Viewpoint

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The Health Impact Fund: incentives for improving access to medicines

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Access to essential drugs has been recognised as a determinant and consequence of inequalities in health, income,[1–4] and development. However, present market forces and intellectual property rights provide little incentive for innovation in the diseases of low-income countries, such as diarrhoeal disease, lower respiratory tract infections, perinatal infections, Burkitt's lymphoma, and other cancers prevalent in poor countries. Sir Andrew Witty, the global chief executive officer of GlaxoSmithKline(GSK), pledged[5] in February, 2009, to reduce prices of GSK's patented drugs in developing countries, invest in local healthcare infrastructure, and form a patent pool to allow sharing of GSK-owned intellectual property. Critics have questioned whether such philanthropic measures are sustainable at a time when new drug development is slowing,[6] especially in the global economic downturn.[7] We propose the creation of the Health Impact Fund (HIF) as an enduring reform that would give pharmaceutical innovators stable financial incentives to develop new medicines that have large effects on global health, and to sell them worldwide at no more than the lowest feasible cost of production and distribution.

Spending on pharmaceuticals represents 66% of health expenditure in developing countries—often leading to household impoverishment during serious illness.[8,9] Prices of drugs affect access to them, even in countries such as the UK that have universal insurance with co-payments.[10] The situation is worse in developing countries. Medicines save lives and improve health only when they are of good quality, available, affordable, and properly used. High prices for drugs are generally justified by patent holders as being a result of the high cost of pharmaceutical research and development, which is typically believed to be at least in the hundreds of millions of dollars per successful product after accounting for risk of failure and cost of capital investment. The average cost to bring a new product to market is thus very high compared with long-term marginal cost of manufacturing and distribution. A pure free-market system, without patent protection, would provide scant incentives for pharmaceutical innovation because competition would quickly drive down the price of a new drug to near its long-term marginal production cost, thereby leaving the innovator unable to recover their research and development investment.

Governments create incentives by providing patents for innovations. A patent grants an innovator exclusive rights to use the patented product, enabling high mark-ups through which innovators can profit if demand for the product is large enough even at high prices. Although monopolies are much criticised by economists as being inefficient and by ethicists as interference in the freedom of people to produce and exchange, patents are widely accepted as a necessary evil. Nonetheless, we have reason to explore whether the existing situation can be improved—this system does not encourage development of drugs for diseases that mainly affect poor people, and through high prices it results in mortality and morbidity. Billions of people are excluded from health benefits that advanced medicines can provide. Panel 1 shows various flaws of the present system.

Until 1994, strict patent rules were mostly confined to high-income countries, whereas developing countries had weak patent protections, if any. The situation changed when a powerful alliance of pharmaceutical and other industries pressured governments of wealthy countries to impose the globally uniform Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.[11] Developing countries agreed to institute TRIPS-compliant systems to qualify for membership in the World Trade Organization. This agreement becomes more constraining as increased numbers of countries implement patent exclusivity. Although TRIPS implementation and drug affordability are not the only factors contributing to access problems,[12–14] TRIPS has widened the health gap between high-income countries and developing countries.

The world has responded to the enormous global health crisis through declarations and summits, intergovernmental initiatives (eg, UNITAID), governmental programmes (eg, the US President's Emergency Plan for AIDS Relief), public–private partnerships (eg, the Global Fund), medicine donations from pharmaceutical companies, efforts to foster new drug development (eg, the Drugs for Neglected Diseases Initiative), various prizes, and advance market and purchase commitments.[15] All these options are working towards improved drug access. However, a system-wide reform of rewards for drug innovation might offer the only sustainable solution. Drawbacks of the newly globalised patent monopoly could be alleviated by a complementary source of incentives and rewards for development of new drugs.[15] An international interdisciplinary team has designed HIF to this end. This fund differs from other intergovernmental initiatives by being an enduring institutional reform that—valuing the health of all people equally—is neither disease specific nor country specific.

