

A New Trade Framework for Global Healthcare R&D¹

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The current system for financing R&D for new medicines is widely regarded as unsustainable. Governments and health insurers are balking at skyrocketing prices and finding ways to deny coverage for the newest and priciest products. In the United States and other countries without a universal public health system, the uninsured simply cannot afford the newest medicines. In developing countries, patent owners price life saving medicines beyond the reach of most people, a morally offensive outcome. When prices differ from one country to the next, patent owners demand extensive and expensive efforts to stop cross border trade, or simply seek to create a single price for the whole world, making the global gap between the rich and the poor even worse. At the same time, taxpayers and consumers in the United States are fed up with paying the lion's share of the global R&D, and US trade officials are lobbying to dismantle price controls or bar the uses of state bargaining power to negotiate lower prices. Strong patent rights are often used as an anticompetitive weapon to block innovation, and too much secrecy slows scientific progress. Drug companies constantly manipulate the patent system to unfairly or even fraudulently extend marketing monopolies, harming consumers and taxpayers. We don't have effective mechanisms to finance medicines for diseases that primarily afflict the poor such as malaria or tuberculosis, and we under-invest in vaccines, and public databases or other public goods that advance science. And this is just a short list of the problems.

Propping up the present system is the widely held belief that the private sector plays a key role in the development of new medicines, and that it is necessary to tie the private sector financing of R&D to a 20-year monopoly on new health care inventions. Every outrageous case of inefficiency, overreaching, greed or unfairness is justified on the grounds this is a necessary evil to get new drugs. And if this were true, it would make sense to tolerate all sorts of bad outcomes, because the fruits of R&D eventually benefit everyone in wonderful ways.

But granting of a 20 year marketing monopoly on a patented invention is just one way to finance R&D, and the shortcoming of the present system are increasingly hard to ignore. We need a new approach, and it should be built upon two main elements.

1. Trade agreements should be reframed to focus on standards for sharing the costs of R&D, rather than standards for granting and protecting property rights in research.
2. We need to implement business models for financing R&D that do not depend upon marketing monopolies for approved products.²

¹ This is based upon my collaboration with Tim Hubbard and the members of the Bellagio Dialogue on a new R&D trade framework, the MSF Neglected Diseases Group and the Trans Atlantic Consumer Dialogue workshops on intellectual property. Other accounts of this work include: James Love, "Fixing the Global R&D problem," Working Conference on Globalisation, 10 December 2003, Ministry of Health, Welfare and Sports (VWS), The Hague, the Netherlands (which is essentially the same paper), James Love, "From TRIPS to RIPS: A better Trade Framework to support Innovation in Medical Technologies." presented at the Workshop on Economic Issues Related to Access to HIV/AIDS care in Developing Countries, Agence nationale de recherches sur le sida, Marseille, France, May 27, 2003, and Tim Hubbard and James Love, "Medicines without barriers," the New Scientist, June 14, 2003. A nice account of Tim Hubbard and John Sulston's work on these issues is given in Kenneth Neil Cukier's "Community Property: Open-source proponents plant the seeds of a new patent landscape," Acumen, Volume 1, Number III.

² This argument is forcefully presented by Burton Weisbrod's op-ed in the Washington Post. Solving the Drug Dilemma. August 22, 2003.

Taken together, these two core steps can completely change world in a positive way. We can raise global R&D levels as a matter of policy, and ensure that resources flow into the areas of the greatest need, and we can do so knowing that the poor and the rich will have access to new inventions at marginal cost.

There will be other benefits as well:

1. Policy makers will be weaned from their current unhealthy addiction to ever higher levels of intellectual property rights as the only instrument to raise R&D levels, a path that has increasingly reached diminishing returns or become counter productive. With new instruments to address the overall levels of R&D investment, policy makers can more constructively address the well-known inefficiencies in the patent system without the fear that global R&D levels will suffer.
2. The system of prescribing medicines will be radically transformed in a healthy way. What passes for marketing of medicines is now a multi billion industry that is devoted to showering doctors with bribes, an unseemly corruption of the evidence upon which prescriptions decisions are based, and an increasingly blatant effort to package medicines like fashion accessories.
3. Without marketing monopolies to protect, there will be far less spent to influence and control the governments that set the rules that regulate such monopolies.

Firms that invest in R&D need a financial payoff, but they don't necessarily require marketing monopolies to get those payoffs. Pharmaceutical marketing monopolies are both an extremely expensive mechanism to get money to researchers, and a highly imperfect mechanism for setting research priorities.

No matter which data you believe, only a small share of the current drug bill is used to finance R&D. According to the US Internal Revenue Service (IRS), the rate of investment in new products represents less than 10 percent of pharmaceutical sales.³ The PhRMA survey of its members, which serves public relations objectives, places the R&D rates at about 16 percent in recent years. PhRMA claims that 12 or 13 percent of turnover is invested in new (as opposed to existing) products. There is considerable reason to question these numbers,⁴ but quite uncontroversial is the fact that most of this is invested in non-innovative products. According to the US Food and Drug Administration (FDA), about 70 percent of new drug approvals are not better than existing therapies, and the non-innovative products have significantly larger clinical trials than the innovative products.⁵ At 2 cents on the dollar invested in innovative products, and a rapidly increasing share of the national GDP, the inefficiency of the current system is increasingly difficult to justify.

