technology Across Europe: on Behalf of Task Force 2 of the Cardiovascular Round Table of the European Society of Cardiology." *European Heart Journal* vol. 25, No. 7: 611-616.
Sanders, Representative Bernard, United States Congressional Record, Extensions of Remarks, E149. Medical

Innovation Prize Fund. 18 May 2005.
Sanjuan, Judit Rius, James Love, Robert Weissman. "Protection of Pharmaceutical Test Data: A Policy Proposal" November, 2006.
Schweitzer, S. O., S. R. Shiota. "Access and Cost Implications of State Limitations on Medicaid Reimbursement for Pharmaceuticals." *Annual Review of Public Health* vol. 13, May 1992: 399-410.
Shavell, Steven and Tanguy van Ypersele. "Rewards versus Rights." *Journal of Law and Economics* vol. 44: 525-547. (Previously published as Discussion Paper No. 246. "Rewards versus Intellectual Property Rights." *Harvard Law School, Olin Center for Law, Economics & Business,* 1998.
Soumerai, Stephen B. "Benefits And Risks Of Increasing Restrictions On Access To Costly Drugs In Medicaid." Health Affairs, 23, no. 1 (2004): 135-146.
Steiger, William, U.S. Department of Health and Human Services. Correspondence to the Honorable J.W. Lee, M.D., Director-General, World Health Organization. 30 Oct. 2003.
Stiglitz, Joseph. "Give Prizes not Patents." *New Scientist* 23 December 2006.
Stiglitz, Joseph. "Scrooge and Intellectual Property Rights: A Medical Prize Fund Could Improve the Financing of Drug Innovations." *British Medical Journal* vol. 333: 1279-80.
Trouiller, P., P. Olliaro, E. Torreele, J. Orbinski, R. Laing, R. Ford. "Drug Development for Neglected Diseases: a Deficient Market and a Public-Health Policy Failure." *The Lancet* vol. 359, iss. 9324: 2188-2194.
TVnz, "Deal reached over cancer drug," 19 Dec. 2005. Tvnz.co.nz. Accessed 19 Dec. 2005.
Veeken, Hans, Bernard Pécoul. "Drugs for 'Neglected Diseases': a Bitter Pill." *Tropical Medicine & International Health* vol. 5(5): 309–311.
Weisbrod, Burton A. "Solving the Drug Dilemma." *The Washington Post* 22 Aug. 2003.
Wittes, Robert E. "Cancer Weapons, Out of Reach." *Washington Post* 15 Jun. 2004.
Woolley, Scott. "Prizes Not Patents." *Forbes Magazine* May 2006.
Wright, Brian. "The Economics of Investment Incentives: Patents, Prizes, and Research Contracts." *The American Economic Review* vol. 73: 691-707.
Yamey, G., and E. Torreele. "The World's Most Neglected Diseases: Ignored by the Pharmaceutical Industry and by Public-private Partnerships." *BMJ* vol. 27, iss. 325(7357): 176-7.