As a global agency underwritten by governments, HIF would offer pharmaceutical innovators the option to register any new product. Registration entitles the innovator to receive, for a defined period (eg, 10 years), a

share of fixed remuneration from a reward pool. The fund would disburse at least US$6 billion yearly, paying each registrant a share that corresponds to the registrant's contribution to the global health effect of all registered products , as estimated with a global health impact assessment exercise (panel 2). In exchange, the registrant would need to sell the medicine wherever it is needed at no more than the lowest feasible cost of production and distribution, and after the end of the reward period offer free licences to enable generic manufacture and sales.

With HIF in place, pharmaceutical innovators would analyse possible research and development projects under two competing settings—profitability with optimum exploitation of patent-protected market exclusivity through high prices, and profitability with best efforts to achieve an effect on global health. Some products might be viable for only one of these settings—for example, products tackling hair loss would be unprofitable with HIF, whereas products combating tropical diseases might be unprofitable with the high-pricing scheme. By contrast, medicines for the diseases that contribute most to the burden of global disease, such as HIV/AIDS or coronary heart disease, could be viable in either setting. In this situation, the innovator's decision would depend on the expected size and perceived reliability of HIF rewards.[15]

The global health impact assessment will draw on the same types of information that agencies such as the National Institute for Health and Clinical Excellence (NICE) now use to make recommendations about listing new drugs, but will continually update this information with data for use of the drug and information from new practical trials. No method of global health impact assessment could be perfect and indisputable in its measurements or the estimates produced from it. However, although these drawbacks are serious, the real comparison is not with a perfect system but with the present situation. In the UK, where drug insurance is universal and NICE assesses the cost-effectiveness of medicines, the present situation might be seen as a reward system in which each sale of a drug creates a reward equal to the difference between the price and the cost of manufacture and distribution. The size of the reward per pill is fixed on the basis of information provided to NICE at the time of drug approval, and is typically not modified to show new information. Thus, the UK system is essentially a simple reward system in which the reward equals the price–cost margin multiplied by the number of units sold.

HIF's global health impact assessment would improve on this standard in at least five important ways (panel 3). All available data would be used to regularly update the assessed average health effect per unit dispensed (compared with the outcome that would have arisen with the standard of care available before the product was introduced). Multiplication of this number with that of units actually dispensed would provide an estimate of the product's total incremental health effect.

An objection that this information is inadequate to form the basis for rewards is implicitly an argument in favour of HIF, because the proposed scheme uses much more information than does the present reward system. Just because global health impact assessments will not have enough information to establish rewards perfectly cannot be an argument for use of even less relevant information. Critics might fear that costs to obtain additional information will outweigh the benefits. However, this outcome is unlikely because the benefits include direct gains in cost-effectiveness produced by HIF, and large ancilliary benefits derivable from an improved understanding of effectiveness of drugs in the real world.

For example, the assessment of simvastatin—had this drug been registered with HIF—would have initially used data from clinical trials to compare the product with pre-existing treatments for the prevention of cardiac

***Panel 1:* Problems with the present patent system**

Exclusion of poor people
A medicine while under patent is sold at a profit-maximising monopoly price, and many people have no access to it.

Neglect of diseases concentrated in low-income countries
For-profit pharmaceutical companies naturally focus their research efforts on products that are saleable to wealthy countries. Products of benefit only to poor nations are less likely to be developed than are those for high-income countries.

Bias towards maintenance drugs
Existing patent systems make symptom-relieving drugs most profitable and thereby biases research and development against curative medicines and especially vaccines.

Wastefulness
Innovators presently have to cover the cost to file and litigate patents in many countries—globally, people bear huge losses from foregone sales above marginal cost and below present monopoly price.

Counterfeiting
Large profit margins encourage illegal manufacture and sale of medicines that, when diluted, often cause drug-resistant strains.

Excessive marketing
High mark-ups encourage pharmaceutical companies to make extensive efforts to improve sales by influencing prescription patterns of physicians, irrespective of therapeutic improvement.

The last mile problem
Pharmaceutical companies have poor incentives to promote the optimum use of their medicine and to ensure that their drugs reach those (and only those) who need them.