One naive and false dichotomy presents only two models for financing R&D -- a government funded centrally managed R&D program, or a system of market driven rewards from the patent system.

There is already considerable overlap between the public and private roles in R&D. We rely extensively on public sector support for R&D -- more than \$27 billion at the US National Institutes of Health (NIH) alone, most of which is distributed to universities, other non-profit research organizations or private firms, typically commercialised by the private sector. Governments globally already play a huge role as the purchaser of patented inventions, at

³ James Love, What do US IRS tax returns tell us about R&D investments?, Van ontwikkelen tot slikken, Pharma Selecta congres, Utrecht, the Netherlands, January 16, 2003. James Love, Evidence Regarding Research and Development Investments in Innovative and Non-Innovative Medicines, September 22, 2003.

⁴ The issues range from overreporting, which has advantages for tax, regulatory, investor, political and public relations purposes, to evidence of waste, and the difficulty to quantify amount of reported R&D that primarily meets marketing objectives. James Love, "Evidence Regarding Research and Development Investments in Innovative and Non-Innovative Medicines," September 22, 2003.

⁵ The FDA estimates that over the past ten years, 69 percent of new drug approvals are considered not significantly better than existing therapies. The products that were not better than existing treatments had clinical trials that were 83 percent larger than the more innovative products. Based upon these data, the share of investments in new products that have significant improvements over existing treatments is estimated to be 20 percent of the total invested in new products.

negotiated prices. The public sector R&D program is often decentralized and privatised, and the private sector R&D program is increasing selling to the public sector.

Importantly, a private sector market for R&D does not depend upon post-development marketing monopolies. Here are only a few examples of business models that might be used to finance R&D, that do not require marketing monopolies on final products.

1. Prize Models.

Firms can compete for rewards for specific R&D outputs -- referred to by economists as a prize model. The prizes could reflect public health priorities, with greater rewards for innovative outputs, products that fill treatment gaps, or which provide databases or other building blocks for R&D. The prize model could be implemented with high or low levels of intellectual property rights, or even without any intellectual property rights.

The key objective would be to design a prize system that would permit the products to be manufactured and distributed by a competitive industry, as generic commodities, so that prices would be reasonably related to marginal costs.

The actual structure of the reward system for a prize model would drive investor incentives. A poor design would work poorly, although it would not have to be perfect to work better than the existing system, which only seems to result in about 2 cents on the industry turnover invested in innovative products.

In a simple formulation, governments could place large sums into a fund that would be allocated every year to firms that bring new products to market. The payment to the innovative firm could retire all intellectual property claims (as compensation for compulsory licenses to IPR claims), and permit rapid introduction of generic competition.

The reward system could be a lump sum payment, eliminating any incentive to continue to market the product, or to engage in activities described by some as corrupting the evidence base for prescribing decisions. Alternatively, the reward system could have a long-term payout structure, which would depend upon evidence of both usage and efficacy.

Prize systems could be designed to be fairly similar to the current system, a sort of "winner take all" compensation approach, with big payoffs for successful entrepreneurs, with the entire set of traditional intellectual property rules in place, but subject to compulsory licensing of claims when the product reaches the market. But even with this "traditional" approach, there would be huge opportunities to improve welfare. The reward system could be more rational than the existing system, allocating greater rewards for innovative products and less for "me too" products that do not work better than existing products. Premiums could be given for therapies that address treatment gaps or for inventions that pave the way to new classes of drugs. The products would be priced closer to marginal costs, reducing the need for health care payers to restrict formularies and ration access to the latest medicines. And the costs of marketing medicines, which today is far higher than the amounts invested in R&D, would be greatly reduced. There would be much less concern over counterfeiting, parallel trade, and the management of price control systems. Most importantly, the poor would have much better access to medicines.

One could also consider "prize" models that made departures from (improvements over) the "winner take all" system. This would be important, because patents are often a poor proxy for actual inventions or investments that were significant to the development of a product.

2. Direct Funding of Drug Development.

Governments could expand direct funding for drug development, either through the exiting structures such as the NIH collaborations with industry and academia, or through non-profit development projects, such as those currently

resourced to address treatments for neglected diseases like malaria and TB.⁶ Examples of such projects are the Medicines for Malaria Venture (MMV), the Global Alliance for TB Drug Development (TB Alliance), the International AIDS Vaccine Initiative (IAVI), the Drugs for Neglected Diseases Initiative (DNDi), and the Institute for OneWorld Health, to mention only a few.

Most of the non-profit development projects have some type of a public private nature, often with most of the hard financing coming from UN agencies, governments, or charitable donors, and a variety of in-kind or contracted or licensed services from the private sector. If exclusive marketing rights were eliminated for pharmaceutical drugs, prices would be far lower, and governments could re-direct significant resources to these types (or different types) of non-profit drug or vaccine development entities.