Panel 2: Key features of the Health Impact Fund

- A global agency, funded by governments
- Features yearly reward pools from which a new medicine can, for 10 years, receive a share that corresponds to that drug's contribution to the global health effect of all HIF-registered drugs
- Optional registration requires the innovator to offer the product at the lowest feasible cost of production and distribution and to provide zero-cost licences at the end of the reward period
- Has benefits for patients, taxpayers, and pharmaceutical companies

Panel 3: Evidence used by the Health Impact Fund's global health impact assessment (GHIA)

Physician survey data about actual use of medicines
In some countries, IMS Health, a global health consultancy firm, already obtains data relating prescriptions to treatment indications. The GHIA would have to gather such data globally for registered medicines.

Evidence for drug use in medical practice through practical trials
In clinical practice, the prescription of drugs might have quite different effects compared with those in clinical trials, because of different patient populations and lowered compliance. Practical trials could help to show actual effects on patient health of a specific drug.[16]

Patient usage data through surveys of patients who were prescribed the drug
Not every prescription is dispensed, and not every dispensed drug is used.

Outcomes data
The GHIA could develop evidence for outcomes with administrative databases such as the General Practice Research Database, which follows about 13 million patients in the UK. IMS Health obtains similar anonymised longitudinal data from several other countries.[5]

Data from post-approval phase 4 clinical trials, especially comparative trials
This evidence would be used to revise assessment of the average health effect per prescription or per pill. Further comprehensive post-marketing studies have great potential therapeutic value, and the HIF's rewards could link to such information.[17]

For **HIF proposal** see www.healthimpactfund.org

disease. Inference would have been needed because of the use of surrogate endpoints to calculate an estimate of quality-adjusted life-years saved. Emerging trials[18,19] led to a change in indications for statins, and would have resulted in upward revisions in the assessed yearly health effect. Evidence that simvastatin was being prescribed to many patients who did not meet the clinical criteria would have led to downward revisions, whereas other data showing that simvastatin like other statins has positive effects in secondary prevention, even for patients without high cholesterol, would have led to upward revisions. Under the structure of HIF, had Merck chosen to register simvastatin, the company could have realised very large global sales of this breakthrough product at generic prices from the outset. The resulting widespread health effects would have enabled the company to capture a large share of HIF's yearly reward payments.

HIF can be thought of as a comprehensive advance market commitment.[20] Unlike conventional advance market commitments, HIF is not disease-specific and is thus much less vulnerable to lobbying by firms and patient groups than are other such commitments. It merely offers to reward any company that produces an effective new drug in proportion to how well the drug works, provided that the innovator agrees to sell it at cost price. HIF pulls research towards the medicines that can do the most good. It can also reward development of new products, new uses for existing products, and clinical testing of traditional medicines that patents alone cannot stimulate. All patients, rich and poor, would benefit from refocusing the pharmaceutical industry's innovation and marketing priorities toward health benefits. HIF gives industry the opportunity to make increased profits by development of new high-effect drugs that would be unprofitable in its absence. By sale of such medicines at cost price, firms avoid having to charge high prices to poor people and pressure to make charitable donations. In these ways, HIF improves the ability of industry to fund high-value research.

HIF will be supported mainly by governments, but taxpayers will benefit from lowered drug prices, mostly cancelling out government and taxpayer costs of financing rewards. This factor is a key point—although HIF would have to pay large rewards every year to encourage innovation and registration, all who pay for medicines would save money, including patients in high-income states and their insurers and governments. The fund is fundamentally a rational reorganisation of how we pay for drugs that is designed to foster innovations we most want while enabling the widest access, rather than being merely another call for money to help the world's poor. Furthermore, HIF mechanism would ensure that taxpayers always obtain value for money because HIF-registered products will generally have a lower cost for a given health effect than will products outside HIF. Taxpayers, as consumers of health, might also benefit from a reduction in risks of pandemics and other health problems that easily cross national borders.