3. Open collaborative public goods models.

Open collaborative public goods models such as those use for the Human Genome Project, could be play an important role, not only for gene sequencing, but in drug development itself. Kenneth Neil Cukier recently surveyed eight such projects in an issue of *Acumen*.

Table 2

Harbingers of an Open-Source Biotech Movement: Several initiatives herald a viable open-source approach to intellectual property in the life sciences. (Source: Kenneth Neil Cukier, "Community Property: Open-source proponents plant the seeds of a new patent landscape," *Acumen*, Volume 1, Number III.)

Human Genome Project (HGP)	<p>Intellectual property approach: Public domain</p> <p>Activity: Six-nation, decade-long program that by 2003 decoded the human genome.</p> <p>Result: created database for DNA sequences that researchers can freely use and refine.</p>
SNP Consortium	<p>Intellectual property approach: Public domain</p> <p>Activity: A public/private collaboration led by the Wellcome Trust that identifies common DNA sequence variations known as SNPs (single nucleotide polymorphisms).</p> <p>Result: Has identified over 1.8 million SNPs and continues to make further discoveries.</p>
Electric Genetics	<p>Intellectual property approach: Open-source ontologies; patented analysis software</p> <p>Activity: Since 1997 has sold genomic data analysis systems and validated drug targets.</p> <p>Result: Free gene expression ontologies increases the value of their software and services.</p>
BioSPICE	<p>Intellectual property approach: Open source</p> <p>Activity: DARPA-funded software system for simulating cell behavior.</p>

⁶ Dean Baker and Noriko Chatani, "Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research," October 11, 2002. Sabine Louët, "Public-private partnerships boost research on neglected diseases," *Nature Biotechnology* 21, 1254 - 1255 (2003).

	Result: Enables research on cell functions not amenable to direct experiment, such as unknown pathogenic agents.
Open Bioinformatics Foundation	Intellectual property approach: Open source Activity: Support hub for open bioinformatics programming languages like BioPerl, BioJava, and the Open Biological Database Access system. Result: Shared, community-vetted code eliminates the need for duplicate programming work.
Microarray Gene Expression Data Society	Intellectual property approach: Public domain standards; open-source software Activity: Industry and nonprofit collaboration started in 1999 to set standards for open microarray data annotation, databases, and software. Result: Sharing standard microarray data will speed up research and lower costs.
BioBricks	Intellectual property approach: Open source Activity: MIT initiative to standardize terms, tools, and process for engineered biological circuits. Result: Enables researchers to work from identical, custom-made genomic materials.
Alliance for Cellular Signaling	Intellectual property approach: Open source Activity: Free online computer tool to test cell reaction to protein alterations. Result: Makes drug-research testing easier and less expensive.

The proponents of the new open and collaborative models for public goods point to the success of GNU/Linux in the software field as evidence that major projects can be undertaken with radically different business models. As noted above, if marketing exclusivity is eliminated for new products, the resource savings could be used to support such efforts.

4. Competitive Intermediators

In a dialogue with Aventis, Tim Hubbard and James Love proposed a new competitive financing scheme that would work through R&D investment intermediators. These R&D funds would be licensed and regulated (like pension funds). Their role would be to manage R&D assets on behalf of consumers. Consumers (or employers) would be required to make minimum contributions into R&D funds. The intermediators would compete to attract funds to invest in R&D.

In this proposal, employers would make contributions to R&D funds much like mandatory contributions to social security or health insurance, or to pension funds. But while the government would set the required contributions (i.e. 100 euros or more per person on a health insurance plan), the employer (or employee) would be free to choose the particular intermediary that received their contributions.

The R&D Funds would compete on the basis of their prowess for drug development, and upon their priorities. The actual business model for financing R&D would be tested in the market. The Intermediators could experiment with prize systems, direct investments in profit or non-profit entities, open collaborative public good models, or other approaches. Business models that were better would attract more funding.

5. Mixed Models

Governments could decide to adopt a mixed model, with a certain percentage of national R&D investments allocated to each of these (or other approaches), and over time, based upon experience, increase or decrease allocations based upon results. The important proposition is that business models could themselves compete, and evolve.

Concluding Comments

We believe the economics of a change in paradigm for funding R&D are highly favourable. The current system is not only unfair, but it is extremely costly and inefficient. The largest inefficiency comes from the enormous marketing outlays that firms undertake to maximize the benefits of the marketing monopoly. The very largest pharmaceutical firms -- big pharma -- have huge global marketing operations that brand and promote products worldwide. The actual innovation sector is competitive, but for many pharmaceutical inventions, only a big pharma firm can maximize the value of a marketing monopoly. Hence, smaller businesses license products to big pharma. But in a system where the economic incentives for marketing are radically changed, and every product becomes a generic commodity, the smaller enterprise becomes more competitive in drug development. Ultimately, more resources can be allocated to actual R&D work, overall costs can fall, and consumers can face marginal cost pricing of innovative new medicines. If implemented worldwide, one of our most vexing ethical dilemmas can be resolved in a manner that actually promotes the Doha Declaration on TRIPS and Public Health mandate to encourage access to medicine for all.