For HIF to become a reality, this proposal will need to be examined, refined, and planned in detail. The fund has begun to take shape, but further consultation with many stakeholders (eg, industry, governments, insurance companies, epidemiologists, non-governmental organisations, lawyers, economists, and doctors) is needed. The next stage would be for governments, supported by their citizens and with collaboration of pharmaceutical firms, to make conditional commitments to support HIF at, for example, 0·03% of gross national income. These commitments then would become binding once a certain threshold (eg, $6 billion per year) is reached. Horton[21] has stated that "access to medicines has become the test above all others by which the rich world will be judged in its dealings with the poor". HIF is a fair, cost-effective way of stimulating research and development of life-saving medicines and making them accessible to all.

Contributors
TP and AH conceived the original idea for the HIF. AB has been a medical adviser to the HIF since 2006. AB wrote the original draft with TP. AH helped to write the final version of the Viewpoint.

Conflicts of interest
We declare that we have no conflicts of interest.

References

1 Global Poverty Report. Okinawa Summit. July 2000. http://www.adb.org/Documents/Reports/Global_Poverty/2000/G8_2000.pdf (accessed July 3, 2009).
2 Chen S, Ravallion M. The developing world is poorer than we thought, but no less successful in the fight against poverty. World Bank Policy Research Working Paper WPS 4703, 2008: 34. http://econ.worldbank.org/docsearch (accessed July 3, 2009).
3 A gateway to the UN System's work on the MDGs. United Nations Millennium Development Goals. http://www.un.org/millenniumgoals/ (accessed July 3, 2009).
4 Von Schirding Y. The World Summit on Sustainable Development: reaffirming the centrality of health. *Global Health* 2005; **1:** 8.
5 Witty A. Big pharma as a catalyst for change. February 13, 2009 Speech to Harvard Medical School. http://www.gsk.com/media/Witty-Harvard-Speech-Summary.pdf (accessed July 3, 2009).
6 The Lancet. Pharmaceuticals, patents, publicity...and philanthropy? *Lancet* 2009; **373:** 693.
7 Garber AM. An uncertain future for cardiovascular drug development? *N Engl J Med* 2009; 360: 1169–71.
8 WHO. The world drug situation. Geneva: World Health Organization, 1988.
9 WHO. Chronic Diseases Report 2005. Chapter 2: chronic diseases and poverty. Geneva: World Health Organization, 2005.
10 Gemmill MC, Costa-Font J, McGuire A. In search of a corrected prescription drug elasticity estimate: a meta-regression approach. *Health Econ* 2007; **16:** 627–43.
11 Trade-related aspects of intellectual property rights agreement. World Trade Organization. http://www.wto.org/English/tratop_e/TRIPS_e/trips_e.htm (accessed July 3, 2009)
12 Attaran A, Gillespie-White L. Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa. *JAMA* 2001; 286: 1886–92.
13 Oliveira MA, Bermudez JA, Chaves GC, Velásquez G. Has the implementation of the TRIPS Agreement in Latin America and the Caribbean produced intellectual property legislation that favours public health? *Bull World Health Organ* 2004; **82:** 8150–21.
14 Attaran A. How do patents and economic policies affect access to essential medicines in developing countries? *Health Affairs (Millwood)* 2004; **23:** 155–66.
15 Hollis A, Pogge T. The Health Impact Fund. Making new medicines accessible for all. Incentives for Global Health 2008. http://www.healthimpactfund.org (accessed July 3, 2009).
16 Tunis SR, Stryer DB, Clancy CM. 2003. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003; **290:** 1624–32.
17 Baciu A, Stratton K, Burke SP, eds. The future of drug safety: promoting and protecting the health of the public, 2007. Washington, DC: National Academies Press, 2007.
18 Scandinavian Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994: **344:** 1383–89.
19 Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; **360:** 7–22.
20 Hollis A. A comprehensive advanced market commitment (2007). Submission to World Health Organization public hearing on public health, innovation and intellectual property. http://www.who.int/phi/public_hearings/second/contributions_section2/Section2_Aidan_Hollis_Full_Contribution.pdf (accessed July 3, 2009).
21 Horton R. WHO: the casualties and compromises of renewal. *Lancet* 2002; **359:** 1605–11.